

## Program at a Glance

## April 7 (Thu.) AM

	Track 1	
8:00	8:00-8:05      Opening Remarks	
	8:05-8:35      Keynote Lecture 1	
	Chairperson: Hideyuki Kawauchi (Emeritus Professor, Shimane University, Japan)	
	KY1-1    Limitations in Managing Obstructive Sleep Apnea	
	Sung Wan Kim (Kyung Hee University, Korea)	
8:30		
	8:40-10:10      Symposium 1	
	Recent advances in OSA	
	Chairpersons: Masaaki Suzuki (Teikyo University Chiba Medical Center, Japan)	
	Sung Wan Kim (Kyung Hee University, Korea)	
9:00	SY1-1	What is the next CPAP? -pharmacology therapy in sleep apnea-
		Yoichi Nishimura (Sleep Disorders Center, Johns Hopkins University, USA)
	SY1-2	Surgical outcomes in Korea
		Ji Ho Choi
		(Department of Otorhinolaryngology-Head and Neck Surgery, Soonchunhyang University College of Medicine, Bucheon Hospital, Korea)
9:30	SY1-3	History of sleep medicine in Japanese insurance system and introduction of HNS
		Shintaro Chiba (Sleep Medicine/ ENT, Ota Memorial Sleep Center, Japan)
	SY1-4	Robotic surgery in OSA
		Hyung-Ju Cho (Otorhinolaryngology, Yonsei University, Korea)
10:00		
	10:20-11:50      Symposium 3	
	Recent advances in medical devices on vestibular science	
10:30	Chairpersons: Noriaki Takeda (University of Tokushima, Japan)	
	Kyu-Sung Kim (Inha University Hospital, Korea)	
	SY3-1	MR imaging of endolymphatic hydrops in Meniere's Disease
		Munehisa Fukushima (Kansai Rosai Hospital, Japan)
	SY3-2	Non-invasive middle ear pressure treatment for intractable Meniere's disease
		Hideo Shojaku (Department of Otolaryngology, University of Toyama, Japan)
11:00	SY3-3	Sensory substitution therapy as a final selection for graded rehabilitation of vestibular system
		Toshiaki Yamanaka (Otolaryngology-Head and Neck Surgery, Nara Medical University, Japan)
	SY3-4	IT-based medical device for the balance disorder
		Jae-Jun Song (Department of Otolaryngology-Head and Neck Surgery, Korea University Guro Hospital, Korea)
	SY3-5	Application of TMS & DCS for dizzy patients
		Ho Yun Lee (ORL-HNS, Ewha Womans University, Korea)
11:30	SY3-6	Clinical implication of VR and AI for patients with vertigo
		Sungkwang Hong (Department of Otorhinolaryngology-Head and Neck Surgery, Hallym University College of Medicine, Korea)
12:00		
	12:00-12:50      Luncheon Seminar 1	
	Chairperson: Shigeru Hirano (Kyoto Prefectural University of Medicine, Japan)	
	LS1-1    Paradigm shift in treatment strategy for head and neck cancer: What is changing, and what is the same?	
	Tomoya Yokota (Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Japan)	
12:30		
	Sponsor: Bristol-Myers Squibb K.K./ONO PHARMACEUTICAL CO., LTD.	
13:00		

Track 2	
8:00	
8:30	
9:00	<div>8:40-10:10     <b>Symposium 2</b> <b>Problems of Dysphagia</b> <b>Chairpersons:</b> <b>Yukio Katori</b> <i>(Department of Otolaryngology and Head and Neck Surgery, Tohoku University Graduate School of Medicine, Japan)</i>                   <b>Young Hak Park</b> <i>(Department of Otolaryngology-HNS, Yeouido St. Mary's Hospital, The Catholic University of Korea, Korea)</i> <b>SY2-1     Swallowing computed tomography and virtual reality</b>                   Rumi Ueha <i>(Swallowing Center, Otolaryngology and Head and Neck Surgery, the University of Tokyo, Japan)</i> <b>SY2-2     Preventive intervention for age-related dysphagia in an increasingly aging society</b>                   Kaori Nishikubo Tanaka <i>(Otorhinolaryngology,Head and Neck Surgery, School of Medicine,Ehime University, Japan)</i> <b>SY2-3     Management of cricopharyngeal dysphagia</b>                   Young Hak Park <i>(Department of Otolaryngology-HNS, Yeouido St. Mary's Hospital, The Catholic University of Korea, Korea)</i></div>
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## Program at a Glance

## April 7 (Thu.) PM

	Track 1	
13:00	<b>12:55-13:55 Keynote Lecture 2</b> <b>Chairperson: Sungwon Chae</b> (Department of Otorhinolaryngology Head & Neck Surgery Korea University School of Medicine, Guro Hospital, Korea) <b>KY2-1 Heads-up Surgery, Paradigm Shift in Ear Surgery</b> Seiji Kakehata (ENT, Yamagata University Faculty of Medicine, Japan)	
13:30	<div style="text-align: right;">領</div> <div style="text-align: right;">※ Credit approved session(For Japanese only)</div>	
14:00		
14:30	<b>14:25-14:55 Keynote Lecture 3</b> <b>Chairperson: Ryuichi Hayashi</b> (Department of Head and Neck Surgery, National Cancer Center Hospital East, Japan) <b>KY3-1 Era of Advanced TORS Using Single Port Surgical Robotic System</b> Se-Heon Kim (Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea)	
15:00	<b>15:00-15:50 Afternoon Seminar</b> <b>Chairperson: Tetsuya Terada</b> (Department of Otolaryngology-Head and Neck Surgery, Osaka Medical and Pharmaceutical University, Japan) <b>AS-1 A New Era in the Treatment of the Olfactory Disorder with Infection and Allergic Rhinitis</b> Eri Mori (Department of Otorhinolaryngology, The Jikei University School of Medicine, Tokyo, Japan)	
15:30	<div style="text-align: right;">Sponsor: TAIHO PHARMACEUTICAL CO., LTD.</div>	
16:00	<b>16:05-17:35 Symposium 4</b> <b>Recent topics of diagnosis and treatment of olfactory dysfunctions</b> <b>Chairpersons: Takaki Miwa</b> (Kanazawa Medical University, Japan) <b>Chang-Hoon Kim</b> (Yonsei University College of Medicine, Seoul, Korea)	
16:30	<b>SY4-1 Does olfactory mucosa regenerate after resection?</b> Eri Mori (Department of Otorhinolaryngology Head and Neck Surgery, The Jikei University School of Medicine, Japan)	
	<b>SY4-2 The value of olfactory scintigraphy to determine the connectivity of olfactory sensory neurons in patients with olfactory dysfunction</b> Hideaki Shiga (Otorhinolaryngology, Kanazawa Medical University, Japan)	
	<b>SY4-3 The YSK olfactory function (YOF) test: Development of a new Korean olfactory test</b> Chang-Hoon Kim (Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea)	
17:00	<b>SY4-4 The feasibility of clinical applications for olfactory testing using fMRI</b> Jin Kook Kim (Otorhinolaryngology-Head & Neck Surgery, Konkuk University Hospital , Konkuk Univeristy School of Medicine, Korea)	
17:30		
18:00		

Track 2	
13:00	
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16:00	<div>16:05-17:35 Symposium 5</div> <div>Recent Topics for Head and Neck Tumors</div> <div>Chairpersons: Ken-ichi Nibu</div> <div>(Department of Otolaryngology-Head and Neck Surgery, Kobe University Graduate School of Medicine, Japan)</div> <div>Yong Bae Ji</div> <div>(Department of Otolaryngology-Head and Neck Surgery, College of Medicine, Hanyang University, Seoul, Korea)</div> <div><div>SY5-1</div><div>Molecular characterization of circulating tumor cells in head and neck squamous cell carcinoma and its clinical application</div><div>Kazuaki Chikamatsu (Otolaryngology-Head and Neck Surgery, Gunma University Graduate School of Medicine, Japan)</div></div> <div><div>SY5-2</div><div>New developments and future directions in systemic therapy for salivary duct carcinoma</div><div>Yuichiro Tada (Department of Head and Neck Oncology and Surgery, International University of Health and Welfare, Mita Hospital, Japan)</div></div> <div><div>SY5-3</div><div>Prognostic factors in surgically treated HPV positive tonsillar cancer</div><div>Young Hoon Joo (Department of Otolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, Korea)</div></div> <div><div>SY5-4</div><div>Inhibition of integrin <math>\beta</math>1 induces radiosensitization and attenuates perineural invasion in oral squamous cell caricnoma</div><div>Sung Joon Park (Department of Otorhinolaryngology-Head and Neck Surgery, Chung-Ang University, College of Medicine, Korea)</div></div> <div><div>SY5-5</div><div>Gender differences in the prevalence of head and neck cancers</div><div>Jun-Ook Park (Department of Otolaryngology-Head and Neck Surgery, The Catholic University of Korea, College of Medicine, Korea)</div></div>
16:30	
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18:00	



Program at a Glance

April 8 (Fri.) PM

	Track 1
13:00	
13:30	<div><div>13:25-14:25</div><div>Keynote Lecture 5</div><div>Chairperson: Eun Chang Choi (Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea)</div><div>KY5-1 Regenerative Medicine for Airway Organs</div><div>Koichi Omori (Department of Otolaryngology Head and Neck Surgery, Kyoto University, Japan)</div></div>
14:00	
14:30	<div><div>14:30-15:20</div><div>Cafe Seminar</div><div>Chairperson: Atsushi Matsubara (Hirosaki University Hospital, Japan)</div><div>CS-1 New endotyping of chronic rhinosinusitis with nasal polyps</div><div>Takechiyo Yamada (Otorhinolaryngology, Head and Neck surgery, Akita University, Japan)</div></div>
15:00	
15:30	<div><div>15:25-16:55</div><div>Symposium 9</div><div>Robotic Head and Neck Surgery</div><div>Chairpersons: Ichiro Tateya (Fujita Health University, Japan)</div><div>Se-Heon Kim (Yonsei University College of Medicine, Korea)</div><div>SY9-1 Current situation and evidence of TORS in Japan</div><div>Akira Shimizu (Department of Otorhinolaryngology, Head and Neck Surgery, Tokyo Medical University, Tokyo, Japan)</div><div>SY9-2 Robotic Head and Neck Surgery at Fujita Health University Hospital</div><div>Hisayuki Kato (Department of Otolaryngology, Fujita Health University School of Medicine, Japan)</div><div>SY9-3 Advance in Robotic Neck Surgery</div><div>Kyung Tae (Department of Otolaryngology-Head and Neck Surgery, Hanyang University, Korea)</div><div>SY9-4 Advance in Robotic Thyroidectomy</div><div>Seung-Kuk Baek (Otorhinolaryngology-Head and Neck Surgery, Korea University Medicine, Korea)</div><div>SY9-5 Robotic Neck Dissection</div><div>Yoon Woo Koh (Department of Otorhinolaryngology / Yonsei Head Neck Cancer Center Yonsei University, College of Medicine, Korea)</div></div>
16:00	
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17:00	<div><div>16:55-17:00</div><div>Closing Remarks</div></div>
17:30	
18:00	

	Track 2
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15:30	<div><div>15:25-16:55</div><div>Symposium 10</div><div>State-of-the-art Pediatric ORL</div><div>Chairpersons: Yukiko Iino (Tokyo Kita Medical Center, Japan)</div><div>Yoo-Sam Chung (Ulsan University, Asan Medical Center, Korea)</div><div>SY10-1 How to cope with pediatric patients with dizziness</div><div>Fumiyuki Goto (Tokai University, Japan)</div><div>SY10-2 Tinnitus in pediatric population: an update</div><div>Jae-Jin Song (Seoul National University Bundang Hospital, Korea)</div><div>SY10-3 Present issue in pediatric allergic rhinitis: How does it develop in early life?</div><div>Sawako Masuda (Department of Otorhinolaryngology, National Hospital Organization Mie National Hospital, Japan)</div><div>SY10-4 Association of adenotonsillectomy with asthma and upper respiratory infection in children: A Nationwide Cohort Study</div><div>Dong-Kyu Kim (Hallym University, Korea)</div><div>SY10-5 Management of obstructive post-tracheostomy granulation tissue in children</div><div>Takaharu Nito (Saitama Medical University, Japan)</div><div>SY10-6 High flow assisted spontaneous ventilation for pediatric airway surgery</div><div>Seong Keun Kwon (Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Korea)</div></div>
16:00	
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17:30	
18:00	



## Poster(Free Papers)

### FP1 Head & Neck (Clinical)

- FP1-1** **Clinical significance of visiting ENT department when cervical lymphadenopathy is recognized in terms of early detection of HNC**  
Kohei Matsumoto (National Hospital Organization Nagasaki Medical Center, Japan)
- FP1-2** **A new staging system for olfactory neuroblastoma**  
Akira Nakazono (Otolaryngology-Head and Neck Surgery, Hokkaido University, Japan)
- FP1-3** **Clinical characteristics of acinic cell carcinoma and secretory carcinoma of the parotid gland**  
Yusuke Ayani (Department of Otorhinolaryngology-Head & Neck Surgery, Osaka Medical and Pharmaceutical University, Japan)
- FP1-4** **Short-term outcome of 69 external auditory canal cancer treated at a single institution**  
Takeshi Tsutsumi (Otorhinolaryngology, Tokyo Medical and Dental University, Japan)
- FP1-5** **Withdrawn**
- FP1-6** **Withdrawn**
- FP1-7** **Surgical strategy for squamous cell carcinoma of the external auditory canal: management of locally advanced cases**  
Naoki Nishio (Otorhinolaryngology, Nagoya University, Japan)
- FP1-8** **Clinical outcomes of Nivolumab and its prognostic factors related to tumor immunity in head and neck malignancies**  
Eiji Kobayashi (Otolaryngology, Head and Neck Surgery, Kanazawa University / Toyama Prefectural Central Hospital, Japan)
- FP1-9** **Protective effects of sodium thiosulfate for Cisplatin -mediated ototoxicity in patients with head and neck cancer**  
Hisashi Sugimoto (Kanazawa University, Japan)
- FP1-10** **Three Cases of Non-Occlusive Mesenteric Ischemia Developed after Head and Neck Cancer Therapy**  
Kotoko Ito (Kagoshima University, Japan)
- FP1-11** **A case report of laryngeal cancer with dermatomyositis**  
Chieko Yokota (Otolaryngology, Osaka City University, Japan)
- FP1-12** **A case of chylothorax after modified radical neck dissection**  
Yuki Yamamoto (Osaka City University, Japan)
- FP1-13** **An experience of salvage surgery after boron neutron capture therapy: a case report**  
Masaaki Higashino (Otorhinolaryngology, Head and Neck Surgery, Osaka Medical and Pharmaceutical University, Japan)

## Poster(Free Papers)

### FP2 Head & Neck (Research)

**FP2-1** Withdrawn

**FP2-2** Relationship between APOBEC3 expression and viral genome hypermutation and integration in HPV-related oropharyngeal cancers

Satoru Kondo (Division of Otolaryngology, Head and Neck Surgery, Graduate School of Medical Science, Kanazawa University, Japan)

**FP2-3** Examination of HPV-related oropharyngeal carcinoma and REV7 expression

Kaho Momiyama (Otorhinolaryngology-HNS, Kitasato University School of Medicine, Japan)

**FP2-4** The p16 Overexpression and Rb Loss Correlate with Transcriptionally Active High-risk HPV Infection in Oropharyngeal Squamous Cell Carcinoma

Rina Jiromaru (Otorhinolaryngology, Kyusyu University, Japan)

### FP3 Laryngology (Clinical)

**FP3-1** Withdrawn

**FP3-2** A case of pemphigoid laryngeal lesions in association with DPP-4 inhibitor use

Sachimi Okamoto (PL Hospital, Japan)

**FP3-3** A Study of Pediatric Cases of Tracheostomy and Laryngotracheal Separation

Sakurako Takano (Osaka City University Graduate School of Medicine, Japan)

**FP3-4** Developmental functional morphology of the preepiglottic space in the human larynx

Kiminori Sato (Department of Otolaryngology-Head and Neck Surgery, Kurume University School of Medicine, Japan)

### FP4 Otology (Clinical 1)

**FP4-1** THE ETIOLOGIES AND DIAGNOSTIC APPROACHES FOR PULSATILE TINNITUS IN A LARGE CASE SERIES

Yoonjoong Kim (Department of Otorhinolaryngology, Chungnam National University Hospital, Korea)

**FP4-2** A Long-Term Surgical Outcome Analysis In Subjects With Pulsatile Tinnitus Originating From The Sigmoid Sinus

Sang-Yeon Lee (Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Bundang Hospital, Seongnam, Korea)

**FP4-3** Development of real-time video-oculography using high quality infrared video Frenzel

Makoto Hashimoto (Department of Otolaryngology, Yamaguchi University Graduate School of Medicine, Japan)

**FP4-4** Withdrawn

## Poster(Free Papers)

- FP4-5** **A case of vestibular migraine/delayed endolymphatic hydrops overlapping syndrome**  
Takaki Inui (Department of Otorhinolaryngology - Head and Neck Surgery, Osaka Medical and Pharmaceutical University, Japan)
- FP4-6** **Persistent postural-perceptual dizziness (PPPD) secondary to BPPV: a case report**  
Koji Otsuka (Otolaryngology, Tokyo Medical University, Japan)
- FP4-7** **Detection of oval window lesion in otosclerosis by ultra-high resolution computed tomography**  
Shunsuke Kondo (Otolaryngology, Head and Neck, University of the Ryukyus, Japan)
- FP4-8** **Study on the relationship of hearing loss and cognitive function: a retrospective study using health screening data**  
Jong Woo W. Chung (Otorhinolaryngology-Head and Neck Surgery, Asan Medical Center University of Ulsan College of Medicine, Korea)
- FP4-9** **Does hearing loss increase postural instability in elderly? Population based study**  
Sungwon Chae (Otorhinolaryngology Head & Neck Surgery, Korea University, College of Medicine, Korea)
- FP4-10** **Withdrawn**
- FP4-11** **Efficacy of the additional effect of HBO in combination of steroid and prostaglandin E1 for idiopathic sudden sensorineural hearing loss**  
Satoshi Hara (Otolaryngology, Juntendo University, Japan)
- FP4-12** **Withdrawn**
- FP4-13** **Test-retest reliability of sound field (SF) audiometry test results between SF system for small audiometric booths and traditional SF system**  
Hyong-Ho Cho (Otorhinolaryngology-Head & Neck Surgery, Chonnam National University, Korea)
- FP4-14** **Development of Sound Field Audiometry System for Small Audiometric Booths and Comparison of Its Equivalence With Traditional System**  
Hyong-Ho Cho (Otorhinolaryngology, Chonnam National University Hospital, Korea)
- FP4-15** **How to manage the Cochlear Dysplasia that causes meningitis**  
Shinichi Kanemaru (Otolaryngology and HNS, Medical Research Institute, Kitano Hospital / Translational Research Informatics Center, The Foundation for Biomedical Research and Innovation, Kobe / Graduate School of Medicine, Kyoto University, Japan)
- FP4-16** **Cochlear Implant and Additional Hearing Aid in the Same Ear: Preliminary Data**  
Oh Seung-Ha (Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Seongnam, Korea)
- FP4-17** **Cochlear duct length determination and prediction of insertion depth angles for CI electrodes using preoperative temporal bone CT**  
Dong-Han Lee (Department of Otorhinolaryngology & Head and Neck Surgery, Seoul National University Hospital, Korea)
- FP4-18** **Change of Vestibular Symptoms and Functions after Cochlear Implant; Its Relevant Factor and Correlation with Residual Hearing**  
Jeong Hun Jang (Ajou University School of Medicine, Korea)

## Poster(Free Papers)

### FP5 Otology (Clinical 2)

**FP5-1** Withdrawn

**FP5-2** Safe Open Cavity Reconstruction Using a Sliced-Cartilage Graft for Poorly Aerated Ears with Cholesteatoma

Masahiro Komori (Otolaryngology, Kochi University, Kochi Medical School, Japan)

**FP5-3** Comparative analysis of butterfly cartilage tympanoplasty versus conventional methods

Masayuki Okamoto (Otorhinolaryngology-Head and Neck Surgery, University of Fukui, Japan)

**FP5-4** Withdrawn

**FP5-5** Reconstruction of the external auditory canal using full-thickness rolled-up skin graft after lateral temporal bone resection

Takeshi Fujita (Otolaryngology-Head and Neck Surgery, Kobe University Graduate School of Medicine, Japan)

**FP5-6** Prediction of appropriate prosthesis length by preoperative CT in TEES for stapes surgery

Yasuyuki Kajimoto (Otolaryngology, Head & Neck Surgery, Osaka City University Graduate School of Medicine, Japan)

**FP5-7** Development of the Near-future type Tympanoplasty by Regeneration of the Tympanic Membrane using Endoscopic Ear Surgery

Shinichi Kanemaru (Otolaryngology and HNS, Medical Research Institute, Kitano Hospital, Japan)

**FP5-8** Multi-layered connective tissue underlay myringoplasty technique with high success rate

Masato Nakashima (Otolaryngology, Saitama Medical University Hospital, Japan)

**FP5-9** Nasopharyngeal pneumococcal carriage as a risk factor for otitis media with effusion

Chisei Satoh (Nagasaki University Hospital, Japan)

**FP5-10** Otitis media with effusion caused by a parapharyngeal tumor

Atsunobu Tsunoda (Otolaryngology, Head & Neck Surgery, Juntendo University, Nerima Hospital, Japan)

**FP5-11** A case of otitis media cholesteatomatosa in a young patient with significant inner ear destruction

Masahiro Oishi (Otolaryngology and Head and Neck Surgery, Osaka City University, Japan)

**FP5-12** Examination of otogenic intracranial complications due to middle ear cholesteatoma in our department

Yuki Koda (Osaka City University, Japan)

**FP5-13** Withdrawn

**FP5-14** Cavernous Hemangioma of the External Auditory Canal in Patients Older than 60 Years: A Rare Tumor

Junhui Jeong (Otorhinolaryngology, National Health Insurance Service Ilsan Hospital, Korea)

## Poster(Free Papers)

### FP6 Otology (Research)

- FP6-1** Eustachian tube function test in two head positions  
Shigeto Ohta (Department of Otolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Japan)
- FP6-2** Trials to establish our rat behavioral model of tinnitus using salicylate  
Koichi Kitano (Department of Otolaryngology-Head and Neck Surgery, Nara Medical University, Japan)
- FP6-3** An Explanatory Model of Tinnitus  
Kazuhiro Noda (Noda Otolaryngology clinic, Japan)
- FP6-4** Transcriptome analysis for deafness: neuroplastic change in the auditory cortex  
Min-Hyun Park (Otorhinolaryngology, Boramae Medical Center Seoul National University Seoul Metropolitan Government, Korea)
- FP6-5** Central Processing of Speech Sounds and Non-Speech Sounds with Similar Spectral Distribution: an Auditory Evoked Potential Study  
Shinsuke Kaneshiro (Department of Otorhinolaryngology - Head and Neck Surgery, Iwate Medical University, Japan)
- FP6-6** Withdrawn
- FP6-7** An examination on abnormally thickened subepithelial extracellular deposit of vestibular end organ in 3 human cases  
Tadao Okayasu (Otolaryngology-Head and Neck Surgery, Nara Medical University, Japan)
- FP6-8** Rat Model of Meniere's Attack: Direction-changing Nystagmus and Reversible Hearing Impairment Induced by Intratympanic KCl Injection  
Takefumi Kamakura (Department of Otorhinolaryngology-Head and Neck Surgery, Osaka University Graduate School of Medicine, Japan)
- FP6-9** Withdrawn
- FP6-10** Gene Therapy and Drug Screening for GJB2 Related Hearing Loss with iPS cells  
Kazusaku Kamiya (Juntendo University Faculty of Medicine, Japan)
- FP6-11** Expression of advanced glycation end-product in the cultured utricles  
Kazuma Sugahara (Department of Otolaryngology, Yamaguchi University Graduate School of Medicine, Japan)
- FP6-12** Preoperative assessment of chorda tympani nerve (CTN) function in patients with middle ear disease  
Tomomi Nin (Otolaryngology Head and neck surgery, Hyogo College of Medicine, Japan)



## Poster(Free Papers)

### FP7 Rhinology (Clinical)

- FP7-1** Usefulness of postoperative endoscopic score for recurrent eosinophilic chronic rhinosinusitis

Takahiro Saito (*Hyogo College of Medicine, Japan*)

- FP7-2** A case of pollen-food allergy syndrome treated with omalizumab for intractable lip edema

Daiki Sakamoto (*Kansai Medical University, Japan*)

### FP8 Rhinology (Research)

- FP8-1** Copy Number Variation in DRC1 is the Major Cause of Primary Ciliary Dyskinesia in the Japanese Population

Kazuhiko Takeuchi (*Mie University, Japan*)

- FP8-2** A novel scoring system of surgical findings at the sinus in patients with chronic rhinosinusitis

Ken Okazaki (*Otolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Japan*)

- FP8-3** Asian Sand Dust Regulates IL-32 Production in Airway Epithelial Cells: Inhibitory Effect of Glucocorticoids

Heung-Man Lee (*Otorhinolaryngology-Head and Neck Surgery, Korea University College of Medicine, Korea*)

- FP8-4** Serum IgG4 as a biomarker reflecting pathophysiology and post-operative recurrence in chronic rhinosinusitis

Mitsuhiro Okano (*Otorhinolaryngology, International University of Health and Welfare / Okayama University, Japan*)

- FP8-5** Efficacy of endoscopic sinus surgery for eosinophilic chronic rhinosinusitis with bronchial asthma

Nobuo Ohta (*Otolaryngology, Tohoku Medical and Pharmaceutical University, Japan*)

- FP8-6** The importance of adipokines in the pathogenesis of eosinophilic chronic rhinosinusitis

Yoshimasa Imoto (*Department of Otorhinolaryngology Head & Neck Surgery, Faculty of Medical Sciences, University of Fukui, Japan*)

- FP8-7** Anti-inflammatory effects of epoxygenated eicosapentaenoic acid metabolite on IL-33-induced innate eosinophilic inflammation in upper airway

Ichiro Tojima (*Shiga University of Medical Science, Japan*)

- FP8-8** Development of an intranasal phototherapy device for allergic rhinitis using LEDs emitting narrowband-UVB

Seiichiro Kamimura (*Otorhinolaryngology, Head-Neck Surgery, Tokushima University, Japan*)

- FP8-9** The association between the human microbiome in the nasal cavity and the number of sensitization in allergic rhinitis

Keisuke Koyama (*Division of Otorhinolaryngology and Head & Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Science, University of Fukui, Japan*)

## Keynote Lecture 1

# Limitations in Managing Obstructive Sleep Apnea

**Sung Wan Kim**

*(Kyung Hee University, Korea)*

Management of OSA patients is still going round in circles other than positive airway pressure (PAP) ventilation therapy because of heterogeneity of the patients' phenotype even though evaluation of sleep apnea patients is looked well-designated and world-widely accepted.

Polysomnography is used for the evaluation of the severity of the patients. Apnea-hypopnea index (AHI) and oxygen parameters have been used as the marker for severity. However, the definition of disease focused on AHI. OSA had been diagnosed by event number of apnea and adapted hypopnea with very little evidence. And the number of events had been changed to index of events. Then, the time factor had been included in the diagnosis. Even the definition of hypopnea has been changed several times. There were very small numbers of evidence used for these changes. We may need more precise indicators for the severity of OSA. Furthermore, OSA is multifactorial disease. Respiratory event is one of the outcome of these multifactorial causes.

For the evaluation of obstruction site, cephalometry, endoscopy, CT, and MRI in an awake state. Then, drug-induced sedation has been introduced for the evaluation of the obstruction site. Fluoroscopy, CT, MRI, and upper airway endoscopy have been used in the drug-induced sleep state. Many studies have been published based on these evaluations. However, drug-induced sleep has limitations such as mimicking sleep and snapshot study. Wrong evaluation should make the wrong decision. That is why positive airway pressure therapy is always better than other anatomy-modifying treatments such as surgery, oral appliance.

Treatment of OSA has advanced in each field. PAP therapy developed from CPAP to BiPAP, pressure reduction mode, Auto PAP, iVAPS, servo-ventilation. All these tools have a limitation of compliance and unavoidable continuous lifelong application without improvement. The oral appliance has been changed from a mono-bloc to a two-piece type, monitoring device. Surgical management also developed from palatal surgery to multilevel surgery, airway reconstruction, and electrical stimulation. However, oral appliance and surgical management showed limitation of partial improvement, lower success rate, and long-term relapse.

## Keynote Lecture 2

# Heads-up Surgery, Paradigm Shift in Ear Surgery

**Seiji Kakehata**

*(ENT, Yamagata University Faculty of Medicine, Japan)*

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2021 can truly be called a special year for the field of ear surgery for a number of reasons. The year 2021 marks the 100th anniversary of the first use of the microscope in any field of surgery. This history-making milestone was achieved by Dr. Nylen, who incorporated the microscope into ear surgery in 1921. In addition, the year 2021 marks the 70th anniversary of introduction of the binocular dissecting microscope. Dr. Wullstein subsequently put it to immediate good use in the development of the groundbreaking tympanoplasty procedure. The year 2021 also marks the 40th anniversary of the work of another pioneer in ear surgery. Dr. Nomura confronted and worked to overcome the limitations of the microscope through the development of a small-diameter endoscope in 1981. This needle otoscope made it finally possible to visualize the hard to reach areas within the ear.

