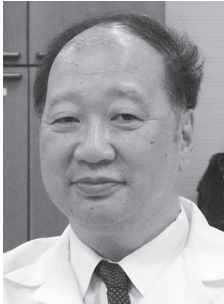


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## Historical Development of Japan-Taiwan Otolaryngology-Head and Neck Surgery—Medicine, Culture and Friendship—



### Kimitaka Kaga

*Professor Emeritus, the University of Tokyo, Tokyo, Japan / National Institute of Sensory Organs, National Tokyo Medical Center / International University of Health and Welfare, Director, Center for Speech and Hearing Disorders*

Kimitaka Kaga, MD, PhD. is a professor of International University of Health and Welfare in Japan, the emeritus director of National Institute of Sensory Organs in National Tokyo Medical Center and the emeritus professor of University of Tokyo. He graduated from the School of Medicine in the University of Tokyo. His academic specialty is otology, neurotology and audiology. His surgical specialty is otological surgery including cochlear implant, cosmetic and functional reconstruction for microtia and atresia, and tympanoplasty. His academic concern is central auditory processing, auditory plasticity and vestibular failure and central compensation in children. He published five books, from Springer: in 2009 1. *Neuropathies of the Auditory and Vestibular Eighth Cranial Nerves.*, 2. *Vestibular Evoked Myogenic Potential-Its Basics and Clinical Application.*, 3. *Central Auditory Pathway Disorders*, in 2013(#1), in 2014(#2). He was the former president of Otological Society of Japan and the committee chairman of sensory organs in research in Science Council in Japan. Now he works in two institutes of The International University of Health and Welfare and The National Institute of Sensory Organs in Tokyo. Present Chairman of Tokyo Branch of the ORL Society of Japan Inc.

Dec. 3

In the old days, Japan and Taiwan practiced Chinese medicine. How did each country adopted Western medicine? Western medicine was brought to Japan by only the Dutch people through Dejima in Nagasaki in 1641-1859 because the Tokugawa Shogunate closed Japan against Western countries except the Netherlands. The aim was to suppress the expansion of Christianity and to prevent invasion by foreign countries. In 1868, modern Japan opened to the world and the new government decided to learn German medicine. It lasted until the end of the Second World War. Thereafter, medical education in Japan has been influenced by American medicine. Meanwhile, in Taiwan, English and Canadian pastors who were doctors also brought Western medicine in 1865-1895, which is called the church medicine period. In 1895, China ceded Taiwan to Japan in the Japan-China Treaty after its defect in the Japan-China War.

Western medicine was then taught by Japanese doctors in medical schools in Taipei. Thereafter, the School of medicine of Taihoku Imperial University was established until the end of the Second World War (1905-1945). After the Second World War, medical education in Taiwan has been influenced by American medicine similar to Japan.

In 1971, Professor Sawaki of Department of Otolaryngology of Yokohama City University visited Taiwan for a collaborative study of the etiology of nasopharyngeal cancer. This was supported by a big Japanese government grant. He conducted this study throughout Taiwan. Through this study, he was deeply impressed by the doctors and people in Taiwan. He thought of an idea to hold a biennial Japan-Taiwan Otolaryngology and Head and Neck Cancer Conference in order to exchange information on medicine and foster friendship. The memorable first conference was held in Tokyo 1992.

In my Keynote Lecture, a medical science movie film entitled "Nasopharyngeal Cancer" which was produced by Prof. S. Sawaki and awarded a gold medal in IFOS meeting (Budapest, 1981) will be presented.

#1: in 2013, 4. *Microtia and Atresia Combined Approach by Plastic and Otologic Surgery* from Karger,

#2: in 2014, 5. *Vertigo and Balance Disorders in Children* from Springer.

## SL1

**Benefit of genetic testing for cochlear implantation candidates****Shin-ichi Usami**

*Department of Otorhinolaryngology, Shinshu University School of Medicine, Nagano, Japan / Department of Hearing Implant Sciences, Shinshu University School of Medicine, Nagano, Japan*

1999-present	Professor, Department of Otorhinolaryngology, Shinshu University School of Medicine
1993-1999	Associate professor, Department of Otorhinolaryngology, Hirosaki University School of Medicine
1992-1993	Assistant professor, Department of Otorhinolaryngology, Hirosaki University School of Medicine
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1986	Research fellow, Department of Otorhinolaryngology and Communicative Sciences, Balor College of Medicine, Texas, U.S.A.
1981-1985	Resident in Otorhinolaryngology, Hirosaki University School of Medicine

Prof. Usami graduated from Hirosaki University in 1981, and did his residency training in the Dept. of Otorhinolaryngology at Hirosaki University Hospital. He spent one year doing basic research at Baylor College of Medicine in 1986. He became Professor and Chairman of the Department of Otorhinolaryngology of Shinshu University School of Medicine in 1999. He is a member of Oto-Rhino-Laryngological Society of Japan, CORLAS and Barany Society. He is interested in various topics including genetics for deafness, cochlear implantation, space science, as well as molecular phylogenetics of alpine butterflies. He has published nearly 200 peer reviewed articles in international scientific journals. He is an Editorial board of *Acta Otolaryngol*, *Audiological Medicine*, *Audiology & Neuro- Otology*, *Otology & Neurotology*.

**Objective**

Cochlear implantation is the most important treatment currently available for profound sensorineural hearing loss. The aim of this study was to investigate the etiology of hearing loss in patients with cochlear implantation, and to compare outcomes.

**Methods**

Japanese hearing loss patients who received cochlear implants (CIs) or electric acoustic stimulation (EAS) in Shinshu University hospital (n=173, pre-lingual onset: 92, post-lingual onset: 81) participated in this study. Invader assay followed by the targeted exon-sequencing of 63 deafness genes using Massively parallel DNA sequencing (MPS) was applied. For pre-lingual patients, additional imaging examination, cCMV screening, and pediatric examination were performed for precise diagnosis.

**Results**

Genetic screening successfully identified the causative mutation in 60% of patients with pre-lingual onset hearing loss and in 36% of those with post-lingual hearing loss. Differences in the kinds of genes identified were observed between the two groups. Although there were marked variations in the outcome of cochlear implantation, patients with specific deafness gene mutations showed relatively good results.

**Conclusion**

The present study showed genetic etiology is a major cause of hearing loss in CI/EAS patients. Patients possessing mutations in a number of deafness genes known to be expressed within inner ear have achieved satisfactory auditory performance, suggesting that the identification of the genetic background facilitates the prediction of post-CI performance. MPS is a powerful tool for the identification of causative deafness genes in patients receiving cochlear implantation. Therefore, determination of the involved region inside/outside of the cochlea by identification of the responsible gene is essential.

## SL2

**Potential application of an inner ear test battery to map the affected territory of vestibular disorders****Yi-Ho Young**

*Department of Otolaryngology, National Taiwan University Hospital, Taiwan*

Education and positions held:

1981 MD, National Taiwan University, School of Medicine

1991 PhD, University of Tokyo, Graduate School

1991 Assistant professor, College of Medicine, National Taiwan University

1995 Associate professor, College of Medicine, National Taiwan University

2004 Professor, College of Medicine, National Taiwan University

Stimulation via air-conducted sound or bone-conducted vibration enables recording of vestibular-evoked myogenic potential (VEMP) from cervical muscles (called cervical VEMP, cVEMP) and extraocular muscles (called ocular VEMP, oVEMP). These two emerging tests expand the test battery available to clinicians for exploring dynamic otolithic function, and create a potential use for the sacculo-collic reflex and vestibulo-ocular reflex, respectively. Coupled with audiometry and caloric test, the inner ear test battery is designed for complete assessment of the inner ear function including the cochlea, saccule, utricle and semicircular canals.

Clinically, the inner ear test battery has been widely adopted in cases of peripheral vestibular diseases such as 1) chronic otitis media with vertigo; 2) radiation-induced otitis media with vertigo; 3) otosclerosis with vertigo; 4) acute acoustic trauma or noise-induced hearing loss; 5) vestibular inflammatory diseases i.e. vestibular neuritis, herpes zoster oticus; 6) sudden deafness; and 7) Meniere's disease.

In central vestibular disorders, the inner ear test battery may help map the affected territory in cases of 8) vestibular migraine; 9) posterior fossa stroke; and 10) posterior fossa tumor. The use of oVEMP and cVEMP tests in vestibular schwannoma patients helps assess the tumor origin from the superior or inferior vestibular nerve. For the brainstem lesion, the oVEMP and cVEMP tests can discriminate it. Additionally, the oVEMP test can differentiate between cerebellar and brainstem lesions. Abnormal oVEMPs in patients with cerebellar disorder may indicate adjacent brainstem involvement.

In conclusion, it is believable that complete assessment of the inner ear function via an inner ear test battery comprising audiometry, oVEMP, cVEMP and caloric tests may stimulate to elucidate the mechanism of peripheral and central vestibular disorders.

## Symposium 1 Cochlear and Middle Ear Implant and Baha

## SY1-1

### 3D-CT analysis of FMT position to RWM after VSB surgery - its correlation to the efficacy in sound transmission -

Katsumi Doi

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#### Introduction

In Japan, the multi-center clinical trial of Vibrant SoundbridgeR (VSB, MedEl) was completed in 2014. Round window vibroplasty (RWV) via transmastoid approach was adopted in the protocol. The bony lip overhanging round window membrane (RWM) and the posterior part of hypotympanum were carefully drilled to get enough space for the placement of floating mass transducer (FMT). The placement of the FMT was checked by 2D-CT scans at postoperatively, however, it must not be possible to see the precise position of FMT to RWM with this routine 2D-CD scans.

#### Materials and Methods

In our institute, twelve patients received VSB implantation, and they were 9 males and 3 females. FMT was placed within RW area in 11 cases, and within oval window (OW) area in one case. No post-operative complication such as facial nerve weakness and sensorineural hearing loss was noted. After VSB surgery, thin-sliced 2D-CT images (0.625 mm slice) with GE Discovery CT750 HDR (GE, USA) were collected and 3D-CT images were reconstructed (Figure 1) by using Zio stationR (Amin, Japan). The location of RWM and OW were identified, and the angle of FMT to RWM/OW (FMT angle) was measured. The correlation between the FMT angle and the efficacy in sound transmission (bone conduction threshold - vibrogram threshold; BC-V threshold) was finally evaluated.

#### Results and Discussions

The FMT angle was scattered from 36.9 degree to 83.9 degree (n=11). The BC-V threshold (averaged at 1-4 kHz) was scattered from 15 to 31.7 dB (n=11, RWV). The correlation between the FMT angle and BC-V threshold did reach to a significant level (P=0.049, Spearman rank correlation), indicating the negative correlation between them ( $y = -0.2494x + 38.21$ ,  $R^2 = 0.36322$ ). The sound transmission (BC-V threshold) after VSB surgery should be better as the FMT angle to RWM became larger (more perpendicular to the surface of RWM). If the measurement of the FMT angle to RW/OW during VSB surgery could be possible in future, it might be able to contribute to the achievement of much better hearing performances with VSB.

## SY1-2

### Electroacoustic Stimulation: Six Years' Experience at University of Miyazaki

Tetsuya Tono

*University of Miyazaki, Miyazaki, Japan*

Electroacoustic stimulation (EAS) is now a viable option for people who have residual hearing at low frequencies and achieve little benefits from conventional hearing aids. In order to receive satisfactory effects from EAS, the patient's residual hearing should be preserved as much as possible during and after cochlear implant (CI) surgery. Owing to recent advances in electrode design, insertion techniques and intra-postoperative steroid administration, hearing preservation rates are reportedly more than 90 % at within 1 or 2 years after CI surgery. However, longer-term hearing results in EAS patients has not been systematically evaluated so far. The aim of this paper is to evaluate low frequency hearing stability over time in our series of 12 EAS patients.

#### Materials and methods

Ten out of 12 patients received a MEDEL FLEX24 electrode, five with PULSER between 2011 and 2012 under the Japan multicenter study setting and 5 with CONCERTO after 2014 under the national health insurance system. The first case patient was implanted with a COMBI40+ using a standard electrode and the latest patient with a CONCERTO using a FLEX28 electrode. All subject received the DUET processor except for the latest patient who uses her own conventional hearing aid in the ipsilateral ear. All subjects except for one latest patient fulfilled the audiological criteria for EAS, with pure tone average hearing levels bilaterally at 65 dB HL for 125 Hz, 250 Hz and 500Hz; 80 dB HL for 200Hz and 85 dB HL for 4000 and 8000 Hz. The electrode insertion was performed by a single surgeon (TT) using the round window approach in all cases.

#### Results

Residual low frequency hearing was well preserved at follow-up periods between 6 months and 2 years after CI surgery in all cases. The first patient implanted with a COMBI40+ using a standard electrode showed a gradually progressive deterioration of the low frequency hearing. We found a late-onset total residual-hearing loss in a patient implanted with a FLEX24 electrode at 38 months after CI surgery. Her Speech perception ability was satisfactorily compensated by CI-only fitting.

#### Conclusion

Trials covering more than 2 years' term would be necessary for more appropriate candidacy criteria in EAS. Further developments not only in electrode design but also in surgical technique may minimize the risk of late-onset acoustic hearing loss.

**SY1-3**

## **Baha - Current State in Japan and Our Experiences**

Yoshihiro Noguchi

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Bone-anchored hearing aid is an implantable bone conduction stimulator. It is composed of a sound processor, an abutment and a titanium implant. The most commonly used device is Cochlear Baha and more than 110,000 Baha users are estimated to exist in the world. Although we had performed Baha surgeries since 2001 under the acceptance by the Institutional Review Board of Tokyo Medical and Dental University, it was finally covered by health insurance in 2013 in Japan. Baha is indicated for individuals who are basically  $\geq 18$  years of age and have bilateral outer and/or middle ear disorders with the mean bone-conduction hearing threshold of  $\leq 45$  dB. Individuals with unilateral hearing loss, such as single-sided deafness (SSD) and unilateral external auditory canal anomaly, are excluded from indication.

Baha has advantages over conventional hearing aids in sound quality and speech perception in noise. We determined the benefit from Baha by assessing the Abbreviated Profile of Hearing Aid Benefit (APHAB) and the Nijmegen group questionnaire. We enrolled 23 unilateral Baha users (gender: 12 males, 11 females; age: 21-79 years) with the follow-up periods of 3-114 months. Etiologies of the hearing impairments were bilateral chronic otitis media post-operative states in 9 patients, bilateral external auditory canal anomaly in 9, unilateral external auditory canal anomaly in 2 and SSD in 3. APHAB scores in 3 of the 4 subscales (ease of communication, background noise and reverberation) showed a significant decrease when comparing both with and without BAHA, suggesting an improvement in benefit. The responses to the Nijmegen group questionnaire showed that most patients, in 18 patients who had previously used conventional air- or bone-conduction hearing aid, preferred Baha with regard to speech recognition in quiet places, sound quality and visibility. In general, 17 patients (94.4%) preferred Baha.

Baha requires surgery and may have postoperative complications including skin reactions and skin overgrowth. In our early series, skin reactions categorized Holgers' grade 1 or more were recognized in nearly 70% of ears during the first postoperative year but most were a grade 1 reaction and skin reactions decreased with time. Most complications were treated in outpatient clinics. However, some ears with repetitive skin overgrowth needed re-operation.

The results of the self-assessment questionnaire showed the superiority of Baha. However, the decision to proceed with Baha surgery required fully informed consent based on knowledge of postoperative complications.

**SY1-4**

## **Long-term follow-up outcomes in 423 cases of cochlear implantation in Chang-Gung Memorial Hospital, Linkow branch**

Che-Ming Wu

*Department of Otolaryngology, Chang-Gung Memorial Hospital, Chang-Gung University, Taiwan*

**Background:** Since 1999, a total of 423 Mandarin-speaking patients have received cochlear implantation (CI) in the cochlear implant center of Chang-Gung Memorial Hospital. This study aimed to retrospectively review the outcomes of CI and related characteristics in these patients for surgical and rehabilitation concerns.

**Methods:** 423 patients received CI between 1999 and 2015 in our cochlear implant center. Tests regarding their auditory performance, intellectual ability, speech and environmental sound perception, speech production, language development, reading skills and academic performance were administered at follow-up visits. Their genetic characteristics and radiological data were also examined.

**Results:** So far, we have published a total of 29 SCI journal articles related to CI. Among the 423 patients, 394 (93.0%) received continuous follow-up over the 15 years, 258 (61.0%) were implanted before 5 years of age. The results of 3-dimensional magnetic resonance imaging (MRI) showed an incidence of 21.2% for cochlear nerve deficiency in all children undergone MRI in our center. Most of the implanted children had normal performance intelligence quotient (IQ), but their verbal IQ dragged behind their normal-hearing peers. A significant prevalence of genetic mutations (33.5%) was identified in children with CIs. The presence of genetic mutations was associated with good long-term auditory performance outcomes after implantation. After 2.5 years of implant use, most of the children were intelligible to people who had a little experience of deaf people's speech and understood common phrases without lipreading. After 4 years of use, they were able to communicate over the telephone with familiar talkers. However, their recognition ability of environmental sounds could not be achieved only by natural exposure to auditory stimuli encountered in daily life if sounds other than speech stimuli were less emphasized in routine verbal/oral rehabilitation program. Although their classroom performances were mostly satisfactory, they fell behind in other areas, such as communication abilities.

**Conclusion:** With 15 years of follow up, we acquire a more comprehensive knowledge of the effectiveness of CI and postoperative rehabilitation. Our patients with cochlear implants show visible improvements in their language and reading skills, and many of them fall within the normal range of their hearing age mates.

SY1-5

## Identifying children with poor cochlear implantation outcomes using massively parallel sequencing

Chuan-Jen Hsu

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Cochlear implantation is currently the treatment of choice for children with severe to profound hearing impairment. However, the outcomes with cochlear implants (CIs) vary significantly among recipients. It is important to identify the genetic determinants of poor outcomes of cochlear implantation (CI). Twelve children with poor CI outcomes (the “cases”) and 30 “matched controls” with good CI outcomes were subjected to comprehensive genetic analyses using massively parallel sequencing, which targeted 129 known deafness genes. Audiological features, imaging findings, and auditory/speech performance with CIs were then correlated to the genetic diagnoses. We identified genetic variants which are associated with poor CI outcomes in 7 (58%) of the 12 cases; 4 cases had bi-allelic PCDH15 pathogenic mutations and 3 cases were homozygous for the DFNB59 p.G292R variant. Mutations in the WFS1, GJB3, ESRRB, LRTOMT, MYO3A, and POU3F4 genes were detected in 7 (23%) of the 30 matched controls. The allele frequencies of PCDH15 and DFNB59 variants were significantly higher in the cases than in the matched controls (both  $P < 0.001$ ). In the 7 CI recipients with PCDH15 or DFNB59 variants, otoacoustic emissions were absent in both ears, and imaging findings were normal in all 7 implanted ears. PCDH15 or DFNB59 variants are associated with poor CI performance, yet children with PCDH15 or DFNB59 variants might show clinical features indistinguishable from those of other typical pediatric CI recipients. Accordingly, genetic examination is of benefit to decision-making for all CI candidates before operation.

## Symposium 2 Geriatric Otolaryngology

### SY2-1

## Cognitive function and hearing in the elderly

Yasue Uchida

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Hearing impairment is highly prevalent among older population. Our estimates of the size of the hearing-impaired population older than 65 years old in Japan have shown to be 15 million based on national demographic statistics 2010 according to the population-based aging study. Age-related hearing impairment is a representative geriatric condition. Cognitive impairment is also a major health concern related to aging. What to do about cognitive impairment is one of the most important issues a longevity society currently faces. There has been a growing interest in the impact of hearing impairment on cognitive decline.

We aimed to assess a change in cognitive function using a nonverbal test during a 12-year period in the community-dwelling elderly with and without hearing impairment. Subjects were participants (age at baseline 60-79 years) of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA), a prospective observational investigation started in 1997. As a cognitive testing, the Digit Symbol Substitution Test (DSST), a component of the Wechsler Adult Intelligence Test, was administered as a nonverbal measure of executive function and psychomotor speed, in which participants code a series of numbers with the corresponding symbol in 90 seconds. In a longitudinal analysis of 1,109 older adults (mean age = 68.7 years), hearing impairment at baseline was associated with faster rates of decline on the DSST score ( $p = 0.0014$ ) compared to those without hearing impairment.

A number of studies have demonstrated the significant link between greater hearing impairment and poorer cognitive function. Frank R. Lin, who is the author of several recent publications, has reported the significant association between hearing impairment and lower scores on the DSST, cross-sectionally in the National Health and Nutritional Examination Survey (NHANES), and longitudinally in the Health ABC (Health, Aging, and Body Composition) Study.

Hypothesized mechanisms to explain the association in the recent publications include a shared neuropathologic origin underlying both hearing impairment and cognitive decline (e.g., vascular disease, inflammation), increased social isolation and loneliness, increased cognitive load due to hearing impairment (termed effortful listening), and changes in brain structure.

The current presentation focuses on the latest findings from both inside and outside the country and prospective view.

### SY2-2

## Olfactory impairment in elderly

Takaki Miwa

*Department of Otorhinolaryngology, Kanazawa Medical University, Ishikawa, Japan*

Like other sensations, smell function of human decreases with aging, too. In this symposium, I'd like to present the problems of olfactory dysfunction by aging and its preventive strategies. It has been reported that 50% of people aged 65 and older and more than 80% of people aged 80 and older have olfactory deficits. The overall prevalence of olfactory impairment increased with age and was more common in men than women. Sinonasal disease, arteriosclerosis and smoking are seemed to be risk factors of olfactory impairment. Pathophysiological changes of olfactory system are observed in everywhere from nasal cavity to central olfactory pathway. Elder persons with olfactory dysfunction have following problems. (1) The most of them aren't aware that they have olfactory dysfunction. (2) They are more likely to be harmed by fire, gas leak or poisoned by rotten food. (3) It is well established that decreased smell function can be an early sign of neurodegenerative diseases as Alzheimer's disease and sporadic Parkinson's disease. The most important thing to prevent olfactory dysfunction is to avoid from risk factors. It is also effective to smell odors consciously in daily living not only to notice decrease of olfactory function in early stage, but to be olfactory training. In the recent research, it was found that regular exercise at least once a week long enough to work up a sweat had decreased risk of olfactory impairment and increasing frequency of exercise was associated with decreasing risk of developing olfactory impairment in future 10-year.

## SY2-3

**Laryngeal Problems in Advanced Age and Cost-Effective Solutions**

Koichi Tsunoda

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In the course of evolution, as a result of an increase in the volume of the frontal lobe and of the descent of the larynx toward the chest, the human vocal tract expanded and the vocal cords acquired the ability to vibrate. Thus, we achieved the ability to communicate through speech. During the act of swallowing, the larynx normally elevates and the epiglottis is sandwiched between the base of the tongue and framework of the larynx. This instantaneous motion prevents aspiration.

Changes in the position of the larynx during evolution made it easier for aspiration to occur, however. Atrophy of the extrinsic laryngeal muscles with age lowers the position of the larynx, and weakening of the muscles makes it difficult to elevate the larynx sufficiently to prevent aspiration while swallowing. Thus, the elderly are more prone to the consequences of aspiration. As a result, one-quarter of the population of Japan consists of people aged 65 years or older, and pneumonia was the third leading cause of death nationwide in 2013.

Age-related atrophic changes in the intrinsic laryngeal muscles commonly cause glottal closure insufficiency, or so-called glottal incompetence. Anatomical and functional problems resulting from glottal closure failure include not only breathy hoarseness or shortening of the maximum phonation time (MPT) but also frequent laryngeal inflow and difficulty in expectoration due to insufficient subglottic pressure to remove aspirated substances through coughing. As a result, continued aspiration can lead to the development of pneumonia. Glottal incompetence resulting from vocal cord atrophy in the elderly can cause so-called aspiration pneumonia of the aged.

Two major defense mechanisms can prevent aspiration: laryngeal elevation; and glottal closure. As a substitute for laryngeal elevation, we recommend that patients draw in the jaw during the act of swallowing. Various treatments are available for insufficient glottal closure. Laryngeal framework surgery, vocal cord augmentation, and vocal cord injection surgery and autologous transplantation of the fascia into the vocal folds (ATFV) technique are performed to improve speech or prevent chronic or recurrent aspiration by allowing the glottis to close adequately. Those surgical techniques can correct anatomical defects such as vocal cord atrophy with aging, however those need a time and cost.

We developed a self-controlled vocal exercise (SCVE) method as a more cost-effective treatment. Here we introduce this cost-effective solutions for laryngeal problems in advanced age.

## SY2-4

**Genetic variations in age-related hearing loss**

Tien-Chen Liu

*Department of Otolaryngology, National Taiwan University Hospital, Taiwan*

Age-related hearing loss (ARHL) is a complex disease involving the interaction of both environmental and genetic factors. The heritability of ARHL has been well demonstrated in previous studies and many genes were reported to be associated with ARHL. We have a cohort of 1481 subjects, and we study the correlation and contribution of GJB2, ADIPOQ, ADIPOR1, GRHL and CDH23 to ARHL in humans, cochlear explants and transgenic mice models. First, we identified an association between GJB2 variant alleles and ARHL in the clinical cohort, with the strongest association between the c.109G>A allele and ARHL under the assumption of the co-dominant model. The pathogenetic effects were then confirmed in a knock-in mouse model segregating the c.109G>A variant: mice homozygous for c.109G>A developed pre-senile hearing deterioration, revealed compromised gap-junction-mediated metabolite transfer in the inner ear sensory epithelium, and appeared more vulnerable to noise exposure. Secondly, the associations between ADIPOQ tagSNPs appear to exist only in subjects with specific ADIPOR1 genotypes, indicating an interaction between adiponectin and AdipoR1. Measurement of plasma adiponectin in 736 subjects revealed that ADIPOQ genotypes might exert their effects on hearing levels via modulation of plasma adiponectin levels. Subsequently, we confirmed the expression of AdipoR1 in the inner ear of mice, and demonstrated antiapoptotic effects of adiponectin in cochlear explant cultures. Furthermore, we showed no positive association between GRHL2 polymorphisms and ARHL in Han Chinese individuals. Population differences might be a key factor leading to non-replication of the association compared to Europeans. Finally, despite that the Ah1 allele of Cdh23 had been implicated with ARHL in mice, we found no positive association of the CDH23 tag SNP in intron 7 with ARHL in Han Chinese.

In this presentation, we would also report a study evaluating speech performance and subjective outcomes for older individuals who have hearing impairment and use digital hearing aids. The outcomes between young and old elderly users were compared. We found that, age by itself is not a limiting factor for older patients with hearing impairment to benefit from digital hearing aids.



SY2-5

## Association and Mechanisms of Obesity and Age-Related Hearing Impairment

Juen-Haur Hwang

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Part one: Association of WC and hearing thresholds in humans.

There were 954 adult and elderly subjects. After adjusting for coronary artery disease (CAD), diabetes mellitus (DM), hypertension (HTN), dyslipidemia, chronic kidney disease (CKD), smoking, drinking, noise exposure and even body mass index (BMI), WC still showed significant positive association with Z scores of middle or high frequencies.

Part two: Association of plasma adiponectin concentration and hearing thresholds in humans.

After adjusting for CAD, DM, HTN, dyslipidemia, CKD, smoking, drinking, noise exposure, and even WC, the plasma adiponectin concentration still showed significant negative association with Z scores of high frequencies.

Part three: Association of plasma ROS concentration and hearing thresholds in humans.

Luminol-dependent chemiluminescence signals, which reflect hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), hypochlorite (HOCl/OCl), and hydroxyl radicals (OH $\cdot$ ) levels, showed significant positive association with Z-low, Z-middle, or Z-high after adjusting central obesity, systemic diseases, habits, and noise exposure. Lucigenin-dependent chemiluminescence signals, which mainly reflect superoxide anion (O<sub>2</sub> $\cdot^-$ ) level, showed significant positive association with Z-low, but not with Z-middle or Z-high after adjusting other variables.

Part four: Effects and mechanisms of diet-induced obesity on hearing degeneration.

Compared to control group, the diet-induced obesity (DIO) group had significant higher body weight, fasting plasma triglyceride concentration, and omental fat weight after ICR/CD1 mice were fed with high fat diet for 16 weeks. The auditory brainstem response thresholds at 16000 Hz and 32000 Hz were significantly higher in the DIO group than the control group. But, the fasting plasma sugar and high-density lipoprotein cholesterol concentration were not significantly different in both groups. Cochlear H&E stain showed that DIO group had thinner diameter with higher vessel wall to radius ratio in the stria vascularis of cochlear basal turn. The cell density of spiral ganglion or spiral ligament was significantly lower in the DIO group than in the control group. But, the degeneration of Organ of Corti was similar in both groups. Cochlear immunohistochemistic stain showed that hypoxia-induced factor-1 $\alpha$ , tumor necrosis factor  $\alpha$ , nuclear factor-kappa B, caspase 3, poly (adenosine diphosphate-ribose) polymerase-1, apoptosis inducing factor stains were significantly denser in the DIO group than in the control group.

Conclusions: Waist circumference or central obesity was a novel independent risk factor for age-related hearing impairment.

## Symposium 3 Nasopharyngeal and Oropharyngeal Cancer

## SY3-1

**Role of Epstein-barr Virus and Alternating Chemoradiotherapy in Nasopharyngeal Carcinoma**

Tomokazu Yoshizaki

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Nasopharyngeal carcinoma (NPC) is chemoradiosensitive and highly metastatic cancer, which is contributed by Epstein-Barr virus (EBV). We have reported that EBV-encoded LMP1 promote metastasis by inducing MMP-1, MMP-9, c-Met, IL-8, VEGF etc. Thus, in addition to improve irradiation technique for controlling local disease, intensive chemotherapy is mandatory for controlling metastatic disease.

The concurrent chemoradiotherapy with 3-course of cisplatin and adjuvant chemotherapy with 3-course of cisplatin + 5FU has been a prevalent regimen for advanced NPC since ISG 0099. However, only 55% could accomplish the protocol treatment. Alternating chemoradiotherapy has been adapted since 1990 and shown better outcome of this treatment. in Aichi Cancer Institute. From December 2003 to March 2006, 90 patients with Stage IIb or more advanced NPC were enrolled in prospective multicenter phase II study. The patients were treated with 3 course of 5-FU (800mg/m<sup>2</sup> x 5days) plus cisplatin (50mg/m<sup>2</sup> x 2days) and 2 course of irradiation (36 Gy between 1st and 2nd chemotherapy, 34Gy between 2nd and 3rd chemotherapy). Three patients were not eligible for the protocol treatment and 87 patients were enrolled for the efficacy analysis. Seventy-four patients (85.1%) completed this therapy. The 5-year overall and progression free survival rate were 78.0% and 68.4%, respectively. Commonly observed acute toxicities of Grade 3 or more were loss of appetite (47.7%), neutropenia (45.5%), and mucositis (31.8%).

This alternating chemoradiotherapy protocol is more effective, less toxic than IGS-0099 protocol, and thus, promising treatment for advanced, and especially, EBV-associated NPC.

## SY3-2

**p16 expression in oropharyngeal and nasopharyngeal carcinoma**Yuki Saito<sup>1</sup>, Tetuo Ushiku<sup>2</sup>, Go Omura<sup>1</sup>, Masafumi Yoshida<sup>1</sup>, Mizuo Ando<sup>1</sup>, Tatsuya Yamasoba<sup>1</sup>*<sup>1</sup>Department of Otolaryngology and Head and Neck Surgery, the University of Tokyo, Tokyo, Japan, <sup>2</sup>Department of Pathology, the University of Tokyo, Tokyo, Japan*

**Objective.** In a previous study, we reported the value of p16 expression and alcohol consumption in oropharyngeal carcinoma in Japan. We now report 1) the clinical significance of human papillomavirus (HPV) status and p16 expression in oropharyngeal carcinoma and 2) the clinical significance of Epstein-Barr Virus (EBV) status and p16 expression in nasopharyngeal carcinoma.

**Subjects and Methods.** Retrospective case comparison study of the pathology database was conducted at the University of Tokyo to identify tumor samples of oropharyngeal and nasopharyngeal carcinoma. We performed 1) immunohistochemistry for the p16 protein, in situ hybridization for HPV-DNA (ISH-HPV), and polymerase chain reaction for the HPV-DNA oncogene E6 (PCR-E6) in oropharyngeal carcinoma, and 2) immunohistochemistry for the p16 protein, in situ hybridization for EBV-DNA (EBER-ISH). We evaluated the HPV status in patients with oropharyngeal carcinoma to determine its prevalence and association with prognosis. We defined HPV(+) and HPV(-) oropharyngeal carcinoma cohorts as those with and without PCR-E6 or ISH-HPV. In addition, we evaluated the EBV status in patients with nasopharyngeal carcinoma to determine its prevalence and association with prognosis.

**Results.** In oropharyngeal carcinoma, the prevalences of p16(+)HPV(+), p16(+)HPV(-), p16(-)HPV(+), and p16(-)HPV(-) were 32% (48/150), 7% (10/150), 2% (3/150), and 59% (89/150), respectively. Low tobacco and alcohol consumption, tonsil or base of tongue localization, but not age, were associated with p16(+)HPV(+). Low alcohol consumption was associated with p16(+)HPV(-). There was a significant difference in overall survival between p16(+)HPV(-) and p16(-)HPV(-). In multivariate Cox regression models, p16 was the independent prognostic factor, regardless of HPV status. In nasopharyngeal carcinoma, the prevalence of p16(+)EBV(+), p16(+)EBV(-), p16(-)EBV(+), and p16(-)EBV(-) were 5% (2/38), 16% (6/38), 50% (19/38), and 29% (11/38), respectively. Keratinizing squamous cell carcinoma (WHO type I) was associated with p16(-)EBV(-). There was a significant difference in overall survival between p16(-)EBV(-) and p16(+)EBV(-) and between p16(-)EBV(-) and p16(-)EBV(+).

**Conclusion.** p16 expression was a reliable prognostic biomarker regardless of HPV status. In addition, p16 expression was also a prognostic biomarker in EBV(-) nasopharyngeal carcinoma.

SY3-3

## Superselective intra-arterial cisplatin infusion and concomitant radiotherapy for base of tongue cancer

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### BACKGROUND:

The purpose of this study was to evaluate the efficacy of superselective intra-arterial cisplatin and concomitant radiotherapy (RADPLAT) for previously untreated patients with the squamous cell carcinoma of base of tongue (SCC-BOT).

### METHODS:

Thirty-one patients were given superselective intra-arterial infusions of cisplatin (100-120mg/m<sup>2</sup>) with simultaneous intra-venous infusions of thiosulfate to neutralize cisplatin toxicity and conventional radiotherapy between 2000 and 2013.

### RESULTS:

Eight patients (25.8%) was diagnosed with T2, 4 (12.9%) with T3, 18 (58.1%) with T4a, and 1 (3.2%) with T4b disease. Lymph-node involvement was present in 24 patients (77.4%); 3 (9.7%) with N1, 1 (3.2%) with N2a, 10 (32.3%) with N2b, and 10 (32.3%) with N2c. During the median follow-up period of 5.6 years (range, 1.8-8.6 years), the 5-year local control and overall survival rates were 90.3% and 78.5% for all patients, respectively. Three patients with persistent/recurrent primary disease had T4a or T4b disease. Four patients died with neck disease (2) or distant metastasis (2) had N2c disease. No patient died as a result of treatment toxicity or experienced a cerebrovascular accident. Osteonecrosis was observed in 6 patients as late adverse reactions. All surviving patients are able to have oral intake without feeding-tube support and normal speech without tracheostoma after treatment.

### CONCLUSION:

Our study found that RADPLAT gave excellent survival rates and organ functions for patients with SCC-BOT. We consider that SCC-BOT is a good indication for RADPLAT and that the angiographic technique is a key to success.

SY3-4

## The utility of useful markers on the detection and management of nasopharyngeal carcinoma

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Nasopharyngeal carcinoma (NPC) is one of the most common types of head and neck cancer in Southeast Asia. NPC is a very radiosensitive tumor, and 5-year overall and disease-free survival rates up to 70% can be obtained by the use of concurrent chemoradiotherapy. However, NPC patients presenting with more advanced disease have worse prognosis and some patients may still develop locoregional and distant failure, thus requiring salvage or palliative therapy. For these reasons, the development of more tailored treatment approaches can ultimately improve clinical outcomes. In our previous studies, the recognition of the importance of Epstein-Barr virus (EBV) in the pathogenesis of NPC led to the discovery of the EBV-derived biomarkers for NPC. Furthermore, the assessment of cell-free EBV DNA load may not only serve for detection of NPC but may also have value for prediction of prognosis and treatment outcomes. For instance, it has been reported that post-treatment EBV DNA levels may be clinically useful for monitoring tumor relapse.

In the past fifteen years, head and neck research group collaborated by Chang Gung Memorial Hospital and Chang Gung University has used various research platforms including the genomic approach (cDNA microarrays, genome-wide association analysis), proteomic approach (2-D electrophoresis, LC-MS/MS, Immunobead-based suspension arrays), and molecular imaging technologies, attempting to search and identify the novel biomarkers for nasopharyngeal carcinoma. Currently, in addition to EBV-derived markers (EBV EA+EBNA1 IgA and EBV copy number), we have found that some biomarkers, such as SNPs and copy number variations at 6p21.3, IHC markers, serum/plasma markers (MIP-3alpha, SCF, cystatin A, VEGF, IL-8, and CXCL9) and functional parameters (tumor TLG and heterogeneity) from molecular imaging, could be used for the purpose of either NPC detection or stratification. In this presentation, I'll share our experience to apply these research platforms to clinical utility in cancer research concerning the potential usage of biomarkers for disease screening and stratification in patients with nasopharyngeal carcinoma.

## SY3-5

## Management of p16 negative advanced tonsil cancer, primary surgery or primary radiation?

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The silencing of p16 by promoter methylation is commonly observed in HNSCC. In contrast, HPV is readily detected in HPV positive tumors and is highly correlated with p16 expression, which is most likely the result of transcriptionally active HPV infection. Generally, the p16 protein could be regarded as the surrogate of HPV infection in the oropharyngeal cancer. According to many researches, the p16 positive tonsil cancer shows a very good clinical outcome when compared with p16 negative tumor. The treatment of tonsil cancer by primary radiation is usually good enough to control the p16 positive tumor. However, the clinical outcomes of p16 negative tonsil cancer remain poor especially of the advanced tumor.

Currently, there are few reports discussing the treatment strategy about this advanced but operable tonsil cancer with negative expression of p16. In this study, we try to figure out which kind of treatment strategy, primary radiation or primary surgery is better for these patients. Between 1996 June and 2013 June, 128 cases of advanced but operable tonsil cancer with negative expression of p16 were enrolled for study. 69 patients were assigned as primary surgery group and 59 patients were assigned as primary radiation group. Patients in primary surgery group showed significantly better 5-year local/regional control rate ( $p=0.001$ ), 5-year disease free survival rate ( $p=0.013$ ), 5-year overall survival rate ( $p=0.024$ ) and 5-year disease specific survival rate ( $p=0.003$ ) when compared with patients in primary radiation group. In conclusion, the surgical intervention should be considered as the primary treatment strategy among patients with advanced but operable tonsil cancer with negative expression of p16 to achieve the better clinical outcomes.

## SY3-6

## Salvage Nasopharyngectomy for rNPC

Sheng-Po Hao

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Nasopharyngeal carcinoma (NPC) is a common cancer among the Chinese people. NPC is a squamous cell carcinoma which originates from the epithelial lining of the nasopharynx. Currently available therapeutic modalities for NPC are radiation therapy (RT), chemotherapy, or a combination of both. NPC is highly radiosensitive and patients presenting with limited stage cancer have a high possibility for cure after RT. Concurrent cisplatin based chemo-radiotherapy with or without neo-adjuvant chemotherapy is currently the standard treatment for patients with advanced locoregional disease. Though NPC is usually a radiosensitive tumor, some do recur after RT. Local failure, either persistence or recurrence, in the nasopharynx, occurs in 10% to 30% of patients with NPC after initial RT.

Salvage nasopharyngectomy has been the mainstay of treatment after RT failure. Surgical access to the nasopharynx has been a challenge to head and neck surgeons for years. Various surgical approaches to the nasopharynx have been developed, such as the transpalatal, transmaxillary, midline mandibulotomy, transpterygoid, facial translocation, and infratemporal fossa approaches. However, in recent years, there is a paradigm shift for nasopharyngectomy, that is from open to endoscopic. Minimally invasive endoscopic nasopharyngectomy has been reported to be a feasible treatment of a small mucosal recurrence. The indication of endoscopic nasopharyngectomy for rNPC includes lesions of the central roof or floor with minimal lateral extension. With the aid of navigation, endoscopic nasopharyngectomy can also be a good surgical intervention in rNPC cases even with skull base bone involvement.

**Symposium 4** Skull Base Surgery

**SY4-1**

**Surgical Management of Acoustic Neuroma - strategy and outcomes of functional preservation of facial nerve and hearing -**

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The goal of acoustic neuroma surgery is complete excision of tumor with functional preservation of the facial nerve and hearing. Use of intraoperative monitoring and team operation with otologists and neurosurgeons enable us to functional preservation of both facial nerve and hearing as well as complete resection of the tumor because otologists have good skill for temporal bone dissection and neurosurgeons for intracranial tumor dissection.

To date, three surgical approaches of translabyrinthine (TL), middle cranial fossa (MCF) and retrosigmoid (RS) are used in acoustic neuroma surgery. Eclectic use of three approaches is also the goal in a managed surgical setting. Our surgical pathways for functional preservation are that (1) use of intraoperative monitoring of facial nerve and hearing, (2) surgical approach is decided depending on tumor size, location and hearing status, (3) otologists take the parts of opening the bony IAC and excision of intrameatal tumor, (4) neurosurgeons take the parts of craniotomy and excision of extrameatal tumor near brain stem in both the MCF and RS approaches. Using above surgical pathways, we have performed 248 acoustic neuromas (MCF: 84, RS: 129, TL: 35) in cooperation with otologists and neurosurgeons during recent 15 years. Hearing was preserved in 71 (84%) patients operated via MCF approach and in 70 (54%) patients operated via RS approach. Facial nerve function of HB grade 1 or 2 was achieved in 34 (97%) patients operated via TL approach, in 82 (99%) patients via MCF approach and in 117 (91%) patients via RS approach. We stress team treatment with neurosurgeons and show our technique for preservation of hearing and facial nerve function.

**SY4-2**

**Strategy, Surgical Procedure and Outcomes of Subtotal Temporal Bone Resection for Advanced Temporal Bone Cancers**

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**Introduction:** A combination of preoperative chemo-radiotherapy (CCR) and en-bloc surgical resection improved survival ratio in T3 and anterior lateral type T4 for squamous cell carcinoma (SCC) of temporal bone (Nakagawa et al. 2006). We performed subtotal temporal bone resection (STBR) by mainly extradural approach. However, how to deal with advanced cases of squamous cell carcinoma of temporal bone is still controversial. We will present treatment strategy for advanced cases, background concept, step-by-step operative procedure for STBR and analysis of the outcomes.

**Subjects and Results:** Subjects were 33 patients with primary advanced SCC of temporal bone. Indication for STBR was a case which extended outside external auditory canal (EAC) without dural invasion, internal carotid canal (ICA) destruction or distant metastasis. Preoperative CCR was performed in most of cases. STBR started with neck dissection from below up to jugular foramen. Medial part was cut along posterior cranial fossa (PCF) dura. Removal of posterior-medial-upper part was middle cranial fossa (MCF) dura from below. ICA and jugular bulb were recognized from below by drilling lateral bone out of those vessels. Blinded medial part was resected from above after a craniotomy of MCF.

5 year-survival ratios were 75% for T3 (n=8) and 40% for T4 lesion (n=25). That for T4 with operation (61%, n=9) was significantly higher than that without operation (27%, n=16). T4a was defined as tumor eroding the cochlea, medial wall of the middle ear, or with extensive soft tissue involvement (>0.5 cm), or evidence of facial paresis. T4b was the tumor eroding petrous apex, carotid canal, jugular foramen or dura. In addition to T stage, the existence of lymph node significantly affected 5 year survival rate. Then we proposed the staging system by T, N and M staging. Stage I to III are tumor of T1 to T3 without positive lymph node and metastasis. Stage IV A is T1 to T3 with positive LN and T4a with any N stage. Stage IV B is tumor with metastasis or T4b with any N stage. Then survival rates were in line by the staging with significance.

**Conclusion:** STBR by en-bloc technique with pre-operative CRT was effective on advanced cases of SCC of temporal bone. T4 was classified to T4a and T4b by either with or without medial invasion. Staging system of temporal bone SCC was proposed in consideration of T and N stage.

## SY4-3

## Complications and treatments for facial palsy in the lateral skull base surgery

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**Introduction:** Lateral skull base surgery manages tumors near the temporal bone and infratemporal fossa. On the other hand, facial nerve runs from the brain to the parotid gland and innervates to facial muscle. That means all lateral skull base surgery may cause facial palsy.

**Cases and method:** In these 10 years, we had done 107 of lateral skull base surgeries. Among these cases, facial nerve was not exposed in 54 cases. Coronal skin incision, facial dismasking flap, pre auricular and post auricular skin incision was applied. Rest of 53 cases, facial nerve manipulated in various way. Managements for facial nerves are only exposure of the nerve (20), reroute of the nerve (5), cut & suture (14) and removed with lesion (14). Among these 14 cases, facial nerve was removed with the lesion and 4 had no immediate reconstruction and 10 had immediate reconstruction surgery (Hypoglossal-Facial N. anastomosis). The patients who showed facial palsy after the surgery, rehabilitation were applied.

**Result:** The facial palsy occurred in 8/54 cases occurred after coronal skin incision and facial dismasking flap and these palsy was observed mainly in the frontal muscle. Traction force to flap elevation during the surgery might be a cause of palsy and 8 cases with facial palsy suffered rehabilitation and recovered.

Among 53 case with facial nerve exposure, 20 patients with only exposure of the nerve and 5 cases suffering reroute of the nerve, facial nerve were anatomically preserved. However, former 3 out of 20 cases showed HB II palsy and latter 5 cases showed HB III to VI immediately after the surgery. The former cases recovered to HB I. The latter remains slight facial palsy of HB II to III, one case remained HB IV. Fourteen case suffering cut & suture and 14 cases with removal with lesion showed total palsy immediate after the surgery. The former cases showed recovery of HB III (7) and HB IV (7). The latter case with immediate reconstruction showed HB III (1) and HB IV (9). The latter case without immediate reconstruction remained total palsy. Plastic surgery underwent for some patients with profound palsy and satisfactory results were obtained.

**Conclusion:** Various degrees of facial palsy depends on facial nerve manipulation in the lateral skull base surgery. Informed consent before surgery, special care to the nerve during surgery and an appropriate rehabilitation were required.

## SY4-4

## Endoscopic Skull Base Surgery- an Otolaryngologist's Perspective

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During the last 2 decades, minimally invasive endoscopic surgeries have emerged as the standard, and frequently preferred, techniques in a number of surgical disciplines including urological, general, and orthopedic surgery due to its minimal invasiveness with short recovery time. However, such operations are not yet a standard procedure in the skull base region because of anatomy complexity in this region. The use of the endoscope, which is so familiar to the otolaryngologist in functional endoscopic sinus surgery, has helped fuel interest in the skull base area. Much improved illumination, endoscopic visualization, navigation, specialized instrumentation, and continued advances in surgical technique have allowed this revolution in the advanced endoscopic skull base surgery. Hence, endoscopic skull base surgery has undergone rapid advancement in the past decade moving from pituitary surgery to suprasellar lesions and now to anterior skull base, central skull base, infratemporal fossa and petrous apex, including benign and malignant lesions. Cosmetic results are not the only factor that has prompted the use of minimally invasive endoscopic skull base surgery. Other potential and important advantages of this approach are to achieve the same results as obtained by traditional surgery, with fewer traumas to the surrounding tissue, reduced operation time, and shorter hospitalization. I conclude that endoscopic skull base surgery for benign disease is largely accepted now but more data is needed to support the role of treatment for malignant disease.

**SY4-5**

## **Lateral Skull Base Surgery in Taipei Veterans General Hospital**

Mao-Che Wang

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### Introduction:

Lateral skull base surgery in Taipei Veterans General Hospital is a team work involving a neurosurgeon and a neurotologist. For large cerebello-pontine angle (CPA) tumors (>3cm) or patients without useful hearing, translabyrinthine approach was the choice of approach for tumor removal. For patients with useful hearing, combination of retrolabyrinthine and infralabyrinthine approaches was used.

### Materials and Methods:

From June, 9th, 2011 to Aug, 11th, 2015, 49 patients received translabyrinthine approach for CPA tumors or other skull base lesions. Nine patients had combination of retrolabyrinthine and infralabyrinthine approaches.

### Results:

For 49 patients received translabyrinthine approach, age ranged from 18 to 76 years old. Acoustic neuroma was noted in 35 patients, meningioma in 8, lower cranial nerve schwannoma in 4, craniopharyngioma in 1 and anaplastic hemangiopericytoma in 1. Tumor size ranged from 2cm to 8cm and 47 of them were larger than 3cm. Total resection was achieved in 13 patients, near total resection in 16, subtotal resection in 16 and partial resection in 4. Six patients had previous surgery and 2 had previous Gamma knife radiosurgery for the lesions. Two patients required further surgery and 9 had Gamma knife radiosurgery for tumor control. Thirty patients (61%) had good facial nerve function (grade I or grade II) after surgery. For 9 patients had combination of retrolabyrinthine and infralabyrinthine approaches, meningioma was found in 3, the others had acoustic neuroma, cholesteatoma, epithelioma, chordoma, lower cranial nerve schwannoma and a giant aneurysm. Total resection was achieved in 2 patients, near total resection in 2, subtotal resection in 4 and clipping of aneurysm in 1. Two patients had transient post-operative facial palsy and hearing preservation in 8 patients except the patient with large acoustic neuroma.

### Conclusion:

Translabyrinthine approach is a safe and effective way in dealing with CPA tumors and other lateral skull base lesions. It can provide excellent exposure of surgical field and good preservation of facial nerve function. The main drawback is the sacrifice of hearing. For patient with useful hearing, combination of retrolabyrinthine and infralabyrinthine approaches can achieve both hearing preservation and tumor control except one case of large acoustic neuroma.

## Symposium 5 Laryngeal and Hypopharyngeal Cancer

## SY5-1

**Hypopharyngeal cancer in the elderly**

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While the population has increased by 6% in the past 5 years Globally, 75+ age group had doubled from 7% to 14%. Japan is the most advanced aging society in the world. One of the main risk factor for developing head and neck cancer is age. As a results, head and neck surgeons in Japan have been struggling to treat elder head and neck cancer patients.

In hypopharyngeal cancer (HPC) treatment, the ratio of chemo-radio therapy (CRT) is increasing for preserving larynx. However, the Evidence of usefulness of CRT is not shown in elderly population. The purpose of this report is to clarify the significance of the surgical treatment in elderly HPC patients.

A retrospective analysis of 208 patients from April 2007 to December 2014 was performed. About 40% of patients were at least 70 years old (82patients).

Because of severe comorbidities and advanced disease, sixteen patient choice palliative care. Remaining 68 patients were treated with curative intent. In general, our institution selected total pharyngolaryngectomy (TPL) with free jejunum transplantation for elder advanced HPC. Thirty-four patients were undertook TPL, CRT was performed in only 9 cases. The five year over all survival rate of TPL group is 47%. There is no significant difference between elder and younger population in treatment results.

The treatment paradigms in the elderly population have not been well defined. These elderly patients may not be considered candidates for aggressive multimodality management due to multiple comorbidities, general debility, and concerns regarding poor treatment tolerance and toxicities.

Our date indicates that TPL is simple and effective procedure to treat advanced HPC elderly.

## SY5-2

**Transoral Videolaryngoscopic Surgery (TOVS) - A Novel Endoscopic Surgery for Laryngopharyngeal Cancers**

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## Backgrounds

We developed a novel easy-to-use surgical environment that combines a distending laryngoscope, rigid high-definition endoscope, and surgical forceps for laparoscopic surgery. This environment provides a wider field of view, which makes it possible to operate with both hands and perform transoral en bloc resection without tracheostomy for supraglottic and hypopharyngeal, cancers. We named this surgery "Transoral Videolaryngoscopic Surgery (TOVS)".

## Methods

Ninety three patients with T1, T2, and selected T3 supraglottic and hypopharyngeal cancer were enrolled in this study. Under general anesthesia with oral endotracheal intubation, the most appropriate surgical view was obtained using an FK retractor (Gyrus ACMI, Southborough, Massachusetts) or a Weerda distending laryngoscope (Karl Storz, Tuttlingen, Germany). Endoeye Flex rigid endoscope (Olympus Medical Systems, Tokyo, Japan), which has a flexible part at its tip, or a laryngeal rigid endoscope with a high-definition camera (Karl Storz) was used for monitoring. The tumor was resected en bloc using 3-mm-diameter laparoscopic surgical instruments (Karl Storz) bimanually while watching the video images on the monitor. Neck dissections were performed for node-positive patients.

The overall survival rate, disease-specific survival rate and laryngeal preservation rate were evaluated. A patient's swallowing function after treatment was also assessed by the patient's Functional Outcome Swallowing Scale (FOSS) stage.

## Results

TOVS enabled us to perform transoral en bloc resection in all cases. For supraglottic and hypopharyngeal cancers, the 5-year overall and disease-specific survival and laryngeal preservation rates were 81%, 98% and 96%, respectively. The patients' FOSS stages were 0-2 in 93.3% of the cases and 3 or 4 in 6.7% of the cases. Four (6.7%) patients received transient tracheostomy.

## Conclusions

TOVS made it possible to perform a safe and reliable transoral en bloc resection for T1-T3 laryngopharyngeal, cancers with satisfactory oncological and functional outcomes, indicating that it could be one of the minimally invasive treatment options for these cancers. TOVS may also be an easy-to-use and low-cost alternative surgical environment for robotic surgery.

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**SY5-3**

## **Endoscopic laryngo-pharyngeal surgery and transoral robotic surgery in Japan**

Ichiro Tateya

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Transoral surgery is a less invasive treatment that is becoming a major strategy in the treatment of laryngo-pharyngeal cancer. It is a minimally invasive approach that has no skin incision and limits the extent of tissue dissection, disruption of speech and swallowing muscles, blood loss, damage to major neurovascular structures, and injury to normal tissue. Transoral approaches to the laryngo-pharynx, except for early glottis cancer, had been limited traditionally to tumors that can be observed directly and manipulated with standard instrumentation and lighting. Since the 1990s, transoral laser microsurgery has been used as an organ preservation strategy with good oncological control and good functional results, although it has not been widely used because of its technical difficulty.

Recently, transoral robotic surgery (TORS) is becoming popular as a new treatment modality for laryngo-pharyngeal cancer, and surgical robots are used widely in the world since United States FDA approval in 2009. In spite of the global spread of TORS, it hasn't been approved by the Japan FDA. A multi-center (Kyoto University, Tokyo Medical University, and Tottori University) clinical study of TORS led by Kyoto University is currently underway to assess the safety and feasibility of TORS and to provide data to the Japan FDA for TORS approval.

On the other hand, the limited access to TORS has led to the development of unique transoral surgical techniques in Japan. Endoscopic laryngo-pharyngeal surgery (ELPS) is one of them and has been developed to treat laryngo-pharyngeal cancer by modifying the endoscopic submucosal dissection (ESD) procedure. The concept of ELPS is the same as that of ESD, however, the resection procedure is performed by a head and neck surgeon with both hands using a ME-NBI and rigid curved laryngo-pharyngoscope. ELPS was indicated initially for carcinoma in situ or invasive laryngo-pharyngeal cancer without muscular invasion, but the indication for this technique becoming broader.

The technical features and clinical outcomes of ELPS and the recent progress and future prospects of TORS in Japan will be presented.

**SY5-4**

## **Screening of esophageal cancer in newly diagnosed primary hypopharyngeal cancer patients with a significant survival benefit**

Cheng-Ping Wang

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Hypopharyngeal cancer (HSCC) has a higher risk associated with primary esophageal cancer (ESCC). In the past 8 years, we have demonstrated the feasibility of transnasal esophagogastroduodenoscopy (EGD) without conscious sedation to evaluate HSCC with tissue diagnosis and to regularly screen the entire esophagus at the same time. Between 2007 and 2014, we evaluated 248 patients with newly diagnosed HSCC, but without previous history of other head and neck cancer and ESCC, by use of this technique. About 45% of the patients had simultaneous esophageal lesions, including ESCC for 15% of patients, esophageal dysplasia without ESCC for 9% and Lugol voiding lesion (LVL) without ESCC or dysplasia for the other 21%. Heavy alcohol drinking and big neck metastasis (N3) of HSCC were the independent risk predictors associated with simultaneous esophageal lesions. The overall survival of patients with HSCC alone was significantly higher than that of patients with simultaneous HSCC and ESCC, which treatment is a very challenging issue I will talk about, too. This risk evaluation also stratifies the HSCC patients with esophageal dysplasia or LVL, who developed metachronous ESCC significantly more commonly than the patients with normal esophagus mucosa and may need regular screening of ESCC after treatment of HSCC. The early stage of ESCC (50%) in this cohort was more common than that of ESCC (25%) diagnosed based on the presence of symptoms in general population in Taiwan. We also demonstrated positive survival benefit of this diagnostic approach compared with the cohort without esophageal screening.

