

# Symposium

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15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery

## Symposium 1 Facial Nerve

## SY1-1

**A new electroneurography (ENoG) method for facial palsy - midline method**

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

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

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

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

**Conclusion:** Lately, the midline ENoG recording method has been widely used in Japan. This method has advantages over the standard method from the viewpoint of electrode setting, and its ENoG value is more useful as a prognostic factor. The presenter will also indicate an important point to adopt a CMAP of facial muscles from recorded waves.

## SY1-2

**Intratympanic steroid therapy for severe facial nerve palsy**

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Bell's palsy and Ramsay Hunt syndrome account for approximately 70% of acute facial palsies worldwide, with yearly incidences of 20 and 5 per 100,000 individuals, respectively. These conditions result from viral neuritis of the facial nerve. Ramsay Hunt syndrome is known to be caused by varicella-zoster virus (VZV), and Bell's palsy is typically caused by herpes simplex virus type-1 (HSV-1). Combination treatment with systemic steroids and antiviral agents is currently widely used in treating patients with these conditions. For Bell's palsy, this approach has led to recovery in 92.6–96.5% of cases. However, the recovery rate remains unsatisfactory in severe cases. For example, for patients with facial nerve degeneration of  $\geq 90\%$  as determined by electroneurography (ENoG), the rate of recovery is only 25–66.7%. Furthermore, in Ramsay Hunt patients, in whom facial paralysis is typically more severe, this approach achieves recovery in only 52.5–58.7% of cases.

In severe cases of Bell's palsy and Ramsay Hunt syndrome, defined as  $\geq 90\%$  facial nerve degeneration, surgical decompression of the facial nerve is an additional treatment option. During this procedure, bulging or herniation of the facial nerve from a dehiscence of the facial canal is sometimes observed, which could facilitate localized delivery of steroids in patients with severe Bell's palsy or Ramsay Hunt syndrome.

The most widely used local steroid treatment for inner ear diseases is intratympanic steroid therapy (ITST), i.e. injection into the tympanic cavity. Although this approach mainly targets the inner ear, steroid can also reach the adjacent facial nerve, especially when the latter extends out of the facial canal. Because the impact of concurrent ITST on the facial nerve has not been characterized, we investigated its efficiency in patients with severe facial palsy (HB grade V or VI) with Bell's palsy and Ramsay Hunt syndrome.

SY1-3

## The regeneration facilitating effects of basic fibroblast growth factor impregnated biodegradable gelatin hydrogel as a novel therapeutic strategy for facial paralysis due to temporal bone fracture

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**Introduction:** Temporal bone fracture occasionally leads to severe facial paralysis. Although facial nerve decompression is indicated when severe facial paralysis occurs after trauma, the outcome of surgery is insufficient overall. Improving surgical intervention outcomes remains a challenge for most otolaryngologists.

Over the last few decades, many growth factors have been found and utilized for practical purposes. Basic fibroblast growth factor (bFGF) is known to promote nerve regeneration following denervation and is currently commercially available as a medication in Japan. Furthermore, biodegradable gelatin hydrogel has been developed as a drug delivery system that released some growth factors continuously over several weeks. Our previous studies demonstrated that bFGF-impregnated biodegradable gelatin hydrogel facilitated regeneration of the damaged facial nerve in an experimental study and the patients with severe Bell's palsy.

**Objective:** The purpose of this study was to determine the regeneration-facilitating effects of bFGF-impregnated biodegradable gelatin hydrogel in patients with severe facial paralysis caused by temporal bone fracture.

**Methods:** Nine patients with severe facial paralysis with a >95% degree of denervation as assessed by electro-neuronography were treated with the new procedure at our institution between 2006 and 2016. The facial nerve around the fractured segment was exposed via the mastoid, while the nerve sheath was not incised to avoid possible damage to the facial nerve. A bFGF-impregnated biodegradable gelatin hydrogel was placed on the exposed nerve. Regeneration of the facial nerve was evaluated by the House-Brackmann (H-B) grading system. The outcomes were compared with 27 patients that had undergone conventional transmastoid decompression surgery at our hospital before this study.

**Results:** The rates of good recovery (H-B grade 1 or 2) in the 2 groups were 88.9% and 48.1%, respectively, with significant differences between the novel treatment and conventional surgery groups.