Great strides were subsequently made in microscopic ear surgery (MES) in the next half century. However, in the past and even today ear surgeons must deal with many challenges when performing MES. These challenges include a tiny field of view, an uncomfortable surgical posture, and a cramped environment during an operation. Ear surgeons were finally able to direct their gaze upwards in the 21st century with the introduction of transcanal endoscopic ear surgery or TEES. TEES offers many advantages including less invasiveness, better ergonomics, enhanced surgical precision, and the ability to surgically expose and access unreachable internal ear structures and spaces. On the horizon is the exoscope which can replace the microscope and enables complete heads-up surgery in combination with TEES. Heads-up surgery enables better ergonomics, reduced surgeon fatigue and discomfort, reduced burden on the patient and sharing of enhanced images in real time. Our ultimate goals of ear surgery are aimed higher at a less invasive, safe, and functional surgical procedure which results in a predictable outcome. So today, the goals can now be achieved with heads-up surgery in combination with TEES and ExES. While the endoscope and exoscope changes the viewpoint of the surgeon, it facilitates good visualization and sure and steady manipulation that surpasses what had been achievable prior to TEES and ExES.

## Keynote Lecture 3

# Era of Advanced TORS Using Single Port Surgical Robotic System

**Se-Heon Kim**

*(Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea)*

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**Background.** The purpose of this study was to evaluate the feasibility and safety of the DaVinci SP system for performing transoral robotic surgery (TORS) in head and neck cancer patients.

**Methods.** From October 2018 to Sep 2021, we retrospectively reviewed the medical records of 210 patients who underwent TORS using the DaVinci SP system.

**Results.** During TORS, three robotic arms could be used to perform a geometric resection of the lesion in a narrow working space. The mean total operation time was 70 minutes and the average time required to set up the robotic system was within 10 minutes. All patients successfully underwent TORS. All robotic arms were inserted through a single port, which widened the working space around the patient's head and allowed for the operative assistant to easily approach the patient during operation. The joggle joint of the robotic arms aided in easy manipulation within the confined working space. Joggle joints of the endoscopic arm were controlled through the navigation system, which was very helpful in securing the superior visualization of the surgical site, especially in the area of larynx and hypopharynx.

**Conclusions.** We confirmed that DaVinci SP provided us technical advantages above the Si/Xi systems for performing TORS. Especially, it was helpful to ensure proper visualization of the surgical field and to perform precise surgery when operating the tongue-base or the laryngo-hypopharyngeal lesion.

## Keynote Lecture 4

# Fitting, Verification and Validation of hearing aids in a BUSY otological clinic

**Yang-Sun Cho**

*(Department of Otolaryngology, Sungkyunkwan University, Samsung Medical Center, Korea)*

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Hearing loss is a common problem that impacts quality of life for the patient, family members, and caretakers. Population with a significant hearing loss is increasing due to growing number of older population and new-born hearing screening. Unfortunately, hearing loss is often undiagnosed and untreated to cause a significant disability and subsequent social burden.

For rehabilitation of these patients, hearing aid is one of the primary choices.

There are many ways to program today's hearing aids for any given patient that provides appropriate audibility, optimum intelligibility and good sound quality. However, the fitting must be verified, and we need to validate, in a reliable manner, that benefit and satisfaction are present in the real-world. The Marketrak VIII survey clearly show that as we add various verification and validation component to the fitting protocol, satisfaction increases accordingly, patient loyalty increases, and follow-up visits are reduced.

In our department, we are running the hearing aids clinic for 15 years with an established protocol. This presentation summarizes the procedure of hearing aids fitting for those whom with hearing loss, which can be implemented into a busy otologic practice. Specifically, the presentation will be focused on fitting and verification procedures and finally, validation using popular self-assessment inventories.



## Keynote Lecture 5

# Regenerative Medicine for Airway Organs

**Koichi Omori**

*(Department of Otolaryngology Head and Neck Surgery, Kyoto University, Japan)*

Airway organs are essential to life-sustaining and social life such as respiration, swallowing and speech. In cases of malignancies or inflammatory lesions, airway reconstruction after surgical resection remains a difficult challenge. Conventionally, for large defect areas, reconstruction by cartilage graft using auricular cartilage, nasal septal cartilage, or costal cartilage, with pedicle flap including deltopectoral flap, pectoral major muscular flap or free vascularized cutaneous flap is performed in order to secure the airway frame. Even with such an invasive treatment, tracheal stoma may remain in several patients. Tissue engineering will contribute to regenerative medicine for airway organs.

Based on our concept “in situ tissue engineering” which is designed to mediate the healing and tissue re-growth in the body, we developed an artificial trachea made from non-absorbable polypropylene mesh tube covered by absorbable porous and microcellular collagen sponge as a scaffold. In proof of concept, an artificial trachea implanted into the defect of the cricoid and trachea in beagle dogs demonstrated no airway obstruction with good epithelization.

With an approval from IRB, the artificial trachea was implanted for repair of the airway defect in patients with cancer invasion or laryngotracheal stenosis as a clinical research. Postoperative endoscopy and CT scan showed well epithelized airway lumen.

For practical use in Japan, it is necessary to comply with official regulations such as biological safety test on GLP, safe production and quality control of medical equipment on QMS, and accurate, ethical and efficient clinical trial on GCP. Clinical trial based on GCP was performed. Translational research and regulatory science are essential to establish regenerative medicine for airway organs.

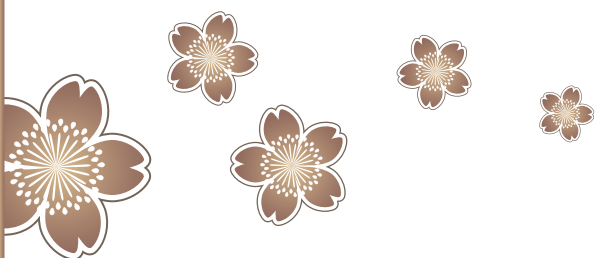
Reverse translational research was also performed for accelerating regeneration of the epithelium and cartilage tissue. Cell sources such as adipose tissue derived stem cells and iPS cells, collagen vitrigel scaffold and regulatory factors were developed and applied. In vitro and in vivo basic studies will contribute to develop new strategy for regeneration of airway organs.



## **Abstract**

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**Symposium, LS(LS1, LS2), CS, AS, Poster(Free Papers)**



## Symposium 1

### Recent advances in OSA

#### SY1-1

#### What is the next CPAP? -pharmacology therapy in sleep apnea-

**Yoichi Nishimura**, Thomaz Fleury Curado,  
Huy Pho, Alan R. Schwartz, Vsevolod Y. Polotsky  
*Sleep Disorders Center, Johns Hopkins University, USA*

The pathogenesis of obstructive sleep apnea (OSA) has been linked to a loss of motor input to the tongue and specifically to the genioglossus muscle during sleep is associated with pharyngeal collapsibility and the development of OSA. There is no effective pharmacology treatment of OSA.

We applied a novel chemogenetic method to improve upper airway patency using chemogenetic approach by deploying designer receptors exclusively activated by designer drug (DREADD) in the hypoglossal motoneurons. DREADD (rAAV5-hSyn-hM3(Gq)-mCherry) and control virus (rAAV5-hSyn-EGFP) were stereotactically administered to the hypoglossal nucleus of C57BL/6J mice. Genioglossus EMG and dynamic MRI of the upper airway were performed before and after administration of the DREADD ligand clozapine-N-oxide (CNO) or vehicle (saline). In DREADD-treated mice, CNO activated the genioglossus muscle and markedly dilated the pharynx, whereas saline had no effect. We applied a novel chemogenetic method to reversibly silence neuromotor input to the genioglossal muscle using DREADD, which was delivered bilaterally to the hypoglossal nucleus in fifteen C57BL/6J mice. The viral administration mice were injected with a CNO or saline followed by a sleep study. Inspiratory flow limitation was recognized by the presence of a plateau in mid-respiratory flow. DREADD injection brain slices of medulla were prepared and individual hypoglossal motoneurons were recorded before and after CNO application. In sleep studies, CNO markedly increased the frequency of flow limitation in NREM sleep and REM sleep compared to saline treatment, but there was no significant oxyhemoglobin desaturation or sleep fragmentation. Electrophysiology recording in brain slices showed that CNO inhibited firing frequency of DREADD-containing hypoglossal motoneurons.

Chemogenetic approach allows to silence hypoglossal motoneurons in mice, which leads to sleep disordered breathing manifested by inspiratory flow limitation during NREM and REM sleep.

Our these results suggest that chemogenetic approach can be considered as a treatment option for OSA and other motoneuron disorders.

#### SY1-2

#### Surgical outcomes in Korea

**Ji Ho Choi**

*Department of Otorhinolaryngology-Head and Neck Surgery,  
Soonchunhyang University College of Medicine, Bucheon  
Hospital, Korea*

Obstructive sleep apnea is characterized by intermittent partial or complete obstructions of upper airway including the nasal cavity, pharynx and larynx during sleep. If diagnosis or treatment is delayed, obstructive sleep apnea can cause diverse symptoms such as excessive daytime sleepiness and significant complications including cardiovascular disease. Therefore, immediate detection and optimal management for obstructive sleep apnea is very critical for alleviating patient health. There are various management options for obstructive sleep apnea such as weight control, positional therapy, positive airway pressure, oral appliance and surgical treatment. Surgical procedures for the treatment of sleep-related breathing disorder have been performed since the 1960s. Currently, varied surgical methods are performed according to the predicted obstruction site: nasal surgery (e.g., septoplasty, turbinate surgery), oropharyngeal procedures (e.g., tonsillectomy, uvulopalatopharyngoplasty [UPPP], uvulopalatal flap [UPF]), hypopharyngeal procedures (e.g., genioglossus advancement, radiofrequency tongue base ablation, partial glossectomy) and global airway procedure (e.g., maxillomandibular advancement). In this presentation, the outcomes of various obstructive sleep apnea surgery in Korea are reviewed.

## Symposium 1

### Recent advances in OSA

#### SY1-3

### History of sleep medicine in Japanese insurance system and introduction of HNS

**Shintaro Chiba**

*Sleep Medicine/ ENT, Ota Memorial Sleep Center, Japan*

Japanese medical insurance is started since 1961, based on following 4 concepts.

- 1 Covering all citizens by public medical insurance
- 2 Freedom of choice of medical institution, we call it free access
- 3 High-quality medical services with low costs
- 4 Based on the social insurance system, spending the public subsidy to maintain the universal health insurance coverage.

Sleep medicine in Japan is also provided under this insurance system too. Initially nocturnal Polysomnography was reimbursed in 1990, OCST followed in 1996, and CPAP treatment was reimbursed in 1998. Japanese do not have much obese patients but still local epidemiological study reported 22.3% of moderate to severe OSA prevalence in male working generation.

Today, approximately 20,000 OCST and 9,000 PSG tests are performed and in a month. Therefore, the number of patients using CPAP have reached 455,000 in 2016 as the number of sleep tests increases. One of the problems is increasing medical cost in our aging society that will come in near future. And another problem is increasing number of CPAP failure patients. Recently, effectiveness of Hypoglossal nerve stimulation is reported as alternative treatment and the patient number who received HNS reached already more than 5000 in US and Germany. In Japan we have not yet started HNS treatment, however, HNS was certified for medical equipment last year and expected to be included in the insurance in this year. Now we, The Otorhinolaryngological Society of Japan, The Japanese Sleep Research Society, The Japanese Respiratory Society and The Japanese Circulation Society, are preparing for introduction and start of HNS. In this lecture we will introduce our progress of HNS introduction in Japan including clinical guidelines being developed.

#### SY1-4

### Robotic surgery in OSA

**Hyung-Ju Cho**

*Otorhinolaryngology, Yonsei University, Korea*

Traditionally, CPAP has been the gold standard of treatment for obstructive sleep apnea OSA. However, a variable but significant number of patients have poor results using CPAP and consider alternative treatments, including surgery. Recently, tongue base obstruction has been recognized as one of the essential anatomic regions that may be challenging to surgeons due to difficult access and limited surgical techniques. With the development of new surgical equipment, tongue directed methods such as coblation tongue base surgery and transoral robotic surgery TORS have become popular therapeutic options for downsizing tongue volume. Among various surgical techniques, TORS has been widely recognized and is now preferred by many sleep surgeons after its first use for OSA treatment in 2010 by Vicini et al. However, many surgeons have concerns or hesitate to apply a robot for sleep surgery due to the cost-benefit effect. Robotic and coblation tongue base resections have their own advantages and disadvantages, but there is a lack of well matched comparison studies that compare the two surgical procedures. The surgical outcomes of TORS were comparable to endoscope guided coblation tongue base resection. Patients who underwent TORS showed non-inferior PSG outcomes, comparable complication rates and prolonged hospitalization. Further studies, including a comparison between TORS and coblation tongue base resection, are necessary to further demonstrate the cost benefits, efficacy, safety and surgical indications for TORS.

## Symposium 2

### Problems of Dysphagia

#### SY2-1

### Swallowing computed tomography and virtual reality

**Rumi Ueha**

*Swallowing Center, Otolaryngology and Head and Neck Surgery, the University of Tokyo, Japan*

The common imaging tests for cervical symptoms during swallowing include videofluoroscopic swallowing study (VFSS), laryngeal endoscopy, and cervical computed tomography (CT). In VFSS, the image quality is insufficient for evaluating hard tissues such as the hyoid bone and styloid process. Laryngeal endoscopy is limited to the assessment of the pharyngolaryngeal lumen. In addition, while cervical CT can provide a detailed view of the tissue structure, it cannot evaluate dynamic structural changes. Swallowing CT and swallowing virtual reality (VR) can overcome these challenges. Swallowing CT studies using a second-generation 320-row CT have been performed since 2011. This technique allowed the understanding of the oro-pharyngo-laryngeal structural changes during swallowing motion three-dimensionally and dynamically. Regarding swallowing VR, we developed a system to display the swallowing CT data in VR, which shortened the time required for 3D image reconstruction and reduced the costs. In swallowing VR, the 3D models were reconstructed from CT image data in DICOM format using the marching cubes algorithm. Superimposing pharyngeal lumen models and bone tissue models enabled simultaneous observation of the dynamics of the pharyngeal lumen and bone tissue during swallowing. Although the reconstruction methods for swallowing CT and VR are different, the image data used are the same; therefore, the evaluator can choose the most convenient method based on the proficiency of the imaging examination ability at the facility.

While swallowing CT and VR are useful for diagnosis, they are not widely recognized because of their novelty and are rarely used in clinical practice. Thus, it is imperative to highlight the benefits of swallowing CT and VR so that they can be more widely adopted. With further technological improvements, precisely reconstructed swallowing CT/VR images are expected to facilitate accurate diagnoses and improved patient treatment and satisfaction. The conditions and diseases that may be amenable to swallowing CT/VR are those in which there is no abnormality at rest, but anatomical abnormalities can be revealed during swallowing. It is anticipated that swallowing CT/VR will be widely used for swallowing evaluation in the future.

#### SY2-2

### Preventive intervention for age-related dysphagia in an increasingly aging society

**Kaori Nishikubo Tanaka**

*Otorhinolaryngology, Head and Neck Surgery, School of Medicine, Ehime University, Japan*

Globally, population aging is progressing rapidly, and the number of patients with dysphagia is simultaneously increasing. It is well known that aging is an important contributor to dysphagia, and presbyphagia, which refers to the decline in swallowing function, is often seen in healthy elderly people. Specific examples of age-related decline in swallowing function have been reported, including: 1) laryngeal ptosis, 2) geniohyoid muscle loss, 3) throat hypoesthesia, and 4) esophageal entrance dilatation. In particular, laryngeal elevation during pharyngeal swallowing affects airway defense, pharyngeal clearance, and esophageal entrance passage, and a decrease in laryngeal elevation is significantly associated with a decrease in swallowing ability. However, dysphagia does not affect all elderly people. Much attention has not been given to compensatory mechanisms for swallowing dysfunction in the elderly. One such compensatory mechanism is an increase in the activity of swallowing-related muscles. Whether the elderly can compensate for the age-related decline in swallowing function is dependent on their ability to maintain safe oral intake. In this talk, we will discuss the compensatory mechanisms for age-related dysphagia and explain the effects of preventive intervention strategies.



## Symposium 2

### Problems of Dysphagia

**SY2-3**

#### Management of cricopharyngeal dysphagia

**Young Hak Park**

*Department of Otolaryngology-HNS Yeouido St. Mary's Hospital,  
The Catholic University of Korea, Korea*

The cricopharyngeal dysphagia refer to the dysfunction of upper esophageal sphincter(UES) caused by the failure of its coordinated relaxation or expansion.

The upper esophageal sphincter refers to the high pressure zone between pharynx and cervical esophagus, which composed of cricopharyngeus muscle, inferior pharyngeal constrictor and cervical esophagus.

Three components are associated with UES opening; relaxation of cricopharyngeus muscle, contraction of UES opening muscle and intrabolus pressure at the hypopharynx. Impairment in harmony of these components inevitably results in dysfunction of the UES opening and thus cricopharyngeal dysphagia.

Many conditions result in cricopharyngeal dysphagia, which clinical manifestations vary depending on the pathologic conditions.

The diagnosis of cricopharyngeal dysphagia may be accomplished with a combination of clinical and instrumental evaluation, including videofluoroscopic evaluation of swallowing, flexible endoscopic evaluation of swallowing, pharyngeal manometry, and EMG.

Management method of cricopharyngeal dysphagia include swallowing exercise, mechanical dilatation, botox injection, and cricopharyngeal myotomy.

Mechanical dilatation is usually used for stricture or stenosis patient.

Botox injection and CP myotomy is successful in cricopharyngeal dysphagia with near normal pharyngeal function.

In case of reduced laryngeal elevation and pharyngeal dysfunction, swallowing exercise can have role to treat cricopharyngeal dysphagia. Swallowing exercises to manage cricopharyngeal dysphagia are head rotation position during swallowing trial and swallowing exercise including tongue base exercise, laryngeal elevation exercise and head lifting exercise.

To achieve improvement of swallowing function in cricopharyngeal dysphagia, It is important to be approached appropriated diagnostic tool for accurate diagnosis, and should managed by multidimensional treatment modality

## Symposium 3

### Recent advances in medical devices on vestibular science

**SY3-1**

#### MR imaging of endolymphatic hydrops in Meniere's Disease

**Munehisa Fukushima**

*Kansai Rosai Hospital, Japan*

Endolymphatic hydrops (EH) is now widely recognized as a histological marker of Meniere's disease (MD), and is associated with its pathogenesis. In the chronic course of MD, the vertigo episodes improve, but both vestibular and hearing function deteriorate. However, the details of how EH behaves in this process remains unclear.

In recent years, visualization of EH using 3-Tesla magnetic resonance (MR) imaging, 4 h after intravenous administration of gadolinium, is routinely performed. Using this in vivo imaging method, we characterized EH enlargement in MD patients during medical treatment. We treated MD patients medically, and observed EH over the medium-to-long term. We repeatedly measured the volumetric change in EH by MR images processing. MR image studies showed that EH in MD patients developed longitudinally with deterioration of inner ear function during medical treatment. Enlargement of the EH was the likely cause of hearing deterioration because the EH volume was significantly correlated with the hearing level of the affected ear.

MD is characterized by recurrent vertigo, which may be related to the rupture of membranous labyrinth in the inner ear. The swollen membranous labyrinth is thought to rupture after EH increases gradually ('rupture theory'). Bilateral EH remained stable in one patient with a 4.5 year course of repeated vertigo, although either side of ears could be involved in vertigo attacks in this patient with bilateral MD. Ruptures of EH were not observed during and after vertigo attacks. This presentation of EH that suggests rupture theory may not be entirely accurate.

## Symposium 3

### Recent advances in medical devices on vestibular science

#### SY3-2

#### Non-invasive middle ear pressure treatment for intractable Meniere's disease

**Hideo Shojaku**

*Department of Otolaryngology, University of Toyama, Japan*

A 12-month follow-up study of patients with intractable Meniere's disease (MD) and delayed endolymphatic hydrops (DEH) showed that middle ear pressure treatment with a transtympanic membrane massage (TMM) device had a similar effect to a Meniett® device. However, the long-term effects are still unclear. We therefore retrospectively compared the effects of pressure treatment with a TMM device to the effects of treatment with a Meniett® device in patients with MD and DEH who were followed for a minimum of 24 months. Twenty-seven patients were treated with the TMM device and 14 patients were treated with a Meniett® device. The insertion of a transtympanic ventilation tube was necessary for the Meniett® device but not for the TMM device. In patients treated with the TMM and Meniett® devices, the frequency of vertigo was significantly improved at 19-24 months after treatment. The distribution of vertigo at 19-24 months after treatment did not differ between the patients treated with the two types of devices. Pressure treatment for  $\geq 8$  months was suitable for achieving remission. Middle ear pressure treatment for  $\geq 8$  months with a TMM or Meniett® device was equally effective and provided minimally invasive treatment options for intractable MD and DEH.

#### SY3-3

#### Sensory substitution therapy as a final selection for graded rehabilitation of vestibular system

**Toshiaki Yamanaka**, Tadashi Kitahara

*Otolaryngology-Head and Neck Surgery, Nara Medical University, Japan*

Some patients with uncompensated vestibular hypofunction have a long-term history of a persistent severe problem in their posture and mobility. Graded vestibular balance rehabilitation for such patients is performed using the stepwise treatment program that includes vestibular adaptation training (Step 1) to promote the vestibular ocular and spinal adaptation process, sensory reweighing training (Step 2) to alter vestibular, visual, and somatosensory input, and vestibular substitution-based biofeedback training (Step 3) to use the sensory substitution system with human (brain)-machine interface in our clinic.

In this study, we investigated the impact of electrotactile biofeedback training (Step 3, final step) using a vestibular substitution tongue device (VSTD) in an effort to correct postural imbalance in 16 patients with unilateral loss of vestibular function that was intractable to any treatment involved in Step 1 and 2 training. The VSTD transmits information on the head position to the brain through the tongue as a substitute for the absent vestibular information. Subjects were trained to maintain a centered body position by appropriately focusing the electrical signals at the center of their tongues. All subjects attended 10-min training sessions 2-3 times per day for 8 weeks, and were followed-up for over 2 years after the cessation of the training program to evaluate the long-term impact of this intervention. The balance functions involving postural stability and gait improved in all subjects after the 8-week training period, and these improvements persisted for up to 2 years after the termination of the training program. Thus, the biofeedback training with a VSTD proved beneficial in both the short and long-term. As an example, we present a case of a disabled archer with severe balance disorder. He underwent successful Step 3 rehabilitation with the VSTD and effect of the treatment was maintained for 7 years, and he has now qualified for the upcoming Paralympic games at Tokyo in 2020.

We conclude that VSTD biofeedback training can be useful for the rehabilitation of individuals with persistent balance disorders. This approach can lead to long-term improvements in balance and motor function and will facilitate improved athletic performance.

## Symposium 3

### Recent advances in medical devices on vestibular science

#### SY3-4

#### IT-based medical device for the balance disorder

**Jae-Jun Song**

*Department of Otolaryngology-Head and Neck Surgery, Korea University Guro Hospital, Korea*

Virtual Reality is a computer technology that makes users feel immersed. Sensorama, developed by Morton Heilig in 1957, and the Head Mounted Display (HMD), developed by Ivan Edward Sutherland in 1968, are key technologies for the current virtual reality. Since then, various attempts have been made to virtual reality, and in the late 1980s, Jaron Lanier finally proposed the term "Virtual Reality", which allows users to feel the 'virtual sense'.

Augmented Reality, on the other hand, is a computer graphics technique that combines virtual objects or information into a real environment and implements them as if they were in the real world. It is the beginning of augmented reality that Thomas Caudell, who worked for Boeing, developed a program that would help his colleagues to work easier. Wearable augmented reality devices are similar to virtual reality in that they realize the screen through any HMD. However, virtual reality emphasizes immersion and interaction in virtual worlds that are disconnected from real world, while augmented reality emphasizes the direct interaction with intelligent enhancement in the extended world that is combined with reality. A new technology called "Mixed reality" is a mixture of these features, including Magic Leap, HoLoLens, and Project Alloy.

The virtual reality and augmented reality markets are growing every year. According to a report by Goldman Sachs, the virtual and augmented reality market is estimated at \$182 billion in 2025. The virtual reality market in Korea is mainly composed of military and architectural fields, and recently it has been expanded to games, animation, video and e-learning. In addition, virtual reality and augmented reality are used for medical purposes, and they are mainly used for diagnosis, operation, training of surgery, and psychiatric treatment. For example, several virtual reality programs for surgical training, medical devices that combines augmented reality, and augmented reality programs for exposure therapy are being used in various medical fields.

In this presentation, we introduce various AR/VR technology for vestibular rehabilitation and future perspectives.

#### SY3-5

#### Application of TMS & DCS for dizzy patients

**Ho Yun Lee**

*ORL-HNS, Ewha Womans University, Korea*

Neuromodulation has been applied to various intractable diseases to conventional treatment such as drug-resistant depression, headache or intractable pain, rehabilitation after stroke, Parkinson's disease, Alzheimer's disease, and tinnitus. For dizziness, changes in the brain network, functional connectivity between the prefrontal cortex and visual and motor regions have been reported in persistent postural-perceptual dizziness, visual-induced dizziness, and phobic postural vertigo. In this presentation, I will review recent neuromodulation and imaging studies applied to dizziness, and the feasibility of neuromodulation for better treatment outcomes will be discussed together.

### Symposium 3

#### Recent advances in medical devices on vestibular science

**SY3-6**

#### Clinical implication of VR and AI for patients with vertigo

**Sungkwang Hong**

*Department of Otorhinolaryngology-Head and Neck Surgery,  
Hallym University College of Medicine, Korea*

Artificial intelligence (AI) and virtual reality (VR) have been widely utilized in numerous fields with the recent advancement in technology. In particular, machine learning technology has been increasingly used in the medical field due to its significant benefits, in which several studies have revealed potential benefits for the diagnosis of hidden several pathological diseases, such as cancers, lung problems. We think that the paring of neurotologic data and AI might also create a new paradigm in diagnosis and treatment in the otologic domain. Additionally, VR can provide a suitable environment for dizzy patients for rehabilitation. The main focus of this talk is to review the clinical applications of AI and VR and introduce our developments using them in the neurotologic domain. The use of such machine learning technologies and VR are expected to be applied to various medical fields in the future, including the diagnosis and treatment of various diseases and the objective evaluation of after-treatment. In particular, the neurotologic domain, the numerous machine learning model, and VR contents will give a new opportunity for the treatment and diagnostic tools.

### Symposium 4

#### Recent topics of diagnosis and treatment of olfactory dysfunctions

**SY4-1**

#### Does olfactory mucosa regenerate after resection?

**Eri Mori**

*Department of Otorhinolaryngology Head and Neck Surgery, The  
Jikei University School of Medicine, Japan*

##### [Introduction]

Resection of the olfactory mucosa (OM) is sometimes unavoidable during sinus surgery. OM is well-known as it's characteristics of regeneration. However, it is not known whether the OM can completely recover thereafter. The aim of this study was to uncover whether the OM fully recovers after mucosal resection and describe the process of OM regeneration.

##### [Method]

Eight-week-old male Sprague-Dawley rats (n = 18) were subjected to OM resection at the nasal septum (NS). Six rats were euthanized for histological examination 0, 30, and 90 days after surgery. Immunohistochemistry was performed to identify olfactory receptor neuron (ORN) lineage cells [mature and immature ORNs and ORN progenitors, and olfactory ensheathing cells (OECs)], as well as dividing and apoptotic cells. Squamous and respiratory metaplasia and inflammatory cell infiltration were also assessed.

##### [Result]

On day 30 after resection, the mucosa had regenerated, and mainly contained thin nerve bundles, basal cells, and immature ORNs, with a few mature ORNs and OECs. On day 90, the repaired nasal mucosa had degenerated into stratified squamous or ciliated pseudostratified columnar epithelia, with reducing ORNs. The lamina propria contained numerous macrophages. Partial regeneration was observed within 1 month after OM resection, whereas subsequent degeneration into squamous and respiratory epithelia occurred within 3 months.

##### [Discussion and Conclusion]

Given the poor persistence of ORNs and OECs, OM resection is likely to result in olfactory impairment. Overall, surgeons should be cautious not to injure the OM during surgery.

## Symposium 4

### Recent topics of diagnosis and treatment of olfactory dysfunctions

#### SY4-2

#### The value of olfactory scintigraphy to determine the connectivity of olfactory sensory neurons in patients with olfactory dysfunction

**Hideaki Shiga**, Takaki Miwa

Otorhinolaryngology, Kanazawa Medical University, Japan

According to previous studies, the prognosis of olfactory dysfunction due to respiratory infection, head trauma, or chronic sinusitis primarily depends on residual function. The larger olfactory bulb volume has been shown to be a predictor of good olfactory recovery in patients with postinfectious and posttraumatic olfactory loss. The patients with small damage in olfactory sensory neurons are likely to show a better response to the treatments. Severe olfactory nerve damage determined using thallium-based olfactory imaging, Olfactory scintigraphy, predicts a worse prognosis in patients with idiopathic olfactory loss treated with the traditional Japanese herbal medicine tokishakuyakusan. The tokishakuyakusan rapidly promotes the expression of nerve growth factor in the olfactory bulb and rescues neurons from damage *in vivo*. The retroneural transport of nerve growth factor in olfactory bulb to the olfactory epithelium induces the differentiation of basal cells in olfactory epithelium. The connectivity of olfactory sensory neurons between olfactory epithelium and olfactory bulb needs to be determined with olfactory scintigraphy for recruiting participants in clinical trials of medicines targeting at the olfactory epithelial regeneration. The Medical Ethics Committees of our institution approved the study protocol of olfactory scintigraphy (trial registration no. jRCTs041180021). The authors declare that there are no conflicts of interest to declare. This study was funded in part by JSPS KAKENHI (grant numbers JP17K11369 and JP21K09592 to HS).