SY5-5

## **Surgical Techniques to Improve Voice Outcomes in Glottic Cancer Patients Underwent Transoral Laser Microsurgery**

Pen-Yuan Chu

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Transoral laser microsurgery (TLM) and radiotherapy (RT) are commonly used in the treatment of early glottic cancer. Both treatment modalities provide high and comparable local control rate and survival. Because of the low morbidities, short treatment duration and excellent oncologic outcomes, there is a trend of increasing use of TLM as primary treatment for early glottic cancer. Previous report showed 5-years local control rate and disease-specific survival was 87% and 96% in early glottic cancer (T1 and T2) treated by TLM in our hospital.

Voice quality is always the main concern of treatment choice for early glottic cancer. The extent of resection and anterior commissure (AC) involvement has been reported the most important factors of post-treatment voice quality after TLM. To improve the voice quality, some surgical techniques of TLM was developed in our hospital.

In 2006, we developed a modified type III cordectomy for early glottic cancer. Unlike classical type III cordectomy to resect the whole layers of epithelium, lamina propria, and vocalis muscles, modified type III cordectomy only resected the upper part of vocalis muscle which was involved by tumor. The lower part of vocalis muscle was preserved as a scaffold to allow granulation formation and fill the surgical defect. This modified technique will improve the glottis closure which is essential for good voice quality. The preliminary data showed most of the voice parameters were significantly better in modified resection and the oncologic result was similar to classical resection.

For those patients who had bilateral vocal fold lesions and AC involvement, two type of technique was designed to avoid anterior glottis web formation. In superficial lesions of AC, staged cordectomy was performed. The first stage cordectomy was done from one side of vocal fold to midline of AC. After epithelization of vocal fold, the second stage cordectomy was then performed. The time interval between two stages cordectomy was around 3 weeks. In deep lesions of AC, single stage type 6 cordectomy was performed. During operation, the resection was made from AC to thyroid cartilage with a cavity. It may help to lessen the anterior glottic web formation after surgery. The preliminary result was satisfactory. In this presentation, we will show the video of surgical techniques.

**Symposium 6** Salivary Gland

**SY6-1**

**Evaluation and management for parotid gland tumors**

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The objective of this study was to analyze the diagnosis and postoperative complications of benign parotid tumors for a series of 633 patients who underwent the same diagnostic methods and operation procedure in a single institute. A series of 633 patients who underwent parotidectomy for benign parotid tumors over a 16-year period was reviewed. There were 345 female and 288 male patients. The site of the tumors was divided into three groups, superficial, deep, and lower pole tumor. The number of each type of the tumor was 342, 122, 169 cases, respectively. The most common pathology of the parotid tumor was a pleomorphic adenoma (372 cases) followed by a Warthin tumor (166 cases). Pleomorphic adenomas and Warthin tumors accounted for 85 % of all benign tumors. The accuracy rate of fine needle aspiration cytology (FNA) for all benign tumors was 71 %, 84 % for pleomorphic adenoma and 72 % for Warthin tumor. Transient facial nerve dysfunction was observed in 130 patients (21%) in 612 cases of primary benign parotid tumors, and only one patient developed a permanent weakness. The incidence of transient facial nerve dysfunction was 18% in superficial tumors, 39% in deep tumors, and 15% in lower pole tumors. Significant risk factors for development of a transient facial palsy were the site of tumors, the size of tumors, operation time, and bleeding volume. Among these risk factors, the site of the tumors, deep lobe was the most important factor in transient facial nerve dysfunction. Transient facial nerve dysfunction recovered within 6 months in 90% patients of all cases. The accuracy rate of FNAC for benign parotid benign tumors was 72%. The incidence of transient facial nerve dysfunction in deep tumors was significantly higher compared to that in superficial and lower pole tumors. According to the rate of facial palsy, operation time, and bleeding volume, benign parotid tumor should be divided into three groups, superficial, deep, and lower pole tumors.

**SY6-2**

**Sialendoscopy: treatment and effects beyond sialolithiasis**

Li-Jen Hsin

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Introduction: Sialendoscopy has been applied for various salivary gland diseases. To the best of our knowledge, the application mainly focused upon sialolithiasis. For other salivary gland diseases such as chronic obstructive sialadenitis, stricture of salivary duct, juvenile recurrent parotitis, the effect of this procedure was still unclear. We intend to provide a brief demonstration of our clinical findings and treatment outcome.

## SY6-3

**Recent Advances in IgG4-related sialadenitis**

Kenichi Takano, Kazuaki Nomura, Ayumi Abe,  
Tetsuo Himi

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Immunoglobulin G4-related disease (IgG4-RD) is a newly categorized disease that has received much attention in the last decade. The hallmarks of IgG4-RD are lymphoplasmacytic tissue infiltration with a predominance of IgG4-positive plasma cells accompanied by fibrosis, obliterative phlebitis, dacryoadenitis, and elevated IgG4 levels. Most often, diagnosis is made in patients with IgG4-related dacryoadenitis and/or sialadenitis (so-called Mikulicz's disease), which was once believed to be a subset of Sjogren's syndrome and type 1 autoimmune pancreatitis (AIP). Immunohistochemical detection of increased IgG4 levels in involved tissues is important because IgG4 is a surrogate marker that enables exclusion of its neoplastic mimics. The involved organ systems are numerous and include the salivary and lacrimal glands, pancreas, bile duct, central nervous system, thyroid, lungs, liver, gastrointestinal tract, kidneys, prostate, retroperitoneum, arteries, lymph nodes, skin, and breast tissues. In particular, a characteristic finding is infraorbital nerve enlargement on CT or MRI examinations. The pathogenesis of this disease remains unclear, but inflammation and subsequent fibrosis occur due to excess production of Th2 cell and regulatory T-cell cytokines. IgG4-positive plasma cell infiltration has been determined in various diseases and clinical conditions. Therefore, rigorous histopathological examination is necessary for definitive diagnosis. The newly proposed criteria emphasize the importance of IgG4-positive plasma cell infiltration along with storiform or swirling fibrosis and obliterative phlebitis in diagnosing IgG4-RD. Therefore, we recommended that although more invasive than labial salivary gland (LSG) biopsy, submandibular gland (SMG) biopsy is more accurate for diagnosing IgG4-RD and for excluding malignant diseases. However, this procedure may be contraindicated for some patients who are unable to undergo general anesthesia or who are unwilling to undergo an invasive procedure. For those patients, determination of sIL-2R levels, increased uptake of 18F-FDG, or both, may enhance our ability to predict infiltration of IgG4-positive plasma cells into LSG tissue before performing a biopsy of the patient's lip. Although glucocorticoids treatment is effective in inducing remission, patients often relapse when doses of these agents are tapered. IgG4-RD has also been associated with an increased incidence of certain malignancies. Systemic screening is necessary to establish the diagnosis of IgG4-RD, and it must be distinguished from neoplastic disease. In this lecture, I will talk about the recent progress in our understanding of the pathogenic mechanisms of IgG4-related disease, and outline considerations for diagnosis and treatment of the condition.

## SY6-4

**Robotic surgery for the salivary gland tumors**

Tsung-Lin Yang

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Surgery remains the therapeutic mainstream of the salivary gland tumors. Conventional open surgery results in obvious scars on the face and neck, which disfigure the esthetic appearance. It is therefore many surgical techniques have been developed for decades to obscure the scars. Compared with other surgical methods, robotic surgery provides appealing surgical approaches and techniques. Here we report the feasibility and efficacy of treating the salivary gland tumors by robotic surgery. We develop a novel robotic surgical technique through the trans-hairline approach. The incision is concealed within hairs postoperatively. Compared with other robotic approaches of the neck, the trans-hairline approach obliterates scars without creating unnecessary long surgical routes. It has been successfully applied in our attempts of treating different types of the salivary gland tumors. Using a novel device, so called the Yang's retractor, the surgical field is maintained automatically through the incision along the hairline. Robotic instruments can be freely introduced into the surgical tunnel without collision. Complete tumor removal was achieved by robotic surgery through the hairline approach in all patients. Neither operative nor postoperative complications were found. An esthetic outcome was maintained by concealing scars within hairs. Our experiences demonstrate that robotic surgery through trans-hairline approach is a feasible alternative to conventional surgery with potential safety and esthetic advantages in treating the salivary gland tumors.

**Symposium 7** Middle Ear and Facial Nerve

**SY7-1**

**The new technology: Canal wall up tympanoplasty with transplantation of tissue-engineered cell sheets**

Hiromi Kojima

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**Objectives:** The likelihood of recurrent retraction and adhesion of newly formed tympanic membrane is high when normal middle ear mucosa is extensively lost during intractable middle surgery. If rapid postoperative regeneration of the mucosa on the exposed bone surface can be achieved, prevention of recurrent tympanic membrane adhesion and cholesteatoma formation can be expected. The aim of this study was to develop a new method to transplant autologous cell-sheets to promote postoperative regeneration of the middle ear mucosa.

**Methods:** We harvested 10-by-10-mm specimens of inferior turbinate mucosal tissue from the patient with acquired middle ear cholesteatoma. Tissue-engineered epithelial-cell sheets were fabricated *ex vivo* by culturing harvested cells for three weeks on temperature-responsive culture dishes in a cell-processing center (CPC) according to good manufacturing practice guidelines. After canal wall up tympanoplasty with mastoidectomy had been performed, sheets of cultured autologous cells that had been harvested with a simple reduced-temperature treatment were transplanted directly into the exposed bone surface of middle ear cavity from which normal mucosa had been defect.

**Results:** During the cultivation, the sterile environment in the CPC was confirmed. Autologous cell sheets were successfully transplanted to human middle ear.

**Conclusion:** This is the first clinical study approved from the Ministry of Health, Labour and Welfare in Japan. Furthermore this is a first-in-man study in the world that the cultured cells were transplanted to the human ear. This novel technology of transplantation might be an effective alternative to the surgical operation on intractable otitis media in the near future.

**SY7-2**

**Facial nerve regeneration surgery using bFGF-gelatin hydrogel in patients with severe Bell's palsy**

Naohito Hato

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Bell's palsy is an idiopathic, peripheral, unilateral facial paralysis of sudden onset and is the most common cause of facial nerve paralysis. Facial nerve decompression surgery is indicated in cases of Bell's palsy suspected to have a poor prognosis, usually within 2 weeks of onset. Currently, most patients are treated medically, and decompression surgery is rarely undertaken. Decompression more than 2 weeks after the onset of paralysis is particularly rare because the surgical procedure is unlikely to facilitate nerve regeneration.

Basic fibroblast growth factor (bFGF) promotes the regeneration of denervated nerves. Our experimental study suggested that bFGF-impregnated biodegradable hydrogel facilitates regeneration of the facial nerve in guinea pigs due to the sustained release of bFGF. Clinically, this therapeutic regimen may be useful for facial nerve decompression surgery, which is indicated for severe facial nerve paralysis. Therefore, we started clinical trial after the approval by the institutional review board of Ehime University Hospital.

Twenty-nine patients with Bell's palsy were treated with the new procedure. The inclusion criteria were: 1) older than 16 years of age; 2) severe or complete facial paralysis corresponding to House-Brackmann (H-B) grade 5 or 6; 3) degree of denervation exceeding 95%, determined using electroneuronography; 4) presenting between 2 weeks and 4 months after the onset of paralysis; 5) clinical follow-ups available for more than 12 months. The facial nerve was decompressed between tympanic and mastoid segments via mastoid. A bFGF-impregnated biodegradable gelatin hydrogel was placed around the exposed nerve. Regeneration of the facial nerve was evaluated by House-Brackmann (H-B) grading system. The outcomes were compared with our previous study, which reported outcomes of the patients who underwent conventional decompression surgery or conservative treatment. The complete recovery (H-B grade 1) rate of the regeneration surgery was significantly better than the rate of conventional decompression surgery and conservative treatment. Every patient in the regeneration surgery group improved to H-B grade 2 or better even when undergone over one month after onset.

To our knowledge, this is the first clinical report of the efficacy of bFGF utilizing a new drug delivery system in patients with severe Bell's palsy. This study revealed the efficacy of a bFGF-impregnated biodegradable hydrogel as a drug-delivery medium in the paralyzed facial nerve surgery. Further clinical studies are necessary to fully evaluate the usefulness of this procedure.

## SY7-3

## Fallopian canal dehiscence in pediatric cholesteatoma

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**Background:** Dehiscence of the fallopian canal is often observed during cholesteatoma surgery. There have been some reports that the presence of fallopian canal dehiscence was less frequent in pediatric patients than adult patients with cholesteatoma.

**Objective:** To investigate the presence of fallopian canal dehiscence in children with middle ear cholesteatoma at the time of surgery, and analyze the clinical characteristics of the cases with the dehiscence.

**Methods:** This study included 37 ears with cholesteatoma in pediatric patients less than 15 years, and 273 ears with cholesteatoma in non-pediatric patients aged 15 years or older. All patients had undergone tympanoplasty under general anesthesia. The incidence of fallopian canal dehiscence was analyzed regarding type of cholesteatoma and coexisting pathological conditions such as missing of the superstructure of the stapes, presence of a labyrinthine fistula and dural exposure.

**Results:** The fallopian canal dehiscence was found in 6 of 37 ears (16.8%) in the pediatric group and 91 of 273 ears (33.3%) in the non-pediatric group ( $P < 0.05$ ). However, missing of the superstructure of the stapes was much more frequently observed in pediatric group than in non-pediatric group. Fallopian canal dehiscence was more frequently accompanied with missing the superstructure of the stapes in non-pediatric group than in pediatric group. In pediatric group, the incidence of fallopian canal dehiscence was low in congenital type, and high in tensa type of cholesteatoma.

**Conclusion:** The fallopian canal dehiscence is not so frequent in children with cholesteatoma except for tensa type, even in cases with missing of the superstructure of the stapes.

## SY7-4

## Feasibility of Transcanal Endoscopic Ear Surgery to Access Cholesteatoma in the Tympanic Sinus by Depth Classification

Seiji Kakehata

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**Objective:** To determine the feasibility of transcanal endoscopic ear surgery (TEES) to access cholesteatomas in the tympanic sinus (TS) based on a classification of the depth of the TS in comparison to the facial nerve.

**Background:** The TS is an anatomical dead corner which is not directly visible microscopically and is a frequent site of residual cholesteatomas. TS depth is classified as A, B and C going from shallow to deep.

**Study design:** A retrospective case series

**Setting:** Tertiary referral center

**Patients:** 110 patients with primary acquired cholesteatoma who underwent surgery between September 2011 and August 2014, including 87 with pars flaccida (PF) and 23 with pars tensa (PT) cholesteatoma.

**Intervention:** Operation records were reviewed to determine the presence of cholesteatoma in the TS. The TS was classified based on a high resolution CT scan.

**Results:** Cholesteatomas extended into the TS in 20 cases (18%), including 9 cases of PF and 11 cases of PT. The TS classification was A (8), B (11) and C (1) with the 12 B and C cases representing deep retractions which are inaccessible microscopically. The cholesteatoma was completely removed from the TS under endoscopic visualization in all cases by either TEES or canal wall down. TEES was performed on 12 out of 20 cases (60%), including 3 PF (33%) and 9 PT (82%), with 3 TS classification of A and 9 of B.

**Conclusions:** TEES is a less invasive approach providing visibility and access to the TS, a hitherto anatomical dead corner.

**SY7-5**

## **Nontuberculous Mycobacterial Otomastoiditis**

An-Suey Shiao, Chien-Fu Yeh, Tzong-Yang Tu

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**Objective:** To evaluate the clinical manifestations and treatment outcomes of the rare disease, nontuberculous mycobacterial otomastoiditis (NTM).

**Study Design:** Retrospective cohort study.

**Method:** Patients diagnosed with NTM otomastoiditis according to mycobacterial cultures were included in this study. Age distribution, gender ratio, clinical manifestations including otorrhea, otalgia, granulation, facial palsy, imaging features, diagnostic methods, treatment modalities and outcomes of these patients were analyzed.

**Results:** The 17 enrolled patients with NTM had a median age of 57 years (range 42~81) with no obvious difference in gender ratio. There were 14 (82.4%) patients with *Mycobacterium abscessus* infection. All patients had otorrhea and 16 (94.1%) patients had granulations in their middle ear. 6 patients (35.3%) had otalgia and 2 (11.8%) had facial palsy. Imaging studies revealed 16 patients had soft tissue density in the middle ear cavity. Ossicular chain destruction was noted in 4(25%) cases during the surgery. The rate of simultaneous lung involvement was 5.9%. All patients received medical treatment, 16 (94.1%) received surgical treatment, and 3 (17.6%) received revision surgery.

**Conclusion:** NTM should be suspected if a patient has chronic refractory otorrhea, granulations in the middle ear, otalgia or facial palsy. Medication and surgery may complement each other to treat this disease.

**SY7-6**

## **Intraoperative continuous facial nerve monitoring in cochlear implant and middle ear surgery**

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**Background:** Iatrogenic facial nerve injury is one of the most severe complications of cochlear implant surgery. Facial nerve paralysis has a significant functional and emotional impact on patients. Intraoperative facial nerve monitoring (IFNM) is used as an adjunctive modality in a variety of neurotologic and temporal bone surgical procedures. Despite the utility of IFNM in reducing the risk of iatrogenic facial nerve injury during neurotologic surgery, the routine use during ear surgery remains controversial. The purpose of this study was to share our experience in the use of IFNM during cochlear implant and middle ear surgery.

**Methods:** This retrospective analysis included 165 patients (85 males and 80 females) who underwent cochlear implant (62 cases) and middle ear (103 cases) surgery. Facial potentials were recorded from needles placed in the orbicularis oculi and oris muscles. Cochlear implantation was performed with a minimally invasive incision and limited mastoidectomy. The facial nerve was directly stimulated with a monopolar stimulator (constant current pulses, 0.1-3.0 mA, 4 Hz, 100  $\mu$ s). An event threshold was set at 100  $\mu$ V.

**Results:** The mean age of the 165 patients was 32.4 years (range 18 months to 69 years). No spontaneous facial nerve dehiscence was noted during CI surgery, however 40.8% (42/105) spontaneous facial nerve dehiscence was noted during middle ear surgery. The monitor sounded a warning when the diamond burr touched the facial nerve sheath of four cases. There was no warning sound at the initial setting (1.0 mA) in 13 patients, of whom nine had the stimulation intensity increased to 1.2 and 2.5 mA. There was also a visible stapes muscle contraction at 2.0 mA stimulation with no warning sound in another case. Chorda tympani nerve stimulation was noted in 108 patients, and a warning sound was emitted in 93 of these cases. No postoperative facial paresis was noted in any of the 165 patients.

**Conclusions:** Although not a substitute for the anatomic identification of the facial nerve, IFNM is of great value in the early identification of dehiscent facial nerve anatomy, assisting in the maintenance of its integrity, and functionality postoperatively. However, false-positive and false-negative results may occur when using IFNM. Nevertheless, IFNM can still be used as an additional technique to optimize surgical success.

## Symposium 8 Basic Science of Otology and Neurotology

## SY8-1

**Translating back and forth in between benchside and bedside by hiPS based-technology and a primate model**

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The technology of iPSCs offers platforms for investigating pathophysiology and development of drugs in various diseases. Particularly, disease modeling using patient-derived iPSCs has an advantage in recapitulating phenotypes of human disease cells that cannot be observed in other animals (e.g. rodents) due to the species gap. We have been investigating the physiology/pathophysiology of monogenic, bilateral, gradual but fluctuating deafness using iPSC technology for understanding intractable cochlear sensorineural hearing loss.

Pendred syndrome (PDS) /DFNB4 is the most frequent syndromic form of deafness, involves bilateral progressive hearing loss, enlargement of vestibular sac and a thyroid goiter. Mutations in the *Slc26A4* gene are known as primarily causes of PDS/DFNB4, yet the pathophysiology of progression in the deafness remains unrevealed due to the lack of disease model that recapitulate the symptom: Knock-out mouse models could only represented malformation phenotypes and failed to recapitulate progressive hearing loss. Knock-in mouse model did not represent any phenotype. The unknown factors that have been predicted by clinical reports to determine the severity and the progression of this condition remain undetermined and therefore PDS is still intractable.

To examine the unknown pathophysiology and treatments of PDS, we generated PDS patient-derived human cochlear cells via iPSCs. The results reveal a novel degenerative phenotype of PDS and propose rational treatment strategy for progressive hearing loss: Mutated proteins involve neurodegenerative phenotypes which result in the gradual decrease in the number of cochlear cells, which may account for progression of deafness. Furthermore, using our iPSC-based in vitro model of the human cochlea, we discovered drugs that ameliorate stress-induced apoptotic cell death.

In this way, iPSC-based in vitro assay is a powerful tool especially in the research of diseases where rodent models do not recapitulate human symptoms. However, the approach could not fully serve detailed information of the species gaps. To circumvent such a pitfall, we have been using a small New World monkey, common marmoset (*Callithrix jacchus*). I will also introduce our data indicating what the difference is in between human and rodent in terms of the physiology and pathophysiology of cochlea related to *Slc26A4* gene, and the reason why rodent models cannot recapitulate hearing loss of PDS.

We anticipate that the combination of iPSC-based in vitro model and a non-human primate in vivo model may be useful for translational studies investigating the pathogenesis of other forms of hereditary deafness, and idiopathic hearing loss, to identify new treatments for these conditions.

## SY8-2

**Maintenance of Cochlear Tight Junction System by Tricellulin**

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Tricellulin is a central component of tricellular tight junction and is distributed to the various epithelial tissues. Although mutations in tricellulin are known to cause deafness in human (DFNB49) and in mice, the influence of its systemic deletion in vivo has not been elucidated. In the current study, we generated *Tric*-KO mice (*Tric*<sup>-/-</sup> mice) and analyzed their phenotype. *Tric*<sup>-/-</sup> mice showed early-onset progressive hearing loss associated with HC degeneration. Hearing loss was the only pathological phenotype and other organs, such as gastrointestinal tract, liver, kidney, thyroid gland, and heart were not affected in the *Tric*<sup>-/-</sup> mice, suggesting the specific requirement of tricellulin in the cochlear function. The EP in *Tric*<sup>-/-</sup> mice was maintained and the HC degeneration is subsequent to the reported period of the EP maturation. The hair cells in *Tric*<sup>-/-</sup> mice was not degenerated when cultured under physiological extracellular ion composition, suggesting that the HC degeneration in *Tric*<sup>-/-</sup> mice is probably consequence of the compromised ion homeostasis surrounding HCs due to increased transepithelial ion permeability. These data demonstrate specific requirement of tricellulin for maintaining ion homeostasis around cochlear hair cells to ensure their survival. The newly established *Tric*<sup>-/-</sup> mouse provides a good model for understanding the distinct role of tricellulin in different epithelial systems and the pathogenesis of DFNB49.



SY8-3

## Regulation of cytoskeleton in hair cells by TRIOBP

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Kohei Yamahara<sup>1</sup>, Tomoko Kita<sup>1</sup>, Takeshi Sakamoto<sup>2</sup>,  
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Actin is the major cytoskeleton that construct inner ear hair cells. Inner ear hair cells detect sound through deflection of mechanosensory stereocilia, that is composed by actin bundle. TRIOBP, a molecule that bind bundle the actin filament, is a good candidate to harmonize actin structure in inner ear via isoform specific matter. Each stereocilium is supported by a paracrystalline array of parallel actin filaments that are packed more densely at the base, forming a rootlet extending into the cell body. TRIOBP-5, a cytoskeleton-associated protein mutated in human hereditary deafness DFNB28, is localized to the stereocilia rootlets in inner ear hair cells. TRIOBP have three major isoforms (abbreviated as T1, T4 and T5). Then, T4/T5 double deficient mice show profoundly deaf. Stereocilia of T4/T5 deficient mice develop normally, but fail to form rootlets and are easier to deflect and damage. It indicates that F-actin of rootlets bundling by TRIOBP provide durability and rigidity for normal mechanosensitivity of stereocilia. Although it has been suggested that each isoforms have their own actin cytoskeleton regulation mechanism, the exact mechanism and function of each isoforms remains obscure. To investigate the role of each TRIOBP isoforms, we generated isoform specific mutant mice. One of them, the T5 deficient mouse became severe hearing loss, but not deaf. It's also suggested that each isoforms have different function. Here we investigate the role of TRIOBP isoform in vivo and in vitro.

We generated T5 specific deficient mice and T1 conditional knockout mice. To evaluate molecular interaction of TRIOBP, we performed biochemical studies such as the fluorescence size exclusion chromatography assay or immune-precipitation.

T5 deficient mice phenotypes are as follow. •Severe Hearing loss. •Stereocilia Rootlets hypoplasia. •Loss of TRIOBP-1 localization at sterocilia rootlets. And from biochemical study, we had the results which indicate that each isoforms make homo oligomer.

We are currently promoting the analysis of molecular mechanisms of TRIOBP. We would like to introduce the results.

SY8-4

## Explore inner ear disorders in humans and mice using next-generation sequencing

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The advent of next-generation sequencing (NGS) has revolutionized our understanding of inner ear pathophysiology in humans and in mice. In the clinical scenario, comprehensive genetic screening for idiopathic sensorineural hearing impairment (SNHI) can be achieved by using the massively parallel sequencing (MPS) technique. Using a MPS panel which targets ~160 known deafness genes, we have increased the detection rates of causative mutations in multiplex and simplex families with idiopathic SNHI to ~67% and ~50%, respectively. Precise genetic diagnoses facilitate genetic counseling in these families, and enable prognosis prediction in the affected patients, such as the outcomes with cochlear implants.

On the other hand, transgenic mice have been demonstrated to be an excellent model for investigating hearing impairment in humans. In the past years, we have generated several transgenic mouse models harboring specific deafness mutations of interest using either the traditional protocols or the newly developed CRISPR/Cas genome editing technique. We are currently exploring the molecular pathophysiology in these mouse models using another NGS-based technique: RNA sequencing (RNA-seq). As compared to the conventional microarray-based method, RNA-seq enables the identification and quantification of transcripts without prior knowledge of a particular gene and provides information concerning alternative splicing and sequence variation. Our experience with regards to the application of MPS and RNA-seq to clinical and animal studies will be presented.

SY8-5

## The clinical significance of assembled inner ear tests in the animal model

Ting-Hua Yang, Yi-Ho Young

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Animal studies sometimes provide more information than clinical studies in the investigation of the otologic disorders, since histological or pathological evidence are difficult to get in human. With appropriate function tests, animal can provide functional and histological results for comparison. Inner ear function tests are frequently required for neurotologic studies. They are used to assess both auditory and vestibular function. Auditory function tests in the animals were well-established and delivered convincing results. On the contrary, vestibular function tests are quite complete in human but not in the animal. We developed a set of assembled tests including auditory brainstem responses (ABR), ocular and cervical vestibular myogenic potential tests (cVEMP and oVEMP) and caloric tests in the animal to evaluate the entire inner ear function. This set of assembled inner ear tests for animals measure function of the cochlea, the otolith organs and semicircular canals in short time. We will present examples of its application on clinical issues such as ototoxicity of known drugs, safety screening of potential new drugs and functional influence of endolymphatic hydrops on the inner ear. Combined with other tools such as genetic or histologic investigation, this system may help unveil unsolved questions in the otology and neurotology.

**Symposium 9** Laryngology and Dysphagia

**SY9-1**

**Future prospects for the laryngeal framework surgery**

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Laryngeal framework surgery (type I, II, III, IV and arytenoid adduction surgery) was established by Isshiki et al. A procedure, history, indication, and how to evaluate the voice function for the laryngeal framework surgery will be explained. Especially, an effort aim to improve the postoperative voice quality for type I in our department will be explained. Type I has been done to improve a breathy hoarseness for patient with glottal closure failure such as unilateral vocal fold paralysis. Many kinds of implant materials such as silicon block, polytetrafluoroethylene, hydroxyl apatite, and titanium has been used as the flange to medialize the paralyzed vocal fold. Arytenoid adduction surgery combined with type I is often used for a patient with severe posterior glottal closure failure. However, some author reported that type I alone without arytenoid adduction is able to improve the breathy hoarseness even in the patient with severe posterior glottal closure failure. Type II has been done to weaken a force of glottal closure. Type II is good indication for a patient with spasmodic dysphonia. Nowadays, a titanium bridge is usually used. Type III has been done to shorten the vocal fold length. This is good indication for patient with boy's voice change disturbance or female to male gender identity disorder to decrease voice pitch. Type IV has been done to get long the vocal fold length. This is good indication for patient with male to female gender identity disorder to increase voice pitch. However, the most difficult framework surgery to get certain improvement result is thought to be type I. The most important point of type I is how to design the shape of frange to correct dislocation of the paralyzed vocal fold. Because the difference of gender, size of body, thickness of thyroid cartilage, and the degree of an angles that thyroid cartilage makes variation for a shape of frange. For the future prospects, we built a three-dimensional larynx model from the DICOM (Digital Imaging and Communication in Medicine) data of the neck CT image of the patient. We designed a flange shape that will be able to ideal vocal fold medialization in computer. However, we outputted the larynx model of the vocal folds level to fill a flange with a 3D printer by the problem of the expense. We will show a type I thyroplasty case whose frange was designed using the larynx output model as a reference.

**SY9-2**

**The Usage of Holmium YAG Laser in Pediatric Laryngotracheal Stenosis**

Kuo-Sheng Lee

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Holmium (Ho) YAG laser is a fiberoptic delivery laser with wave length of 2100 micrometers. Its advantages include fiberoptic delivery that can be used in trachea bronchial lesions, less thermal penetration in tissue than KTP, Nd YAG and Diode laser, less water resorption than CO2 laser, good function of bone ablation, and good hemostasis. It had been widely used for lithotripsy in sialoendoscopy and urology. However, there were few studies discussing about application in the airway procedures. Subglottic stenosis is complicated in children and was not uncommon in paediatric airway disease. There were scarring or cicatrix of trachea, subglottis, glottis or supraglottis that can lead to airway obstruction. We treated the laryngotracheal lesions with Holmium YAG laser including subglottic or tracheal stenosis, subglottic web, recurrent respiratory papillomatosis, ductal cyst, etc. The laryngotracheal stenosis was dilated with Holmium YAG laser by lysis the annular scar formation, then intralesional steroid injection into the laser wound and residual scar. The intralesional steroid injection may inhibit the synthesis of fibroblast, enhanced the resorption of fibrous tissue and minimize the systemic side effect of steroid.

Application of Holmium laser then intralesional steroid injection to the stenotic scar had benefit in the treatment of laryngotracheal stenosis. This technique may avoid the tracheostomy or laryngotracheal reconstruction (LTR), and may be a savage procedure of LTR. We will present our surgical technique and outcome in the conference.

## SY9-3

**Fetal airway management - EXIT procedure**

Wei-Chung Hsu

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Fetuses with upper airway obstruction such as large congenital oral or cervical neck masses presenting major difficulties in management of the neonatal airway at delivery and in the perinatal period have a high mortality rate if immediate airway rescue is not administered after delivery. Recent advances in prenatal three-dimensional (3D) ultrasound and fetal magnetic resonance imaging (MRI) facilitate a prenatal diagnosis and well preparation of neonatal airway rescue before delivery. An airway treatment plan can then be formulated and modified in relation to the airway presentation at birth.

The attempts at pre-delivery management of obstructed fetal airways have focused on the EXIT (ex-utero intrapartum treatment) procedure, which allows sufficient time to establish the fetal airway through preservation of utero-placental gas exchange while the utero-placental circulation is still maintained. The prognosis of such neonates has much improved after the introduction of this procedure.

The EXIT procedure could successfully rescue the fetal airway under a well-planned and organized multidisciplinary cooperation among the obstetrician, neonatologist, anesthesiologist, and pediatric otolaryngologist.

## SY9-4

**Simple and semi-quantitative scoring system for flexible endoscopic evaluation of swallowing and its clinical significance**

Masamitsu Hyodo, Kahori Hirose, Asuka Nagao

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Recently, swallowing disorder has become a critical issue medically and socially with the background of an increasing of aging population. To treat patients with dysphagia appropriately, objective assessment for their swallowing functions is mandatory. In the Clinical Practice Guideline for swallowing in Japan, flexible endoscopic evaluation of swallowing (FEES) is positioned as a necessary examination. However, it lacks standardized evaluation criteria to date. Thus, we have developed a simple and semi-quantitative scoring system for FEES and discussed on its clinical significance. The scoring system includes four major parameters; 1) degree of saliva pooling at the vallecula and piriform sinuses, 2) glottal closure reflex induced by contacting the tip of the endoscope to the epiglottis or arytenoid, 3) elicitation of swallowing reflex assessed by the timing of white-out, and 4) pharyngeal clearance after blue-dyed water swallow. Each parameter is categorized into "0" as normal, "1" as mild impairment, "2" as moderate, or "3" as severe. Nasopharyngeal insufficiency, pharyngeal inflow before swallow, laryngeal paralysis, and etc. are described as other abnormal findings.

Scores of major parameters collected from experienced otolaryngologists for swallowing were significantly correlated with those from non-experienced otolaryngologists and speech-language-hearing therapists. This indicates that our scoring system is easy to evaluate and objective. FEES clearance score correlated with pharyngeal clearance by videofluorography. Severity of aspiration also correlated with summed scores of the four parameters with statistical significance. The methods of feeding showed significant relationships with the summed scores, indicating that the scoring system can be a useful tool for deciding oral food intake. Consequently, our new scoring system is simple, semi-quantitative, and reliable for evaluating severity and feature of dysphagia and is enough worth introducing into the clinical use in treating dysphagic patients.

SY9-5

## Treatment of dysphagia in patients with head and neck cancer

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Patients with head and neck cancer are frequently suffered dysphagia because they are mainly faced two problems which decrease swallowing function: the first is a structural deformity of oral cavity and pharynx, and the second is a functional insufficiency by palsy and/or inflammation. Both problems could be caused by cancer itself and the therapy required: surgery, radiation and chemotherapy. The treatment of dysphagia in the cancer patients is very important not only for preserving a quality of life such as 'enjoying oral food deglutition', but also for decreasing risks of aspiration and suffocation. The latter is essential because the respiratory problems such as aspiration pneumonia could delay the cancer therapy and sometimes become life-threatening.

The treatment of dysphagia consists of two parts: evaluation and rehabilitation. Video endoscopic and video fluoroscopic examinations are useful for the evaluation of swallowing function, and those information lead important suggestions for the rehabilitation. Several rehabilitation maneuvers, for examples, neck rotation, chewing, blowing, glottis closure, body positioning, food processing, are challenged. Oral treatment is essential to keep oral hygiene and to improve transportation of the food. Artificial tooth, dental implant and palatal augmentation prosthesis are sometimes useful for the patient with oral tissue defect. For the patient treated by radiation therapy, the moisture and cleanliness is necessary for smooth passage of swallowing bolus. Pain control is also necessary, especially for the patient with mucositis and ulcer by the radiation therapy. During the chemoradiotherapy for the pharynx, many patient give up the eating by the pain and have to use the gastrostomy tube or nasogastric tube. The tube feeding can keep nutritional condition of the patient, but is also known to delay oral food intake after the cancer therapy.

Surgical treatment is a good option for the dysphagia in head and neck cancer patient. Laryngeal suspension and cricopharyngeal myotomy is effective and sometimes planned at the first surgery of tumor excision and tissue reconstruction. Endoscopic balloon dilatation could be effective for the patients with esophageal narrowing. For the case with an intractable aspiration after the cancer treatment, the surgery preventing aspiration such as glottis closure or narrow field laryngectomy is considered.

Treatment described above should be indicated for each patient, considering the pathophysiology of dysphagia, therapeutic schedule for the cancer, and the body condition. In the symposium, the cases of oral and pharyngeal cancer are presented and the treatments of dysphagia for each cases are discussed.

## Symposium 10 Rhinology

## SY10-1

**Mucosal route of Immunotherapy with Transgenic rice Seeds expressing Whole T Cell Epitopes of Cryj1 and Cryj2 -an experimental study in a murine cedar pollinosis model-**

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Sublingual immunotherapy with cedar pollen extract is most recently developed and permitted in Japan to be utilized in clinical routine as a more safe and effective method. For the last decade, we have been investigating the effective mechanism of mucosal route of immunization in murine allergic rhinitis models to attenuate nasal symptoms and downregulate Th2 responses. In this study, we have examined the effect of sublingual administration or natural feeding with protein bodies (PB) of transgenic rice seeds expressing hypoallergenic whole T cell epitopes of Cryj1 and Cryj2 (PB-Tg rice), in murine model of cedar pollinosis. The numbers of sneezing after final intranasal challenge in sublingually treated mice with PB-Tg rice powder were significantly decreased in comparison with no sublingual treatment group of mice. Histopathological findings correspondingly demonstrated that the number of eosinophils infiltrating into nasal mucosa decreased and the damage of epithelial cells was less found in sublingually treated mice. IL-13 level in culture supernatants of spleen cells was significantly reduced with sublingually treated mice, but no difference in IL-5 production. In analyses of cervical lymph node cells, IL-13 and IL-5 production seemed to decrease in sublingually treated mice. But, on the contrary, IFN-gamma increased in those mice. Furthermore, the numbers of sneezing after final intranasal challenge in mice naturally fed with PB Tg-rice powder were significantly decreased in a dose dependent manner, with less doses, in comparison with those of whole Tg-rice powder. Histopathological findings correspondingly demonstrated that the number of eosinophils infiltrating into nasal mucosa decreased and the damage of epithelial cells was less found in each group of mice. These data indicate that mucosal route of immunotherapy with this Tg-rice is a promising treatment strategy for attenuating nasal symptoms of cedar pollinosis and now clinical trials have been on-going to confirm the beneficial effects on patients with cedar pollinosis.

## SY10-2

**Apolipoprotein A-IV is a new target molecule for allergic rhinitis**

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**Background:** Sublingual allergen-specific immunotherapy (SLIT) is the available treatment that can alter the natural course of allergic rhinitis. We performed proteomic in the patients treated with SLIT. Apolipoprotein A-IV (ApoAe-IV) was significantly increased in SLIT-treated patients but not in placebo-treated patients. The serum level of ApoA-IV correlated with the clinical symptom-medication scores and quality of scores in the case of SLIT-treated patients. In this study, we investigated the function of ApoA-IV in the allergic rhinitis.

**Methods:** Histamine release from the basophils in vitro was examined after the addition of recombinant ApoA-IV. We made ApoA-IV knock out mice (ApoA-IV<sup>-/-</sup>) and administrated antigen to ApoA-IV<sup>-/-</sup>. Recombinant ApoA-IV was administrated to monkey with allergic rhinitis caused by Japanese cedar pollen.

**Results:** The addition of recombinant ApoA-IV reduced histamine release from human basophils in the presence of antigen. Frequency of sneezing and nasal itching was decreased after antigen challenge in ApoA-IV<sup>-/-</sup>, compared to wild type. However, cytokine (Th1 and Th2) and IgE production, and eosinophil infiltration in the nasal mucosa in ApoA-IV<sup>-/-</sup> were same level to those to those in wild type. The administration of recombinant ApoA-IV increased nasal flow in allergic monkey, but the recovery rate was smaller than topical corticosteroid treatment.

**Conclusion:** Although biological ability of ApoA-IV is not strong, ApoA-IV works to increase nasal flow and decrease histamine release in SLIT-treated patients.

SY10-3

## Interaction between coagulation and upper airway inflammation

Takeshi Shimizu

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Airway inflammation is associated with increased vascular permeability and leakage of plasma coagulation factors, leading to activation of the coagulation system in the extravascular space. Tissue factor (TF) is an important initial upstream protein in the extrinsic coagulation cascade. Leakage of coagulation factors into the tissues induces factor VIIa (FVIIa) to bind to TF on the cell surface, and the resulting complex binds to factor X (FX), converting it to the activated form, factor Xa (FXa), ultimately leading to thrombin (FIIa) formation and fibrin deposition. Tissue factor pathway inhibitor (TFPI) regulates this initial step in the coagulation cascade, and antithrombin III inactivates thrombin through formation of a thrombin-antithrombin III complex (TAT).

We found significant concentrations of thrombin and TAT in nasal secretions from patients with allergic rhinitis (AR) and chronic rhinosinusitis (CRS), and they were significantly high in patients with eosinophilic CRS. These results provide clear evidence of activation of the coagulation system in sinonasal inflammation. We also found that nasal epithelial cells and infiltrating eosinophils express TF and that nasal secretions contain significant concentrations of TF and TFPI, which are released by cultured nasal epithelial cells upon stimulation with thrombin or TNF-alpha. These results indicate that the nasal epithelium initiates and regulates coagulation activity, which leads to thrombin generation and fibrin deposition.

Coagulation factors such as thrombin (FIIa), FVIIa, and FXa play important roles not only in thrombosis and homeostasis, but also in inflammation through interactions with protease activated receptors (PARs), expressed on epithelial cells, fibroblasts, and vascular endothelial cells. The PAR family consists of 4 subtypes (PAR-1, -2, -3 and -4). We found that all PARs are expressed in nasal epithelium, and that thrombin stimulates the secretion of MUC5AC mucin and profibrotic cytokines (PDGF and VEGF) from nasal epithelial cells via PAR-1. Thrombin can also promote inflammatory responses by stimulating the production of inflammatory cytokines and growth factors including L-6, IL-8, PGE2, and CCL-2 from airway epithelial cells. Coagulation factors FVIIa and FXa activate PAR-2. PAR-2 plays an important role in the initiation and development of allergic airway inflammation by stimulating the secretion of epithelial cell-derived Th2 cytokines; TSLP and IL-25.

These results indicate that PARs-mediated responses provide a direct link between coagulation and airway inflammation, and the coagulation system may be potential therapeutic targets for airway inflammation. The inhibitory effects of anticoagulants; activated protein C (APC) and heparin, on upper airway inflammation were also demonstrated.

SY10-4

## Primary ciliary dyskinesia in the Japanese population

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**[Background]** Primary ciliary dyskinesia (PCD) is a genetic disease inherited in an autosomal recessive manner. The prevalence of PCD is estimated to be 1 in 20,000 live births. Congenital abnormality of the primary cilia results in situs inversus in 50% of patients. Decreased function of motile cilia causes chronic rhinosinusitis, otitis media with effusion, bronchiectasis and infertility. Cases with situs inversus are considered to show "Kartagener's syndrome", and diagnosis is not difficult. However, in cases without situs inversus, the diagnosis is much more troublesome. PCD without situs inversus is thus probably underdiagnosed. The diagnosis of PCD requires the presence of the characteristic clinical phenotypes and either: 1) specific ciliary ultrastructural defects identified by transmission electron microscopy in biopsy samples of respiratory epithelium; or 2) identification of mutation in one of the genes known to be associated with PCD. The purpose of the study is to find novel gene mutations causing PCD in the Japanese population.

**[Materials and methods]** We performed transmission electron microscopy studies and genetic analyses for 21 patients (age 1~35 years old, 10 males and 11 females) who were suspected clinically of PCD. For genetic analysis, we sequenced known hot-spots of DNAH5 and DNAI1 first, because mutations in DNAH5 or DNAI1 genes can be found in about a third of the patients with PCD. Next we performed whole-exome sequencing. The results of whole-exome sequencing were validated by Sanger sequencing.

**[Results]** In four patients (19%), novel mutations in the previously known genes were identified. They were compound heterozygous mutations of DNAH5 in one patient, a homozygous mutation of DNAI1 in two siblings, and a heterozygous mutation of DNAH11 in one patient.

**[Conclusion]** This is the first report of novel mutations of PCD found by whole-exome sequencing in the Japanese populations.

## SY10-5

**Thermal effects in nasal physiology**

Ching-Yin Ho

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Airway temperature has been suggested to represent a marker of mucosal inflammation and remodeling in asthmatic children being related with mucosal eosinophilia and vascular remodeling. Previous study has also showed exhaled breath temperature is related to the degree of airway inflammation in asthma. Allergic rhinitis and asthma are shared same pathogenesis that was well documented. There are only few reports mention about the relationship between nasal temperature and allergic rhinitis. Even, the physiologic nasal mucosa temperature change was reported also only in few studies. The intranasal temperature was different in different measured location. It also was different in the phases of respiration. We measured intranasal temperature at the anterior part of inferior turbinate and anterior rhinomanometry in allergic rhinitis patients and normal subjects. We found that the intranasal temperature of allergic rhinitis patients is higher than normal subjects. The higher nasal resistance is the higher intranasal temperature. The intranasal temperature decreased when nasal symptoms controlled in allergic rhinitis patients. The previous studies showed that the high nasal resistance has high risk of obstructive sleep apnea. The possible mechanisms were unbalance of autonomic nerve system. According the previous studies, intranasal temperature is a useful marker to predict the inflammation conditions.

## SY10-6

**Searching 'epimmunome' of sinonasal mucosa**

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The sinonasal epithelial cell (EC) consistently encounters external intruders and is therefore one of the most frequent immune reactive sites in the human body. "Epimmunome", a term introduced recently by Swamy and colleagues (2010), describes all molecules and pathways used by ECs to instruct immune cells. The role of the ECs as a switchboard to initiate and regulate immune responses is altered through inhaled substance exposure. The details of the interplay between ECs and immune cells are not yet fully understood. We have used cell culture models (including cell line and primary cell culture), microarray study and molecular biology method to gain knowledge about potential mechanisms.

In result, nasal ECs are known to constitutively equip with all toll-like receptors (TLRs). Selective ligands: CL419(TLR2 ligand), Poly(I:C)(TLR3 ligand), LPS(TLR4 ligand) and ODN2006(TLR9 ligand) were used to stimulate A549 cell line and primary cultured ECs in order to investigate the production of epithelial-derived cytokines. TSLP in ECs is induced by treatment with a TLR2 and TLR3 ligands. High expression of TSLP in cultured ECs from nasal polyp responded to BLP (bacterial like particle) stimulation via TLR2 signaling. Poly(I:C) mainly stimulate A549 cells to express TSLP mRNA by using QPCR analysis. This is in accordance with previous publication. LPS may also stimulate IL-25 and CL 419 stimulate IL-33. On the contrary, LPS showed inhibition of TSLP and IL-33 in primary cultured nasal epithelial cells. And ODN206 inhibit IL-25 expression. In other hand, ODN2006 effectively increased TSLP. LPS and Poly(I:C) increased IL-25 expression.

Therefore,

1. Epithelial cell line may not behave the same way as primary cultured epithelial cells. Any interpretation extrapolated from cell lines should be carefully evaluated.
2. Our results indicated that via TLR stimulation, the epithelial cell derived cytokines may be modulated and thus downstream inflammatory reaction would be directed.
3. Due to tremendous variable phenotype of chronic rhinosinusitis patient, the tissue sample collected must be carefully categorized.

In conclusion, increasing our understanding about the role of ECs in respiratory immunity may yield novel therapeutic targets to modulate downstream diseases.



**Symposium 11** Sensorineural Hearing Loss

**SY11-1**

**Promises and challenges of next generation sequencing in personalized medicine for sensorineural hearing loss**

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Genetics plays an important role in sensorineural hearing loss, especially for congenital hearing loss. Approximately 70% of patients with congenital hearing loss are known to be caused by genetic causes. Significant proportion of adult-onset hearing loss is also predicted to be caused by genetic causes. Each gene has specific genotype-phenotype correlations which can be of help in understanding clinical condition as well as in making decisions on medical intervention and family planning. Because of the enormous genetic heterogeneity of deafness genes, it was not possible to identify mutations in the majority of patients with SNHL until recently. However, the situation has changed dramatically since the development and introduction of next generation sequencing (NGS) into the clinic.

Because most of small changes in DNA sequences can be detected with NGS, the probability of genetic diagnosis has significantly increased. Identification of novel genes and mutations has become rapid, which increased the probability of definite diagnosis and facilitated understanding genetic causes of SNHL. Classification of patients according to genetic causes provided novel opportunity to conduct clinical trials in patients with the same molecular mechanism. On the other hand, current NGS technology has several limitations. Firstly, evaluation of data obtained by NGS is frequently ambiguous. Pathological significance of identified mutations cannot be proved in many cases. This has to be overcome by epidemiological approach as well as experimental approach. In addition, NGS cannot reliably detect certain types of mutations such as copy number variation and chromosomal rearrangement. Mutations in introns and regulatory regions are also out of target for NGS except for whole genome sequence which is hardly available for clinical study at present. These weak points may be overcome by development of new technologies and improvement of current system.

Future studies should be planned for effective and efficient strategies to use NGS, especially for patients who have the clinical features indicating candidate genes in order to reduce the burden associated with analysis of many genes. Studies for genetic counseling are also necessary. Each patient and physicians should be given the probability of definitive genetic diagnosis, expected genes and their clinical information before genetic tests. Detailed clinical characteristic including later clinical course should be explained in association with appropriate options for medical intervention at the time of reporting the results of genetic tests. In order to develop novel clinical intervention, functions of deafness genes and their controls have to be elucidated.

**SY11-2**

**Measurement of the vestibular aqueduct in the prediction of developing Meniere's disease from Acute-Low-tone sensorineural hearing loss**

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**Objective:** Most of acute low-tone sensorineural hearing loss without vertigo (ALHL) improves over time; however some of them develop into typical Meniere's disease (MD), suggesting the association of ALHL and MD. The aim of this study was to investigate the association of ALHL and MD from the viewpoint of development of the vestibular aqueduct.

**Study Design:** Case-control study.

**Setting:** Tertiary referral center.

**Subjects and Methods:** In 53 patients with unilateral ALHL (16males, 37females; mean age, 43.5 years), 38 patients with unilateral MD (15males, 23females; mean age, 52.5 years) and 11 normal controls (11 males; mean age, 33.3 years), length of the external aperture of the vestibular aqueduct (EAVA) were measured by 3-dimensional computed tomography (3-D CT) and compared the results among ALHL patients, MD patients and controls.

**Results:** The Mean length of the EAVA was  $5.7 \pm 2.5$  mm in ALHL patients,  $4.2 \pm 2.0$  mm in MD patients, and  $6.5 \pm 1.5$  mm in controls. The length of EAVA was significantly shorter in MD than in ALHL or controls. Among ALHL patients, length of the EAVA was significantly shorter in patients with recurrence ( $4.5 \pm 1.9$  mm) than in those without recurrence ( $6.3 \pm 2.5$  mm).

**Conclusion:** Hypoplasia of the endolymphatic sac may be a predisposing factor for recurrence of ALHL and / or MD because development of the endolymphatic sac is known to correlate with the length of the EAVA.

## SY11-3

**Speech discrimination test with mixed noise**

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**Objective:** To evaluate discrimination of Japanese monosyllables by patients with sensorineural hearing loss under noisy circumstances and to optimize the condition to detect the handicap.

**Methods:** We classified patients with sensorineural hearing loss due to cochlear impairment into three grades according to hearing threshold at 4000 Hz: Group 1: < 45 dB; Group 2:  $\geq$  45 dB and < 70 dB; Group 3:  $\geq$  70 dB. Speech discrimination test (SDT) was performed using twenty monosyllables included in the 67-S speech audiometric test approved by the Japan Audiological Society. Weighted random noise, with a flat spectrum at 125-1000 Hz and -12 dB/oct at 1000-6000 Hz, was added to the signals in audiometer (RION AA-H1) and presented to tested ears.

After measuring hearing thresholds and the best speech discrimination without mixed noise, signal of monosyllables was set at the minimal level where the best discrimination was achieved. Mixed noise was first set to implement S/N = 10 dB. Discrimination rate of the monosyllables was repeatedly measured with noise attenuated in 5 dB steps. Normal adults, who fulfilled the condition: hearing threshold at 4000 Hz  $\leq$  40 dB and the best speech discrimination rate  $\geq$  90% in quiet condition, were enrolled as controls.

**Results and Discussion:** Discrimination rate in Group 1 was as high as that in controls in the quiet condition. With mixed noise of S/N = 10 dB or 5 dB, discrimination of monosyllables was clearly degraded in Group 1. When noise level was elevated to implement S/N = 0 dB, the discrimination rate in some controls was as low as in Group 1. Patients with mild sensorineural hearing loss usually encounter difficulty in speech comprehension in noisy circumstances although hearing thresholds and SDT in quiet condition do not detect such handicap in daily life. SDT with mixed noise which fulfill S/N of 5-10 dB can be easily set up and performed in a short time and a promising tool for clinical test.

## SY11-4

**Speech Perception of Children with Bilateral Cochlear Implants**Yukihiko Kanda<sup>1,2</sup>, Haruo Yoshida<sup>2</sup>, Minoru Hara<sup>2</sup>, Kensuke Hatachi<sup>2</sup>, Takeshi Watanabe<sup>2</sup>, Akiko Ito<sup>1</sup>, Chiharu Wakasugi<sup>1</sup>, Natsumi Ohshima<sup>1</sup>, Ayana Koga<sup>1</sup>, Sachiko Hayashida<sup>1</sup>, Haruo Takahashi<sup>2</sup>*<sup>1</sup>Kanda ENT Clinic, Nagasaki Bell Hearing Center, Nagasaki, Japan, <sup>2</sup>Department of Otolaryngology Head and Neck Surgery, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan*

**[Goal of the presentation]** The clinical effect of cochlear implant (CI) in infants is well established not only in unilateral but also bilateral cases. We have previously reported 1) about binaural effectiveness on bilateral CI in 19 children who acquired language with either CI or HA using various audiological tests. In this presentation, we will investigate further results and evaluate the clinical effectiveness on bilateral CI in children.

**[Methodology]** Since we started CI surgery in 1997, amongst the 221 children undergoing CI rehabilitation in our clinic, 100 children (45%) had bilateral CI for at least a year prior to Feb. 2015.

We evaluated word recognition scores (WRS) and speech discrimination scores (SDS) under silent & noisy conditions in various settings on 62 children with bilateral CI who acquired language with the aid of either CI or hearing aids over 1 year after 2nd CI. We excluded cases with severe anomalies and late development children.

**[Results]** As our initial research shows 1), binaural hearing using bilateral CI is better than first CI in all speech understanding tests. Especially, comparing the results with the first CI, there were marked improvements with bilateral CI on SDS, SDS at 1 m from second CI side speaker (SP), WRS at 1 m from second CI side SP, SDS under the noise (S/N=80/70) and WRS under the noise (S/N=80/70). Further, upon examination of 36 bilateral CI children at every age, a second CI proved to be very effective. However, the results were better in those who had CI under 6-years-old than 6-years-old on the mean WRS, SDS in silent and under the noise (S/N=80/70) on second CI. Binaural hearing using bilateral CI is better than hearing before 2nd CI in all speech understanding tests. We would like to report about the results using various implanted device and education received before CI.

**[Conclusions]** Binaural hearing using bilateral CI is very effective for children having severe-to-profound hearing loss.

1) Kanda Y, Kumagami, H, Hara, et al: Bilateral Cochlear Implantation for Children in Nagasaki, Japan. Clin Exp Otorhinolaryngol. 2012 April; 5(Suppl 1): S24?S31, 2012

**SY11-5**

## **Effects of Ginkgo Biloba Extract (GBE) on Cochlear Ischemia**

Chiader Lin

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The cochlea, an end-artery organ with high metabolic activity, is sensitive to disturbance of blood flow. Perturbations in the inner ear microcirculation have been implicated in the pathophysiology of various kinds of sensorineural hearing loss. Although many chemicals have been proved to provide variable degrees of protective effects, there is still no effective neurotherapeutic agent for cochlear ischemia. Ginkgo biloba extract (GBE) has been widely used for treatment of neural damage and disorders. GBE may exert its therapeutic effect through the blood flow improving or neuromodulation effects. Ginkgo biloba extract is said to be effective to ameliorate common inner ear disorders such as idiopathic tinnitus or dizziness. However, the role of GBE on cochlear ischemic neuropathy is still controversial. This presentation will present a systemic review of GBE on cochlear dysfunction. Then, a series of basic researches about the cochlear ischemia in our laboratory will be presented. First, we establish an animal model of reversible cochlear ischemia through cervical ventral approach to explore the labyrinthine artery via auditory bulla and selectively occlude the labyrinthine artery using microclamps. The revival time of cochlea after of transient ischemia may be more than one hour in guinea pigs. Orderly functional and cellular changes in cochlea are demonstrated after different ischemia duration. A differential base-to-apex gradient of cochlear turns exists to the susceptibility to ischemia. Then, the interaction of aminoglycoside ototoxicity with ischemia was explicated via a caspase-dependent programmed cell death pathway. Finally, the therapeutic role of ginkgo biloba on cochlear ischemia was studied. Our data showed that ginkgo biloba extract may be effectively treat or prevent cochlear damage from temporary ischemia. The therapeutic effect was most significant immediately after the cochlear ischemia happened.