**Conclusion:** The efficacy of this novel treatment is advantageous in the cases of severe facial paralysis following temporal bone fractures. This is the first clinical report of bFGF efficacy in a drug delivery system for patients with facial nerve paralysis due to a temporal bone fracture.

SY1-4

## A systemic approach to decrease the chance of marginal mandibular branch injury during level Ib neck dissection

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Injury to marginal mandibular branch (MMB) of the facial nerve is a complication not uncommonly seen during neck dissection in head and neck (HNC) patients. The reported rate of MMB injury in HNC patients receiving neck dissection ranges from 0% to as high as 28%. Injury of MMB will lead to weakness of depressor anguli oris and depressor labii inferioris, resulting in asymmetry of the lower lip and mouth angle when smiling. In a previous study conducted on HNC patients receiving neck dissection, 41% of patient reported a minor change of their smiling, 5% was bothered by their asymmetric smiling, and 3% reported limitation of their activities due to their disfigured smiling. Thus, it is important to minimize inadvertent injury of MMB during neck dissection to improve life quality of HNC patients.

In submandibular gland/tumor operation, MMB is traditionally protected by the well-known Hayes-Martin maneuver, which denotes ligation the facial vein at a level approximately two finger-breadths below the mandible, followed by retraction of the superficial layer of the deep cervical fascia with the subplatysmal plane until the lower margin of mandible. However, such approach will inevitably result in suboptimal dissection of supramandibular/perifacial lymph nodes, which is apparently at risk of metastasis in oral cavity cancer patients. Therefore, a consistent way to safely clear the supramandibular/perifacial lymph nodes while minimize the chance of inadvertent injury of MMB is needed.

Reviewing literature, although a variety of surgical approaches has been proposed to locate MMB intraoperatively, only a few studies have been focused on the identification of MMB during neck dissection. Despite it is possible to routinely identify every ramus of MMB during neck dissection, such kind of approach will inevitably increase the time of operation. In this presentation, I'll (1) briefly discuss the anatomical location and potential variation of MMB (2) describe the rationale of our surgical approach (3) share our experiences and results in conducting such an approach.

## SY1-5

## The facial nerve in parotid surgery

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Surgical intervention is the standard management for parotid gland neoplasms. The risk of facial paralysis after parotid surgery is the primary concern of both surgeons and patients. Facial nerve dysfunction not only causes cosmetic and social problems, but also increases ocular complications and significantly impacts on a patient's quality of life. Surgeons and researchers have continued to look for more reliable landmarks to identify facial nerve and better ways to reduce the incidence of iatrogenic facial nerve dysfunction.

Intraoperative facial nerve monitoring in parotid surgery has been investigated for decades to reduce patients' morbidity. However, its effectiveness in abating the occurrence or severity of transient facial nerve dysfunction remains controversial.

However, the rate of postoperative facial paralysis after parotidectomy remains high. Transient facial nerve dysfunction has been reported in 20% to 40% of patients, whereas permanent facial nerve dysfunction occurs in 0% to 5% of cases.

Several risk factors have been identified for post-parotidectomy facial nerve dysfunction, including older age, malignancy, larger tumor size, tumors involving the deep lobe of a parotid gland, surgery for chronic inflammatory diseases and reoperation. In general, these factors are based on patient characteristics known at the time of diagnosis. For patients who develop immediate post-parotidectomy facial nerve dysfunction, the prognosis and the period of recovery of function are always concerned. Those with anticipated spontaneous recovery should be observed rather than scheduled to undergo surgery for facial reanimation. It is important to clarify the expected duration of facial nerve dysfunction, and to know the predictors of final facial nerve function in these patients. In this presentation, we will also share the results and time to recovery in patients with immediate facial nerve dysfunction after parotid surgery in our hospital. The influences of different clinical and pathological parameters were also analyzed to determine the prognostic factors in this group of patients.

## Symposium 2 Rhinology

### SY2-1

#### Novel clinical practice guidelines for the management of olfactory dysfunction in Japan

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**Objective:** To provide an evidence-based recommendation for the management of olfactory dysfunction (OD) in accordance with the consensus reached by the Subcommittee of the Japanese clinical practice guideline for olfactory dysfunction in the Japanese Rhinologic Society.