#### SY4-3

#### The YSK olfactory function (YOF) test: Development of a new Korean olfactory test

**Chang-Hoon Kim**

Department of Otorhinolaryngology, Yonsei University College of Medicine, Korea

Olfaction is related to a person's quality of life, beyond the instinctive sense of simply smelling food and recognizing danger. Recently, research has focused on its association with various diseases, such as neurodegenerative disease or anosmia after viral infection. The evaluation of olfactory function must consider the cultural experience of the target group. A new Korean culture friendly olfactory function test, the YSK olfactory function (YOF) test, uses safe odorants, such as phenyl-ethyl alcohol (PEA) (not n-butanol), for the threshold test. Furthermore, odorants of the YOF identification test reflect each of the eight major chemical functional groups. The diagnostic cut-off for anosmia was a TDI score of  $\leq 14.5$  and for hyposmia was  $14.5 < \text{TDI} \leq 21.0$ . The YOF test showed relevant diagnostic validity for olfactory dysfunction with the Korean version of the Sniffin' Stick-II test. In this talk, we share our experiences developing this new Korean-friendly olfactory function test.



## Symposium 4

### Recent topics of diagnosis and treatment of olfactory dysfunctions

#### SY4-4

### The feasibility of clinical applications for olfactory testing using fMRI

**Jin Kook Kim**, Won-Jin Moon

*Otorhinolaryngology-Head & Neck Surgery, Konkuk University Hospital, Konkuk University School of Medicine, Korea*

Advances in Neuroimaging techniques have been applied to the evaluation of the visualization and functionality of the olfactory region. Several studies have evaluated systematic and objective tools for assessing olfactory function; in particular, previous work has examined the diagnostic utility of single-photon emission CT and MR imaging. Previous MR imaging studies in patients diagnosed with anosmia (esp. traumatic anosmia) based on the clinical olfactory test have found that 61%~88% of the study population had gross damage to the olfactory system. Studies using SPECT have detected abnormalities that were previously undetectable on MR. But even normosmic subjects showed abnormality on SPECT. Therefore, functional imaging, as well as structural imaging, is important, and fMRI is a representative tool. Olfactory fMRI is now used for the study of olfactory deficits in neurodegenerative diseases, schizophrenia, and congenital hyposmia. And it can be used to measure the functional activity or connectivity in patients with smell disorders and can enhance our fundamental understanding of the olfactory system. Therefore, findings from fMRI studies may lead to better prognosis and improved treatment strategies. While olfactory fMRI can provide additional information regarding brain function, task instructions can be difficult for patients with olfactory dysfunction due to accompanying cognitive problems. Furthermore, olfactory fMRI studies have provided various results due to the heterogeneity of olfactory tasks, overlapping functional areas responsible for sniffing and olfaction, and habituation of the olfactory systems. Resting-state fMRI appears to be a promising evaluation tool for understanding functional activity and connectivity without specific stimuli or tasks. In this respect, rs-fMRI may have additional benefits compared to odor-stimulated task-based fMRI for the evaluation of olfactory dysfunction in patients with smell disorder. rs-fMRI studies on olfactory dysfunction have been rarely reported to date, specifically in those with post-traumatic anosmia. In this session, we will consider the clinical feasibility of olfactory fMRI and rs-fMRI as an objective tool of olfactory function assessment.

## Symposium 5

### Recent Topics for Head and Neck Tumors

#### SY5-1

### Molecular characterization of circulating tumor cells in head and neck squamous cell carcinoma and its clinical application

**Kazuaki Chikamatsu**, Hiroe Tada,

Hideyuki Takahashi

*Otolaryngology-Head and Neck Surgery, Gunma University Graduate School of Medicine, Japan*

A circulating tumor cell (CTC) is a cell that has shed into the bloodstream from a primary tumor, and regards as attractive biomarkers for monitoring disease progression in cancer patients. For the clinical application of CTCs in head and neck squamous cell carcinoma (HNSCC), evidence has shown that the existence or enumeration of CTCs is associated with various clinical factors, such as clinical stage and prognosis. Here, we performed the molecular detection and characterization of CTCs in patients with HNSCC and analyzed whether the molecular characteristics of CTCs was associated with clinical outcome. CTCs captured by microfilter were analyzed for the expression of multiple epithelial markers (*EPCAM*, *MET*, *KRT19*, and *EGFR*) by RT-qPCR. Twenty-eight (63.6%) of the 44 untreated HNSCC patients were positive for at least one epithelial-related gene. *EPCAM* was detected in 7 (15.9%), *MET* in 13 (29.5%), *KRT19* in 22 (50.0%), and *EGFR* in 7 (15.9%) patients. Of note, patients with *MET*-positive CTCs showed a shorter progression-free survival (PFS) than those with *MET*-negative CTCs. CTC-positivity was significantly correlated with treatment resistance, locoregional recurrence, and a shorter PFS. Thus, the presence of CTCs was closely related to local recurrence as well as distant metastasis, which may represent the ability of CTCs to return to and grown in primary site. For further molecular characterization, the CTC-positive samples were analyzed for the expression of 10 genes (*PIK3CA*, *CCND1*, *SNAI1*, *VIM*, *CD44*, *NANOG*, *ALDH1A1*, *CD47*, *CD274*, and *PDCD1LG2*). Interestingly, patients with *CD274*-positive CTC showed prolonged PFS and overall survival compared to those with *CD274*-negative CTC, suggesting that *CD274* (PD-L1) expression on CTCs may partially reflect the tumor immune microenvironment, that is, increased immune cell infiltration and PD-L1 overexpression in tumor cells. Taken together, molecular characterization by the gene expression of CTCs clearly indicated their effects on clinical outcome in patients with HNSCC. CTC-relating technologies may become a powerful tool towards cancer precision medicine.



## Symposium 5

### Recent Topics for Head and Neck Tumors

#### SY5-2

#### New developments and future directions in systemic therapy for salivary duct carcinoma

**Yuichiro Tada**

*Department of Head and Neck Oncology and Surgery, International University of Health and Welfare, Mita Hospital, Japan*

Salivary gland cancer (SGC) is a rare cancer, accounting for 0.2% of all cancer incidences and 0.3% of all cancer deaths according to the Global Cancer Statistics 2020. The Japanese cancer statistics estimate that the incidence rate is 1.4/100,000 people/year, with about 1,800 cases per year.

Developing systemic therapy for SGC is challenging given its rarity, and biologic and clinical diversity, with more than 20 subtypes defined by the 2017 WHO classification. In recent years, however, advances in molecular biology of SGC have led to the identification of genetic characteristics of each subtype, and the results of several clinical trials on molecular therapies have been reported. The systemic treatment options for SGC in the NCCN Guidelines have been updated annually since 2018. Currently, various agents are recommended for the treatment of metastatic lesions of SGC based on the results of HER2 status, androgen receptor (AR) status, NTRK fusion gene, tumor mutation burden (TMB), microsatellite instability (MSI), and genomic analysis by NGS.

In this presentation, I will review the findings and future prospects of anti-HER2 and anti-AR therapies, which have been established as useful treatments for salivary duct carcinoma, including the experiences of these two prospective studies conducted in our department.

#### SY5-3

#### Prognostic factors in surgically treated HPV positive tonsillar cancer

**Young Hoon Joo**

*Department of Otolaryngology-Head and Neck Surgery, College of Medicine, The Catholic University of Korea, Korea*

Oropharyngeal cancer is the most common head and neck cancer, and its prevalence is increasing. Human papillomavirus (HPV) + oropharyngeal cancer represents a distinct disease compared to HPV-negative oropharyngeal cancer. In general, HPV+ oropharyngeal cancer patients have a more favorable prognosis than do patients with HPV- disease. Initial treatment options for HPV+ oropharyngeal cancer include surgical resection or nonsurgical treatment with radiotherapy or chemoradiotherapy. Radiotherapy, however, has significant morbidity of its own, which is compounded by the frequent use of systemic therapy. In the last decade, transoral surgery has facilitated effective treatment along with reduced morbidity. More than half of all head and neck cancer patients require primary surgical treatment, and typically more than two thirds will have to undergo a surgery at some point during their treatment.

The previous data show that treatment failures occur regularly in HPV+ HNSCC. Treatment failure can occur locoregionally or at distant sites. For clinical practice, it is important to look at differences in the clinical characteristics of these recurrences. This section therefore aims at identifying patterns of disease recurrence in the HPV + population and its differences compared to HPV- cancers. In oropharyngeal carcinomas, the study by Ang et al. is a retrospective analysis of stage III/IV oropharyngeal carcinoma (no significant difference in survival after treatment with accelerated fractionation RTx+ cisplatin or standard fractionation radiotherapy + cisplatin). 206 (63.8 %) of 323 patients with oropharyngeal carcinoma were HPV positive (HPV ISH & p16). After 3 years, the tumor had relapsed locoregionally significantly more often in HPV-negative than in HPV-positive patients (35.1 %, 95 %CI 26.4–43.8 vs. 13.6 %, 95 %CI 8.9–18.3). The frequency of distant metastases did not differ significantly between both groups. A retrospective analysis by Rischin et al. identified 106 (57 %) of 185 stage III or IV oropharyngeal carcinomas (treated with radiotherapy and cisplatin ± tiranzapine) that were p16 positive. After 2 years,

## Symposium 5

### Recent Topics for Head and Neck Tumors

#### SY5-4

### Inhibition of integrin $\beta 1$ induces radiosensitization and attenuates perineural invasion in oral squamous cell carcinoma

**Sung Joon Park**

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Locoregional failures were observed more often in the HPV-negative group (14 % vs. 7 %,  $p = 0.091$ ) with similar rates of distant failure in both groups. The study by Posner et al. identified 56 (50 %) HPV-positive (HPV PCR) carcinomas among 111 patients with locally advanced oropharyngeal carcinomas. After 5 years, local-regional failure was significantly less common in HPV positive than in negative carcinomas but no significant difference was seen in the rate of distant metastases. The study by Huang et al. identified 457 p16+ patients among 624 patients with oropharyngeal cancer treated with definite radiotherapy or chemoradiation. The median follow-up was longer in p16+ patients (4.2 vs. 3.3 years). 27 (6 %) p16+ patients had locoregional failure as compared to 35 (21 %) p16- patients. Distant metastases (with or without concurrent locoregional recurrence) were identified in 54 (12 %) p16+ and 25 (15 %) p16- patients. Taken together, these results suggest that locoregional recurrences were less common in HPV+ carcinomas, whereas the rate of distant metastases was similar.

In this symposium I will discuss about the clinicopathological predictors on risk of recurrence and survival in patients with HPV-positive tonsil cancer undergoing surgical treatment.

**Purpose:** Radioresistance and perineural invasion are big hurdles in treatment of oral cavity squamous cell carcinoma (OSCC). We tried to evaluate the importance of integrin  $\beta 1$  on radiosensitivity, perineural invasion, and aggressiveness of OSCC by conducting in vitro study using radiosensitive and radioresistant OSCC cell lines.

**Materials and Methods:** Radioresistant OSCC cells which mimic real radiotherapy protocol were used. The expression of integrin  $\beta 1$  was inhibited by shRNA. The adhesion to neuronal cells, sensitivity to radiation, aggressiveness reflected by invasion and migration potential of radioresistant OSCC15 and 25 cells were evaluated with or without inhibiting integrin  $\beta 1$  expression and compared these results with that of radiosensitive OSCC15 and 25 cells.

**Results:** We found that adhesion to neuronal cell, invasiveness, and migration were increased in radioresistant OSCC15 and 25 cells compared with radiosensitive cells. In addition, the expression of integrin  $\beta 1$  was also increased in radioresistant OSCC15 and 25 cells compared with radiosensitive cells. When the expression of integrin  $\beta 1$  was inhibited, adhesion to neuronal cell, invasiveness, migration, and even the radioresistance of OSCC15 and 25 cells were attenuated to the level of radiosensitive cells.

**Conclusion:** Our data suggest that integrin  $\beta 1$  critically contributes to the maintenance of radioresistance along with adhesion to neuronal cell of radioresistant OSCC cells. Furthermore, integrin  $\beta 1$  was associated with the aggressiveness of radioresistant OSCC cells. Future in vivo experiments are warranted to evaluate the targeting integrin  $\beta 1$  as a novel emerging therapeutic target in radioresistant OSCC patients.

## Symposium 5

### Recent Topics for Head and Neck Tumors

#### SY5-5

### Gender differences in the prevalence of head and neck cancers

**Jun-Ook Park**

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The incidence of cancers varies by sex/gender; these may influence the cancer risk in different ways. The complex and dynamic interactions between sex and gender throughout the lifespan may affect health care; cancer susceptibility, perception, and progression; and treatment compliance. Descriptive epidemiologists have repeatedly reported that males are more susceptible to head and neck cancers. We performed a retrospective cohort study using the Korean National Health Insurance Service database on 9,598,085 individuals who underwent regular health checkups from January 1 to December 31, 2009. We sought head-and-neck cancers developing during the 10-year follow-up. A total of 10,732 (incidence rate [IR] per 1,000 person-years 0.25) individuals were newly diagnosed with head-and-neck cancer among the 9,598,085 individuals during the 10-year follow-up. The IR was 0.19 in males (8,500 affected) and 0.06 in females (2,232 affected). Notably, the male-female ratio increased with age below 70 years, but decreased thereafter. The male-female difference was most apparent for laryngeal cancer; the male IR was 11-fold higher in the 40s and 20-fold higher in the 60s, followed by hypopharyngeal cancer (6.8- and 24.2-fold). Males smoked more and drank more alcohol than females ( $P < 0.0001^*$ ,  $P < 0.0001^*$ ). When never-smokers/-drinkers (only) were compared, males remained at a 2.9-fold higher risk of head-and-neck cancer than females. The hazard ratios for head-and-neck cancers in males tended to increase in the lower part of the upper aerodigestive tract: larynx (13.9) > hypopharynx (10.9) > oropharynx (4.4) > nasopharynx (2.9) > sino-nasal region (1.8) > oral (1.6). Only the salivary gland cancer incidence did not differ between the sexes; the gland is not in the upper aerodigestive tract. In summary, males were much more susceptible to head-and-neck cancers than females regardless of whether they drink alcohol or smoke tobacco. Sex differences in the incidence of head and neck cancer were most evident in the 60s in the lower part of the upper aerodigestive tract such as the larynx and hypopharynx. Further research is needed.

## Symposium 6

### Problems of tinnitus research

#### SY6-1

### Clinical consideration on tinnitus pathophysiology -hidden hearing loss as a possible cause of tinnitus-

**Tetsuaki Kawase<sup>1</sup>**, Yusuke Kusano<sup>1</sup>,  
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<sup>2</sup>Tohoku Medical and Pharmaceutical University

Tinnitus is thought to arise from the pathological changes along the entire auditory pathway, which develops as a consequence of initial cochlear lesions. Decreased neural input from the auditory periphery thought to be one of the important factors affecting tinnitus development. Even for tinnitus patients in whom decrease of neural input from the auditory periphery seems not to be indicated by routine audiogram, reduction of neural input caused by synaptopathy between inner hair cells (IHCs) and type I cochlear neurons and neural degeneration (as known hidden hearing loss, or HHL) has been speculated.

In the present study, the possible involvement of HHL mechanism in development of tinnitus were examined in patients with unilateral hearing loss. The possible existence of HHL was assessed by comparing the supra-threshold auditory functions between affected and unaffected ears for the point at which hearing recovery was confirmed based on the audiograms. Then, the relation between subjective tinnitus perception and the possible existence of HHL were examined.

Results obtained from the present study appear to indicate 1) that HHL pathology was developed, at least in some subjects, after the unilateral hearing loss at recovery stage, 2) but that the association between the existence of possible HHL and tinnitus might not be straightforward, as indicated in the relation between general hearing loss and the development of tinnitus. That is, although HHL pathology might be an essential factor leading to the development of tinnitus, not everybody with possible HHL develops tinnitus. Factors other than the decrease of neural input from the auditory periphery might be involved in the development and recognition of tinnitus.

The possible significance of HHL pathology in the development of tinnitus will be discussed.

## Symposium 6

### Problems of tinnitus research

#### SY6-2

### Functional neuroimaging signatures determining the development of tinnitus in subjects with hearing loss

**Jae-Jin Song**

*Seoul National University Bundang Hospital, Korea*

As the human brain works in a Bayesian manner to minimize uncertainty toward external stimuli, the deafferented brain may generate tinnitus to fill in missing auditory information. However, not everybody with hearing loss develops tinnitus. Understanding the differences between people with hearing loss who develop tinnitus versus those who do not offers a unique opportunity to unravel critical brain areas involved in the generation of a phantom sound.

In the first study, we compared electroencephalography data between 65 hearing loss patients with tinnitus (HL-T) and 65 without tinnitus (HL-NT) to identify signatures that may reveal prerequisites for the selective development of tinnitus in subjects with hearing loss. Compared to the HL-NT group, the HL-T group showed significantly higher activity in the right parahippocampus for the beta 1 frequency band, in the left inferior parietal lobule (IPL) for the beta 2 band, and in the right IPL for the beta 3- and gamma bands. These results suggest that tinnitus may be perceived only if auditory memory stored in the parahippocampus is actively linked to the IPL-based "circuit breaker" system and the circuit breaker signal is connected to the default mode network (DMN). Thus, when the circuit breaker system regards tinnitus secondary to peripheral deafferentation as a salient event and then the DMN regards tinnitus as a norm, subjects with hearing loss may consciously perceive tinnitus.

In the second study, we investigated the differences between 65 HL-T and 104 HL-NT using a EEG data-based volume entropy model of the brain network, by comparing the afferent node capacities, that quantify the contribution of each node to the spread of information, of all Brodmann areas. While the HL-T group showed increased information flow in areas involved in Bayesian inference and auditory memory storage, the HL-NT group showed increased afferent node capacity in hub areas of the DMN (the right posterior cingulate cortex and the right medial temporal gyrus). These results suggest that the balance of activity between the Bayesian inferential network and DMN determines whether phantom auditory perception occurs in a brain with decreased peripheral auditory input.

#### SY6-3

### What is the prognostic factor worsening tinnitus ?

**Sho Kanzaki, Kaorue Ogawa**

*Otolaryngology, Keio University, Japan*

**Aim)** The associations between tinnitus distress and psychological factors such as depression and anxiety has been reported. However, the prognostic factor is unknown because there is a few reports on the associations between tinnitus distress and genetic background. We analyzed the associations between the genetic background related with tinnitus and the grade of tinnitus distress and searched for prognostic markers.

**Subjects)** The patients The subjects were 138 patients with chronic tinnitus lasted for more than 3 months.

**Methods)** THI (an index of distress) of those patients was confirmed. The association between genetic background associated with depression / anxiety and tinnitus distress was evaluated. The SNPs targeted for this study were limited to those with a Minor allele frequency (MAF) of 0.1 or more at HAPMAP Japan, among the OMIMs that had been reported to be associated with depression, anxiety disorder, and obsessive-compulsive disorder as described above. In this study, THI score  $\leq 56$ : mild or moderate, score  $\geq 58$ : severe / most severe, SDS score  $\leq 43$  in normal group, SDS score  $\geq 44$  in non-normal group Then, Fisher's exact test was performed for the target SNP. Furthermore, the relationship between SNP and the severity of THI, SDS, and STAI was also evaluated by Trend's test. The significance level in each of the above tests was 5%.

**Results)** The association between SNP rs131702 of BCR gene and Tinnitus handicap inventory (THI), which is an index of tinnitus distress, was found to be severe. In addition, the association with the severity of the State-Trait Anxiety Inventory (STAI), an index of state anxiety, was also recognized. On the other hand, no association was found with the Self-rating Depression Scale (SDS), an index of depression.

**Discussions)** Our results indicated that the SNP of this gene is independent of depression and is considered to be a prognostic factor unique to tinnitus. Patients with BCR (rs131702) often had severe tinnitus cases, suggesting that it may be associated with severe tinnitus. However, since the number of cases is small, we should increase the number of cases since tinnitus is not caused by a single gene, and more likely that multiple genes are related.

## Symposium 6

### Problems of tinnitus research

#### SY6-4

#### Which is more important for the occurrence of tinnitus, "the aging or hearing loss"?

**Yong-Hwi An**

*Eulji University, Korea*

The prevalence of tinnitus and hearing loss (HL) increased with age. So presby-tinnitus can be termed as tinnitus that accompanies the progressive HL of presbycusis (i.e. age-related HL). There is a difference of the prevalence pattern of tinnitus and HL in the elderly; the prevalence of tinnitus does not increase above a certain level of old age, while HL does continue to increase with age above 65 years. Most epidemiologic studies showed the prevalence of tinnitus itself seemed to be related not to age but to audiometric threshold by the comprehensive statistical analysis. Despite the age-dependent occurrence of HL, there was no such age dependency for tinnitus when the effects of HL was excluded in those surveys. This is thought to be due to other compounding factors including noise injury, metabolic or vascular dysfunction, and genetic predisposition other than age. It is necessary to investigate the prevalence of newly defined tinnitus disorder (when associated with emotional distress, cognitive dysfunction, and/or autonomic arousal, leading to behavioral changes and functional disability) for the accurate evaluation of the relationship among tinnitus, HL and the aging.

#### SY6-5

#### Current status of cognitive behavioral therapy for tinnitus in Japan

**Mariko Takahashi**

*Otolaryngology-Head and Neck Surgery, Aichi Gakuin University School of Dentistry, Japan*

Tinnitus is a condition in which the patient experiences a continuous sensation of sound in the ears or the head, although it is not perceptible externally. At least 10% of the population in Japan has reportedly experienced tinnitus, with 1-3% of these cases being severe. Although the prevalence of tinnitus is relatively high in Japan, at about 15%, a systematic treatment protocol has not yet been proposed, and patients are often kept away in an outpatient clinic without adequate treatment. Against this backdrop, the Tinnitus Clinical Practice Guidelines were first published in Japan in May 2019, and recommended cognitive behavioral therapy (CBT) based on strong evidence. However, in Japan, CBT is used only for treating disorders such as depression, and is rarely considered for the treatment of tinnitus.

CBT captures the human mind from four aspects - emotion, behavior, cognition, and body - and each of them is interrelated, it has occurred a vicious cycle. CBT is a collective term for treatment approaches aimed at alleviating symptoms and distress using various behavioral and cognitive techniques to improve a patient's behavioral and cognitive capabilities.

The use of CBT for tinnitus has been recommended not only in Japan but in other countries such as Germany, the USA, the Netherlands, and Sweden as well. However, CBT has been designated for treating only conditions such as depression, anxiety disorders, panic attacks, chronic pain, and so on, in Japan, and is rarely used for the treatment of tinnitus presently.

One of the reasons why the use of CBT has not been treated for tinnitus in Japan may be that otolaryngologist treat tinnitus, compared to other countries, where psychiatrists treat tinnitus. Furthermore, there are a few doctors in Japan who use CBT in psychiatry, and CBT has been recognized by insurance providers only as a treatment for depression, anxiety disorder, panic disorder, post-traumatic stress disorder and so on. At present, CBT is gaining more attention, and we hope that CBT will be designated for treating tinnitus in Japan in the future.



## Symposium 6

### Problems of tinnitus research

**SY6-6**

#### Neuromodulation for tinnitus

**Ho Yun Lee**

*ORL-HNS, Ewha Womans Univeristy, Korea*

In the generation of tinnitus, changes of the auditory cortex and various brain networks are involved, causing the tinnitus to be perceived, salient, and persisted. Considering these, neuromodulation may be a fundamental method close to the pathophysiology of tinnitus. Various neuromodulation methods have been introduced. In this presentation, among the neuromodulation studies published for ten years from 2010 to 2021, the methodology and the results of the most representative studies conducted will be reviewed.

## Symposium 7

### How to manage eosinophilic chronic rhinosinusitis (ECRS)

**SY7-1**

#### Biologic drugs for the treatment of chronic rhinosinusitis with nasal polyps

**Tetsuji Takabayashi**

*The Division of Otorhinolaryngology Head and Neck Surgery,  
Department of Sensory and Locomotor Medicine, , University of  
Fukui, Japan*

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases worldwide. CRS is a heterogeneous disease, and racial or geographical differences of inflammatory pattern in nasal or paranasal mucosa are major concerns. Eosinophilic chronic rhinosinusitis (ECRS) is a subgroup of chronic rhinosinusitis with nasal polyps (CRSwNP), which is associated with severe eosinophilic infiltration and intractable.

Treatment options of nasal polyps of ECRS are to target the type 2 inflammation, which is characterized by a prominent role of cytokines, such as IL-4, IL-5, IL-13 and IgE. Anti-IL-4R-alpha chain Ab (dupilumab) improved nasal polyp score, CT score by Lund-Mackay score, QOL scores and the olfactory test score. Most recently, promising results of an international phase III trial of dupilumab for CRSwNP with high polyp scores has been published. Anti-IL-5R Ab (benralizumab) had been effective for limited patients with ECRS. These results provide us the precise mechanisms of ECRS, and precision medicine using biologics will improve the therapeutic efficacy for the patients with ECRS.



## Symposium 7

### How to manage eosinophilic chronic rhinosinusitis (ECRS)

#### SY7-2

#### The role of *Staphylococcus aureus* in the development of eosinophilic chronic rhinosinusitis

**Dae Woo Kim**

*Otorhinolaryngology Head and Neck Surgery, Seoul National University College of Medicine, Boramae Medical Center, Korea*

*Staphylococcus aureus* colonization has been observed more frequently in patients with CRSwNP compared to control subjects. CD4 T cells which express staphylococcal enterotoxins-targeting T cell receptor Vb genes are expanded in nasal polyps so that they can drive polyclonal IgE production and contribute to Th2 inflammation in the airway mucosa. Besides its superantigenic properties, *S. aureus* actively modulates the host immune response by releasing proteins that facilitate bacterial invasion and colonization. Exoproducts from *S. aureus* induced lower repair rates and reduced lamellipodial protrusion length and velocity in primary nasal epithelial cells from CRSwNP than those from control subjects, implying *S. aureus* induced physical epithelial dysfunction. Additionally, aberrant immune responses of nasal polyp tissues facilitate entry of *S. aureus* into tissues. *S. aureus* directly contributes to the initiation of Th2 inflammation by fast induction of epithelial-derived innate cytokines including thymic stromal lymphopoietin and IL33 in nasal polyp tissues, not in healthy turbinate mucosa whereas *S. epidermidis* did not induce these cytokines. In addition to the direct role of bacterial substances in developing Th2 inflammation, nasal bacteria may be causative allergens in CRS, especially refractory CRSwNP. 10% - 37% of isolated IgE antibodies specifically recognized surface structure of nasal bacteria including *S. aureus*, *S. pyogenes* and *H. influenza* and contained relatively large numbers of mutations in the variable regions of immunoglobulin heavy chain. Through High-throughput DNA sequencing immunoglobulin analysis, it proved that NP-derived IgE shared connectivity with IgG and IgA but not IgM, indicating class-switching to IgE within lineages after accumulation of somatic mutations in NPs. Nasal bacteria-specific IgE in nasal polyps originated from polyp-residing IgG+ and IgA1+ germinal center B-like cells. In brief, protective antibacterial response in healthy conditions can be converted into Th2 inflammatory responses in CRSwNP. Lastly, this speaker will present his study results about the role of superantigens in the activation of Th2 cells in CRSwNP in detail.

#### SY7-3

#### How to treat eosinophilic chronic rhinosinusitis in patients with bronchial asthma -Total care for type2 airway inflammation

**Mikiya Asako**

*Department of Otolaryngology, Head & Neck Surgery, Allergy Center, Kansai Medical University Medical Center, Japan*

Eosinophilic chronic rhinosinusitis (ECRS) is a serious, chronic inflammatory disease that predominantly displays a type 2 inflammatory signature. ECRS and type 2 asthma share the same inflammatory pathophysiology and are frequent comorbidities, as up to 67% of patients with ECRS have comorbid asthma. ECRS with BA is definitely the systemic disease of airway, although the patients are treated separately with ENT doctor and respiratory medicine doctor.

As a rational therapeutic strategy, we focused on the ICS exhalation through the nose (ETN) treatment for asthmatics with ECRS. We have been treated the patients with ECRS have comorbid asthma, with ENT & Internal Medicine doctor in the same room of our clinic. Airway medicine is the concepts for the total airway treatment with ICS ETN combined with full-house ESS. The endpoints for the surgical therapy is to make a drug delivery root for sinuses and the reduction of the inflammatory mucosa and eosinophilic mucin to control the airway inflammation. Although airway medicine is reasonable and the half recurrence rate compared to JESREC study, the additional therapy is required for severe cases.