**SY11-6**

## **Effect of Tone Performance on Speech Intelligibility in Mandarin-speaking Cochlear Implanted Children with Profound Sensorineural Hearing Loss**

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**Objectives:** Speech intelligibility is one index of the performance of speech development after cochlear implantation (CI), and it may be influenced by tone performance for Mandarin, a kind of tonal language. The purpose of this study was to examine the predictive value of tone perception and tone production on speech intelligibility in Mandarin-speaking cochlear implanted children with profound sensorineural hearing loss.

**Materials & methods:** Forty-one children with bilateral profound sensorineural hearing loss who received CI were enrolled. Their mean age 13.7 years (range, 8.5-17.7 years). The mean age of surgery was 3.3 years and the duration of CI use was 10.3 years in average. Tone perception test based on monosyllabic utterances, tone production test using disyllabic utterances, and Speech Intelligibility Rating (SIR) scale were conducted for all participants, and the results were scored by two normal hearing adults then counted by computers. Pearson correlation and stepwise regression analysis were used to estimate the correlation among tone perception, tone production and SIR.

**Results:** The mean score for tone perception was 75.27% (SD = 12.54%). The mean score for tone production was 89.86% (SD = 6.50%). The mean score for SIR was 4.06 (SD = 0.48). Moderate positive correlation was found between tone perception & tone production, tone production & SIR, and tone perception & SIR in Pearson correlation. When tone production as a valid constant and SIR as a dependent variable, SIR could be contributed by tone production.

**Conclusions:** The findings suggested that profoundly hearing-impaired children who received CI with sufficient duration of implant use did perform well in speech intelligibility, and the speech intelligibility could be predicted by the tone performance.

## Symposium 12 Dizziness and Vestibular Disorder

## SY12-1

**Somatosensory input influences the vestibule-ocular reflex**

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The vestibulo-ocular reflex (VOR) generates smooth eye movements that are compensatory for head movements to ensure gaze stabilization during head rotations. The VOR is under adaptive control that corrects VOR performance when visual-vestibular mismatch arises during head movement. During normal visual-vestibular interaction, cooperation between the VOR and vision results in stabilization of retinal image. Adaptive VOR recalibration occurs whether visual-vestibular mismatch arises through the manipulation of visual feedback during head movement or by lesion-induced modification of vestibular input. Considering how important VOR is in stabilizing gaze, one could predict that when VOR is lost, patients would be severely disabled by retinal image movement due to head movement. To compensate for vestibular deficits, the vestibular center uses the other substitutes such as visual and somatosensory information for the lost vestibular signals.

To investigate the contribution of somatosensory signal upon VOR, especially upon semicircular-ocular reflex (ScOR), we examined the plasticity of the ScOR using vestibular-somatosensory interaction and the effect of the adaptive plasticity of the ScOR by somatosensory stimulation.

We made two different conditions as somatosensory stimulations during rotation tests as follows; 1) Subjects grasped an earth-fixed metallic bar with their right hands so that their right arms always kept moving. 2) Subjects' outer side of the upper arms were stimulated alternatively by pressure using pressure chamber mounted on the rotatory chair.

We demonstrated a reasonably consistent effect of adaptation of ScOR gain using a somatosensory stimulation paradigm.

Our data suggest that the ScOR and somatosensory signals share common neural pathways in such a way that a change in the synaptic efficacy of one pathway is accompanied by a change in the other. The role of a neural store that receives input from both the semicircular canals and the somatosensory system to maintain a spatial orientation is discussed.

## SY12-2

**Morphological and functional changes in a new animal model for Meniere's disease**

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## [Background]

Meniere's disease (MD) is histologically characterized by endolymphatic hydrops (EH) in the inner ear. EH is considered to be the result of dysfunction of inner ear water homeostasis, which involves excessive production of endolymph and/or reduced absorption of endolymph. Furthermore, temporal bone study revealed that the endolymphatic sac (ES) showed fibrosis and/or hypoplasia in MD patients. This histopathological findings indicates that malabsorption of endolymph in the ES is one of the possible mechanism underlying the development of EH. However, fluctuating hearing loss and episodic vertigo attack are inexplicable based only on retention hydrops. Until recently, the detailed mechanisms underlying the over-accumulation of endolymph were unclear. Clinical studies suggest that stressful lifestyle and a stress modulating hormone, vasopressin (VP), correlate with disorder of the inner ear homeostasis. There is considerable evidence that water homeostasis in the inner ear is regulated partly via the vasopressin-aquaporin2 (VP-AQP2) system. We examined both morphological and functional changes of the inner ear system in our novel animal MD model, involving the surgical obliteration of the ES and the administration of desmopressin (VP type 2 receptor agonist; V2 agonist).

## [Methods]

In experiment No. 1, guinea pigs used in morphological studies underwent surgical obliteration of the ES in the left ear and maintained for 1 or 4 weeks, and divided into groups with or without desmopressin administration. We quantitatively assessed EH in the cochlea, vestibules and semicircular canal. In experiment No.2, we performed vestibular examination. We recorded spontaneous nystagmus and observed the presence or absence of balance disorder in the normal control group, desmopressin administration group and surgically treated groups with (combined) or without (surgical) desmopressin administration.

## [Results]

In experiment No. 1, both the increase ratio of the scala media area and the proportion of the endolymphatic space in the saccule were significantly higher in the combined group than in the surgical group. There were no significant differences in the degree of hydrops in the utricle or semicircular canal among the ear groups. In experiment No. 2, all animals of the combined group showed spontaneous nystagmus and balance disorder; whereas the surgical group was asymptomatic.

## [Conclusions]

Our experimental animals not only presented severe EH in the cochlea and the saccule, but also showed balance disorders and nystagmus. EH may be exacerbated due to ES dysfunction and the effects of desmopressin; acute V2 phenomenon, which may accompany vestibular abnormalities that are similar to vertigo attack in MD patients.

**SY12-3**

**Usefulness of the diuretic induced cervical vestibular evoked myogenic potentials in the patients with the Meniere's disease and delayed endolymphatic hydrops**

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The pathogenesis of Meniere's disease (MD) and delayed endolymphatic hydrops (DEH) is the endolymphatic hydrops. In order to evaluate the endolymphatic hydrops of the saccule, two kinds of the diuretic induced cervical vestibular evoked myogenic potentials (VEMP) have been reported. It is not clear whether the usefulness of the glycerol-induced VEMP is similar as that of the furosemide-induced VEMP (FVEMP). So, this study performed to compare the GVEMP with the FVEMP in the patients with the MD and DEH.

The patients with the MD and DEH who had a neurological examination in the University Hospital of Toyama were the test subjects in this study. Thirty-six patients were the subjects for the GVEMP, while 62 patients were for the FVEMP. In the GVEMP, the positive rate in the patients with the MD and DEH was 58%, and that was 57% in the FVEMP, suggesting that the two kinds of the diuretic induced VEMP are the similar utility to evaluate the endolymphatic hydrops of the saccule.

**SY12-4**

**Optimal stimulation mode for obtaining galvanic ocular vestibular-evoked myogenic potentials**

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**Introduction:** The BCV-oVEMP test alone cannot localize the pathology that affects the afferents between the otolithic organs and vestibular nuclei. Nevertheless, BCV-oVEMPs coupled with GVS-oVEMPs may help to topographically delineate the lesion site.

**Objectives:** This prospective study aimed to establish the most effective galvanic intensity and duration for evoking oVEMPs.

**Methods:** Twenty healthy volunteers underwent oVEMP tests via bone-conducted vibration (BCV) and galvanic vestibular stimulation (GVS) modes of various intensity (1, 2, 3, 5, and 6 mA at 1.0 ms) and duration periods (0.1, 0.2, 0.5, and 1.0 ms at 5 mA intensity). All subjects were questioned about the painful sensation experience in each test using an 11-point numeric rating scale (NRS-11) and a 100-mm visual analog scale (VAS). The prevalence, nI and pI peak latencies, nI-pI interval, amplitude and pain level of each stimulation mode were compared.

**Results:** Since more than half of subjects were not able to tolerate the galvanic stimulation at 6 mA/1.0 ms, this level was dropped from further study. Galvanic stimulation at 3 mA/1.0 ms, 5 mA/0.5 ms, or 5 mA/1.0 ms exhibited the highest prevalence (90% - 100%). In terms of GVS-induced pain, there was no significant difference among these three stimulation modes. In terms of the GVS-oVEMPs, the group receiving 5 mA/1.0 ms had exhibited a significantly larger nI- pI amplitude than the 3 mA/1.0 ms or 5 mA/0.5 ms group, but the latencies and nI- pI interval did not differ significantly among them. In addition, BCV-oVEMPs had significantly longer latencies and a larger amplitude than the GVS-oVEMPs evoked by 5 mA/1.0 ms, whereas the nI-pI interval was similar between them.

**Conclusions:** Galvanic stimulation at 5 mA/1 ms yields a higher response rate and larger nI-pI amplitude of oVEMPs relative to less intense stimuli without exceeding the tolerable level of subjective pain. Hence, the preferable stimulation mode for eliciting GVS-oVEMPs is optimally set at an intensity of 5 mA with a duration of 1 ms.

SY12-5

## Horizontal BPPV

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**Objectives:** Different from posterior benign paroxysmal positional vertigo (P-BPPV), the treatment of horizontal benign paroxysmal positional vertigo (H-BPPV) requires more efforts to achieve a good resolution due to varied mechanisms. The aim of this study is to find a simple, fast, yet effective treatment algorithm in the ENT outpatient department (OPD) for all subtypes of H-BPPV

**Material & methods:** a retrospective study of 490 patients with BPPV in our OPD was reviewed. Among these 490 patients, 86 (17.6%; 86/490) H-BPPV variants (54 female and 32 male patients, ranging in age from 18-92 y; mean age 56.2 y) were diagnosed with the supine roll test (McClure- Pagnini test).

**Results:** Among 86 H-BPPV patients, 74.4% (64/86) were hypothesized as the canalithiasis type, 20.9% (18/86) hypothesized as the cupulolithiasis-utricle type (Cup-U) and 4.7% (4/86) hypothesized as the cupulolithiasis-cupula type (Cup-C). The main treatment maneuver was the forced prolonged position (FPP) maneuver. For 3 patients suffering from refractory symptoms, we also introduced the Gufoni maneuver along with the FPP. The total average successful rate of treatment is 96%.

**Conclusions:** We had concluded that for H-BPPV with an initial geotropic nystagmus, the forced prolonged position without combination of the barbecue rotation maneuver, had a good treatment control rate. However, for apogeotropic patients, an observation to see a transformation of nystagmus was necessary before further treatments. For apogeotropic patients due to cupulolithiasis with refractory to single FPP treatment, keeping it with addition of Gufoni's maneuver was needed.

**Keywords:** horizontal benign paroxysmal positional vertigo (H-BPPV), forced prolonged position (FPP) maneuver, canalithiasis, cupulolithiasis.

**Symposium 13** Chemoradiotherapy and Targeted Therapy

**SY13-1**

**The role of targeted therapy in the treatment of locally advanced head and neck cancers**

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Radical surgery for locally advanced head and neck cancers inevitably causes loss of important organ functions such as speech and swallowing. In the past three decades locally advanced laryngopharyngeal cancer management has undergone a paradigm shift from surgical dominance to non-surgical organ preservation strategies. The organ preservation concept was based on the findings of pivotal trials by the Veterans Affairs, European Organization for Research and Treatment of Cancer group and Radiation Therapy Oncology Group. Concurrent chemoradiotherapy was thus advocated as the treatment of choice for locally advanced head and neck cancers. During the last decade, there were a couple of targeted therapeutic agents coming into play. The long-term treatment results of chemoradiation in organ preservation have also been re-evaluated. Following the publication of The Cancer Genome Atlas (TCGA) studies, more therapeutic agents targeting frequently mutated genes in head and neck cancers are under clinical trials. In this talk, I will summarize what we have learned from the current evidence-based results of implementing targeted therapeutic agents in the treatment of locally advanced head and neck cancers. I will also talk on the major breakthrough implementing immune checkpoint inhibitors in the treatment of head and neck cancers.

**SY13-2**

**Concurrent use of cetuximab with radiation for oropharyngeal and hypopharyngeal squamous cell carcinomas**

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Cetuximab has been approved to use for the treatment of head and neck cancer since Dec. 2012 in Japan. There are only a few reports on cetuximab based bioradiotherapy (BRT) in Japan. We examined the primary outcome of radiation therapy with cetuximab for the patients with oropharyngeal or hypopharyngeal cancer in our department, and also the influence on the regulatory T cells which play a critical immunosuppressive role in patients with head and neck cancer.

A total 30 patients were treated with BRT between Jan. 2013 and Apr. 2014, and cetuximab was weekly administrated 5-8 times. Their completion rates were 89 % and response rates were 100%. Complete remission was observed in 82% and 71% of the patients with oropharyngeal and hypopharyngeal cancer, respectively. Serious adverse events occurred in three patients. These results were comparable with 86 patients who had been treated with chemoradiation therapy using cisplatin from 2008 to 2012. Most of the patients started their treatment with BRT at the out-patient clinic, a fact that contributed the shortening the hospitalization time.

Activated regulatory T (aTreg) cells increased in the peripheral mononuclear cells (PBMCs) of these head and neck cancer patients compared with those of the age matched healthy control subjects. These regulatory cells also inhibited the proliferation of CD3 T cells and NKT cells. Cetuximab significantly blocked the expression of foxp3 of these regulatory T cells in vitro, however the ratio of aTreg/ CD4 T cells of PBMCs did not decrease after BRT in these patients.

These results suggest that BRT using cetuximab could be expected as a useful treatment for head and neck cancer, but further studies need to clarify the role of cetuximab in the immune suppression observed in the patients with head and neck cancer.

## SY13-3

### Predictive and prognostic value of metabolic tumor volume in patients with laryngeal carcinoma treated by radiotherapy / concurrent chemoradiotherapy

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**Aim:** To evaluate the predictive and prognostic value of pretreatment metabolic tumor volume (MTV) in patients with treated by radiotherapy (RT) or concurrent chemoradiotherapy (CCRT).

**Methods:** We reviewed the records of 118 patients with newly diagnosed laryngeal carcinoma, who had been treated by RT or CCRT. Pretreatment positron emission tomography (PET) was performed, and MTV values were obtained by contouring margins of standardized uptake value. Clinical factors and MTV were analyzed for their association with survival.

**Results:** Patients with residual disease showed a significantly higher MTV than those with a complete response (CR) after primary treatment. Univariate analysis showed that the patients with a high MTV had a significantly lower disease-free survival (DFS) ( $p < 0.001$ ). Subsite ( $p = 0.010$ ), T-stage ( $p < 0.001$ ), nodal metastasis ( $p < 0.001$ ) and clinical stage ( $p < 0.001$ ) also correlated significantly with DFS. In the multivariate analysis, MTV and clinical stage were both found to be independent prognostic factors for DFS ( $p = 0.001$ ,  $p = 0.034$ , respectively). The 3-year DFS for patients with a high MTV were significantly poorer than those with a low MTV ( $p < 0.001$ ).

**Conclusions:** MTV of the primary tumor is a significant prognostic factor for DFS in patients with laryngeal carcinoma treated by RT or CCRT. The results imply that MTV could be an important factor when planning treatment and follow-up for patients with laryngeal carcinoma.

## SY13-4

### Multimodality treatment for oropharyngeal cancer based on HPV status

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Human papillomavirus (HPV) infection is a major carcinogenic factor for oropharyngeal cancer (OPC). The prevalence of OPC with HPV infection is growing in the world. Japan Cooperative Study Group for Basic Research in Head and Neck Cancer performed multicenter prospective study to clarify the prevalence of HPV and treatment results with or without HPV in OPC. Patients without prior treatments were registered from May 2009 to March 2011 and tissue samples were collected from 21 institutes covering all over Japan. OPC tissue samples from 157 patients were tested using polymerase chain reaction. High-risk HPV was detected in 79 (50.3%) of 157 OPC patients. When analyzed survival by HPV status, the 2-year and 3-year estimated overall survival rates were 89% (95% CI: 0.80-0.94) and 77% (95% CI: 0.53-0.91) for the HPV-positive patients, and 61% (95% CI: 0.48-0.71) and 53% (95% CI: 0.39-0.65) for the HPV-negative patients. The disease-free survival rates were 80% (95% CI: 0.70-0.88) at 2 years and 80% (95% CI: 0.70-0.88) at 3 years for HPV-positive patients, and 59% (95% CI: 0.47-0.70) at 2 years and 57% (95% CI: 0.44-0.68) at 3 years for HPV-negative patients. Significant differences in overall survival rates (log-rank test,  $p = 0.0028$ ) and disease-free survival rates (log-rank test,  $p = 0.0047$ ) were observed between patients with and without HPV infection. HPV positive patients who were treated with CRT had an improved overall survival rate compared with HPV-negative patients (log-rank test,  $p = 0.006$ ). Many studies including our study show that of HPV-positive patients have better prognosis compared with negative patients. The decision of treatment modification according to HPV infection is an important issue in future.



**SY13-5**

**Comparison of concurrent chemoradiotherapy versus  
neoadjuvant chemotherapy followed by radiation in patients  
with advanced nasopharyngeal carcinoma in endemic area:  
experience of 128 consecutive cases with 5 year follow-up**

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**Background:** Combined radiotherapy and chemotherapy is considered the standard of care for locally advanced nasopharyngeal carcinoma (LA-NPC) in Epstein-Barr virus infection endemic area. This study compared the long-term outcomes between LA-NPC patients treated with neoadjuvant chemotherapy followed by radiotherapy (NACT) and those treated with concurrent chemoradiotherapy (CCRT).

**Methods:** From 2003 to 2007, a total of 128 histopathologically proven LA-NPC patients receiving either NACT or CCRT were consecutively enrolled at the National Cheng Kung University Hospital in Taiwan. NACT consisted of 3-week cycles of mitomycin, epirubicin, and cisplatin on day 1 and fluorouracil and leucovorin on day 8 (MEPFL) or weekly alternated cisplatin on day 1 and fluorouracil and leucovorin on day 8 (P-FL). CCRT comprised 3-week cycles of cisplatin (Cis 100) or 4-week cycles of cisplatin and fluorouracil (PF4). The first failure site, disease free survival (DFS), overall survival (OS), and other prognostic factors were analyzed.

**Results:** Thirty-eight patients (30%) received NACT. Median follow-up duration was 53 months. More patients with advanced nodal disease (N2-N3) (86.8% vs 67.8%,  $p=0.029$ ) and advanced clinical stage (stage IVA-IVB) enrolled in the NACT group (55.2% vs 26.7%,  $p=0.002$ ). For NACT, both MEPFL and P-FL had similar 5-year DFS and OS (52.9% vs 50%  $p=0.860$  and 73.5% vs 62.5%,  $p=0.342$ , respectively). For CCRT, both PF4 and Cis 100 had similar 5-year DFS and OS (62.8% vs 69.6%,  $p=0.49$  and 72.9% vs 73.9%,  $p=0.72$ , respectively). Compared to CCRT, NACT had similar 5-year DFS and OS (51.5% vs 65.1%,  $p=0.28$  and 71.7% vs 74.3%,  $p=0.91$ , respectively). Among patients who were recurrence-free in the first 2 years after treatment, those treated with NACT experienced poorer locoregional control compared to those treated with CCRT (Hazard ratio =2.57, 95% confidence interval: 1.02 to 6.47,  $p=0.046$ ).

**Conclusions:** For LA-NPC, both CCRT and NACT were similarly efficacious treatment strategies in terms of long-term disease control and survival probability. Close locoregional follow-up is recommended for patients receiving NACT, because these patients are more prone to develop locoregional failure than patients receiving CCRT.

## Paper 1 Head and Neck 1

### O01-1

#### Anti-IgE therapy to Kimura's disease

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Eosinophilic granuloma of the soft tissue (Kimura's disease) was first described by Kimura et al, in 1948. This disease is a chronic benign inflammatory disease of unknown etiology, and often presents as a tumor-like swelling in the subcutaneous soft tissue of the head and neck region with formation of lymphoid follicles and infiltration of eosinophils. Blood tests often show eosinophilia and elevation of serum IgE. It is thought to be an IgE-mediated disease. There is still no definitive treatment for this disease, although various therapies - including surgery - have been applied.

Omalizumab, a monoclonal antibody, has recently been suggested as a potential new systemic treatment for IgE-mediated disease, based on its efficacy in treating asthma and allergic rhinitis. Omalizumab binds to free IgE in the blood, thereby preventing IgE from bindings to basophiles and mast cells, inhibits activation of inflammatory cells and inhibits their release of such inflammatory mediators as histamine, leukotrienes, etc. We report a study of three patients with Kimura's disease who received anti-IgE treatment (omalizumab). Omalizumab was administered to them by injecting it subcutaneously at 300 mg/day in a total of 8 cycles given at two-week intervals. The size of tumorous regions was evaluated by MRI at baseline and after 4 months of treatment. Blood samples were taken every two weeks. In each of the patients, the size of tumorous regions and the peripheral blood eosinophil and basophil counts were all decreased after the treatment. These results suggest that omalizumab may be valuable for treatment of Kimura's disease.

### O01-2

#### Sialoendoscopy Experience In Taiwan

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Sialoendoscopy was developed in the 1990s to provide a minimally invasive gland-preserving approach for the treatment of obstructive sialoadenitis. Sialoendoscopy is efficient to manage structural ductal disease by removing stones, stenosis dilatation, scar lysis and also intra-ductal drug delivery ( e.g. antibiotics, corticosteroid).

Since 2013 September, MacKay Memorial Hospital established sialoendoscopy and performed 200+ sialoendoscopic procedures till now. First In this presentation, we will describe our settings and surgical equipments. The second part, we will present how we treating the different kinds of obstructive sialoadenitis including : stones, ductal stenosis, ranula, sialoectasis and chronic sialoadenitis. The 3rd part we will present the experience of pediatric sialoendoscopy. As a children hospital, we met several pediatric cases e.g. stones, juvenile recurrent parotitis. Finally, we will present our results of sialoendoscopy and sialostent experience.

O01-3

### Is the ultrasound alone adequate for pre-operative detection and evaluation of parotid tumor?

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Ultrasound (US) is a good tool for head and neck otolaryngologist to assess head and neck region. To determine sufficiency of the ultrasound alone for pre-operative assessment of parotid tumor, we collected 6302 head and neck US records in National Taiwan University Hospital from October, 2003 to May, 2015.

Of these records, 287 patients were diagnosed of parotid tumor by US. And a total of 129 people with 131 parotid tumors (2 patients had bilateral parotid tumors) who had had US and either cross-sectional imaging (computed tomography (CT) (n = 95) or magnetic resonance (MR) (n = 34) as part of their preoperative assessment. There were 64 male and 65 female with a mean age of 53.2 years (range 5?85). Among 95 patients with both US and CT examination, we found 12 patients (12.6%) had negative finding on CT. Among 34 patients with US and MR, we found 3 patients (8.8%) had negative finding on MR. Six of these 20 patients with positive finding on US and negative finding on CT or MR, had surgery and all had positive finding in pathology. We compared the features of US to the findings of CT or MRI for these patients. And we also evaluate the difference between ultrasounds features of parotid tumor and operative finding. Our data contributes to a preliminary result that US is an adequate tumor detection tool and also can provide adequate pre-operative assessment.

O01-4

### Kikuchi-Fujimoto disease; evaluation of the prognostic factors and analysis of the pathologic findings

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Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a benign and self-limiting condition characterized by mainly affecting the cervical lymph nodes. Although most affected patients recover without any treatments, this disorder is sometimes difficult to be differentiated from malignant lymphoma or tuberculous lymphadenitis especially in the cases with long disease duration. In the present study, the records of 57 patients who were histopathologically diagnosed as KFD between April 2001 and March 2014 were reviewed retrospectively to identify prognostic factors and predictive factors of recurrence. As a result, the cases with fever >37 degrees and developed in spring and summer were more likely to have longer period between symptom onset and relief. We could not find any predictive factors of recurrence. The histopathological features of affected lymph nodes in KFD are on occasion, notably similar to those of systemic lupus erythematosus (SLE), and pathogenic linkage between SLE and KFD has been proposed. Thus we also reviewed the histopathologic findings of each of these cases in detail and discussed the relationship between KFD and SLE or other autoimmune diseases.

O01-5

## An ulcerating Warthin's tumor that resulted with a formulation of a granulation tissue

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Skin ulceration of a tumor is commonly known as a characteristic of malignancy. However, Warthin's tumors have been reported to result with skin ulcers consequent to growth. We too, have experienced several cases of Warthin's tumors resulting with skin ulcerations, suggestive of malignancy or Tbc of the parotid gland. Amongst them, we present a rare clinical case of a 68 year-old male, whose Warthin's tumor ulcerated its overlying skin with a mass of granulation tissue after refusing to receive surgical treatment for over ten years.

### Case History

Three months prior to his visit to our hospital, the patient noticed redness to the skin over the tumor. He first visited a local clinic, where he was prescribed with a week of CFPN-PI. A few weeks later, however, the tumor disrupted the skin with a discharge of purulent exudates.

Upon his arrival to our out-patient's clinic, the tumor presented with a skin ulceration of about three centimeters in diameter. From within the ulceration grew a cauliflower-like granulation tissue, with a clear and saliva-like discharge, of about five centimeters in height. There was very little bleeding from the tumor, and no signs of necrosis. The patient denied of tenderness nor trismus, and no symptoms of facial nerve paralysis was seen. The contrast enhanced CT presented the tumor to be well differentiated from the normal parotid gland. The macroscopic findings alone made it difficult to differentiate malignancy, but the overall clinical features of the case suggested more of infection. Post-admission, we first began an antibiotic therapy of CEZ (2 g/day, div). Twelve days later, the amount of purulent discharge decreased, so we continued on with CAM (400 mg/day, po). Antibiotics, however, did not ameliorate the size of the tumor or its ulceration, leading us on to surgical treatment. It had been a month after admission, when the tumor was excised and submitted for pathological examination.

### Pathological Examination

Histologically, the tumor consisted of parotid gland tissues with hyperplastic lesions of eosinophilic oncocytic epithelial cells as papillary cystadenoma lymphomatosum, suggestive of "Warthin's tumor with inflammatory change."

Although we have experienced several cases of Warthin's tumors resulting with skin ulcerations, the gross appearance of this case had a striking resemblance to a malignant tumor. To our knowledge, there have been only been a few cases of gross granulation tissues reported. Thus, ulcerating Warthin's tumors may require an exceptional prudence when differentiating them from malignancy.

O01-6

## Basaloid squamous cell carcinoma arising in inverted papilloma in the nasal cavity

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Basaloid squamous cell carcinoma (BSCC) is a histologically distinctive variant of squamous cell carcinoma composed of two parts, basal cell carcinoma and squamous cell carcinoma. BSCC shows an aggressive behavior and carries a poor prognosis because of frequent lymph nodes and distant metastases. BSCC occurs preferentially in cervix, thymus and esophagus, and is uncommonly found within the head and neck region. BSCC in the nasal cavity or paranasal sinus is particularly rare. Inverted papilloma is uncommon benign tumor that present propensity to be associated with malignancy, however BSCC arising from inverted papilloma has never been reported in English literature. We report herein on a case of BSCC arising from inverted papilloma in the nasal cavity.

A 56-year old female was referred to our hospital with complaints of epistaxis, nasal congestion and dysphagia. We observed a tumor completely occupied the left nasal cavity. A biopsy specimen histologically revealed papilloma. Computed tomography demonstrated a tumor with heterogeneous contrast effect occupied the left nasal cavity however extra nasal tract extension was not observed. No metastatic region was detected by US and PET/CT. We performed endoscopic excision of the tumor. Microscopic findings confirmed the diagnosis of BSCC arising from inverted papilloma. No tumor recurrence has been observed for 1 year after surgery.

**Paper 2** Otology 1

O02-1

## Clinical Analysis of Five Patients Suspected to have Superior Canal Dehiscence Syndrome

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### 【Background】

Superior canal dehiscence syndrome (SCDS) is a recently discovered condition in which vestibular symptoms are elicited by sound or pressure secondary to the dehiscence over the superior semicircular canal (SSC). The dehiscence leads to the formation of a “third window” in the inner ear, which is a consequence of abnormal mobility of the endolymph, and reduction in the threshold of bone conduction. Normally, SCDS is detected by traditional high-resolution computed tomography (HRCT); however, the high rate of false positives is a problem, especially when faced with dehiscence.

### 【Materials and Methods】

The clinical data obtained from 5 patients who were diagnosed with dehiscence or thin over SSC upon HRCT appearances from 2010 to 2015 were retrospectively reviewed. We compared the clinical history and audiogram results as well as the results of the VEMP and ENG of these 5 patients. Traditional HRCT images significantly overestimate the prevalence of canal dehiscence because of its lack of sufficient spatial resolution. To compensate for this, we used thin-slice HRCT findings reconstructed in a parallel plane of the SSC.

### 【Results】

Three patients had unusual sounds and pressure-induced vestibular symptoms, along with hearing loss as detected on the audiograms. None of the patients showed evoked nystagmus. In 2 of the 3 patients, HRCT reconstructed along with a plane of the SSC demonstrated that the other dehiscence on the roof of the SSC was a false positive finding. In both the patients who were reviewed, the amplitude of the VEMP waveform in an SCDS ear was greater than that in the ear without dehiscence. HRCT reconstructed along with a plane of the SSC was useful for the diagnosis of SCDS. The possibility of false positive findings is much lower with this technique. Further this technique made it possible for us to define the diagnosis of SCDS. SCDS should be diagnosed by not only symptom coronal HRCT finding but also audiograms, VEMP and HRCT findings reconstructed in a parallel plane of the SSC.

### 【Conclusion】

The diagnosis of SCDS is based upon characteristic symptoms, specific findings on clinical examination, and VEMP, as well as on the HRCT findings reconstructed in a parallel plane of the SSC. Further research is necessary and could aid in the diagnosis and treatment of SCDS.

O02-2

## Superior Semicircular Canal Dehiscence Syndrome: Case Report

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Superior canal dehiscence (SCD) syndrome is a recently described vestibular and hearing condition caused by an absence of bone over the arc of the superior semicircular canal. Patients with such condition present a variety of perplexing symptoms including conductive hearing loss, hyperacusis, vertigo, autophony, and eye movement in response to sound and pressure. We will present a care of 70-year-old man who suffered from chronic dizziness, especially during straining or coughing and left ear autophony. VEMP response revealed low threshold in left ear. Temporal-bone computed tomography (CT) confirmed a diagnosis of left ear superior semicircular canal dehiscence syndrome. Surgical plugging of SCD via middle cranial fossa cured vestibular symptoms.

## O02-3

**Can Presbystasis be cured?**

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**【Introduction and aims of the study】**

Japan has entered into a period of an aging society. Presbystasis is a state of dizziness and balance disorder which is caused pathophysiologically by aging. It is a progressive condition due to aging and worsen with time, just like cancer, without intervention or treatment. Presbystasis in Japan seems to have as the population ages. In this study, we tried to see if presbystasis could be improved or cured with intervention.

**【Purpose】**

The purpose of this study is to find out whether or not presbystasis can be improved or cured.

**【Methods】**

After categorizing dizziness and disequilibrium patients from the outpatient clinic into those whose symptoms are caused by presbystasis, we conducted simple physical therapies.

**【Results】**

Dizziness patients were categorized into four groups. A few cases of presbystasis could be improved and patients were relieved from their balance disorders.

**【Conclusions】**

Presbystasis is a pathophysiologically progressive condition just like cancer that worsens overtime without intervention. According to our results, some simple physical therapy seems to have relieved patients of some of their symptoms and improved their conditions.

## O02-4

**No association between plasma adiponectin levels and central auditory function in adults**

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Adiponectin might play a protective role in cardiometabolic and peripheral auditory disorders, but its role on central auditory function was still unclear. The aim of this study was to examine whether there is an association between plasma adiponectin levels and central auditory function in adults. We recruited 297 adults, with normal or symmetrical sensorineural hearing loss and normal cognitive functions. Multivariate linear regression was performed to assess the association between plasma adiponectin concentrations and pitch pattern sequence (PPS) score, which was one of central auditory tests. The results showed that there were 224 (75.4%) women and 73 (24.6%) men in this study. The mean age was  $58.1 \pm 8.4$  years, the mean waist circumference (WC) was  $81.1 \pm 8.3$  cm, and the mean body mass index (BMI) was  $24.0 \pm 3.0$  kg/m<sup>2</sup>. The mean PPS score was  $71.5 \pm 14.1$  %, and plasma adiponectin concentration was  $12.7 \pm 5.5$  g/mL. After adjusting for age, gender, WC, coronary artery disease, hypertension, diabetes mellitus, chronic kidney disease, smoking and drinking, plasma adiponectin concentrations (coefficient  $\pm$  standard error,  $\beta \pm SE = -0.09 \pm 0.16$ ,  $p = 0.563$ ) were found to have no significant associations with PPS score. When WC was excluded from these variables in the multivariate linear regression model, plasma adiponectin concentrations ( $\beta \pm SE = -0.03 \pm 0.15$ ,  $p = 0.855$ ) were still not significantly associated with PPS score. In conclusion, plasma adiponectin levels were not significantly associated with PPS score, which was one of central auditory function tests. More studies should be conducted for the underlying mechanisms of obesity-related central auditory dysfunction.

O02-5

## Inner Ear Deficits in Irradiated Nasopharyngeal Carcinoma Survivors

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**Objectives/Hypothesis:** Despite the advancement of concurrent chemoradiotherapy, inner ear symptoms such as hearing loss, tinnitus, or vertigo/dizziness are still experienced in irradiated nasopharyngeal carcinoma (NPC) survivors. This study utilized an inner ear test battery to assess the causes and sequence of inner ear deficits in irradiated NPC survivors with a mean interval of 10 years after radiotherapy. **Study Design:** Retrospective study. **Methods:** Thirty-six irradiated NPC survivors were enrolled. Otoscopy and an inner ear test battery comprising audiometry were performed, as well as ocular vestibular-evoked myogenic potential (oVEMP), cervical VEMP (cVEMP), and caloric tests.

**Results:** Otoscopic examination revealed middle ear complications in 37 ears (51%), including radiation-induced otitis media in 32 ears and otitis media with effusion in five ears. Percentages of abnormal cVEMP test, oVEMP test, boneconducted mean hearing level, and caloric test were 91%, 75%, 67%, and 39%, respectively, exhibiting a significantly declining sequence in inner ear deficits. Most (67%) NPC survivors had inner ear deficit originated from peripheral vestibular lesion, mainly due to sequela of otitis media. In contrast, 33% of them had inner ear deficit caused by central vestibular disorder.

**Conclusions:** A significant sequential decline in inner ear function of irradiated NPC survivors was observed from the saccule to the utricle, cochlea, and semicircular canals. Most of them were due to sequela of otitis media, followed by central vestibular disorder.

O02-6

## Evolution of post-irradiated sudden deafness during the past two decades

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**Objective:** The beneficial effect of intensity-modulated radiotherapy (IMRT) on reducing the prevalence of post-irradiated sudden deafness (PISD) in nasopharyngeal carcinoma (NPC) survivors has never been mentioned. This study investigated the evolution of PISD in NPC survivors during the past two decades.

**Methods:** Of the 3,206 NPC patients who underwent radiotherapy during the past two decades, 32 patients (34 ears) had PISD. Twenty-nine patients (30 ears) received two-dimensional radiotherapy (2DRT) and were assigned to Group A, whereas 3 patients (4 ears) undergoing IMRT were assigned to Group B. An inner ear test battery including audiometry, and ocular vestibular-evoked myogenic potential (VEMP), cervical VEMP and caloric tests was performed for comparison between the two groups.

**Results:** Group B (0.2%) showed significantly lower prevalence of PISD than Group A (2%). Percentages of abnormal pursuit, saccade and optokinetic nystagmus test results did not significantly differ between Groups A and B. Likewise, both groups did not differ significantly in the percentages of abnormal mean hearing level, cervical VEMP test, and caloric test. However, significant hearing improvement after treatment was identified in Group B ( $p < 0.01$ ), but not in Group A ( $p > 0.05$ ), probably because mean radiation dosage to the cochlea of Group B ( $35.0 \pm 0.4$  Gy) was less than Group A ( $50 \pm 3$  Gy).

**Conclusion:** Compared to 2DRT, both radiation dosages to the cochlea and radiation damage to tissues surrounding the inner ear are lessened by IMRT. Therefore, NPC patients who received IMRT have a low prevalence of PISD with significant hearing improvement after treatment.

002-7

## Development of A Mobile Phone-based Otitis Media Auto-Diagnostic System (MP-OMADx)

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**Objective:** The demand for new point-of-care testing, consumer-oriented diagnostics, patient-centered devices to support telemedicine has rapidly emerged as a trend to adopt wireless technology into medical device systems. In this study, we aim to develop a mobile phone-based otitis media (OM) auto-diagnostic system (MP-OMADx).

**Study Design:** We prospectively collected and coded 1181 digitized otoscope images. We used the sparse representation technique via dictionary learning for classification and object recognition of the 22 types of OM. The sparse representation allows a high performance classification of high dimensional data of OM images to solve the L1-minimization problem. The algorithm was used to develop a diagnostic engine; the engine was embedded in an android-based mobile phone. A specialized ear speculum was designed to mount on a wireless camera device.

**Setting:** otolaryngology department of a tertiary referral center. **Patients:** 1181 digitized otoscopic images from 591 OM patients were used to develop the diagnostic algorithm. Another 1000 images from 100 adult patients (20 control, 80 with chronic OM-COM) captured by the device were used to validate the MP-OMADx. **Intervention:** Through synchronization, the images captured by the camera can be transmitted to the mobile phone for analysis and diagnosis. **Main Outcome Measure(s):** sensitivity, specificity, and accuracy. **Results:** The algorithm was capable to diagnose adult COM with sensitivity of >91%, specificity>86%, and accuracy>89%. The sensitivity, specificity, and accuracy for MP-OMADx to diagnose adult COM exceeded 90%. **Conclusions:** The MP-OMADx proves capable to provide real time clinical decision support for professional or personal health management. It has the potential to improve COM diagnosis with less expense.



**Paper 3** Otolology 2

O03-1

**A novel approach for treatment of congenital cholestatoma using a semiconductor laser**

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Different approaches are available to the surgeon for treatment of congenital cholesteatoma depending on the location and extent of cholesteatoma. The introduction of endoscopic ear surgery makes it possible to remove a small congenital cholesteatoma located in only the tympanic cavity with a minimal invasion. However, such a procedure may have risks of residual cholesteatoma. We introduce two cases removed a congenital cholesteatoma located only anterior to the malleus by resecting the malleus handle using a semiconductor laser. The first case is a three-year-old girl with a white mass in contact with the malleus handle behind the anterior-superior quadrant of the left ear. Preoperative temporal bone CT imagines showed a soft tissue shadow in only the anterior-superior part of the tympanic cavity. After tympanomeatal flap elevation, a cholesteatoma was found behind the malleus handle. The cholesteatoma was removed completely after resecting the malleus handle using a semiconductor laser. Packing of the external auditory canal made the tympanic membrane contact with the malleus neck. Post-operative left ear average hearing level by the four divided method was 26.3dB HL. Postoperative temporal bone CT imagines and endoscopic findings of the left tympanic membrane showed no residual cholesteatoma.

The second case is a two-year-old boy with the same otoscopic, preoperative imagine and operative findings in the right ear as the first case. The cholesteatoma was removed completely after resecting the malleus neck, and a piece of cartilage was used to connect both amputated ends of the malleus. Postoperative endoscopic findings of the right tympanic membrane showed no residual cholesteatoma.

In the conventional surgery for such cholesteatomas, the malleus and/or the incus are removed to extirpate a cholesteatoma completely and the subsequent type II or type IIIc tympanoplasty is performed to restore hearing. In endoscopic ear surgery, residual cholesteatoma may occur because the base of cholesteatoma is not put under vision and is not exfoliated even using oblique mirrors and instruments which we can use at present. Our methods may provide a clue to solve this conflicting problem.

O03-2

**Preservation of chorda tympani nerve in cholesteatoma surgery - Is "sacrificing" the nerve still appropriate?**

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**Background**

Although there are a few studies on post-operative gustatory function in middle ear surgery, reports on the preservation of chorda tympani nerve itself have been rare. Some suggest intentional "sacrifice" of the nerve when involved in the lesion. The authors modified surgical procedures more conservatively and try to preserve the nerve in principle. In this paper, we evaluate morphological (anatomical) preservation of chorda tympani nerve in cholesteatoma surgery.

**Subjects and Method**

Included were 189 ears of 184 patients who underwent first-time or staged (second) surgery for cholesteatoma between April 2011 and May 2015. Evaluated were 1) preservation rate of chorda tympani nerve at the first surgery, and 2) sites of recurrence at the second, staged surgery.

**Results**

1) Two ears were excluded since no funicular structure was found in the mesotympanum. Of 187 ears, involvement of chorda tympani nerve was observed in 108 ears. Preservation of the nerve was achieved in 175 ears (93.6%). The nerve was intentionally severed in 4 ears. Once identified nerve disappeared in the lesion in 6 ears. In 2 ears, preserved nerve was severed accidentally. As reference, preservation rate for first-time non-cholesteatoma surgery (118 tympanoplasties and 58 stapes surgeries) during the same period were also evaluated, which gave 100% preservation. The difference in preservation rates between cholesteatoma and non-cholesteatoma surgery reached significance ( $p < 0.001$ ).

2) Recurrent cholesteatoma was found in 12 of 76 ears (16%) who underwent staged surgery (12 residual cholesteatomas and 1 reformation, permitting overlap). However, no recurred lesion touched chorda tympani nerve, including simple invagination of the ear drum.

**Discussion**

Recent advances in surgical equipments have been remarkable. Surgical microscopes with Xenon lamps provide clear, well-lighted view, without heating up the surgical field. By using a nerve stimulator, surgeon can test a funicular structure in the mesotympanum, whether it is a branch of facial nerve or not. Tiny sharp-edged scalpels help dissect the chorda tympani nerve. Thanks to these technological enhancements, a relatively good preservation rate was attained, even at a University Hospital to which advanced cases are referred. However, since the risk of severing the nerve in cholesteatoma surgery was significantly higher than in other middle ear surgeries, pre-operative informed consent should be taken carefully. The notion that chorda tympani nerve, if involved, should be sacrificed no longer holds true, for no lesion was found involving the nerve in the staged (second) surgery.

## O03-3

## The efficacy of color mapped fusion images together with a T1 weighted image in the postoperative follow-up evaluation for residual cholesteatomas

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Transcanal Endoscopic Ear Surgery (TEES) is a less invasive procedure for the treatment of cholesteatomas through the ear canal without the need for a large, invasive retroauricular incision. However, TEES can only be used to treat cholesteatomas located in the attic and antrum. Therefore, preoperative evaluation of the anatomical location of a cholesteatoma is crucial in determining whether a patient is indicated for TEES even in the case of residual cholesteatomas. Diffusion-weighted imaging (DWI), a variation of conventional MRI, has been used in recent years to detect cholesteatomas. Non-EPI DWI has been reported to be more reliable than EPI DWI in identifying cholesteatomas. However, non-EPI DWI has a major drawback in that the anatomical location is harder to identify because of lower image resolution. However, we were able to solve this problem by combining a 1-mm thin slice non-EPI DWI with MR cisternography (MRC) to clarify the anatomical location of cholesteatomas. We also incorporated color mapping to further enhance the visualization of the cholesteatoma. The resulting image is called a color mapped fusion image (CMFI), which together with a T1 weighted image (T1WI) has proved to be useful in the accurate detection of cholesteatomas. We thus use a CMFI and a T1WI for the preoperative evaluation of cholesteatomas and for the postoperative follow-up evaluation to check for residual cholesteatomas. We were able to identify early-stage residual cholesteatomas with CMFI and T1WI. Therefore CMFI and T1WI are thus a reliable diagnostic modality for not only preoperatively identifying cholesteatoma but also postoperatively identifying early-stage residual cholesteatomas and determining whether TEES is indicated for treatment.

## O03-4

## Clinical findings of the congenital cholesteatoma: focusing on Potsic stage III prognosis

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**Objectives:** Thirty patients with congenital cholesteatoma in the middle ear who underwent surgery at the Mitsui Memorial Hospital from 2009 to 2015 were studied. The symptoms at initial onset, otoscopic findings, configuration of the cholesteatoma, type of surgical procedure, and surgical outcome were investigated.

**Study design:** Retrospective chart analysis of consecutive patients with congenital cholesteatoma.

**Patients:** Between February 2009 and July 2015 conclusive thirty patients underwent primary procedure.

**Intervention:** The diagnosis of congenital cholesteatoma with Potsic staging system and the therapeutic operation were performed.

**Result:** Patients were from 3 to 47 years old (mean 6 years), with 83% aged 15 years or younger. 60% held diseases in right side of the ear. Male to female ratio is 1.14.

Of thirty cases, 6 cases were classified in Potsic stage I, 1 in stage II, 19 in stage III and 4 in stage IV.

In stage I and II, all patients didn't notice hearing loss and showed white mass behind the ear drum. In contrast, more than half (14 cases) complained conductive hearing loss in stage III and IV. Cholesteatoma localized to the anterior mesotympanum without ossicular involvement in stage I and II, otherwise mostly located in the posterior mesotympanum in stage III and IV.

Patients showed normal hearing in stage I or II (26.7dB and 25.0dB), but showed moderate hearing loss in stage III or IV (42.3dB and 47.8dB, respectively) preoperatively. Postoperatively, those of stage III showed manifest improvement in both mean pure tone average (PTA) and Air-Bone gap (ABG), but no significant change was shown in stage I, II or IV patients.

Mastoidectomy was underwent in 13 cases, 1 in stage I, 8 in stage III and all in stage IV, respectively. In stage I or II cases, single-stage tympanoplasty type I was performed. Of stage III patients, 13 were planned to second-stage ossicular reconstruction, 7 of which needed mastoidectomy, but canal wall were preserved. In stage IV, 2 patients required radical mastoidectomy.

Recurrence was found in 7 cases at present, 5 cases in stage III. All patients were followed for more than one year.

**Conclusion:** Patients in stage III occupied almost two thirds in our study. They showed not only improvement in hearing, but also various locations of disease, methods for operative intervention and favorite site of recurrence. We will discuss about surgical indication, operative intervention and prognosis focusing on Potsic stage III patients.

O03-5

## Management of intractable petrous apex cholesteatoma combined trans labyrinthine-sphenoidal approach

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### Background:

It is difficult to remove completely lesion for petrous apex cholesteatoma.

As it is for a long period of time, the lesion may involve vital structures such as the sigmoid sinus, jugular vein and artery.

We report a case of a petrous apex cholesteatoma which was managed with combined surgery, translabyrinthine approach and endoscopic sinus surgery.

### Case presentation:

A 71-year-old Japanese man underwent right tympanoplasty 7 years ago.

For recurrence of petrous apex cholesteatoma, he visited our hospital.

He had mixed hearing loss in his right ear and atresia of right external auditory meatus.

In imaging procedure, cholesteatoma invaded sphenoid sinus and had extensively spread to nearby carotid artery and jugular vein.

As surgical method, translabyrinthine approach was performed to remove cholesteatoma as possible, trans-sphenoidal approach was used to create drainage hole.

### Conclusions:

We experimented intractable petrous apex cholesteatoma. Operative procedure combined trans-sphenoidal approach can maintain debris drainage, and observe lesion from sphenoid sinus. This therapy would lead to the future complications prevention.

O03-6

## Endoscopic Trans-Canal Management of Pediatric Congenital Cholesteatoma

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Background: Endoscopic Ear Surgery (EES) has become one of the most influential methods to deal with cholesteatoma. The goal of this paper is to discuss the feasibility of Endoscopic Trans-Canal Management of Congenital cholesteatoma in pediatric patients.

### Case Presentation:

Case 1: The first case is a 5 y/o girl. She came for help because of left side hearing impairment. She had no prior history of otitis media and the left ear drum was intact with a hidden white shadow beneath post-superior quadrant. The Audiometry shows a conductive hearing loss on the left ear. And the High resolution temporal bone tomography (HRCT) revealed a soft tissue mass filled in the attic and post-superior quadrant of tympanic cavity. Then the total trans-canal endoscopic ear surgery (ESS) was performed, elevating the tympanomeatal flap, drilling out the scutum, removing the cholesteatoma and decayed incus concomitantly. Since the supra-structure of stapes was also absent, we rebuilt the scutum and ossicle chain simultaneously with a piece of tragal cartilage and TORP (4mm, polycel).

Case 2: The second case is a 9 y/o girl, who had received postauricular approach, microscopic Atticotomy 5 years ago to eradicate the congenital cholesteatoma in the posterior half of middle ear. Unfortunately, during the 5-year follow-up, a white mass behind the intact ear drum was found. And the HRCT also revealed a soft tissue mass in the post-inferior quadrant of tympanic cavity. This time we adopted total trans-canal endoscopic ear surgery (ESS) to remove the recurrent cholesteatoma thoroughly.

There are no complications after the surgeries and these patients were followed up for months with excellent clinical appearance and hearing improvement.

Conclusion: In Taiwan, Most of the congenital cholesteatoma appears in the posterior half of the middle ear where contains a lot of hidden recesses and are difficult to deal with via Microscopic trans-canal approach. Endoscopic ear surgery was proved to be a satisfying alternative to the traditional microscopic surgery in the management of congenital cholesteatoma even in pediatric patients. However, the challenge is that one-hand surgery is more skillful and needs more practice.

O03-7

## Lateral attic cholesteatoma with intact ossicular chain: long-term safety of limited atticotomy with ossicular chain preservation

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**Objective:** Advances in technology have enabled early diagnosis of middle ear cholesteatoma which previously could not be identified until huge damage is done. In our experience, increasingly new cases have been found to be small and localized in the lateral attic with an intact ossicular chain. The study aimed to determine the long-term anatomical safety of limited atticotomy with ossicular chain preservation.

**Method:** During a 17-year period (1993 - 2010), we reviewed 26 cases of lateral attic cholesteatoma with intact ossicular chain. None of them had previous mastoidectomy for chronic otitis media with or without cholesteatoma. The middle ear mucosa was intraoperatively assessed as normal in all cases. The intention of the surgery was to completely remove the disease without ossicular chain interruption. Conchal cartilage was used for attic reconstruction. All of the surgeries were performed by Dr. Lien. Surgical success was defined as a recidivism-free condition at last visit.

**Results:** Of the 26 eligible cases, 22 (85%) were included in this study, and 4 were excluded due to lost to follow-up. The mean age at the time of surgery was 38 years (range 11-67 years). The mean follow-up period was 13 years (range 4-21 years). Twenty (91%) ears had a follow-up period of 5 years or longer, 15 (68%) ears 10 years or longer, and 10 (45%) ears 15 years or longer. Eardrum perforation was observed in 2 ears (9%), 4 and 15 years after surgery, respectively. During a 13-year observation, eardrum retraction or disease recidivism was not identified in any of the patients.

**Conclusion:** In lateral attic cholesteatoma with intact ossicular chain, our long-term evidence supports that limited atticotomy with ossicular chain preservation would not compromise the anatomical outcome. Further investigation is warranted to clarify the reservation of acoustic transmission function in a long-term manner.

**Paper 4** Rhinology 1

**O04-1**

**Real-time Ultrasonography Imaging during Nasal Endoscopic Transsphenoidal Surgery**

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**Objectives:** Pituitary tumors are commonly treated by nasal endoscopic transsphenoidal surgery (TSS). However, the navigation systems used during surgery does not provide real-time information. The objective was to obtain clear real-time images of the pituitary tumor and carotid arteries during nasal endoscopic TSS using ultrasonography (US).

**Case 1:** A 59-year-old Japanese man presented with bilateral visual impairment and tunnel vision. A pituitary gland tumor was diagnosed, and nasal endoscopic TSS was performed. After the nasal septal cartilage and vomer were partially removed, the US probe was extended to contact the tumor surface and the left and right carotid arteries and the pituitary gland tumor were clearly visualized. The clarity of the US image was enhanced when the sphenoid sinus was filled with physiological saline. Histopathological analysis of the resected specimen revealed a pituitary adenoma.

**Case 2:** A 72-year-old Japanese man presented with narrowing of visual acuity in both eyes. Pituitary gland tumor was diagnosed, and nasal endoscopic TSS was performed. The US image clearly showed bilateral carotid arteries and the pituitary gland tumor. The size of the tumor decreased at the end of the surgery.

**Case 3:** A 40-year-old Japanese woman presented with visual impairment in both her eyes. Cyst formation in the pituitary gland tumor was clearly visualized on the US image.

**Case 4:** A 40-year-old Japanese man developed narrowing of visual acuity in his left eye. He was diagnosed with a pituitary adenoma cyst. Both carotid arteries and a pituitary gland tumor were clearly visualized. The US image also showed cyst formation in the tumor. The adenoma was totally resected via US.

**Results:** US conducted during nasal endoscopic TSS can be used to avoid damage to the carotid arteries and to show the extent of tumor penetration. Doppler US imaging is particularly useful for visualization of the arteries.

**Conclusion:** Clear real-time US images of the pituitary tumor and the carotid arteries can be obtained during nasal endoscopic TSS. US imaging is a promising technique for tumor resections at the base of the skull, which are performed via the nasal endoscopic approach.

**O04-2**

**Clinical study of 56 cases of sinonasal inverted papilloma**

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**Introduction:** Inverted papilloma (IP) is a benign but locally aggressive tumor that originates from sinonasal epithelium. It is estimated to represent 0.4% to 4.7% of all surgically removed nasal tumors. According to some reports, the recurrence rate is about 15% to 20%, and the rate of malignant association is approximately 10%. The only treatment of IPs has been complete operative resection. The introduction of new endoscopic sinus surgical techniques and improvements in radiological studies led to a trend toward endonasal endoscopic excision. We report our institution's experience with the operative treatments of IP during about 10 years.

**Material and method:** 56 patients were diagnosed with sinonasal IP treated between 2004 and 2013 at Juntendo university hospital. We performed a retrospective analysis of these 56 cases. The basic surgical concept such as tumor debulking, subperiosteal dissection plane, and underlying bone drilling continue to be the mainstay of our surgical procedures. Concretely we performed attachment-oriented endoscopic surgery.

**Result:** The subjects consisted of 47 male and 9 female, with a mean age of 60.7 years.

The mean follow-up was 30.7 months. All patients had been treated by surgical procedure. 44 patients had a first treatment and 12 patients had a history of previous nasal surgery. According to Krouse's staging system 44 new treatment patients were classified as T1 in 3 cases, T2 in 27 cases, T3 14 cases. Recurrences were noted in 3 cases. Of the 56 cases, 52 patients were resected with purely endoscopic technique and 3 patients were resected with open procedure. One patient had synchronous malignancy. Among the 56 patients, 3 (5.3%) had recurrence, with the mean time to recurrence at 18 months. The recurrence rate in the 2 patients who had performed a previous surgery for IP was 16.6%, and was 2% in the 1 patient who had no previous surgery.

**Conclusion:** The recurrence rate in the 2 patients who had performed a previous surgery for IP was 16.6%, and was 2% in the 1 patient who had no previous surgery. Because secondary cases had high recurrence rate, first complete resections were most important things for IP treatment.

O04-3

## Invasive Nasal Septal Aspergillosis

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**Objective:** We report an unusual case of invasive aspergillosis related nasal septal perforation, without involvement of the paranasal sinuses.

**Case Report:** A 76-year old man with diabetes presented complaining of progressive nasal pain for one month. Sinusoscopic examination revealed a dry necrotic mass occupied the inferior part of nasal septum. The paranasal magnetic resonance imaging demonstrated that there is no soft tissue mass of the paranasal sinuses, except thinning of the inferior nasal septum. The patient underwent endoscopic resection of the mass lesion and its surrounding tissues, during which an irregular eroded hole of the inferior nasal septum was found. Histopathological examination revealed fungal infection with tissue destruction and necrosis. Septate hyphae of acute angle branching like *Aspergillus* species were identified by the Periodic acid-Schiff stain.

**Conclusion:** Aspergillosis of the nose and paranasal sinuses has been found that four forms: allergic aspergillus sinusitis, aspergilloma, invasive aspergillosis and fulminant aspergillosis. Invasive aspergillosis typically seen in debilitated or immunocompromised patients is a slowly progressive but destructive infection. A malignant neoplastic process is usually suspected until biopsy confirms the diagnosis. Management of both fulminant and invasive aspergillosis requires systemic antifungal treatment and surgery. Although a survey of the reports in the literature indicated that the occurrence of isolated nasal septal perforation is a rare complication of invasive fungal sinusitis, it should be considered in the differential diagnosis of sinunasal pathology.

O04-4

## An unexpected route for otolaryngology bacterial contamination with a Venturi atomizer

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**Background:** The Venturi-principle atomizer is a commonly used device in otolaryngology practices. The purpose of this study is to evaluate the possible route of bacterial contamination from the nasal vestibule to the atomizer tip through the jet airflow created during the use of the Venturi atomizer.

**Methods:** Thirty nostrils from 15 enrolled volunteers were tested. The aerosols generated by spraying sterilized saline into the nostrils were collected using a specially made aerosol-collecting nozzle cap. The collected samples were sent for bacterial culture, and nasal vestibular swab cultures were performed for comparison.