**Methods:** The following seven clinical questions (CQs) for the management of OD [CQ 1-7] were formulated: [CQ1] medical therapy in chronic rhinosinusitis (CRS); [CQ2] endoscopic sinus surgery (ESS) in CRS; [CQ3] medical therapy in allergic rhinitis (AR); [CQ4] effective treatments in post-viral OD (PVOD); [CQ5] effective treatments in post-traumatic OD (PTOD); [CQ6] contribution of OD as a predictor of early diagnosis of neurodegenerative diseases; and [CQ7] effect of corticosteroids on OD. The literatures published between April 1990 and September 2014 using the PubMed, Cochrane Library, and Japanese Ichushi Web databases were searched. Based on the results of the literature review and the expert opinions in the Subcommittee, four levels of recommendation in each CQ: [A] strongly; [B] moderately; [C] weakly recommended; and [D] not recommended, were finally adopted for the management of OD.

**Results:** [CQ1] Both topical and systemic administration of corticosteroids have been the most recommended medicines for patients with OD due to CRS with high levels of evidence by randomized-controlled trials (RCTs) (level A). [CQ2] Most reports have described as observational studies, and their mean improvement ratio was approximately 70% after ESS in CRS patients with OD (level B). [CQ3] Nasal steroid spray and antihistamine drugs have been moderately recommended for patients with OD due to AR (level B). [CQ4] Olfactory training using odorants has been reported to be effective for improving PVOD, though no drugs have been deemed to be truly effective by RCTs (level C). [CQ5] Although Kampo medicines, corticosteroids, vitamin, and adenosine triphosphate are used to treat for PTOD in Japan, the efficacy of these medicines has not been supported by high levels of evidence (level C). [CQ6] Olfactory testing is useful for differential diagnosis, prediction of disease progression, and early detection of cognitive decline in neurodegenerative diseases (level A). [CQ7] Corticosteroid treatment with attention to the pituitary/adrenal system suppression, are effective in patients with OD due to CRS and/or AR. On the other hand, the efficacy of corticosteroid treatment on the OD without any sinonasal inflammation, including PVOD, PTOD, and idiopathic OD, is limited (level B).

**Conclusion:** The clinical practice guideline has been developed and used for the management of various aspects of OD in Japan.

### SY2-2

#### Effects of Biologic drugs for chronic rhinosinusitis with nasal polyps

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Eosinophilic chronic rhinosinusitis (ECRS) is a subgroup of chronic rhinosinusitis with nasal polyps (CRSwNP), which is associated with severe eosinophilic infiltration and intractable. Its symptoms include dysosmia, nasal obstruction, and viscous nasal discharge. The precise mechanisms by which ECRS represents Th2 dominant eosinophilic inflammation remain unclear. Several studies suggested that *Staphylococcus aureus* and its enterotoxins are involved in stimulating the Th2 system to promote IgE production and eosinophil infiltration through various pathways. One of the important histopathological features of ECRS is prominent tissue edema and less collagen formation.

We previously demonstrated that the coagulation system is activated, and the fibrinolytic system is suppressed, leading to excessive fibrin deposition in nasal mucosa, which cause nasal polyp development. Actually, degradation of fibrin mesh of nasal polyp tissue significantly shrinks nasal polyp tissue. Therefore, a fibrin-degrading agent could also be a new treatment for ECRS.

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. Clinical studies of these biologics, anti-IL-5 antibody (Ab), anti-IL-5 receptor (IL-5R) Ab, anti-IgE Ab and anti-IL-4R $\alpha$  chain Ab, have been performed for severe CRSwNP. Anti-IgE Ab (omalizumab) improved nasal obstruction, hyposmia and nasal secretion scores in ECRS patients with aspirin induced asthma. Placebo-controlled double-blind study of anti-IL-5 Ab (mepolizumab) demonstrated to decrease nasal polyps and to improve CT findings in patients with large nasal polyps. 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. Precision medicine using biologics will be performed to ECRS patients in the future.