Biologics, including anti IgE, anti IL-5, anti IL-5Ra, and anti IL-4Ra have strong efficacy to control of type2 airway inflammation.

Here, we present our strategy for type2 upper and lower airway inflammation based on the concepts of airway medicine in this symposium.

## Symposium 7

### How to manage eosinophilic chronic rhinosinusitis (ECRS)

#### SY7-4

#### How to manage eosinophilic chronic rhinosinusitis (ECRS): Medical treatments for ECRS

##### Jin-Young Min

Department of Otorhinolaryngology, Head & Neck surgery, Kyung Hee University, School of Medicine, Korea

Chronic rhinosinusitis (CRS) is characterized by local inflammation of the sinonasal mucosa, with symptoms persisting for at least 12 weeks. Although most investigators accept a classification based on phenotypes including CRS with nasal polyps and CRS without nasal polyps, a shift of approach strategy from phenotypic towards endotyping is necessary for implementation of precision medicine.

Among the endotyping classification, CRS can be subdivided into two types based on eosinophilic inflammation: eosinophilic CRS (ECRS) and non-eosinophilic CRS (Non-ECRS). ECRS and Non-ECRS show distinct clinical features, prognosis, and immunopathologic characteristics. As tissue eosinophilia has been implicated in treatment outcome, strategies for blocking eosinophil recruitment could contribute to treatment for ECRS. Up to now, topical glucocorticosteroids, short-term oral glucocorticosteroids, and long-term antibiotics (doxycycline) are considered for ECRS treatment.

Glucocorticosteroids target type 2 inflammatory responses better than non-type 2 responses. However, glucocorticosteroid resistance has been observed even in type 2-dominant CRS patients, thus the use of glucocorticosteroids might not be efficacious in some patients with ECRS. Long-term doxycycline treatment can also be used in ECRS patients. Additionally, antagonists of oral prostaglandin D2/chemoattractant receptor-homologous molecule expressed on TH2 cells also can target type 2 immune reactions in ECRS patients.

Another treatment option for ECRS especially in patients with nasal polyp is biologics, targeting the type 2 inflammatory mediators such as IL-4, IL-5, IL-13, and IgE resulting in reduction of eosinophilia as a secondary phenomenon. Mepolizumab primarily target activation and survival of eosinophils in tissue and peripheral blood. Omalizumab targets free total serum IgE. Dupilumab acts as an antagonist IL-4-receptor alpha. Recently, the U.S.FDA has been approved dupilumab to treat adult with CRSwNP. This is the first treatment approved for inadequately controlled CRSwNP.

Altogether, identification of underlying immunopathologic mechanisms of ECRS is key to developing medical treatment strategies for ECRS, especially in patients with uncontrolled severe disease.

#### SY7-5

#### Endoscopic sinus surgery for olfactory dysfunction caused by eosinophilic chronic rhinosinusitis

##### Masayoshi Kobayashi

Department of Otorhinolaryngology-Head and Neck Surgery, Mie University Graduate School of Medicine, Japan

##### I. Introduction

Eosinophilic chronic rhinosinusitis (ECRS) is a refractory disease and induces conductive olfactory dysfunction in most cases. An endoscopic sinus surgery (ESS) is often applied to cases in which treatment with steroid is not so effective or steroid is difficult to use for its side effects. Critical points of the ESS for improving olfactory dysfunction are to restore airflow of the olfactory cleft and superior meatus of nose and to open the ethmoidal sinus. However, inappropriate operation in olfactory cleft may cause mucosal adhesion and idiopathic olfactory loss. Therefore, delicate and careful manipulation is required. Here we show how to perform ESS for ECRS to improve olfactory dysfunction.

##### II. Methodology

For ECRS cases, full-house ESS is applied to make sinonasal airflow condition better. Since olfactory cleft is narrow and its mucosa bleeds easily, suctioning tools as suction curette and microdebrider are helpful to get clear surgical view and remove polyps in the olfactory cleft. Especially, rectangle microdebrider is useful for safe manipulation in the cleft, preventing damage to the cribriform plate. If many polyps occupied the olfactory cleft and wounded surface is wide after removing polyps, we insert gelatin sponge into the olfactory cleft and inject steroid solution into the sponge to prevent mucosal adhesion and scar formation.

##### III. Results

In the ESS cases, 81% of the cases could restore their olfactory function after the surgery. In the cases applied the gelatin sponge-steroid method, 86% of the cases could restore their olfactory function after the ESS.

##### IV. Conclusion

ESS is useful to restore olfactory function caused by refractory ECRS when using appropriate surgical techniques.

## Symposium 7

### How to manage eosinophilic chronic rhinosinusitis (ECRS)

**SY7-6**

#### Surgical treatments for ECRS

**Ilho Park**

*Korea University College of Medicine, Korea*

Type 2 inflammation is characterized by cytokines IL-4, IL-5 and IL-13 as well as activation and recruitment of eosinophils and mast cells. Recent research has revealed that patients with type 2 endotype tend to be much more resistant to current therapies. It has been shown repeatedly in several studies that patients with eosinophil dominant CRSwNP (ECRS or type 2 endotype CRS) have the high level of polyp recurrence after surgery.

So far, there has been no significant disagreement on the appropriate surgical timing for the treatment of ECRS. In the treatment of CRS, earlier surgery after diagnosis was beneficial to patients compared with prolongation of pharmacologic treatment and later surgery. However, high recurrent rate of ECRS raises the question of whether surgery is the right choice for the treatment of sinusitis. If the effect of surgery lasts only a few months, we should reconsider the need for surgery in the treatment of ECRS. Furthermore, eosinophilic CRS has been shown not to be associated with ostiomeatal occlusion.

There are two strategies to maintain long-lasting effects of surgery. The one strategy is to operate more extensively compared to conventional functional surgery. Reboot approach, focusing on removal of the inflamed mucosa from all sinuses was introduced a few years ago. Preliminary data showed that the reboot approach resulted in fewer recurrences. Even if the surgery is not as extensive as a reboot surgery, some studies showed that radical surgery for ECRS prolongs recurrence time and improves olfaction, rhinorrhea, and quality of life. The other strategy is to delay or prevent recurrence by coupling FESS with postoperative continued medical therapy.

## Symposium 8

### Otologic Surgery

**SY8-1**

#### Swing-Door Overlay Tympanoplasty: Surgical Technique & Results

**Shi Nae Park**

*Department of Otorhinolaryngology-HNS, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Korea*

Classical overlay tympanoplasty is one of the well-known surgical technique for chronic otitis media. Disadvantages of overlay tympanoplasty are its difficulty in surgical technique, frequent lateralization of the graft and longer healing time compared to underlay tympanoplasty. Swing-Door overlay tympanoplasty is a modified technique of classical overlay tympanoplasty which takes all advantages of overlay tympanoplasty while overcomes the disadvantages of classical one. It is a highly successful surgical technique suitable for all types of tympanic membrane perforations. No gelfoam packing in the middle ear cavity is possible in this technique. Therefore, earlier and better hearing results after the surgery can be achieved compared to the tympanoplasty with gelfoam packing. Overall graft uptake rate of our swing-door overlay tympanoplasty was over 98.5% and the air-bone gap less than 20dBHL after the surgery has been observed up to 85% of the patients. In this talk, a step by step surgical technique of swing-door overlay tympanoplasty will be introduced with its long-term surgical results.

## Symposium 8

### Otologic Surgery

#### SY8-2

### Strategies for approaching the round window in patients with congenital aural atresia

**Hiroshi Hidaka<sup>1</sup>**, Ryoukichi Ikeda<sup>2,4</sup>,  
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Congenital aural atresia (CAA) is a relatively common anomaly that occurs in approximately 1 in 10,000 to 20,000 people. It is not only due to the hypoplasia of the external auditory canal (EAC) but also represents underdevelopment of the whole temporal bone such as the auricle, middle ear, and occasionally the inner ear structures.

Both audiologic and radiologic evaluation prior to any intervention is essential to select the most appropriate therapy. Middle ear reconstruction, Vibrant Soundbridge (VSB, MedEL, Innsbruck, Austria), and Bone Conduction Implants have been reported to restore the hearing in patients with CAA. A higher Jahrsdoerfer score or modified Jahrsdoerfer score predicts a better post-middle ear reconstruction hearing outcome.

The VSB is a semi-implantable hearing aid with an external audio processor and internal implant that includes the floating mass transducer (FMT). Although FMT can be coupled to a variety of middle ear structures in patients with conductive or mixed hearing loss, dislocation of the facial nerve (FN) or absence of a mobile stapes would result in unfavorable outcomes. Comparable benefits from round window (RW) FMT placement have recently been described in patients with mixed or conducting hearing loss. First, we report that VSB placement to the RW via the retrofacial approach with partial removal of the stapedial muscle which can be a feasible alternative in CAA cases associated with an anteriorly and laterally positioned aberrant FN.

Although the FN has been reported to be more laterally and anteriorly displaced in CAA patients, findings of these previous studies have been attributed to comparisons between CAA patients and other cases with normal auricles. Conversely, unilateral atresia would offer ideal comparisons between the normal ear with patients who are completely age and sex matched. Again, detailed investigations of the stapedial muscle

(SM) in atresia patients have yet to be adequately conducted. Secondly, we thus analyze image variations in the mastoid segment of the FN and SM in 9 patients with unilateral CAA. According to the CT measurement, the SM is located more posteriorly to the FN in CAA patients, and this is mainly attributed to the laterally and anteriorly displaced FN.

## Symposium 8

### Otologic Surgery

#### SY8-3

#### Malleo-stapedotomy: indication, procedure & outcome

**Ja-Won Koo**

*Seoul National University Bundang Hospital, Korea*

The most frequent and initially considered surgical procedures for stapes fixation is incus stapedotomy. Hearing outcome is excellent in most patients. However, revision surgery may be necessary when hearing outcome is not satisfactory after initial surgery, and the revision surgery frequently be more complicated than the initial surgery. Many unwanted surgical problems or anatomical alterations can be encountered even in the initial stapes surgery in which piston wire prosthesis cannot be anchored to the incus long process necessitating malleo-stapedotomy (MS). Possible situations considering MS are hypoplastic Incus long process, iatrogenic removal of incus before evaluating stapes mobility, fracture of incus long process, incus body or malleus head fixation and etc. Out of 198 stapes surgery, 13 MS was performed in 12 patients. Etiology of stapes fixation, complications, surgical outcome of MS, and prior surgeries before MS were reviewed. Since 6.6% of the stapes surgeries were MS, the surgeon must prepare for the procedures during stapes surgery with the possibility of MS in mind.

#### SY8-4

#### Hearing Rehabilitation with Percutaneous Bone-Anchored Hearing System

**Il Joon Moon**

*Samsung Medical Center, Sungkyunkwan University, Korea*

Osseointegrated titanium implants were successfully introduced into clinical fields in the late 1970s by Tjellstrom et al. Since then, more than 100,000 of these devices have been implanted in patients with conductive, mixed, and unilateral sensorineural hearing loss. Although percutaneous bone-conduction implants (pBCI) are accepted as a gold standard therapy among bone-anchored hearing system, there are some complications of pBCIs mainly related to the skin around the abutment, such as skin overgrowth, infections, graft necrosis, and implant loss. Thus, recently, transcutaneous bone-conduction implants (tBCI) have been favored to reduce skin problems and obtain better cosmetic results. However, for the purpose of sound transmission and MRI compatibility, pBCIs still have advantages over tBCIs. To improve outcomes and overcome disadvantages, both the implant design and the surgical technique have evolved over the last few decades. In this lecture, clinical outcome of newly-introduced pBCI, Ponto (Oticon Medical) will be discussed. Overall, pBCIs are effective in the rehabilitation of conductive/mixed and unilateral hearing loss when conventional hearing aids cannot be used. However, advantages and limitations in terms of audiological and surgical perspectives should be carefully considered.

## Symposium 8

### Otologic Surgery

#### SY8-5

## Cochlear implantation has a positive influence on QOL in elderly adults

**Yumi Ohta**

*Osaka University, Japan*

#### Introduction:

As Japan has become a super-aging society, the increase in patient with dementia is a major social issue. The Lancet Commission showed that hearing loss was the largest potentially modifiable risk factor for dementia. Because pharmacologic therapy for dementia only has symptom-modifying effects, preventive strategies focused on the reduction of risk factors for dementia is more beneficial. But there is insufficient evidence that interventions in elderly patients with deafness can prevent the onset of dementia. In this study, we investigated whether cochlear implantation affects cognitive function in elderly with severe hearing loss.

#### Material and methods:

Data for patients that underwent CI surgery for profound bilateral sensorineural hearing loss were collected prospectively. Patients aged 65 years and older were recruited at our university hospital from 2013 to 2017. 21 patients (age range: 65-80 years) were included in this study.

The primary outcome measurement was the change in cognitive function three points assessed by Mini-Mental State Examination (MMSE): preoperatively, and at 1 and 2 years after surgery. The secondary outcome measurements were the followings; the Nijmegen Cochlear Implant Questionnaire (NCIQ), the Self-Rating Depression Scale (SDS), and hearing and speech recognition threshold assessment before CI, and 1 and 2 years after CI. The correlations between MMSE scores and NCIQ subdomain scores 2 years after surgery were evaluated.

#### Results:

The mean MMSE score, hearing threshold and speech recognition were significantly improved. The NCIQ scores were statistically significantly improved in all 6 subdomains after surgery. The scores of SDS were slightly improved but it was not statistically significant. Analysis of correlation between MMSE scores and NCIQ scores at 2 years after surgery showed only correlation

between MMSE and speech production among 6 subdomains of NCIQ.

#### Conclusion:

Since severe deafness has a higher risk of dementia, it is important result that cognitive function improved after cochlear implantation. The MMSE scores were correlated with the scores of speech production among 6 subdomains of NCIQ. It suggests that talking as an active activity supported by hearing may lead to maintenance of cognitive function.



## Symposium 8

### Otologic Surgery

#### SY8-6

### The benefits of cochlear implantation in congenital Single Side Deafness

**Jae Young Choi**

*Yonsei University College of Medicine, Seoul, Korea*

According to the recent systemic review paper regarding Cochlear Implantation in congenital single side deafness (SSD). The children shows benefits in Sound Localization Speech hearing, Spatial hearing and hearing quality. We experienced 5 cases of CI in congenital SSD. They have one side normal hearing ear and the other ear is totally deaf. The age at CI ranges from 22M to 97M. One patients have hypoplastic cochlear nerve and another one child experienced CMV infection. In addition to basic audiologic test, We evaluated the patient speech understanding in noisy condition. And we also evaluated the localization ability. Every child uses the device more than 6 hr per day. The hearing threshold is similar to the bilateral deaf patient Ling 6 score range from 0 to 6 and the average CAP score with CI is 4.5. The HINT test shows improved SNR with CI expect noise to deaf ear condition. The SSQ score improved in every 3 aspects. Although these optimistic results, there are several issues regarding the CI in congenital SSD. Especially, the critical age for CI in case of SSD is unclear and the rehabilitation is another big issue after CI in SSD. Site-specific stimulation is essential.

#### SY8-7

### Role of hearing preservation surgery for small and medium-sized vestibular schwannomas: hearing-focused strategy

**Naoki Oishi**

*Keio University, Japan*

The incidence of diagnosed sporadic unilateral vestibular schwannoma has increased since the 1970s primarily due to increasing access to MRI. When hearing preservation surgery is considered for small or medium-sized tumors, the natural history of the tumor is critical. The attempt of hearing preservation surgery should be considered only in the cases of possible tumor progression and hearing deterioration. The intraoperative continuous hearing monitoring system application offers excellent help for surgeons to achieve hearing preservation in vestibular schwannoma surgery. Based on our clinical cases, patients showing shorter auditory brainstem response (ABR) wave V latency (< 6.5 msec) or a higher otoacoustic emission (OAE) response during preoperative analysis were good candidates for the present hearing preservation surgery by the retrolabyrinthine approach. We have adopted a hearing-focused strategy for small to medium-sized tumors based on the preoperative ABR/OAE results.

## Symposium 9

### Robotic Head and Neck Surgery

#### SY9-1

### Current situation and evidence of TORS in Japan

**Akira Shimizu<sup>1</sup>**, Ichiro Tateya<sup>2</sup>, Kazunori Fujiwara<sup>3</sup>,  
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Japan

In Japan, da Vinci surgical system was introduced in 2009. At present, there are more than 350 systems nationwide. Transoral surgery; TORS began as a clinical trial in 2011. It was approved by pharmaceutical equipment in 2018 and the TORS training program was started in 2019. Insurance for TORS has been attached since April this year.

The systems currently operating in Japan are Si, Xi, and X, but Sp has not been installed. For this reason, in this session the main topic is about oropharyngeal cancer.

1. Conditions for starting TORS
2. TORS training courses in Japan
3. Results of cases of pre-Insurance acceptance
4. The current state of treatment for oropharyngeal cancer cases in the world and Japan
5. The future prospects

All TORS procedure regulates under committee of Japan Society for Head and Neck Surgery. The committee announce several restrictions.

The conditions for starting TORS are following.

- (1) facility requirements; ethical approval, team simulation, trouble shooting, invitation proctor for first case
- (2) operator requirements; Certificate of TORS advance training, specialist for head and neck cancer treatment, experience of over 20 transoral surgery cases or over 10 cases of TORS.

Advance training is mandatory in Japan. Advance course holds in Fujita health university cadaver surgical center. There are 3 proctors for advance training who had been learn the proctor training course in Germany.

Between August 2011 and January 2018, 56 patients underwent TORS in our country. There was no

conversion case. The 3-year and 5-year OS and DFS rates of all patients were 87.3% and 84.2%, and 77.9% 72.0%, respectively. There were 40 patients, which include 16 p16 positive patient, had oropharyngeal squamous cell carcinoma. The 5-year OS and DFS rates of p16 positive oropharyngeal cancer cases were 100%, and 79.1%, respectively. This reports included recurrence cases or previous head and neck or esophagus cancer treatment accepted. No significant difference was observed in either group, but the prognosis tended to be better in the p16-positive group and the group without prior treatment.

From 2019 to March 2022, it was operated under the training program, and the number of enforcement facilities was 15 and the number of cases was 105. Most of these cases were fresh cases. After the cases evaluation by the committee, the indication was decided for safety operation. Postoperative bleeding of Grade 3 or higher was observed in 3 cases, but no G5 case. We recommend risk management and ligation of the feeding artery for decreasing postoperative catastrophic bleeding.

The problem of case accumulation in Japan is that a lot of facilities will become to do TORS in the near future. If the facilities procedure different methods, it will be difficult to uniformize treatment and surgical strategies. So, the training programs and case registration systems will play an important role. We expect establish on the evidence of TORS from Japan.

## Symposium 9

### Robotic Head and Neck Surgery

#### SY9-2

#### Robotic Head and Neck Surgery at Fujita Health University Hospital

**Hisayuki Kato<sup>1</sup>**, Yusuke Hiei<sup>1</sup>, Shigeaki Mori<sup>1</sup>,  
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<sup>3</sup>Center of Head and Neck & Thyroid Endoscopic Surgery, Fujita University Hospital

Transoral Robotic Surgery (TORS) was approved in Japan on August 2018 as an indication of the Pharmaceuticals and Medical Devices Act. After that, the Japan Society for Head and Neck Surgery presented the guidelines and processes for performing TORS and has developed systems for performing physicians and facilities.

In our department, we performed a basic course using a pig on April 2019 and an advanced course using a cadaver donor in May. In July 2019, the first TORS in our hospital was performed using the DaVinci Xi surgical system.

We will report on the initial experience of TORS for 11 cases with early T stage oropharyngeal cancer (9 cases in the lateral wall, 1 in the superior wall, and 1 in the posterior wall) underwent from July 2019 to May 2021. Concurrent or preceding neck dissection was performed in 6 patients. The average time to carry out the TORS procedure was 99 min. Surgical complications were observed in 4 cases (tongue injury in 3 cases, tooth and tongue injury in 1 and postoperative bleeding in 1). The median fasting period following surgery was 2 days (1-18 days). The average hospital stay period was 15.5 days. The median observation period was 610 days (205-885 days). Locoregional recurrence was observed in two patients, one of whom died of the primary disease.

In the United States, more than 80% of T1/2 oropharyngeal cancer are treated mainly by surgery, including TORS, according to the national cancer database. As approximately 60-70% of oropharyngeal carcinomas are T1-2 cases in Japan, there are potentially a lot of cases indicated for TORS. The insurance coverage is expected for the spread of TORS in Japan.

In addition to TORS, our institution is in the process of preparing for Robot Assisted Transaxillary Surgery (RATS) and Transoral Robotic Thyroidectomy (TORT) with cadaver surgical training.

#### SY9-3

#### Advance in Robotic Neck Surgery

**Kyung Tae**

Department of Otolaryngology-Head and Neck Surgery, Hanyang University, Korea

To hide neck scarring and improve postoperative cosmesis, various remote access thyroid and parathyroid surgery via axillary, breast, anterior chest, postauricular facelift, or transoral approaches have been developed in the past 20 years. In addition to remote access approaches for thyroid and parathyroid, robotic or endoscopic procedures are used for submandibular gland, neck dissection, and benign neck masses, such as TGDCs and branchial cleft cysts.

Each method of endoscopic/robotic thyroid surgery has its advantages and disadvantages. Therefore, we need to understand the advantages and disadvantages of various endoscopic/robotic thyroid surgery. However, recently, transoral thyroidectomy has been increasingly adopted. It is less invasive than the transaxillary approach, BABA, and the facelift approach because the dissection area for the working space is smaller. In addition, it makes it easier to perform total thyroidectomies than the transaxillary and facelift approaches because it provides midline access to both thyroid lobes.

Robotic or endoscopic neck dissection has been developed for head and neck cancer using a modified or postauricular facelift approach to avoid long trans-cervical scars. Robotic SND or MRND via a postauricular facelift approach is feasible and safe, and a postauricular and occiput hairline incision is, on its own, sufficient for dissecting levels I-V. Also, various remote access approaches have been developed for lateral neck dissection for thyroid cancer. On the history of endoscopic and robotic lateral neck dissection for thyroid cancer, a minimally invasive video-assisted lateral neck dissection approach was performed in 2007. Since then, lateral neck dissection using axillary, breast, retroauricular, and BABA approaches have been developed. Also, recently, robotic lateral selective neck dissection using the transoral approach has been introduced. The surgical outcomes of robotic SND were comparable to conventional SND in selected patients with head and neck cancer and thyroid cancer.

In this session, I would like to present the evolution and advances in robotic and endoscopic neck surgery for thyroid cancer, head and neck cancer, and other neck procedures.

## Symposium 9

### Robotic Head and Neck Surgery

#### SY9-4

#### Advance in Robotic Thyroidectomy

##### Seung-Kuk Baek

*Otorhinolaryngology-Head and Neck Surgery, Korea University  
Medicine, Korea*

As the da Vinci robot was applied to thyroid surgery, various approaches have been introduced, and there have been many studies on the usefulness, oncological stability, and postoperative complications of robotic thyroid surgery. Currently, there are transaxillary approach, bilateral axillo-breast approach, retroauricular facelift approach, and transoral approach, which can be implemented in various ways depending on the strengths and weaknesses of each and the preference of surgeons or patients. The most significant advantage of robotic thyroidectomy are excellent postoperative cosmesis. However, the disadvantages of robot surgical devices being very expensive and the problems that they cannot be used in various medical institutions are still not resolved. In addition, cultural differences, longer operative times, and medicolegal issues are a barrier to the diffusion of robotic thyroidectomy. Even though robotic thyroid surgery is still lacking in its superiority compared to conventional thyroid surgery that has been performed in the past, the development of various approaches and the gradual development of robotic technology are expected to overcome these limitations in the future.

#### SY9-5

#### Robotic Neck Dissection

##### Yoon Woo Koh

*Department of Otorhinolaryngology / Yonsei Head Neck Cancer  
Center Yonsei University, College of Medicine, Korea*

## Symposium 10

### State-of-the-art Pediatric ORL

#### SY10-1

#### How to cope with pediatric patients with dizziness

**Fumiyuki Goto**

*Tokai University, Japan*

The number of pediatric patients complaining dizziness is much less than adults. However there is certain number of patients complaining dizziness in pediatrics. The etiology of pediatric cases is much different from adult cases. We should be aware of the full spectrum of disorders to reach a correct diagnosis, leading to prompt and effective treatment. It is sometimes difficult to make the correct diagnosis because children are often unable to describe their complaints. They may also find it hard to say how long attacks last and what provokes or accompanies them. A correct diagnosis, however, not only obviates unnecessary investigations and alleviates parental worries; it is the prerequisite for successful therapy. Careful clinical examination of oculomotor and vestibular function is the key step on the way to diagnosis. All disorders that are known in adults also occur in childhood, but the epidemiology differs and presentation is often atypical. There is no doubt that migraine-related vertigo syndromes are very common in children and adolescents 1). The differentiation of vestibular migraine and BPV of childhood is still a matter of debate, despite the fact that both are defined in the new edition of the classification of the International Headache Society.

Migraine-related syndromes account for about half of diagnoses in children with vertigo and dizziness 2). Somatoform vertigo 3) 4) is also a common condition, particularly in adolescence. The vast majority of vertigo and dizziness syndromes in childhood are benign. Although the prognosis of episodic forms is usually benign, the correct diagnosis is a prerequisite for targeted treatment.

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#### SY10-2

#### Tinnitus in pediatric population: an update

**Jae-Jin Song**

*Seoul National University Bundang Hospital, Korea*

Tinnitus is not an uncommon symptom in the pediatric population. However, despite its relatively high incidence, is still an unrecognized problem, particularly in children with normal hearing. Also, there is no consensus regarding the management of tinnitus in children. For instance, medications for pediatric tinnitus are not widely used due to a lack of evidence-based information. As tinnitus is frequently described by adults without any hearing loss, reports of tinnitus can be obtained also from a group of children without otological pathology. Recent studies distinguish pediatric tinnitus from adult tinnitus in terms of lower association with lower likelihood of reported anxiety and higher likelihood of improvement and resolution. Also, recent reports suggest that pediatric tinnitus is likely to have a higher chance of improvement by counseling alone or combination therapy without medication. In this talk, although still not widely studied, an update on pediatric tinnitus particularly focusing on its clinical features and treatment options will be discussed.

## Symposium 10

### State-of-the-art Pediatric ORL

#### SY10-3

#### Present issue in pediatric allergic rhinitis: How does it develop in early life?

**Sawako Masuda**

Department of Otorhinolaryngology, National Hospital Organization  
Mie National Hospital, Japan

Allergic rhinitis (AR) is one of the common diseases in children. The prevalence of AR in Japanese children is markedly increasing to the age of 10. In recent years, many medicines for children have been on the market, and sublingual immunotherapy has become one of the common treatments. However, many children were sensitized to various inhalation allergens in their early life. The sensitization rate to mites and cedar pollen are high in Japanese children. It is important to clarify how allergic rhinitis develops in young children.

The establishment of diagnostic criteria of AR in infants is the basic issue. It is difficult for young children to evaluate and express their own symptoms correctly. Invasive examinations are also hard to perform. We set up allergic rhinitis diagnostic chart for infants based on the presence of persistent nasal symptoms, nasal eosinophilia, and sensitization to house dust mite (HDM). Based on this chart, we classified children's rhinitis into eight groups, namely, Classical AR, Eosinophilic rhinitis, Suspicious AR, Non-Allergic rhinitis, Subclinical AR, Local eosinophilia, Sensitization, and No rhinitis.

To investigate the development of AR, we prospectively observed 304 infants under 2 years of age with atopic dermatitis and/or food allergy. The prevalence of Classical AR and AR-like phenotype (Eosinophilic rhinitis, Suspicious AR, and Subclinical AR) increased from 3.0% to 29.5%, and 18.4% to 65.0% in 2 years, respectively. Thus, the prevalence of an HDM-related AR and AR-like phenotype was markedly increased during infancy in high-risk children with atopic dermatitis and/or food allergy.

Is it possible to prevent children from developing AR? Several studies have suggested that allergen immunotherapy prevents novel allergen sensitization. However, there are still many problems to be solved.

#### SY10-4

#### Association of adenotonsillectomy with asthma and upper respiratory infection in children: A Nationwide Cohort Study

**Dong-Kyu Kim**

Hallym University, Korea

**Background:** Adenotonsillectomy is a common pediatric surgery for treating obstructed breathing or recurrent inflammation. However, despite the important roles played by the adenoid and tonsils in the development and function of the immune system, few concerns exist regarding long-term health consequences. This study investigated the potential association between adenotonsillectomy and the development of asthma and upper respiratory infections.

**Methods:** This propensity score-matched cohort study was conducted using data from the National Sample Cohort 2002-2013. In the asthma cohort, we used a Cox-proportional hazards model to analyze the hazard ratio of adenotonsillectomy for asthma events. In the upper respiratory infection cohort, equivalence tests of postoperative visits for upper respiratory infections were performed.

**Results:** The incidence of asthma was 66.97 (1000 person-years) in children who underwent adenotonsillectomy and 30.43 (1000 person-years) in those who did not. Adjusted hazard ratios of asthma were 2.25 (95% confidence interval, 1.96-2.57) in the adenotonsillectomy vs. non-adenotonsillectomy groups. In a subgroup analysis, children aged 5-9 years and living in metropolitan areas showed a higher incidence of subsequent asthma than those of other ages and residing in other areas. However, we could not identify any significant difference between the groups in terms of upper respiratory infection events in the 1 to 11 years postoperative period.