**Results:** In the aerosol-exposed group, 18 out of 30 samples (60%) were positive for bacterial growth, confirming the bacterial contamination from the nasal vestibule to the atomizer tip through the reverse jet airflow. The bacteria species in 8 of the 18 positive samples were identical to those from the nasal swab culture results from the same nostril.

**Conclusion:** In ordinary otolaryngology practices, there are significant risks for bacterial contamination from the nasal vestibule to the tip of the Venturi atomizer even without direct contact. Clinicians must be more aware of this pattern of contamination, which has not been reported in the existing literature.

O04-5

## Ethnic Variation in Paranasal Sinus Anatomy

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### INTRODUCTION

London is widely recognised as one of the most ethnically diverse cities in the world. In the 2011 Census, of the population of 8,173,941, 59.8% classified themselves as 'White' (including English, Scottish, Irish and others), 18.4% as Asian (Indian, Pakistani, Bangladeshi, Chinese etc) and 13.3% as 'Black' or of 'Afro-Caribbean' origin.

The aim of our study is to assess whether there is a significant variation in the paranasal sinus anatomy between the most common ethnic groups undergoing Functional Endoscopic Sinus Surgery (FESS) at Guy's and St Thomas' Hospital.

### METHOD

The most common population groups were identified by the 2011 Census data. We assessed all patients who underwent FESS between August 2013 and 2015. Of those with their ethnicity recorded, 73.44% were white, 17.05% Black and 4.59% Asian. Consecutive pre-operative CT sinus scans were assessed for variations in: ethmoid sinus height, measured from fovea ethmoidis; Keros classification and angle of lateral lamella to fovea ethmoidis. Patients who were excluded included those without ethnicity data, with gross abnormalities or who had undergone previous sinus surgery.

### RESULTS

White patients had the highest asymmetry between left and right ethmoid heights (average 9.1mm vs 5.1mm for Black patients and 3.9mm for Asian patients). There was no significant difference between left and right asymmetry for Keros classification. The majority of White and Black patients were classified as Keros type 2. Asian patients had the highest proportion of Keros type 3 patients (approximately 40%). Average ethmoid sinus height was 29.00mm, 30.71mm and 32.54mm for White, Black and Asian patients, respectively with a Standard Deviation of 1.45. Similarly, average lateral lamella height was 4.76mm, 5.21mm and 6.72mm, respectively with a Standard Deviation 0.84.

### CONCLUSION

Some previous studies have shown significant differences when comparing variation in paranasal sinus anatomy. However, none have specifically assessed the population groups found most commonly in the Greater London area. Appreciation of variations in the anatomy of the ethmoid roof that can occur in different patient populations is important for an ENT surgeon in order to minimize the risk of complications in Functional Endoscopic Sinus Surgery.

O04-6

## Nasal Plasmid Flt3 Ligand And CpG ODN Alone Enhances Immediate, Influenza Virus-Specific Recall Secretory IgA Ab Responses

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Due to the progress of aging society, health care of elderly including vaccination becomes an important issue. The elderly have already experienced various pathogens and thus possess pathogen-specific Abs, whose titers are too low to combat reinfection. Thus, it would be of great benefit to the aged population if one could use an innate adjuvant system alone, without vaccine, in order to enhance mucosal immunity against past respiratory infections. We tested whether a combined plasmid Flt3 ligand (pFL) and CpG ODN adjuvant would enhance influenza virus-specific recall Ab responses without a need for additional vaccination. Young adult mice were nasally immunized with A/Puerto Rico/8/34 (PR8) hemagglutinin (HA) plus cholera toxin as mucosal adjuvant three times at weekly intervals. Seven months later, these mice were given nasal pFL and CpG ODN only or combined adjuvant together with PR8 HA. Saliva and plasma samples were collected two weeks later and PR8 HA-specific IgA Ab responses were evaluated. Both groups of mice showed significantly increased and comparable levels of anti-PR8 HA secretory IgA Ab responses in saliva when compared with those responses seen without innate adjuvant. The increase in total IgG Ab responses in mice given pFL and CpG ODN were limited when compared with those seen after primary nasal immunization. Total plasma IgE Ab titers in mice given nasal pFL and CpG ODN only were essentially the same as IgE levels seen in naive mice. These results suggest that nasal pFL and CpG ODN alone can enhance pre-existing Ag-specific Ab responses without adverse effects in the elderly.

**Paper 5** Laryngology 1

O05-1

**The contribution of the retrotrapezoid nucleus/parafacial respiratory group to the regulation of coughing and swallowing in guinea pigs**

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The laryngeal muscles function as a part of respiratory system under normal conditions, contributing to the regulation of the airflow during breathing. This respiratory regulation of the larynx is controlled by the respiratory neuronal circuits in the brain stem. On the other hand, the network organization that controls the laryngeal motoneurons can change in order to produce the non-respiratory behaviors such as the airway protective reflexes, such that the larynx can successfully achieve the multifunctional motor control. The airway protective reflexes including coughing and swallowing are generated by the specific neuronal circuits in the brain stem, which possibly include the respiratory neuronal networks. Indeed, many respiratory neurons in the brain stem altered their activity in synchrony with these behaviors, participating in the generation of these reflexes. The retrotrapezoid nucleus/parafacial respiratory group (RTN/pFRG) located ventral to the facial nucleus plays a crucial role in the regulation of active expiration caused by enhanced expiratory muscle activity under hypercapnia. In order to clarify the roles of the RTN/pFRG in generating these non-respiratory behaviors, during which the expiratory activity drastically changes, we analyzed the motor output patterns of the laryngeal and respiratory nerve activities during coughing and swallowing before and after brain stem transection at the rostral and caudal margins of the RTN/pFRG region in decerebrate paralyzed guinea pigs. The cough-related activity patterns of those nerves were preserved after removal of the RTN/pFRG, although the cough-related abdominal nerve activity was attenuated by the transection at the caudal most level of the RTN/pFRG. In addition, the swallowing-related recurrent laryngeal nerve activity was elicited by stimulation of the superior laryngeal nerve after the caudal level transection. These findings imply that the RTN/pFRG could have a minor contribution to the generation of coughing-induced active expiration, but may not be included within the core networks involved in coughing and swallowing.

O05-2

**PEAK Plasma Blade as one of the choices for excision of distal tracheal obstructive granulation in patients following tracheostomy**

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Tracheal granulation is one of the common long term complications in patients with tracheostomy. Hypertrophic tracheal granulation may cause airway obstruction and further operation may be needed for re-creating airway. Distal tracheal granulation is clinically troublesome due to its position and surgical field limitation. This is a retrospective case review study to evaluate the outcomes of PEAK plasma Blade assistant tracheal surgery in patients with distal tracheal granulation. 11 patients who accepted PEAK assistance tracheal surgery were reviewed. The average operation time is 112 minutes. NO intraoperative complication was met among all the patients. 100% of patient free of recurrent granulation over 6 months. PEAK assistance tracheal surgery is one of the choices for the treatment of distal tracheal granulation or tracheal benign lesion. Besides, it is also a useful alternative for patients who have difficulties of opening mouth and neck extending position.



O05-3

## Preliminary Experiences in Trachea Scaffold Tissue Engineering with Whole Organ Decellularization

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### Objective

Ideal methods for reconstructing the tracheal structure and restoring tracheal function following damage to or removal of the trachea have not been developed. The purpose of this study is to evaluate the feasibility of using a whole segment decellularized tracheal scaffold to reconstruct the trachea.

### Study Design

Prospective experimental design.

### Setting

In vivo rabbit model.

### Methods

Trachea scaffolds were created using our previously developed freeze-dry-sonication-SDS (FDSS) decellularization process. After histological and mechanical testing, the scaffolds were transplanted orthotopically into segmental defects in New Zealand White Rabbits (n=9). Two weeks after transplantation, the grafts were evaluated endoscopically and histologically.

### Results

The mechanical properties of the decellularized trachea segment did not differ significantly from the fresh native trachea (Max. resisting strength  $327.8 \pm 125.30 : 440.1 \pm 141.86$  kPa,  $p=0.36$ ; Young's modulus  $1.54 \pm 0.655 : 1.39 \pm 0.539$  MPa,  $p=0.77$ ). After transplantation, whereas the autograft in the control group showed full integration and functional recovery, all of the rabbits in the decellularized scaffold transplantation group died within 7~24 days. Although significant collapse of the tracheal tubular structures were noted, full respiratory epithelium regeneration was also observed in the rabbits that survived more than two weeks.

### Conclusion

The FDSS decellularization process is effective in creating whole segment decellularized trachea scaffolds. However, although the respiratory epithelium regeneration on the inner surface appeared to be satisfactory, the tubular structures were not able to be maintained after transplantation, which ultimately led to the death of the animals.

O05-4

## Evaluation of Outcomes after Endoscopic Management of Paediatric Subglottic Stenosis

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### OBJECTIVE:

To evaluate the outcomes and any adverse events related to endoscopic surgical management of paediatric subglottic stenosis.

### METHODS

All patients who had undergone microlaryngoscopy and bronchoscopy (MLB) between 2012 and 2014 with at least 6 months follow-up were evaluated. Their electronic medical records were reviewed to identify those who had undergone balloon dilatation. We evaluated treatment outcome using the NICE audit tool (interventional procedure guidance 425).

### RESULTS

A total of 48 MLB and endoscopic balloon dilatations in 22 patients were identified. 3 patients were excluded from analysis due to insufficient information. 74% of patients had acquired subglottic stenosis secondary to intubation (n=14) and 26% of patients had congenital stenosis (n=5). The average number of dilatations per patient was 2.52. No adverse events were reported in our case series. Symptomatic improvement after primary procedure not requiring further intervention was recorded in 37% of patients (n=7). 42% of patients required 2 balloon procedures before adequate improvement in symptoms (n=8) and 21% required 3 procedures (n=4). Over the three-year period, 3 patients required re-intubation post-operatively, all for respiratory distress. Of these, 2 were successfully extubated after 24 hours. 1 patient required unplanned repeat dilatation due to failure to extubate.

### CONCLUSION

Endoscopic techniques have an increasing role in the literature in the management of paediatric subglottic stenosis. However, concerns have been voiced regarding failure and complication rates. This case series has demonstrated endoscopic balloon dilatation to be a feasible and reliable technique when compared to more invasive surgical approaches such as laryngotracheal reconstruction.

O05-5

## Postoperative swallowing and survival in multiple system atrophy

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### Background:

Patients with multiple system atrophy (MSA) may require a surgical management such as tracheostomy and laryngeal closure due to the progression of disease, including severe dysphagia and respiratory disorder. Only a few reports have discussed the relationship between dysphagia and vocal cord abductor paralysis (VCAP), as well as postoperative feeding in MSA patients, and few studies have investigated the postoperative clinical course of MSA patients. The aim of this study is to describe the management strategy for dysphagia and respiratory disorder in MSA.

### Methods:

From 2001 to 2014, 18 MSA patients (13 males and 5 females) underwent tracheostomy (TR), laryngeal closure (LC) or both. Their age ranged from 52 to 76 years old (mean 64 years). Vocal fold movement impairment, the degree of dysphagia and pre/post-operative oral ingestion, the duration between the onset of dysphagia or dyspnea and surgery, and postoperative survival time were evaluated retrospectively. Swallowing function was assessed using the penetration aspiration scale (PAS).

### Results:

TR and LC were performed in 11 and 12 patients, respectively. Five patients underwent LC after TR. TR was performed due to respiratory disorder in 7 patients and due to dysphagia in 4 patients. Preoperatively, 11 patients had severe dysphagia and 15 exhibited bilateral vocal cord fixation in a median position (severe VCAP). PAS scores ranged 1-8 in TR patients and 7-8 in LC patients. Seven of 11 patients who underwent TR displayed worsened PAS scores, and no patients displayed improved PAS scores following TR. All patients who underwent LC regained complete or partial oral intake after surgery. The period from the onset of MSA to TR or LC ranged from 3 to 145 months (median 64.5 months). There were no significant differences in postoperative survival time between the two groups.

### Conclusions:

In MSA patients, TR sometimes negatively influenced swallowing, while LC enabled them to take food orally, regardless of the severity of preoperative dysphagia. Considering the impacts of TR and LC on survival time, postoperative feeding and swallowing, LC is a good option for treating MSA patients with dysphagia.

O05-6

## The results of Kaplan-Meier and multivariate analyses of etiological factors related to the outcome of combined pharmacological therapy against laryngeal granuloma

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**Objectives:** To assess the effects of the combined usage of an inhaled corticosteroid plus oral tranilast administration and/or a proton pump inhibitor on the size of granulomatous lesions, and to reveal the etiological factors related to the outcome using the Kaplan-Meier method and a subsequent multivariate analysis. The factors examined included the gender, age, gastroesophageal reflux diseases (GERD), tracheal intubation, habitual intensive vocal fold collision and habitual cigarette smoking. **Methods:** sixty-two patients with laryngeal granuloma (male: 42; female 20, median age: 58 years old; range: 23-81 years old) were enrolled. All patients were initially evaluated based on their medical history including their history of surgery under general anesthesia, ventilator use, laryngeal abnormal laryngeal sensation (irritation, lumps), typical reflux symptoms (heartburn, belch, regurgitation), habitual intensive vocal fold collision (cough symptom, voluntary throat clearing, the use of a loud voice) and habitual cigarette smoking (the Brinkman index of more than 100). With regard to GERD-associated laryngeal signs, using a rigid-type laryngoscopy, we noted the presence of only three points for the inflammatory status of the Reflux Finding Score: the arytenoid, vocal folds and subglottis. An inhaled corticosteroid plus tranilast (300mg/day) and rabeprazole (20mg/day) were administered to all of the patients, and only to those diagnosed to have GERD, respectively. The size of granulomatous lesions was measured for each patient at the initial visit and every four weeks. Subsequently, at 48 weeks, the Kaplan-Meier plots for lesion disappearance rate were compared between groups with and without each of the etiological factors, followed by Cox proportional-hazards regression. **Results:** Almost all of the patients showed a progressive decrease in their lesion size during the 48 weeks after the start of pharmacological therapy. The lesion disappearance rates for the whole population 48 weeks after the start of pharmacological therapy were 82.3%. Although the prevalence of GERD-related laryngeal findings and tracheal intubation showed a significant gender difference, the Kaplan-Meier analysis exhibited significant differences between patients separated by GERD diagnosis, habitual intensive vocal fold collision and smoking. Only GERD were identified as an independent etiological factor affecting the resolution of the lesion by a multivariate analysis using Cox's proportional-hazards regression. **Conclusions:** The present results indicate that the existence of GERD is an independent etiological factor predicting retardation of the resolution of laryngeal granuloma, suggesting that lifestyle modification as well as the administration of gastric acid-secretion inhibitor is required for early resolution of laryngeal granuloma.

O05-7

## How to make a permanent tracheostoma to prevent postoperative complications

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Safe creation of a permanent tracheostoma during total laryngectomy is important. Ischemia or necrosis at the tracheal end often causes severe problems, including stenosis, infection, carotid artery exposure, and the need for repeat surgery. It is a particularly important concern for patients undergoing salvage procedures after concurrent chemoradiotherapy. Here, I would like to describe some techniques that will aid in preventing complications. First, the blood supply to the trachea should be carefully preserved. The thyroid lobe should be spared not detached from the tracheal end, if possible. The branch of the inferior thyroid artery supplying the trachea can be preserved by meticulous paratracheal dissection. The perichondrium of the trachea should not be peeled off, and the fat tissue anterior to the trachea can be preserved in cases of hypopharyngeal cancer. Second, any tension between the skin and trachea should be released during suturing; the tracheal end should not be pulled up and the cervical skin flap should not be pulled down for suturing. If the cervical skin flap is pulled down, it often results in the creation of a dead space in the submental region and increases the risk of pharyngeal fistula formation. The anterior chest skin flap should be adequately elevated. Cutting off the clavicular head obliquely and the placement of anchor sutures for approximating the anterior chest skin flap with the periosteum of the clavicular head is one of the best ways to release tension. Finally, the suture technique should be appropriate. The skin flap is always de-epithelized according to the shape of the tracheal end. The placement of subcutaneous buried sutures to approximate the skin with the tracheal end is a useful technique. The tracheal cartilage must not be uncovered. After suturing, it is important to pick up the skin around the sutures and confirm minimum tension.

## Paper 6 Oral Cavity

### O06-1

#### How to trim uvula undergoing uvulopalatopharyngoplasty for sleep apnea patients

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UPPP(uvulopalatopharyngoplasty) is an effective surgical therapy for sleep apnea to enlarge pharyngeal space, however, it may cause scar formation as a recurrent complication. Recent reports suggested that additional Z-plasty was available to avoid the issue. In some UPPP reports revealed incision of uvula for Z-plasty.

The uvula is a highly sophisticated structure, capable of producing a large quantity of fluid saliva that can be excreted in a short time. The musculus uvulae, which lies entirely within the uvula, shortens and broadens the uvula. This changes in contour allows the soft palate to adapt closely to posterior pharyngeal wall to help close the nasopharynx during swallowing or vocalizing. Thus losing uvula may cause dis-function of swallowing or vocalizing.

We divided our surgical plans to three groups, completely leave uvula(group A), remove 50%(group B), and 75%(group C). Twelve months result of 8 cases will be presented. Although cases is not enough to conclude, it seemed group B might be the best treatment as from it remained shape.

Since uvula plays an important role in swallowing or vocalizing, and the issue is rarely discussed, we would like to ask frank suggestion or discussion.

### O06-2

#### Carotid intima-media thickness measurement for cardiovascular risk assessment in obstructive sleep apnea and post neck radiation

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##### Background

Patients who underwent radiation therapy (RT) or with obstructive sleep apnea (OSA) are associated with increased the risk of cardiovascular disease (CVD). The aim of this study is to measure the carotid intima-media thickness (CIMT) and the CVD risks in patients with OSA, or post neck irradiated patients comparing to normal adults.

##### Material and methods

The ultrasound was performed with Toshiba Aplio MX (Tokyo, Japan) using a 7-18 MHz broad band linear array transducer. We defined CIMT as the distance from the front edge lumen-intima interface to the media-adventitia interface in the far wall of the vessels. CIMT distal to the carotid bifurcation (CCA), bulb, and internal carotid artery (ICA) were measured bilaterally manually. The presence of any carotid plaque was also recorded. Patients were considered at high risk for developing CVD when the mean CIMT (CCA, bulb, ICA) is >75th percentile for normal adults or in the presence of a carotid plaque. The means CIMT among normal adult, OSAS and post irradiated patients were compared with ANOVA tests. A univariate and multivariate logistic regression models were used to test significant predictors for high risk of CV events.

##### Results

From Jan to July 2015, 21 normal adult, 20 post irradiated cancer patients and 21 OSA patients were recruited. The mean CIMT were 0.75±0.14 (mean±SD), 1.19±0.36 and 0.83±0.19 mm for post RT, OSA and normal adults, representatively. The mean CIMT of post RT patients was significantly thicker than that of OSA patients and normal adults (p<0.05 in ANOVA test). The 75th percentile for normal adults was 0.83 mm and set as a cut-point for high risk of CVD. 95% (19/20) in post RT patients; 52% (11/21) in OSA patients were high risk for CVD. After adjustment with gender, age, and hypertension; post RT patients (12.37, 3.16~48.4, p<0.01) and OSA patients (3.11, 1.80~9.68, p=0.05) were still significantly predictors for high CV risk.

##### Conclusions

CV risks were higher for post RT and OSA patients than normal adults. Ultrasound can help to identify the patients at high risk and may lead to more effective prevention in CV events.

O06-3

## Positional therapy for treatment of snoring in non-obese patients with positional obstructive sleep apnea syndrome

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Sleep position can play a role in the pathogenesis of obstructive sleep apnea syndrome (OSAS). However, clinical significance of position therapy remains unclear. To investigate the effect of position therapy using a head-positioning pillow (HPP) and impact of body weight status on reducing snoring sounds in patients with mild-to-moderate positional OSAS, 25 adults with polysomnography-confirmed positional OSAS (apnea-hypopnea index [AHI]  $\leq 30$  and an AHI in supine position: AHI in non-supine position  $\geq 2$ ) were prospectively enrolled. The patients were asked to use their own pillows at home on the first night (N0), and the HPP on the second and third nights (N1 and N2). The primary outcome measures were snoring severity (SS; visual analogue scale, 0-10) and snoring index (SI; the number of snoring events per hour), which were recorded for three consecutive nights. Median SS significantly decreased from 5.0 to 4.0 (N0 versus N2), and median SI significantly decreased from 218.0 to 115.0 in the whole study group. Although the overweight group had a significantly improved SS, the reduction in SI was not statistically significant. In contrast, the normal-weight group had both significantly improved SS and SI. Long-term effectiveness of the HPP remains unknown and warrants further study.

O06-4

## Assessing the Standard of Practice in Performance of Tonsillectomies at a Central London Teaching Hospital

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### INTRODUCTION

Here we present a multi-faceted project of 268 adult patients who underwent a tonsillectomy between 2014 and 2015 at Guy's and St Thomas' Hospitals, London.

Patients were assessed for:

1. Indications for surgery against National Guidelines
2. Post-Operative re-bleed rates against National Prospective Tonsillectomy Audit (NPTA) (2005) rates
3. Adherence of Operation Notes to Royal College of Surgeons Guidelines (2008)

### METHOD

268 patients' electronic medical notes were reviewed for operation notes, details for re-admissions, complications and re-bleeding. Referral letters were reviewed for indications for surgery.

### RESULTS

268 patients underwent tonsillectomy, with an average age of 30 (age range 17 to 62). 47 were performed with an additional procedure: 76.60% UPPP, 12.77% adenoidectomy, 10.63% other. 64.02% of patients underwent tonsillectomy for recurrent tonsillitis, 14.77% for obstructive sleep apnoea, 7.95% for snoring, 6.06% for quinsy and 7.2% for others including tonsiloliths. Of the 169 patients with recurrent tonsillitis, only 44% had the number of episodes and duration recorded with 90.54% adhering to the SIGN National Guidelines.

Operation notes were assessed against 18 different criteria which are recommended by the Royal College of Surgeons' 'Good Surgical Practice' (2008) and The NPTA (2005) recommendations. Documentation of these criteria were present in operation notes between 1.67% and 100% of the time, with no single operation note recording all of the recommended criteria.

Of the 268 patients who were assessed, 1 patient suffered a primary haemorrhage and 30 patients were recorded as having secondary post-operative haemorrhages. This represents a 0.37% primary bleed rate (compared to 0.6% from the NPTA). However, the secondary haemorrhage rate was 11.19%, 373% higher than the nationally reported rate of 3%. Bleeding occurred an average of 6.23 days after surgery (range 2 to 15 days). 5 patients (16.67%) returned to theatre for further surgery and 1 (3.33%) received a transfusion. Additional complications included long-term change to sense of taste, ongoing post-operative pain and nasal regurgitation. The prescription of post-operative antibiotics was shown to have no significant effect on post-operative haemorrhage (73% vs 27%,  $p = 0.5$ ).

### DISCUSSION

While our post-operative haemorrhage rates were significantly higher than the NPTA rates, we did assess only adult patients; who have a higher risk of postoperative haemorrhage. However, given the significant difference we have begun a prospective cohort study comparing adult intra-capsular coblation tonsillectomies to standard bipolar dissection tonsillectomies.

O06-5

## Analysis of regional post-tonsillectomy bleed data and evaluation of a newly introduced tonsillectomy operation record: A quality improvement project at the Northwest London Hospitals

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### Objectives:

The main objectives of this audit and quality improvement project were to (1) to retrospectively analyse regional post-tonsillectomy haemorrhage data, (2) to introduce a new electronic tonsillectomy operation record and (3) to evaluate and validate its use and usefulness in improving documentation.

### Material and methods:

The retrospective audit component and the prospective audit and quality improvement component were carried out at the Northwick Park Hospital and Central Middlesex Hospital. 642 tonsillectomy records (2012-2014) were reviewed and documentation as well as various factors in relation to post-tonsillectomy haemorrhages were analysed. Documentation before and after the introduction of (a) a new paper-based and (b) electronic surgical record proforma was reviewed (2014-2015).

### Results:

Over a two year period 62 of the 642 (9.7%) audited tonsillectomy patients had a post-tonsillectomy haemorrhage and 19 of these (2.9%) had to return to theatre for surgical arrest of the haemorrhage. Bipolar diathermy was the most commonly used technique. During this period documentation in the surgical operation notes was limited in the majority of cases and significantly improved after the introduction of the paper-based proforma. The compliance was further improved after the introduction of an electronic version.

### Conclusion:

The introduction of the electronic tonsillectomy surgical proforma which replaced operation notes for tonsillectomies at Northwest London Hospitals has significantly improved documentation. This will allow a concise and detailed re-audit which is subject to further study. Based on these findings we suggest that proformas incorporated in the electronic medical record system shall be evaluated for other operation in the region to further increase the compliance with concise documentation.

O06-6

## Deglutition and Respiratory Patterns During Sleep in the Aged

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**Objectives:** Deglutition is a vital function, and the clearance of the pharynx by deglutition, which removes matter that could be aspirated, is important in protecting the airways and lungs against aspiration. Certain clinical disorders, such as reflux-related and aspiration-related diseases, may be related to nocturnal deglutition. Recently aspiration pneumonia has become an important cause of death in the aged. There have been some investigations into deglutition during sleep in human adults (Lear et al, 1965) (Lichter et al, 1975) (Sato et al, 2006, 2011), and children (Sato et al, 2007). However, deglutition and respiratory patterns during sleep in the aged are not clear. The deglutition, electroencephalographic arousal and respiratory phase patterns during sleep in the healthy aged were investigated in this study.

**Methods:** Ten aged adults (average age 71) were examined via time-matched digital (computed) recordings of polysomnography and surface electromyography of the muscle (thyrohyoid and suprahyoid muscles) related to swallowing.

**Results:** During sleep, swallowing was infrequent and absent for long periods. The mean number of swallows per hour during total sleep time was 0.8 and the mean longest deglutition-free period was 135 minutes. Most deglutition occurred in association with spontaneous electroencephalographic arousal both in REM (rapid eye movement) and non-REM sleep.

Deglutition was related to the sleep stage. The deeper the sleep stage, the lower the mean deglutition frequency. There was no deglutition during deep sleep. Overall muscle tone during REM sleep was inhibited and surface EMG amplitude dropped to its lowest level of recording during REM sleep. However, deglutition also occurred in association with spontaneous EEG arousal as frequently as in non-REM sleep stage 2. The deeper the sleep stage, the lower the mean arousal frequency, and the lower the mean ratio of arousal with deglutition to arousal. Approximately 39% of swallows were followed by expiration, 34% were followed by arrested breathing and 28% were followed by inspiration.

**Conclusion:** Deglutition was infrequent and displayed unique patterns during sleep in the aged. Sleep-related deglutition may adversely influence aspiration-related (aspiration pneumonia, etc) diseases in the aged.

O06-7

## Drug-induced sleep CT scan for obstructive sleep apnea patients

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**Purpose:** The purpose of this study is to identify the sites, direction and severity of airway obstruction during sleep using drug-induced sleep computer tomography(CT) scan for decision-making of surgical plan. By delicate identification of obstruction sites and tailor-made surgical treatment, it is expected to increase success rate, avoid unnecessary operation, and develop a new diagnosis and treatment model for OSA.

**Method:** The study plan to enroll 40 moderate to severe OSA patients who are intolerant or unwilling to CPAP therapy and seeking for surgical treatment. Subjects need to fit in with inclusion criteria and eliminate from exclusion criteria. After fully understanding the whole process and rights, they sign informed consent to be the study subjects. Subjects will be arranged to receive high-speed 320 CT scan during quiet respiration and then drug-induced (propofol) sleep CT scan of the upper airway under the monitor of sedation degree by bispectral index. Reconstructive image can provide a dynamic change in the levels of obstruction and demonstrate the direction and severity of collapse. Tailor-made multi-level surgical treatment for each subject is decided accordingly. The whole examination will be repeated 6 months after operation.

**Anticipatory results:** ① We anticipate that sleep CT scan can clearly show the obstruction levels and severity of airway. Besides, soft palate is presumed to be the most common obstruction site, followed by tongue base, lateral pharyngeal wall and supraglottis. Multi-level obstruction will be the majority in this study population (moderate to severe OSA) and combined supraglottic obstruction may exist only in severe OSA patients. ② Sleep CT scan is expected to display more obstructions in the tongue base, lateral pharyngeal wall and supraglottis that are usually ignored in physical examination and nasopharyngoscopy with Muller's maneuver. ③ Post-operative airway dimension is expected to be significantly increased when compared with pre-operative status and the enlargement of airway dimension are likely to be negatively correlated with the decrease of AHI.

**Clinical significance:** ① Sleep CT scan can observe sequence, direction, severity and interaction of airway obstruction, which is helpful in developing the mechanism of sleep apnea in OSA patients. ② Using the sleep CT scan as a standard, we can elucidate the difference in levels and severity of obstruction with physical examination / endoscopy. ③ The decision making of management based on the study is very likely to increase surgical success and develop a new assessment and treatment model.

## Paper 7 Otology 3

O07-1

## Mechanism of eosinophil infiltration to the inner ear in animal model of eosinophilic otitis media

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**Background:** Eosinophilic Otitis Media (EOM), which is first reported by Tomioka et al., is an intractable otitis media with eosinophil-enriched middle ear effusion associated with bronchial asthma (1993). EOM is known to be a high risk disease often involving severe sensory hearing loss, therefore it is important to clarify its etiology for the purpose of establishing the effective therapy. We have succeeded in constructing the model animal of EOM, and reported that the number of eosinophils infiltrating to the intratympanic space and middle ear mucosa increases as the period of inflammation prolongs (Nishizawa H, 2012). Additionally, we observed eosinophil infiltration to the inner ear, which damages the structure of the cochlear (Matsubara A, 2014).

**Objectives:** The purpose of the present study was to elucidate the mechanism of eosinophil infiltration to the inner ear through histological study of the sections from model animals. Immunohistological analysis was also performed for the chemokines which were considered to play a key role in eosinophilic inflammation.

**Methods:** We constructed the model animals of EOM by systemic and topical sensitization using Ovalbumin (OVA): after intraperitoneal injection of OVA, daily intratympanic injection was continued for 7days, 14days, and 28days. We examined the infiltrating cells in the inner ear and the extent of inner ear damage by histological study. In addition, the immunoreactivities for Eotaxin and RANTES were observed in the same specimens.

**Results:** In the inner ear of 7-day stimulation side, a few eosinophils were seen in the scala tympani, although no structural damage of inner ear was observed. In the 14-day antigen stimulation side, the number of eosinophils infiltrating to the scala tympani increased. In the 28-day stimulation side, we observed more inflammatory cells infiltrating to the perilymph than 14-day stimulation side, accompanied with severe morphological damage of the organ of Corti. The infiltrating cells contained eosinophils, lymphocytes, and plasma cells. Although no immunoreactivity for Eotaxin was seen in scala tympani, immunopositive cells were observed in the middle ear mucosa of both 7-day and 14-day stimulation side. The number of the immunoreactive cells increased in the latter. We observed similar tendency for the RANTES immunopositive cells in the middle ear mucosa.

O07-2

## Protective Effect of Astaxanthin Nano Emulsion in Hair Cells

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### Introduction

It was known that aminoglycoside induced hair cell death was related with the free radical generation. Many kinds of molecules can protect hair cells against aminoglycoside ototoxicity. Astaxanthin is a kind of carotenoid and provides the red color of salmon meat and the red color of cooked shellfish. Astaxanthin has the strong antioxidant activity. Therefore, the dietary supplement and cosmetics which contain astaxanthin were manufactured in many countries. However, Astaxanthin was difficult to transit to the living tissue, because the molecule is a lipophilic material. Nano nano emulsion of astaxanthin was developed in Fuji film company (Japan). The nano emulsion can diffuse into water and transit to the living tissue. In the present study, we evaluated the protective effect of nano emulsion of astaxanthin on the inner ear sensory cells against neomycin ototoxicity.

### Materials and Methods

Cultured utricles of CBA/N mice were used. Cultured utricles were divided to three groups (Control group, Neomycin group, Neomycin + Astaxanthin group). In the Neomycin group, utricles were cultured with neomycin (2 mM) to induce hair cell death. In Neomycin + Astaxanthin group, utricles were cultured with neomycin and Astaxanthin (100 - 1  $\mu$ M). Twenty-four hours after exposure to neomycin, the cultured tissues were fixed with 4% paraformaldehyde. To label hair cells, immunohistochemistry were performed using anti-calmodulin antibody. The rate of survival vestibular hair cells was evaluated with the fluorescence microscope. In addition, immunohistochemistry against 4-hydroxy-2-nonenal was performed to evaluate the product of hydroxy radical.

### Results

The survival rate of hair cells in Neomycin + Astaxanthin group was significantly more than that in Neomycin group. The signals of 4-hydroxy-2-nonenal were inhibited in neomycin + Astaxanthin group.

### Discussion

As the clinical effects of astaxanthin, the inhibition of diabetic complications, eye diseases, cancer prevention, and anti-fatigue action has been reported. In this study we showed that nano emulsion of astaxanthin protects sensory hair cells against neomycin-induced death in mammalian vestibular epithelium. The nano emulsion of astaxanthin can be used as the protective drug in the inner ear.



O07-3

## The sequential changes and cellular death forms of hair cells after transient cochlear ischemia in guinea pigs

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**Objective:** Perturbation of cochlear microcirculation is a one of the major causes of hearing impairment. The detailed cellular form after cochlear ischemia still remained to be elucidated. Therefore, we intended to examine the chronological morphological, functional, and molecular changes in the cochlea in the early stage following ischemia and reperfusion.

**Methods:** We developed an animal model of transient cochlear ischemia via ventral cervical approach in guinea pigs. The associated morphological, functional, and molecular changes in the cochlea were studied by rhodamine-coupled phalloidin staining and the TUNEL assay.

**Results:** A substantial amount of TUNEL-positive cells appeared at 12 h after 1-hour of transient cochlear ischemia, and then, significant hair cell loss followed, which may indicate the beginning of necrotic cell death.

**Conclusions:** Cochlear hair cells may exhibit both apoptotic and necrotic cell death after transient ischemia, in which apoptosis may precede the necrotic process.

O07-4

## An animal model for genetic lineage tracing of supporting cells after hair cell regeneration

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**Objective:** Damage of cochlear hair cells is usually permanent because hair cells do not regenerate in mammals. We have described a population of cochlear supporting cells that can act as progenitors for hair cells, and, therefore, methods to label and lineage trace supporting cells are important after genetic or pharmacologic manipulation to regenerate hair cells from supporting cells. In this study, we validate the inducible form of Cre using the estrogen receptor (ER) under the transcriptional control of the Sox2 promoter in a Sox2-Cre-ER genetic model for the study of hair cell generation from supporting cells. By crossing this mouse to an inducible tdTomato mouse, Sox2-expressing supporting cells are labeled.

**Materials and methods:** We crossed the Sox2-Cre-ER mouse to the tdTomato mouse. Upon Cre-mediated excision of a stop sequence this drove tdTomato reporter expression in Sox2-expressing supporting cells. Tamoxifen was administered twice to mothers of Sox2-Cre-ER-tdTomato litters at postnatal day (P) 0 or 2, for transfer to the pups via the milk. Cochleae were analyzed at P6 by immunohistochemical labeling of hair cells (myosin VIIa) and supporting cells (Sox2).

**Results:** Quantification of tdTomato reporter-positive supporting cells showed that over eighty percent of Sox2-positive supporting cells expressed reporter activity in all regions of the cochlea. Consistent with our previous results, reporter expression was also seen in hair cells in an apical-to-basal gradient: as we have reported, 50% of apical hair cells, 2.5% of mid-turn hair cells, and less than 1% of basal hair cells were positive for reporter when tamoxifen was injected at P0. When tamoxifen was injected at P2, less than 10% of apical hair cells and less than 1% of mid-turn and basal hair cells were positive for reporter expression.

**Conclusions:** Our data demonstrate that perinatal labeling of hair cells in the Sox2-Cre-ER model can be subtracted from treated samples and that the model is ideal for tracing cell fate of newborn cochlear supporting cells in studies of hair cell regeneration.

O07-5

## Mn-SOD affects Noise Induced Hearing Loss

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**Background:** The generation of reactive oxygen species (ROS) is thought to be one of the mechanisms underlying noise-induced hearing loss (NIHL). Manganese superoxide dismutase (Mn-SOD), one of the antioxidant enzymes acting within the mitochondria, converts toxic superoxide to hydrogen peroxide. To investigate the pathological role of mitochondrial antioxidant stress in the cochlea, we generated systemic Mn-SOD heterozygous knockout (HET) mice, and investigated hearing loss and hair cell damage after noise exposure. **Material and methods:** HET mice were generated by crossbreeding of homozygous Mn-SOD lox/lox mice with the chicken actin promoter-crd transgenic mice, and their littermate wild-type (WT) C57BL/6 mice were enrolled as controls (N=6, each). Both HET and WT mice were exposed to 120 dB SPL 4 kHz octave band noise, for 4 h. Animals in each group underwent measurements for auditory brain stem responses (ABR) before and 1h, 1, 3, 7, and 14days after noise exposure. At 14days after noise exposure, animals were euthanized for evaluation of cochlear pathology. The paraffin-embedded cochlear sections were stained with Haematoxylin and Eosin, and were analyzed for inner/outer hair cell survival rates in the basal, middle, and apical turns of the cochlea. **Results:** The mean ABR thresholds at all frequencies, particularly in 4 kHz, were significantly worse on post-noise days 7 and 14 in HET mice compared to WT, although both groups showed similar hearing loss 1h after noise exposure. Histologically, outer hair cell damage in HET mice were significantly greater in all turns, particularly in apical turns, compared with WT mice, whereas inner hair cell survival rates revealed only a slightly greater in the apical turn in HET mice. **Conclusion:** These findings suggest that Mn-SOD has important role to reduce ROS production in hair cell, thereby protecting from NIHL.

O07-6

## The effect of G-CSF for promoting regeneration of severed facial nerves in rats

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**Background:** In the treatment of severe facial paralysis with a high degree of Wallerian degeneration, it is ideal that the degenerated nerve fibers get to be regenerated as early and sufficiently as possible. Recently, administration of various drugs, such as growth factors and neurotrophic factors, have been tried experimentally as a new therapeutic strategy for this. In recent years, several reports have been made that Granulocyte colony-stimulating factor (G-CSF), which is well-known hematopoietic growth factor, has an effect on the treatment for the central nervous injury such as cerebral infarction and spinal cord injury. G-CSF already have been safely administered in clinical setting for hematologic disease.

Here we have examined the effect of G-CSF on promoting regeneration of nerve in rat facial nerve paralysis model. In administration of G-CSF, we made use of the gelatin hydrogel together as the drug delivery systems.

**Methods:** 25 male SD rats were used. In the group A (10 rats), 10mm of left facial nerve bundles including main trunk and its branches were excised at outside the temporal bone. G-CSF soaked in the gelatin hydrogel was administered to 5 rats subcutaneously in the back 2 and 4 weeks after excision as a G-CSF subgroup. In the other 5 rats, saline, instead of G-CSF, was used as the control group. In group B (15 rats), facial nerves were cut and sutured end-to-end immediately in the main trunk. Of these 15 rats, 5 rats were assigned to the G-CSF subgroup. Other 5 rats were assigned to the control group. The rest 5 rats were also assigned to the G-CSF subgroup, but G-CSF was administered immediately and 2 weeks after surgery. Electrophysiological evaluation was performed 2, 4, 8, and 12 weeks after the surgery.

**Results:** In the evoked electromyogram, rats in Group B showed better recovery of the wave amplitude than those in Group A. In group B, wave amplitudes of the G-CSF subgroups recovered significantly better than those of the control group. In addition, earlier timing of G-CSF administration resulted in quicker recovery of the wave amplitude.

**Conclusion:** Our data implied that the G-CSF is effective for promoting nerve regeneration in the severe facial nerve paralysis model of rat.

**Paper 8** Head and Neck 2

O08-1

**NSQIP surgical risk calculator:  
Actual vs. predicted surgical  
mortality and morbidity in South  
Australian tongue cancer patients**

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**Purpose:**

Patient selection for tongue cancer patients considering surgery is critical in ensuring the optimal outcomes for patients. The American College of Surgeons NSQIP risk calculator is a validated web based tool, developed to assess patients 30-day post-operative risk assessment based on 21 patient-specific factors, and provide surgeons with information to guide decision making. Use of the risk calculator in an Australian population has not been published to date.

**Methodology:**

A retrospective review of actual mortality and morbidity of Head and Neck cancer patients was undertaken to investigate validity of this tool for South Australian patients treated from 2009 - 2012 (the period of the NSQIP risk calculator data-set collection). Post-operative 30-day outcomes for patients undergoing glossectomy (partial/complete) with or without modified radical neck dissection in South Australian public teaching hospitals were included in the study. Results from the study were compared to the predicted mortality and morbidity using NSQIP risk calculator, incorporating surgeon-assessed relative risk category.

**Results:**

There were n=128 patients identified in the study. The predicted mortality and morbidity was significantly different from the actual mortality and morbidity identified in the case notes. Multiple factors for this were identified and will be explored in the presentation.

**Conclusion:**

This risk calculator tool has value in optimising the decision making process for tongue cancer patients and clinicians in the Australian healthcare system undergoing major head and neck surgery.

O08-2

**Symptomatic internal jugular vein  
occlusions after conservative neck  
dissections**

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The neck dissection (ND) procedure has advanced to provide better quality of life for head and neck cancer patients. The conservative ND (CND) has now become a standard procedure in the surgery of head and neck cancer. We already know about ND-related symptoms that result from injury of nerves, such as accessory nerve, lingual nerve, facial nerve, and hypoglossal nerve. However, the advantage of preserving internal jugular vein (IJV) has not been reported enough. This is the reason why we examine the patency of IJV after neck dissections and the symptoms that are derived from occlusion of IJV.

We surveyed on neck computed tomography (CT) and magnetic resonance (MR) images of head and neck cancer patients after receiving ND in the period from January 2011 to March 2015 at the department of otolaryngology-head and neck surgery of Tohoku University Hospital. We performed NDs in 362 sides' neck (285 patients) in the period. Except for cases ineligible for assessment or of resected IJVs, among 159 preserved IJVs, 15 were occluded. The rate of occlusion was 7.7%, and most of the IJV occlusions were found within a year after NDs. In most of the cases the occlusion was not resulted in any symptoms, but in some cases it could be related to the symptoms that contain facial swelling, neuralgic pain, and diplopia.

We experienced a case in which the patient complained diplopia derived from the IJV occlusion 2 years after receiving CND. We will report the case as an example of rare but significant complication caused by IJV occlusion

O08-3

## Retrospective review of patients who underwent gastrostomies after radical radiotherapy in a tertiary referral unit

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**Introduction:** Patients with advanced stage head and neck cancer experience nutritional depletion requiring enteral supplementation. This can be achieved by nasogastric tube or gastrostomy, the latter being more long-term. The aim of this project was to review patients who had gastrostomies following radical radiotherapy at differing levels comparing the length of time feeding was required.

**Materials and Methods:** Retrospective review of all patients who had gastrostomies after radical radiotherapy over 2 years. A comparison was made on the length of gastrostomy feeding based on the level at which radiotherapy was applied. Patients were followed up for 1 year.

**Results:** 30 patients having radiotherapy at the level of the oropharynx underwent gastrostomy feeding, compared to 10 patients having radiotherapy at the level of the hypopharynx. Analysis revealed there no significant differences in length of gastrostomy feeding between the groups.

**Conclusion:** There is no significant difference in length of time a gastrostomy is required, based on the level at which radiotherapy is required. Despite claims that radiotherapy is a more anatomically preservative treatment option, the physiological disturbance from radiotherapy at any level results in equal nutrition supporting needs.

O08-4

## Superselective intraarterial chemotherapy for the locally advanced lacrimal sac cancer : a report of two cases

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Squamous cell carcinoma of the lacrimal sac is a rare epithelial neoplasm. The treatment of primary lacrimal sac carcinomas includes wide surgical resection followed by radiation therapy and chemotherapy. Locally advanced cases may require an orbital exenteration which may reduce quality of life of the patients.

We report the two cases of squamous cell carcinoma of the lacrimal sac with extensive involvement of the orbital soft tissue. The first patient was a 72-year-old woman presenting exophthalmus, diplopia, epiphora and swelling of the right orbit region. She was treated with radiotherapy and concomitant intraarterial chemotherapy using cisplatin and docetaxel. After the treatment she has no residual tumor at PET scan and her vision was normally preserved. The second patient was a 68-year-old man with a history of treatment of maxillary sinus cancer 30 years before, presenting swelling of the left orbit region, diplopia and slight left visual disorder. He was treated with superselective intraarterial chemotherapy followed by CyberKnife radiotherapy. His left eyesight was maintained and the tumor was disappeared by PET evaluation.

With multidisciplinary therapy using intraarterial chemotherapy, the visual function can be preserved in patients with locally advanced lacrimal sac squamous cell carcinoma.

O08-5

### The different nature of mucositis between cetuximab-based bioradiotherapy and platinum-based chemoradiotherapy in malignancies of the upper aerodigestive tracts

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**Background.** The efficacy of cetuximab-based bioradiotherapy (BRT) in locally advanced head and neck squamous cell carcinomas (HNSCC) has been established. We evaluated the acute toxicities in cetuximab-based BRT and platinum-based chemoradiotherapy (CRT) and focused on the different nature of radiation mucositis.

**Methods.** We retrospectively analyzed 15 patients who underwent cetuximab-based BRT and 29 patients who underwent platinum-based CRT to compare the incidence of acute toxicities. In cetuximab-based BRT group, an initial cetuximab loading dose of 400 mg/m<sup>2</sup> was delivered over 120 min, one week before the start of radiotherapy. Seven weekly infusions of 250 mg/m<sup>2</sup> of cetuximab followed during the definitive radiotherapy. In platinum-based CRT group, cisplatin was administered at a dose of 40mg/m<sup>2</sup> weekly during the definitive radiotherapy. Acute toxicities were evaluated according to Common Terminology Criteria for Adverse Events (CTCAE) version 3.

**Results.** The BRT group had a higher incidence of Grade $\geq$ 3 radiation dermatitis than did the CRT group (47% vs 3%, respectively; Fisher's test, p=0.01). The incidence rate of Grade $\geq$ 3 mucositis/stomatitis was 66.7 % and 41.4% in the BRT and CRT group, respectively (log-rank test, p=0.1167), while the incidence rate of the inability to feed orally was 35.7% and 55.2%, respectively (log-rank test, p=0.1502). Radiation mucositis with white-coated pseudomembrane was observed specifically in patients treated by cetuximab-based BRT.

**Conclusions.** Treatment with cetuximab-based BRT was likely to increase the incidence of Grade $\geq$ 3 mucositis, but to decrease the incidence of inability to feed orally in comparison to platinum-based CRT. It is possible that the characteristics of mucositis caused by cetuximab-based BRT differ from those of mucositis caused by platinum-based CRT. The nature of mucositis in cetuximab-based BRT patients may be advantageous in terms of oral feeding.

O08-6

### Plate Exposure After Anterolateral Thigh Free-Flap Reconstruction in Head and Neck Cancer Patients With Composite Mandibular Defects

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**Background.** This study aimed to identify the risk factors for postoperative plate exposure in head and neck cancer patients with composite mandibular defects undergoing tumor ablation followed by bridging plate and anterolateral thigh (ALT) flap transfer.

**Methods.** Between January 2007 and June 2012, 1,452 patients who underwent free tissue transfer after head and neck cancer ablation were retrospectively reviewed. Only ALT flap coverage with a bridging plate for segmental mandibular defects was included. The Jewer's classification was used to define the type of mandibular defect.

**Results.** The study enrolled 123 men and 7 women. The incidence of plate exposure was 37.7 % (49/130). The follow-up time ranged from 0.5 to 5.4 years (mean, 2.4 years). The 5-year probability of a plate exposure-free rate was 32.8 % for the patients with postoperative radiotherapy (RT) (n = 33) and 64.3 % for the patients without it (n = 97). Patients reconstructed with a fasciocutaneous or chimeric type of ALT flap had higher rates of plate exposure than those reconstructed with a musculocutaneous type of ALT flap (p = 0.002). As shown by logistic regression, the significant predictive risk factors for postoperative plate exposure still were postoperative RT [adjusted odds ratio (OR) 2.76, 95 % confidence interval (CI) 1.09-6.99, p = 0.031] and intraoperative blood loss (adjusted OR 2.37, 95 % CI 1.13-4.99, p = 0.022).

**Conclusions.** The type of ALT flap, postoperative RT, and intraoperative blood loss were the predisposing factors for increased risk of postoperative plate exposure in the specific disease group.

O08-7

## Rhinosinusitis and otitis media with effusion in nasopharyngeal carcinoma patients treated by IMRT

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The current study aimed to investigate the occurrences of post-irradiation otitis media with effusion (OME), chronic rhinosinusitis (CRS), and their interrelationship in nasopharyngeal carcinoma (NPC) patients treated by intensity-modulated radiotherapy (IMRT). A retrospective review of medical records and magnetic resonance imaging for NPC patients across a 5-year follow-up was conducted. Rhinosinusitis was diagnosed and staged by Lund-Mackay system. A total of 102 patients were enrolled in the study. On the 5th year following IMRT, 30 patients (29.4%) and 17 patients (16.7%) suffered from post-irradiation OME and CRS, respectively. Analysis by logistic regression showed a lack of association between the occurrence of post-irradiation OME and CRS ( $P=0.06$ ). These observations indicated that the modern radiotherapy technique exhibits capability in decreasing the incidences of CRS comparing to the data of traditional radiotherapy. But post-irradiation OME was still encountered in more than one quarter of long-term survivors of NPC. Of note, rhinosinusitis in NPC survivors does not predispose to the development of post-irradiation OME, suggesting nasal irrigation might be unnecessary for the management of OME following radiotherapy.

**Paper 9** Head and Neck 3

O09-1

### Treatment outcomes following orbital preservation surgery for cancers with orbital invasion

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**Objective:**

The indications for orbital preservation surgery (OPS) are unclear. OPS has generally been specified for patients with no orbital fat invasion. The aim of this study was to identify treatment outcomes and to clarify the indications for orbital preservation surgery.

**Methods:**

We retrospectively analyzed 27 patients with orbital invasion cancers. The median follow-up period was 36 months. The tumors had invaded the orbit without periorbital invasion in 13 patients, had invaded the periorbital in 6 patients, and had invaded the orbital fat beyond the periorbital in 8 patients. Pathological examination identified 19 carcinomas and 8 sarcomas. Six patients underwent orbital exenteration. Twenty-one patients underwent OPS of which eight patients also underwent periorbital resection. The types of OPS surgical resections in this study were as follows: two skull base surgeries, eight total maxillectomies, and eleven partial maxillectomies. Twelve patients with positive or close surgical margins underwent postoperative radiotherapy. Moreover, we analyzed the treatment outcomes, three-year orbital control rate (OCR), disease-specific survival (DSS), functional eye preservation rate (fEPR), and risks for orbital recurrence.

**Results:**

Among the 21 OPS patients, the three-year OCR and DSS were both 68%. The presence of positive surgical margins had a significantly poor three-year OCR (41% vs. 91%;  $p = 0.04$ ). The orbital apex and the periorbital were the most predominant locations for positive margins. Only two of the six orbital recurrences were salvaged by orbital exenteration. The overall fEPR was 67%. Severe diplopia persisted in 40% of patients that had exposure of the extraocular muscles during surgery. Among the six orbital exenteration patients, the three-year OCR and DSS rates were 80% and 60%, respectively.

**Conclusion:**

In conclusion, 68% patients retained good orbital function after an OPS. Positive surgical margins significantly correlated with orbital recurrence. Wide periorbital invasion and microscopic apex invasion were risk factors for positive margins difficult to orbital preservation. Salvage surgery for orbital recurrence was not an easy process. The exposure of extraocular muscle also tended to result in severe diplopia.

O09-2

### Efficacy of weekly cisplatin chemoradiotherapy for patients with pyriform sinus squamous cell carcinoma

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**【Background】**

Among head and neck cancers, hypopharyngeal cancer, particularly that originating from pyriform sinus, has one of the worst prognoses. We treat patients with pyriform sinus squamous cell carcinoma by weekly cisplatin chemotherapy with concomitant radiotherapy for the purpose of preserving larynx and evaluated the treatment outcomes.

**【Methods】**

We evaluated 40 patients with pyriform sinus squamous cell carcinoma who underwent weekly cisplatin chemoradiotherapy at our institution between August 2006 and November 2013. The patients included 39 men and 1 woman. Cisplatin was administered at a dose of 40mg/m<sup>2</sup> on weeks 1, 2, 3, 5, 6, and 7 of the radiotherapy course. Ten patients underwent induction chemotherapy with docetaxel, cisplatin, and 5-fluorouracil followed by weekly cisplatin chemoradiotherapy.

**【Results】**

All patients completed radiotherapy at a median dose of 70 Gy (range 64-70 Gy). Cisplatin was administered concomitantly at a median of five times (range 2-6 times). On limiting the analysis to patients who underwent induction chemotherapy, the median radiotherapy dose was 70 Gy and cisplatin was administered at a median of five times.

The 5-year overall survival rate was 73.7%. The 5-year locoregional control rate and larynx preservation rate were 85.3% and 66%, respectively.

**【Conclusion】**

Generally, completion of induction chemotherapy followed by chemoradiotherapy is challenging because of severe adverse events. With our regimen, patients who underwent induction chemotherapy did not have a lower concomitant chemoradiation therapy completion rate. Weekly cisplatin chemoradiotherapy is likely an effective therapy for patients with advanced pyriform sinus squamous cell carcinoma.

O09-3

## The distribution of SUVs in light accumulation lesions of the larynx on PET-CT

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<sup>18</sup>F-FDG PET/CT is a useful tool for the diagnosis and evaluation of the primary tumor, neck lymph node metastasis, distal metastasis, and double cancer in head and neck cancer patients. Today, the determination between a benign and malignant lesion depends to a large extent on the single voxel presenting the maximum standardized uptake value (SUV<sub>max</sub>). Recently, tumor standardized uptake values (SUVs) is an area of active research. For example, the metabolic tumor volume derived from SUVs is reported as a new prognostic factor for chemoradiation therapy. In head and neck cancer, light accumulation lesions (with 3 to 6 SUV<sub>max</sub>) are difficult to differentiate between physiological and pathological accumulations. In this study, we analyzed the distribution of SUVs in light accumulation lesions of the larynx among 30 patients with laryngeal or hypopharyngeal cancer to determine its efficacy as a diagnostic factor.

O09-4

## A comparison of oncological outcomes in the treatment of advanced stage oropharyngeal squamous cell carcinoma treated with either chemoradiation or a primary surgical protocol

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Introduction:

The incidence of oropharyngeal squamous cell carcinoma (OPSCC) in the western world is increasing, with the disease becoming more prevalent in younger, non-smoker and non-drinker patients. High-risk human papillomavirus (HPV) has been implicated for this observed trend. The treatment choices for advanced stage OPSCC include primary surgery with appropriate adjuvant therapy versus primary chemoradiation (CRT). Whilst the oncological results are similar, depending on HPV status, the patterns of failure for each treatment modality are not clearly understood.

Aims:

To review the patterns of oncological failure following a primary surgery protocol versus primary chemoradiotherapy for advanced OPSCC.

Methods:

Review of prospective head and neck cancer database. One hundred patients with locoregionally advanced OPSCC treated with curative intent over a 5-year period (2008 to 2012), following head and neck cancer multidisciplinary team discussion at our tertiary unit, were included in the study. Clinicopathological characteristics including TNM stage, HPV status, treatment modality, recurrence free and overall survival were collated. There was a minimum of 24 months follow-up post treatment.

Results:

Two-thirds of patients underwent a primary surgical protocol, whilst the remainder had primary CRT. The rate of recurrent disease was 14% in the primary surgery cohort and 37% in the primary CRT group. All the primary surgery oncological failures were regional or distant recurrences, compared to the primary CRT group that had local, regional, and distant failures.

Conclusion:

We report higher rates of disease control for OPSCC treated in the primary surgical group compared to the primary chemoradiation group.



O09-5

## Evaluation of Lymphatic and Vascular Invasion in Relation to Clinicopathological Factors and Treatment Outcome in Oral Cavity Squamous Cell Carcinoma

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### Objectives

This study evaluated the associations between lymphatic and vascular invasion of oral cavity squamous cell carcinoma (OSCC) and clinicopathological manifestations, as well as their impact on patient outcomes after treatment.

### Materials and Methods

In total, 571 patients with primary OSCC who underwent surgery with or without adjuvant therapy were enrolled.