## SY2-3

## Direct approach to the anterior and lateral part of the maxillary sinus with an endoscope

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**Objective:** The Caldwell-Luc (CL) approach with a sublabial incision is used to manipulate the anterior wall of the maxillary sinus. Paresthesia is one of the major complications associated with the CL approach. We developed a new method, “direct approach to the anterior and lateral part of the maxillary sinus with an endoscope” (DALMA), that negates the need for a sublabial incision and minimizes dental paresthesia by reducing the risk of anterior superior alveolar nerve injury. This study aimed to describe how to perform the DALMA technique, and to review its effectiveness and associated complications.

**Methods:** We retrospectively reviewed 10 patients who had received DALMA.

**Results:** Ten patients underwent DALMA. The anterior superior alveolar nerve was identified in all patients. Access to the lateral side beyond the infraorbital canal and anterior wall of the maxillary sinus was achieved.

**Conclusions:** DALMA is a simple, effective, and minimally invasive technique that can be used as an alternative to CL with sublabial incision.

## SY2-4

## The Influence of Eosinophils on the Manifestation and Surgical Outcomes of CRSwNP

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**Background and aim:** Eosinophilic chronic rhinosinusitis with polyp (CRSwNP) is more predominant in the western countries than in the EAST. The disease entity is typically presented with more extensive sinus disease and higher polyps recurrence after surgery. Although lacking the consensus in the diagnostic criteria, studies have shown the prevalence is keeping increased in some Asian areas. Thus Rhinologists have concerned the impact of the quality of life for who suffered from Eosinophilic CRSwNP. The study aims to understand how eosinophils influence the disease-specific quality of life, clinical manifestations, and surgical outcomes for patients with CRSwNP.

**Materials & Methods:** A retrospective analysis was conducted of 21 chronic rhinosinusitis with polyps (CRSwNP) patients who underwent FESS between Jan. 2019 and May, 2019 at China Medical University Hospital. Demographic data, history of atopy, pre-operative and post-operative SNOT22, and tissue eosinophils were collected. The correlation between eosinophils and disease-specific quality of life, symptoms, and surgical outcomes are analyzed.

**Results:** CRSwNP patients with higher tissue eosinophils presented with worse quality of life and symptoms, especially in rhinologic domain and extra-rhinologic domain. On the other hand, Patients who have higher tissue eosinophils can obtain more symptoms Improvements after FESS.

**Conclusion:** The level of eosinophils in polyps tissue will influence the disease-specific quality of life, clinical manifestations, and surgical outcomes of patient with CRSwNP.



SY2-5

## Rhinoplasty in Rhinology

Chih-Wen Twu

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The Nose is a respiratory organ, an olfactory organ and a vomeronasal organ. Meanwhile, the nose is a prominent facial feature.

Traditional rhinoplasty corrects only the aesthetic deformities; however, restoration of both aesthetic and physiological function is mandatory in modern septorhinoplasty.

Proper diagnosis is the gate to the success in managing both functional and aesthetic rhinoplasty. A detailed and thorough analysis of the nasal deformities includes inspection, palpation, endoscopic examination, functional tests like acoustic rhinometry and rhinomanometry, imaging studies like computed tomography scan. Photography is crucial for surgical planning and for discussing surgical options with the patients.

Specific deformities then can be manipulated with precise surgical planning. Topics including nasal valve stenosis, caudal septal deviation, twisted nose, etc. will be discussed in this session. For example, while we're facing the deviated nose associate with breathing problem, we can follow the logic in surgical procedures. Since the aesthetic and functional deviated noses come from deformities in skin-soft tissue envelope, bony-cartilaginous framework and internal lining, the topics discussed in this session will be:

1. Anatomical and Functional aspects of the deviated nose
2. Management of the deviated septum
3. Management of the bony and cartilaginous vault
4. Management of the asymmetric tip
5. Other skills for deviates nose like arrangement of camouflage

SY2-6

## Updates in the management and mechanism of olfactory dysfunction

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Olfactory dysfunction is a common disease and caused by rhinosinusitis, upper respiratory tract infection, head trauma, neurodegenerative diseases and ischemic brain injury. Olfactory dysfunction can impair the quality of life and is a potential life-threatening disease. Corticosteroid can be effective in some cases with olfactory dysfunction after rhinosinusitis, viral infection, or head trauma. Olfactory training is another treatment for olfactory dysfunction, and its effect can be found in some cases. Other potential therapies such as zinc, vitamin A and theophylline have been proposed; however, the evidence of these therapies are limited. There are still some patients with olfactory dysfunction who have no improvement after the current management. Thus, the management and the mechanism of olfactory dysfunction is still under investigation.