**Conclusions:** Adenotonsillectomy in children is associated with an increased incidence of pediatric asthma, with no significant impact on postoperative visits for upper respiratory infections.



## Symposium 10

### State-of-the-art Pediatric ORL

#### SY10-5

#### Management of obstructive post-tracheostomy granulation tissue in children

**Takaharu Nito**

*Saitama Medical University, Japan*

Recently, tracheostomy has been increasingly performed in infants and children, aligned with the improvements in neonatal and pediatric ICU care. The most frequent late complication of tracheostomy is the formation of granulation tissue (GT). GT can occur at various sites within the trachea—either at the stoma, the cuff site, or the distal tip of the tracheostomy tube (TT). In particular, it is important to manage GT at the distal tip of TT because it may cause airway narrowing or occlusion. Irritation of the tracheal mucosa by TT causes ulceration, and GT forms accompanied by infection. One of the major causes of infection in children who had undergone tracheostomy is aspiration. The fundamental strategy against GT formation is removal of its cause. First, the distal tip of TT should be prevented from causing irritation by using the appropriate TT (in terms of material, size, length, angle, and cuffed or uncuffed) and adjusting the insertion depth of TT. Adjustable flange TTs are useful. In addition, steroids are administered systemically or by inhalation to reduce GT. When GT nearly occludes the trachea, direct injection of steroids to GT or GT excision using an electrocautery snare should be carried out. If the patient has chronic aspiration, surgery for preventing aspiration may be carried out. Because it is very important to detect the formation of GT as early as possible, the trachea should be observed by bronchoscopy during the time of tracheostomy tube exchange.

#### SY10-6

#### High flow assisted spontaneous ventilation for pediatric airway surgery

**Seong Keun Kwon**

*Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Korea*

Airway surgery requires an anesthetic technique that provides good exposure of the larynx while maintaining adequate oxygenation, ventilation, and depth of anesthesia. Since placing an endotracheal tube disturbs the field of vision, tubeless anesthetic techniques have been developed. Recent developments in critical care have found that high flow nasal oxygen, which provides heated and humidified oxygen via high flow nasal cannula, is a useful method to support breathing in patients who need respiratory supportive care, preoperative or postoperative oxygenation, or ventilatory support during bronchoscopy. High flow nasal oxygen has several physiological benefits including a lower dilution of inspired oxygen, generation of positive end expiratory pressure, and reduced upper airway resistance. High flow nasal oxygen contrasts with other tubeless anesthetic technique such as apneic anesthesia or jet ventilation in that it can supply warm and humidified oxygen at a high flow rate. To date, there have been few studies which applied the combined method of spontaneous respiration and high flow nasal oxygen to patients undergoing airway surgery. To our knowledge, there has been no previous research using this technique in airway surgery of children. The main purpose of this presentation is to highlight the feasibility and its clinical applications on pediatric airway surgery. We applied this technique since 2017 to pediatric airway surgery. The median age was 16.0 (1-215) months and the median weight 10.2 (2.4-38.5) kg. The median duration of spontaneous respiration was 40 (10-140) minutes. The airway procedures included diagnostic microlaryngoscopy, tracheocutaneous fistula excision, balloon dilatation, supraglottoplasty, laryngeal cleft repair, tracheoesophageal fistula cauterization, injection laryngoplasty, papilloma excision, and subglottic cyst removal. During these procedures, this anesthetic technique facilitated the evaluation of dynamic obstruction of the airway and the immediate outcome of surgical treatment, provided good surgical view, and thus allowed us to avoid tracheostomy. We conclude this method is an highly effective and safe option of anesthesia for pediatric airway surgery.

## Luncheon Seminar 1

### Paradigm shift in treatment strategy for head and neck cancer: What is changing, and what is the same?

#### LS1-1

### Paradigm shift in treatment strategy for head and neck cancer: What is changing, and what is the same?

#### Tomoya Yokota

*Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Japan*

Recent breakthrough in cancer immunotherapy employing immune checkpoint inhibitors (ICIs) has evolved into number of clinical trials with antibodies against PD-1, PD-L1, and CTLA-4 for patients with squamous cell carcinoma of head and neck (SCCHN). nivolumab and pembrolizumab as ICIs targeting PD-1 have a significant impact on the current treatment standards for recurrent and metastatic disease. The phase III clinical trial CheckMate-141 demonstrated that nivolumab is a standard therapy for patients with platinum-refractory diseases. The results of KEYNOTE-048 suggest that pembrolizumab monotherapy and pembrolizumab plus platinum-based chemotherapy are novel standards for platinum sensitive diseases. The use of nivolumab and pembrolizumab has been approved for clinical use in the treatment of patients with recurrent and metastatic SCCHN in Japan. These practice-changing data open the door to a new era of tailor-made medicine in treatment of recurrent and metastatic SCCHN, based on tumor burden, clinical stability, and PD-L1 status (CPS). Furthermore, ICIs in combination with chemoradiotherapy or in perioperative setting have been investigated for locoregionally advanced disease.

## Luncheon Seminar 2

### EAS in Japan & Korea

#### LS2-1

### EAS with longer electrodes

#### Hidekane Yoshimura

*Dept. of Otorhinolaryngology, Shinshu University, Japan*

Electric-acoustic stimulation (EAS) has emerged as a standard treatment for patients with high-frequency hearing loss. EAS is usually performed with short electrodes of 16–24 mm in length. However, most EAS recipients may gradually lose residual acoustic hearing in the implanted ear over time. In these cases, EAS eventually needs to be converted to pure ES via cochlear implants (CIs), thus increasing the disadvantages for patients treated with short electrodes if residual hearing is lost or if it is unsuitable for EAS. To avoid this dilemma, EAS using longer electrodes, without causing significant intra-cochlear damage would be ideal.

We have previously reported that hearing preservation (HP) is independent of the length of the inserted cochlear implant (MED-EL FLEXsoft [31.5 mm] vs. FLEX28 [28 mm] vs. FLEX24 [24 mm]) (Yoshimura et al., 2020a). We have also documented that in cases meeting the EAS criteria with longer electrodes, residual hearing can be preserved in all patients (Yoshimura et al., 2020b). EAS with longer electrodes can offer broader cochlear coverage, resulting in natural frequency matching compared with shorter electrodes. Therefore, reliable HP after deep insertion of longer electrodes could extend the indications for CI to cases with less severe deafness and more residual hearing, as in EAS cases.

We previously reported that genetic testing could provide the etiology of hearing loss as well as further information regarding the state of residual hearing (Usami et al., 2012). For example, most patients with CDH23 mutations initially present with high-frequency hearing loss. Subsequently, their residual hearing at low frequencies deteriorates gradually over time, suggesting that the clinician should provide longer electrodes for broader coverage of the frequency range. Additionally, even when the causative gene of hearing loss is not identified, ongoing low-frequency hearing loss is sometimes observed in the implanted ear or in both ears, indicating that longer electrodes should be selected. Taken together, the clinician should select the proper array length for each individual according to the “future” (not current) status of residual acoustic hearing based on the etiology and/or the natural course of hearing loss to allow EAS users to optimize mapping toward more natural hearing.

## Luncheon Seminar 2

### EAS in Japan & Korea

#### LS2-2

### EAS in Japan – Current Status & Future

#### Hiroshi Yamazaki

*Hearing Research Division, Kobe City Medical Center General Hospital Center for Clinical Research and Innovation, Japan*

In Japan, Electrical Acoustic Stimulation (EAS) using the FLEX24 electrode has been available since 2009 for people with high-frequency hearing loss. EAS employs acoustic stimulation (AS) in the low-frequency range combined with electrical stimulation (ES) via a cochlear implant (CI). Recently, an increasing number of patients with residual hearing (RH-CI cases), not high-frequency hearing loss, undergo cochlear implantation. Several studies demonstrated that the residual hearing could be preserved even with the standard length of electrodes, longer than FLEX24. However, there is no established way to utilize their residual hearing in the RH-CI cases. Focusing on the long-term course of the adult EAS cases in our hospital, the low-frequency residual hearing on the implanted side slowly deteriorated over time. Although the efficacy of AS reduces as residual hearing worsens, EAS reprogramming prevented deterioration of EAS hearing performance. These results suggest that even patients who eventually become deaf can be gradually switched from EAS to CI while maintaining their hearing performance. Interestingly, many EAS users who have residual hearing below the EAS criteria several years after implantation feel that the addition of AS to ES improves sound quality. These data suggest that AS may also be helpful in RH-CI patients who show similar residual hearing to long-term EAS users.

We have one RH-CI patient who felt that at least shortly after cochlear implantation, the addition of the hearing aid improved his hearing compared to the CI alone. Considering that a CI processor and a hearing aid are worn in the same ear, the hybrid audio processor designed for EAS may be more practical for this patient. Since the current Japanese health insurance system does not allow the use of an EAS hybrid processor with a conventional CI, extending the EAS processor to RH-CI patients may improve the quality of hearing in this group.

As the number of RH-CI patients increases, the roles of EAS will become increasingly important as a hearing device that provides a smooth transition from hearing aids to CI.

#### LS2-3

### EAS in Korea – Current status & Future development

#### You-Ree Shin

*Soree Ear Clinic East Center, Seoul, Korea*

The combined electric acoustic stimulation (EAS) of one ear is a topic that has received considerable attention over the last 10 yrs. We are trying to preserve residual hearing (RH) as much as possible (surgical technique, electrode selection, gene analysis and preoperative cochlear measure et al.) and fit optimally according to RH change. Hearing habilitation should be individualized for each patient. We encourage patients and family support.

Questions about EAS:

Q 1. RH can be preserved?

In almost patients, the remaining hearing was sufficient to apply the planned EAS before the surgery. RH over a period of time (6 years after EAS) showed fluctuations below 2-4%/yr were the same as adults and children.

Q 2. Benefit through EAS?

EAS users benefited from more than one performance in objective evaluations (music or speech). The reason for not seeing the benefits in some cases was the loss of RH and the experience or willingness to use HAs. Directional gain was also observed in many EAS users, especially adults.

Q 3. How EAS users prefer EAS and keep EAS longer?

The majority of EAS users who had objective gains showed subjective satisfaction. Some users who did not experience HAs before surgery tend not to use EAS despite the objective gain. Most users were able to use EAS satisfactorily and continuously even though their hearing was deteriorated. If the hearing was not enough to be able to support EAS, it could be successfully switched to CI only. Among EPS users, there was a case that the natural acoustic hearing should be switched to EAS mode, in which case training was need to adapt.

Q 4. Special EAS considerations to the congenital deaf children?

Difficult to gather adequate information from infants on the amount of RH but we must measure behavioral thresholds for actual RH. Most of congenital deaf

## Luncheon Seminar 2

### EAS in Japan & Korea

children has RH even though ABR no response and can be benefited from HAs. A period of acoustic stimulation with HA prior to CI is critical. So early fit HAs and try to auditory training. Even if a low-frequency RH remains a little, the hearing should be preserved as much as possible and the EAS should be tried.

In the future, the robot-assisted surgery will allow for high precision surgery and reliable hearing preservation. Local drug delivery will focus on suppression of trauma reaction and local regeneration. Also biological therapies (gene therapy, stem cell transplantation) will support. Future electrode design will most likely improve the neuronal health by reducing insertion trauma, minimizing the inflammatory reaction and will focus on better electrode-nerve interfaces. Smaller device has continuously developed and improved coding strategies can enhance temporal and spectral resolution.

## Cafe Seminar

### New endotyping of chronic rhinosinusitis with nasal polyps

#### CS-1

### New endotyping of chronic rhinosinusitis with nasal polyps

**Takechiyo Yamada**, Yui Miyabe, Hiroki Tomizawa

*Otorhinolaryngology, Head and Neck surgery, Akita University, Japan*

**Background:** In allergic inflammation, the cells existing in the mucosa take up antigens and present them to produce specific IgE, but there is no clinical study that quantifies antigens that cause allergies in local tissues. Fungi can induce the formation of nasal polyps via epithelial damage and type-2 inflammation. *Aspergillus fumigatus* is the most common environmental allergen; however, the involvement of its specific antigens in local allergic reactions in nasal polyps has not yet been reported.

**Objective:** To investigate local allergic reactions to the *Aspergillus fumigatus* antigen, Asp f 1 in patients with CRSwNP.

**Materials and Methods:** Nasal polyp tissues were collected from 103 patients with CRSwNP during surgery and homogenized. Tissue eosinophil counts and Asp f1, *Aspergillus*-specific IgE, type 2 cytokines and galectin-10 levels were measured in nasal polyps.

**Results:** Eighteen cases (15.9%) of 103 patients were positive for Asp f 1 and were divided into two groups based on Asp f 1 levels. Asp f 1 levels positively correlated with *Aspergillus*-specific IgE levels ( $r=0.68$ ,  $p<0.01$ ). *Aspergillus*-specific IgE ( $p<0.01$ ) levels in nasal polyps were significantly higher in the high Asp f 1 group than in the low Asp f 1 group although no significant differences were observed in IgM levels between these groups. Furthermore, Asp f 1 levels positively correlated with tissue IL-4 levels ( $r=0.85$ ,  $p<0.0005$ ) or tissue galectin-10 levels ( $r=0.54$ ,  $p<0.01$ ).

**Conclusion:** This is the first study to quantify the levels of *Aspergillus fumigatus* antigen in the nasal polyps of patients with CRSwNP. The presence of Asp f 1 might explain the local type 2 allergic reaction to *Aspergillus fumigatus* in CRSwNP.

## Afternoon Seminar

### A New Era in the Treatment of the Olfactory Disorder with Infection and Allergic Rhinitis

AS-1

#### A New Era in the Treatment of the Olfactory Disorder with Infection and Allergic Rhinitis

**Eri Mori**

*Department of Otorhinolaryngology, The Jikei University School of Medicine, Tokyo, Japan*

In contrast to other sensory organs, the sense of smell had attracted less medical attention. As information associated with life is mainly obtained through visual and auditory means, loss of the sense of smell is sometimes less likely to be subjectively recognized and may have less impact on our daily lives. While vision and hearing tests are part of the physical examination, olfaction is not as common, and people will have less opportunity to be aware of it. In addition, not many medical and educational institutions assess the degree of olfactory disorder before treating it. Therefore, neither assessment nor treatment has been well established.

However, the situation surrounding olfactory disorder is dramatically changing by COVID-19 pandemic. Patients infected of COVID-19 have often experienced olfactory and gustatory abnormalities, the fact of which had attracted considerable media attention. And people all over the world could become aware of their sense of smell and taste again. Therefore, this is an opportunity to make further development in the assessment and treatment of olfactory disorder.

The loss of the sense of smell deprives sufferers of their quality of life as well as the options in life. While chronic sinusitis is the most common cause of olfactory disorder, post upper respiratory infectious (post-URI) olfactory dysfunction and the idiopathic olfactory dysfunction with no identifiable cause are also relatively common. The association with allergic rhinitis and neurodegenerative diseases has also attracted attention.

In this seminar, I will talk in simple terms about the mechanisms of olfactory perception and the pathology and treatment of olfactory disorder. I would hope that you feel free to join the discussion of this short session.

## Poster (Free Papers)

### Head & Neck (Clinical)

FP1-1

#### Clinical significance of visiting ENT department when cervical lymphadenopathy is recognized in terms of early detection of HNC

**Kohei Matsumoto<sup>1</sup>**, Chisei Satoh<sup>2</sup>,  
Fujinobu Tanaka<sup>1</sup>, Yoshihiko Kumai<sup>2</sup>

<sup>1</sup>National Hospital Organization Nagasaki Medical Center, Japan

<sup>2</sup>Department of Otolaryngology-Head and Neck Surgery, Nagasaki University

#### [Objective]

To clarify the conditions of selection of the initial clinical department according to the typical symptoms of head and neck cancer (HNC) patients

#### [Study Design]

Retrospective study

#### [Materials and Methods]

One hundred twenty five HNC patients who underwent chemoradiotherapy at ENT department of Nagasaki University Hospital (April 2013 to March 2019) were involved. We examined the effects of differences with initial clinical departments on both waiting period for the treatment and recurrence-free survival. Additionally, to clarify which clinical department to choose when the initial symptoms peculiar to HNC were actually recognized, we conducted a questionnaire survey on 114 new patients who visited ENT department at Nagasaki Medical Center.

#### [Results]

The waiting period for treatment in cases other than ENT department was 17 days longer than those visited to ENT department ( $p < 0.0001$ ), and the recurrence-free survival time was shorter ( $p = 0.0443$ ). Cases with cervical lymph node metastasis were less likely to visit other than ENT department. ( $P = 0.0005$ ). These were statistically significant. In a questionnaire survey, the percentage of subjects who chose to visit ENT department for cervical lymphadenopathy (12%) were significantly lower than other symptoms peculiar to HNC, such as swallowing pain (54%;  $p = 0.0193$ ), and hoarseness (54%;  $p = 0.0193$ ), respectively.

#### [Conclusion]

Cervical lymphadenopathy is significantly less frequent at first visit to ENT department when it is initially recognized, compared to other symptoms peculiar to HNC. It should be strongly enlightened to visit ENT department soon when cervical lymphadenopathy is recognized.



Poster (Free Papers)

Head & Neck (Clinical)

FP1-2

# A new staging system for olfactory neuroblastoma

**Akira Nakazono**, Hiroaki Motegi, Yuji Nakamaru, Masanobu Suzuki, Shigeru Yamauchi, Yukitomo Ishi, Aya Honma, Shogo Kimura, Miki Fujimura, Akihiro Homma

*Otolaryngology-Head and Neck Surgery, Hokkaido University, Japan*

**Background:** Olfactory neuroblastoma (ONB) is a rare malignant tumor arising from the olfactory neuroepithelium. Endoscopic skull base surgery has become a standard of care for ONBs; however, there has been no staging system on which to base the selection of endoscopic skull base surgery. The aim of this study was to design a new staging system for the selection of different surgical approaches.

**Methodology/Principal:** Twenty patients with ONB treated between 2003 and 2019 were included. We developed the new staging system (Hokkaido staging system) in consideration of the indications for endoscopic skull base surgery and evaluated its usefulness retrospectively.

**Results:** In the Hokkaido staging system, 2 patients were diagnosed with stage I, 7 with stage II, 10 with stage III, and 1 with stage IV. All the cases with stage I and II underwent endoscopic skull base surgery alone, and all the cases with stage III required craniotomy. The 10-year overall survival rate for stage I, II, III, and IV was 100%, 100%, 100% and 0%, respectively ( $p < 0.001$ ). The 10-year disease-free survival rate for stage I, II, III, and IV was 100%, 85.7%, 66.7%, and 0%, respectively ( $p < 0.001$ ). The 10-year local control rate for stage I, II, III, and IV was 100%, 100%, 66.7%, and 0%, respectively ( $p < 0.001$ ).

**Conclusions:** The Hokkaido staging system appears to be useful for selection of the appropriate surgical approach as well as in the prediction of the prognosis for ONB.

FP1-3

# Clinical characteristics of acinic cell carcinoma and secretory carcinoma of the parotid gland

**Yusuke Ayani**, Takaki Inui, Masaaki Higashino, Tetsuya Terada, Shin-Ichi Haginomori, Ryo Kawata

*Department of Otorhinolaryngology-Head & Neck Surgery, Osaka Medical and Pharmaceutical University, Japan*

**Purpose:** Mammary analogue secretory carcinoma (SC) of the parotid gland is a relatively uncommon cancer associated with the ETV6-NTRK3 fusion product similar to breast cancer. The clinical characteristics and outcome of treatment were reviewed for patients with this tumor at our hospital. **Methods:** In this retrospective case series, 24 patients with a diagnosis of acinic cell carcinoma (AcCC) of the parotid gland were classified as having either SC or AcCC based on analysis of the ETV6-NTRK3 fusion gene. These two groups were compared with respect to their clinical and imaging characteristics (MRI/US), cytologic findings, accuracy of fine-needle aspiration cytology and frozen section, treatment outcomes, and immunohistochemical findings. **Results:** Based on re-classification by ETV6-NTRK3 fusion gene analysis, the diagnosis was SC in 14 patients and AcCC in 10 patients. The SC group had a significantly higher proportion of male patients and was also significantly younger than the AcCC group. Imaging studies revealed that SC was significantly more likely to show internal heterogeneity. Correct grading of both tumors was comparable by fine needle aspiration, with the rate being 60% for AcCC and 50% for SC. Diagnosis by frozen section biopsy diagnosis obtained the correct grade in 90% of the AcCC group and 93% of the SC group. **Conclusions:** In 24 patients previously diagnosed with AcCC, re-analysis of the ETV6-NTRK3 fusion product indicated that 14 patients actually had SC. Although AcCC and SC show similarities of their biological aggressiveness and prognosis, patients with SC were significantly more likely to be male and younger.



Poster (Free Papers)

Head & Neck (Clinical)

FP1-4

**Short-term outcome of 69 external auditory canal cancer treated at a single institution**

**Takeshi Tsutsumi**, Takahiro Asakage,  
Yoshiyuki Kawashima, Yosuke Ariizumi  
*Otorhinolaryngology, Tokyo Medical and Dental University, Japan*

External auditory canal cancer is an extremely rare entity, with an annual incidence of 1 in a population of 1 million. Due to its rarity and surgical difficulty caused from complex anatomy of the temporal bone, no general consensus has been reached yet on the treatment protocol. In this paper, we present the short-term outcomes of 69 cases with external auditory canal cancer, managed from July 2015 to March 2021 in Tokyo Medical and Dental University Hospital.

Fifty-seven cases were treated with surgery (42 primary / 6 salvage surgical group) consisted of lateral temporal bone resection (n=43), subtotal temporal bone resection (n=12), and partial resection (n=2), while 12 cases without surgery (non-surgical group) consisted of TPR-RT (n=6, TPF-RT group), CDDP-RT (n=1) and heavy particle therapy (n=4). In the surgical group, 48 patients were pathologically diagnosed as SCC, 5 ACC, and 4 adenocarcinomas, while in the non-surgical group, 8 patients were diagnosed as SCC and 4 ACC.

Analyses of the short-term outcomes of cases with SCC revealed no statistically significant difference of OS, DSS, and DFS between the primary surgical group and the TPF-RT group. In the primary surgical group, postoperative recurrences occurred within a year of surgery in most cases. Only the positive surgical margin, determined by postoperative histopathology, was associated with poorer outcomes. Patients with postoperative recurrence consisted of 4 cases with salvage surgeries, 3 cases with rapid preoperative progressions, and 4 with recurrent neck lymph node metastasis. Among the cases with advanced disease, no statistically significant differences in the outcomes were observed between the primary surgical and TPF-RT groups.

FP1-5

Withdrawn

Poster (Free Papers)

Head & Neck (Clinical)

FP1-7

**Surgical strategy for squamous cell carcinoma of the external auditory canal: management of locally advanced cases**

**Naoki Nishio**<sup>1</sup>, Seiya Goto<sup>1</sup>, Kenichiro Iwami<sup>2</sup>,  
Tadao Yoshida<sup>1</sup>, Takashi Maruo<sup>2</sup>,  
Nobuaki Mukoyama<sup>1</sup>, Hidenori Tsuzuki<sup>1</sup>,  
Sayaka Yokoi<sup>1</sup>, Akihisa Wada<sup>1</sup>, Mariko Hiramatsu<sup>1</sup>,  
Yuichiro Hayashi<sup>1</sup>, Yuzuru Kamei<sup>1</sup>, Masazumi Fujii<sup>3</sup>,  
Yasushi Fujimoto<sup>2</sup>, Michihiko Sone<sup>1</sup>

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<sup>2</sup>Aichi Medical University

<sup>3</sup>Fukushima Medical University

**Objective:**

Surgical indications for advanced-stage squamous cell carcinoma (SCC) of the external auditory canal (EAC) are highly dependent on the skull base surgery team. The aim of this study was to evaluate the surgical outcomes in patients with SCC of the EAC and to clarify the surgical indication of far advanced cases using the T4 subclassification.

**Methods:**

Patients with SCC of the EAC who underwent curative treatment from 2002 to 2021 at our hospital were retrospectively reviewed. Clinical and surgical results, including operative data, overall survival (OS), and disease-specific survival (DSS), were analyzed. To clarify the surgical indication for advanced-stage tumors, we proposed the T4 subclassification.

**Results:**

In the 46 patients included in the study, 8 patients had T1 tumors, 10 had T2 tumor, 5 had T3 tumors, and 23 had T4 tumors. The 5-year DSS with T1, T2, T3, and T4 tumors were 100, 85.7, 100, and 61.7%, respectively. No prognostic impacts for margin status were found between the 5-year OS and DSS ( $p=0.23$  and  $0.13$ , respectively). Patients with far-advanced-stage (T4b) tumors were significantly associated with shorter DSS than those with early-stage (T1/T2) and advanced-stage (T3/T4a) tumors ( $p=0.007$  and  $0.03$ , respectively).

**Conclusion:**

The present study focused on patients with SCC of the EAC at a university hospital over a period of 20 years, especially with skull base involvement, and a T4 subclassification was proposed. Complete tumor resection in an en bloc fashion could help achieve a good survival rate even in patients with locally advanced tumors.

FP1-8

**Clinical outcomes of Nivolumab and its prognostic factors related to tumor immunity in head and neck malignancies**

**Eiji Kobayashi**<sup>1,2</sup>, Satoru Kondo<sup>1</sup>,  
Hisashi Sugimoto<sup>1</sup>, Tomokazu Yoshizaki<sup>1</sup>

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<sup>2</sup>Toyama Prefectural Central Hospital, Japan

Nivolumab, an anti-programmed death 1 (PD-1) monoclonal antibody, has been approved as the first immune checkpoint inhibitor in head and neck malignancies. The agent has a completely novel mechanism and is expected to improve prognosis of patients refractory to conventional therapies. Several reports suggest that cetuximab or radiotherapy affect response to nivolumab by modulating tumor immunity and that nivolumab could have unique prognostic factors different from that of conventional agents.

We performed retrospective analysis of 39 cases of head and neck malignancies which were administered nivolumab before September 2020.

Mean age were 67.3 (43 - 85) years old. 30 were male, and 9 were female. 30 were squamous cell carcinoma (SCC), 4 were malignant melanoma, and 5 were other histologies. 9 cases have primary sites in oral cavity, 8 in hypopharynx, 7 in larynx, and 7 in nasal cavity or paranasal sinus. Median duration of follow-up was 235 days. Median overall survival (OS) was 10.1 months, and median progression free survival (PFS) was 3.0 months. Overall response rate (ORR) was 17.9%, and disease control rate (DCR) was 46.2%. Analysis exclusive to SCC had similar results.

We also performed stratification by history of treatment by cetuximab or radiotherapy. SCC cases with prior treatment by cetuximab tended to have better OS than cases without prior treatment by cetuximab, though statistically not significant. Prior or post treatment by radiotherapy showed no clear difference.

These results demonstrated efficacy of nivolumab in real-world data, similar to that of Checkmate 141 trial. Our results suggest that administration of nivolumab should be considered in relatively early phase of therapeutic sequence, especially prior to cetuximab.

Poster (Free Papers)

Head & Neck (Clinical)

FP1-9

**Protective effects of sodium thiosulfate for Cisplatin -mediated ototoxicity in patients with head and neck cancer**

**Hisashi Sugimoto**, Eriko Ishikawa, Miyako Hatano, Tomokazu Yoshizaki  
*Kanazawa university, Japan*

**Conclusions:** Intra-arterial high-dose cisplatin chemoradiation (CRT-IA) with sodium thiosulfate causes relatively less severe cisplatin ototoxicity than intravenous cisplatin chemoradiation without sodium thiosulfate (CRT-IV). The results of this study also suggest that early detection of ototoxicity is possible by testing the hearing loss at ultra-high frequencies.

**Objectives:** To investigate protective effects of sodium thiosulfate (STS) against Cisplatin ototoxicity.

**Methods:** Between 2011 and 2013, 18 patients with head-and-neck carcinomas were treated with intra-arterial infusions of high-dose cisplatin (range 100 mg/body-180 mg/body, mean 111 mg/body, range 2-5 courses, mean 3.6 courses) and systemic administration of cisplatin (range 66-185 mg/body, mean 130 mg/body, range 1-3 courses, mean 2.6 courses) and concurrent radiation therapy (range 60-70 Gy, mean 69 Gy). Cisplatin was neutralized by STS in CRT-IA not in CRT-IV.

**Results:** Intra-arterial infusion in the high-dose cisplatin group caused significant hearing loss at ultra-high frequencies 10 and 12 kHz ( $p = 0.028, 0.039$ ). Whereas the group receiving systemic administration of cisplatin had significant hearing loss at high frequencies of 8 and 10 kHz ( $p = 0.016, 0.027$ ).

FP1-10

**Three Cases of Non-Occlusive Mesenteric Ischemia Developed after Head and Neck Cancer Therapy**

**Kotoko Ito**, Hiromi Nagano, Hirohisa Matsuzaki, Mizuo Umakoshi, Junichiro Ohori, Yuichi Kurono  
*Kagoshima University, Japan*

Non-occlusive mesenteric ischemia (NOMI) causes intestinal necrosis due to irreversible ischemia of the intestinal tract despite the absence of organic obstruction in the mesenteric blood vessels. The disease has extremely poor prognosis. We report three cases of NOMI developed after head and neck cancer therapy.