### Results

Lymphatic and vascular invasion were found in 28 (5%) and 16 (3%) patients, respectively. Significant associations were found between lymphatic and vascular invasion and overall stage ( $P < 0.001$  and  $P = 0.020$ , respectively), tumor stage ( $P = 0.009$  and  $P = 0.025$ , respectively), nodal metastasis (both  $P < 0.001$ ), extracapsular spread (both  $P < 0.001$ ), perineural invasion (both  $P < 0.001$ ), bone invasion ( $P = 0.004$  and  $P = 0.001$ , respectively), depth of invasion ( $P < 0.001$  and  $P = 0.001$ , respectively), and pathologic differentiation ( $P = 0.002$  and  $P < 0.001$ , respectively). In the analysis of adverse events during follow-up, neither lymphatic nor vascular invasion was statistically associated with local recurrence, neck recurrence, and distant metastasis. Although lymphatic invasion exhibited significant associations with poorer overall survival ( $P < 0.001$ ), disease-specific survival ( $P < 0.001$ ), and disease-free survival ( $P = 0.01$ ), it was not demonstrated to be an independent prognostic factor in all multivariate analyses. Twenty-six (93%) of 28 and 13 (81%) of 16 OSCC patients with lymphatic and vascular invasion received post-operative adjuvant treatments, respectively. In other words, only two cases of OSCC patients with lymphatic invasion and three cases with vascular invasion did not receive any post-operative treatment. Due to these limited numbers, we could not analyze the survival benefit of post-operative treatment in the patients with these two pathological factors.

### Conclusion

According to our study, both lymphatic and vascular invasion are associated with many clinicopathological manifestations. Besides, the poorer prognosis is related to the lymphatic invasion in the survival analysis. There is still no conclusions whether adjuvant therapy is mandatory upon only lymphatic or vascular invasion respectively due to limited case numbers.

O09-6

## Transoral Videolaryngoscopic Surgery (TOVS) for oropharyngeal cancer – Non-Robotic Transoral Surgery –

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**Background:** Several types of minimally invasive transoral approaches have been reported for resection of oropharyngeal cancer. We previously reported en bloc resection under surgical microscope. Transoral Robotic Surgery (TORS) is widely distributed all over the world, especially in United States and Korea. However, surgical robot and its running cost are expensive, and it is not applicable in some institution. In Japan Robotic surgery for head and neck cancer has not been approved by the government yet. Recently, we adopted Transoral Videolaryngoscopic Surgery (TOVS) which was developed in Japan.

**Patients and Methods:** For 3 years, 20 oropharyngeal cancers were resected with TOVS. The pharynx was exposed with FK-retractor or Davis mouth gag. The tumor was resected en bloc under the clear view provided with deflectable-Tip EndoEYE.

**Results and Discussion:** The operative field was successfully exposed, and the surgical view was much improved with TOVS. The base of tongue could be also well exposed. En bloc resection was carried out in all cases and the post-operative function was satisfactory. There was no major post-operative complication. The swallowing and speech function were satisfactory. No local relapse was observed and regional relapse was seen in 2 cases. The merit of TOVS introduction will be discussed comparing with TORS.

**Paper 10** Head and Neck 4

**O10-1**
**A prediction model for predicting malignant cervical lymph nodes after neck irradiation**

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**Objective:** To construct a real-time predictive scoring system based on demographic data and sonographic findings on the picture archiving and communication system (PACS) for predicting malignant cervical lymphadenopathy after neck radiotherapy (RT).

**Methods:** After neck irradiation, one hundred forty four neck lymph nodes, receiving ultrasonography and ultrasound-guided fine needle aspirations (USgFNAs), were used to construct a predictive model.

**Result:** A predictive scoring model was proposed by multivariate logistic regression analysis:  $1.35 \times (\text{L axis}) + 2.03 \times (\text{S axis}) + 2.27 \times (\text{Margin}) + 1.48 \times (\text{Echogenic hilum}) + 3.7$ . Cervical lymph node after neck RT was regarded as malignant with a score  $\geq 7$ . The formula will be programmed into a synchronized, computerized sonographic reporting system. Internal validation of this predictive tool showed sensitivity (82.3%), specificity (83.1%), and overall accuracy (82.6%).

**Conclusions:** A real-time and practical sonographic scoring system was built and validated to provide the physician prompt and reliable probability guidance for performing US-FNA cytology in managing cervical LN after RT.

**O10-2**
**Epstein-Barr virus (EBV) encoded microRNA BART7 alters the susceptibility of nasopharyngeal carcinoma to ionizing radiation**

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Radiotherapy is the major therapeutic regime for primary undifferentiated NPC treatment as EBV-associated NPC is highly susceptible to ionizing radiation. Existence of cancer cells which are intrinsically resistance to radiation may lead to treatment failure resulting in disease recurrence. We hypothesized that the viral microRNA BART7 (miR-BART7) plays a part in modulating the responsiveness of NPC to radiotherapy. Our results shown that cancer cells with high level of miR-BART7 are less tolerant to the extrinsic radiation. The colony forming ability was reduced significantly with higher portion of apoptotic cells in the miR-BART7 expressing NPC cells after radiation treatment. To confirm the in vitro data, we developed a zebrafish model to assess the effects of miR-BART7 expression on the changes of radiosensitivity in HONE1 cells. Forced expression of miR-BART7 resulted in obvious reduction of the xenograft size as opposed to the mock control. In addition, we noticed that miR-BART7 could inhibit the signaling pathways mediated by transforming growth factor beta 1 (TGF $\beta$ 1), a pleiotropic cytokine with the potency to trigger self-renewal and damage-repair machinery in cancer cell after radiotherapy. Taken together, the results revealed that miR-BART7 plays a positive role in modulating radiation sensitivity in NPC cells. Establishing the functional significance of miR-BART7 could be helpful in tailoring the therapeutic dosage of radiotherapy for individual patients to prevent over-treatment and unnecessary side effects. Further, miR-BART7 could possibly be used as a non-invasive blood-borne marker to monitor residual cancer cells after primary treatment and predict disease recurrence.

O10-3

### Tumor-suppressive microRNA-451a inhibits cancer cell migration and invasion through targeting ESDN/DCBLD2 in hypopharyngeal squamous cell carcinoma

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**Background:** In spite of considerable advances in multimodality therapy, including surgery, radiotherapy and chemotherapy, the overall survival rate for patients with hypopharyngeal squamous cell carcinoma (HSCC) is only 15-45%. Therefore, understanding the molecular mechanisms of metastatic pathways underlying HSCC using currently available genomic approaches might improve therapies for and prevention of the disease. MicroRNAs (miRNAs), member of ncRNA are endogenous small ncRNA molecules (19-22 bases in length) that function to regulate protein-coding gene expression by repressing translation or cleaving RNA transcripts in a sequence-specific manner. A substantial amount of evidence has suggested that miRNAs are aberrantly expressed in many human cancers and play significant roles in human oncogenesis and metastasis. In this study, we constructed the miRNA expression signature of HSCC using clinical specimens. Our expression signature showed that miR-451a was downregulated in cancer tissues, suggesting that it might act as tumor suppressor in HSCC. The aim of this study was to investigate the functional role of miR-451a, and identify genes or pathways regulated by miR-451a in HSCC.

**Result:** The expression levels of miR-451a were significantly downregulated in cancer tissues and cell lines than normal tissues. The restoration of miR-451a significantly suppress migration and invasion in cell lines. Genome-wide gene expression assays revealed that five genes (SPC25, MIF, ESDN/DCBLD2, AKR1B1, C4orf46) were significantly downregulated by miR-451a transfectants. Among these candidate genes, we focused on ESDN/DCBLD2 because its expression levels were the most upregulated in tumor tissues and was shown negative correlation between expression levels of miR-451a in HSCC clinical specimens. The luciferase reporter assay revealed that ESDN/DCBLD2 was a direct target of miR-451a in SAS. The mRNA or protein expression levels of ESDN/DCBLD2 were significantly downregulated transfected miR-451a. The loss of function study revealed that cell migration and invasion were significantly inhibited in si-ESDN/DCBLD2 transfectant.

**Conclusion:** Downregulation of miR-451a was frequently observed in HSCC clinical specimens, and miR-451a act as tumor-suppressive miRNAs in this disease. ESDN/DCBLD2 was a direct regulator of miR-451a in HSCC cells. Overexpression of ESDN/DCBLD2 was detected in HSCC clinical specimens, and functional assays showed that ESDN/DCBLD2 promoted cancer cell invasion and migration, indicating this gene as an oncogene in HSCC cells. Elucidation of cancer genes and pathways regulated by miR-451a might be extended to the treatment of HSCC.

O10-4

### Rapid detection of hypopharyngeal cancer using activatable fluorescent probe for dipeptidyl peptidase-4

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Hypopharyngeal cancer (HPC) is one of the commonest malignancies in head and neck region, but has one of the highest mortality rates mainly because of delayed diagnosis. To overcome this problem, a lot of effort has been put to develop a new method to diagnose HPC at early stage. Narrow band imaging (NBI) has been reported to be an effective tool, though experienced skill is required. A novel, simple and practical diagnostic method, therefore, has been required for a long time.

Recently, an innovative method for rapid cancer detection using a fluorescent probe for gamma-glutamyltranspeptidase (GGT), of which activity is up-regulated in cancer cells, such as ovary cancer or breast cancer was established. In the same way, we applied several fluorescent probes for aminopeptidase to HPC, aiming to establish a novel method for detecting HPC by fluorescent imaging. Surgically resected tissues of HPC were used in this study. Within several hours after resection, fluorescent probe was applied to each specimen by topically spraying, following the fluorescent imaging study.

Of various probes tested, a probe for dipeptidyl peptidase-4 (DPP-4) is ideal to detect early HPC. Increment of the fluorescent intensity is so rapid and enough to detect even with the naked eyes in tumor site, whereas the fluorescence was almost absent in normal epithelium. We expect this novel DPP-4 probe can be widely applied for clinical practice, including HPC screening by fiberoptic scope and intraoperative assessment of surgical margins.

## O10-5

## Prognostic role of Regenerating gene-I (REG-I) in patients with stage IV Head and Neck Squamous Cell Carcinoma

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Regenerating gene (REG) family is composed of antiapoptotic factors and growth factors that affect the epithelial cells within the digestive system. REG-I expression has been proved in thoracic esophageal cancer so, we investigated the expression of REG-I in head and neck SCC and its relevance to patient survival rates.

**Materials and Methods:** The medical records of 60 patients with stage IV head and neck SCC were reviewed. Untreated biopsy specimens were examined for the expression of REG-I and the results were correlated with patient survival times.

**Results:** Incidence of lymphatic permeation, vascular invasion and pathological lymph nodes was significantly higher in REG-I negative group ( $p = 0.008$ ,  $0.030$  and  $0.015$ , respectively). Overall and cancer-free survival rates were significantly higher in REG-I positive group ( $p = 0.0008$  and  $0.0004$ , respectively). Multivariate analysis showed that REG-I was an independent prognostic factor for predicting long-term overall and disease-free patient survival rate ( $p = 0.003$  and  $0.004$ , respectively).

**Conclusion:** REG-I is a good prognostic factor for advanced head and neck SCC.

## O10-6

## PBK/TOPK Expression Predicts Prognosis in Head and Neck Cancer

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**Background:**

Oral squamous cell carcinoma is a common cancer related to various factors. This study was aimed to evaluate the expression of PBK/TOPK (PDZ-binding kinase/T-LAK cell-originated protein kinase) and its clinical significance in oral squamous cell carcinoma.

**Materials and methods:**

PBK/TOPK expression was detected in 287 patients of oral squamous cell carcinoma, 114 patients of early stage (stage I, II) and 179 patients of late stage (stage III, IV). Then, the correlation between PBK/TOPK expression and clinicopathological features was quantitatively analyzed by immunohistochemical analysis.

**Results:**

Using immunohistochemical analysis of oral squamous cell carcinoma tissue samples, our study showed that a high PBK/TOPK expression level correlates strongly with better overall survival. Moreover, in combination with high PBK/TOPK expression and other pathologic staging factors showed significant better overall survival in young patient ( $p < 0.05$ ), patient with smoking habit ( $p < 0.05$ ), and late stage ( $p < 0.05$ ) compared with in low PBK/TOPK expression.

**Conclusions:**

Our results suggest that PBK/TOPK expression is closely associated with oral squamous cell carcinoma. High PBK/TOPK expression, either alone or in combination with other pathologic staging factors, may serve as a good prognostic marker for oral squamous cell carcinoma.

O10-7

## Identification of chemoresistance factors for head and neck carcinoma by analysis with iTRAQR and Microarray

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Background: Anticancer drugs such as cisplatin are important in the treatment of head and neck squamous cell carcinoma (HNSCC); at present, cisplatin is the key anticancer drug for advanced HNSCC although not all cases respond well to the drug and some tumors show cisplatin resistance. In addition to its expensive cost, administration of cisplatin in tumor-resistant cases would provide little curative effect and may increase risks of adverse drug reactions, which is a clear disadvantage. If chemoresistance could be determined before treatment, unnecessary drug administration could be avoided. Here, we investigated chemoresistance factors by comprehensive analyses at protein and RNA levels.

Material and Methods: Four human HNSCC cell lines used were as follows: cisplatin-sensitive UM-SCC-23, acquired cisplatin-resistant UM-SCC-23-CDDPR, naturally cisplatin-resistant UM-SCC-81B, and acquired 5-fluorouracil (5-FU)-resistant UM-SCC-23/WR cell lines. Extracted proteins were labeled with iTRAQR and analyzed by tandem mass spectrometry (LC-ESI-MS/MS). MS/MS data searches were conducted using the ProteinPilotR software. Moreover, we combined spectrometry results with corresponding results of microarray analysis to identify chemoresistance-related proteins.

Result: We identified proteins that may mediate anticancer drug resistance by analysis with iTRAQR. Seven proteins suspected of being cisplatin-specific chemoresistance factors (lower levels in UM-SCC-23 and UM-SCC-23/WR cells but higher levels in UM-SCC-23-CDDPR and UM-SCC-81B cells) and 13 proteins suspected of being multi-chemoresistance factors (lower levels in UM-SCC-23 cells but higher levels in UM-SCC-23/WR, UM-SCC-23-CDDPR, and UM-SCC-81B cells) were discovered. However, results of microarray analysis indicated hundreds of proteins. Nevertheless, two proteins were common between the analyses: one is a suspected cisplatin-specific chemoresistance factor and the other is a suspected multi-chemoresistance factor.

Discussion: From the perspective of therapies for HNSCC, this is the first report of the use of both recent proteome technologies, such as the iTRAQR method and LC-ESI-MS/MS, and the previous method for transcriptome analysis, microarray analysis, to investigate mechanisms of anticancer-drug resistance against cisplatin and 5-FU. We discovered two common proteins as chemoresistance factors because of a simultaneous encyclopedic analysis at mRNA and protein levels, which was considered extremely precise. Our results indicate that the discovered proteins can be biomarkers for chemoresistance. Moreover, by using inhibitors of these proteins, we may be able to develop new treatment strategies for HNSCC in the near future.

## Paper 11 Rhinology 2

## O11-1

**Murine nasal Natural Killer cells in mucosal immunity**

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**Background:** Natural killer (NK) cells in the upper respiratory airways have not been well characterized. In the current study, we sought to characterize and functionally assess murine nasal natural killer cells.

**Methods:** We used immunohistochemistry and flow cytometry to compare nasal NK cells with their splenic and pulmonary counterparts. For this purpose, we adopted Ncr1-GFP knock-in mice, whose NK cells were identifiable by their production of green fluorescent protein (GFP). In addition, we conducted in vitro analyses of expression of surface markers by flow cytometry, as well as functional analyses, including degranulation and cytokine production of nasal NK cells of these mice. Furthermore, C57BL/6 mice were treated with PK136 antibody to deplete NK cells and then nasally infected with influenza virus PR8, to analyze the in vivo functions of nasal NK cells.

**Results:** Immunohistochemical analysis confirmed the presence of NK cells in the lamina propria of nasal mucosa. Flow cytometry showed that the nasal NK cells were of NK cell lineage. The expression patterns of Ly49 receptors, CD11b/CD27 and CD69 revealed that nasal NK cells had an immature and activated phenotype compared with that of their splenic and pulmonary counterparts. Effector functions including degranulation and IFN- $\gamma$  production after in vitro stimulation with phorbol 12-myristate-13-acetate/ionomycin or IL-12/IL-18 were dampened in nasal NK cells, and the depletion of NK cells resulted in increase of influenza virus titer in nasal passages.

**Conclusions:** NK cells reside in the nasal passage, and they belong to conventional NK cell lineage. They show characteristic immature and activated phenotype. Despite their hyporesponsiveness in vitro, they play important roles in host defence against nasal influenza virus infection in vivo.

## O11-2

**Pathogenicity of memory Th2 cell changes and is linked to stage of allergic rhinitis**

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**Background:** The patients with Japanese cedar pollinosis show strong nasal symptoms between February and April, and the number of patient is increasing. In allergic disease, we have proposed that memory Th2 cells with additional functions have pathogenic potential.

Allergic rhinitis has three stages: a non-sensitized stage, asymptomatic sensitization stage, and symptomatic stage. We investigated these three stages of seasonal allergic rhinitis caused by Japanese cedar pollen and analyzed with "pathogenic Th2 cells" by focusing on the influence of IL-33.

**Methods:** Patients with Japanese cedar pollinosis and healthy volunteers were divided into "non-sensitized," "asymptomatic sensitization," and "pollinosis" groups based on three factors: the presence of Japanese cedar specific IgE (immune CAP method), presence of seasonal symptoms, and results of nasal provocation test. We analyzed the Japanese cedar-specific T cell in peripheral blood mononuclear cells (PBMCs) using flow cytometry and real-time polymerase chain reaction.

**Results:** Few ST2 positive Japanese cedar-specific CD4T cells were found in PBMCs in the "non-sensitized" and "asymptomatic sensitization" groups, but markedly larger number of these cells was observed in the "pollinosis" group. Different patterns of Th2 cytokine production were observed in each of the three groups with Japanese cedar and IL-33 stimulation.

**Conclusions:** Our study showed that pathogenicity of memory Th2 cell is linked to sensitization and the allergic rhinitis stage. ST2-expressing memory Th2 cells may be involved in the onset of allergic rhinitis and play pathogenic roles in the progression of its stages.

O11-3

## The expression of CST1 in eosinophilic chronic rhinosinusitis

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Eosinophilic chronic rhinosinusitis (ECRS) is the inflammation disease of nasal sinuses characterized by significant eosinophilic infiltration and is progressively increasing in Japan. Patients with ECRS have nasal polyps which are refractory and recurrent easily and can have complications; severe hyposmia, asthma, and eosinophilic otitis media. It is very hard to treat ECRS, yet the pathogenesis of ECRS is largely unknown.

Cysteine proteases are widely expressed proteolytic enzymes that play role in inflammatory tissue destruction. The proteolytic activity of these enzymes is controlled by a family of inhibitors known as the cysteine superfamily, and cystatins inhibit cysteine proteases by forming tight but reversible complexes with their target enzymes.

Cystatin SN (CST1) is protease inhibitor and is one of the type 2 cysteine subfamily. CST1 is expressed in the submandibular gland, bladder, and ureter. CST1 has been shown to bind tightly to the cysteine protease, papain, which is a potent allergen, and to inhibit the cysteine protease activity of papain. Thus, the cysteine family may play protective roles against allergens with protease activity.

In the previous study, we performed a microarray analysis of nasal epithelial cells from seasonal allergic rhinitis (SAR) patients to the Japanese cedar and control subjects. We observed that the expression of CST1 was upregulated specifically in SAR patients during natural allergen exposure. Immunohistochemical staining confirmed the increased expression of CST1 in the nasal epithelial cells of SAR patients. We have been analyzing the function of CST1 in allergic rhinitis. Additionally, we think that CST1 has the important role in eosinophilic chronic rhinosinusitis, which is the representative chronic inflammation disease such as allergic rhinitis.

In this study, samples of nasal mucosa and nasal polyp of ECRS patients and non-ECRS patients were collected and compared the expression of CST1. Furthermore, we analyzed the function of CST1 by using cultured mast cells.

O11-4

## Serum level of interleukin-21 is elevated in chronic rhinosinusitis

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(1) Background: Chronic rhinosinusitis (CRS) is an inflammatory disease of the sinuses and mucosa with unclear pathogenesis. Interleukin (IL)-21 is mainly expressed in activated cluster of differentiation (CD)4+ T cells and has potent regulatory effects on the immune system.

(2) Objective: This study is to determine whether IL-21 in the blood is correlated with CRS.

(3) Methods: The blood samples from CRS patients and normal controls were analyzed in correlation with clinical features. The eosinophil percentage was counted, and serum levels of total immunoglobulin E (IgE) and IL-21 were analyzed by enzyme-linked immunosorbent assay (ELISA). In addition, IL-21 and interferon (IFN)- $\gamma$  secreted from stimulated peripheral blood mononuclear cells (PBMCs) were measured by ELISA, and their mRNA expression levels were analyzed by real-time quantitative polymerase chain reaction (RT-qPCR). Disease severity was scored based on computed tomography (CT) scan, nasal endoscopy, and global osteitis scoring scale (GOSS).

(4) Results: A total of 55 CRS and 37 healthy subjects were recruited. The average levels of serum total IgE were 20 kU/L in normal group, 290 kU/L in CRS with nasal polyps (CRSwNP), and 187 kU/L in CRS without nasal polyps (CRSsNP). IL-21 levels were 28 pg/mL in normal group, 54 pg/mL in CRSwNP, and 71 pg/mL in CRSsNP. Both IgE and IL-21 were significantly elevated in both CRS patient subgroups. However, no significant difference was found between these two patient subgroups. The serum IL-21 levels correlated well with the disease severity in the patients. In addition, the secreted IL-21 was enhanced significantly in the patient's PBMCs stimulated by phytohemagglutinin (PHA).

(5) Conclusion: IL-21 could be a target for diagnosis and treatment of CRS.

## O11-5

## Synergistic action of nectins and cadherins establishes the mosaic cellular pattern of the olfactory epithelium

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The olfactory epithelium is a sensory neuroepithelium involved in olfaction. The olfactory epithelium is a pseudostratified columnar epithelium in which supporting cells, olfactory cells, and basal cells are arrayed in layers, from the apical to the basal surface. In the apical surface of the olfactory epithelium, olfactory cells and supporting cells are arranged in a characteristic mosaic pattern, in which olfactory cells are enclosed by supporting cells. This cellular pattern is established by cellular rearrangements during development. However, the mechanism of the cellular patterning remains unknown. Cell-sorting caused by cell adhesion molecules is assumed to be one of the mechanisms for cellular patterning. Nectins, a family of immunoglobulin-like adhesion molecules, comprise four members: nectin-1, -2, -3, and -4. Nectins first form cell-cell contact sites and recruit cadherin-catenin complex to the contact sites via alpha-catenin, leading to mature cell-cell adhesion. Nectins can interact homophilically and heterophilically. Their heterophilic interactions are stronger than their homophilic interactions in the following order: nectin 1-3 > nectin 2-3 > nectin 1-1, 2-2, 3-3. We have shown that heterophilic interaction between nectin-1 and -3 played a key role in checkerboard-like cellular patterning of the mouse auditory epithelium. In this study, we investigated the roles of nectins and cadherins in the mosaic cellular patterning of the mouse olfactory epithelium. We revealed that the olfactory cells expressed nectin-2, N-cadherin, and the supporting cells express nectin-2, nectin-3, E-cadherin, and N-cadherin. The heterophilic interactions between nectin-2 on olfactory cells and nectin-3 on supporting cells recruit cadherin-catenin complex to the heterotypic boundaries, which leads to differential distributions of cadherin-catenin complex depending on types of boundaries. The differential distributions of cadherin-catenin complex among boundaries promote intercalation of supporting cells between attached olfactory cells, resulting in the separation of attached olfactory cells. In this way, synergistic action of nectins and cadherin-catenin complex makes the differential adhesion force depending on types of boundaries, which contribute to the mosaic cellular patterning of the olfactory epithelium.

## O11-6

## The administration of nasal drops in the "Kaiteki" position allows for delivery of the drug to the olfactory cleft: a pilot study in healthy subjects

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[Background] About 5 % of the general population exhibit functional anosmia. Prevalence of olfactory impairment in adults older than 53 years is 25%. Sinunasal diseases are among the most frequent causes of olfactory dysfunction. Treatment of sinunasal olfactory dysfunction is problematic. While systemic treatment with corticoids shows therapeutic effects, few patients benefit from intranasal topical drug application. This may partly be due to access of the intranasal spray or head position of nasal drop to the olfactory epithelium. Some head positions, which were reported, are uncomfortable and lead poor compliance. Furthermore these positions have not been proven to reach the olfactory cleft. The aim of the present study was to investigate how nasally applied substances distribute within the new head position. Specially, we used a technique that was first described by Japanese researchers based on work in cadaver heads.

[Material and Methods] A total of 13 healthy volunteers participated (5 men and 8 female) in the study. Mean age was 30.0±8.4 years (range 22-50 years). None of them reported nasal problems. The tilted head position is lying on the side with upper neck turning from 20 to 30 degrees and with heading up from 20 to 40 degrees. This position was first described by utilizing a cadaver head in Japan (J. Miyazaki et al. New method for effective instillation of nasal drops in patients with olfactory dysfunction, *Jibi-rin* 97; 697-705, 2004). This is named "Kaiteki" position meaning for "comfortable" in Japanese. Approximately 5 minutes before application, the nasal mucosa was decongested using 2 sprays of xylometazoline hydrochloride. And blue food dye was used to visualize the intranasal distribution of the liquid. The investigation was carried out using nasal endoscopy immediately; two independent observers judged the intranasal distribution of the dye.

[Results] Nasal drops reached the olfactory cleft in 12 cases (92.3%). In addition, the blue dye was widely distributed in the nasal mucosa.

[Conclusions] The present data suggest that using the Kaiteki position lying sidewise, it seems likely to present the drugs more effectively and comfortably to the olfactory cleft. Thus, it may be hypothesized that therapy could be more effective using the Kaiteki position.



O11-7

## Investigation of prognostic factors for post-traumatic olfactory dysfunction

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**Background:** Post-traumatic olfactory dysfunction is common but has a poor prognosis. The purpose of this study was to analyze the effect of clinical features on improvements in post-traumatic olfactory dysfunction.

**Methods:** From 2007 to 2013, patients with post-traumatic olfactory dysfunction were enrolled. Olfactory function was assessed using the Sniffin' Sticks test at the first and final visits. Olfactory improvement was defined as a change in olfactory state to an improved level. Variables with a potential effect on improvements in olfactory dysfunction, including age, sex, time from trauma to first visit, initial olfactory function, observation time, and olfactory bulb integrity, were entered into logistic regression analysis.

**Results:** In total, 107 patients were included, with a mean age of 40 years. The mean follow-up period was 9.4 months. Eighteen patients (16.8%) had improvements with regard to olfactory function. No clinical factors were found to influence olfactory recovery in univariate and multivariate analyses (all  $p > 0.05$ ). In addition, there were no differences in clinical features between the patients with and without olfactory recovery (all  $p > 0.05$ ).

**Conclusion:** No significantly favorable prognostic factors for post-traumatic olfactory recovery were identified, reflecting, to some extent, the poor prognosis of post-traumatic olfactory damage. The results of this study provide useful information that clinical physicians can use when counseling patients with post-traumatic olfactory disorder regarding the prognosis, observation choice, and possible treatment strategy.

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### O12-1

#### Feasibility and Advantages of Myringoplasty using Transcanal Endoscopic Ear Surgery (TEES)

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**Introduction:** When performing transcanal myringoplasty under a microscope, the total circumference of the perforation can be difficult to confirm in patients where the external ear canal is narrow and/or protruded. In such patients, a retroauricular incision approach is usually employed. However, we have developed a transcanal endoscopic myringoplasty procedure, and the microscopic and endoscopic views are compared herein. The feasibility and advantages of transcanal endoscopic myringoplasty were examined.

**Patients:** Transcanal endoscopic myringoplasty was performed on 73 ears in 66 patients with chronic otitis media between 2011 and 2014.

**Methods:** Microscopic and endoscopic views were compared for each patient. The two fields of views were both recorded and evaluated to determine the advantages and disadvantages of microscopes and endoscopes. Myringoplasty was performed using an endoscopic technique while comparing views arbitrarily.

**Results:** Endoscopic views revealed the entire tympanic membrane in a single field with clear visualization of the perforation edges even when the ear canal was curved. This clear visualization facilitated reliable refreshing of the perforation edges and grafting. The anterior edge of the perforation was not visible under microscopy in 20% of total ears. Under an endoscopic wide view, the tympanic cavity was observable through the perforation, and the orifice of the tube, ossicular chain and tympanic isthmus were visible especially with large perforations. Transcanal endoscopic myringoplasty was successfully performed with a simple underlay technique or with an intracanal incision in cases of marginal perforation and total perforation.

**Conclusion:** Comparison of microscopic and endoscopic views revealed superior visualization and operability of endoscopic approach as opposed to transcanal simple underlay myringoplasty. Transcanal endoscopic myringoplasty does not require surgical exposure such as a retroauricular skin incision to get an anterior view. Our results demonstrated that transcanal endoscopic myringoplasty can be performed, regardless of the perforation size and the narrowness and/or protrusion of external ear canal.

### O12-2

#### Efficacy of transcanal endoscopic ear surgery in chronic otitis media

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Middle ear surgery is commonly treated using a surgical microscope. A binocular stereomicroscope is often used in ear surgery because this instrument offers many advantages including binocular stereoscopic vision of the surgical field; no obstruction of the view by blood, mucus, or bone dust on the lens; high magnification, besides being hands-free. Conversely, the narrow-angle view is a disadvantage of using a microscope for middle ear surgery. Moreover, there are several blind areas behind important structures, such as the facial nerve, that cannot be avoided. The use of an endoscope offers several advantages over the use of a microscope during middle ear surgery, particularly the wider field of view. Therefore, endoscopic ear surgery, especially transcanal approach, has been developing recently. The aim of this study is to endoscopically examine surgical outcome for chronic otitis media after endoscopic ear surgery comparing microscopic ear surgery. Eighty-four consecutive patients who underwent tympanoplasty for chronic otitis media. Transcanal endoscopic ear surgery was performed in 25 patients, transcanal microscopic ear surgery in 15, and postauricular incision microscopic ear surgery in 44. Hearing outcome of air conduction threshold, bone conduction threshold, air-bone gap was assessed. Outcome of hearing levels after transcanal endoscopic ear surgery was significantly better than postauricular incision microscopic ear surgery. Transcanal endoscopic ear surgery is advantageous to approach to the attic and perform tympanoplasty for sound transmission. Surgical outcome of transcanal endoscopic tympanoplasty for chronic otitis media is excellent.

O12-3

## The Outcome of Endoscopic Ossiculoplasty with Artificial Prosthesis

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**Background:** Endoscopic Ear Surgery has aroused a lot of attention all over the world in these years. The goal of this study is to estimate the feasibility of Ossiculoplasty performed with endoscope as an alternative procedure.

**Methods:** 24 patients who had received Endoscopic Ossiculoplasty with artificial prosthesis during Jan. 2014 to Jul. 2015 were enrolled in this study, including 6 cases of ossicle chain defect with merely Endoscopic Ossiculoplasty (Group O: PORP (3) and TORP (3)) and 18 cases of COM with or without Cholesteatoma that had received concomitant Ossiculoplasty (Group C: PORP (15) and TORP (3)) during Endoscopic Ear Surgery. We analyze the surgical outcome, Pre-OP and Post-OP hearing level, average surgical time and hospitalization days of these patients to evaluate the efficiency and efficacy of Endoscopic Ossiculoplasty.

**Results:** The Group O was all performed under local anesthesia with average surgical time of  $51 \pm 13.44$  mins, while the Group C was all performed under general anesthesia with average surgical time of  $161.14 \pm 24.38$  mins ( $p=0.002$ ). The hospitalization days for Group C:  $2 \pm 0.82$  vs. Group O:  $0.43 \pm 0.79$  ( $p=0.008$ ).

The average Air-Bone Gap for Group C: Pre-OP:  $32.71 \pm 7.22$  vs. Post-OP:  $13.4 \pm 6.72$  ( $p=0.03$ ) and Group O: Pre-OP:  $37.13 \pm 8.29$  vs. Post-OP:  $14.9 \pm 8.53$  ( $p=0.04$ ).

**Conclusion:** Endoscopic Ossiculoplasty was proved to be a satisfying alternative to the traditional microscopic surgery. However, the challenge is that one-hand surgery is more skillful and needs more practice.

O12-4

## Technical Considerations of Transcanal Middle Ear Surgery

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Transcanal middle ear surgery is to repair a drum defect and possibly reconstruct an interrupted ossicular chain directly through the ear canal without a standard endaural or postauricular incision under an operating microscope with the assistance of an endoscope. The application of transcanal surgery is not confined to a small perforation with a wide canal as most otologists might think and do. In fact, a near-total perforation repair and an ossiculoplasty can be performed through an advanced transcanal surgery in experienced hands. From 1999 to 2013, a total of 1307 middle ear surgeries for chronic otitis media were performed by the senior author. The annual rate of transcanal middle ear surgery was increased from 45% to 80%, while that of endaural approach was decreased from 55% to 20%. Both surgical approaches showed good ear drum healing rates and hearing results for type I tympanoplasty. During the year 2007 to 2013, among the 39 attempted transcanal ossiculoplasty, two-thirds of them succeeded with transcanal approach and one-third shifted to endaural approach due to limited exposure of ossicles. The hearing outcome was comparable between the two groups.

Advanced transcanal middle ear surgery is a delicate procedure that requires careful preoperative evaluation, intraoperative decision making, and mastery of difficult surgical techniques to achieve a good result. The operator must learn to manipulate two instruments with both hands at the same time. Precise coordination between surgeon's eyes through a microscope and hands through instruments are important prerequisites for a successful surgery. To overcome the natural curvature of ear canal, a standard ear speculum is placed to straighten the ear canal. The ear drum is shown through the speculum by carefully adjusting the position of speculum opening by surgical instruments under the microscope. The condition of ossicular chain and other middle ear structures can be further inspected with the assistance of an endoscope. However, in case of unexpected difficult exposure, the transcanal surgery is changed to endaural approach during surgery instead. The surgical results are comparable with those of traditional endaural and/or postauricular approach middle ear surgery. The advantages of transcanal approach include a minimal incision, a short operation time, good wound healing, cosmetic result and patient acceptability.

O12-5

## The feasibility of transcanal endoscopic tympanoplasty with no surface wound

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**Background/Purpose:** In recent decades, the endoscope has been incorporated into ear surgery. It has been also suggested that preservation of as much normal middle ear mucosa with the endoscope can promote the reeration of the mastoid cavity leading to better hearing outcomes in surgery. However, there is still a need to minimize the wound size and no surface wound especially in young children and the elderly. Herein, we try to develop a new way and evaluate the feasibility of total transcanal endoscopic tympanoplasty to repair the eardrum perforation. **Materials/Methods:** This retrospective study included patients with chronic otitis media who need to receive surgery. All patients did not have a haircut and underwent the transcanal endoscopic surgery. A graft was taken from the posterior surface of the tragus, and middle ear cavity and external ear canal were packed with Gelform soaked with antibiotics. The whole procedure involved the wounds limited to the posterior aspect of the tragus, tympanomeatal flap and the margin of perforated eardrum. Patient were observed the side effects postoperatively such as dizziness, tinnitus, hearing loss, wound pain, incision side numbness or signs and symptoms of facial nerve damage. All patients were follow-up at outpatient department once weekly for 3-4 times before removing the gelforms carefully and checked the healing condition. Continue to follow up for at least six months period and perform hearing test again to evaluate the outcome of the procedure. **Results/Discussion:** None of the patient suffered any significant symptoms such as sensation of the facial nerve injury, vertigo or hearing loss. The detail results and discussion will be presented at the conference. **Conclusion:** The present study demonstrates that transcanal endoscope applied to the middle ear surgery with no surface wound seen is feasible when the patients are chosen appropriately, and its successful rate is comparable with conventional microscopic surgery. However, postoperative infection still needs closely observing, particularly otomycosis, and processing timely.

O12-6

## Endoscopic ear surgery as a tool for surgical training

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Transcanal endoscopic ear surgery (TEES) is an emerging technique in the field of otologic surgery. We have performed 226+ TEES cases since 2012, which included tympanoplasty, cholesteatoma resection, ossiculoplasty, and stapes surgeries.

We have employed the TEES as a tool for surgical training of trainees. During ear surgeries, which are usually performed under microscope, it is difficult to give explanations of the important structures and landmarks in surgical fields and to teach how to manipulate the instruments in specific scenes, since the surgeon under training is looking into the microscope and the trainer behind her/him is watching the monitor.

With TEES, however, surgical fields on the monitor can be shared by the trainer and the trainees, and the trainer can give instructions in a timely manner. The trainer can even show the approach routes and give direction of the manipulation over the shared monitor, so that the trainee can comprehend them more easily than during microscopic ear surgery.

It is suggested that the surgical training using TEES is an effective method on the trainees who are under training of otologic surgery.

O12-7

## Underwater endoscopic management for inner ear diseases

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We propose a novel technique of “underwater” endoscopic ear surgery (UWEES) to preserve inner ear function for inner ear diseases. This technique provides a clear operative field without requiring suction and protects the inner ear from unexpected aeration that may damage its function. The mastoid cavity was filled completely with saline water by perfusion for the appropriate management of the site of inner ear diseases. Saline water perfusion is provided through an Endo-scrub lens cleaning sheath (Medtronic) covered on 0 degree 2.7mm diameter high-definition endoscope (Storz) that cleared the surgical field and prevented refraction effects.

A several cases of labyrinthine fistula were performed by UWEES to remove the matrix of cholesteatoma. Surgery was performed for removal of the cholesteatoma and closure of the fistula of the semicircular canal. The cholesteatoma was extirpated except for the island lesion of the matrix over the fistula under the operating microscope. Subsequently, by UWEES, the island residual matrix was exfoliated and plugged with temporal bone and fascia endoscopically and the fascia covered with bone paste.

A 36-year-old male had suffered from superior canal dehiscence syndrome (SCDS) in the left ear. He developed hyperacusis at the age of 34 and had tullio phenomenon. Computed tomography (CT) revealed SCDS on his left ear. UWEES was successfully performed for plunging of the superior semicircular canal by transmastoid approach.

Cochlear fistula, which is rarely encountered, may cause difficult situations to preserve hearing functions because of the vulnerability. UWEES was also applied for cochlear implantation to identify the scala tympani with clear surgical view. A 77-years old woman was suffered from chronic otitis media due to aspergilloma infection on both sides. Her hearing level was deteriorated after the twice episodes of acute inflammation periods, the former one concomitant with facial palsy on her right side. Two staged surgeries were planned, and cochlear implantation was performed on her left ear by UWEES successfully six months after blind sac closure of the outer ear canal at the first staged operation. UWEES was suitable to cochlear implantation when cochlear fistula existed.

UWEES has a great potential in ear surgery for preventing the risk to inner ear function, specifically in other interventions such as stapes surgery and temporal bone destruction corrective surgery. Furthermore, UWEES is expected as an efficient and safe method for drug delivery into the inner ear.

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## O13-1

## Bilateral Electric Acoustic Stimulation (EAS) improves sound localization detection and speech perception in noise

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### Background:

The electric acoustic stimulation (EAS) system improves hearing ability for patients with high-frequency hearing loss in whom standard hearing aids are ineffective. Meanwhile, bilateral cochlear implants (CIs) been shown to have several advantages over a unilateral CI in improving hearing performance through binaural hearing. However, the potential risks of vestibular dysfunction and taste disorders should be considered before deciding on a second implantation; moreover, the risk is higher with a second implantation.

Here, we report our results for two cases of adults with bilateral EAS implanted sequentially, and discuss the benefits they obtained based on conventional speech recognition and sound localization testing, as well as the safety of the procedure.

### Cases and Methods:

Two female patients, aged 38 (Case 1) and 45 years (Case 2), respectively, received bilateral EAS sequentially. To insert the electrode array, the round window approach was applied to reduce insertion damage to the cochlea. Pure-tone audiometry was performed preoperatively and postoperatively to evaluate the hearing preservation at the lower frequencies. Speech perception outcomes in quiet and noise, as well as sound localization were assessed for unilateral and bilateral EAS. To evaluate the safety and conservation of postoperative vestibular function, vestibular evoked myogenic potential (VEMP) and caloric response were also analyzed.

### Results:

Residual hearing at the lower frequencies was well preserved after insertion of electrodes using the round window approach. After bilateral EAS, speech perception was improved in quiet and even more so in noise. The Japanese monosyllable test (67S, at 65 dB SPL) score in noise improved from 55% correct (first EAS only) and 60% correct (second EAS only) to 80% correct (bilateral EAS) in Case 1 and from 45% correct (first EAS only) and 70% correct (second EAS only) to 75% correct (bilateral EAS) in Case 2. In addition, the sound localization ability of both cases with bilateral EAS improved remarkably. No changes in the caloric test and VEMP test results were observed after EAS surgery in Case 1. The caloric test and VEMP test results indicated normal vestibular response after EAS surgery in case 2.

### Conclusions:

Bilateral EAS is beneficial in noisy conditions and improves sound localization ability. The EAS surgical concept must be used for bilateral CI surgery. These results indicate that bilateral EAS was effective and can be recommended for patients with high-frequency hearing loss.

## O13-2

## The assessment of the ability of hearing in noise, music perception, and QOL with new processor

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[Introduction] Newly released speech processor by Cochlear, Neucleus® 6 (N6) processor, has the program that automatically recognizes the sound environment and selects the best hearing mode. In this study we aimed to examine whether N6 processor can improve hearing and QOL in Japanese population.

[Material and method] Six adult CI users who use Freedom® or Esprit™ 3G processor participated in our study. N6 processor with the same mapping program was provided. After one month trial, speech in quiet, speech in noise, music perception and QOL scale was assessed and compared with that of previous processor. CI 2004 in quiet and in noise (S/N 10dB) was used to evaluate speech discrimination, and J-CAMP - Japanese version of the University of Washington Clinical Assessment of music Perception Test (UW-CAMP) - was applied to evaluate music perception. Translated version of the Speech, Spatial and Qualities of Hearing Scale (SSQ) was used to evaluate QOL.

[Result] Three subjects with Esprit™ 3G and two subjects with Freedom® completed this study. One with Freedom processor couldn't perform music test, because he refused. The average CI 2004 score with their previous processor and N6 in quiet were 88% and 85%, respectively, and those in noise were 60% and 57%, respectively. The average pitch discrimination with their previous processor and N6 were 3.6 and 3.5 semitones. The average melody recognized percentages were 11% and 13%, and timbre percentages were 26% and 27%. SSQ score went up to -10 from -29 by renewing their device.

[Conclusion] Improvement of speech in quiet, speech in noise, music perception and QOL by upgrading was evaluated. Although there were no significant differences in hearing in noise and music perception, QOL tend to be improved. Accumulation of cases and long term evaluation will be needed for further study.

O13-3

## The Brainstem Process of Voice Pitch in Newborns

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### [Objective]

Pitch processing at the brainstem level, as reflected by the scalp-recorded frequency-following response, has been reported. However, our scarce understanding in such a response for newborns impedes the development of the frequency-following response technology.

### [Methods]

A set of four contrastive, monosyllabic Mandarin pitch contours that mimicked the American vowel /yi/ was used to elicit frequency-following response in ten American and ten Chinese newborns. A control condition was also conducted for quality control.

### [Results]

Data demonstrated that the rising and dipping pitch contours produced significantly better tracking accuracy and larger response magnitudes than the falling pitch contour ( $p < 0.05$ ). Additionally, the frequency-following response elicited by each pitch contour were significantly better ( $p < 0.05$ ) than those obtained in a control condition.

### [Conclusion]

These findings expand our knowledge in pitch-processing and suggest the use of a rising or dipping pitch contour when recording frequency-following response in newborns who were born in a tonal or non-tonal linguistic environment.

O13-4

## Written Language Ability in Mandarin-Speaking Children with Cochlear Implants

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**Objectives.** To examine narrative writing in cochlear implant (CI) children and understand the factors associated with unfavorable outcomes. **Materials and Methods.** Forty-five CI children in grades 2-6 participated in this study. They received CIs at  $4.1 \pm 2.1$  years of age and had used them for  $6.5 \pm 2.7$  years. A story-writing test was conducted and scored on 4 subscales: Total Number of Words, Words per Sentence, Morphosyntax, and Semantics. Scores more than 1.5 SD lower than the mean of the normal-hearing normative sample were considered problematic. Language and speech skills were examined. **Results.** Significantly more implanted students were problematic on "Total Number of Words" ( $p < 0.001$ ), "Words per Sentence" ( $p = 0.049$ ), and "Semantics" ( $p < 0.001$ ). Poorer receptive language and auditory performance were independently associated with problematic "Total Number of Words" and "Semantics", respectively. "Semantics" problem was more common in lower graders (grades 2-4) than in higher graders (grades 5-6;  $p = 0.016$ ). **Conclusion.** Implanted children tend to write stories that are shorter, worse-organized, and without a plot, while formulating morphosyntactically correct sentences. Special attention is required on their auditory and language performances, which could lead to written language problems.

O13-5

## A quaternary unit detailed analysis of symptoms at, and causes of Cochlear Implant failure over a 10-year period

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### 1. Objectives

Cochlear implantation rates have increased substantially since the introduction of the neonatal screening program. Each device has the inherent risk of failure in performance, which is the most common reason for implant removal. Our aims were to analyse the symptoms preceding device failure and to compare the causes and rates of failure for the various devices.

### 2. Method

Retrospective analysis of 83 consecutive cochlear implant failures at the Royal National Throat, Nose and Ear Hospital (RNTNEH) between 1993 and 2014. All three major cochlear implant companies' devices are implanted at RNTNEH. Data collected included implant type, failure interval, cause of failure, and symptoms preceding failure. Analysis was performed using Microsoft Excel.

### 3. Results

The mean time to failure was 11 years 1 month. Generally the cause of failure is categorised into device failure (83%) and medical failure (17%). The most common cause of device failure was hermeticity failure (45%). The commonest preceding symptom was reduced sound quality (57%). Other symptoms included: pain, excessive loudness and non-auditory stimulation.

### 4. Conclusions

Our mean time to failure was longer than those of previously published series. This may be related to the lower proportion of medical failures in our patient cohort. Meticulous surgical technique, early identification of problems and timely intervention may reduce rates of medical failure. Cochlear implants will always have a natural lifespan, which could increase with technological advancements. Our study demonstrated considerable variation between manufacturers however further investigation is required.

O13-6

## Effects of cochlear implantation on vestibular function in children

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### Introduction

Injury to the vestibular system is one of the risks of cochlear implant (CI) surgery. Studies on vestibular function in children who undergo CI have been limited, and the risks are not well known. In our institute, we routinely evaluate the vestibular function of children prior to CI surgery. In cases of sequential bilateral CI, we can assess both pre- and post-CI vestibular function. In this study, we aimed to analyze pre- and post-CI vestibular function in children and determine the influence of CI on vestibular function.

### Material and Methods

Fourteen children who underwent sequential bilateral CI and preoperative vestibular function tests were included in this study. Preoperative vestibular function tests included caloric and cervical vestibular evoked myogenic potential (cVEMP) tests. Pre- and postoperative vestibular functions were defined from the findings of vestibular function tests before the first and second CI surgeries, respectively. Nystagmus and dysequilibrium were considered symptoms of postoperative vestibular dysfunction. CI24RE cochlear implants with Contour Advance (CA) electrodes were used in 12 patients and CI24RE implants with Straight (ST) electrodes in two. Electrodes were inserted through cochleostomy in all patients.

### Results

All patients exhibited normal responses in the caloric test before surgery. Of these, one exhibited loss of response after surgery. This patient did not exhibit cVEMP responses on both sides before CI, indicating that it had limited vestibular dysfunction prior to surgery. Eleven patients underwent cVEMP tests and 7 patients exhibited good cVEMP responses before surgery, with two losing their responses after surgery. The three patients with postoperative vestibular dysfunction showed no obvious vestibular symptoms.

### Conclusions

In this study, 7% and 18% patients exhibited loss of response in the caloric and cVEMP tests, respectively. Vestibular functional loss could not be detected from postoperative vestibular symptoms. These results suggest that the incidence of vestibular functional loss after CI surgery is relatively small. However, vestibular function should be carefully evaluated, particularly in patients requiring second CI surgery, because some patients have inherently limited vestibular function.



O13-7

## **Congenital Cytomegalovirus Sensorineural Hearing Loss**

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### **INTRODUCTION**

Congenital infections are a well defined cause for neonatal mortality and morbidity. Of the many pathogens which cause these infections, Cytomegalovirus (CMV) is amongst the most prominent - particularly as a cause for sensorineural hearing loss and other neurodevelopmental disruption.

There has been much progression in recent years in terms of indications for cochlear implants, the use of paediatric neuroimaging and innovations in novel medical treatments.

Here we present a retrospective study which provides an overview of the assessment and preoperative work up for patient diagnosed with congenital CMV (cCMV) and their cochlear implant outcomes. We also discuss the latest developments in multidisciplinary management of these patients.

### **METHODS**

We assessed all children with cCMV who underwent cochlear implants insertion at St Thomas' Hospital from 2014 to 2015. We analysed their preoperative imaging and audiology as well as their neurological assessment. Cochlear implant outcomes were measured using the Speech Transmission Index, category of auditory performance and The Infant-Toddler Meaningful Auditory Integration Scale.

### **RESULTS**

Patients had an average age of 2.1 years at assessment and 4.0 at implantation. 18% received left-sided implants only. 55% were performed bilaterally in the same surgery while the remaining 27% were performed sequentially. Those performed sequentially had an average of 5.97 years between implantations. 45% of patients suffered severe to profound hearing loss at initial assessment, while 55% of patients presented with bilateral profound hearing loss. Patients had age appropriate hearing tests done at initial assessment and at follow-up. All patients showed a significant improvement in hearing test outcomes. 36% of patients presented with associated neurological comorbidities ranging from balance issues to cerebral palsy and 27% of patients also suffering some degree of neurocognitive dysfunction.

### **CONCLUSION**

Our results show that while overall cochlear implant outcomes were mixed, all children benefited. Importantly, our data also highlights the significant neurodevelopmental comorbidities associated with cCMV. With the recent developments in medical treatment, this underlines the importance of utilising a multidisciplinary management, including neuroradiology, paediatric neurology and paediatric infectious disease team members.

## Paper 14 Laryngology 2

### O14-1

### Effectiveness of medialization laryngoplasty on swallowing function of patients with unilateral vocal fold paralysis

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**Objectives:** Medialization laryngoplasty (ML) is a well-known phonosurgical procedure for unilateral vocal fold paralysis (UVFP). Although better glottic closure could theoretically contribute to better swallowing function, limited literatures have assessed the swallowing pathology after ML. The purpose of this study was to assess the impact of ML on the swallowing function in the patients with UVFP.

**Methods:** Thirty patients with UVFP who underwent ML between April 2013 and December 2014 were incorporated. Of these, 10 patients underwent type I thyroplasty with simultaneous arytenoid adduction (TPI+AA), 13 patients underwent CaHA injection, and 7 patients underwent collagen injection. Pre- and post-operative flexible endoscopic swallowing evaluations (FEES) were performed using clinic-based scoring proposed by Hyodo. Aerodynamic parameters (MPT and MFR) were measured as glottic functions and were comparatively assessed with FEES results.

**Results:** All the patients achieved satisfactory voice after MLs. Preoperative FEES represented abnormal findings in 27 (90%) patients. While glottal closure reflex and swallowing reflex initiation were normal in most of the patients, salivary pooling degree (SP) and pharyngeal clearance (PC) were disturbed in multiple patients. Although improved scores of these parameters were observed after MLs in 14 patients (52%), PC remained disturbed in the patients with high vagal paralysis (n=3) and idiopathic UVFP (n=3) after surgeries. Furthermore, postoperative values of aerodynamic measurements were relatively poor in 7 patients (MFR<250ml/s and/or MPT<10s) with unimproved postoperative PC. Among multiple surgical options, CaHA injection provided especially quick and successful recoveries of SP and PC.

**Conclusions:** Phonosurgical ML procedures could affect the swallowing functions of the patients with UVFP. Future studies including the assessment on potential limitations of ML to improve swallowing functions are warranted.

### O14-2

### Surgical planning of medialization laryngoplasty using an open-source DICOM viewer

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**Objectives:** The aim of this study was to determine the efficacy of preoperative planning of medialization laryngoplasty (type I thyroplasty and/or LCA-pull) using the OsiriX DICOM viewer.

**Methods:** Seven patients with unilateral vocal cord paralysis and severe, breathy dysphonia were recruited. Multi-detector computed tomography (MDCT) DICOM data was obtained and breath-holding was performed during image acquisition. Using three-dimensional multi-planar reconstruction (3D-MPR), the upper level of the vocal folds were located, the optimal location for a window was outlined, and the angle between the midline of the thyroid cartilage and the line indicated by the upper level of the vocal folds and distance from the thyroid notch to the presumed point of anterior commissure were measured. Type I thyroplasty and/or LCA-pull was performed using Isshiki's original method and Iwamura's method, and only the placement of the window was decided according to the preoperative simulation point. Postoperative CT and evaluation of voice were performed 3 months after operation.

**Results:** All patients are now free from breathy dysphonia, and their glottic closures resolved satisfactorily. Postoperative CT revealed that appropriate implant positioning resulted in a successful surgical intervention.

**Conclusions:** Preoperative surgical planning of medialization laryngoplasty with the OsiriX DICOM viewer can be used for strategic and predictable type I thyroplasty and LCA-pull.

O14-3

## Hemodynamic Impacts of Office-Based Laryngeal Procedures

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**Background:** With the progress in modern endoscopic technology, various studies had demonstrated that office-based laryngeal procedure (OBLP) can be an effective alternative modality for benign vocal fold disorders. This study intends to investigate the potential influence of OBLP on the patients' hemodynamic profiles.

**Design:** We prospectively recruited patients who received vocal fold steroid injection, injection laryngoplasty, and angiolytic laser in the out-patient clinic under local anesthesia (LA) from April 2015. A detailed history concerning dysphonia were recorded during the first clinical visit, including underlying comorbidities and medical prescriptions. We measured heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) and oxygen (O<sub>2</sub>) saturations at baseline, after LA, after procedure, and 20 minutes after the completion of procedures.

**Results:** A total of 92 patients (31 male and 61 female) were included, with a mean age of 45.7 +/- 14.6 years (range 21 ~ 77 years). Following LA, 29 and 23 patients report tongue/oral numbness and lumping throat (31% and 25%, respectively). Only 2 and 4 patients report palpitation and chest tightness after LA, without risky elevation of BP or HR, and the procedure can be completed uneventfully. The SBP significantly elevated from 117 mmHg (baseline) to 129 mmHg (after LA,  $p < 0.001$ ), 127 mmHg (after procedure,  $p < 0.001$ ), and 122 mmHg (20 minutes after procedure,  $p < 0.001$ ). DBP also showed similar trend of significant elevation throughout the procedure. HR elevated in female subjects after LA (from 76.6 to 81.7,  $p < 0.001$ ), which returned to normal level after the procedure. O<sub>2</sub> saturation did not show significant alteration peri-operatively. No significant differences were noted between three treatment modalities.

**Conclusion:** Through systematically data collection, this study provides comprehensive information of hemodynamic change following OBLP. Subsequent recruitment of more cases shall provide further information on the influence from underlying comorbidity and concurrent medical prescriptions.

O14-4

## Quantitative analysis of vocal fold vibration in normal and pathological voices using high-speed digital imaging

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**Purpose:** Although various analysis methods for high-speed digital imaging (HSDI) exist, each method has merits and demerits, and to the best of our knowledge, no single analysis method that exists today is sufficient enough to fully clarify spatiotemporal vibratory characteristics of vocal fold vibration in a quantitative manner. Hereby, the authors propose a combination of several analysis methods as a routine HSDI evaluation.

**Method:** From the HSDI data of 46 vocally healthy speakers and 304 patients with various laryngeal disorders, vibratory characteristics were quantitatively evaluated using several methods such as visual-perceptual rating with an assessment form, laryngotopography, digital kymography and glottal area waveform.

**Result:** Normative values obtained from vocally healthy subjects generally matched the values in the literature. There were gender- and age-related normal variations in selected parameters such as fundamental frequency, open quotient, speed index, location of glottal gap, lateral peak and longitudinal phase difference. In comparison with the normal group, the pathological group revealed greater period irregularity, greater asymmetry in amplitude, mucosal wave, phase and lateral peak, and poorer glottal closure with larger open quotient, smaller speed index and larger minimum glottal gap.

**Discussion:** A combination of different analysis method attempted in the present study was effective in quantitatively documenting normal variation and differentiating normality and abnormality. However, the present result is tentative, and further investigation as to the choice of method or parameter will be called for.