Microglia are the brain resident macrophages, and its activation in the olfactory bulb has been reported to develop olfactory dysfunction in animal models of traumatic brain injury, neurodegenerative diseases and ischemic brain injury. Activated microglia releases proinflammatory cytokines including interleukin (IL)-1 $\beta$ , IL-6, tumor necrosis factor- $\alpha$ . These cytokines increase the degree of neuroinflammation and is associated with olfactory dysfunction. We have used a selective soluble epoxide hydrolase (sEH) inhibitor in rats with ischemic brain injury and olfactory dysfunction. We found the sEH inhibitor can attenuate microglia activation and proinflammatory cytokines expression. Besides, it can also decrease the degree of olfactory dysfunction in rats.

In this presentation, I will review the current management of olfactory dysfunction and share our novel discovery of mechanism and therapy of olfactory dysfunction.

## Symposium 3 Skull Base

## SY3-1

**Lateral skull base surgery: A single-center experience in the last 5 years**

Noritaka Komune

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The temporal bone's complex, intricate structure is a product of its close association with vital organs; anatomical structures it houses, in whole or in part, include the internal carotid artery, otic capsule, jugular bulb, superior and inferior petrosal sinuses, internal auditory canal and, trigeminal and lower cranial nerves. Due to its complexity, lateral skull base surgery is still challenging. Around the temporal bone, a variety of tumors may arise including schwannoma, external auditory canal carcinoma, glomus tumor, cholesteatoma and so on. There are a variety of surgical approaches reported for the lateral skull base surgery. Recently, the application of the endoscopic endonasal approach has extended to the lateral skull base region such as the petrous apex as its surgical techniques have advanced. Thusly the choice of an appropriate approach should be based on the tumor's histopathology and location.

The establishment of the multidisciplinary surgical team is the most essential in the modern skull base surgery, which is one of the recent achievements in my institution. The multidisciplinary team comprises of otorhinolaryngologists, neurosurgeons and plastic surgeons. After the establishment of our surgical team, we can discuss all types of skull base pathologies once a month to choose the surgical corridor, size of craniotomy, surgical approaches, reconstruction methods, skin incision. The advance of the surgical tracking devices is also important for the lateral skull base surgery. A textbook knowledge of anatomical landmarks is still essential, but no longer sufficient enough to perform surgery up to current, modern safety standards. The surgical tracking devices however, now make it possible to confirm "patient-specific" anatomy during surgery. Thusly, we use the electromagnetic navigation system to make the lateral skull base surgery more accurate, gentle and safe.

In this talk, we reviewed the skull base cases in the last 5 years and will show a variety of the lateral skull base surgeries performed in our institution. It includes subtotal temporal bone resection of the external auditory canal carcinoma, the resection of the glomus tumor in the jugular foramen, infrapetrous approach for the petrous apex cholesterol granuloma, transotic approach for the cochlear schwannoma and others.

## SY3-2

**Recent advantage of craniofacial resection for anterior or anterolateral skull base malignancy**

Yasushi Fujimoto

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Craniofacial resection of sinonasal carcinoma has been used widely since Ketcham et al first reported it in 1963, and many authors have reported good results with favorable prognoses and low complication rates for craniofacial resections of malignant skull base tumors. At Nagoya University Hospital, 134 patients underwent craniofacial resection during 27-year period. Among them, 101 patients underwent anterior or anterolateral cranial base resections for nasal or paranasal malignant tumors.

The 5-year survival rate was 77.5% among anterior skull base, and 60.6% among antero-lateral skull base cases, respectively. Univariate analysis showed that surgical margin, recurrent disease and skin invasion had a significant effect on the five-year overall survival and disease-free survival. Complications occurred in 14 patients, including two mortalities resulting from cerebral infarctions or meningio-encephalitis after cavernous sinus resection. Most severe complications were occurred during the first decade, and amount of bleeding and operation time was significantly longer than today. Successful en-bloc tumor resection requires a complex and precise surgical technique, and outcomes of craniofacial resection depend on clinical experience and surgical expertise.