**Case 1:** A 74-year-old man. The diagnosis was T2N0M0 stage 2 oropharyngeal carcinoma. The patient complained of abdominal pain during five days after chemoradiotherapy. Abdominal computed tomography (CT) revealed mesenteric ischemia and intestinal emphysema. The patient was diagnosed as NOMI, and an emergency operation was performed. However, he died seven months after the operation because of recurrence of cancer.

**Case 2:** A 69-year-old man. The diagnosis was T2N2bM0 stage 4A hypopharyngeal carcinoma. The patient complained of abdominal pain during TPF chemotherapy. Abdominal CT revealed mesenteric ischemia and intestinal emphysema. The patient was diagnosed as NOMI, and an emergency operation was not performed because of blood pressure was unstable. However, he died on the day.

**Case 3:** A 82-year-old man. The diagnosis was T2N2bM0 stage 4A hypopharyngeal carcinoma. The patient complained of abdominal pain and decreased the level of consciousness during five days after total laryngopharyngectomy. Abdominal CT revealed mesenteric ischemia, intestinal emphysema, portal vein gas and bloodstream of the mesenteric artery. The patient was diagnosed as NOMI, and an emergency operation was performed on the same day. He moved another hospital four months after the operation.

We therefore suggest that ENT physicians must be aware of this complication during head and neck cancer therapy.

## Poster (Free Papers)

### Head & Neck (Clinical)

#### FP1-11

#### A case report of laryngeal cancer with dermatomyositis

**Chieko Yokota**, Yuichi Teranishi, Masahiro Oishi,  
Kishiko Sunami  
*Otolaryngology, Osaka City University, Japan*

Dermatomyositis is an inflammatory myopathy of unknown cause, and known to be associated with malignant tumor in 20~30%. Gastric cancer, lung cancer and breast cancer are common for underlying malignancies, but head and neck cancer is uncommon. We report a case of laryngeal cancer with dermatomyositis.

70 years old man had erythema with itching in head skin and eyelids from X-3months. Once these symptoms were improved by oral antihistamine and topical steroids, but facial erythema appear again at X-1months. At the same time, he noticed weakness in right upper limb, and this was getting worse gradually. Left upper limb's strength was also weakened at X-2weeks, so he visited dermatologist in our hospital (day X). He was diagnosed dermatomyositis, and referred to our department because laryngeal tumor was pointed out by upper gastrointestinal endoscopy for screening malignant tumors.

The tumor existed from tongue side of epiglottis to vestibular fold, and we diagnosed laryngeal cancer (squamous cell carcinoma cT2N0M0). He wanted good meals rather than voice preservation, so we planned total laryngectomy.

Before surgery, he received steroids and IVIG therapy for weakness of upper limbs. Just before surgery, he was possible to maintain a sitting position, but difficult to get up and transfer by himself, and fasting due to aspiration pneumonia. After surgery, his muscle strength improved gradually, and he was able to walk and eat on the 15th day.

Now a days, more than 5 years have passed since the operation, neither laryngeal cancer nor dermatomyositis has recurred.

#### FP1-12

#### A case of chylothorax after modified radical neck dissection

**Yuki Yamamoto**, Chieko Yokota, Yuichi Teranishi,  
Masahiro Oishi, Kishiko Sunami  
*Osaka City University, Japan*

The chylothorax is very rare among complications to occur after the neck dissection.

We must need attention because may occur serious respiratory disorder and circulatory disturbance.

This report describes rare postoperative complications occurring after left modified radical neck dissection.

The case is 86 years old man.

His diagnosis of left cancer of parotid gland (adenocarcinoma) cT4aN2bM0.

We showed curative treatment, but he chose the left modified radical neck dissection and heavy ion radiotherapy for origin. Because he thinks that oneself is old and quality of life is important.

The case showed sufferings from breathing and pleural fluid in chest X-ray two days later after surgery.

The results of the pleural effusion puncture were chylothorax.

Conservative treatment was successful including techniques such as local compression, drainage, nutritional management and/or IVH.

We diagnosed this case relatively early, and good results was able to be obtained by conservative treatment.

Poster (Free Papers)

Head & Neck (Clinical)

FP1-13

**An experience of salvage surgery after boron neutron capture therapy: a case report**

**Masaaki Higashino**, Teruhito Aihara, Akiko Ozaki, Naonori Ko, Koji Ono, Keiji Nihei, Yoshitaka Kurisu, Ryo Kawata

*Otorhinolaryngology, Head and Neck Surgery, Osaka Medical and Pharmaceutical University, Japan*

Salvage surgery after radiation therapy known to be associated with a high incidence of postoperative complications. We describe a case of successful salvage surgery after boron neutron capture therapy. In our patient with head and neck carcinoma, cervical lymph node recurrence with adhesion to a large vessel occurred after conventional irradiation. This lesion responded well to boron neutron capture therapy irradiation. Salvage surgery was subsequently performed to remove the residual tumor. Histopathologically, the isolated tissue contained tumor cells in its center and the surrounding tissue showed severe fibrosis. However, the tissue outside of the irradiation area had almost no fibrosis. Boron neutron capture therapy may facilitate salvage surgery after radiotherapy because it causes less injury to the surrounding tissue than conventional irradiation. Our experience suggests that boron neutron capture therapy may be a feasible preoperative treatment in patients with inoperable lesions or in those who strongly desire preservation of function.

Poster (Free Papers)

Head & Neck (Research)

FP2-2

**Relationship between APOBEC3 expression and viral genome hypermutation and integration in HPV-related oropharyngeal cancers**

**Satoru Kondo**, Naohiro Wakisaka, Tomokazu Yoshizaki

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The prevalence of human papillomavirus (HPV)-related oropharyngeal cancers (OPCs) have been increasingly reported in developed countries. If current trends continue, the annual incidence of HPV-positive OPC cases in the USA could surpass that of cervical cancers soon. Therefore, it is imperative to identify the mechanism of HPV carcinogenesis to prevent further increases in the prevalence of HPV-related cancers. We recently demonstrated that an antiviral factor, apolipoprotein B mRNA-editing catalytic polypeptide 3 (APOBEC3), can induce hypermutation of HPV DNA in vitro.

In the present study, we found numerous C-to-T and G-to-A hypermutations in the HPV16 genome in biopsy samples of OPCs, by 3D-PCR and sequencing. A3s were more abundantly expressed in HPV16-positive OPCs than in HPV-negative OPCs as assessed by immunohistochemistry and RT-qPCR, and interferons upregulated A3s in a HPV16-positive OPC cell line. Furthermore, qPCR analysis of HPV DNA suggested that A3A expression is strongly correlated with the integration event of HPV DNA. These results suggest that HPV16 infection upregulates A3A expression, thereby increasing the chance of viral DNA integration. The role of A3A in HPV-induced carcinogenesis is discussed.

Poster (Free Papers)

Head & Neck (Research)

FP2-3

**Examination of HPV-related oropharyngeal carcinoma and REV7 expression**

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In recent years, human papillomavirus (HPV) -related cancers attract attention in the head and neck region. In particular, it is reported that HPV-related cancer has a better prognosis than non-HPV-related cancer when a chemoradiation therapy is performed. On the other hand, a chemoradiation therapy has anticancer effects by causing single- and double-stranded DNA damage. Cancer has a mechanism to stop the repair of DNA damage against it and is refractory. This mechanism is called DNA damage tolerance. There are two types of repair, trans-damage repair and template switch repair. Rev7, which is involved in trans-injury repair, is known to be involved in cell cycle and transcription factor regulation. High expression of Rev7 is associated with a chemoradiation therapy sensitivity and is known as one of the poor prognostic factors in ovarian cancer, testicular cancer, diffuse large B-cell lymphoma, etc.

This time, we focused on oropharyngeal cancer. The subjects were patients diagnosed with oropharyngeal carcinoma in our department from January 1, 2008 to December 31, 2013, who had been treated and had an observation period of more than three years.

We immunostained the biopsy specimens or the surgical specimens of the subjects, and the expression of p16 / Rev7 was confirmed. In addition, we examined the relationship between the degree of each expression and the five-year survival rate and treatment sensitivity.

FP2-4

**The p16 Overexpression and Rb Loss Correlate with Transcriptionally Active High-risk HPV Infection in Oropharyngeal Squamous Cell Carcinoma**

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Overexpression of p16 is a highly sensitive but not a perfect surrogate marker for transcriptionally active high-risk human papillomavirus (HR-HPV) infection in oropharyngeal squamous cell carcinoma (OPSCC). Beside HPV specific testing, more cost-effective marker is required. In this study, we examined expression status of p16 and Rb by immunohistochemistry and transcriptionally active HR-HPV infection by mRNA in situ hybridization in 177 cases of OPSCC. HR-HPV and p16 was positive in 105 (59.3%) and 113 (63.8%) cases, respectively, and thus, 8/113 cases (7.1%) of p16-positive tumors were HPV negative. Rb status was divided into preserved expression (>90%, n=69), partial loss (PL) (10-90%, n=97) and complete loss (CL) (<10%, n=11). Among HPV-positive cases (n=105), Rb pattern was typically PL (97 cases, 92.4%) and rarely CL (8 cases, 7.6%) but not preserved expression (0%). In contrast, among HPV-negative cases (n=72), Rb pattern was typically preserved expression (69 cases, 95.8%) and rarely CL (3 cases, 4.2%) but not PL (0%). As compared with p16 alone, the combination of p16 overexpression and Rb partial/complete loss showed equally excellent sensitivity (each 100%) and improved specificity (97.2% vs 88.9%) and positive predictive value (98.1% vs 92.9%). By prognostic analysis, p16+/HPV- group and p16-/HPV- group showed similarly worse OS than p16+/HPV+ group (p=0.0610, p=0.0004, respectively). Among HPV-positive cases, Rb status (PL vs CL) did not show prognostic difference. The results suggest that combined use of p16 and Rb immunohistochemistry could be a reliable and cost-effective method to predict HR-HPV infection for better prognostication in OPSCC.



Poster (Free Papers)

Laryngology (Clinical)

FP3-1

Withdrawn

FP3-2

**A case of pemphigoid laryngeal lesions in association with DPP-4 inhibitor use**

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The case was a 52-year-old man. He noticed sore throat from 1 month ago and pain during swallowing from 2 weeks ago. He visited our department. Medical history is diabetes. Laryngeal endoscopic findings at the first visit showed white coat adhering to the right side of the epiglottis, and edematous mucosa in the right arytenoid. Herpes laryngitis was suspected based on physical findings, and Hangeshashinto was taken orally, but the symptoms did not improve. Bacterial tests were also performed on only indigenous bacteria. Therefore, a biopsy was performed from the epiglottis, and the result was that there was no atypical cell and a small number of inflammatory cells were found. One month after the first visit, the lesion had decrease slightly, so the patient was followed up with only a gargle. Two months after the first visit, the patient complained the pain in the oral cavity, and aphthous lesions extending from the soft palate to the buccal mucosa was observed. Therefore, a systemic lesion was suspected, and an additional blood test was performed, and an increase in anti-BP180 antibody was observed. When he came to ask for the results of the blood test, he was suspected of having pemphigoid, so I instructed him to go to a dermatologist. DPP-4 inhibitor (dipeptidyl peptidase-4 inhibitor) has few contraindications and is widely used in daily clinical practice. However, there have been occasional reports of autoimmunity-related events such as arthritis and bullous pemphigoid. The onset time is wide, ranging from 2 weeks to 15 months after administration. Since discontinuation of the DPP -4 inhibitor does not mean immediate improvement, it is basically a tapering dose of steroids. We report a case of pemphigoid laryngeal lesions with a DPP-4 inhibitor.

Poster (Free Papers)

Laryngology (Clinical)

FP3-3

# A Study of Pediatric Cases of Tracheostomy and Laryngotracheal Separation

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Pediatric tracheostomy is indicated for securing the airway in cases of upper airway stenosis or obstruction, when long-term respiratory management is required, and when securing the lower airway with an endotracheal stent. The ability to secure a stable airway has the advantage of allowing the patient to transition from hospitalization to home. On the other hand, after discharge from the hospital, there is a burden on family members to acquire medical procedures such as suctioning and tracheostomy care, and there is also the problem of complications such as granulation due to tracheostomy. In many cases, not only preoperative but also postoperative and post-discharge management is required, and cooperation with other departments including pediatrics is essential. The purpose of this study is to examine the primary disease, indications for surgery, and postoperative and post-discharge status of patients who underwent tracheostomy and laryngotracheal separation at our hospital.

FP3-4

# Developmental functional morphology of the preepiglottic space in the human larynx

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**Objectives:** The distribution of preepiglottic space is important in understanding its functional significance. However, its growth and development are enigmatic.  
**Methods:** Five normal human newborn and five adult larynges were investigated and compared with each other using whole organ serial section technique.  
**Results:** In adults, the preepiglottic space existed astride the epiglottis. On the other hand, the topography of the human newborn preepiglottic space differed considerably from that of adults. The newborn preepiglottic space was immature and occupied a small area anterior to the epiglottis. The epiglottis lay on a somewhat horizontal axis and was partially obscured behind the hyoid bone. The hyoid bone overlapped the thyroid cartilage, partially obscuring the superior thyroid notch. The thyroid cartilage was present close to the hyoid bone and the thyrohyoid membrane ran between the superior surface of the thyroid lamina and, not the anteroinferior, but the posteroinferior surface of the hyoid bone. The preepiglottic space was located anterior, lateral and posterolateral to the thyroepiglottic ligament. However, the preepiglottic space was located anterior to the epiglottic cartilage.  
**Conclusions:** In order to acquire the human adult vocal tract for speech production, the human larynx descends as the child grows. And likewise, the preepiglottic space, occupying a small area anterior to the epiglottis, likely grows as the larynx descends and acquires the vocal tract. And its distribution likely allows the epiglottis to more effectively play the role of retroflexion during swallowing in order to prevent aspiration.

Poster (Free Papers)

Otology (Clinical 1)

FP4-1

# THE ETIOLOGIES AND DIAGNOSTIC APPROACHES FOR PULSATILE TINNITUS IN A LARGE CASE SERIES

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## Objectives

To summarize the etiologies of and diagnostic approaches for pulsatile tinnitus (PT) in a large case series.

## Materials and Methods

Medical records of subjects diagnosed with PT from January 2011 to July 2017 at a single tertiary hospital were reviewed. Patients who underwent temporal bone CT angiography (TBCTA), brain MRI/A, or transfemoral catheter angiography (TFCA) were included (n=198).

## Results

There were 80 patients who had no abnormal findings on radiologic examination. Among the 118 with abnormal findings on radiologic exam, 3 had non-vascular lesions such as glomus tumor or meningocele. The findings of the 115 subjects with vascular etiologies were as follows, 25 of which had overlapping findings; high jugular bulb (JB) (19.7%), dominant sigmoid sinus (SS) (11.6%), dural arteriovenous fistula (dAVF) (9.6%), SS dehiscence (9.6%), SS diverticulum (8.1%), JB dehiscence (7.6%), JB diverticulum (1.5%), internal carotid artery (ICA) stenosis (1.0%), superior petrosal sinus dehiscence, dural sinus thrombosis, aberrant ICA, and emissary vein dilatation (all 0.5%). All the anatomical abnormalities responsible for PT can be detected by TBCTA, except for dAVF. For the dAVF, the diagnostic yield of TBCTA was very low (2/13). And even through brain MRI/A (n=15), two patients showed false negative for dAVF. They could be diagnosed as dAVF only by TFCA.

## Conclusion

The radiologic examination such as TBCTA, MRI, or TFCA can reveal the etiologies of PT in about 60% of subjects. All the anatomical abnormalities responsible for PT can be diagnosed by TBCTA, only except for dAVF. Considering its potentially catastrophic consequence, when clinically strongly suspected of dAVF, TFCA should be performed regardless of TBCTA or MRI/A results.

FP4-2

# A Long-Term Surgical Outcome Analysis In Subjects With Pulsatile Tinnitus Originating From The Sigmoid Sinus

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Etiology-specific and secure reconstruction using a firm material is vital to achieve optimal outcomes in pulsatile tinnitus (PT) caused by a dominant sigmoid sinus (SS) with dehiscence and/or diverticulum (SSDD). Here, we aimed to evaluate the long-term efficacy of transmastoid resurfacing/reshaping using bone cement and discuss the possible underlying pathophysiology. We conducted a retrospective review of 20 PT patients who were diagnosed with unilateral SSDD, underwent transmastoid SS resurfacing/reshaping using bone cement, and were followed up for more than 1 year after surgery. They underwent individualized surgical approaches according to their pathology: resurfacing for SS diverticulum and reshaping for severely dominant SS dehiscence or thinning. After surgery, immediate and long-term changes (>1 year) in visual analog scale (VAS) loudness and annoyance were analyzed. Additionally, pre- and postoperative objective measurements of PT using transcanal sound recording and spectro-temporal analysis (TSR-STA), imaging results, and audiological findings were comprehensively reviewed. A significant improvement in PT was noted immediately after surgery, which was sustained or enhanced for >1 year. Neither major postoperative complications nor aggravation were observed in our cohort during the long-term follow-up period. From TSR-STA, both peak and root mean square (RMS) amplitudes decreased after surgery, and average pure-tone threshold at 250 Hz was also significantly improved. Taken together, the long-term improvement of PT perception was demonstrated subjectively by VAS loudness and annoyance and objectively by TSR-STA and PTA. Therefore, stringent selection of candidates and patient-tailored surgical approaches may be key to successful treatment.

Poster (Free Papers)

Otology (Clinical 1)

FP4-3

FP4-4

**Development of real-time video-oculography using high quality infrared video Frenzel**

Withdrawn

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Background

It is essential to use an infrared CCD camera in clinical examination of the vestibular system. Devices are currently available that can quite accurately record human eye movements, based on the principle of video-oculography (VOG). We devised an original VOG (HI-VOG) system using a commercialized infrared CCD camera, a personal computer and public domain software program (ImageJ) for data analysis. In the present study, we revised the VOG and image filing system for real-time 3D analysis of nystagmus, and developed high quality video Frenzel (yVOG-Glass).

Methods

The video image from a Frenzel with high quality image camera was captured at 60 frames per second at a resolution of 640\*480 pixels. For real-time analysis of the horizontal and vertical components, the X-Y center of the pupil was calculated. For real-time analysis of torsional components, the whole iris pattern was overlaid with the same area of the next iris pattern, and the angle at which both iris patterns showed the greatest match was calculated.

Results

Accurate measurements of horizontal, vertical and torsional eye movement were taken while recording the video image in real-time. For quantitative analysis, the slow phase velocity of each occurrence of nystagmus and the average value of the slow phase velocity were analyzed automatically.

Conclusion

Using the yVOG-Glass system, it was possible to perform real-time quantitative 3D analysis of nystagmus from video images recorded with high quality video Frenzel.

Poster (Free Papers)

Otology (Clinical 1)

FP4-5

**A case of vestibular migraine/delayed endolymphatic hydrops overlapping syndrome**

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Vertigo and headache are both common physical symptoms and may co-occur. Vestibular migraine (VM) is characterized by recurrent vertigo attacks with concomitant headache fulfilling the criteria for migraine. It is important to distinguish VM from Meniere's disease (MD), because the symptoms are similar and MD often co-occurs with VM. "VM/MD overlapping syndrome" has been suggested for cases in which different types of vertigo attributable to VM and MD occur simultaneously. Delayed endolymphatic hydrops (DEH) is a clinical entity characterized by recurrent vertigo developing years to decades after severe sensorineural hearing loss; the etiology is similar to that of MD. We report our experience of a case of simultaneous VM and DEH.

A 65-year-old male with right ear deafness following sudden deafness 15 years prior visited us complaining of recurrent vertigo and headache. He was diagnosed with VM; his dizziness and headache diary revealed simultaneous onset of vertigo and migrainous headache. He was also diagnosed with DEH because the administration of isosorbide resolved both the vertigo and headache; the prior lomerizine hydrochloride administration improved these symptoms, but did not resolve completely. Since the right ear improved on the results of caloric test after treatment, he was diagnosed with ipsilateral DEH.

We diagnosed this case with VM/DEH overlapping syndrome, given the cooccurrence of VM with DEH signs and symptoms. This case indicates the relationship between VM and endolymphatic hydrops, not only MD but DEH.

FP4-6

**Persistent postural-perceptual dizziness (PPPD) secondary to BPPV: a case report**

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Persistent postural-perceptual dizziness (PPPD) was defined for the International Classification of Vestibular Disorders in 2017. It is a chronic vestibular disorder that manifests with waxing and waning symptoms of dizziness, unsteadiness, or nonspinning vertigo that last for 3 months or more and are exacerbated by upright posture, active or passive motion of self, and exposure to environments with complex or moving visual stimuli. Triggers of PPPD include a wide variety of conditions that may cause vestibular symptoms or disrupt balance functioning, including neuro-otologic and other medical conditions and psychological distress.

Herein, we report the case of a 35-year-old woman who developed PPPD secondary to benign paroxysmal positional vertigo (BPPV). She felt spinning vertigo by head movement and visited to our hospital from a nearby ENT clinic. She had direction-changing positional nystagmus and diagnosed posterior canal BPPV. She still felt dizziness though the nystagmus was disappeared after epley maneuver. We instructed her to do rolling-over maneuver twice a day for several months. We let her to consult a psychiatrist because she felt difficulty for looking at large store displays and took a temporary leave from a drug store job. Her symptoms were reduced gradually by taking selective serotonin reuptake inhibitors (SSRI). Dizziness handicap inventory (DHI) and Niigata PPPD questionnaire were both improved after administration of SSRI.

Poster (Free Papers)

Otology (Clinical 1)

FP4-7

**Detection of oval window lesion in otosclerosis by ultra-high resolution computed tomography**

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**Introduction:** Aquilion PrecisionTM (hereafter AP) is one of the ultra-high resolution computed tomography which has 0.25 mm X 1792 channel, 0.4 mm X 0.5 mm focal spot, 2 times better accuracy, and 2048 matrix UHR MBIR reconstruction. Since it has better spatial resolution than multi-detector raw CT (hereafter MDCT), it may be useful to detect anatomical information related otologic surgery.

**Subjects:** Retrospective case review. Subjects were 40 patients with chronic otitis media, sudden deafness, or facial palsy as control and 5 cases (2 males and 3 females) with 3 otosclerosis and 2 ossicular chain malformation with stapes fixation confirmed by surgery.

**Methods:** Compared the thickness of footplate and the bony change around oval window between the control group and the stapedial surgery group. Image analysis was carried out using Ziostation 2 software.

**Results:** The mean and standard deviation of foot plate thickness in the control group was  $0.46 \pm 0.08$ mm in the right ears and  $0.46 \pm 0.08$ mm in the left ears, respectively. The otosclerosis cases had 1.08 mm in affected ears and 0.82 mm in the unaffected ears, respectively. The bony changes were identified in all affected ears and there was no subject with such bony change in the control. The thickness of footplate in ossicular malformations was 1.08 mm in the affected ears, and 0.58 mm in the unaffected ears, respectively. The bony fixation of stapes and surrounding bone were observed in all malformation cases.

**Conclusion:** The result of this study suggests that the measurement of the thickness of foot plate and the bony change of oval window with AP image would be useful for diagnosis of otosclerosis and stapes fixation. And the CT information obtained by AP will be useful to prepare surgical procedure before surgery.

FP4-8

**Study on the relationship of hearing loss and cognitive function: a retrospective study using health screening data**

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**Background:** Hearing loss may contribute to cognitive impairment and dementia. The purpose of this study was to investigate the association between hearing impairment and cognitive function using health screening data.

**Methods:** This study includes the data obtained from non-demented healthy people who received health screening with cognitive function tests. Hearing loss was defined by an average of hearing thresholds at 0.5, 1, 2, and 4kHz in the better hearing ear. Korean version of the Mini-Mental State Examination(MMSE) and the Korean version of the 7-Minute Screen for the detection of early-stage Alzheimers disease were used for the cognitive test.

**Results:** 791 patients were recruited for this study. 591 of them had normal hearing(<20dB in the better ear on PTA), 156 had mild hearing loss(21-40dB in the better ear on PTA), and 44 had moderate hearing loss(>40dB in the better ear on PTA). In univariate analysis, there was a significant association between the degree of hearing loss and cognitive function. However, the degree of hearing loss was significantly associated with the age of the patients. When age and sex were adjusted, there was no significant correlation between the degree of hearing loss and cognitive function. In multivariate analysis, only moderate hearing loss was associated with the prediction rate of dementia. In addition, abnormal findings such as diffuse atrophy, chronic ischemic change, small vessel disease, leukoaraiosis, microbleeds, tumor and aneurysm in brain MRI were not associated with cognitive function.

**Conclusion:** In this cross-sectional study, the relationship between hearing loss and cognitive impairment was not obvious. More age-adjusted studies for the relationship between hearing loss and cognitive function are needed.



Poster (Free Papers)

Otology (Clinical 1)

FP4-9

# Does hearing loss increase postural instability in elderly? Population based study

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**Objective:** Hearing loss(HL) and postural instability are common age-related changes and they are related to each other. Many patients with age-related HL also suffer from dizziness. But there have been few studies about the relationship between HL and postural instability. In addition, the criteria for hearing rehabilitation as an intervention of postural instability has not been proposed. In this study, we aimed to elucidate the risk of postural instability according to the degree of HL and suggest a criterion for hearing rehabilitation for postural instability.

**Methods:** Korean National Health & Nutrition Examination Survey V(KNHANES V, 2010-2012) data, the fifth cross-sectional survey for the South Korean population performed by the Korean Ministry of Health and Welfare was used. Pure tone audiometry was performed on both the left and right sides, and each was classified into normal, mild HL and moderate HL. Postural instability was defined as the failure to maintain the stance in condition 4 of the foam balance test.

**Results:** A total of 3,864 men and women over 40 years old were included in the study. Women were at higher risk of postural instability than men, and as they grew older, the risk of postural instability increased. There was no increase in the risk of postural instability in unilateral and bilateral mild HL, but there was a statistically significant increase in the risk of postural instability when there was moderate HL on at least one side.

**Conclusions:** Female, aging, and HL were associated with postural instability on our analysis. If moderate HL was at least on one side, the odds of postural instability increased significantly.

FP4-11

# Efficacy of the additional effect of HBO in combination of steroid and prostaglandin E1 for idiopathic sudden sensorineural hearing loss

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**Purpose:**

The efficacies of hyperbaric oxygen therapy (HBO), systemic steroid, prostaglandin E1, or the combination of any two modalities have been reported in patients with idiopathic sudden sensorineural hearing loss (ISSNHL). However, little is known about the combined efficacy of HBO, systemic steroid, and prostaglandin E1 for this disorder. We aimed to investigate the efficacy of HBO combined with systemic steroid, and prostaglandin E1 as triple therapy in patients with ISSNHL.

**Materials and Methods:**

We retrospectively evaluated the records of 67 patients with ISSNHL who were treated with systemic steroid and prostaglandin E1, with (n=38) or without (n=29) HBO. The inclusion criteria included a diagnosis of ISSNHL within 14 days of symptom onset, age  $\geq 15$  years, treatment according to the protocol, and clinical follow-up of at least 1 month. The patients' hearing levels were evaluated 1 month after hearing loss onset. The primary outcome was hearing improvement on pure tone audiometry. We also evaluated the demographic profiles of patients.

**Results:**

Patients treated with triple therapy showed significantly greater hearing improvement ( $p < 0.01$ ) than those treated without HBO, despite some differences between the two treatment groups. Multivariate logistic regression analysis revealed a significant positive correlation between pure tone audiometry improvement and hyperbaric oxygen therapy, after adjustment for confounding factors (odds ratio=7.42; 95% and confidence interval=2.37-23.3;  $p=0.001$ ).

**Conclusion:**

HBO with systemic steroid and prostaglandin E1 administration conferred significant therapeutic benefits for ISSNHL. Therefore, routine use of triple therapy is recommended for patients with ISSNHL.

Poster (Free Papers)

Otology (Clinical 1)

FP4-12

Withdrawn

FP4-13

**Test-retest reliability of sound field (SF) audiometry test results between SF system for small audiometric booths and traditional SF system**

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**Background and objectives**

The purpose of this study is to compare the SF test results (test-retest reliability) between the traditional SF audiometry system and the newly designed SF system for use in small audiometric booths.

**Subjects and Methods**

In order to evaluate the reliability of the SF audiometry system, the following tests are performed with wearing a hearing aid. 1) Warble tone hearing test using the traditional SF audiometry system, 2) speech audiometry test using the traditional SF audiometry system, 3) Warble tone hearing test using the newly designed SF audiometry system for small audiometric booth, 4) speech audiometry test using the newly designed SF audiometry system, 5) repeat steps 1)-4).

A total of 39 adults (56 ears) who wore hearing aids participated in the study. The comparative parameters included warble tone audiometry threshold, a speech reception threshold (SRT), and a speech discrimination score (SDS).