O14-5

## Frequency of Electroglottographic Fluctuations in the Expiration Phase during Throat Clearing as a Useful Functional Index

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**INTRODUCTION:** Throat clearing (TC) is a cooperative movement associated with the larynx for the removal of foreign bodies or discharges in the lower airway. However, methodologies for estimating the laryngeal condition during TC remain developed compared with phonation and swallowing. In the present study, using high-speed digital imaging (HSDI) and electroglottography (EGG), to clarify the characteristics of EGG waveforms reflecting the efficiency of TC, we investigated the associations between the maximal frequency of fluctuations in EGG signals during the expiration phase of TC and aerodynamic parameters in normal participants and patients showing unilateral vocal fold paralysis (UVFP).

**MATERIALS AND METHODS:** Twenty healthy adult participants and 20 patients with UVFP were included. Each participant was fitted with EGG electrodes followed by the insertion of a transnasal flexible fiberoptic connected to a high-speed camera, and subsequently asked to perform weak and strong TC in order while recording the HSDI movies and acoustic/EGG signals. The maximal frequency of EGG fluctuations of the expiration phase was calculated using Praat. In addition, the expiration phase rise time (EPRT), peak expiratory cough flow (PECF) and volume acceleration (VA) were measured in each patient using a spirometer with a face mask. These obtained values were compared between the tasks and between the groups. The associations between these measurements and the parameters of EGG fluctuation were analyzed.

**RESULTS:** In the normal participants, EGG fluctuation and vibration of the vocal folds/supraglottic structures were observed in the post-compression expiration phase of TC. Strong TC induced significantly higher values for the maximum frequency of the vocal fold fluctuation, PECF and VA than weak TC. In addition, the normal group showed significantly higher values of these measurements than the UVFP group. In the analysis of the correlations between the aerodynamic parameters and the maximal frequencies of EGG fluctuation, the PECF values showed the highest correlation coefficient with the frequencies of EGG fluctuations in the whole group and only the male group ( $r=0.62$ ,  $r=0.74$ , respectively).

**CONCLUSION:** EGG fluctuation during the expiration phase of TC was observed concomitantly with strenuous vibration and repeated contact of the vocal folds/supraglottic structures, suggesting that the maximal frequency of the vocal fold fluctuation is dependent on the subglottic pressure and the mass of the vocal folds. This can explain our present results. The measurement of the maximal frequency of EGG fluctuation may be a useful indicator for estimating the efficiency of TC even in patients with poor performance.

O14-6

## Epidemiology of vocal fold paralysis in Taiwan: a population-based study using the National Health Insurance Database

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**Introduction:** Vocal fold paralysis is a considered a relatively common problem of the vocal folds that can have a significant impact on a patient's quality of life. Despite this, studies examining the basic epidemiology of this condition are rare, and as a result, the actual disease burden for this problem is not well known.

**Objective:** The goal of this study is to investigate the epidemiology of vocal fold paralysis (VFP) among the adult population in Taiwan using the National Health Insurance claims database.

**Methods:** A retrospective cohort study was conducted using claims data of National Health Insurance. Claims data were retrieved for patients 20 years or older with a diagnosis of vocal fold paralysis (International Classification of Diseases, Ninth Revision, Clinical Modification codes 478.3 ). The authors describe the demography of vocal fold paralysis and the medical resource utilization associated with its treatment. **Results:** An increase in incident cases of vocal fold paralysis was seen from 2001-2011. Males were slightly more likely to be diagnosed than females (53% v 47%). The majority of cases were found in those over age 40, with a median age of diagnosis of 56.5 years. Treatment at time of diagnosis was not common, as 82.5% of those diagnosed opted for no treatment. Of those undergoing treatment, voice therapy was the most common form selected.

**Conclusion:** The number of individuals diagnosed with VFP in Taiwan has increased steadily from 2001 to 2011. Incidence increases with age, with a median age of diagnosis of 56.5 years. Despite several clinically established treatment options, few are receiving care following initial diagnosis.

O14-7

## **Photocoagulation therapy for laryngeal dysplasia using angiolytic lasers**

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**Objectives:** In the management of laryngeal pre-cancerous lesions such as dysplasia or carcinoma in situ (CIS), it is important that lesion regression occurs without any complications. In order to minimize damage to the vocal fold and subsequent scar formation, photocoagulation therapy using angiolytic lasers has been attracting attention. Therapeutic effects have been reported for this type of treatment, however, vocal function after treatment has not been well discussed. In this retrospective case series, we examined the therapeutic effects of photocoagulation therapy on laryngeal dysplasia and the impact on vocal function.

**Study design:** Retrospective case series

**Methods:** Twenty-four patients with laryngeal dysplasia or CIS were treated with photocoagulation therapy using angiolytic lasers from 2007 to 2013 at Kyoto University Hospital. Their ages ranged from 55 to 85 years (average, 70.8 years). Eighteen had a unilateral lesion (right: 8, left: 10), five had bilateral lesions and one had a lesion at the anterior commissure. Two patients were treated under general anesthesia, the remaining 22 patients were treated with topical anesthesia. The extent of the lesions was evaluated by endoscopic examination before and after treatment to assess the therapeutic effects of photocoagulation therapy. Voice assessments consisted of aerodynamic and acoustic examinations.

**Results:** Laser irradiation was easily performed in all patients without any complications. More than 50% disease regression was observed in 20 of 24 patients. Acoustic and aerodynamic analyses revealed improvement in pitch perturbation quotient (PPQ) with no impairment in other parameters.

**Conclusions:** Our case series demonstrates the usefulness and safety of photocoagulation therapy using angiolytic lasers in the treatment of pre-cancerous glottal lesions.

## Paper 15 Otolology 6

## O15-1

## Correlation of sitting 3-D CT findings of Eustachian tube with subjective and objective findings in Patulous Eustachian tube patients

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Patients with patulous Eustachian tube (PET) suffer from symptoms such as aural fullness, autophony, and hearing their own breathing, as a result of persistent opening of the normally closed Eustachian tube (ET). These symptoms are usually masked in the recumbent position, which has detracted from the advantages of modern imaging for the diagnosis of the PET, because computed tomography (CT) and magnetic resonance imaging (MRI) are performed in the recumbent position. However, the horizontal CT system such as three-dimensional CT (3-D CT) was recently developed, and that is useful for diagnosis of PET (Yoshida H et al, *Acta otolaryngol.* 2004, Kikuchi T et al, *Otol Neurotol* 2007). In this study, we observed the correlation of sitting 3-D CT findings of Eustachian tube with subjective and objective findings in PET patients.

## O15-2

## Temporal Bone CT Findings and Hearing Profiles in 25 Children with Charge Syndrome

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### [Introduction]

CHARGE syndrome is a condition in which 4 or more of abnormalities including coloboma(C), central nervous system anomalies, heart defects(H), atresia choanae(A), retardation of growth and/or development(R), genital hypoplasia(G), ear anomalies(E), and hearing impairment or deafness are concurrent. Its severity varies widely, and its incidence is reported to be 0.1 to 1.2/1,000 live births. In 60–70% of children mutations of the CHD7 gene have been reported as the etiology of this syndrome. Hearing loss is observed in more than 90%, and its type is reportedly diverse, being conductive or mixed or sensorineural hearing loss (SNHL).

In this study, we analyzed HRCT of the temporal bone images, and hearing profiles, and compared with the literature of CHARGE syndrome.

### [Methods]

Total of 25 consulted our division of Otolaryngology in our children hospital. All of 25 patients had undergone the Department of Genetics at our hospital and/or elsewhere. 15 patients with mutations of the CHD7 gene were found, 10 patients were definitively diagnosed with major and minor criterions of CHARGE syndrome (by Pagon et al.).

We studied all of 25 patients (50 ears), of the HRCT of the temporal bone images, and hearing profiles examined by the ABR/COR/Audiometry tests which were selected depending on their ages and physical conditions.

Patients ages ranged from 7 months to 29 years old and were 15 females and 10 males. Two of them died of systemic complications.

### [Results]

On HRCT, abnormalities were classified into middle ear, cochlea and semi-circular canals(SCCs). At the middle ear, there found small middle ear cavity 86%(43/50), ossicles deformities 54%(27/50), ankyloses 56%(28/50), no stapes 4%(2/50). At the cochlea, there found of common cavity 4%(2/50), Incomplete Partition type I 22%(11/50), Incomplete Partition type II 50%(25/50). At the SCCs, there found of absent 72%(36/50), incompleting 8% (4/50), and only superior SCCs 12%(6/50).

Hearing impairment was found in all of 25 patients (49ears) and classified by 21-40dBnHL 41-70dBnHL 71-100dBnHL and profound hearing loss. Hearing threshold of 21-40dBnHL:8%(4/50), 41-70dBnHL:24%(12/50), 71-100dBnHL:18%(9/50), profound:48%(24/50). Only one ear indicated as normal hearing. Types of hearing loss indicated, conductive 2%(1/50), mixed 10%(5/50), SNHL 70%(35/50), unable to identify 16%(8/50). We performed cochlear implantation for 2 patients (2/50).

### [Conclusions]

In CHARGE syndrome temporal bone CT is very useful to find diverse abnormalities which could suspect the causes of the hearing loss. This study could help guide the clinical managements including hearing aids and Cochlear Implantations in CHARGE syndrome.

O15-3

## Significance of cVEMP and oVEMP tests for early diagnosis of acoustic neuroma

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When we treat patients with acoustic neuroma (AN), early diagnosis is mandatory to keep their QOL. So far it has generally been known that ABR is the most sensitive test battery for making diagnosis. Recently it has become possible to examine the function of superior vestibular nerve and inferior vestibular nerve separately. When we consider the fact that the tumor originates from inferior or superior vestibular nerve, the detection rate of acoustic neuroma will become much better than that of the usual examination methods. From these background, we have examined cVEMP and oVEMP in addition to canal function along with ABR in cases with intracranial tumor cases. Abnormality rates were as follows; oVEMP:69.6%, cVEMP:71.7%, CP:72.5%, and ABR: 86.6%. Either cVEMP or oVEMP abnormality: 92.5%. Two cases had normal results in all of those tests.

Thus so far, no test will be available to detect small acoustic neuroma with 100% positive. However, detection rate will become better employing both VEMPs for AN suspected case.

O15-4

## Perioperative bone-conducted vestibular-evoked myogenic potentials in patients with otosclerosis

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**Introduction:** Stapes surgery is an effective and safe treatment for otosclerosis. However, several studies have shown that some patients report vestibular symptoms such as unsteadiness, dizziness, or vertigo following stapes surgery. The mechanisms underlying these vestibular symptoms remain unclear. Stapes surgery may cause otolithic disorders because of the anatomical proximity of the footplate to the otolithic organs. Vestibular evoked myogenic potentials (VEMPs) can be used to evaluate the function of the otolithic organs. Cervical VEMP (cVEMP) characterized by a positive peak (p13) and subsequent negative peak (n23) is associated with saccular organs, and ocular VEMP (oVEMP) characterized by a negative peak (n1) and subsequent positive peak (p1) is associated with utricular organs. Air-conducted VEMP cannot be recorded in patients with conductive hearing loss. We therefore performed bone-conducted (BC) cVEMP and oVEMP using a mini-shaker (Bruel & Kjar) to induce bone-conducted vibrations.

**Object:** To investigate BC VEMPs using a mini-shaker before and after stapes surgery.

**Patients:** Nine otosclerosis patients (age range, 20-67 years) who underwent primary stapes surgery (8 stapedotomies, 1 stapedectomy) between October 2014 and April 2015. All patients were females with no history of previous surgery.

**Methods:** We performed cVEMP and oVEMP with BC vibration through a mini-shaker on the midline forehead before and after stapes surgery. The p13-n23 amplitude in cVEMP and n1-p1 amplitude in oVEMP were measured. Asymmetry ratio was then calculated. Postoperative hearing results were evaluated according to the 2010 guidelines for reporting hearing results in middle ear and mastoid surgery by the Japan Otological Society.

**Results:** Overall success rate in terms of postoperative hearing was 88.9% (8/9 patients). Four patients complained of temporary postoperative dizziness, but none showed spontaneous nystagmus. Both p13-n23 amplitude in BC cVEMP and n1-p1 amplitude in BC oVEMP did not differ significantly ( $p = 0.18$  and  $p = 0.96$ , paired t test) between before and after surgery. No significant differences in asymmetry ratio were seen between BC cVEMP ( $p = 0.77$ ) and BC oVEMP ( $p = 0.08$ ), either. In one patient, the asymmetry ratio in BC oVEMP increased after surgery.

**Conclusion:** These findings suggest that stapes surgery causes no or only undetectably small otolithic disorders at the VEMP level.

## O15-5

## Auditory Change in Cleft Patients Undergoing Orthognathic Surgery

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**Background/Purpose:** Orthognathic surgery (OGS) is widely performed to correct congenital and acquired dentofacial discrepancies. Jaw deformity can be corrected by a well-designed OGS, despite of inducing changes of pharyngeal muscles and postoperative swelling which usually result in dysfunction of middle ear and otitis media. However, the effects of OGS on hearing sensitivity and middle ear function in cleft patients remained uncertain till now.

**Materials/Methods:** We conducted a prospective study with 32 cleft patients undergone OGS. Clinical auditory examinations including pure tone audiometry and speech audiometry were performed at three sequential time points: pre-operation, 1 week post-operation and 3 months post-operation. Middle ear tympanometry was recruited to evaluate variations of middle ear status, and wireless digital video otoscope was used to record status of tympanic membrane at the above time points. These tests help us to seek and clear the related factors of hearing changed in cleft patients after OGS through long term tracking.

**Results/Discussion:** Totally 32 cleft patients were enrolled in this study. Negative middle ear pressure was observed in many patients and otitis media with effusion developed in 9.4% of cases after surgery under general anesthesia. Negative middle ear pressure was found 1 week and also 3 months after operation. Hearing sensitivity was not influenced.

**Conclusion:** Negative middle ear pressure was observed in many cleft patients, and otitis media with effusion (OME) developed in 4.7% of ears after OGS under general anesthesia. Although hearing sensitivity may be insignificant silent, close observation of the middle ear pressure for cleft patients after OGS is still in need at the outpatient department to avoid possible auditory system dysfunction.

## O15-6

## Good outcomes of Balloon dilatation of Cartilaginous Eustachian Tube

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### OBJECTIVES:

To study the safety/efficacy of balloon dilation of the cartilaginous eustachian tube (ET) in patients with ET dilatory dysfunction.

### STUDY DESIGN:

Prospective with subjects as their own historical controls since Sep. 2014.

### SETTING:

Tertiary refer center.

### SUBJECTS AND METHODS:

Fifteen consecutive adult patients with longstanding aural fullness sensation that were difficult to autoinsufflate their ET by Valsalva, swallow, or yawn. At the time of intervention, 2 of 15 had a tube. All of 15 had intact TMs, None with OME and tympanogram type A. Balloon dilation of the cartilaginous ET was performed with balloon dilation instruments via transnasal endoscopic approach under general anesthesia in a day surgery setting. Inflation was to a maximum of 12 atm for 2 minute.

### OUTCOME MEASURES:

Ability to Valsalva, rating of ET mucosal inflammation, tympanogram, Blue stone nine steps inflation-deflation test, ETD Q7 questionnaire and otoscopy findings.

### RESULTS:

All cases successfully dilated. 13 of 15 could self-insufflate by Valsalva ( $P < .001$ ); At base line, only 3 ETs of 2 patient pass the nine steps test before surgery and 17 of 21 ETs (13 of 15 patients) passed after surgery ( $P < .001$ ). The ETD Q7 improved. Procedures were well tolerated, without pain or complications related to dilation.

### CONCLUSION:

Balloon dilation of the cartilaginous ET was beneficial and without significant adverse effects in the treatment of ET dilatory dysfunction.



O15-7

## A new electroneurography method for patients with facial palsy - midline method

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Background: Electroneurography (ENoG), which was first described by Esslen in 1973, is widely used for determining the degree of facial nerve damage and evaluating the prognosis in facial palsy. The ENoG value, which is the ratio of the compound muscle action potential (CMAP) on the paralyzed side to that on the healthy side, multiplied by 100, reflects the percentage of facial nerve degeneration on the paralyzed side. In the standard ENoG measurement, the two recording electrodes are applied to the nasolabial fold for CMAP recording. The problem of this method is that the nasolabial fold cannot be easily detected in severe facial palsy, and the optimal bilateral electrode placement is difficult due to facial asymmetry.

Recently, we have used new electrode positions for measuring CMAPs from the facial muscles in which one electrode is placed on the mental protuberance, and the other is placed on the philtrum over the orbicularis oris muscle, the midline method. This method is simple in terms of electrode setting and is not influenced by any resting asymmetry of the face in patients with unilateral facial palsy. In the present study, we compared these methods for clinical use.

Patients and Methods: Sixty-four patients with peripheral facial palsy were enrolled. CMAPs were recorded using the midline and standard methods simultaneously. Percutaneous electrical stimulation was applied to the main trunk of the facial nerve. The amplitudes of the CMAPs and the relationship between the ENoG values, calculated using the CMAPs, and the period to full recovery from the facial palsy were compared.

Results: The midline method had larger CMAP amplitudes in both sides and a stronger negative correlation in the relationship between the ENoG value and period to full recovery from palsy than the standard method (-0.52 vs. -0.33,  $P=0.001$ ) statistically.

Conclusions: The midline ENoG method may have advantages over the standard method in terms of ease of electrode setting, and the ENoG value may be a useful prognostic factor. We also propose a criterion for the ENoG value for clinical use of the midline ENoG to evaluate the prognosis of the facial palsy.

**Poster** Head and Neck 1

P01

**High Level of Plasma EGFL6 Is Associated with Clinicopathological Characteristics in Patients with Oral Squamous Cell Carcinoma**

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**Background:**

EGFL6 is a secreted protein that promotes endothelial cell migration and angiogenesis. The current study investigated the association between the clinicopathological characteristics and plasma level of EGFL6 in patients with oral squamous cell carcinoma (OSCC).

**Methodology and Principal Findings:**

Plasma EGFL6 concentration was determined by ELISA in 330 male OSCC patients. In addition, the metastatic effects of EGFL6 knockdown on oral cancer cells were investigated by cell migration assay. The results showed that plasma EGFL6 levels were significantly higher in the patients with advanced T status ( $p=0.002$ ), distant metastasis ( $p=0.001$ ), and higher TNM stages ( $p=0.033$ ).

**Conclusion:**

The plasma level of EGFL6 may be useful to assess disease progression, and especially advanced T status and higher TNM stage, in patients with OSCC.

P02

**Surgical treatment of substernal goiter: An analysis of 41 secondary mediastinal goiters and 1 primary mediastinal goiter**

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**Background.** Substernal goiter is defined as a thyroid mass where more than 50% is located below the thoracic inlet. Substernal goiters are classified as primary or secondary intrathoracic goiters. Here, we report the diagnosis, symptoms, treatment, and postoperative complications of 42 substernal goiters.

**Methods.** A retrospective chart review of 334 patients undergoing thyroidectomy at the Department of Otolaryngology-Head and Neck Surgery of the Tokyo Metropolitan Tama Medical Center. Between 2009 and 2014, 42 patients underwent surgery for substernal goiter.

**Results.** The frequency of primary and secondary mediastinal goiters was 0.3% (1/334) and 12.3% (41/334), respectively. The preoperative symptoms were neck mass (76.2%), dyspnea (9.5%), and dysphagia (11.9%). Eight patients (19.1%) were asymptomatic. Thirty-seven patients had benign masses (88.1%) and 5 patients had malignant masses (11.9%). Most patients were operated on for adenomatous goiters (50.0%). In eight cases beyond the aortic arch, the tumors were benign and there were six cases of adenomatous goiter. All patients underwent a successful transcervical incision without sternotomy. Even the primary intrathoracic goiters were extracted after total thyroidectomy via the cervical approach without complications. Although a postoperative complication caused a unilateral recurrent nerve paralysis in one case, phonetic function improved in 6 postoperative months. No instances of postoperative bleeding or definitive hypoparathyroidism occurred, and tracheostomy was not performed in any of the cases.

**Conclusion.** The cervical approach was safely performed in almost all substernal goiters without an extracervical procedure. Select cases of primary mediastinal goiter may be excised via the cervical approach.

P03

## Treatment of cervical tuberculous lymphadenitis - An analysis of 19 cases

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### (Objectives)

After tuberculous pleurisy, lymphadenitis arising from cervical lesion is the second most common form of extrapulmonary tuberculosis. It is generally treated with antituberculosis agents, but some patients resist chemotherapy. In such patients, surgical resection is often considered as an alternative treatment. This study aims to evaluate the therapeutic outcome of cervical tuberculous lymphadenitis and the future course of treatment of this disease.

### (Patients & Methods)

We retrospectively reviewed the clinical charts of patients diagnosed at the Department of Otolaryngology-Head and Neck Surgery of the Tokyo Metropolitan Tama Medical Center between 2005 and 2015 and identified 19 cases of cervical tuberculous lymphadenitis.

### (Results)

Patient ages ranged from 26 to 85 years old (average: 55.5 years), and the male-to-female ratio was 10:9. The range of tuberculosis progression was as follows: 14 in only the cervical lymph node, 2 in the mediastinal lymph node, 1 in the lung and vertebrae lumbales, 1 in the lung, and 1 in the pleural membrane. All 19 patients were initially treated with antituberculous drugs at the Department of Pulmonary Medicine. In five cases, the antituberculous drugs were replaced due to side effects. Two cases involved a single drug-resistant strain, and one case involved a double drug-resistant strain. Sixteen patients were controlled by only chemotherapy. The three patients resistant to chemotherapy were successfully treated through neck dissection.

### (Conclusion)

Local therapy could prove effective in cervical tuberculous lymphadenitis patients who exhibit an inadequate response to drugs.

P04

## Hybrid carcinoma of the parotid gland: a case report (epithelial-myoepithelial carcinoma and squamous cell carcinoma)

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Hybrid carcinomas of the parotid gland are a recently defined and rare tumor entity, consisting of two histologically distinct type of carcinoma with in the same topographic area. These are very rare lesions, as they represent less than 0.1% of all salivary gland neoplasms. We present a 63-year-old man with enlarging mass in the right parotid lesion for a month. Physical examination disclosed a 3.7 x 3.2 cm, hard, painless and mobile mass without right facial palsy. Magnetic resonance imaging (MRI) revealed a low-intensity area on T1-weighted images and a non-homogenous low-intensity area on T2-weighted images. The images of the tumor demonstrated high intensity on a post-gadolinium contrast T1 image. The results of fine needle aspiration was a class II tumor that was presumed to be pathologically benign. The patient underwent total parotidectomy without facial nerve, because histopathology of the tumor revealed suspicious of pleomorphic adenoma during the operation. The final pathological diagnosis was hybrid carcinoma (epithelial-myoepithelial carcinoma and squamous cell carcinoma) of the parotid gland. Local recurrence was observed 5 months after the first surgery, and was removed with skin. Pathological examination revealed the recurrence of squamous cell carcinoma. Post-operative radiation was added. After the treatment, he did well without recurrence or facial paralysis for five years.

P05

### Suppression of SESN1 depresses cisplatin and hyperthermia resistance in human maxillary cancer cells

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Cisplatin plays an important role in the therapy of the head and neck cancers. However, some head and neck cancers have cisplatin resistance, leading to a difficulty in treatment and poor prognosis. To analyze the mechanisms of resistance, we established cisplatin-resistant IMC3CR cell line from human maxillary cancer cell line IMC3. Cisplatin-induced genes were analyzed in IMC3CR cells by PCR array. Among the genes whose expressions were increased by cisplatin, we focused on SESN1 in this study. SESN family regenerate peroxiredoxin and suppress oxidative DNA injury by reactive oxygen species (ROS), which could be induced by chemotherapeutic agents such as cisplatin. In addition, it was reported that ROS participated in apoptosis induced by cisplatin or hyperthermia. We found that SESN1 could be induced by cisplatin treatment in IMC3CR cells by real time PCR and Western blotting. Suppression of SESN1 by specific RNAi reduced cell viability through enhancement of ROS after cisplatin. Moreover, RNAi for SESN1 enhanced cell-killing effect of hyperthermia, but not radiation. In this study, we analyzed the participation of SESN1 in cisplatin and hyperthermia resistance of human maxillary cancer. And we examined possibility of SESN1 as a candidate of novel molecular targeted therapy for human head and neck cancers.

P06

### A Case of Primary Submandibular Gland Oncocytic Carcinoma

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Primary submandibular gland oncocytic carcinoma is a rare pathology, with only 10 cases being reported to date. We encountered a case of primary submandibular gland oncocytic carcinoma and report it herein. The patient was a 69-year-old man who came to our hospital with right submandibular cancer as the main complaint. Based on the results of computed tomography and magnetic resonance imaging, submandibular gland tumor was diagnosed. Preoperative cytodiagnosis suggested class III oncocytic carcinoma. Resection of the right submandibular tumor was performed along with right neck dissection. Postoperative histopathological diagnosis was oncocytic carcinoma. As of 3 years following surgery, no recurrence has been identified.

P07

## Interstitial Lung Disease associated with Cetuximab for Patients with Head and Neck Carcinoma: A single-institution experience in Japan

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Interstitial Lung Disease(ILD) induced by monoclonal antibody against EGFR such as Cetuximab has been rarely reported and consequently the incidence and the clinical features of ILD in patients with squamous-cell carcinoma of the head and neck are unknown in any detail. We retrospectively reviewed the records of patients who were treated for LASCCHN and R/MSCCHN by Cetuximab in our hospital between March 2013 and June 2015. The incidence of ILD was 13% (6/46) at our hospital. The average age was 70.2 years old (range59-81) when ILD was developed. All patients had smoking history. 2 patients were death for ILD and another patients are alive. Some studies suggested that smoking history, poor PS, pre-existing lung disorder elderly are risk factors of drug induced ILD. We consider that administration of Cetuximab for SCCHN patients should be deliberate because many patients of SCCHN are elderly, with smoking habit and pre-existing lung disorders such as pulmonary emphysema which decreases normal lung capacity.

P08

## Pilomatricoma of the Neck -Case Report

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Pilomatricoma is a benign skin appendage tumor derived from the outer sheath cell of hair follicle and is usually locating on head, neck and upper extremities. It is most commonly seen in children , adolescents and presents with a painless superficial skin mass. We report a 12-year-old boy presenting with a painless, slow-growing mass in right posterior neck for 4 months. The physical examination revealed a movable solitary firm nodule. The computed tomography scan revealed a well-demarcated and non-homogenous calcified mass with estimated size of 1.5 × 0.8 cm. The tumor was totally removed under general anesthesia, and the histopathology reported a pilomatricoma. There was no evidence of recurrence after 6 months follow-up.

P09

## Identification of nonrecurrent laryngeal nerve by intraoperative NIM nerve monitoring systems

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The most notorious complication of thyroid surgery is injury to recurrent laryngeal nerve (RLN), which may induce (1) breathy voice and choking when swallowing if unilateral palsy and (2) airway compromise if bilateral vocal palsy. The incidence of nonrecurrent laryngeal nerve (NRLN) was very rare, about 0.5% to 1% on the right side and 0.04% on the left side, associating with situs inversus. The NRLN is consistently associated with vascular anomalies of the aortic arch, which might be found with neck CT, MRI or angiography. Because the standard image study of thyroid is high resolution ultrasound instead of CT, MRI or angiography, the NRLN can only be found preoperatively if there are other indications for neck CT, MRI or angiography. The risk of injury to the NRLN was reported high up to 75% if it was not identified preoperatively.

The intraoperative nerve monitoring (IONM) provides applications including facilitation of initial nerve identification through neural electrophysiological mapping, identification of impending neural injury through continuous vagal IONM, and postoperative neural functional prognostication by vagal stimulation at the conclusion of lobectomy.

We report a rare case of right side NRLN, which was confirmed by IONM and visualization during the thyroid surgery and also review NRLN in literature.

P10

## Regulation of Tumor Progression via the Snail-RKIP Signaling Pathway by Nicotine Exposure in Head and Neck Squamous Cell Carcinoma

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**Background:** Recent studies suggest that long-term exposure of the carcinogen.

4-methylnitrosamino-1-3-pyridyl-1-butanone (NNK) found in tobacco smoke is involved in the progression of head and neck squamous cell carcinoma (HNSCC). The underlying nicotine-mediated mechanism remains unclear.

**Methods:** An analysis of SCC-25 and Fadu cells with or without NNK exposure focusing on the evaluation of migration and invasion abilities, the expression of epithelial-mesenchymal transition, drug-resistance-related genes, properties of cancer stem cell and anti-apoptosis was performed.

**Results:** Long-term NNK exposure dose-dependently enhances migration and invasion with morphological alterations. Furthermore, NNK exposure also up-regulates snail, promotes sphere-forming ability and overexpresses ALDH1, Nanog, OCT4, ABCG2 and MDR1.

**Conclusions:** The current study confirmed that long-term NNK exposure plays a role in HNSCC by increasing anti-apoptosis and therapeutic resistance via the Snail-RKIP signaling pathway. Our data also suggest that  $\alpha 7$ -nAChR inhibition or targeting Snail may provide a feasible rationale for preventing the progression of HNSCC.

P11

## Adenoid Cystic Carcinoma of the Nasal Cavity-Case Report

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The sinonasal tract is an uncommon primary site for malignant disease. The incidence of sinonasal cancer is predicted to be one in 100,000 per year. It comprises approximately 3% of all the upper aerodigestive tract malignancies and less than 1% of all the cancers. Because early manifestations mimic inflammatory diseases such as chronic rhinitis and rhinosinusitis and because the paranasal sinuses are air-filled spaces, diagnosis is often delayed and is usually found in advanced stages. The most common histology of cancers arising in the nasal cavity and the paranasal sinuses is squamous cell carcinoma and is followed by malignancies of salivary gland origin. Adenoid cystic carcinoma (AdCC) is the most common salivary gland tumor in the sinonasal tract and accounts for 10% to 25% of all head and neck AdCC. AdCC is a rare malignant tumor that affects major and minor salivary glands, lacrimal glands, ceruminous glands, and occasionally excretory glands of the female genital tract. AdCC is well known for its prolonged clinical course and the tendency for delayed onset of distant metastases. A 66 y/o man with intermittent blood-tinged rhinorrhea for 6 months. There's also nasal obstruction, post-nasal drip and blood-tinged sputum noted. Except that bilateral nasal lesions were displayed by endoscopy, no abnormality was found in upper respiratory tract. His chest X ray revealed no remarkable findings. Sinus CT revealed an enhanced soft tissue mass (2.7\*1.5\*2.7cm) over middle and lower meatus with tumor extension into left pterygopalatine fossa; expansion of sphenopalatine foramen without bone remodelling noted. Endoscopic intra-nasal tumor excision was arranged. The microscopic findings of the specimens with hematoxylin and eosin staining revealed picture of adenoid cystic carcinoma composed of intermediate cells arranged in nests or cords with cribriform appearance. He then received adjuvant CCRT and under ENT and medical oncology outpatient department follow-up.

P12

## Swallowing outcomes following primary surgical resection and primary free flap reconstruction for oral and oropharyngeal squamous cell carcinomas: A systematic review

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### Introduction:

Treatment modalities for oral and oropharyngeal squamous cell carcinoma has significantly progressed over recent years, with treatments now aimed at organ preservation and quality of life as well as survival. Dysphagia is still a treatment related morbidity as organ preservation does not always translate into function preservation despite advances in treatment modalities. The purpose of this systematic review is to review the swallowing outcomes of patients with oral or oropharyngeal squamous cell carcinoma following primary surgery with primary free flap reconstruction with or without adjuvant therapy.

### Methods:

The MEDLINE database was searched with identification of text words and index terms. Second search using identified keywords and index terms were undertaken across all included databases (MEDLINE, CINAHL, Embase, Scopus, Cochrane). Papers selected for retrieval were assessed by two independent reviewers regarding study design, study population, interventions, outcome measures, results and conclusions for each article. Inclusion criteria were articles that included histological diagnosis of oral or oropharyngeal squamous cell carcinoma in patients 18 years or older, swallowing evaluation at six months or later following curative treatment with locoregional control at time of evaluation. Exclusion criteria consisted of mandibular or maxillary involvement requiring osseous free flap reconstruction, distant metastasis at diagnosis, presence of other malignancies and diagnosis of dementia, stroke or other neurological disease prior to treatment.

### Results:

699 articles were initially retrieved, of which, 16 articles consisting of 537 patients meeting selection criteria were included in this review. Gastrostomy tube dependency was the most commonly reported functional outcome with swallowing evaluations conducted at 6 to 91 months following curative treatment. Swallowing outcomes were found to be satisfactory in most articles, however, this was also dependent on size and location of resection. It was also observed that swallowing outcomes are negatively affected by adjuvant chemoradiotherapy.

### Conclusion:

Predictors of swallowing function include TNM staging, adjuvant therapy, method of resection and reconstruction. It would appear advanced TNM stage and use of adjuvant chemoradiotherapy had negative impacts on swallowing function. Majority of patients were able to have gastrostomy tubes removed at 6 months following curative therapy. Enlarged flap volume for the reconstruction of oral and oropharyngeal defects appears to improve swallowing outcomes. Due to the complexity of dysphagia, a wide variety of swallowing evaluations have been employed by various researchers. Further research is required with a standardised evaluation of swallowing outcomes with utilisation of objective and subjective measures.

P13

## Transoral videolaryngoscopic surgery (TOVS) with a navigation system for excision of a metastatic retropharyngeal lymph node: report of two cases

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Surgical approach to the retropharyngeal space (RPS), which is located in the deepest region of the head and neck, is generally difficult, so adequate tumor visualization and precise surgical orientation must be ensured for avoidance of damage to the surrounding critical nerves and vessels. A transcervical approach is conventionally used to access the RPS, but in our cases, scar tissue after neck dissection may have been problematic. We experienced two cases in which we could remove a metastatic retropharyngeal lymph node (RPLN) using transoral videolaryngoscopic surgery (TOVS) with a navigation system.

Case 1: An 86-year-old woman with tongue cancer (cT2N0M0) underwent partial glossectomy and left selective neck dissection. Three months postoperatively, a left metastatic RPLN was identified on follow-up MRI. The metastatic RPLN was successfully excised by TOVS with a navigation system. After postoperative irradiation, she had no recurrence more than 1 year after the surgery.  
Case 2: A 62-year-old woman with papillary thyroid carcinoma (cT3N1M0) underwent right thyroid lobectomy and resection of right paratracheal lymph nodes. Three years postoperatively, a right retropharyngeal, supraclavian and prelaryngeal LN metastasis were identified on follow-up PET-CT. We performed residual thyroid lobectomy, right selective neck dissection and the metastatic RPLN was successfully excised by TOVS with a navigation system. She had no complication postoperatively.

In both cases, visualization of the RPS by high-definition endoscopy and a navigation system were effective in facilitating the safe performance of surgery. And we devised preoperative CT: we did preoperative CT with the mouth open so that we could simulate a real operative situation, which was very useful in the actual operation. We will discuss preoperative planning, surgical indications and pearls of surgical procedure for excision of a metastatic RPLN.

P14

## Surgical management of Eagle's syndrome: An approach to shooting craniofacial pain

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**Objectives:** To determine the surgical outcome of intra-oral resection of the styloid process (IRSP) for Eagle's syndrome (ES) and to compare preoperative findings between ES and glossopharyngeal neuralgia (GPN) for the surgical management of shooting craniofacial pain.

**Materials and Methods:** In total, 14 symptomatic patients who presented with typical shooting craniofacial pain, had a styloid process longer than 25 mm, were examined with CT, and underwent surgical intervention or medication alone from 2011 to 2015 were involved. They were divided into two groups: Group I included eight patients who underwent surgery following 3 months of medication failure, and Group II included six patients who received medication alone. Preoperative physical and radiographic findings and surgical outcomes were examined.

**Results:** In Group I, the pain was located from the base of the tongue to the middle ear. Symptoms were triggered by swallowing, except for one case whose pain was triggered by phonation. The presence of a rigid process in the tonsillar fossa was detected in all but three cases. The presence of vascular contact with the glossopharyngeal nerve (VCG), diagnosed with MRI, was detected in six cases. Six cases received IRSP with complete relief from symptoms and were confirmed as ES. Two cases received microvascular decompression (MVD). One showed complete relief from symptoms, and was confirmed as GPN. The other case showed recurrence 1 year postoperatively, received IRSP with complete relief from symptoms, and was confirmed as ES. In Group II, the presence of a trigger point and of a rigid process in the tonsillar fossa was detected in all six cases. VCG was not detected in any case. Three cases experienced complete relief from symptoms with 3 months of medication with no surgical intervention or recurrence up to at least 1 year of follow up. Of the three remaining cases, two experienced relief from symptoms with 2 months of medication; however, symptoms recurred in 3 months and 1 year, respectively. The remaining case refused surgical intervention and continued to suffer from symptoms despite a long period of treatment with medications.

**Conclusions:** IRSP is an effective treatment for ES. There was no clear difference in preoperative findings between ES and GPN, suggesting difficulty in making a preoperative differential diagnosis between the two conditions. Because MRI findings suggesting the presence of VCG may not guarantee true vascular contact with the glossopharyngeal nerve, IRSP should be prioritized in MVD considering its physical aggressiveness.



## Poster Otolaryngology 1

P15

**Otitis Media in Fiji: Prospective Surveillance 2015**Te-Yung Fang<sup>1</sup>, Pa-Chun Wang<sup>1</sup>, Chen-Hsu Wang<sup>2</sup>,  
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**Objective:** Otitis media (OM), as a common infectious disease, is a major cause of hearing impairment among general population. Even though the prevalence of otitis media (OM) has declined over time globally owing to the introduction of new antibiotics and universal vaccination coverage; the OM remains a major public health threat in the pacific islands. The risks OM have not been thoroughly explored in this region. The objectives of this study are to investigate the incidence, clinical features, and quality-of-life impacts of OM in Fiji. **Materials and Methods:** In the medical service trip entitled "Healing and Hope - Taiwan Cathay Heart and Hearing Medical Mission to Fiji", we conducted a prospective surveillance study in Suva and Sigatoka areas (Korolevu, Cuvu, and Lomawai) in the summer of 2015. OM were diagnosed and documented by 2 senior otologists. The otitis media - 6 (OM-6) and the Chronic Ear Survey (CES) were used to survey the OM-related quality of life. **Results:** In the 980 patients screened; 12 out of 392 children (3%) have AOM, 33 (8.4%) have OME, 15 (3.8%) have COM. For the patients aged between 13-17, 5 (7.2%) have OME, 3 (4.3%) have COM. 16 out of 509 adults (3.1%) have OME, 19 (3.7%) have COM. The incidence of OM is not different between ethnic Indian and Fijian people ( $P > 0.05$ ). The OM patients have worse OM-6 ( $P < 0.05$ ) and CES (adults,  $P < 0.05$ ) scores than normal controls. **Conclusion:** The OM is an important primary care diseases in Fiji that remains under-served. It is critical to educate professionals, parents, and patients as well to improve care for OM.

P16

**Use of the apparent diffusion coefficient of conventional echo-planar imaging to differentiate between cholesteatomas and abscesses of the temporal bone**Hiroko Monobe, Chikako Tamada, Katsumi Takizawa,  
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As therapeutic alternatives and technologies have advanced, the use of non-invasive modes of therapy to avoid surgery has increased. From this perspective, diffusion-weighted (DW) imaging and the apparent diffusion coefficient (ADC) can be valuable diagnostic tools. The focus of this study was to evaluate the diagnostic benefit of the ADC in conventional echo-planar magnetic resonance imaging (MRI) as a means of differentiating between cholesteatomas and acute inflammatory lesions with abscess formation. We evaluated three patients with suspected temporal-bone cholesteatomas, one infected cholesteatoma and three with acute inflammatory lesions by using MRI, including standard T2-weighted spin-echo and echo-planar DW/ADC sequences, and computed tomography (CT) as aligned with regions of interest (ROIs) determined in DW imaging. The ADC values in the selected ROIs were calculated by using a 2-point linear regression method ( $b = 0$  and  $b = 1000$  s/mm<sup>2</sup>). To test the reliability, all measurements were performed twice; the coefficient of correlation was 0.94. Three of the patients with suspected cholesteatoma and one patient with temporal-lobe abscessation due to temporal-bone inflammatory lesions subsequently underwent surgical confirmation and excision or drainage of their lesions. Because it was considered an unnecessary procedure, the remaining three patients did not undergo surgical confirmation of their lesions. We followed all seven patients for at least 6 months. The ADC values were  $0.759-0.915 \times 10^{-3}$  mm<sup>2</sup>/s (mean,  $0.840 \times 10^{-3} \pm 0.0586$  mm<sup>2</sup>/s) for cases of uninfected cholesteatoma,  $0.538-0.573 \times 10^{-3}$  mm<sup>2</sup>/s (mean,  $0.555 \times 10^{-3} \pm 0.0141$  mm<sup>2</sup>/s) for infected cholesteatomas, and  $0.905-1.272 \times 10^{-3}$  mm<sup>2</sup>/s (mean,  $1.063 \times 10^{-3} \pm 0.123$  mm<sup>2</sup>/s) for inflammatory lesions. These ADC values differed significantly (one-way analysis of variance:  $F(2,11) = 18.1$ ,  $P < 0.05$ ). In addition, none of the 3 patients with inflammatory lesions who did not undergo surgery developed lesions suggestive of cholesteatoma or progression of disease during the 6-month follow-up period. Therefore, the ADC value can be used preoperatively to differentiate between temporal-bone cholesteatomas (infected versus uninfected) compared with abscesses. However, the ROIs of such temporal-bone lesions are small; furthermore, heterogeneous internal structures can yield different signal intensities in DWI/ADC, leading to blurring of the images. Consequently, T2-weighted, FIESTA, or CISS images must be matched carefully to temporal-bone CT scans to accurately define ROIs. **Abbreviations:** ADC, apparent diffusion coefficient; CT, computed tomography; DW, diffusion-weighted; MRI, magnetic resonance imaging; ROI, region of interest; FIESTA, fast imaging employing steady-state acquisition; CISS, constructive interference in steady state.

P17

## Comparison of CT findings and the postoperative outcomes on Japanese otosclerosis patients

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**Purpose:** The aim of this study was to compare CT findings and the postoperative outcomes on Japanese otosclerosis patients. We reviewed preoperative CT findings and postoperative outcomes in patients who underwent surgery for otosclerosis.

**Materials:** Clinical data were obtained in 81 ears from 67 patients (29 men, 38 women) who underwent initial stapes surgery examined by CT scanning of the temporal bone and the various examinations.

**Methods:** The presence or absence of decalcification in the anterior oval window and pericochlear regions was determined from preoperative CT findings. Postoperative outcomes were assessed using the criteria proposed by the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS). The postoperative pure tone average was within 10 dB were considered to have improved hearing acuity.

**Results:** Based on CT scans findings, there were 48 ears (59.3%) diagnosed as fenestral type, 8 ears (9.9%) as retrofenestral type with decalcification involving the cochlea, and 25 ears (30.9%) as none of positive findings. Eight ears (9.9%) showed the narrowing of the oval window and 18 ears (22.2%) thickening of the footplate of the stapes. As the surgical results, the operation was successful in 64 (79.0%) of the 81 ears. The surgical treatment was successful in 3 of the 7 ears with oval window narrowing and in 12 of the 18 ears with footplate thickening on CT scans. The surgical success rate was low in the patients with CT-confirmed oval window narrowing or stapedia footplate thickening.

**Conclusions:** CT scans were confirmed to be useful to confirm otosclerotic foci and diagnose otosclerosis. The rate of positive CT findings for otosclerosis in our series was about 69.2%. The extent of the hypodense lesion did not correlate with the preoperative hearing levels and influence the surgical outcomes.

P18

## Surgical technique for reduction of complication rate in cochlear implantation

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**Objective:**

This presentation describes complications occurring after cochlear implantation which lead to revision surgery at Toranomon hospital, and discuss about surgical technique to avoid complications in cochlear implantation.

**Materials and Methods:**

Between 1987 and March 2015, 510 patients had cochlear implantation placed at Toranomon hospital, and thirty patients had received revision surgery. Causes of postoperative complications which lead to revision surgery were reviewed retrospectively.

**Results:**

Thirty patients had complications which lead to revision surgery.

As for complications, nine patients had device failure (two patients had head injury), four patients had wound infection and necrosis with or without the receiver-stimulator extrusions, three patients had facial nerve stimulation, three patients had electrode exposure at external auditory canal, two patients had electrode problems caused by treatment of ear canal, two patients had poor performance after activation, two patients had recurrent middle ear infection, two patients had cholesteatoma, one patient had misinsertion of electrode, one patient had slip out of electrode, and one patient required surgery to take out magnet before MRI.

As for revision surgery, eighteen patients had received re-implantation on the same side, three patients had taken out initial device without re-implantation, and eight patients had received re-implantation on the other side.

**Discussion:**

Most frequent cause of revision surgery was device failure which is not able to avoid. But it will be possible to reduce numbers of complications related to skin, flap and external ear canal. Design of skin incision, fixation of electrode, fixation and tie down of receiver stimulator, and canal wall reconstruction are important to avoid complications.

**Conclusions:**

Safety and reliability of surgery will increase the numbers of cochlear implantation patients.

Incision and fixation of device will be important to avoid complications. Long term follow up is also important in order to find complication early.

P19

## Meatoplasty of congenital aural atresia and stenosis without microtia; a report of 3 cases, 4 ears

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### Background

Surgery of congenital aural atresia (CAA) and congenital aural stenosis (CAS) provides hearing amelioration and maintenance, as well as cosmetic improvement. Restenosis of the external auditory canal is the main postoperative problem encountered after surgery correction of CAA and CAS. In previous studies, middle ear malformation was associated with microtia. This report reviews the outcome of surgical management done on three patients with CAA or CAS without microtia.

### Methods

From January 2014 to July 2015, in the National Hospital Organization Tokyo Medical Center, Department of Otolaryngology, 3 patients (4 ears) with CAA or CAS but without microtia underwent transmastoid meatoplasty.

### Results

At the time of surgery, Patients' ages ranged from 5 to 16 years, with an average of 9 years. Postoperatively, patients were followed up assessing audiometry for a period of 4 months to 1 year 11 months, with an average of 1 year 3 months. There was deficiency of the handle of malleus with 3 ears in 4 ears, while auditory ossicular chain and mobility were favorable. Using the Jahrsdoerfer grading scale, which predicts postoperative hearing improvement, all 4 ears were assigned a score of 9 (maximum score: 10). On long-term follow-up, physical examination of 3 ears shows that all hearing improvement was obtained just after surgery. However, it was noted that hearing loss recurred in 2 ears in 3 ears. No postoperative restenosis of reconstructed external canal was noted in any of the patients, supporting the effect of meatoplasty using pedicle flap for CAA and CAS to avoid postoperative restenosis of the external auditory canal.

### Conclusions

In conclusion, in this study, 4 ears with CAA or CAS without microtia were not accompanied severe middle ear malformation. It was only 1 ear in 3 ears that maintained better hearing long-term, despite a favorable grade of 9 in the Jahrsdoerfer grading scale. Because of lateralized tympanic membrane and auditory ossicle re-fixation, it is challenging to maintain better hearing in post-operative patients.

P20

## A Kinect-based Fall Detection System for Patients with Vestibular Dysfunction

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**Objective:** According to the statistics from Taiwan Patient-safety Reporting system, fall incidents are one of the most important security issues in hospital. Therefore, we developed a Kinect-based fall detection system to detect and prevent fall incidents for in-hospital patients with chronic vestibular dysfunction or patients who are assessed to be high-risk of falls.

**Study Design:** Three experimental scenarios were designed to test the performance of the fall detection system.

**Setting:** A Kinect-based depth camera was installed at the ceiling of a ward in a hospital. An effective fall detection algorithm was developed to process the depth images acquired from the depth camera to detect fall incidents.

**Patients:** Patients with chronic vestibular dysfunction or patients who are assessed to be high-risk of falls.

**Intervention(s):** Non-invasive warning system to detect events of falls at wards in a hospital.

**Main Outcome Measure(s):** The precision ratio and the recall ratio were adopted to measure the performance of the proposed fall detection system.

**Results:** The performance of the proposed system was verified by three experimental scenarios. The first experimental scenario is designed to test whether false alarms would happen under normal daily movements. The second experimental scenario is designed to test whether falls could be correctly detected under no change of environments. The third experimental scenario is designed to test whether falls could be correctly detected if there are some changes in environments. Among 90 fall events, the precision ratio and the recall ratio were 94% and 96%, respectively.

**Conclusions:** An effective fall detection system was developed to detect fall incidents happened at wards. It provides more safety for patients with chronic vestibular dysfunction or patients who are assessed to be high-risk of falls.

**Keyword:** In-hospital fall incident, Chronic imbalance, Vestibular dysfunction.

P21

## Age-related changes in caloric response

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**Objective:** To analyze age-related changes in caloric response.

**Patients:** Data from 2609 patients that underwent audiometry and caloric testing between October 2010 and September 2013 were evaluated. Subjects with spontaneous, positional, and/or positioning nystagmus, and those with bilateral Meniere disease or vestibular schwannoma were excluded. Finally, 110 subjects (11-86 years) were included.

**Intervention:** The mean hearing level at high frequencies (4000Hz and 8000Hz) and the maximum slow-phase eye velocity of caloric nystagmus (MSPEV) were evaluated using pure tone audiometry and electronystagmography, respectively. The mean hearing level and MSPEV were compared between 4 age-groups: <50 years-old (n = 40), 50-64 years-old (n = 23), 65-74 years-old (n = 29), and ≥75 years-old (n = 18).

**Main outcome measures:** Age-related changes in mean hearing threshold levels and MSPEV during warm and cold-air stimulation.

**Results:** The mean hearing level at high frequencies progressively worsened as age advanced. The mean hearing threshold was significantly greater according to age. The mean MSPEV under cold-air stimulation was significantly faster compared with that under warm-air stimulation. During warm-air stimulation, there were no significant differences in MSPEV between the groups. During cold-air stimulation, the mean MSPEV in the >75 year-old group was significantly slower compared with that in the <50 year-old group.

**Conclusions:** In caloric testing, age-related changes in the mean MSPEVs were only apparent during cold-air stimulation. During cold-air stimulation, the mean MSPEV was significantly slower in subjects >75 years-old compared with subjects aged <50 years-old.

P22

## Persistent stapedia artery with stapes ankylosis

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The persistent stapedia artery (PSA) is a very rare, congenital, vascular anomaly. It presents as a pulsatile middle ear mass and sometimes causes conductive hearing loss. The diagnosis of the presence of a PSA is always accidental, because it is so rare and difficult to predict. CT findings include the absence of the foramen spinosum and a soft-tissue prominence in the region of the tympanic segment of the facial nerve. The risks of surgery include facial palsy, hemiplegia caused by coagulation of the PSA, and bleeding due to injury of the carotid artery during surgery in cases of aberrant internal carotid. We report a case of PSA with stapes ankylosis for which we performed malleus-stapedotomy using a Teflon wire piston. We didn't coagulate the PSA. Nevertheless the PSA attached to the prosthesis, the patient presented significant improvement in hearing level and had no complaint of pulsating tinnitus. Thus, we have shown that attachment of the prosthesis to the PSA does not necessarily disturb improvement of hearing level after malleus-stapedotomy for otosclerosis with PSA. Based on our experience, many cases can be treated by stapedotomy using a prosthesis and without coagulating the PSA.

P23

## Features of audiogram configuration in multiple-system atrophy C and cortical cerebellar atrophy

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**Conclusion:** The ratio of low tone hearing loss (LTHL) is significantly frequent in spinocerebellar degeneration (SCD) with cerebellar predominance, including multiple-system atrophy C (MSA-C) and cortical cerebellar atrophy (CCA).

**Background:** SCD is a rare disease affecting the cerebellum and the brainstem. Basing on disease phenotypes, SCD can be divided into subtypes such as MSA and CCA. CCA is diagnosed when the pathologic phenotype is restricted to the cerebellar symptoms. MSA is also subdivided into MSA-C (cerebellar predominance), MSA-P (parkinsonism predominance) and Shy-Drager syndrome (predominance in the autonomic nervous system). The clinical symptoms of familial SCD with autosomal-dominant inheritance, SCA36 (spinocerebellar ataxia 36), which is prevalent in western Japan is characterized by sensorineural hearing loss with late-adult onset. Abnormality in Auditory Brainstem Response is reported in MSA-C patients. Based on these observations, we hypothesized that SCD with cerebellar predominance, MSA-C and CCA may involve auditory symptoms. In order to distinguish hearing loss specific for SCD from presbycusis in the high frequencies, we focused on hearing loss in the low frequencies in MSA-C and CCA.

**Methods:** We retrospectively reviewed the pure tone audiograms of the patients with MSA-C (n=47; 23 males, 24 females; 61.6±8.9 years old) and CCA (n=16; 7 males, 9 females; 62.8±9.5) by comparison to age-matched control (n=169; 62.5±10.7). We excluded the patients who had ever had any ear disease such as sudden hearing loss or any ear surgery. The shapes of audiograms in the right and left ears were classified into the 5 categories ("high frequency sloping", "flat", "low frequency ascending" (LFA), "mid-frequency U-shape", and "mid-frequency reversed U-shape" (MFRU)) according to the definitions of audiometric configuration used in previous reports. We also used the definition of LTHL; an audiogram shape as LFA or MFRU and mean threshold at 125/250/500 Hz was >25 dB. In addition, only when all 3 certified audiologists judged independently an audiogram shape as LFA or MFRU and mean threshold at 125/250/500 Hz was >25 dB, the audiogram was considered to show LTHL as the final selection.

**Results:** According to the criteria, the odds ratio for LTHL in MSA-C compared to the control cohort was 2.492 (95%CI: 1.208-5.139; p=0.015, Pearson's chi-square test). The odds ratio for LTHL in CCA was 2.194 (95%CI: 0.709-6.795). Based on the more strict verification by the 3 audiologists, the odds ratio in MSA-C and CCA is significant (MSA-C odds ratio: 3.243; 95%CI: 1.320-7.969; p=0.014) (CCA odds ratio: 3.692; 95%CI: 1.052-12.957; p=0.054).

P24

## Anatomical Variations of the Supratubal Recess: A Cone-Beam CT Study

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### 【Purpose】

Supratubal recess (STR), located anterior to the epitympanum and superior to the bony Eustachian tube is clearly demarcated by a bony partition. It described by Hoshino and Suzuki as the anterior attic bony plate (AABP) and by Sheehy as a "cog" referring to its unique shape. Several anatomical studies on the STR have shown a considerable variation even among normal adult temporal bones. The purpose of this study is to reevaluate the anatomical variations of the anterior attic wall and the STR using a cone-beam computed tomography (CBCT).

### 【Materials and Methods】

We used ten cadaveric temporal bones (right 5 : left 5) for this study. Double oblique images were obtained using a Multi-Planar Reconstruction technique, allowing visualization of the Eustachian tube, the STR and the attic in one slice. Yamasoba classified the structure of the STR into three types and measure the depth of the STR from their temporal bone dissection study in 1990. We adopted their classification and measurement to compare CBCT images of fine bony structures related to the STR morphology.

### 【Results】

The STR was identified by the existence of AABP in 9 temporal bones. The STR could be classified into 3 structural types accordingly to Yamasoba's classification. Type A, the STR is bordered by the AABP and a thick bony plate related to the tensor tympani semicanal, can be seen in 4 ears. Type B, the STR is separated into 2 compartments by a bony ridge in addition to above mentioned bony plate, in 3 ears. Type C, the STR slopes down to the Eustachian tube without distinct bone plates related to the tensor tympani semicanal, in 2 ears. Type C was the deepest compared Type A and B with regard to the depth of the average length of the STR.

### 【Discussion】

Owing to the sagittal projection obtained with double oblique CBCT images, we could clearly identify the STR. CBCT allowed us to evaluate fine bony structures bordering the STR from the attic and from the Eustachian tube. We could confirm the anatomical classification proposed Yamasoba, with the similar occurrence rates.

### 【Conclusion】

The STR is a surgically accessible space where pathologies may be hidden by the AABP. Removal of the AABP and mucosal folds is also an important surgical technique to create an anterior drainage and/or aeration route. CBCT can be a useful tool for preoperative evaluation for this procedure.

P25

## Standardized Facial Nerve Monitoring for Early Localization and Identification of Facial Nerve during Cochlear Implantation Surgery

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Background: Cochlear implantation is a relatively safe & effective procedure for severe to profound sensorineural hearing loss patient. However facial nerve injury, although not deadly, is still devastating for not only surgeon but the patient and their family.

The aims of this paper is to share the experience in standardizing Facial Nerve Monitoring (FNM) in CI surgery by using different amount of electric current of FNM during surgery to identify the nerve and prevent possible injury.

Methods: Different amount of electrical current (Medtronic NIMR) are used in different stage of operation. After identifying incus, 2.0mA is used to locate the possible tract of nerve. After the mastoid air cell was removed and the compact bone was encounter, 1.0mA is used to identify aberrant nerve. And when facial recess is nearly drilled out, 0.5mA is used to confirm the facial nerve and prevent injury until the facial nerve is visually observed.

Results: More than 86 cases of CI surgeries were enrolled in this study. There was no permanent facial palsy or paresis noted in all the cases. Under our standardized surgical technique, with the stimulus of 2.0mA; 1.0mA; 0.5mA, the average voltage of the facial nerve EMG is 1370.7 $\mu$ V; 1625.4 $\mu$ V; 1942.0 $\mu$ V. And there are certain patterns noticed between the three stimuli and the EMG.