We have tried to minimize surgical invasion by 1) construction of team approach among neurosurgeons, plastic surgeons, and head and neck surgeons, and 2) introduction of the 3D virtual surgical simulations.

The 3D virtual surgical simulations are performed with the Virtual Surgiscope, which uses a volume rendering method to generate the 3D virtual environment from CT images. The Surgiscope allows the surgeon to view anatomic structures from various viewpoints and directions. Key anatomic structures can be rendered in different colors by extracting these regions from the CT images in advance. By means of appropriate feedback that can highlight disparities between a surgical simulation and the actual surgery could help to reduce complication rates and improve prognoses.

Preoperative surgical simulation and postoperative feedback can contribute to training for surgeons and surgical support in patients undergoing skull base surgery for sinonasal carcinoma.



SY3-3

## Endoscopic endonasal surgery for sinonasal carcinoma

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Endoscopic endonasal surgery for sinonasal carcinoma is becoming popular these days.

The surgery is often performed as a definitive therapy especially for olfactory neuroblastoma, which is regarded as low-grade carcinoma. For high-grade carcinoma, however, its surgical indication has not been established, otherwise, chemoradiation or particle beam therapy such as proton or carbon ion beam is the first choice.

Among high-grade carcinoma, we think mucosal malignant melanoma can be applicable to endoscopic endonasal surgery. Regarding squamous cell carcinoma, patients who develop primary failure after radiotherapy can undergo excisional biopsy or salvage surgery with endoscopic endonasal approach.

In this symposium, we show the surgery videos of representative cases who underwent endoscopic endonasal surgery for malignant tumors. In addition, important surgical anatomy for this approach will be reviewed with cadaver dissection videos.

SY3-4

## Microvascular free flaps and the applications of 3D-printing in head and neck reconstructions

San-Fu Hong

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To maximize function and restore cosmetics, head and neck reconstruction is necessary for patients with head and neck tumors surgery. The microvascular free flaps can provide several versatile flaps for the complex anatomy of the head and neck region and achieve the goal of reconstruction functionally and aesthetically. 3D printing-assisted surgery, including preoperative virtual surgical planning, intraoperative cutting and reconstructive guides is highly accurate and reduce operation time in fibular flap mandibular reconstruction.

From January 2016 to September 2019, more than 300 consecutive microvascular free flap reconstructions were performed by author. The rate of successful flap transfer was 96%. Otolaryngologists have abundant experience and expertise in anatomy and physiology of the head and neck. After microvascular surgery training, otolaryngologists can perform microsurgical reconstruction of the head and neck.

## SY3-5

## Bilateral smell preservation is routinely possible following endoscopic endonasal approach for sellar/suprasellar lesions

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**Background:** The endoscopic endonasal approach (EEA) has been shown to be an effective means to access sellar and parasellar lesions. However, there are limited studies centered on evaluating olfactory function after surgery. In current study, we assessed the pre- and postoperative olfactory function of patients who underwent EEA for sellar lesions. The impact of nasoseptal flap use on olfaction was further analyzed.

**Methods:** We retrospectively reviewed patients with sellar and suprasellar lesions who had underwent EEA surgery from August 2015 to March 2018. The patients' olfactory function were examined pre- and postoperatively using Sniffin' Sticks' odor identification test. Data regarding demographics, olfactory scores, pathology, reconstructive technique, graft usage, and extent of resection were retrieved.

**Results:** A total of 106 subjects were enrolled. The mean age was 51 years old, with 36 males and 70 females. There were 76 pituitary tumors, 12 Rathke's cleft cysts, 7 craniopharyngiomas, 7 meningiomas, and 4 other lesions. The nasoseptal flap was used in 39 cases for skull base reconstruction, and these patients had no statistically significant change between pre- and postoperative olfactory scores ( $p = 0.283$ ). Moreover, statistically significant improvement of olfactory scores was found in patients who did not have a nasoseptal flap for skull base reconstruction.