**Results**

Warble-tone hearing thresholds and SRT were similar in both systems ( $p>0.05$ ). However, the SDS was significantly higher in the newly developed system ( $p<0.05$ ). Further, the TOST results showed equivalent SF audiometry results using either system. CV% of test-retest hearing thresholds results on 500Hz, 1kHz, 2kHz, 4kHz, and the average values of the four frequencies were 6.62, 6.22, 6.21, 6.6 and 4.24 % respectively in the traditional SF system and 5.63, 4.93, 5.99, 4.87 and 3.79 % respectively in the newly designed SF system,

**Conclusion**

The audiometric results of the newly developed SF audiometry system were equivalent to those of a traditional system. Furthermore, the reliability of test-retest was higher in the newly designed SF system than the traditional SF system.

Poster (Free Papers)

Otology (Clinical 1)

FP4-14

# Development of Sound Field Audiometry System for Small Audiometric Booths and Comparison of Its Equivalence With Traditional System

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## Objectives

Sound field (SF) audiometry tests are usually conducted in audiometric booths measuring greater than 2 x 2 m in size. However, most common private ENT clinics carry about 1x1 m sized audiometric booths, making SF audiometry testing difficult to perform. The aims of this study were to develop an SF audiometry system for use in smaller audiometric booths and compare its performance with traditional system.

## Methods

The newly developed SF audiometry system can yield an SF signal at a distance of about 30 cm from the subject's ears. Its height can be adjusted according to the subject's head height. We compared SF hearing results between the new SF system and the traditional SF audiometry system in 20 adults with normal hearing (40 ears) and 24 adults with impaired hearing levels (38 ears) who wore hearing aids. Comparative parameters included warble tone audiometry threshold, a speech reception threshold (SRT), and a speech discrimination score (SDS).

## Results

Among participants with normal hearing, warble tone hearing thresholds of 0.5, 1, 2, and 4 kHz, average values of these four frequencies, and SRT were similar between the two systems (all  $P>0.05$ ). Participants with hearing aids showed similar warble tone threshold and SRT ( $P>0.05$ ) in both systems except for threshold of 4kHz ( $P=0.033$ ). TOST results showed equivalent SF audiometry results using either system.

## Conclusion

Audiometric results of the newly developed SF audiometry system were equivalent to those of a traditional system. Therefore, the small SF audiometry system can be used at small audiometric booths present in most private ENT clinics.

FP4-15

# How to manage the Cochlear Dysplasia that causes meningitis

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## Objective:

Although there are many reports of Mondini dysplasia with cerebrospinal fluid leakage (CSFL) and meningitis, few of them discuss the surgical repair technique for the fistula. The failure rates for fistula repairs are reportedly 30-60%. In this case report, we introduce a more effective operative technique for repairing this type of fistula.

## Method:

We describe a 7-year-old male with unrecognized, unilateral Mondini dysplasia who presented with CSFL and meningitis after acute otitis media. The CSFL was repaired surgically using the tympanoplastic approach with an endaural incision. We performed a new surgical technique for the repair of the bone defect by not only packing the vestibule with soft tissues and covering them with bone/bone pate but also by applying pressure from the incus.

## Results:

The CSFL did not recur, and there was no postoperative complication. The image of CT scan showed that defects in the bony wall of the vestibule were perfectly regenerated two years after the operation.

## Conclusion:

Our new surgical technique, a combination of packing the vestibule with autologous soft tissues, covering them with bone/bone paste, and applying pressure on the tissues via the incus is an easy, simple and effective method for the repair of a bone defect with CSFL.

Poster (Free Papers)

Otology (Clinical 1)

FP4-16

# Cochlear Implant and Additional Hearing Aid in the Same Ear: Preliminary Data

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Current soft implant surgery often preserves the residual hearing with variable levels. Conventional solution for better outcome was known as an electroacoustic stimulation (EAS) that offers considerable advantages in pitch perception, speech perception, listening in background noise, and music appreciation. In this study, we want to address whether electroacoustic stimulation is beneficial even for the patients who do not meet the conventional audiological EAS criteria. In these cases, electric stimulation covers whole frequencies and acoustic stimuli are fully overlapped. We conducted comprehensive audiological evaluations in two different strategy (Added CI vs. CI only). Out of 18 eligible cases, nine CI patients using off-ear processor were agreed to be included in this study and three were completed. Their residual hearing at 125 and 250Hz were <70dB, and at 500Hz were <90dB. After 4 weeks of HA trial, another 4 weeks of rehabilitation session was completed. After wearing hearing aids and rehabilitation, subjective scores specified to audiological abilities and quality of life (sound response, audibility, communication, concentration, pitch specification, preferences), were markedly improved than pre-hearing aids status. Compared with only electrical stimulation, added CI had higher audibility in terms of lower hearing threshold higher word recognition scores at the latest evaluation. Speech perception of added CI were same or better than CI only condition in all patients. Small case number prevents any statistically significant conclusion, But, Added CI appears to explicit the robust performance compared with only electrical stimulation in terms of higher audibility, greater accuracy, and good localization and hearing in noise.

FP4-17

# Cochlear duct length determination and prediction of insertion depth angles for CI electrodes using preoperative temporal bone CT

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## Objectives

To determine the cochlear duct length (CDL) using preoperative temporal bone computed tomography (TBCT) in patients with hearing loss and to evaluate whether the final insertion depth angle (IDA) of cochlear implantation (CI) electrode is related to the cochlear size.

## Material and methods

We retrospectively reviewed medical records of 35 patients underwent CI from 2014 to 2018. Measurement of CDL, distance A (the largest diameter of basal turn), and distance B (the diameter perpendicular to the distance A) was performed on preoperative TBCT using two softwares (MEDIP and OTOPLAN).

Postoperative cochlear view images were analyzed and IDA was measured. Pearson correlation analysis was performed to determine whether the IDA is related to the cochlear size.

## Results

The mean CDL, distance A, and distance B in both temporal bones of 35 patients were 36.20mm, 8.67mm, and 5.73mm, respectively. The mean IDA was  $431.45 \pm 38.42^\circ$ . There is no significant correlation between CDL and IDA ( $r = -0.2333$ ,  $P > 0.05$ ). There is significant negative correlations between distance A and IDA ( $r = -0.7643$ ,  $P < 0.0001$ ); distance B and insertion depth angle ( $r = -0.7118$ ,  $P < 0.0001$ ), respectively. In patients with normal cochlear, the CDL results predicted by two different softwares were generally consistent. However, in cochlear anomalies, CDL measurements using MEDIP showed better correlation with postoperative IDA than OTOPLAN measurements.

## Conclusions

The cochlear size, especially the diameter of cochlear basal turn, was significantly correlated with the IDA. The preoperative estimation of the cochlear size and IDA would be helpful to choose the correct electrode size for the individual patients and to precisely adjust the insertion depth during CI surgery to preserve residual hearing.

Poster (Free Papers)

Otology (Clinical 1)

**FP4-18**

**Change of Vestibular Symptoms and Functions after Cochlear Implant; Its Relevant Factor and Correlation with Residual Hearing**

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**Purpose:** To evaluate the vestibular loss after cochlear implantation (CI) and relationship between vestibular and hearing changes. **Methods:** Seventy-five patients with CI were enrolled and classified accordingly; normal preoperative caloric function (Group I) and normal preoperative waveform in cervical-vestibular evoked myogenic potential (Group II). The relationship between hearing and changes in the vestibular system was analyzed preoperatively and at 3 and 6 months (3m, 6m) postoperatively. **Results:** In Group I, unilateral weakness on the implanted side was detected in five (7.7%) and eight patients (12.3%) at 3m and 6m post-CI, respectively. By 3m post-CI, the total slow-phase velocity (SPV; warm and cold stimulations) was significantly different between implanted and non-implanted sides ( $P=0.011$ ), and the shift in total SPV from pre- to post-CI significantly correlated with the average hearing thresholds at 6m post-CI. In Group II, an abnormal c-VEMP was detected on the implanted side in six patients (16.2%) at 3m post-CI, and in six more patients (20.0%) at 6m post-CI. Significant changes were noticed in P1 and N1 amplitude at 3m post-CI ( $P=0.027$  and  $0.019$ , respectively). **Conclusions:** Vestibular function and residual hearing function should be afforded equal and simultaneous consideration in terms of preservation.

Poster (Free Papers)

Otology (Clinical 2)

**FP5-2**

**Safe Open Cavity Reconstruction Using a Sliced-Cartilage Graft for Poorly Aerated Ears with Cholesteatoma**

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**Objective:** To establish a surgical treatment for ears with very poor middle ear aeration.

**Methods:** Seventeen ears of 16 patients underwent canal-wall-down tympanoplasty (CWD) with a single smooth sliced cartilage graft (triple S-C graft) for recurrent cholesteatomas, reoperation after CWD, or poorly aerated ears. Eardrum findings and hearing outcomes were evaluated at five years postoperatively. Middle ear aeration was classified as follows: grade 0, no aeration; and grade 1, only the mesotympanum was aerated.

**Results:** We encountered no recurrence caused by formation of a deep eardrum retraction pocket at 5 years postoperatively although shallow retraction was encountered in the grade 0 aeration ears. Median (average +SD) of postoperative air-bone gap were 35dB (32.0 +10.2) for ears with recurrence cholesteatoma after CWD, 33.1dB (30.6 +8.9) for ears with recurrence after canal-wall-up tympanoplasty and 23.75 (25.3 +16.1) for ears with initial surgery. In terms of relationships of preoperative middle ear aeration, the median (average +SD) of postoperative air-bone gap were 37.5dB (38.4 +7.6) for preoperative grade 0 aeration ears and 21.25dB (21.9 +8.6) for preoperative grade 1 aeration ears.

**Conclusions:** Our new surgical procedure can be used to treat recurrent cholesteatoma, or very poorly aerated ears with cholesteatoma. This condition is relatively rare, but our procedure will aid in control of recurrent cholesteatoma. Triple S-C grafting yielded appropriately shaped eardrums. The small tympanic cavity facilitated aeration of grade 1 (mesotympanum aeration only), associated with favorable long-term surgical outcomes. We believe that our new procedure can be used to create a dry, safe open cavity when repeated conventional surgery fails to eradicate cholesteatoma.



Poster (Free Papers)

Otology (Clinical 2)

FP5-3

**Comparative analysis of butterfly cartilage tympanoplasty versus conventional methods**

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Since the first report of myringoplasty in the 1950s, various graft materials and methods have been used to close tympanic membrane perforation such as fascia, connective tissue, perichondrium or cartilage in underlay, inlay or overlay fashion. Myringoplasty using butterfly cartilage is a relatively new method that first reported by Eavery in 1998. This technique does not require tympanomeatal flap elevation and it can be performed under local anesthesia, less operating time, minimal scarring due to transcanal approach, and lack of ear packing. We retrospectively evaluated the medical records of patients who underwent butterfly cartilage tympanoplasty at University of Fukui Hospital between November 2018 and December 2019. 6 patients who were diagnosed with noncomplicated chronic otitis media and underwent microscopic or endoscopic transcanal butterfly cartilage tympanoplasty in this period. Age, gender, patient background, follow-up time, operating time, pre- and postoperative pure tone audiometry thresholds, pre- and postoperative air-bone gap were evaluated. To clarify the advantages and disadvantages of butterfly cartilage myringoplasty, we compared with other procedures that performed perforation closure at the same time. We suggest that butterfly cartilage tympanoplasty can be safely performed even in patients with complications or old patients, and hearing outcomes and successful closure rate are similar to those of other surgical methods.

FP5-5

**Reconstruction of the external auditory canal using full-thickness rolled-up skin graft after lateral temporal bone resection**

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**Objective:** To present our results of the external auditory canal (EAC) reconstruction procedure using rolled-up full-thickness skin graft with tympanoplasty after lateral temporal bone resection (LTBR) for early-stage EAC carcinoma.

**Patients and methods:** A retrospective review of 15 patients who had undergone LTBR with reconstruction of the EAC for T1 and T2 EAC cancer between 2016 and 2020.

**Results:** Postoperative mean air-bone gap was 30.7 decibel hearing level. Although a few patients experienced chronic granulation, persistent otorrhea, and/or laterization of the tympanic membrane, most patients showed no serious complications related to the EAC reconstruction.

**Conclusions:** EAC reconstruction using a full-thickness skin graft in combination with tympanoplasty is useful for minimizing the hearing loss, maintaining the cosmetic appearance, and facilitating the observation into the ear cavity.



Poster (Free Papers)

Otology (Clinical 2)

FP5-6

# Prediction of appropriate prosthesis length by preoperative CT in TEES for stapes surgery

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Transcanal Endoscopic Ear Surgery (TEES) is becoming more popular in otologic surgery because of its advantages over conventional microscopic ear surgery, including a clear, magnified field of view with fewer blind spots, no need for posterior incision in the ear, and less postoperative pain due to less bone removal. However, on the other hand, it has the disadvantage that it requires one-handed surgical operation and that it is difficult to grasp the three-dimensional position of the prosthesis inserted due to the two-dimensional observation of the surgical field. Thus, the indications for TEES must be carefully determined, especially in stapes surgery. In this study, we report a case series of TEES for stapes surgery, focusing on the estimation of appropriate prosthesis length by preoperative Computed Tomography (CT) based on postoperative hearing results.

We retrospectively examined 31 cases of TEES for stapes surgery. Postoperative hearing result was good in 27 cases, but poor in 4 cases. We reviewed the preoperative CT of all patients and measured the straight-line distance from the I-S joint to the oval window in the coronal images, and assumed it to be the "Appropriate Prosthesis Length (APL)". The actual length of the prosthesis inserted at operation, compared to the APL, was shorter in three of four cases without postoperative hearing improvement. In the remaining case, the postoperative CT revealed that the position on the prosthesis was clearly inappropriate. The measurement of APL using preoperative CT could contribute to the improvement of postoperative hearing outcomes of stapes surgery with TEES.

FP5-7

# Development of the Near-future type Tympanoplasty by Regeneration of the Tympanic Membrane using Endoscopic Ear Surgery

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**Background:** We developed a new regenerative treatment for the tympanic membrane (TM) perforations without the need for conventional surgical therapy. It is not necessary for this regenerative treatment to incise the skin and to harvest auto-tissue for repair the TM. As the next strategy, we applied this regenerative treatment to patients with middle ear diseases by using the endoscope. We named this Tympanic Membrane Regeneration in Endoscopic Ear Surgery-Tympanoplasty (TREES-TP).

**Aim:** To investigate the usefulness of TREES-TP.

**Methods:** One-hundred-seven patients (Age:4-92,M=45,F=62) were selected. There were patients with 37 cholesteatomas, 11 tumors, and 59 chronic otitis media. They classified into three groups based on the size for the regeneration of TM perforation. Materials used for the TM repair were a gelatin sponge with b-FGF and fibrin glue. After removal of lesions/washing out of the tympanic cavity through TM perforation, a gelatin sponge immersed in b-FGF was placed under/over the perforation. Fibrin glue was dripped over the sponge. The effectiveness of this therapy was evaluated three months after the treatment. The treatment of TM repair was repeated up to 4 times in the out-patient clinic for cases in which complete closure of the TM perforation was not achieved after one round of the treatment.

**Results:** Complete closure of the TM perforation was achieved by 86.0% (n=92/107). The average hearing levels of all patients with successful TM repair were improved or maintained. No serious sequelae were observed in any patient.

**Conclusions:** The TREES-TP is a simple, safe, cost-effective, and minimally invasive treatment. By this regenerative treatment, a part of tympanoplasty and most of myringoplasty will not be necessary for the near future.

Poster (Free Papers)

Otology (Clinical 2)

FP5-8

**Multi-layered connective tissue underlay myringoplasty technique with high success rate**

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**Background:** Various surgical techniques have been developed for the treatment of tympanic membrane perforation. One of the most common procedures is simple underlay myringoplasty with fibrin glue (SUM) developed by Dr. Yuasa. Compared to conventional tympanoplasty, SUM is less invasive. The drawbacks of SUM are medialization and dislocation of the underlying connective tissue. These two complications can lead to re-perforation, of which the incidence has been previously reported to be about 20%. The hearing improvement rate of SUM has been reported to be around 80%.

We have developed a modified SUM, namely multi-layered connective tissue underlay myringoplasty (MCUM). This new, simple technique does not require fibrin glue. Also, our preliminary study showed it has even higher success rates because properly placed the multiple-layered connective tissue does not cause dislocation.

**Method:** In the present study, we retrospectively examined 61 patients 68 ears operated by MCUM who had more than a one-year follow-up period.

**Results:** The tympanic membrane perforation closure rate and hearing improvement rate was 96% and 94%, respectively. These success rates were equivalent to or higher than that of the previously reported conventional methods such as SUM. Moreover, this study also revealed that even large perforations could be successfully closed. The follow-up CT scans and audiometry revealed the volume of underlaid connective tissue has been reduced and eventually absorbed, and did not cause any harmful effect to the tympanic cavity aeration and hearing outcomes.

**Conclusion:** We have developed MCUM and this new technique brings high perforation closure rate and hearing improvement rate. MCUM can be applied to large sized perforation without using fibrin glue.

FP5-9

**Nasopharyngeal pneumococcal carriage as a risk factor for otitis media with effusion**

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**Purpose:** Otitis media with effusion (OME) commonly occurs and persists in young children. It can cause hearing impairment and future complications. We aimed to determine the prevalence and association of *Streptococcus pneumoniae* in the nasopharynx of healthy children before the introduction of a pneumococcal conjugate vaccine. **Methods:** In October 2016, nasopharyngeal swabs collection and otoscope examinations were conducted in children aged less than 24 months in Nha Trang, Vietnam. OME was diagnosed as the presence of middle ear fluid using a digital otoscope equipped with a pneumatic otoscope. Quantitative PCR targeting pneumococci-specific *lytA* (the major autolysis gene) and bacterial culture were performed to detect *S. pneumoniae*. The point prevalence of OME in the study area was estimated. The association between OME and *S. pneumoniae* in the nasopharynx was evaluated using a multivariable logistic regression model. **Results:** Among the 274 children who underwent bilateral ear examinations and nasopharyngeal swab collections, 47 had OME (17.2%, 95% confidence interval [CI] 12.9-22.1%) and 96 were colonized with *S. pneumoniae* (35.0%, 29.4-41.0%). OME and nasopharyngeal *S. pneumoniae* carriage were positively associated in children aged less than 12 months (adjusted odds ratio [aOR] 3.83, 1.40-10.51). Day-care attendance and living in a rural area were independently associated with OME (aOR 5.87, 2.31-14.91, and aOR 3.77, 1.58-8.99, respectively). **Conclusions:** The nasopharyngeal pneumococcal carriage was associated with OME among children aged <12 months.

Poster (Free Papers)

Otology (Clinical 2)

FP5-10

# Otitis media with effusion caused by a parapharyngeal tumor

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Otitis media with effusion (OME) is a common disease and it causes deafness. The objective of this study is to evaluate OME among parapharyngeal tumor patients. We have experienced 82 parapharyngeal tumor cases and encountered 14 patients complaining of hearing loss due to OME as the initial symptom. These patients showed normal nasopharyngeal findings and presence of tumor had detected long time after beginnings of their hearing symptoms (4 months to 13 years, median 2.5 years). Six patients had undergone ventilation tube insertion on the affected ear, which may lead to delay in diagnosis. Pathological examination was performed in 76 of 82 patients. Among these 76 patients, 13 showed OME. Seven patients had malignant lesions, whereas 6 had benign lesions. Therefore, malignant lesions are prone to occur with OME and its relative risk was 2.26 (95% confidence intervals 1.16-4.42). This difference was statistically significant ( $p=0.044$  Fisher-test).

OME is well known as a primary symptom of nasopharyngeal carcinoma. Therefore, nasopharyngeal observation is necessary for patients with intractable middle ear effusion. However, once the nasopharynx is revealed to be normal, additional examination is not usually done. In such a situation, myringotomy or ventilation tube insertion are usually performed. Nevertheless, present 14 patients with OME showed normal nasopharyngeal findings and finally found after an imaging study. From our data, otitis media with effusion is an important but go-by symptom of parapharyngeal tumors. Imaging studies are potentially useful for such patients with intractable OME, especially when accompanied by additional facial symptoms such as numbness or pain on the same side.

FP5-11

# A case of otitis media cholesteatomatosa in a young patient with significant inner ear destruction

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## Introduction

Although some patients with otitis media cholesteatomatosa have experienced bone destruction, such condition is relatively rare in young population. Here, we report our experience of otitis media cholesteatomatosa in a young patient with widespread bone loss in the semicircular canals.

History of present illness: A 14-year-old male has experienced recurrent otitis media since childhood. One month prior to visiting this department, he presented to a local clinic for persistent right otorrhea and earache; however, no improvement was observed, and thus he was referred to our department. Ear findings: A protruding torose lesion was found in the right external auditory canal. Temporal bone CT and MRI showed a highly likely diagnosis was otitis media cholesteatomatosa. Preoperative pure tone audiometry: Right 51.3 dB, left 6.3 dB. Surgical findings: Outer ear posterior wall had widespread destruction. There were callus lesions in the antrum mastoideum, but the external semicircular canal and posterior semicircular canal labyrinth was collapsing, and the interior of the ampullae were full of cholesteatoma. Cholesteatoma inside the membranous labyrinth was excised, but no lymph leakage was found. There was loss of the incus bone, but no fusion found in the stapes. Postoperative pure tone audiometry: Right 37.5 dB and left 1.3 dB. No worsening of bone conduction was found in the right ear.

## Conclusion

The patient may have had lesions for a considerable period of time, based on recurrent otitis media since childhood, and significant calluses in intraoperative findings. Hence, membranous labyrinth was already occluded at the time of surgery, which may be a reason that he did not experience hearing loss despite partial excision of the membranous labyrinth.

Poster (Free Papers)

Otology (Clinical 2)

FP5-12

FP5-13

**Examination of otogenic intracranial complications due to middle ear cholesteatoma in our department**

Withdrawn

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Introduction: Otogenic intracranial complications include purulent meningitis, epidural abscess, subdural abscess, brain abscess, and dural venous sinus thrombosis. The number of cases of onset and aggravation due to the development of antibiotics tends to decrease. However, if it develops, it may be a potentially life threatening. In many cases, collaboration with a neurosurgeon is required. In addition, it is often accompanied by underlying diseases such as diabetes, and it is necessary to cooperate with other departments for treatment. We report a case of intracranial complications caused by middle ear cholesteatoma from April 2012 to December 2019.

Method / result: From June 2012 to December 2019, we examined 5 cases treated in our department. The average age was 59 years (36-69 years), and all genders were male. The affected side was right: left = 2: 3. All cases were intracranial complications from middle ear cholesteatoma, and the main complaints were otorrhea, ear pain, headache, fever, dizziness, impaired consciousness, and speech disorder. The intracranial complications were meningitis in 1 case, meningitis + sigmoid sinus thrombosis in 2 cases, ventricular inflammation + meningitis in 1 case, and brain abscess in 1 case. Other ear complications were semicircular canal fistulas in 2 cases. As for surgical treatment, 2 out of 5 cases were treated with drainage + antibiotics in brain surgery, followed by mastoidectomy and tympanoplasty. Two were treated with antibiotics, followed by mastoidectomy and tympanoplasty. In one case, the cholesteatoma was spontaneously excreted by antibiotic treatment + local treatment (ear treatment), meningitis and local findings were alleviated, and subjective symptoms improved.

Poster (Free Papers)

Otology (Clinical 2)

FP5-14

# Cavernous Hemangioma of the External Auditory Canal in Patients Older than 60 Years: A Rare Tumor

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Hemangioma is a benign vascular soft tissue tumor and the most common soft tissue tumor in children. More than 60 percent of hemangiomas occur in the head and neck region, but they are rare in the external auditory canal. We present two cases of cavernous hemangioma involving only the external auditory canal. In these cases, a rare vascular cystic mass was excised and the symptoms of aural fullness and tinnitus improved.

A 62 years old woman visited our otorhinolaryngology clinic with symptoms of aural fullness in right ear that began several months prior. On physical examination, a soft, pinkish, cystic mass was observed in the right external auditory canal and it almost occluded the canal. In microscopic surgery under local anesthesia, the mass was excised completely via a retroauricular approach. After excision, the skin defect was minimal. After surgery, symptom of aural fullness in the right external auditory canal improved. Histopathologic findings revealed cavernous hemangioma, which consisted of thick-walled vessels. The vascular channels were covered with keratinized stratified squamous epithelium. A 69 years old woman visited our otorhinolaryngology clinic with symptoms of aural fullness and tinnitus in the left ear that began several years prior. On physical examination, a soft, purple, cystic mass was observed in the left external auditory canal.

In microscopic surgery under local anesthesia, the mass was excised completely via a transcanal approach. As in the former patient, pathology revealed cavernous hemangioma. After surgery, symptoms of aural fullness and tinnitus in the left external auditory canal improved.

Poster (Free Papers)

Otology (Research)

FP6-1

# Eustachian tube function test in two head positions

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**Objective:** Ear symptoms caused by a patulous eustachian tube (PET) are relieved by the head-down posture. We devised a postural change eustachian tube (ET) function test (Ohta Method) and evaluated it with two head positions using sonotubometry.

**Methods:** The JK-05AD ET function meter (RION, Japan) was used for sonotubometry in this study. A microphone was inserted into the subject's ear canal and a speaker was inserted into the subject's ipsilateral nostril. The presentation sound pressure (PSP) of an octave-band noise that was introduced into the nasopharynx was first measured, with the subject in the upright sitting position. Once the test device was reset, the PSP was measured with the subject in the head-down sitting position (sitting in a chair with the head between the knees). Finally, the ear canal sound pressure (ECSP) was measured as the subject's posture changed from the head-down to the upright sitting position. In this study, an ET function test with two head positions was performed in 92 ears of 46 healthy volunteers and 127 ears of 91 patients diagnosed with PET (68 ears of 51 patients with definite PET and 59 ears of 40 patients with possible PET).

**Results:** The average change in the ECSP was significantly higher both in the definite PET group (mean  $\pm$  SD,  $13.0 \pm 8.7$  dB) ( $P < 0.001$ ) and the possible PET group ( $7.7 \pm 8.6$  dB) ( $P < 0.001$ ) than in healthy volunteers ( $0.51 \pm 1.1$  dB). An increase of more than 5 dB in the ECSP after postural changes from the head-down to the upright sitting position was considered indicative of a PET. The overall rate of positive findings with Ohta Method was 91.2% (62/68 ears) in definite PET and 55.9% (33/59 ears) in possible PET.

**Conclusion:** This new postural change ET function test is a useful method for diagnosing PET.



Poster (Free Papers)

Otology (Research)

FP6-2

## Trials to establish our rat behavioral model of tinnitus using salicylate

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Tinnitus is a symptom-based complaint and is difficult to be evaluated objectively in basic as well as clinical studies. In order to understand tinnitus in animals, behavioral models of tinnitus using salicylate has been proposed since the 1980s, such as using drinking behavior, climbing rods, a Gap detection test, and electrical footshock (Kizawa-K et al. Neuroscience 2010; 165: 1323-1332). In this study, we adopted the last one in our laboratory to examine the effects of herbal medicines on tinnitus.

In this behavioral model, animals, male Wistar rats, were trained to perform an active avoidance task: animals were conditioned by electrical footshock to move to the other side of the conditioning box when hearing a sound. Animals received a single injection of salicylate (400 mg/kg i.p.) and "false positive responses", which means that animals feel tinnitus-like sound and move to the other side of the box, were measured 2 h after injection as the number of movements during a silent period. The number of false positive responses in salicylate-treated animals was highest when the conditioned stimulus was 60 dB sound pressure level (SPL) and 16 kHz. This indicates that animals could feel tinnitus 2 h after salicylate injection, equivalent to that induced by 60 dB SPL and 16 kHz.

We conditioned 88 rats, and checked at 4, 12, 16, 20 kHz in 60 dB SPL. Our study showed that the number of false positives at 16 kHz, 60 dB SPL tended to increase. We are now planning to establish this rat tinnitus model by conditioning additional numbers of rats to obtain much more reliable results, and to observe behavioral changes caused by various kinds of treatments in addition to herbal medicines.

FP6-3

## An Explanatory Model of Tinnitus

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Most conventional models of tinnitus cannot adequately explain the majority of tinnitus features. For instance, although tinnitus generally appears within minutes after entering a silent environment, most models postulate that tinnitus emerges over a much larger timescale. Similarly, there is a limited understanding of how the severity of tinnitus can differ in patients with a similar degree of hearing loss. To address this important knowledge gap, we have formulated a new explanatory model of tinnitus, the Perceptual Update (PU) model. The PU model proposes that the inner ear communicates auditory changes to the auditory cortex via the auditory N1 response. The auditory N1 is a prominent cortical electroencephalographic response to the onset (On-N1) and offset (Off-N1) of an auditory stimulus and changes (Change-N1) in pitch or timbre of a continuous tone. Recent studies revealed that ON-N1, OFF-N1 and Change-N1 are generated by the same neural mechanism and are part of the change detection system based on sensory memory. If the brain derives sound intensity based on a change in the auditory input, it is necessary to integrate the actual value of change. The PU model assumes that sound perception is continuously updated within the auditory system by determining at any given moment the relative change in input from the immediately preceding moment. This is similar to the function of data compression technology used for music and images called differential pulse code modulation (PCM).

In the case of hearing impairment, the PU model determines that the auditory system is in an uncertain state and must predict perception based on previous stimulus parameters, which may lead to the appearance of tinnitus.