Conclusion: (1)By practicing the principles mentioned above, all the cases of CI surgeries were carried out in our hospital and there was no permanent facial palsy or paresis. (2)By using standardizing monitoring, we could narrow down the location of the facial nerve before encountering it. Therefore largely decrease the possibility of injury.(3) When the visual cues of the facial nerve are difficult to certain, the standardized facial nerve monitoring data and the EMG outcome could be used as alternative conformation.

Poster Laryngology 1

P26

### Two cases of partial laryngeal paralysis after tracheal intubation

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**Introduction:**Diagnosis of the cause of vocal fold impairment is important in the management of hoarseness after tracheal intubation. Partial laryngeal paralysis, that only a branch of the recurrent nerve paralyzes, is sometimes difficult to distinguish from arytenoid cartilage dislocation only by endoscopic laryngeal examination. We report two cases of partial laryngeal paralysis after tracheal intubation.

**Case presentation:** Patient 1 was a 56-year-old man who was extubated on the seventh day after living-liver transplantation and complained of hoarseness. On the twelfth day after surgery, he received a medical examination from this department. Endoscopic laryngeal examination revealed that though the right arytenoid moves toward midline and the abduction movement of the right vocal fold was normal, the adduction movement of it was insufficient. The vocal process did not contact in phonation, and bowing of the right vocal fold was observed. The laryngeal computed tomography (CT) showed the right arytenoid cartilage was located outer rearward. Laryngeal electromyography examination showed the nerve dysfunction of right thyroarytenoid muscle and right lateral cricoarytenoid muscle, thus we diagnosed the vocal fold impairment as partial laryngeal paralysis. The movement of right vocal fold restored of itself after 1.5 month of the appearance of symptoms.

Patient 2 was a 52-year-old man. He suffered from ventricular fibrillation and received life support measures including intubation. Two days later, he was extubated and complained of hoarseness. His previous doctor suspected of dislocation of arytenoid cartilage and he received a medical examination from our hospital after 1 month of the appearance of symptoms. Endoscopic laryngeal examination revealed that the adduction movement of left vocal fold was insufficient though the abduction movement of the right vocal fold was normal. The vocal process did not contact with each other in phonation, and bowing of the left vocal fold was observed. The laryngeal CT did not show the translocation of left arytenoid cartilage. Laryngeal electromyography examination showed the nerve dysfunction of left thyroarytenoid muscle and left lateral cricoarytenoid muscle, thus we diagnosed the left vocal fold impairment as partial laryngeal paralysis. The movement of left vocal fold and his hoarseness restored of itself gradually from two months of the appearance of symptoms.

**Conclusion:** We experienced two cases of partial laryngeal paralysis after tracheal intubation. Electromyography was useful to diagnose correctly vocal fold impairment after tracheal intubation. Laryngologist should keep in mind this pathogenesis.

P27

### Melanocytic tumor with uncertain malignant potential of hypopharynx- a case report

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A 33-year-old man was found to have an increased number of small pigmented papules along with erythematous halo over trunk, lower extremities, shoulder, upper extremities, and buttock in recent two years. He was admitted to dermatology under the suspicious of paraneoplastic syndrome. Selective skin lesion biopsies were performed and the pathology reported melanocytic nevus with spitzoid feature. Serum screen and urinalysis all were normal. Otolaryngologist was consulted for possible mucosa lesions over upper digestive tract. Fiberscope was arranged and showed two blackish lesions over left aryepiglottic fold and left pyriform sinus. Excisional biopsy was performed through laryngomicroscopic surgery. The pathology reported melanocytic tumor with uncertain malignant potential (MELTUMP). The term MELTUMP derives from the diagnostic difficulty in classifying these lesions as benign or malignant. Lesions in oral mucosa were extremely rare in case report. The outcome of "MELTUMPs" in series studies suggests as a preliminary observation that these lesions as a group exist and that they may be biologically different from conventional melanoma and benign melanocytic nevi.

P28

## The effect of CC10 on endotoxin induced inflammation in bronchial epithelial cells

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### Background:

We have shown that bacterial lipopolysaccharide (LPS) induces IL-8 secretion in differentiated normal human bronchial epithelial (NHBE) cells. It is reported that LPS increases MUC5AC secretion via NF- $\kappa$ B and ERK activation. Club cell 10-kDa protein (CC10) is an anti-inflammatory protein, produced by mucosal epithelial cells and decreased in airway inflammation. The aim of the study is to examine the effects of CC10 on MUC5AC and IL-8 production in NHBE cells stimulated by LPS.

### Methods:

NHBE cells were cultured at air liquid interface (ALI) for 14 days with recombinant human (rh) CC10 or vehicle. Cells were stimulated by LPS on day 13. MUC5AC and IL-8 secretion were measured in cell supernatants by ELISA and PCR on day 14. Western blotting was used to evaluate NF- $\kappa$ B and ERK activation. Cells were stained using hematoxylin & eosin (H&E) and Periodic- acid Schiff (PAS) to examine cell morphology.

### Results:

RhCC10 attenuated LPS stimulated MUC5AC secretion, and MUC5AC mRNA expression. RhCC10 also decreased IL-8 secretion exposed to LPS. NF- $\kappa$ B and ERK 1/2 phosphorylation were inhibited by rhCC10. Histology showed that rhCC10 did not affect cell differentiation.

### Conclusions:

CC10 may attenuate LPS induced airway inflammation, in part due to inhibition of NF- $\kappa$ B and ERK phosphorylation.

P29

## Submucosal elastic laminae of the middle and lower pharynx: a histological study using elderly cadaveric specimens

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**Purpose:** The distribution of elastic fibers in the pharyngeal wall was investigated to consider the elasticity of the pharynx.

**Method:** Histological sections of the mid and lower pharynx from 15 elderly donated cadavers were observed, under the principles of the Declaration of Helsinki and the approval of institutional research ethics review committee.

**Result:** Two distinct submucosal tissue layers with a high content of elastic fibers (tentatively termed "laminae") were identified. The inferolateral elastic lamina was restricted to the level from the upper part of the arytenoid to lower end of the inferior cornu of the thyroid cartilage. It originated from the pharyngeal submucosa, extended laterally along the inner aspect of the thyropharyngeal muscle, and inserted into the periosteum or perichondrium at posterior margin of the thyroid cartilage. The posteromedial lamina extended along the supero-inferior axis from a level above the greater horn of the hyoid bone to reach the muscularis mucosae of the cervical esophagus. The inferolateral and posteromedial laminae were connected at levels below the cricoarytenoid joint. Individual variations were evident in their thickness as well as the extent of connection between them.

**Conclusion:** Two distinct submucosal elastic laminae were newly described in the middle and lower pharynx. In association with striated muscle function, the inferolateral lamina seemed to suspend the lower pharyngeal mucosa, while the posteromedial lamina seemed to provide mucosal fold forcing smoothly peristaltic conveyance of a bolus during swallowing.



P30

## **An Unusual Side Effect of Olanzapine - Bilateral Vocal Cord Paresis and Dysphagia**

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### **Introduction:**

Tardive dyskinesia is a rare side effect of antipsychotics, more commonly presenting in the form of oromandibular stereotypies. The literature has only one other reported case of vocal cord dystonia, in association with antipsychotics and organic brain disease.

We present the first reported case of laryngopharyngeal tardive dyskinesia, secondary the antipsychotic olanzapine.

### **Case:**

Our patient, a 55-year-old female, has a five-year history of progressive shortness of breath, intermittent stridor and swallowing difficulty. The onset of symptoms coincides with the initiation of regular olanzapine for her depression. In 2015 she had an acute deterioration in her breathing and severe weight loss. She was diagnosed with bilateral vocal cord paresis, requiring a surgical tracheostomy, and dietary management with a pureed-diet.

### **Conclusion:**

Olanzapine is a widely prescribed antipsychotic, however it is difficult to predict which patients will develop the severe side effects of laryngopharyngeal tardive dyskinesia. This case highlights the need for routine medication review for all patients presenting with stridor and dysphagia to elicit the cause.

P31

## **A case of mucosa-associated lymphoid tissue lymphoma of the larynx presenting with chronic cough: a case report and literature review**

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Lymphoma in the larynx is an uncommon situation given the paucity of lymphatic node systems and drainages of this area. What's more, primary laryngeal mucosa-associated lymphoid tissue (MALT) lymphoma is exceedingly rare which represents below 1% of malignant neoplasms of this location.

The most common presenting symptom is hoarseness and dysphagia. We present a case of primary laryngeal MALT lymphoma with unspecific presentation of chronic cough. Laryngoscopic examinations revealed movably smooth contour lesion over left arytenoid that favored a cyst as first impression. After systemic evaluation, he was staged as IEA. Irradiation with a dose of 3060 cGy in 17 fractions to the tumor was completed. The irradiation related acute and late side effects were mild. There is few consensus has been achieved regarding to MALT lymphoma to our knowledge, we disclose this case of symptoms, management and follow up.

## Poster Rhinology 1

P32

**Two cases of glomangiopericytoma in nasal cavity**

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Glomangiopericytoma is a sinonasal type hemangiopericytoma that accounts for less than 0.5% of all sinonasal neoplasms. It is classified into low-grade malignancy according to the WHO classification and causes distant metastasis rarely. The patients who have this tumor have severe nasal bleeding because it has rich blood flow. Then, it is very important to control bleeding in the surgery. We report two cases of glomangiopericytoma successfully treated by endoscopic surgery.

**Case 1.** A 41-year-old male complained repeated massive nasal bleeding from his left nose for 6 months. He received blood transfusion in another hospital because of progression of anemia. He was diagnosed glomangiopericytoma by biopsy under general anesthesia and referred our hospital. A large soft tissue mass was observed in his left nose by CT. It was confirmed that the feeder was ophthalmic artery by angiography. After ligation of left ethmoidal artery by transorbital approach, the tumor was removed by endoscopic surgery. Bleeding volume in surgery was 140ml. The tumor was diagnosed glomangiopericytoma by pathological examination. There is no recurrence after surgery.

**Case 2.** A 60-year-old male visited the other clinic complained with headache and diplopia for a few days. He was diagnosed paralysis of left oculomotor nerve and consulted our hospital. CT and MRI showed the left sphenoid sinus lesion and mass in front of sphenoid sinus. We performed endoscopic resection of tumor and opening of left sphenoid sinus. Bleeding volume in surgery was 20ml. The tumor was diagnosed glomangiopericytoma by pathological examination. There is no recurrence after surgery.

P33

**Endoscopic Vasculized Nasoseptal Flap Repair of Anterior Skull Base Meningocele**

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Nasal meningocele is a rare anomaly resulting from meningeal herniation into the nasal cavities through a bone defect in the skull base. We report a case of intranasal meningocele originated in anterior skull base repaired by endoscopic surgery with pedicled nasoseptal flap. A 36-year-old male visited to a neurosurgery clinic with the chief complaint of a headache and repeated watery rhinorrhea from right nose. The patient was consulted our clinic because a soft tissue mass in right nasal cavity by CT scan. A polyp like tumor with pulsation was observed by endoscopic examination. CT scan showed a bony defect of cribriform plate and a soft tissue lesion in both olfactory cleft and anterior ethmoid sinus. MRI confirmed right frontal lobe ptosis. Glucose was detected from watery rhinorrhea. The patient was diagnosed anterior basal meningocele with cerebrospinal fluid leakage. The patient was operated through a transnasal endoscopic approach. The defect in skull base was successfully repaired with the use of vasculized nasoseptal flap.

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## Caloric Restriction in Mice Reduces Basal Cell Proliferation and Neuroepithelial Regeneration Following Olfactotoxic Mucosal Damage

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Caloric restriction (CR) effects on mouse olfactory neuroepithelial cell dynamics were investigated. Eight-week-old male C57BL/6 mice were fed either a control (104 kcal/week) or 36% calorie restricted (67 kcal/week) diet. The uninjured olfactory neuroepithelium cytoarchitecture and its regeneration after exposure to methimazole, an olfactotoxic chemical, were compared between mice fed with control and CR diets. The effect of the timing of CR intervention on neuroepithelial regeneration after injury was also examined. In uninjured olfactory mucosa, the neuroepithelial thickness and number of olfactory marker protein (OMP)-positive olfactory receptor neurons (ORNs) in septal olfactory mucosa were not significantly different between groups at 1 month, but there were significantly fewer 5-bromodeoxyuridine (BrdU)-positive proliferating basal cells in the CR group. At 3 months, the CR group showed a significantly thinner neuroepithelial thickness containing significantly fewer OMP-positive ORNs and BrdU-positive proliferating basal cells. Methimazole-induced mucosal injury increased the number of BrdU-positive basal cells in both groups, but the induction was lower with CR. Final neuroepithelium recovery was less complete in mice kept under CR before methimazole administration than those under CR after the administration. In conclusion, CR may be disadvantageous to olfactory neuroepithelial maintenance and renewal, particularly after injury.

P35

## Nasal septal abscesses. Report of three cases

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Nasal septal abscess is uncommon disease. The causes of nasal septal abscess are vary, such as trauma, infection of surrounding tissues, and idiopathic. We experienced three cases of nasal septal abscess due to different causes.

First case is 67 years old male. He complained facial swelling, redness, pain. He had dental examination and the dentist pointed out infection of a maxillary tooth root, a radicular cyst. He had intravenous antibiotics. He had improvement in his facial pain, but still had nasal swelling, and then he had an otolaryngological examination. He had nasal septal swelling, and CT scan showed an abscess in the nasal septum. A needle puncture and oral antibiotics were performed. Once the nasal swelling improved, however, the swelling recurred in two days. Then drainage was made and his symptoms and swelling were cured.

Second case is 58 years old female. She has diabetes mellitus. She was treated nasal bleeding by cauterization. One month after the treatment, she realized bilateral nasal obstruction and a saddle nose. Otolaryngeal examination and CT scan showed nasal septal swelling and an abscess in the nasal septum. Oral antibiotics and following drainage improved her symptom, but a saddle nose remained.

Third case is 52 years old male. Bilateral nasal obstruction and nose swelling began to appear from 3weeks ago and he was referred to our office. Examination showed nasal septal swelling, and CT scan reveled an abscess and an aberrant tooth with a radicular cyst under the abscess. Drainage after a puncture and oral antibiotics were performed. The abscess was successfully treated, but nasal obstruction was not improved. Nasal septum mucosae were thick and fibrosis of mucosae were suspected. We are planning to have deviatomy and odontectomy.

All three patients were negative for trauma history. Odontogenic infections were considered as causes of nasal septal abscesses in case1 and case3. Cauterization for nasal bleeding was suspected to be related to the cause in case 2.

We present these three cases of nasal septal abscesses, and discuss with the causes, treatment, and prognosis of this condition.

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## Evidence for filaggrin expression in the human nasal mucosa

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### Introduction

Variants of the human filaggrin gene (FLG) are considered to be associated with rhinitis, but the underlying mechanisms are not well understood. Here, we first examined the presence of FLG mRNA as well as re-examination of the localization and distribution of filaggrin immunoreactivity.

### Material and Methods

Nasal biopsies of inferior turbinates from nonatopic subjects (n=5) were analyzed in this immunohistochemistry study. We used skin biopsies (n=3) from nonatopic controls as positive controls.

The levels of mRNA for filaggrin were determined by real-time PCR. Total RNA was isolated from three primary cultures, after they reach subconfluence, using the RNeasy Mini kit. Normal human epidermal keratinocytes (NHEK), nasal epithelial and bronchial epithelia cells were purchased from Kurabo (Osaka, Japan), PromoCell (Heidelberg, Germany) and Lonza (Walkersville, MD), respectively.

### Result

Moderate immunoreactivity of filaggrin was mainly observed in the apical region of the epithelium of the nasal mucosa. The filaggrin mRNA levels in cultured nasal epithelial cells were significantly increased as compared with those of bronchial epithelial cells whereas no statistically significant difference was observed between those of nasal epithelial cells and keratinocytes. Thus, the filaggrin expression in the nasal mucosa may explain a strong link between FLG variants and allergic rhinitis despite of the unknown function of filaggrin in the upper airway.

P37

## The effects of menthol on isolated human nasal mucosa

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**Objectives:** Menthol is used as a constituent of food and drink, tobacco and cosmetics nowadays. This cold receptor agonist has been used as a nasal inhalation solution in the daily life. The effect of menthol on nasal mucosa in vivo is well known; however, the effect of the drug on isolated nasal mucosa has been rarely explored. The aims of this study were to explore the effects of menthol on isolated human nasal mucosa.

**Methods:** We obtained nasal mucosal specimens from patients with/without allergic rhinitis. We used our preparation to test the effectiveness of menthol on isolated human nasal mucosa. A 10-12 mm long portion of nasal mucosa was submersed in 30 ml Krebs solution in a muscle bath at 37°C. Changes in nasal mucosa contractility in response to the application of a sympathetic mimetic agent were measured using a transducer connected to a Pentium III computer equipped with polygraphy software. The following assessments of menthol were performed: (1) effect on nasal mucosa resting tension; (2) effect on contraction caused by 10<sup>-6</sup> M methoxamine as a sympathetic mimetic; (3) effect of the drug on electrically induced nasal mucosal contractions.

**Results:** Results indicated that addition of a sympathetic mimetic to the incubation medium caused the nasal mucosa to contract in a dose-dependent manner. Higher dose of menthol had significant spasmolytic effect on the nasal mucosa precontracted with methoxamine. Meanwhile, menthol inhibited the spike contraction induced by EFS, even at low dose. However, it alone had a minimal effect on the basal tension of nasal mucosa as the concentration increased.

**Conclusions:** The degree of drug-induced nasal mucosa contraction or relaxation was dose-dependent. The finding of the TRPM8 immunoreactivity may partially explain the response of the nose in cooling and its physiological role in temperature regulation. The anti-adrenergic effect on precontracted nasal tissues showed opposite clinic observation. Therefore, the subjective improvement of nasal patency seemed to be a result of the activation of the intranasal trigeminal nerve of cold receptors after menthol stimulation.

P38

## **Anosmia as the initial presentation of olfactory meningioma-Case report**

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Anosmia is commonly caused by paranasal sinus disease, upper respiratory tract infection, trauma or chemical irritation. And intracranial tumors may also cause anosmia, however when the patient only presents anosmia without other neurological symptoms, intracranial lesions may be ignored. We demonstrate a 65 years old man complaining of anosmia for two years. Patient deny stuffy nose, purulent nasal discharge, nasal fetid odor, facial pain and other sinusitis related symptoms. Moreover, the patient had no history of head injury, and his working environment is non-chemical irritated. Patients had been taking medication at the clinic for weeks, but anosmia was not improved, then was referred to our hospital. Transnasal fiberoptic endoscopy demonstrates negative finding. Brain MRI is arranged that revealed a mass with dural tail in the frontal lobe, an olfactory meningioma is suspected. We transferred his patient to neurosurgery department for further treatment.

P39

## **Endoscopic sinus surgery with powerful instruments in treating difficult cases of post-operative maxillary cyst**

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**Objective:**

The present study investigates effect of endoscopic sinus surgery (ESS) with powerful instruments in treating difficult cases of post-operative maxillary cyst.

**Patient & method:**

All patients received radical Caldwell-Luc procedure before and investigated with CT scan excluding cases with monocular membranous wall cyst. In 2007~2012, 13 patients (5 male, 8 female) including 7 recurrent cases were treated traditional ESS before. The principle of procedure is like the mastoidectomy to have wide opening to expose cysts, and remove septum to fuse the multiple cysts in one and preserved mucosa as possible.

**Result:**

We followed these patients at least 2 years. The successful rate was 92% without significant complication.

**Conclusion:**

ESS with powerful instruments is an effective procedure for difficult cases of post-operative maxillary cyst.

P40

### Narrow-band-ultraviolet-B-irradiation suppresses phorbol ester-induced up-regulation of histamine H1 receptor mRNA in HeLa cells without induction of apoptosis

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**Background:** The phototherapy with narrowband-ultraviolet B (NB-UVB, wavelength from 308 to 313 nm) has been proved to be effective to treat skin immuno-allergic disease such as psoriasis and atopic dermatitis, so the NB-UVB can be efficient for the treatment of allergic rhinitis. It was reported that up-regulation of histamine H1 receptor (H1R) mRNA was observed in the nasal mucosa of patients with pollinosis and we have demonstrated that the H1R mRNA level was correlated with the severity of allergy symptoms in patients with pollinosis. In the present study, we examined the effect of NB-UVB on H1R gene expression.

**Objective:** To clarify whether NB-UVB suppresses up-regulation of H1R gene expression and inhibits the symptom of allergic rhinitis, we first investigated the effects of irradiation with NB-UVB at wavelength of 310 nm on phorbol-12-myristate-13-acetate (PMA)-induced up-regulation of H1R mRNA in HeLa cells expressing endogenous H1R, and compared it with those of 305nm and 315nm that is out of NB-UVB. In addition, we evaluated whether 310nm NB-UVB induced apoptosis. **Methods:** HeLa cells were treated with PMA after irradiation with UVB of 305, 310 or 315 nm at doses from 50 to 200 mJ/cm<sup>2</sup>. The mRNA levels of H1R in HeLa cells were measured using real-time quantitative RT-PCR. In addition, we evaluated whether NB-UVB induces apoptosis with Hoechst 33342 staining and Annexin V/Propidium Iodide staining. **Results:** 310nm NB-UVB dose-dependently, reversibly and significantly suppressed up-regulation of H1R mRNA without inducing apoptosis at low dose of less than 150mJ/cm<sup>2</sup>. But, 310nm NB-UVB suppressed up-regulation of H1R mRNA with inducing apoptosis at high dose of more than 200mJ/cm<sup>2</sup>. 305nm UVB suppressed up-regulation of H1R mRNA with inducing apoptosis by non-specific cytotoxicity, 315nm UVB showed no suppressive effect at any dose.

**Conclusion:** These findings suggest that low dose irradiation with NB-UVB of 310 nm at less than 150mJ/cm<sup>2</sup> wavelength-specifically and dose-dependently suppresses up-regulation of H1R gene expression without induction of apoptosis. Intranasal NB-UVB irradiation can be used as the phototherapy to suppress nasal symptoms of allergic rhinitis.

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### Rhinolaryngofiberscopic Removal of a Displaced Dental Implant in Right Maxillary Sinus - Case Report

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Dental implants migrate into maxillary sinus is an uncommon complication in dental surgical procedure. It may be happened during surgery or a period of time after implantation. The dental implant also migrate to other paranasal sinuses (ethmoid or sphenoid). Foreign body in paranasal sinuses may induce infectious symptoms, therefore, removal of displaced implants is needed. Many route had been reported to removal of displaced implant in maxillary sinus, example as through implant site, or Caldwell Luc procedures or prelacrimial duct access into the maxillary sinus by endoscopic nasal approach. In this article, we described a case which presented displaced endodontic materials in the right maxillary sinus, was removed by Caldwell-Luc approach with minimal window on anterior maxillary wall by means of fiberscope with working channel. After the surgery, soft tissue over right cheek had less swelling. There were also no antrum-related complaints, and the wounds healed completely.

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## **Idiopathic bilateral antral exostoses: A rare case in maxillary sinus**

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Exostoses of the external auditory canal have long been recognized clinically; however, exostoses of the paranasal sinuses are vanishingly rare. We report on a healthy and asymptomatic 25-year-old woman who receiving panoramic x-ray before teeth implantation, the ectopic teeth in the maxillary sinus is suspected. Computed tomography further reveals bony protrusion in the bilateral maxillary sinus and antral exostoses is diagnosed. In the literature review, most paranasal exostoses are relating to nasal irrigation with cold solution, but these evidence is lacking in our case. Thus we present this idiopathic bilateral antral exostoses, and effort should be made to find the causes.

## Poster Other 1

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## A case report: IgG4-related rhinosinusitis preceded appearance of the Mikulicz's disease

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IgG4-related disease (IgG4-RD) is a newly recognized disorder, characterized by massive IgG4+ lymphocyte and plasma cell infiltration and fibrosis, causing enlargement, nodules or thickening of various organs. IgG4-RD includes various diseases, such as Mikulicz's disease, autoimmune pancreatitis, retroperitoneal fibrosis. Recently, it was reported that IgG4 may relate with several cases of the rhinosinusitis, especially eosinophilic chronic rhinosinusitis (ECRS). We experienced a case of the ECRS-like IgG4-related rhinosinusitis which preceded appearance of the Mikulicz's disease.

A 59-year-old woman presented to our hospital in March 2015. She complained of a prolonged cough and bilateral nasal obstruction. A transnasal endoscopy detected bilateral multiple nasal polyps derived from the middle nasal meatus. A paranasal sinus CT showed the bilateral ethmoid sinus-dominated shadows and a blood examination showed high rate of the eosinophil subsets. She was diagnosed with the ECRS and performed the endoscopic sinus surgery under the general anesthesia. The pathological finding of the nasal polyps was the infiltration of eosinophils and lymphoid cells, corresponding to the feature of the ECRS. Her postoperative status was stably-maintained. However, after two month from the surgery, she appeared the painless and symmetrical enlargement of her lacrimal glands and salivary glands. We suspected the IgG4-RD containing the Mikulicz's disease and performed blood examination, CT, biopsies of the labial minor salivary gland and submandibular gland, and re-immunostaining of the nasal polyps with IgG4 antibody. As results of these examinations, we could detect the elevation serum levels of IgG4 (390mg/dl) and infiltration of the IgG4-positive cells in the nasal polyp tissues (IgG4+ cells/IgG+ cells > 40%). We diagnosed her as Mikulicz's disease and initiated drug therapy with oral steroids. The enlargement of her lacrimal glands and salivary glands was immediately decreased.

IgG4-related rhinosinusitis is a new concept, therefore there are few reports about this disease. This is a curious case report about an IgG4-related rhinosinusitis which preceded appearance of the other IgG4-RD. According to the past reports, several cases of rhinosinusitis and Churg-Strauss syndrome include IgG4-related rhinosinusitis. When we treat rhinosinusitis, it may be important to consider a possibility of coexisting IgG4-RD.

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## A study of Facial Nerve Neurinoma

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The facial nerve neurinoma is rare tumor. But, in recent years, reports have been increasing due to the advances of CT or MRI. We experienced 16 patients with facial nerve neurinoma who underwent surgical treatment. 16 patients with facial nerve neurinoma were operated in our hospital between 2008 and 2014. There were 5 males and 11 females. Mean age was 40.9 years [range 10-61]. All of 16 patients had facial paralysis. 13 patients had hearing loss. The tumor extended to the inner auditory canal portion was observed in 4 patients, the labyrinthine portion was observed in 6 patients, the geniculate ganglion was observed in 13 patients, the tympanic portion was observed in 14 patients, and the mastoid portion was observed in 10 patients. As the initial symptoms, 6 out of 16 patients had tinnitus or hearing loss, 10 out of 16 patients had facial paralysis. Among the patients whose initial symptoms were tinnitus or hearing loss, the tumor extended to the inner auditory canal portion was observed in 3 patients, the labyrinthine portion was observed in 3 patients, the geniculate ganglion was observed in 6 patients, the tympanic portion was observed in 6 patients, and the mastoid portion was observed in 4 patients. Among the patients whose initial symptoms were facial paralysis, the tumor extended to the inner auditory canal portion was observed in 1 patients, the labyrinthine portion was observed in 3 patients, the geniculate ganglion was observed in 7 patients, the tympanic portion was observed in 8 patients, and the mastoid portion was observed in 6 patients. The average value of the House-Brackmann score is 3.6 in whole, 4.8 in the inner auditory canal portion, 4.3 in the labyrinthine portion, 3.7 in geniculate ganglion, 3.8 in tympanic portion, and 3.6 in mastoid portion.

The first symptom of facial nerve neurinoma is often facial paralysis. So there are reports that some patients with facial nerve neurinoma were diagnosed as sudden deafness because their first symptoms were hearing loss. This study suggests that if the tumor exists in the inner auditory canal portion, vestibular disorders and hearing loss prior to the facial nerve paralysis, and when the facial nerve paralysis occur, it tends to be severe. In such cases that hearing loss is not improved by conservative therapy, we need to suspect out facial nerve neurinoma.



P45

## Nasal Tip Plasty Using Complete Autologous Cartilages - Case Report

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Graft selection remains the greatest challenge for surgeons performing rhinoplasty. The preferred choice thus far for nasal reconstruction would be autograft compared to allograft due to its lower rate of infection and extrusion as it does not induce an immune response. Numerous grafting techniques have been developed to sculpt the nasal framework in rhinoplasty over time. These basic techniques have evolved from the principal that maintenance of major supporting structures of the nose is fundamental for aesthetic and functional purposes. However, the type of graft, its shape, position, and usage may vary depending on the situation and the objectives of the surgeon. Despite the advances and the multiple techniques that have been described in the literature, it can be a steep learning curve and a daunting task for the aspiring rhinoplasty surgeon. The surgeon's attention to functional, reconstructive, and aesthetic principles is paramount in ensuring optimum rhinoplasty results, much to the satisfaction of both the patient and the surgeon. For achieving the desired nasal tip refinements in Asian patients, sufficient septal cartilage must be needed for the ideal tip projection and lengthening of the nose by the septal extension graft, columellar septal strut graft, and onlay tip graft, shield graft. Actually there are many cases having insufficient septal cartilages in Asian augmentation rhinoplasty. We present a case of complete autologous cartilaginous tip plasty using caudal septal extension graft, spreader graft and multiple cap grafts.

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## Geriatric Otolaryngologic Emergencies at a Teaching Hospital in Taiwan

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**BACKGROUND:** Many diseases are more common in older people than in younger people, and it may be more difficult to make a diagnosis because older patients often have nonspecific symptoms. The purpose of this study was to analyze the clinical features, diagnosis, and treatment modalities of geriatric patients treated in an otolaryngology emergency room at a Taiwanese teaching hospital over a 5-year period.

**METHODS:** A retrospective review was performed on patients older than 65 years of age who presented in otolaryngology emergency rooms from January 2010 to December 2014. The retrieved data included age, gender, clinical presentations, and treatment modalities for further analysis.

**RESULTS:** A total of 502 patients (287 males and 215 females ranging from 65 to 100 years of age with mean age of  $75.7 \pm 7.6$ ) were enrolled in the study. The most common need was pharyngology (n=274; 54.6%) followed by otology (n=128; 25.5%), rhinology (n=77; 15.3%), and head and neck surgery (n=23; 4.6%). Acute upper respiratory tract infection was the most frequent diagnosis. Foreign bodies were mostly found in the throat followed by the ears. Most patients with epistaxis sustained anterior nasal septum bleeding. Of the dizzy patients, 62.8% were vestibular disorders and 37.2% were non-vestibular disorders. More than 65% of the patients (335/502; 66.7%) were true emergencies.

**CONCLUSIONS:** Of geriatric patients presenting in otolaryngology emergency rooms, about two thirds presented true emergencies. The non-emergent disease, acute upper respiratory tract infection was the most frequent diagnosis. Although geriatric patients had a variety of medical conditions, most can be managed with a conservative treatment strategy.

**Poster** Head and Neck 2

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**Assessment of preoperative MRI for predicting surgical risks of carotid body tumors**

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**Background and Purpose:** Carotid body tumors (CBTs) are the most common head and neck paragangliomas. Shamblin's classification is widely used for evaluating the adhesion of the tumor to internal carotid artery (ICA). Shamblin's group3 CBTs need to be removed with ICA. Thus, the reconstruction of ICA is necessary for most of group3 tumors, which may increase a risk of stroke and massive hemorrhage. Moreover, the surgical removal of CBTs has some possibility of postoperative neurological damage. To predict Shamblin's classification and cranial nerve involvement before operation is an ideal for surgical planning. The purpose of this study was to establish objective criteria anticipating those risks of surgery on preoperative MRI.

**Materials and Methods:** Eleven CBTs in 10 patients were resected at Keio University Hospital between 2005 and 2014, and their clinical data and preoperative MRI were reviewed. The surgical records were blinded to the radiologist, who measured the size of CBTs and the maximum contact angle with the ICA by the tumor (MCA-ICA) on axial imaging. The correlation between the measurements on MRI and the surgical results was analyzed.

**Results:** There were 4 group1, 3 group2, 4 group3 tumors. The median tumor's anteroposterior, horizontal and vertical diameter were 28.3mm (18.8-37.1mm), 26.6mm (16.1-36.1mm) and 33.0mm (17.6-39.9mm). The tumor size didn't differ among Shamblin's classification. However, the MCA-ICA of group3 tumors was more than 180°, meanwhile those of group1 and 2 were less than 180°. Any of MRI measurements did not relate to neurological damages in this study.

**Conclusions:** MCA-ICA on preoperative MRI may enable to predict Shamblin's group3 tumors. Our findings contribute to diminish surgical risks of CBTs surgery.

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**Utility of Real-time Ultrasound Elastography for Determination of the Excision Area in Patient with Thyroid Gland Cancer**

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**Objective:** It is important to evaluate the distribution of intraglandular metastasis in the patients with thyroid gland cancer, in order to avoid the postoperative recurrence in the residual lobe. Real-time ultrasound elastography (USE) is a newly developed procedure for an evaluation of nodules in thyroid gland. The purpose of this study is to evaluate utility of USE for precisely detecting intraglandular metastases.

**Materials and Methods:** In this study, patients were included, who were diagnosed as papillary carcinoma with fine-needle biopsy, and USE was performed to evaluate intraglandular metastatic foci. The elasticity was in degree scored as 1 (high), 2 (intermediate), or 3 (low), and pathological examination was followed postoperatively. However clinical outcome cannot be evaluated because of shortage of the postoperative follow up period.

**Results:** Out of 93 nodules evaluated with USE, 89 nodules were pathologically diagnosed as papillary carcinoma and their elasticity were exceptionally scored 2 or 3, being strongly predictive of malignancy. On the other hand, 4 nodules scored 1, were respectively diagnosed as benign.

**Conclusions:** USE is a useful tool not only for the diagnosis of intraglandular metastasis in patients with thyroid cancer, but also an appropriated decision making of surgical resection of thyroid gland. Otherwise papillary cancer may recur in residual gland postoperatively.

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### **Predictive markers, including total lesion glycolysis, for the response of lymph node(s) metastasis from head and neck squamous cell carcinoma treated by chemoradiotherapy**

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**Background:** Chemoradiotherapy (CRT) has been applied to cervical lymph node(s) metastatic head and neck cancer patients. The evaluation and treatment of lymph node(s) after CRT is important to improve the prognosis.

**Methods:** Prior to CRT, TNM stage was examined by visual and imaging examinations. Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were calculated by the results of FDG-PET. After CRT, patients were divided in two groups, i.e., complete response (CR) and non-CR. These responses were compared with the clinical characteristics.

**Results:** T4, N2b, N2c and  $TLG_{2.5} \geq 18.8$  were statistically significant predictive index before CRT. The odds ratio, 95% confidence interval and p value were as follows; T4, 2.73, 1.15-6.51, 0.0230; N2b, 6.96, 1.50-32.3, 0.0132; N2c, 11.80, 2.37-58.50, 0.00258;  $TLG_{2.5} \geq 18.8$ , 6.25, 2.17-18.00, 0.000672.

**Conclusions:** Prior to treatment for the metastatic lymph node(s) by CRT, TLG can be a new good predictive factor. After the treatment, FDG-PET is high specific and useful as negative screening.

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### **Impact of lower selective neck dissection on supraclavicular lymph node metastases from endometrial carcinoma**

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Supraclavicular lymph node metastases from uterine carcinoma are rare but affect the patient's prognosis. If the supraclavicular lymph nodes metastases are detected from uterine cervical cancer, there are possibilities of another distant metastasis. The prognosis with supraclavicular lymph nodes metastases from uterine cervical cancer are considered dismal. They often receive palliative radiotherapy for relief of symptoms and improved quality of life.

However, supraclavicular lymph node metastasis from endometrial carcinoma is much rarer than that from uterine cervical cancer and there has been no report regarding systematic neck dissection as a salvage treatment. In this report, we describe the neck dissection for a 74-year old woman with supraclavicular lymph node metastasis from endometrial carcinoma to diagnose histologically. The patient's past medical history included two cancers which were a rectal cancer 7 years before and an endometrial adenocarcinoma 4 years before. We indicate the lower selective neck dissection for this case according to preoperative FDG-PET study and tumor marker. This surgery proved supraclavicular lymph node metastasis from endometrial carcinoma histologically. The lower selective neck dissection is expected to improve patient's prognosis without spoiling the patient's active daily life, quality of life and postoperative shoulder function. Her postoperative course was good by now and we need follow up her carefully for a long time.

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## A case of parotid gland tumor with tumor-induced osteomalacia

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Tumor-induced osteomalacia is a paraneoplastic syndrome characterized by osteomalacia, which occurs as a result of decreased renal phosphate reabsorption and reduced renal vitamin D activation, both caused by fibroblast growth factor (FGF) 23 secreted by the tumors. We report our experience with a case that showed improvement in the subjective symptoms and hypophosphatemia following parotid tumor resection after the diagnosis of tumor-induced osteomalacia. The patient was a 77-year old male. At the age of 70, he developed low back pain and bilateral lower leg pain of gradually worsening severity. Magnetic resonance imaging (MRI) performed at the Department of Orthopedics, revealed findings suggestive of spinal canal stenosis, which was however ruled out based on clinical examinations. Because of the presence of extensive compression fractures of the thoracic and lumbar spine, systemic osteoporosis, and hypophosphatemia, tumor-induced osteomalacia was suspected at the Department of Nephrology and Endocrinology. A detailed examination revealed a high blood FGF23 level. In addition, fluorodeoxyglucose (FDG) - positron emission tomography (PET) revealed accumulation of FDG below the left ear. Systemic venous sampling of FGF23 revealed a markedly high concentration (1320.0 pg/mL) in the left external jugular vein as compared to that in a peripheral vein (206.9 pg/mL) (reference value: 10-50 pg/mL). This suggested that the tumor-induced osteomalacia was probably caused by a parotid gland tumor. The patient was referred to our department for resection of the parotid gland tumor. Preoperative clinical examination revealed no obvious mass, but there was tenderness below the left ear. Computed tomography (CT) revealed a well-demarcated contrast-enhancing mass measuring 20 mm in diameter in the deep lobe of the left parotid gland. A left parotid lobectomy was performed. Intraoperative findings showed no obvious tumor infiltration into the mandible. The histopathological diagnosis was FGF23-secreting phosphaturic mesenchymal tumor. After the tumor resection, the patient showed improvement of not only the subjective symptoms, but also of the hypophosphatemia, and decrease of the peripheral blood levels of FGF23. Tumor-induced osteomalacia has most frequently been reported to be caused by tumors in the head/neck region and lower limbs. There have been no reports of a parotid gland tumor as the causative tumor. This disease can be cured by tumorectomy. For patients presenting with musculoskeletal pain or hypophosphatemia, parotid gland tumor must be borne in mind in the differential diagnosis.

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## Complications of surgery for total laryngectomy and pharyngolaryngectomy -Is the incidence of fistula higher in salvage surgery?-

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Introduction: Recently, the number of radiotherapy (RT) or chemoradiotherapy (CRT) as an organ-preservation therapy is increasing. This causes increasing number of salvage surgery after failure of initial treatments. It is known that previous CRT is a risk factor of surgical complications in salvage total laryngectomy (TL). Especially pharyngo-cutaneous fistula is a major complication, which trouble head and neck surgeons. On the other hands, in total pharyngolaryngectomy with free jejunum transfer (TPLE), a few report describe that previous RT or CRT is not a risk factor of fistulas. However, there is no established evidence about the incidence of fistula in salvage surgery of TPLE. In this study, we retrospectively investigate complications, especially the incidence of fistulas, in TL and TPLE. The rate of fistula is compared with initial treatment group and salvage operation group.

Patients and methods: Patients underwent TL or TPLE between April 2008 and December 2004 in Kochi University Hospital were subjects of this study. Patients with reconstruction with free or pedicle musculocutaneous flap were excluded from this study. The postoperative diagnosis, sex, age at operation, stage of the disease, presence or absent of diabetes mellitus, serum albumin level, bilateral or ipsilateral neck dissection, previous therapy (RT or CRT), and postoperative complications were investigated by retrospective chart study.

Results: Thirty-seven patients underwent TL (Group TL) and 36 patients underwent TPLE (Group TPLE). Former included 29 laryngeal cancers and 8 hypopharyngeal cancers and latter included 4 laryngeal cancers, 28 hypopharyngeal cancers, one oropharyngeal cancer, two cervical esophageal cancers and one thyroid cancer. In Group TL, 35% of the patients had previous RT and 22% had CRT. In Group TPLE, 31% of the patients had previous RT and 19% had CRT. The incidence of fistulas including both minor and major fistulas was 32% in TL group and 11% in Group TPLE ( $p<0.05$ ). In salvage surgeries with previous RT, 7 of 12 patients had fistulas in Group TL, while 2 of 13 patients had fistulas in Group TPLE, which indicates statistical difference ( $p<0.05$ ). In Group TPLE, incidence of fistula was 2 of 25 patients without RT and 2 of 11 patients with previous RT (N.S.).

Conclusion: In salvage surgery, Group TL had higher rate of fistulas than Group TPLE had. In Group TPLE, there was no difference in the incidence of fistula between patients with RT and without RT.

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### Three cases of arytenoid non-malignant mucosal lesion after radiotherapy

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We report three cases of arytenoid non-malignant mucosal lesion after radiotherapy or chemoradiotherapy for head and neck cancer. Arytenoid mucosal lesion like leukoplakia was detected in two cases and brownish area by NBI was detected in one case. All these lesions were detected within a year after treatment against laryngeal or hypopharyngeal squamous cell carcinoma and detected in different region to primary tumor. These mucosal lesions were resected per orally. The pathological diagnoses of three cases were dysplasia, atypical epithelium and dilated capillary. Probably these lesions were induced by radiotherapy, and watchful waiting may be allowed. However these mucosal lesions include dysplasia and sometimes differential diagnosis of cancer is required, so biopsy or resection should be performed actively. We will examine the generating mechanism of these mucosal lesions.

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### Case Report: Coexistent Angiosarcoma and Pleomorphic Adenoma in Submandibular Gland

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Primary angiosarcomas of the submandibular gland are very rare. Treatment is challenging and the prognosis is usually poor because of the high rates of local recurrence. Here we reported an extremely rare case of coexistent angiosarcoma and pleomorphic adenoma in submandibular gland. This patient had a rapid progressing mass in right submandibular region for three months. Head and neck computed tomography (CT) revealed a highly suspected malignant tumor with heterogeneous enhancement. Excision of right submandibular tumor was performed and pathology showed angiosarcoma mixed with pleomorphic adenoma. Local recurrence was noted three months after first-time surgery and revision was done. Owing to the high risk of local recurrence, post-operative radiotherapy was performed and multimodality local therapy is critical to the management of most angiosarcomas.

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### Case Report: Neck Lymph Nodes Recurrence as Papillary Thyroid Carcinoma with De-differentiation into Squamous Cell Carcinoma after Total Thyroidectomy

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Here we reported a rare case of metastatic recurrent papillary thyroid carcinoma (PTC) converting to squamous cell carcinoma (SCC) in upper cervical lymph nodes following total thyroidectomy and radioiodine I-131 treatment 1 year ago due to previous PTC. A 61-year-old woman found left neck painful mass with rapid enlargement for 4 months. The mass was firm at left level II, about 3x3 cm with irregular border. Fibroscopy and oral cavity examination showed no positive finding. Fine needle aspiration cytology showed suspicious malignancy. Neck computed tomography (CT) showed multiple lymph node metastases in neck at left level II, III. Pathology of resected tumor was composed of coexistence of PTC with SCC. Thyroid origin of the latter is confirmed by presence of areas of papillary carcinoma merging imperceptibly with SCC, and PAX-8 positivity in both components in immunostains. Owing to the highly aggressive pattern of thyroid SCC, the conversion of PTC to SCC should be suspected in patients with previous PTC underwent total thyroidectomy exhibiting highly aggressive behavior.

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### Neck IgG4 related disease - A case report

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IgG 4 related disease is a newly named disease within the past 10 years. This is a systemic disease with possible multiple organs involved, causing affected organ fibrosis and chronic inflammation, leading to tissue swelling. Diagnosis depends on elevated serum IgG4 concentration and specific histopathological features. High-dose corticosteroids is used as the first-line treatment, in some asymptomatic patients observation is sufficient. This article reports a 57 years old patient complained of bilateral parotid glands and submandibular glands painless swelling for 3 years. Fine-needle aspiration was performed in another hospital but lacking definite diagnosis. Open biopsy was performed due to no resolution of above condition. IgG4 associated diseases is confirmed by histopathological examination. Conservative policy was suggested because there were no obvious physical symptoms.

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## **Impact of lymph node ration on survival of patients with hypopharyngeal and laryngeal squamous cell carcinomas**

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Lymph node ratio (LNR) has previously been reported to reliably predict survival in several solid malignancies. We have presented the reliability of LNR as a prognostic predictor for patients with head and neck squamous cell carcinoma (HNSCC) previously. However, there was the pitfall of our previous study that included multiple subsites of HNSCC, while different subsites might have different lymphatic drainage pathway. We therefore validated the concept of LNR for patients with hypopharyngeal and laryngeal squamous cell carcinomas in this study.

We retrospectively reviewed our institutional records of patients with hypopharyngeal and laryngeal squamous cell carcinomas who underwent resection of the primary tumor combined with neck dissection to assess the prognostic significance of LNR on survival in comparison with pathological adverse factors such as the presence of extracapsule spread, the presence of positive margin, and the number of positive lymph node metastasis.

LNR (number of positive lymph nodes/number of lymph nodes excised) was categorized into two groups:  $<0.18$  and  $\geq 0.18$  according to our previous result of Receiver-operating characteristic plots. The number of positive lymph nodes was also categorized into two groups:  $<5$  and  $\geq 5$  according to our previous result of Receiver-operating characteristic plots.

We then examined the prognostic significance of LNR on overall, cause-specific, progression-free and loco-regional survival in comparison with these pathological adverse factors using univariate analysis, multivariate analysis and the Kaplan-Meier method with the Wilcoxon log-rank test.

## Poster Otology 2

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### Efficacy of concurrent superselective intra-arterial chemoradiotherapy for late-stage squamous cell carcinoma of the temporal bone

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**Introduction:** Advanced squamous cell carcinoma of the temporal bone is a poor-prognosis disease because of the cranial base and the great vessel located, respectively, superior and medial to the ear, which pose anatomical barriers in performing en bloc resection with an appropriate safety margin.

**Objective:** The aim of this study was to analyze and discuss on the local control rate, disease-free survival rate, adverse events, and cisplatin dosage in 12 patients treated with superselective intra-arterial chemoradiotherapy.

**Methods:** In our institution and related facilities, 12 patients with advanced squamous cell carcinoma of the ear (both T3 and T4 cases) were treated with superselective intra-arterial chemoradiotherapy from 2007 to 2014. Eight patients were treated with cisplatin at a total of 200-600 mg in 2-6 courses. Four patients were treated at a fixed dose of 150 mg/body ×5 courses (total 750 mg/body of cisplatin).

**Results:** Eight of the 12 patients presented successful local control. In the Kaplan-Meier analysis, the estimated cumulative survival rate was 66.7%. No exacerbation of adverse reactions was observed even after increasing the cisplatin dose to 750 mg. The facial palsy developed in two patients several days after the first intra-arterial chemotherapy session. Steroids were administered and both patients fully recovered.

**Conclusion:** To confirm a curative effect with superselective intra-arterial chemoradiotherapy, a multicenter randomized trial may need to be conducted.

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### Expression pattern of Wolframin, the Wolfram syndrome 1 gene (WFS1) product, in Common Marmoset (*Callithrix jacchus*) inner ear

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Wolfram syndrome (OMIM: 222300) is an autosomal recessive disorder of the neuroendocrine system, known as DIDMOAD (Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness) syndrome. Patients show mutations in the WFS1 gene. The WFS1 gene encodes an 890 amino acid protein, called Wolframin, that is predicted to have nine helical transmembrane segments in the endoplasmic reticulum (ER). Wolframin functions in ER calcium homeostasis and unfolded protein responses. Dysregulation of these cellular processes results in the development of ER stress, leading in apoptosis. Hearing loss associated with Wolfram syndrome is typically a high frequency sensorineural hearing loss, although low frequencies may become affected as well (1)(2). Limited literatures describing temporal bone pathology indicate both hair cell loss in the lower basal turn and the atrophy of stria vascularis in the apical turn (3). On the contrary, the expression of Wolframin protein in mice was observed widely and uniformly in the sensory epithelium but was absent in the stria vascularis (4). While WFS1 gene knockout mice suffer diabetes, the hearing level of the strain was completely normal.

In order to elucidate the discrepancy of the phenotype among species, and to explore the pathophysiology of deafness associated with WFS1 gene mutation, we examined expression of Wolframin in the Common Marmoset (*Callithrix jacchus*), non-human primate, inner ear.

Young adult marmosets (n=5) were transcardially perfused with saline followed by fixative with 4%PFA. The fixed temporal bone of marmoset was prepared in the cryosection after decalcification by EDTA. Immunohistochemistry for WFS1 was performed with rabbit anti-WFS1 antibody 1:200 (HPA029128, SIGMA-ALDRICH). The result revealed strong immunoreactivity in outer hair cells, external sulcus cells, Claudius cells, Hensen cells, spiral ganglion and stria basal cells.

The expression pattern of WFS1 in Common Marmoset inner ear was different from that of mouse. In stria vascularis and organ of Corti where strong immunoreactivity of WFS1 found in Common Marmoset, prominent mutations like atrophy or loss are observed in human inner ear of Wolfram syndrome. The pattern may account for the hearing phenotypes in Wolfram syndrome patients. Common Marmoset would be a powerful and extensive tool for investigating pathophysiology of human auditory disorder that cannot be explained by rodent mutant models.

**Reference**

(1) Cremers et al. 1977, (2) Higashi et al. 1991, (3) Hilson et al. 2009, (4) Cryns et al. 2003



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## Three cases with traumatic otolith vertigo revealed by VEMP

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### Introduction

Disequilibrium after traffic accident is often seen but tricky to detect the etiology. Brandt and Daroff propounded the entity of traumatic otolith vertigo in 1980. They described that accelerated impact due to head trauma injures the otolith organ and then the tonus imbalance between the organs in both sides causes disequilibrium. The patients suffer from non-rotatory to-and-fro vertigo and unsteadiness of gait similar to walking on pillows. But such entity has never been confirmed by clinical examination. We experienced three cases with traumatic otolith vertigo revealed by otolith examination as vestibular evoked myogenic potential (VEMP).

### Case reports

Case 1: a 31 year-old female had a rear-end accident 4 months ago. She complained of pain in shoulders and back and unsteadiness of gait. The local orthopedist diagnosed as whiplash injury and treated with cervical traction, but the symptoms including unsteadiness has still remained. Case 2: a 44 year-old female had a rear-end accident 4 months ago. She had a stiff neck and complained of unsteadiness every time. The local orthopedist diagnosed as whiplash injury and treated with physical therapy, and then the symptoms had slightly improved. However, she has still suffered from unsteadiness when her head moved. Case 3: a 34 year-old female had a rear-end accident 13 months ago. Then, she suffered from pain in shoulder, back and knees. She complained of constant unsteadiness for few days later. She was treated with cervical traction by local orthopedist, however unsteadiness has still remained. All cases did not show any spontaneous, positional or positioning nystagmus. Their head MRI and CT image did not indicate any abnormal findings. Their caloric testing and cervical VEMP testing showed normal results, however ocular VEMP obtained abnormal results in all cases. This suggested that their traumatic otolith vertigo were caused by the disturbance on the utricle rather than those on the saccule.

### Discussions

The pathogenesis of the utricle is suggested as follows. Brandt speculated that traumatic otolith vertigo is attributable to dislodged otoconia. All cases were injured by rear-end accident in this study. Their heads impacted anterior-posterior directions. It is suggested that the utricle whose macula lies on the horizontal plane is more fragile by anterior-posterior acceleration concussion than the saccule whose macula lies on the sagittal plane.

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## The Incidence and Treatment of Otitis Media with Effusion in Cases of Cleft Palate

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**Objective:** Approximately 75% of children with cleft palate have Otitis Media with Effusion (OME) histories. The conservative treatment does not always provide satisfactory recovery, so surgical treatment may be unavoidable. The purpose of this study was to determine the incidence of OME in children with cleft palate and to investigate the ratio of operative methods (ventilation tube insertion or only myringotomy) as a part of treatment for OME in children with cleft palate.

**Material and Methods:** A retrospective study was done on 117 children (65 males and 52 females) with non-syndromic cleft palate who underwent palatoplasty from 2010 to 2015. Otoscopy examinations were done in all the cases. We also confirm the existence of OME by using tympanometry and auditory brainstem response (ABR) estimated hearing threshold. All of the children with OME were periodically followed by using otoscopy, tympanometry and audiometry at least 6 months.

**Results:** A majority of 117 children were in the age group of 0-to-1 year. In this study, 91 of 117 children (77.8%) with cleft palate have OME histories. 75 of 91 children with OME (82.4%) were taken ventilation tube insertion. 6 of 91 children with OME (6.6%) were taken only myringotomy. 69 of 75 children were taken ventilation tube insertion when they underwent palatoplasty.

**Conclusion:** The significantly higher prevalence of OME in the children with cleft palate was confirmed in this study. It was considered that ventilation tube insertion was necessary in children with cleft palate with severe OME.

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## Plasticity of the human vestibulo-ocular reflex during off-vertical axis rotation

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We investigated whether adaptive plasticity of the vestibulo-ocular reflex in humans occurs in response to visual-vestibular conflict stimulation during rotation about a 30° incline (off-vertical earth axis rotation, OVAR). Subjects were 26 healthy adults (17 males and 9 females), ranging in age from 22 to 33 years (mean: 24.4) with no history of neurotological symptoms. Each testing session consisted of a pre-test, an adaptation period, and a post-test. The pre-test and the post-test were performed in complete darkness with the subjects' eyes opened. Subjects were rotated sinusoidally at 0.16Hz under OVAR, with a maximum angular velocity of 60°/sec for 30 seconds. Subjects were divided into two groups depending on the kind of visual stimulation. One group of subjects was rotated sinusoidally at 0.16 Hz and 60°/sec peak velocity under OVAR for 20 minutes while viewing optokinetic stripes, which moved at the same frequency and peak velocity as the rotational chair but in the opposite direction (X2 adaptation paradigm). The other group of subjects were rotated sinusoidally at 0.16 Hz and 60°/sec peak velocity under OVAR for 20 minutes while viewing optokinetic stripes, which moved at the same frequency and peak velocity as the rotatory chair but in the same direction (X0 adaptation paradigm). There was no significant difference in gain before or after adaptation using the X2 adaptation paradigm. VOR gain decreased significantly after adaptation using the X0 adaptation paradigm.

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## Auditory varieties of candidates for cochlear implant of Electric-Acoustic Stimulation (EAS)

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**Objectives:** New cochlear implant (CI) combining electrode for electric stimulation with hearing aid for acoustic stimulation, Electric-Acoustic Stimulation (EAS), has been covered by medical insurance since 2014 in Japan. EAS is applied to individuals with severe high-frequency hearing loss and low-frequency residual hearing, "ski-slope type" hearing loss. Little is known about this type of hearing loss fulfilling the auditory criteria for EAS. The purpose of this study is to investigate the auditory varieties of EAS candidates, such as prevalence and etiologies, and hearing levels.

**Materials and methods:** Subjects were 4,758 patients with hearing loss who were diagnosed in first consultation of our department from 2011 to 2014. Their pure-tone and speech audiograms were reviewed to confirm the types of hearing loss fulfilling the criteria for each device of EAS and standard CI. Further, hearing levels at each frequency of EAS candidates were calculated.

**Results:** In pure-tone audiometry of 4,758 subjects, 58 individuals (1.22%) fulfilled the criteria for EAS. In contrast, 129 individuals (2.77%) fulfilled those for standard CI. Primary diseases of hearing loss on EAS and standard CI candidates were idiopathic (EAS 44, standard CI 102 Individuals), middle ear disease (5, 9), inner ear disease (3, 5), acoustic neuroma (0, 5), drug-induced (6, 5), respectively. That is, prevalence of drug-induced hearing loss among EAS candidates was more than that of standard CI. Age of EAS candidates (65.0±18.0) was older than that of standard CI (50.7±27.4). This result may be due to the fact that congenital hearing loss was common primary disease of standard CI candidates than that of EAS. In the audiograms of EAS candidates, averages of hearing levels at 1 kHz were approximately 68 dB, while standard deviations of hearing levels at 1 kHz were 16-18 dB which were similar to those at 500 or 2 kHz in spite of no criteria on 1 kHz hearing level. In 46 ears of 23 EAS candidates who were repeatedly examined in pure-tone audiometry, 16 ears (34.8%) of 10 candidates showed spontaneous hearing deteriorations more than 10 dB during non-implanted time courses for 6 months or more. In the 16 ears, furthermore, 8 ears (50%) showed deteriorations of averaged-hearing levels at 125-500 Hz. In speech audiometry of Japanese speech intelligibility test, 23 EAS candidates showed scores of 5-80% (47.1±18.9%), and 13 candidates (56.5%) fulfilled the criteria for EAS.