**Conclusion:** Olfactory function may be reliably preserved after EEA, with or without nasoseptal flap harvest and use.

## SY3-6

## Clinical Outcome of Endonasal Endoscopic Prelacrimal Approach in Managing sinonasal Pathologies

Yu-Hsuan Lin

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Endoscopic prelacrimal recess approach (EPLA), also called the modified nasal lateral wall resection, has been widely applied in treating tumors located within maxillary sinus, pterygopalatin fossa and infratemporal fossa. Because the surgical corridor might offer unobstructed view of almost any aspect of maxillary inner linings and improved the operating field, the appliance of the EPLA has been reported to provide results comparable to those of conventional external procedures in treating sinonasal neoplasms. It was of great value for its intuitive views in clinical practice meat to be incooperated into a patient's treatment.

In the presentation, we aimed to provide our experience in using the unsophisticated surgical method to effectively manage various sinus diseases. Limitation of EPLA and our rationale in treating diseases other than neoplasms were also addressed. In addition, we also reported our recent clinical outcomes of consecutive 22 patients (23 lesions) treated with EPLAs. We found patient with non-papilloma lesions had significant improvements in S22-item Sino-Nasal Outcomes Test (SNOT-22) and 10-point visual analogue scales (VAS) ( $p$ -value=0.012), while those with papillomas had only marginally significant improvements in VAS ( $p$ -value=0.061). The most common adverse event to be transient cheek or tooth numbness but they usually subsided within 6 months. Thus, with adequate patient counseling, symptoms reduction and improvements in life quality can be expected after receiving surgical treatment of sinonasal lesions using EPLAs.

**Symposium 4** Otology

**SY4-1**

**How to use surgical navigation right and make it useful in otological procedures?**

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Otological procedures deal with 3-dimensionally located complex anatomy that are buried in the bone. Surgical navigation systems that can locate hidden structures within the bone should be helpful. However, there has been a long struggle to manage the required accuracy while reducing the invasiveness to minimal. We have been using commercially-available surgical navigation systems along with developing our own systems to evaluate different functions during the surgery. The presenter will share some of the lessons we have learned in the past decade to improve the accuracy and usability of surgical navigation systems in temporal bone surgery.

1. The reference frame should be secured on bone, or teeth. There is no way that the reference sticker on the skin provides submillimeter accuracy. The reference frame should be treated with extra care throughout the surgery, because once the reference frame is detached, navigation is no longer reliable.
2. The registration should be performed while the patient head is in "CT" position, not the "operating" position. The skin shift during head rotation is more than 5 mm. The registration should be repeated until the operator feels sure that the accuracy has reached the limit. The accuracy should be evaluated in the ear canal, not the pinna.
3. The image screen should show 3-dimensional view with extrapolation of the navigation probe. In otological procedures, the surgeon wants to see the "future" position of the probe, not the current position. Two-dimensional slices with cross marks do not provide necessary information to the surgeon.

**SY4-2**

**Underwater endoscopic ear surgery – The dawn of inner ear ultrafine surgery**

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Over the last few decades, high-definition video imaging endoscopy has emerged as a useful technique for ear surgeons, allowing much closer work and providing clear surgical views for transcanal endoscopic ear surgery (TEES). This technique has a low degree of invasiveness, and can now be applied for a variety of conditions, including acoustic neurinoma, and paraganglioma in the middle ear. Endoscopy can now be applied to endoscope-assisted ear surgery. Currently, endoscopes can be applied directly, irrespective of whether or not a microscope is also needed. In this situation, we prefer to employ a novel technique, underwater endoscopic ear surgery (UWEES), because of its considerable advantages in specific conditions.

The purposes of UWEES are (1) to provide a clear operative view and (2) to maintain the internal environment of the inner ear. Although a recent high-spec endoscope has the potential to provide high-quality visualization of the surgical field, the "underwater" operating condition enhances the magnification 1.33-fold due to the refractive index of water. Constant perfusion of the solution ensures the surgical field remains clear of minor bleeding and bone dust resulting from use of a drill or ultrasonic instrument, and that the temperature of the medium does not increase, which could potentially lead to damage of surrounding tissues, such as nerves and the inner ear organs. The tip of the endoscope is constantly immersed, allowing the surgeon to operate without any visual interference due to reflection or refraction. Thus, UWEES yields a unique operative view, minimizing the risk of inner ear damage and allowing more precise dissection, particularly in the membranous labyrinth. With regard to preservation of inner ear function, the most common indication for UWEES is surgery of the labyrinthine fistula of semicircular canals, which often needs to be done in cases of advanced cholesteatoma and chronic otitis media. Plugging for SCDS is similarly indicated for manipulation in the membranous part of the canal. Even if the dehiscence located on SPS, this technique is advantageous in safety and feasibility by approaching from underneath. The setting of this technique, adaptations, and the postoperative results will be demonstrated.