Poster (Free Papers)

Otology (Research)

FP6-4

# Transcriptome analysis for deafness: neuroplastic change in the auditory cortex

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**Objective:** Hearing loss leads to synaptic changes in auditory neurons and their networks, and functions as a consequence of the interplay between genes and proteins. However, cellular and molecular mechanisms leading to deaf-induced neuroplasticity in the auditory cortex (AC) remain unclear.

**Methods:** Cochlear ablation-induced bilaterally deafened Sprague-Dawley rats were maintained for 12 weeks and their ACs were harvested. RNA-seq analysis was performed to reveal transcripts and the genes expressed in each sample, this information was then used for comparative analysis of DEGs between samples.

**Results:** RNA-seq analysis identified 72 DEGs, of which 19 were upregulated ( $\geq 1.5$ -fold change;  $P < .05$ ) and 53 were down-regulated ( $< 1.5$ -fold change;  $P < .05$ ) after bilateral deafening in the ACs. Gene ontology analysis revealed the potential involvement of mitogenic-activated protein kinases, tumor necrosis factor, and cyclic adenosine 3,5 monophosphate signaling pathways in regulating changes in gene expression. The DEGs of interest, including c-Fos, Arc, Ntf3, and Gli1, from the RNA-seq analysis were consistent with result of real-time quantitative polymerase chain reaction.

**Conclusion:** RNA-seq analysis revealed that auditory deprivation in adult rats elicited the changes in gene expression, transcription factors, and their complex interaction at specific gene promoters in the auditory cortex.

FP6-5

# Central Processing of Speech Sounds and Non-Speech Sounds with Similar Spectral Distribution: an Auditory Evoked Potential Study

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**Objective:** The purpose of this study was to measure the auditory evoked potentials for speech and non-speech sounds with similar spectral distributions.

**Materials and Methods:** We developed two types of sounds, comprising naturally spoken vowels (natural speech sounds) and complex synthesized sounds (synthesized sounds). Natural speech sounds consisted of 5 Japanese vowels. Synthesized sounds consisted of a fundamental frequency and its second to fifteenth harmonics equivalent to those of natural speech sounds. The synthesized sound was filtered to have a similar spectral distribution to that of each natural speech sound. These sounds were low-pass filtered at 2000 Hz. The auditory evoked potential elicited by the natural speech sound /o/ and synthesized counterpart for /o/ were measured in 10 righthanded healthy adults with normal hearing.

**Results:** The natural speech sounds were significantly highly recognized as speech compared to the synthesized sounds (74.4% v.s. 13.8%,  $p < 0.01$ ). The N1 peak amplitudes and latencies evoked by natural speech sounds were not different from those evoked by synthesized sounds ( $p = 0.58$  and  $p = 0.28$ , respectively). The P2 amplitudes evoked by natural speech sounds were not different from those evoked by synthesized sounds ( $p = 0.51$ ). The P2 latencies evoked by natural speech sounds were significantly shorter than those evoked by synthesized sounds ( $p < 0.01$ ).

**Conclusion:** The early P2 observed may reflect central auditory processing of the 'speechness' of complex sounds.

Poster (Free Papers)

Otology (Research)

FP6-7

# An examination on abnormally thickened subepithelial extracellular deposit of vestibular end organ in 3 human cases

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**Background:** The cause of degeneration of the neuroepithelium of the cristae ampullares with a thickened subepithelial extracellular deposit (SED) is unknown. This otopathological study describe the 3cases with thickened SED. These patients had vestibular symptoms during life. A thickened SED was present bilaterally in all three cristae. Therefore, we searched for possible causative factors of the unique pattern of the vestibular end organs by comparing the thickness of SEDs in the 3 study cases with several controls.

**Objective:** The purpose of this study was to characterize the vestibular degeneration, to measure the thickness of SED, and to evaluate the effect of vestibular disease and age.

**Methods:** The SED of the vestibular end organs of the three study cases were studied using H&E, PAS and Gomori trichrome staining. Immunostaining for anti-collagen 4a1 was also done. The thickness of the deposit as measured by light microscopy was compared to that of control groups (age-matched controls, patients with unilateral Meniere's disease, vestibular neuritis, cupulolithiasis, severe non-focal degeneration of the vestibular neuroepithelium, Alport syndrome).

**Results:** Thickened SEDs were found in all three cristae of the 3 study cases. The thickness of SED in the three cristae of the 3 study cases was significantly greater than that of all controls. In the three cristae of normal controls, the SED demonstrated a positive correlation with age.

**Conclusion:** Our results suggested that age and degeneration of the vestibular neuroepithelium is factors associated with the thickness of the SED in this unique pattern of degeneration.

**Acknowledgements:** We would like to thank members of Otopathology Laboratory at Massachusetts Eye and Ear/ Harvard Medical School.

FP6-8

# Rat Model of Meniere's Attack: Direction-changing Nystagmus and Reversible Hearing Impairment Induced by Intratympanic KCl Injection

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Meniere's disease is characterized by episodic vertigo, fluctuating hearing loss, and tinnitus. Direction-changing spontaneous nystagmus is a characteristic vestibular finding in Meniere's disease. In the acute stage, spontaneous nystagmus beating to the affected side (irritative) is often observed, while beating to the healthy side (paralytic) is found in the chronic disease stage. These symptoms have been reproduced in guinea pigs by increasing the potassium ion concentration in the perilymph. The objectives of the current study were to observe hearing and nystagmus changes induced by increasing the potassium ion concentration in the rat perilymph.

We allocated 22 rats to four groups and injected potassium chloride (KCl) solution or distilled water into the tympanic cavity of the right ear and monitored nystagmus: rats in Groups 1, 2, 3, and 4 received 3.4 M KCl solution, 2 M KCl, 1 M KCl, and distilled water, respectively. We also allocated 8 rats to two groups and injected KCl or distilled water into the tympanic cavity, and monitored hearing changes using auditory brainstem responses (ABR): Group 5 received 2 M KCl, and Group 6 received distilled water.

Rats in Groups 1 and 2 showed spontaneous irritative nystagmus followed by paralytic nystagmus. Rats in Group 3 mainly showed irritative nystagmus but rarely showed paralytic nystagmus. Rats in Group 4 showed no nystagmus. Rats in Group 5 showed significant hearing impairment 30 min after KCl injection which recovered 20 h later. Rats in Group 6 showed no significant hearing changes.

The current study showed that hearing impairment with direction-changing spontaneous nystagmus induced by intratympanic KCl injection in rats was reversible and similar to that observed in Meniere's attack.

Poster (Free Papers)

Otology (Research)

FP6-10

## Gene Therapy and Drug Screening for GJB2 Related Hearing Loss with iPS cells

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Mutation of the Gap Junction Beta 2 gene (GJB2) is the most frequent cause of hereditary deafness worldwide and accounts for up to 50% of non-syndromic sensorineural hearing loss. GJB2 encodes connexin (CX) 26, a component in cochlear gap junction. We have demonstrated that the degradation of gap junction plaque (GJP) macromolecular complex composed of CX26 and CX30 are critical pathogenesis starting at the embryonic days (Kamiya, J Clin Invest, 2014). We also demonstrated that the cochlear gene delivery of Gjb2 using Adeno Associated Virus (AAV) significantly improved the GJPs and auditory responses of Cx26 deficient mice (Iizuka, Hum Mol Genet, 2015). As several AAV serotypes has different cell tropism to cochlear cell types such as hair cells without gap junction and supporting cells with gap junctions, we examined various AAV serotypes to develop the effective gene therapy for GJB2 related hearing loss. For the disease modeling, we developed a novel strategy to differentiate induced pluripotent stem (iPS) cells into functional CX26-GJP-forming cells that exhibit physiological properties typical of the developing cochlea (Fukunaga, Stem Cell Reports, 2016). To establish the disease model cells from the patients, we generated human iPS cells from the patients with Japanese and East Asian typical GJB2 mutations, GJB2 V37I, G45E+Y136X and 235delC. To utilize disease model cells for the drug development, we established a gap junction based screening system with high throughput imaging cytometer. This screening system will enable us to develop the drugs and gene therapy vectors for GJB2 related hearing loss.

FP6-11

## Expression of advanced glycation end-product in the cultured utricles

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### Introduction

It is known that the prevalence of hearing loss is high in the patients with diabetes. We have reported that the model mice of metabolic syndrome showed the progressive hearing loss. Advanced glycation end products (AGEs) are proteins that become glycosylated after exposure to sugars. AGEs are prevalent in the diabetic vasculature and contribute to the development of atherosclerosis. We have shown that the formation of AGEs in the inner ear plays an important role in the progressive hearing loss with diabetes.

In this study, we report that AGEs were generated in the cultured utricles after the exposure to the high concentration of glucose.

### Materials and Methods

Cultured utricles of CBA/N mice were used. The utricles were divided to 3 groups (Control group, High glucose group, High fructose group). In the high glucose group, utricles were cultured with glucose (60 mM). Five days after exposure to glucose, the cultured tissues were fixed with 4% paraformaldehyde. To evaluate the expression of AGEs, immunohistochemistry was performed using anti-AGEs antibody. The signal intensity was evaluated with the fluorescence microscope.

### Results

The signal intensity of immunohistochemistry against AGEs were stronger in the high glucose group and fructose group than in the control group. The formation of AGEs was observed in the whole cultured utricles, not hair cell specific. The hair cell degeneration was not observed in both groups.

### Discussion

The results suggested that the inner ear tissues exposed to high concentration glucose accumulate AGEs. AGE is closely related to the tissue damage in the patients with diabetes. The relationship between inner ear damage and AGE formation have been unknown. However, I would like to clarify the role of AGE in inner ear disorders.

Poster (Free Papers)

Otology (Research)

FP6-12

**Preoperative assessment of chorda tympani nerve (CTN) function in patients with middle ear disease**

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**Objective:** To identify differences in the CTN function among patients with middle ear disease. In this study, not only taste function but also lingual trigeminal sensation was assessed, because the CTN contains general somatic afferents from the mandibular region but no special visceral afferents.

**Patients:** Four hundred twenty three patients underwent primary middle ear surgery from January 2006 to December 2017. The subjects consisted of 164 men and 259 women (194 ears with chronic otitis media, 104 ears with pars flaccida retraction-type cholesteatoma, 41 ears with pars tensa retraction-type cholesteatoma, and 84 ears with non-inflammatory diseases.)

**Methods:** All patients underwent the EGM and the FPD for the assessment of taste function in the regions controlled by the CTN before surgery. The SW test and the 2-point discrimination were performed in 134 patients for the assessment of lingual trigeminal sensation. In addition, the electrostimulator test was performed in 89 of them.

**Results:** Among the 4 groups, the patients with pars tensa retraction-type cholesteatoma had the highest the EGM and the FPD thresholds, but the differences were not significant. The frequency of abnormal right versus left difference ( $\geq 6$  dB) was significantly more in the patients with pars tensa retraction-type cholesteatoma than the other groups ( $p < 0.001$ ). The frequency of the abnormal FPD threshold ( $\geq 3.5$ ) in the the group was also significantly more than the other groups ( $p < 0.001$ ). The thresholds of lingual trigeminal sensation were not significantly different among the 4 groups.

**Conclusion:** Our findings suggest that taste function is affected most in patients with pars tensa retraction-type cholesteatoma and the trigeminal lingual sensation is not affected by middle ear inflammation.

Poster (Free Papers)

Rhinology (Clinical)

FP7-1

**Usefulness of postoperative endoscopic score for recurrent eosinophilic chronic rhinosinusitis**

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**Objective.** We retrospectively analyzed the postoperative endoscopy score (E score) for determining treatment in the patients with eosinophilic chronic rhinosinusitis (eCRS) undergoing endoscopic sinus surgery (ESS).

**Method.** The subjects were 339 adults who underwent bilateral initial ESS for eCRS diagnosed by the JESREC criteria from April 2007 to July 2021. There were 193 men and 146 women with median aged 52 years (22-82 years). Depending on the postoperative treatment, patients were divided into two groups: group A ( $n = 118$ ) that required steroid [systemic (prednisolone  $\geq 5$  mg/day) or local steroid treatment], dupilumab, or revision surgery after the initial ESS; and group B ( $n = 221$ ) that did not require any above treatments as a control showing good clinical course. Using a receiver-operating-characteristic (ROC) curve, the cutoff values of the E score for determining treatment at the time of recurrence was investigated.

**Results.** The optimal cutoff value for E score in the group A that required postoperative steroid treatment was 30% ( $n < 0.001$ ). In addition, the optimal cutoff for the E score in group A who resisted steroid treatment and required dupilumab or revision surgery was 65% ( $n < 0.05$ ).

**Conclusion.** It was suggested that the E score of postoperative eCRS can be used as an index for determining treatment at the time of recurrence.

Poster (Free Papers)

Rhinology (Clinical)

FP7-2

# A case of pollen-food allergy syndrome treated with omalizumab for intractable lip edema

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Background: Pollen-food allergy syndrome (PFAS) is a common adverse reaction occurring within a few minutes after the consumption of uncooked fruits and vegetables in patients with a pollen allergy. PFAS is an immunoglobulin E (IgE)-mediated allergic disease caused by cross-reactions among pollens and vegetables. The treatment for PFAS involves the avoidance of the consumption of the triggering food in a raw state, while other therapeutic options for PFAS are still under discussion. Here, we show a patient with intractable PFAS who was treated with sublingual immunotherapy (SLIT) and omalizumab.

Case description: A 12-year-old boy who had multiallergen pollinosis developed oral swelling after eating fresh fruits and vegetables, such as oranges, apples, peaches and tomatoes one year ago. Serum-specific IgE antibodies to 8 kinds of pollen, 3 kinds of fruit and 3 kinds of vegetables were detected. He showed positive reactions to several vegetables and fruits on the prick-to-prick skin test and tested positive on component-resolved diagnosis, such as pectate lyase, profilin and PR-10. We educated the patient to avoid fresh fruits, vegetables and treated him with pharmacotherapy such as antihistamines, intranasal corticosteroids and antileukotriene to reduce the symptoms. Furthermore, we treated him with Japanese cedar pollen (JCP) sublingual immunotherapy (SLIT) as he suffered from severe nasal symptoms during the JCP dispersal season. These treatments improved nasal symptoms; however, persistent oral swelling remained. Additional omalizumab treatment for two seasons reduced his oral swelling, suggesting that the combination therapy of SLIT for targeting the allergen component and omalizumab may be effective for refractory PFAS patients.

Poster (Free Papers)

Rhinology (Research)

FP8-1

# Copy Number Variation in DRC1 is the Major Cause of Primary Ciliary Dyskinesia in the Japanese Population

**Kazuhiko Takeuchi**  
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Primary ciliary dyskinesia (PCD) is a rare genetic disorder caused by functional impairment of cilia throughout the body. The involvement of copy number variation (CNV) in the development of PCD is largely unknown. We examined 93 Japanese patients with clinically suspected PCD from 84 unrelated families. CNV was examined either by exome sequencing of a PCD gene panel or by whole-exome sequencing (WES). The identified alterations were validated by PCR and Sanger sequencing. Nasal ciliary ultrastructure was examined by electron microscopy. Analyses of CNV by the panel or WES revealed a biallelic deletion in the dynein regulatory complex subunit 1 (DRC1) gene in 21 patients from 17 families, which accounted for 49 % of the PCD families in whom a disease-causing gene was found. Sanger sequencing of the PCR product revealed a 27,748 bp biallelic deletion including exons 1 to 4 of DRC1 with identical breakpoints in all 21 patients. The ciliary ultrastructure of the patients with this CNV showed axonemal disorganization and the loss or gain of central microtubules. The deletion of DRC1 is the major cause of PCD in Japan and this alteration can cause various ciliary ultrastructural abnormalities.



Poster (Free Papers)

Rhinology (Research)

FP8-2

**A novel scoring system of surgical findings at the sinus in patients with chronic rhinosinusitis**

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Outcome Objective:

This study aimed to propose a surgical scoring system at functional endoscopic sinus surgery (FESS) and to evaluate recurrence in patients with chronic rhinosinusitis (CRS).

Methods:

We retrospectively analyzed 496 patients with bilateral CRS who underwent FESS at our hospital between 2009 and 2019. Patients were followed-up for  $\geq 3$  months after FESS (mean,  $23.6 \pm 22.1$  months). Intra-operative endoscopic appearance in all sinuses and olfactory cleft (OC) was scored (OP score, 0-60 points). Mucosal lesions were scored as 0, normal; 1, edema; and 2, polyp. Contents were scored as 0, none; 1, mucopurulent; and 2, viscous. Post-operative endoscopic score (E score, %) was calculated as the maximum score on each operated sinus and OC (0, normal; 1, partially diseased; 2, completely closed). Since the OP score has many items of 30, a simplified OP score (ESS score) reduced to 16 items (0-32 points) was proposed in consideration of the correlation coefficients with the E score and clinical significance. The E score more than 50% was defined as recurrence. According to the results of the E score, the ESS score and pre-operative clinical findings were analyzed using univariate and multivariate analysis.

Result:

The E score and all sites of the OP score correlated ( $P < 0.05$ ). On the multivariate analysis, the ESS score was a significant factor of recurrences ( $P < 0.05$ ). In the ROC curve, the area under the phase was 0.759. When the cutoff value of the ESS score was determined to be 22 points, the sensitivity was 0.710 and the specificity was 0.718.

Conclusion:

The OP score could be simplified and used easily. Intra-operative findings can be a predictor of post-operative treatment for CRS.

FP8-3

**Asian Sand Dust Regulates IL-32 Production in Airway Epithelial Cells: Inhibitory Effect of Glucocorticoids**

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Epidemiologic studies have reported that Asian sand dust (ASD) is associated with chronic inflammatory diseases of the respiratory system. Glucocorticoids (GCs) have potent anti-inflammatory properties. The aims of this study were to evaluate the effects of GCs on ASD-induced interleukin-32 (IL-32) expression and to identify the underlying signaling pathways in airway epithelial cells. Methods: A MTT assay was used to evaluate cytotoxicity in A549 and human primary nasal epithelial cells. Expression levels of IL-32 messenger RNA and protein were measured by Western blot, real-time polymerase chain reaction, ELISA, and immunofluorescence staining. Signaling pathways were analyzed using specific inhibitors of Akt, MAPK, or NF- $\kappa$ B. The effects of GCs on the expression of ASD-induced IL-32 were confirmed with ex vivo organ cultures of the nasal interior turbinate. ASD (0 - 400 ng/mL) had no significant cytotoxic effects in A549 cells and human primary nasal epithelial cells. Expression levels of IL-32 were dose-dependently upregulated by ASD treatment in A549 cells. ASD induced phosphorylation of Akt, MAPK, and NF- $\kappa$ B, whereas GCs and specific inhibitors of Akt, MAPK, and NF- $\kappa$ B downregulated these activations and the expression of IL-32. These findings were further confirmed in human primary nasal epithelial cells and ex vivo organ cultures of the nasal interior turbinate. GCs have an inhibitory effect on ASD-induced IL-32 expression via the Akt, MAPK, and NF- $\kappa$ B signaling pathways in airway epithelial cells.



Poster (Free Papers)

Rhinology (Research)

FP8-4

**Serum IgG4 as a biomarker reflecting pathophysiology and post-operative recurrence in chronic rhinosinusitis**

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**Background:** Type 2 chronic rhinosinusitis (CRS), especially eosinophilic CRS (ECRS), is an intractable upper airway inflammatory disease. Establishment of serum biomarkers reflecting the pathophysiology of CRS is desirable in a clinical setting. As IgG4 production is regulated by type 2 cytokines, we sought to determine whether serum IgG4 levels can be used as a biomarker for CRS.

**Methods:** Association between the serum IgG4 levels and clinicopathological factors was analyzed in 336 CRS patients. Receiver operating characteristics (ROC) analysis was performed to determine the cut-off value of serum IgG4 levels that can be used to predict the post-operative recurrence.

**Results:** Serum IgG4 levels were significantly higher in patients with moderate to severe ECRS versus those with non to mild ECRS. The levels were also significantly higher in asthmatic patients and patients exhibiting recurrence after surgery compared to controls. ROC analysis determined that the best cut-off value for the serum IgG4 level to predict the post-operative recurrence was 95 mg/dL. The corresponding sensitivity and specificity were 39.7% and 80.5%, respectively. When we combined the two cut-off values for the serum IgG4 and periostin, patients with high serum levels of either IgG4 or periostin exhibited a high post-operative recurrence (OR: 3.95) as compared to patients having low serum levels of both IgG4 and periostin.

**Conclusions:** The present results demonstrate that the serum IgG4 level is associated with disease severity and post-operative course in CRS. In particular, the combination of serum IgG4 and periostin could be a novel biomarker that predicts post-operative recurrence.

FP8-5

**Efficacy of endoscopic sinus surgery for eosinophilic chronic rhinosinusitis with bronchial asthma**

**Nobuo Ohta**, Naoya Noguchi, Yutaro Saito, Muneharu Yamazaki, Yutaka Tateda, Shiori Kitaya, Takahiro Suzuki, Fumi Shoji, Yuji Yaginuma, Yusuke Ishida

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**Background** There is growing evidence that eosinophilic chronic rhinosinusitis (ECRS) is associated with bronchial asthma. Recent reports suggest the effectiveness of endoscopic sinus surgery (ESS) in ECRS patients with bronchial asthma, but whether ESS has a positive effect on the clinical course of asthma is still unknown. We investigated this point. **Materials and methods** We evaluated the effectiveness of ESS in 36 ECRS patients with bronchial asthma. We evaluated changes in symptoms, medication use, and pulmonary function in patients before and after ESS by an asthma control test questionnaire and pulmonary function tests. **Results** Following ESS, there were significant improvements in asthma control score (wheezing, coughing, shortness of breath), medication use, and pulmonary function. **Conclusions** This study provides corroborative subjective and objective evidence that ESS is feasible and effective in the management of ECRS with bronchial asthma.

Poster (Free Papers)

Rhinology (Research)

FP8-6

**The importance of adipokines in the pathogenesis of eosinophilic chronic rhinosinusitis**

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Chronic rhinosinusitis (CRS) is a heterogeneous chronic inflammatory disease generally divided based on presence or absence of nasal polyps (NPs). It had been reported that metabolic disorder may affect airway inflammation. To date, some reports showed that asthma may be related to metabolic disorder, however, the relationship with CRS had not been well understood. Adipokines can influence on both metabolic disorder and eosinophilic inflammation. In this study, we measured the serum levels of adipokines from patients with eosinophilic CRS (ECRS) and non-ECRS. We also demonstrated the relationships between the level of adipokines and the severity of ECRS according to Japanese Epidemiological Survey of Refractory Eosinophilic Chronic Rhinosinusitis Study (JESREC Study). The results showed that the levels of leptin in serum may reflect the severity of ECRS. Our finding may indicate that ECRS may be related to metabolic disorders.

FP8-7

**Anti-inflammatory effects of epoxygenated eicosapentaenoic acid metabolite on IL-33-induced innate eosinophilic inflammation in upper airway**

**Ichiro Tojima**, Shiori Hara, Keigo Nakamura, Sayuri Yamamoto, Masatomo Toyama, Hiroyuki Arai, Hideaki Kouzaki, Shino Shimizu, Takeshi Shimizu

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**Background:** 17,18-epoxyeicosatetraenoic acid (17,18-EpETE), one of the eicosapentaenoic acid metabolites, has attracted attention as a new class of pro-resolving lipid mediators. However, its biological importance in upper airway inflammation remains poorly understood.

**Objective:** To elucidate the effects of 17,18-EpETE and its metabolite, 17,18-diHETE, in innate eosinophilic inflammation of upper airway, in vitro effects on the cytokine production from group 2 innate lymphoid cells (ILC2s), and in vivo effects on IL-33-induced inflammation in mouse nasal mucosa were examined.

**Methods:** ILC2s were sorted from human peripheral blood by flow cytometry. ILC2s were stimulated with IL-33 and the inhibitory effect of 17,18-EpETE on IL-5 production was examined. Naive mice were treated by intranasal instillation of IL-33, and the effects of intranasal or intraperitoneal administration of 17,18-EpETE were examined in nasal mucosa and lung tissues.

**Results:** Human ILC2s expressed 17,18-EpETE receptor, GPR40. 17,18-EpETE attenuated IL-33-induced IL-5 production from ILC2s. Treatment with a GPR40 receptor antagonist abolished the inhibitory effect of 17,18-EpETE. Intranasal administration of 17,18-EpETE ameliorated IL-33-induced mucus productions and eosinophil infiltrations in nasal mucosa, and IL-5/IL-13 productions in bronchoalveolar lavage fluids and lung tissues, but intraperitoneal administration of 17,18-EpETE did not show any inhibitory effects. Intranasal administration of 17,18-diHETE also had similar anti-inflammatory effects.

**Conclusions:** 17,18-EpETE ameliorated innate eosinophilic inflammation induced by IL-33 in upper airway. These results indicate that 17,18-EpETE may have a therapeutic potential for the treatment of eosinophilic chronic rhinosinusitis.

Poster (Free Papers)

Rhinology (Research)

FP8-8

# Development of an intranasal phototherapy device for allergic rhinitis using LEDs emitting narrowband-UVB

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Narrowband-ultraviolet B (NB-UVB) phototherapy was clinically used for the treatment of atopic dermatitis (AD). Allergic rhinitis (AR) is a TH2-dominant disease as well as AD. Therefore, NB-UVB phototherapy may also be effective for the treatment of AR. Recently, we developed light-emitting diodes (LEDs) that emit their energy at wavelength of 310nm NB-UVB with the cooperation of a company. Developed LEDs are small enough for the use of intranasal phototherapy. In order to develop a device of NB-UVB phototherapy for AR, we first examined the effects of NB-UVB irradiation on the histamine H1 receptor (H1R) gene expression in HeLa cells. We demonstrated that low-dose irradiation with NB-UVB wavelength-specifically, dose-dependently, and reversibly suppressed PMA-induced up-regulation of H1R mRNA without inducing apoptosis of HeLa cells. We then conducted an in vivo study using toluene 2,4-diisocyanate (TDI)-sensitized allergic rhinitis model rats. We demonstrated that intranasal irradiation with low-dose NB-UVB dose-dependently suppressed TDI-induced nasal symptoms and up-regulation of H1R mRNA in the nasal mucosa of model rats without inducing DNA damage in the nasal mucosal cells. These results suggest that low-dose of NB-UVB phototherapy could be effectively and safely applied for the treatment of AR. Finally, we have developed a prototype of intranasal NB-UVB phototherapy device for AR and demonstrated its safety in phase 1 and early phase 2 clinical trials. Next, we are planning a doctor-initiated clinical trial for AR patients.

FP8-9

# The association between the human microbiome in the nasal cavity and the number of sensitization in allergic rhinitis

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Allergic rhinitis significantly reduces the quality of daily life in a wide range of age groups. In a 2016 epidemiological survey in Japan, the prevalence of allergic rhinitis was reported to be about 40%, and the prevalence was further increasing (Sakashita M, et al.).

The increase in prevalence is thought to be due to various factors such as lifestyle, living environment, diet, and the human microbiome. In asthma and inflammatory bowel disease, the human microbiome has been reported to affect the risk of disease onset and severity by causing dysbiosis, which means a change in the composition and abundance of the human microbiome compared to healthy individuals.

However, there are few reports on the human microbiome in the field of otorhinolaryngology. The purpose of this study is to investigate the human microbiome of the nasal cavity, saliva, and stool in allergic rhinitis.

The epidemiological survey was conducted during the staff health examination of 1472 employees of the University of Fukui and the Tannan Hospital in 2016. A questionnaire about the allergic disease and total IgE and antigen-specific IgE levels were measured by blood sampling. Of those, 341 who gave consent were included in the study, and samples of nasal swabs, saliva, and stool were collected.

Microbe-derived DNA was extracted from the collected samples, PCR amplification and indexing of the V3-V4 region of the 16S rRNA gene were performed, and the genome sequence was measured using Illumina MiSeq. The measured data were used to identify microorganisms to the genus level using Quantitative Insights Into Microbial Ecology 2 (QIIME2) and the analysis software R. We report the results of bacterial composition ratio, diversity analysis, and metabolic function prediction with clinical data.

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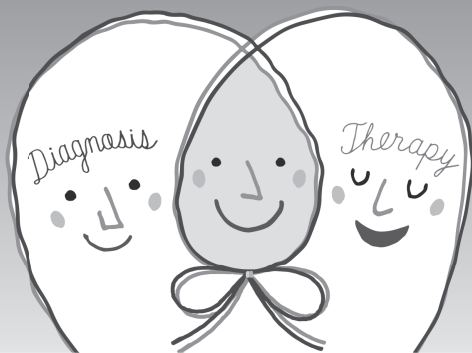
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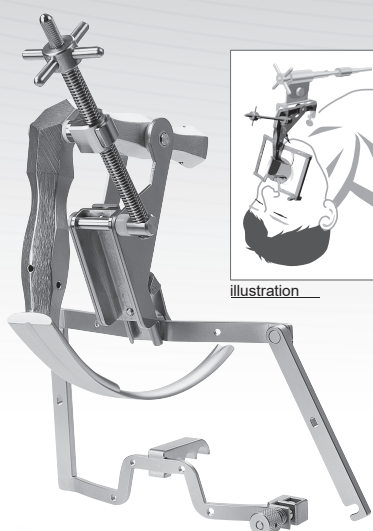


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