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## Measurement of fetal heart rate and auditory evoked potential induced by sound stimulation in human fetuses

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**Objective:** In order to examine fetal auditory perception in the period between 30 to 37 weeks gestational age, we aimed to establish for two kinds of methods to diagnostic parameters in the prenatal period and detect the degree of hearing development in a fetus.

**Methods:** We developed a suitable device for fetal auditory stimulus. This screening system consists of a function generator, a piezo-driver, and a piezo-electric vibrator. Prenatal hearing screening (PHS) was applied to 20 healthy women in the period of 30 to 37 weeks gestational age. Burst tones were used and delivered through the piezo-electric device at an intensity of 45 to 75dB. The changes in the heart rate before and after sound exposure were measured by Cardiotoco monitors and were evaluated to estimate the hearing ability.

The second method is measuring by auditory evoked potential (AEP), placing a different electrode of unipolar induction on the abdominal wall above the fetal head and placing an indifferent electrode on the femur. A piezo-electric vibrator was placed on the abdominal wall of the pregnant woman above the fetal temporal bone which stimulates a sound over a 1,000 times.

**Results:** An increase in the heart rate can be notice in fetuses older than 36 gestational weeks in accordance with the sound stimulation.

On AEP, a peak on the wave was recognized 6msec-12msec after the stimulus and can be noticed repetitively on the same fetus older than 36 gestational weeks.

**Conclusion:** A noticeable change in the fetus heart rate and AEP during the late pregnancy period caused by the sound stimulation described above can be a referent to the orienting reflex.

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## Deformation of the Outer Hair Cells and the Accumulation of Caveolin-2 in Connexin 26-Deficient Mice

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Mutations in GJB2, which encodes connexin 26 (Cx26), a cochlear gap junction protein, represent a major cause of pre-lingual, non-syndromic deafness. The degeneration of the organ of Corti observed in Cx26 mutant-associated deafness is thought to be a secondary pathology of hearing loss. Here we focused on abnormal development of the organ of Corti followed by degeneration including outer hair cell (OHC) loss. Here we investigated the crucial factors involved in late-onset degeneration and loss of OHC. We analyzed the change in the protein expression and localization in the organ of Corti in our Cx26-deficient mice (Cx26f/fP0Cre). In ultrastructural observations of Cx26f/fP0Cre mice, OHCs changed shape irregularly, and several folds or notches were observed in the plasma membrane. Furthermore, the mutant OHCs had a flat surface compared with the characteristic wavy surface structure of OHCs of normal mice. We investigated the factors that contribute to the deformation and degeneration of the organ of Corti of Cx26f/fP0Cre mice. Cochleae of Cx26f/fP0Cre mice were subjected to proteomic analysis, which revealed an increase in the level and abnormal localization of caveolin-2 (CAV2) in the organ of Corti. Diffuse labeling of CAV2 was observed in the organ of Corti of control mice, but there was remarkable accumulation of CAV2 in Cx26f/fP0Cre mice. In particular, this accumulation of CAV2 was mainly observed around OHCs, and furthermore this accumulation was observed around the shrunken site of OHCs with an abnormal hourglass-like shape. The deformation of OHCs and the accumulation of CAV2 in the organ of Corti may play a crucial role in the progression of, or secondary OHC loss in, GJB2-associated deafness. Investigation of these molecular pathways, including those involving CAV2, may contribute to the elucidation of a new pathogenic mechanism of GJB2-associated deafness and identify effective targets for new therapies.

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## Clinical presentation of Acoustic neurinoma

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Acoustic neurinoma (AN) is Schwann cell-derived tumor of the eighth cranial nerve, commonly arising from the vestibular nerve. Symptoms of AN are well known such as auditory, vestibular and others. The most common complaint of AN patients is unilateral hearing loss. Typically, the hearing loss progresses gradually over several months or years. However AN patients sometimes present sudden hearing loss. In addition, they may also complaint other atypical symptoms. With recent improvement in Magnetic Resonance Imaging (MRI), we often have diagnosed AN cases with atypical presentation. The purpose of this report is to analysis clinical symptoms and course to diagnosis with AN patients.

A retrospective chart review was conducted of patients with AN seen at the Department of Otorhinolaryngology, Mitsui Memorial Hospital during the years 1992 through 2015. Eighty-eight patients were identified with the diagnosis of AN, without prior treatment of surgery or radiation. There were 53 males and 35 females, ranging from 24 to 78 years old (mean age 54.9).

Unilateral hearing loss was the most common complaint (52 cases, 59.1%), followed by tinnitus (40 cases, 45.5%), dizziness (18 cases, 20.5%), vertigo (18 cases, 20.5%). Twenty-one (23.9%) patients had presented sudden hearing loss before their first visit to our department. Other symptoms included trigeminal neuralgia (8 cases, 9.1%), hemifacial spasm (1 case, 1.1%), dysgeusia (1 case, 1.1%), headache (3 cases, 3.4%) and syncope (2 cases, 2.3%). Although many patients presented ipsilateral symptoms, a few patients presented contralateral symptoms. While Combination of several symptoms was shown with 54 (61.4%) patients, two (2.3%) of patients whose tumor was detected incidentally had no symptoms. Most patients were diagnosed at our department, and some patients were diagnosed at other department (20 cases, 22.7%) such as neurosurgery, sometimes through medical checkup (3 cases, 3.4%). Duration from symptoms appearance to visits ranged from within one week to over thirty years. A variety with initial tumor size was shown from small node such as 2 mm to large tumor which press cerebellum or brainstem. Duration of their symptoms and initial tumor size were not related. Initial hearing level ranged from normal to scale out.

AN is always taken in consideration even if the symptom is atypical, because clinical presentation of AN is various. Also it is important for us carefully to do neurootological and neuroradiological examination. In our study, there were more cases of sudden onset hearing loss in comparison to previous studies.

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## Congenital cholesteatomas in the middle ear and ossicular anomalies

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### Introduction

Congenital middle ear cholesteatomas are relatively rare diseases. In some cases, ossicular chain anomalies coexist with middle ear cholesteatoma, and these are of interest in terms of pathogenesis of congenital cholesteatomas. Here we present a case report of congenital middle ear cholesteatoma with ossicular chain anomaly, with progression of conductive hearing loss.

### Case presentation

A 12-years-old Japanese male presented with left-sided hearing loss, with no history of otitis media. He had been referred to us three years ago for abnormal hearing of right ear by school physical examination, but his hearing was normal at that point by pure tone audiometry. This time he complained left-sided hearing loss since a year and a half ago. External auditory canal and tympanic membrane of both sides were examined and normal. Pure tone audiometry showed 44 dB conductive hearing loss, and tympanometry showed type C on the left ear. High resolution CT showed defect of the long process of the incus and the head and the cru of the stapes, as well as a shadow near the stapedial tendon. We suspected ossicular chain anomaly and treated by surgery. The ossicular defect was proved as expected during the operation. The shadow found in the CT turned out to be soft tissue extending from the stapedial tendon to the round window niche, presumed to be a cholesteatoma. We removed the tissue and reconstructed ossicular chain by tragal cartilage. Pathological examination proved cholesteatoma. And pure tone audiometry showed 23.8dB after 3weeks from operation.

### Discussion

In our case, the progression of conductive hearing loss suggests that the cholesteatoma destructed ossicular bones. Though we speculate our case was incidental coexistence of congenital middle ear cholesteatoma and ossicular chain defect according to the surgical findings as follows; 1) the normal tympanic membrane without perforation, 2) the small and membranous cholesteatoma without adhesion to the ossicular chain.

Some reports are available about congenital middle ear cholesteatoma with ossicular chain anomaly, and the pathogenesis is still under discussion. As the long process of the incus and the head and the cru of the stapes are absent in most of such cases, they speculate that developmental anomalies of the joint of first and second branchial arch resulted in formation of congenital cholesteatomas. Our case supports this hypothesis.

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## Objective tinnitus by closing of the bite attributed to the connection between the temporomandibular joint and middle ear

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**Objectives:** To describe of objective tinnitus coincided with opening of the bite, which was related to the connection between the mandibular joint and middle ear.

**Methods:** Clinical case records (including computed tomography [CT] and audiological data).

**Results:** A 41-year-old man presented with tinnitus, ear fullness and hearing loss with his mouth opening in the left ear. His hearing thresholds on the ipsilateral side, which were evaluated with opening of the bite, showed elevations with approximately 20 dB in the frequencies below 1000 Hz. Again, the peak of tympanogram deviated negatively to -220 mmH<sub>2</sub>O with the condition of opening the bite without changing the tympanometric peak pressure. CT showed a connection between the tympanic cavity and mandibular disc, which was revealed by a gas collection around the joint capsule evaluated by 2 phases (with and without mouth closing). The ear symptom resolved after the myringotomy.

**Conclusions:** Although an influence of the temporomandibular disorder on tinnitus perception has been debated, it is still an open question as to whether this association is casual or fortuitous. The present case represents a unique feature of tinnitus attributed a connection between the temporomandibular and middle ear.

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## Surgical results of congenital stapes footplate fixation in Japan

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**Objective:** The aim of the study was to describe the audiometric results after stapes surgery in a series of patients with stapes footplate fixation combined with or without another ossicular middle ear anomaly.

**Methods:** 14 ears (8 women; 6 men) ranging in age from 7 to 29 years underwent a CO<sub>2</sub> laser assisted-stapedotomy with Teflon piston between January 2010 to January 2014. All patients had a preoperative workup comprising clinical examination, audiometric data review, and a systemic computed tomographic (CT) scan of the temporal bone. At least 1 year minimum follow-up data were available for 5 patients. Postoperative testing was performed at approximately 6 weeks postoperatively and yearly thereafter.

**Results:** Overall, a mean gain in air conduction of 26.9 dB (from 52.3 dB to 25.4 dB) and a mean postoperative air-bone gap of 13.1 dB (mean preoperative AB gap, 32.4 dB) were observed. The AB gap closure was 20 dB or less in 100% of cases. Stapes surgery for congenital stapes footplate fixation combined with or without another ossicular middle ear anomaly can worthwhile hearing improvement.

**Poster** Laryngology 2

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**New modified laryngotracheal separation for patients with severe neuromuscular diseases**

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Lindeman's tracheoesophageal diversion (TED) has been considered a very effective, reversible procedure for the prevention of intractable aspiration. The advantages of TED are that it is reversible and may allow vocalization. However, the indications for TED are limited, and sedation may be needed for days after the operation to inhibit involuntary neck movement, which can cause complications such as a tracheocutaneous fistula. The longer the sedation that is needed after operation, the more serious the disuse syndrome is that develops in patients with neuromuscular disorders. Recently, it has been reported that a new laryngotracheal separation (LTS) procedure could facilitate postoperative management (Nakaya 2011). We modified this new LTS method for patients with severe neuromuscular diseases in our hospital. This paper describes our surgical technique and reports the outcomes.

The operations were performed under general anesthesia. A wineglass-shaped skin incision was made and skin flaps were elevated with subcutaneous tissue and platysma. The isthmus of the thyroid gland was dissected. The anterior cricoid arch was resected, preserving its perichondrium. A reverse U-shaped anterior tracheal wall incision was made at the level of the lower edge of the cricoid cartilage, and the tracheostomy was created. A laryngeal mucosal incision was made circularly at the same level through the perichondrium of the cricoid, and the stump of laryngeal mucosa was sutured to achieve tracheal closure. The closure was covered with an upper musculocutaneous flap.

A total of 30 patients with neuromuscular disease who underwent the new modified LTS method in Tokyo Metropolitan Neurological hospital were evaluated retrospectively. The breakdown of the subjects was 19 males and 11 females, and the age ranged between 2 and 76 years (mean 36.8 years). The mean surgery time was 124.9 minutes (range, 80 to 225 minutes), and the mean amount of intraoperative bleeding was 12.8 mL (range, 1 to 60 mL). Postoperative complications included only one abscess, with no fistula formation, and postoperative management was simplified. The mean postoperative follow-up period was 13.7 months (range, 0.75 to 55 months). No patients developed postoperative aspiration pneumonia.

This study suggests that our modified LTS procedure might be very effective and more useful for patients with severe neuromuscular disorder because it could prevent their disuse syndrome and allow the patients to maintain their activities of daily living postoperatively.

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**A case of Ewing sarcoma of larynx**

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## Introduction

James Ewing first described Ewing sarcoma in 1921. Ewing sarcoma is a malignant small, round, blue cell tumor. It is a rare disease in which cancer cells are found in the bone or in soft tissue. The most common areas in which it occurs are the pelvis, the femur, the humerus, the ribs and clavicle. This tumor comprises the second most common bone tumor in children and adolescents. Genetic exchange between chromosomes can cause cells to become cancerous. Most cases of Ewing's sarcoma are the result of a translocation between chromosomes 11 and 22. This case report describes an extraskelatal Ewing's sarcoma of the larynx.

## Case report

A 84-year-old female with a past medical history of colon carcinoma, treated 3 years earlier with colectomy was referred to our department with larynx mass which founded in CT. Flexible laryngoscopy showed tumefaction located to the anterior part of the larynx, occupying the anterior commissure, both vocal cords and the laryngeal ventricles with a left-sided predominance. Surgical resection of a part of larynx tumor was performed by means of a videolaryngoscopic surgery after tracheotomy. Microscopically, all the sections revealed a monomorphic proliferation and peritheliomatous arrangement of small round cells with scanty cytoplasm. Immunohistochemistry showed strong cytoplasmic positivity for MIC-2. Vimentin was positive. But S-100 protein, neuron-specific enolase (NSE), synaptophysin, chromogranin, leukocyte common antigen (LCA) and cytokeratin were negative. We proposed postoperative radiotherapy, but the patient and her family rejected for her age. She is living with tumor for six months.

## Conclusions

This is a report of an apparently unique case of extraskelatal Ewing's sarcoma arising in the larynx in an elderly woman. This neoplasm should be included in the differential diagnosis of small round cell tumors in this site.

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## Differentiation of mouse induced pluripotent stem cell into tracheal epithelial cells

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**Introduction:** Autologous tissue implantation techniques using skin or cartilage are often applied in tracheal defected cases with laryngeal inflammatory lesions and malignant tumor invasion. However, these techniques are both invasive and unstable about clinical outcome. The patients of tracheal deficiency undergo minimal invasive operation if artificial materials are able to be used for regeneration of tracheal defect. The purpose of this study was to investigate regeneration in a tracheal defect site of nude rats by implanting ciliated epithelium differentiated from induced pluripotent stem cells.

**Methods:** The embryoid bodies (EBs) were formed from mouse induced pluripotent stem cells. They were cultured with growth factors for five days, and then cultured on the condition of air-liquid interface (ALI) to promote differentiation to ciliated epithelium. The maturation distance for implantation was determined by histological findings and the results of real-time polymerase chain reaction. Artificial materials were implanted into nude rats with tracheal defect. EBs including ciliated epithelium were implanted into nude rats with artificial material by being embedded into type I collagen gel: 'ALI model'. The two models used for comparison were the 'without ALI model', which contained EBs that were not adhered to the ALI, and the 'control model', which contained no EB. Histological evaluation was performed 7 days after implantation.

**Results:** In vitro examination, ciliated epithelial structures were first observed in EBs on 26 days of adhesion culture. In vivo examination, ciliated epithelial structures survived at the lumen side of regenerated tissue in 'ALI model'. It was demonstrated that these structure composed of ciliated epithelial cells by immunohistochemical staining analysis.

**Conclusion:** Our findings demonstrate the potential use of induced pluripotent stem cells for regeneration of tracheal epithelium.

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## Palatal Implantation for Severe Obstructive Sleep Apnea

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**Objectives:** To analyze the subjective and objective outcomes of palatal implantations for patients with severe obstructive sleep apnea.

**Design:** Retrospective analysis of polysomnograms and questionnaires.

**Setting:** A single-institution, retrospective review.

**Patients or Participants:** A total of 10 patients were enrolled in this study.

**Interventions:** Palatal implantation.

**Measurements and Results:** There were statistically significant improvements in subjective outcomes, including visual analog scale scores of snoring ( $8.4 \pm 1.1$  to  $4.1 \pm 1.9$ ,  $P=0.004$ ) and sleep quality ( $3.8 \pm 1.9$  to  $7.4 \pm 1.8$ ,  $P=0.005$ ) and Epworth Sleepiness Scale ( $8.2 \pm 5.1$  to  $5.4 \pm 4.4$ ,  $P=0.012$ ). We defined a reduction in respiratory disturbance index of  $\geq 50\%$  and a subsequent respiratory disturbance index of  $< 20$  as surgical success, and two of the 10 (20%) patients achieved these criteria. Improvements in respiratory disturbance index ( $51.9 \pm 5.0$  to  $37.5 \pm 5.7$ ,  $P=0.009$ ) and minimum O<sub>2</sub> saturation ( $68.6 \pm 3.7\%$  to  $73.5 \pm 3.6\%$ ,  $P=0.033$ ) were significant. Percentage change in RDI was negatively associated with prominent retrolingual collapse ( $P=0.019$ ) and soft palate length ( $P=0.05$ ).

**Conclusions:** Certain patients with severe obstructive sleep apnea may benefit from palatal implantation.

## Poster Rhinology 2

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**The roles of type 2 innate lymphoid cells (ILC2) in chronic rhinosinusitis (CRS)**

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**Background:** Chronic rhinosinusitis (CRS) is one of the most frequent chronic diseases, and little is understood about its pathogenesis. Eosinophils are considered to play a major role in its pathology, but we still know little which is causing chronic immune activation and persistent eosinophilic inflammation in CRS. Recently, type 2 innate lymphoid cells (ILC2s, lineage (-), CD45 (+), CD127 (+), CD294 (+)) were identified as a candidate, which produce highly levels of Th2 cytokines such as IL-5 and IL-13, which activates eosinophils. We hypothesized that ILC2s are enriched in blood and nasal polyps in patients with eosinophilic CRS (ECRS) and are associated with its pathology.

**Methods:** The patients with CRS or pituitary adenoma (normal sinus) who underwent Endoscopic sinus surgery (ESS) in Jikei University Hospital were enrolled. We used PBMC and nasal polyps (NPs) from patients with CRS or normal subjects, and analyzed the amount of ILC2 by flow cytometry. We also investigated the distribution of ILC2s in NPs by immunohistochemistry. EDN and cytokines in NPs were measured by ELISA to investigate correlation with ILC2s. Lineage negative cells from nasal polyps were cultured in vitro with IL-33 or/and IL-2 to investigate the amount of cytokine produced by ILC2s.

**Results:** EDN and Th2 cytokines are significantly higher in ECRS than non-eosinophilic CRS (NECRS). EDN had strongly correlated with the numbers of ILC2s in NPs. The counts of ILC2s in NPs were significantly higher in ECRS than NECRS. Immunostained ILC2 were showed accumulated in nasal polyps of ECRS, but not in NECRS or normal subjects. ILC2's CD25 surface expression in PBMC was significantly higher in ECRS than NECRS. ILC2's IL-17RB surface expression in NPs was significantly higher in NECRS than ECRS. Lineage negative cells from ECRS' NP, but not from NECRS', produced IL-5 and IL-13 in both IL-2 and IL-33 stimulation.

**Conclusions:** ILC2 are considered as candidate of the commander in ECRS, which strongly induce Th2 inflammation. There are possibility that ILC2s have several subtypes and the characteristic of ILC2s are differ from their environment.

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**Recent situation of the treatment of odontogenic cyst in paranasal sinus**

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Odontogenic cyst is generated from Odontogenic epithelium of Jawbone, and is formed with odontopathy or eruption process of tooth. Odontogenic cyst is defined as two types, inflammatory type and developmental type. Radicular cyst, categorized as inflammatory type, is the most typical case and dentigerous cyst, categorized as developmental type, is the typical second case.

Odontogenic cyst is, in many case, treated by oral surgery. But, in case for large radicular cyst or developmental cyst treatment, paranasal sinus region could be the main region for treatment. The region for treatment affects the determination of leading department between oral surgery or otorhinolaryngology, or both. In consideration with the broadening target for endoscopic paranasal sinus surgery, supported by the development of operative procedure and medical equipment, the approaches for these pathologies are still on the further development. In recent years, Nakayama et al. reported that effective procedure for odontogenic maxillary cyst, which enable preservation of the inferior turbinate and nasolacrimal duct, and named as Endoscopic modified medial maxillectomy (EMMM) . Our hospital started to use EMMM approach for the effective case in recent years and has a good result for treatment.

In this report, we report about treated odontogenic cyst in the oral surgery and otorhinolaryngology, concretly, treatments, coordinated cases between oral surgery and otorhinolaryngology, postoperative courses, recent developments of treatment for current situation and treatment in our hospital.



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## Repairing nasal septum perforations: outcome of 30 cases

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**Objectives:** Nasal septum perforation can occur due to external or self-induced trauma, Wegener's granuloma, the use of cocaine, aggressive cauterization of the nasal mucosa, or nasal septal surgery such as septoplasty or deviatomy. Nasal septum perforations accompanying symptoms such as recurrent epistaxis, nasal obstruction, crusting, pain and whistling often require surgical treatment because conservative treatments do not significantly improve symptoms. We report the 5-year outcome in a series of 30 patients who underwent surgery to repair a symptomatic septum perforation.

**Patients and Methods:** From 2010 to 2015, 30 patients with symptomatic nasal septum perforation underwent surgery. The average age was 43.4 (16-66) years old and the average extent of the major axis of a perforation was 22.3 (8-45) mm. The causes of septum perforation were: nasal septal surgery (n=19), cauterization of the nasal mucosa (n=3), and nose-picking (n=4). Four cases had septum perforations due to unknown reasons; systemic diseases such as Wegener's granuloma were ruled out in these cases. The surgical procedure starts with elevation of the bilateral mucosal flaps under an endoscopic view. A releasing incision is made across the nasal floor on one side and across the lateral cartilage on the other side. The flaps are slid up- and downward, respectively. The perforation is then sutured. The follow-up period was a minimum of 6 months. A perforation was considered to be successfully closed when no re-perforation was observed 6 months after surgery.

**Results:** The post-operative follow-up period was 6 months to 5 years after surgery. Nasal septum perforation was successfully closed by the first surgery with no re-perforation observed in the 6 month follow-up period in 26 of the 30 patients (86.7%). Most of the symptoms complained of before surgery resolved except for nasal obstruction. In 4 patients re-perforation was observed within 6 months of surgery: 1 patient had diabetes, 1 patient had taken corticosteroids for several years, and 1 patient had large and multiple perforations. In 3 of the 26 patients whose perforation was successfully fixed, re-perforation was observed more than 1 year after surgery (76.7% 18 after surgery). Among these 3 patients, 1 patient had diabetes, and 2 patients' perforation was due to compulsive nose-picking. These patients required additional closure.

**Conclusion:** The success rate for repairing a nasal septum perforation was 86.7% 6 months after surgery and 76.7% 18 months after surgery. Risk for re-perforation seemed to be associated with corticosteroid use, diabetes, large perforations and nose-picking.

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## A randomized control trial with intranasal mometasone furoate and fluticasone furoate for seasonal allergic rhinitis in train driver

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**Objective:** Allergic rhinitis (AR) treatment should not only reduce symptoms but also improve quality of life (QoL), sleep disturbance, and work productivity. Seasonal AR (SAR) causes rhinitis-disturbed sleep (RDS), although the relationship between RDS and driving safety has not been studied. The aim of this trial was to evaluate the efficacy and safety of early interventional treatment (EIT) with intranasal corticosteroids (INS) of SAR in train drivers.

**Methods:** Fifty East Japan Railway Company (JR-EAST) drivers diagnosed with SAR were administered intranasal mometasone furoate (MF) or intranasal fluticasone furoate (FF) for 90 days in a randomized, double-blind, parallel-group study. Medication was started from the beginning of early symptoms, immediately after the start of cedar pollen dispersal. Efficacy and safety between baseline and end of treatment as primary endpoints were assessed using the Japanese Rhinoconjunctivitis Quality of life Questionnaire (JRQLQ), and secondary endpoints were assessed using the Japanese version of the Epworth Sleepiness Scale (JESS) score, Work Productivity and Activities Impairment-Allergy Specific (WPAI-AS) score, and plasma cortisol concentrations.

**Results:** Forty individuals completed the study. The magnitude of change of JRQLQ, JESS, WPAI-AS, and plasma cortisol concentrations between MF group and FF group did not present significantly difference. Compared with baseline, all JRQLQ items were significantly improved but the JESS scores did not change. Analysis of JESS scores showed that RDS was prevented during the trial. WPAI-AS scores showed improvement, but plasma cortisol concentrations increased.

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## A case of primary ciliary dyskinesia examined by genetic analysis

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Primary ciliary dyskinesia (PCD) is an autosomal recessive genetic disorder of ciliary function, causing impairment of ciliary clearance, leading to chronic sinusitis, otitis media, chronic bronchitis and male infertility. In this study, we reported a 13-year-old boy whose chief complaints were nasal discharge and productive cough. Since birth, he had been suffering from rhinorrhea, otorrhea and productive cough. CT findings of nasal sinuses and lung revealed chronic rhinosinusitis and bronchiectasis. He was diagnosed as chronic rhinosinusitis at 12-year-old, and had endoscopic sinus surgeries twice. The serum levels of IgG subclasses were normal. The concentration of nasal nitric oxide was 160 ppb, which was very low. Electron microscopic analysis of nasal cilia demonstrated the defects of inner dynein arms. His family history was negative for PCD. However, heterozygous mutation in DNAH11 was found. He was diagnosed as PCD. The diagnosis of PCD is not always differentiated as its less frequency. We should always keep in mind the possibility of PCD in patients presenting with atypical chronic sinusitis, chronic otitis media, and bronchiectasis. Early diagnosis and treatment allows improvement of the quality of life.

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## Olfactory Dysfunction caused by Temporal Lobe Epilepsy

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### Background

Phantosmia is the perception of a smell by an individual when no odorant molecules are present, and is often caused by temporal lobe epilepsy (TLE). However, only few reports have focused on olfactory functions of patients with TLE. We report two cases with olfactory dysfunction associated with TLE.

### Material and Method

Case 1; A 64-year-old man had hyposmia for three years before he was diagnosed as TLE, and anosmia and phantosmia were present for 2-3 weeks after seizure-like attacks.

Case 2; A 16-year-old woman with TLE had parosmia and phantosmia for a week after seizure-like attacks.

Olfactory functions of these patients were examined by an odor threshold and identification test (T & T olfactometry).

### Result

Case 1; Both odor detection and identification were worsen after seizure-like attacks, and were gradually recovered, though an impairment of odor detection was not so severe.

Case 2; Despite the presence or absence of seizure-like attacks, odor detection was almost normal, but odor identification was poor.

### Conclusion;

In our two cases, odor detection was not affected by the seizure-like attacks, however odor identification was poor. These results indicate that temporal lobe may play a role for the identification of odorant.

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## Vascular leiomyoma of the nasal septum: case report

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95% cases of leiomyomas arise from the smooth muscle of the female genital tract. Less than 1% occur in the head and neck area, and only 3% of leiomyomas in the head and neck occur in the nasal cavity. Intranasal leiomyoma is extremely rare. After the first case of nasal vascular leiomyoma described by Maesaka et al. in 1966, another 30 cases have been reported in the English literature, and an additional 50 cases in the Japanese literature. They are most commonly found in patients between the ages of 40 and 60 years, with female predominance. Most cases develop from the inferior turbinate, nasal vestibule or the nasal septum. The slow-growing benign neoplasm may cause nasal obstruction or epistaxis. The treatment of choice is surgical excision. We hereby present a case of vascular leiomyoma arising from the nasal septum, its clinical and histological features, the treatment and literature review.

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## Perioperative coronary artery spasm after functional endoscopic sinus surgery - a case report

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Perioperative coronary artery spasm, which is a rare condition in otorhinolaryngological surgery, is shown to play an important role in the pathogenesis of myocardial infarction.

Oriental elderly male patients with coronary risk factor are shown to be more prevalent in this condition; however, the incidence is less than 0.05% in non-cardiac surgery according to the reported literature.

In this report, we presented a 47-year-old male heavy smoker, who underwent functional endoscopic sinus surgery, suffered from two episodes of myoclonus, chest tightness and hypotension after fluid supplement during the postoperative period. Electrocardiography revealed mild ST elevation over Lead II,III and aVF; however, laboratory study showed no cardiac enzyme abnormality. Consciousness change and cardiac arrest with ventricular fibrillation were noted subsequently. Cardio-pulmonary-cerebral resuscitation was performed and the patient was sent for percutaneous coronary intervention after return of spontaneous circulation. The PCI showed proximal right coronary artery spasm with distal thrombus formation. The patient recovered gradually after the procedure and echocardiography later reported good left ventricle contractility (LVEF:69%) with very mild left ventricle regional wall motion abnormality over right coronary artery territory. He was then discharged from our hospital under fair condition.

Although the incidence of perioperative coronary artery spasm was quite low, this could be a lethal situation without early detection and appropriate management.

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## Suggestions on the CT classification and the surgical classification on opening the sphenoid sinus

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There is no effective classification method for the opening of the sphenoid sinus. The objective of this study was to examine the effectiveness of identification of the Onodi cell and classification of the sphenoid sinus using sagittal computed tomography (CT) for sphenoidotomy.

CT classification: Using sagittal CT, the relationships between the lateral side of the anterior wall of the sphenoid sinus and the skull base, the optic canal, and the Sella were studied. Images were classified as demonstrating skull base type, optic canal type, Sella type, and infra-Sella type.

Surgical classification: There are several operative roots in the sphenoid sinus. Namely; the olfactory root, the ethmoid root and the septal root. These roots are different from the difficult operative levels and the safety operative levels. And we have selections for these operative roots basing on the pathological conditions of the sphenoid sinus. But still now, there isn't any specific useful operative method; classified for a clinical application that can be carried out. This time, we classified the operative procedures for the sphenoid sinus this way:

Type1 :(Simple drainage). Type2 :(Lateral drainage). Type3 :(Combined drainage) and Type4 :(Median drainage).

Type1 (Simple drainage): Open the natural ostium of the sphenoid sinus from the olfactory root.

Type2 (Lateral drainage): Open the anterior wall of the sphenoid sinus from the ethmoid root.

Type 3 (Combined drainage): Mix or combine the methods of Type1 and Type2.

Type 4 (Median drainage): Remove the septum of the sphenoid sinus.

Additional two subtypes are added for supplementary purposes or methods.

Subtype-a: The treatment of the superior turbinate.

Subtype-b: Treatment of the posterior septal branch of the sphenopalatine artery.

This new classification of the operative method of the sphenoid sinus is very useful for planning a safe and exact procedure before the surgery. So here is a show on the new findings we've made on the CT classification depending on the operatives on the sphenoid sinus.

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## Increasing prevalence of Japanese cedar pollinosis among children in Akita, Northeast Japan

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**Background:** The prevalence of Japanese cedar (JC) pollinosis is the major seasonal allergic disease in Japan. We investigate time trends in the prevalence of JC pollinosis and the sensitization for JC pollen in two areas of Akita in northeast Japan with contrasting levels of exposure to JC pollen. **Methods:** The study population consisted of elementary school students (10-11 years of age) from the coastal and mountainous areas of Akita in 2005-2006 (339 students) and 2015 (185 students). A questionnaire about symptoms of allergic rhinitis was filled out by the students' parents. A blood sample was taken to determine specific IgE antibodies against JC pollen, mite and grass. **Results:** The prevalence rates of JC pollinosis (10.0% vs 20.6%,  $p < 0.005$ ) and sensitization for JC pollen (31.9% vs 37.8%) increased between 2005-06 and 2015. However, there was no significant change in the prevalence of allergic rhinitis and sensitization for mite. The mean pollen count in the mountainous areas was two times higher than that in the coastal areas. The rates of nasal allergy symptoms and sensitization for JC pollen were significantly higher in the mountainous areas than in the coastal areas.

**Conclusion:** The prevalence of JC pollinosis increase but there is no change with prevalence of persistent allergic rhinitis for the last 10 years in Akita, Japan.

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## The Efficacy of Minimal Invasive Turbinate Reduction Surgery

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**Aim:** The role of inferior turbinate hypertrophy in the reduction of nasal airflow is well established. When it causes symptomatic nasal obstruction, patient's quality of life is significantly impaired. Several methods of turbinate reduction had been used to improve this phenomenon. An ideal surgery can balance adequate tissue resection and preserving functional turbinate tissue. We propose a new minimal invasive turbinate reduction surgery and exam its efficacy and safety.

**Method:** From Aug., 2013 to July, 2015, 216 cases with chief complaint of nasal obstruction underwent turbinate reduction surgeries are included. Conditions with sinus diseases, nasal tumor, previous nasal or facial trauma or surgery are excluded before cases are selected. 92 patients received submucosal resection of septum with submucosal turbinectomy (SMT group), whereas 124 patents received submucosal resection of septum with minimal invasive turbinate reduction (MITR group). MITR is a combination of submucosal microdebridering of turbinate and chocha bone removal via a minimal mucosa incision. Change of SNOT-22, Saccharine transport time (STT), and postoperative pain and bleeding are examined between these two groups.

**Results:** In MITR group, the 1-month postoperative total score of SNOT-22 is decreased by 31.83 (from 43.33 to 11.5,  $p < 0.01$ ). Postoperative pain score is significantly less in MITR group than in SMT group (3.75 vs 7.62,  $p < 0.01$ ). Postoperative bleeding is not noticed in MITR group, compared to 2.17 % in SMT group.

**Conclusion:** MITR can significantly improve nasal obstruction. Compared with SMT, it has less postoperative pain and bleeding. It's mucosa function is also less impaired than the traditional turbinate surgery.

P85

## Retinoids Activate The Production of Tissue Plasminogen Activator in Human Epithelial Cells

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**Rationale:** Recent data from our lab suggested nasal polyp (NP) in chronic rhinosinusitis which is type 2-related inflammation was related to fibrin deposition. This is likely to be caused by potent decrease of tissue plasminogen activator (t-PA) in NP tissue. The aims of present study are to investigate how t-PA gene expression is altered by various stimulants, and to study whether t-PA is stored and/or released by normal human bronchial epithelial (NHBE) cells.

**Methods:** NHBE were stimulated by Cytokines (IL-1b, IL-4, IL-6, IL-13, IL-17, IFN $\gamma$ , TNF $\alpha$ ), Growth factors (TGF $\beta$ , EGF, VEGF, bFGF), Dexamethasone, Retinoic acid (RA), Vitamins (Vitamin A, Vitamin D), Histon deacetylase inhibitors (Butyrate, Trichostatin A) and Statins (Symbastatin, Fluvastatin) for 24hr. The expression of t-PA mRNA was analyzed by real-time PCR. t-PA protein from supernatant and cell lysate were analyzed by ELISA.

**Result:** IL-13(100ng/ml) significantly reduced t-PA mRNA expression by 40%, while RA ( $1 \times 10^{-6}M$ ) and Vitamin A ( $1 \times 10^{-6}M$ ) induced 3 to 6 times higher than control ( $p < 0.05$  respectively). In supernatant, IL-13 significantly reduced t-PA protein, while RA induced significantly compared to control (65.9 vs 229.3 vs 121.1 ng t-PA protein respectively). Similar trend were found in cell lysate (16.4 vs 64.3 vs 36.1 ng t-PA protein respectively).

**Conclusion:** t-PA protein is synthesized and released by NHBE. Type 2 cytokine and RA and Vitamin A have potent relevance to alter the t-PA production in NHBE. The amount of released t-PA is higher than in cell lysate which suggests epithelial cell plays a role in consistent production of t-PA.

## Poster Other 2

P86

**Up-regulation of CX3CR1 on tonsillar CD8+ T cells in patients with IgA nephropathy**

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IgA nephropathy (IgAN), the most common form of primary glomerulonephritis, is recognized as one of the tonsillar focal disease. Although tonsillectomy and steroid pulse therapy has been attracting attention as a treatment preventing IgAN patients from chronic renal failure, relationship between IgAN and tonsils is not fully proved by basic research. Recently, circulating CX3CR1+ T cells reportedly have a role in pathogenesis of IgAN. In this study, we focused on CX3CR1 expression of tonsillar T-cells in IgAN patients. Immunohistochemical analysis revealed that CX3CR1-positive cells were found more often on the section of the tonsils from IgAN patients than from non-IgAN patients. Moreover, the positive cells were also found on the section of kidney biopsy samples from IgAN patients. Two-color flow cytometric analysis revealed that percentages of tonsillar CX3CR1+ CD8+ T cells were significantly higher in IgAN patients than in non-IgAN patients ( $p < 0.05$ ). In vitro stimulation with CpG oligodeoxynucleotides (CpG-ODN) enhanced CX3CR1 expression on tonsillar CD8+ T cells in IgAN patients ( $P < 0.05$ ), but not in non-IgAN patients. The chemotactic response of tonsillar mononuclear cells to CX3CL1 (CX3CR1 ligand) was significantly higher in IgAN patients than in non-IgAN patients ( $P < 0.05$ ). Percentages of peripheral blood CX3CR1+ CD8+ cells were significantly higher in IgAN patients than in non-IgAN patients ( $p < 0.05$ ). Moreover, the percentage significantly decreased after tonsillectomy in IgAN patients ( $P < 0.05$ ). These results suggest that a novel immune response to CpG-ODN may enhance CX3CR1 expression on tonsillar CD8+ T cells in IgAN patients, and CX3CR1+ CD8+ T cells may move to blood circulation, resulting in recruitment to target renal lesions. This may play a role in the pathogenesis of IgAN as tonsillar focal disease.

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**Otorhinolaryngologic Problems Among Children With Down Syndrome**Kentaro Ichijo<sup>1</sup>, Masato Yagi<sup>1</sup>, Masae Ono<sup>2</sup>, Emi Matsuda<sup>1</sup>, Kaori Kanaya<sup>1</sup><sup>1</sup>*Department of Otolaryngology, Tokyo Teishin Hospital, Japan,*<sup>2</sup>*Department of Pediatrics, Tokyo Teishin Hospital, Japan*

Many people with Down syndrome have the common facial features and no other major birth defects. However, some people with Down syndrome might have one or more major birth defects or other medical problems. Some of otorhinolaryngologic problems among children with Down syndrome are listed below. Hearing loss (up to 75% of people with Down syndrome may be affected). Obstructive sleep apnea, which is a condition where the person's breathing temporarily stops while asleep (between 50 -75%). Ear infections (between 50 -70%). Eye diseases (up to 60%), like cataracts and eye issues requiring glasses. Heart defects present at birth (50%)<sup>1</sup>. In short, many children with Down syndrome might have more or less otorhinolaryngologic problems.

In our hospital, 75 children with Down syndrome visited the department of pediatrics between January in 2012 and July in 2015. Among them, 46 children were referred to otorhinolaryngologists for the otorhinolaryngologic problems suspected, Otorhinolaryngologic problems had been discovered in 39 cases. On 29 cases with hearing disorder suspected, auditory brainstem response (ABR) was performed. As a result, 12 children had abnormal findings. According to other otological tests, 7 children were suspected a conductive hearing loss, and 5 children a sensorineural hearing loss. Hearing threshold in 2 children had an improvement in the follow-up. Eight children had otitis media with effusion (21%). Yamashita et al studied 22 children with hearing loss, mental retardation, and Down syndrome who visited the Fukuoka Welfare Center. Among them, 10 children had otitis media with effusion. Hearing threshold in 14 children had an improvement in the follow-up<sup>2</sup>). It is well-known that children with Down syndrome often have the airway trouble. Two children had obstructive sleep apnea syndrome (5%), and 5 children seemed to have laryngomalacia (13%). We recommend children with Down syndrome to have otorhinolaryngologic checks regularly, because they might have various otorhinolaryngologic problems, besides the problems are easily changeable.

## Reference

- Centers for Disease Control and Prevention: Facts about Down Syndrome—Other Health Problems Among Children With Down syndrome—
- Yamashita M et al :Hearing loss in children with Down syndrome. *Otologia Fukuoka* 56: 139-144, 2010.

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## A clinical investigation of deep neck abscesses

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**Purpose:** This study reviews our experience with deep neck abscess and tries to identify the predisposing factors of severity.

**Method:** A retrospective review was conducted of patients who were diagnosed as having deep neck abscess in the Department of Otolaryngology, head and neck surgery at Kansai medical university hospital from 2006 to 2014. Their etiology associated systemic disease, bacteriology, radiology, treatment, duration of hospitalization, complications, and outcomes were reviewed.

**Results:** Forty-six patients were reviewed; 29 were men, and 17 were women, with a mean age of 58.8 years. There were 21 patients (46%) who had associated systemic diseases. Peritonsillar abscess and odontogenic infections were the two common causes of deep neck abscess. Streptococcal groups were the most common organisms identified through pus cultures. The cultures of 14 cases were results in mixed polymicrobial aerobic and anaerobic infections. There were 9 patients with acute necrotizing mediastinitis. The most common source of acute necrotizing mediastinitis were deep neck abscesses secondary to peritonsil abscesses (7 cases; 2 superior abscess and 5 inferior abscess). In two cases acute necrotizing mediastinitis originated from odontogenic infections. The two patients with fatal outcome died as a result of multiple organ failure.

**Conclusion:** Accurate diagnosis and application of early surgical drainage with antibiotic therapy are essential for a successful outcome of deep neck abscesses. Prompt recognition of acute necrotizing mediastinitis can be challenging because there may not be clear symptoms and signs, especially inferior peritonsillar abscesses.

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## Withdrawn

P90

## The role of phosphorylcholine in the adherence of *Streptococcus pneumoniae* and *Haemophilus influenzae*

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### Objective

Phosphorylcholine (PC) is a structural component of a wide variety of pathogens including *Streptococcus pneumoniae* (Spn) and nontypable *Haemophilus influenzae* (NTHi) which are major pathogens of upper respiratory infection. We have reported that the adherence of Spn to epithelial cells is mediated by the interaction between the PC expressed on pathogen and the platelet-activating factor receptor (PAF-R) expressed on epithelial cells. Thus, we examined that the expression of PC on various strains of Spn and NTHi and the adherence of those bacteria to epithelial cells to clarify the mechanisms of adherence ability of bacteria.

### Materials and methods

Ten strains of Spn and 9 strains of NTHi were cultured overnight on blood agar or chocolate agar plate at 37°C in a 5%CO<sub>2</sub> incubator and fixed with formalin. The expressions of PC on these bacteria were evaluated by ELISA. Oral epithelial cells (OEC) were harvested from human buccal mucosa and used for bacterial adherence assay to examine the correlation of PC expression on bacteria with its adherence ability to OEC.

### Results

Spn and NTHi fixed with formalin express PC and either strains adhere to OEC. The adherence of Spn to OEC was reduced by pretreatment with PAF-R antagonist but not in NTHi.

### Conclusion

The interaction between PC and PAF-R might be one of the mechanisms of Spn adherence ability to OEC. Further, there may be differences in adherence mechanism between Spn and NTHi because NTHi adherence was not reduced by pretreatment with PAF-R antagonist.

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## Precise Carving of Autologous Costal Cartilage Graft for Aesthetic Rhinoplasty - Case Report

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Rhinoplasty is one of the most commonly performed aesthetic surgeries in Taiwan today. A typical Taiwanese nose is short length with excess nostril show, wide dorsal vault, round tip and lack of projection. Dorsal augmentation with a large volume graft is needed frequently in Taiwan. There is a variety of alloplastic materials available for this purpose. However, autologous cartilage is safer and preferable. Small to moderate volume of dorsal augmentation can be managed with septal or conchal cartilage used alone or in combination. However, if the projection needs to be increased substantially or when the grafts need to be placed in multiple locations, the two above mentioned cartilages may not provide enough volume. Therefore, costal cartilage is needed. Warping is the inherent tendency of costal cartilage to deform when subjected to trauma or surgeon's knife. The outer layer of the compressed cartilage has a natural tendency to expand, but this is prevented by the taut perichondrium. If the incision is only on one side, that surface will expand causing the cartilage to bend. While carving a piece of cartilage, if the surface incisions are of equal depth, and are equally spread on the opposing surfaces, both the surfaces will equally expand and the piece will not warp. However, warping phenomenon is not yet fully understood. Rather than its prevention, it may be allowed to happen, in a controlled, programmed manner so that it can be used to straighten a curved piece of cartilage, the manner in which cartilage warps is not capricious, but very much predictable. We present a case of costal cartilage rhinoplasty using concentric and eccentric carving method.



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## **Precise Tunneling in Subperiosteal Plane for Augmentation Rhinoplasty - Case Report**

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For oriental noses, there are many aesthetic problems such as broad base, low dorsum and short nose. The majority of rhinoplasty in Taiwanese nose involves augmentative procedures. A major postoperative unsatisfaction after rhinoplasty is misalignment.

It is believed that subperiosteal layer insertion of dorsal augmentation graft or implant is the key of this problem. Several techniques have been published to place graft or implant in the subperiosteal layer. In some studies, the dissection was done in supraperichondrial plane at rhinion and followed by sharp periosteal elevator dissection in creating the subperiosteal tunnel over the nasal bone. From the study of Rojvachiranonda et al in Thai augmentation rhinoplasty, periosteal coverage was always incomplete and did not provide immediate graft or implant fixation. We believe that augmentation rhinoplasty by using graft or implant insertion in subperiosteal plane, at least the nasion area, makes it more natural look, stable and can prevent misalignment. We present a case of augmentation rhinoplasty using precise midline subperiosteal tunneling method.

**Luncheon Seminar 1****LS1****Philosophy of MED-EL**

Melissa Waller<sup>1</sup>, Florian Feichtner<sup>2</sup>

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MED-EL is a research driven company, and in this presentation we are proud to introduce our new SYNCHRYONY cochlear implant system and our philosophy Triformance.

We have a new audio processor SONNET and implant SYNCHRYONY.

For our users, we not only deliver sound, but aim for how “natural” the sound is. We believe this is possible with our philosophy Triformance, and the SONNET features add on new values and expand the possibility of hearing. This is due to our new microphones which we will introduce you to in the presentation as well.

There is a large variety of range in people in need of cochlear implants, and we want to minimize the limitations caused by using an implant. Our SYNCHRYONY is MRI safe up to 3.0T without magnet removal, and the magnet can also be removed when needed. An MRI is not only important for elderly patients, but for young patients as well. In the presentation we will dig into the importance and need of MRI.

## Luncheon Seminar 2

### LS2

## Probing Vestibular Function from Postural Stability

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Postural stability in human is maintained by muscular outputs governed by the processing of the central nervous system. The central processing integrates the information from vestibular, visual, and somatosensory inputs. Dysfunction of any components of this system can cause postural instability, leading to increase in the risk of falls. Static posturography measures spontaneous movement of the center of pressure (COP), which is a good parameter of the center of mass during upright stance. To scrutinize the different sensory inputs involved in the maintenance of balance, dynamic posturography using a platform or a foam rubber surface has been developed to selectively manipulate vision and somatosensation. Our group originally developed a foam posturography analysis system to detect peripheral vestibular dysfunction by putting a foam rubber on a firm platform of common posturography. This system showed high sensitivity and high specificity for detecting bilateral as well as unilateral vestibular dysfunction 1). It is also useful for assessing equilibrium even at the chronic stage after acute unilateral vestibular dysfunction 2). An analysis of the frequency-domain characteristics of postural instability by performing a power spectral analysis of the COP during foam posturography is useful for characterize the movement of COP observed in patients with peripheral dysfunction and those with psychogenic dizziness and aged people.

As a clinical research using the foam posturography, I am going to introduce our recent research about noisy galvanic vestibular stimulation (GVS). GVS has been traditionally used to estimate retrolabyrinthine vestibular function. Recently, small intensity of noisy GVS has been shown to improve motor function in patients with spinocerebellar degeneration and autonomic function in Parkinson's disease. The mechanism underlying this effect is considered to be stochastic resonance, which is a phenomenon wherein the response of a nonlinear system to a weak periodic signal is optimized by a presence of a particular, non-zero level of noise. We examined the effect of noisy GVS on postural stability in patients with bilateral vestibulopathy and healthy subjects, and showed that noisy GVS with appropriate intensity could significantly improve postural stability in both of the groups 3). Noisy GVS was also effective for improving the stability in walking. I am also going to present our new results about the effects of noisy GVS with long duration on postural stability.

#### References

- 1) Fujimoto et al. Clin Neurophysiol 2009
- 2) Fujimoto et al. Otol Neurotol 2012
- 3) Iwasaki et al. Neurology 2014

**Luncheon Seminar 3**

LS3

**Therapeutic strategy with cetuximab for head and neck cancer**

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Cetuximab, an antagonist of EGFR, was approved for head and neck cancer in late 2012 in Japan, and have made some changes in the therapeutic strategy.

Chemoradiotherapy with tri-week cisplatin (CRT) is now the standard treatment for head and neck squamous cell carcinoma, but the long-term adverse effects have become a problem caused by high toxicity of high dose cisplatin, which can make the quality of survivor (QOS) poor. Radiotherapy with cetuximab (ERT) is expected to cause better QOS because of the lower toxicity as compared to CRT. The issue is that it has not been clarified if BRT has similar effects with CRT, because Bonner trial only indicated superiority of BRT to RT alone. In many institutes in Japan, BRT has been applied to the cases that cannot tolerate CRT because of elderly, kidney dysfunction, etc. This is also the case with our experience, and the preliminary results show similar therapeutic effects of BRT to CRT, but more severe mucositis was observed in BRT which led to prolonged swallowing problems. It is warranted to clarify the therapeutic and adverse effects of BRT as compared to CRT in similar patient population.

Induction chemotherapy (ICT) is a tool for organ preservation by down-staging locally advanced cancers which can lead to less-invasive treatment. TPF is the standard ICT regimen, however, the toxicity is so high that CRT is difficult to complete after ICT. TREMPIN trial indicated better completion rate of BRT following ICT with same therapeutic effects to CRT. BRT is now recommended as the 1st line treatment after ICT by NCCN guideline, and our experience has also shown that BRT after ICT has better completion rate and initial anti-tumor effects. TPE, a new ICT regimen consisting of taxan, platinum, and cetuximab, is now under clinical trial in Europe, and is expected to be less toxic as compared to TPF. We also have some preliminary results of TPE as ICT for locally advanced cancer.

Cetuximab has been proven to be useful for the treatment of recurrent and metastatic cancers. EXTREME trial indicated that FPE (platinum, 5FU, cetuximab) was better than FP only in response rates and overall survival for recurrent and metastatic cancers, which has made FPE as the 1st line regimen. PE, paclitaxel + cetuximab, is another promising regimen for cases that cannot tolerate FPE, which allows outpatient treatment with less toxicity.

## Luncheon Seminar 4

### Advances of Surgical Procedure in Otology and Neurotology

#### LS4-1

### Tips and Tricks in Transcanal Endoscopic Ear Surgery

Yu Matsumoto

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In recent years, Transcanal Endoscopic Ear Surgery (TEES) has received much attention as less invasive alternative to standard microscopic ear surgery (MES). Although TEES and MES share most of the instruments, the way in which they are used is quite different. We present our basic surgical techniques such as tympanomeatal flap elevation, incudostapedial joint disarticulation, incus removal, and type IIIi-M tympanoplasty. We also introduce our newly developed bone curette handle that enforces torque. More use of bone curette would avoid the use of microdrills, and eventually account for less bone dust and better visualization.

#### LS4-2

### Endolymphatic Sac Surgery: Endolymphatic Sac Exposed Adequately at Rugose Portion and Opened for the Drug Delivery

Tadashi Kitahara

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Patients with intractable Meniere's disease were divided into 3 groups. Group I (G-I: n=100) consisted of patients who took endolymphatic sac drainage and steroid-instillation surgery that involved the application of a mass of prednisolone followed by absorbable gelatin sponges soaked in a high concentration of dexamethasone into the sac lumen as endolymphatic sac expanding surgery. Group II (G-II: n=47) consisted of patients who took endolymphatic sac expanding surgery for opening the sac adequately. Group III (G-III: n=50) consisted of patients who declined surgery. According to the established criteria in AAO-HNS 1995, seven-year-results showed that definitive spells were completely controlled in 78.8% in G-I, 79.2% in G-II and 25.0% in G-III. Hearing was improved in 36.5% in G-I, 8.3% in G-II and 0.0% in G-III.

LS4-3

## Recent Strategies in the Management of Traumatic Facial Nerve Paralysis

Naohito Hato

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In total, 66 patients with facial nerve paralysis after temporal bone trauma were studied retrospectively. The rate of good recovery in patients undergoing decompression surgery within 2 weeks after trauma reached 92.9%, resulting in a significantly better outcome than later decompression surgery. The ideal time for decompression surgery for the traumatic facial nerve paralysis was the first 2 weeks in patients with severe, immediate-onset paralysis. Recently, we modified the later decompression surgery using bFGF in a gelatin hydrogel to promote the regeneration of denervated nerves. The efficacy of the novel decompression surgery will be presented.

**Evening Seminar 2****ES2****Pathophysiology of Meniere's disease: Does endolymphatic hydrops cause Meniere's attack?**

Akinobu Kakigi

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Yamakawa first reported endolymphatic hydrops (EH) in a patient with Meniere's disease (MD) in 1938. In the same year, Hallpike and Cairns also reported the association between MD and EH, and established the modern diagnosis of MD. This association is now widely accepted; however, doubts have recently been raised. A recent human temporal bone study review could not conclude whether the association is an epiphenomenon or EH causes MD.

The mechanism of EH development still remains an enigma. There is a large amount of evidence that water homeostasis in the inner ear is regulated partly via the vasopressin-aquaporin2 (VP-AQP2) system, suggesting that EH reflects the malregulation of the VP-AQP2 system in inner ear fluid. Moreover, the unfavorable development of the endolymphatic sac (ES) and duct and ES fibrosis have been reported in the temporal bones of MD patients. Based on these results, we hypothesized that a combination of ES dysfunction and the dysregulation of endolymph might induce Meniere's attacks.

Clinically, it is well-known that Meniere's attacks are related to stress. Moreover, the plasma level of VP, a stress hormone, increases in patients with MD. We recently developed an animal model which is considered to be better suited for studying MD, because this model consists of a combination of ES dysfunction and the dysregulation of endolymph. In contrast to previous animal models that very rarely showed episodes of imbalance, spontaneous nystagmus, or vertiginous attacks, even though they are distinct in EH, they are clearly evident in our model. Moreover, our model shows hearing impairment.

Furthermore, we experimentally investigated the mechanisms underlying the formation of EH and its clinical pictures. We revealed that there is no difference in the hydrostatic pressures recorded in the perilymph and endolymph despite the presence of significant hydrops. Moreover, the increase of the hydrostatic pressure in the inner ear did not induce nystagmus. Conversely, EH increased perilymphatic K which contributed to the vertigo and/or hearing loss.

In this paper, clinical observations and experimental evidence suggesting that EH causes MD in addition to stress will be presented mainly based on our recent studies.

## Sponsored Lecture

SpL

**Registration strategy for image-guided temporal bone surgery using commercially available navigation system**

Nozomu Matsumoto

*Department of Otorhinolaryngology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

Image-guided surgery (IGS) has become a helpful tool for surgeons to accomplish surgical objectives with improved accuracy and safety, particularly in the surgical fields of paranasal sinus and skull base. However, IGS in temporal bone surgery is less popular although this region shares the same property with paranasal sinus and skull base, that the surgical field is concealed in the bone and that the small and undetected error in orientation may lead to serious surgical complications. IGS in temporal bones requires two competing factors. First, temporal bone surgery only allows noninvasive registration methods because surgery in middle ear or shallow region in lateral skull base is relatively noninvasive in nature. Second, small anatomical structures in middle and inner ear require submillimetric accuracy of the IGS. The difficulty in developing a system for image-guided temporal bone surgery lies in balancing the noninvasiveness and accuracy. There are a few custom-made navigation systems, including ours, which fulfill both factors to be used in temporal bone surgery. However, technologies and techniques used in these systems are applicable only in limited devices and not for commercially available navigation systems. Thus, we started a research project to bring the lessons we have learned during developing our IGS for temporal bone surgery to a broadly available system.

In this lecture, the presenter will show the recommended procedures to prepare image-guided temporal bone surgery using commercially available electromagnetically-tracked surgical navigation system. In IGS of temporal bone, a reference frame to compensate patient's movement is mandatory. We describe a reference frame that can be secured in a noninvasive manner. Next, although the currently popular noninvasive surface-matching registration is always less accurate compared to more invasive registration methods, there is a way to improve the accuracy by bringing the registration centroid to the operating area. Third, a CT dataset of the temporal bone often includes a set of low-resolution data of the whole head and a pair of high-resolution data of magnified temporal bones of both sides. The registration must be performed using the CT dataset of the whole head, but then can be replaced by a high-resolution dataset so that the intraoperative view in the navigation screen can be improved. The theoretical background with some experimental data as well as our clinical procedures will be demonstrated.