## SY4-3

**Development of innovative treatment for middle ear mucosal regeneration by cell sheet technologies**

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Recurrence of cholesteatoma is mainly caused by poor mucosal regeneration in the middle ear cavity and mastoid cavity. Conventional canal wall up tympanoplasty often results in a lack of mucosal regeneration in the resected area of the mastoid cavity. In particular, mucosal regeneration in a poorly pneumatized mastoid cavity is extremely difficult. If regeneration of the damaged middle ear mucosa were possible in the early postoperative period, it would be possible to prevent re-adhesion of the tympanic membrane and recurrence of adhesive otitis media. Additionally, regeneration of middle ear mucosa would prevent recurrence of cholesteatoma. To overcome these limitations, we developed a novel treatment method combining tympanoplasty and autologous nasal mucosal epithelial cell sheet transplantation for postoperative regeneration of the middle ear mucosa. In clinical research, we endoscopically removed an approximately  $10 \times 10$  mm<sup>2</sup> piece of inferior nasal turbinate mucosal tissue. Tissue-engineered autologous nasal mucosal epithelial cell sheets were fabricated by culturing the harvested cells in an aseptic environment in a good manufacturing practice-compliant cell processing facility. The cultivated cell sheets were transplanted, during tympanoplasty, onto the exposed bony surface of the middle ear cavity where the mucosa had been lost. To our knowledge, this clinical research is the world's first-in-human study to transplant cultured cells into the human middle ear. This treatment simultaneously preserves the external ear canal morphology, as in standard canal wall up tympanoplasty, and incorporates autologous cell sheet transplantation, which enables prevention of recurrence of cholesteatoma. This study represents a great step forward in the development of a new surgical approach for treating adhesive otitis media and cholesteatoma.

## SY4-4

**Consumption of betel quid contributes to sensorineural hearing impairment through arecoline-induced oxidative stress**

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Betel quid is one of the most widely used psychoactive substances, and is consumed by approximately 10% of the world's population. In addition to its carcinogenicity, betel quid has also been reported to affect many organs, including the brain, heart, lungs, gastrointestinal tract, and reproductive organs. As betel quid contains several neurotoxic ingredients, we hypothesize that it also possesses ototoxicity and may lead to sensorineural hearing impairment (SNHI). In this study, we investigated the contribution of betel quid consumption to SNHI in a large clinical cohort, and validated the pathogenetic mechanisms in *ex vivo* tissue explants. We enrolled a total of 2364 volunteers, and determined their audiologic results based on Z-scores converted from their original frequency-specific hearing thresholds. Using generalized linear regression, we identified a positive correlation between betel quid consumption and the Z-scores across different frequencies. Subsequently, we explored the toxicity of arecoline, the main neuroactive component of betel quid, on tissue explants from murine cochleae. Arecoline reduced cell activity in the explant cultures and induced apoptosis in the hair cells, probably through the effects of oxidative stress. These findings have expanded the potential hazards of betel quid to common neurological disorders, and provide insights into preventive strategies against SNHI caused by neurotoxic substances.

SY4-5

## Precision medicine for cochlear implantation in the genomic era: the Taiwan experience

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Cochlear implantation is currently the treatment of choice for children with severe to profound sensorineural hearing impairment (SNHI). However, the outcomes with cochlear implants (CIs) vary significantly among recipients. In the past decade, we have been exploring the correlation between genetic results and the outcomes with CIs. Our results reveal that genetic diagnoses and imaging results are the two predominant factors determining the outcomes with CIs. Mutations in most deafness genes are associated with excellent long-term auditory and speech performance with CIs, probably because the pathology is confined to the inner ear and the auditory nerve is preserved. However, mutations in *PCDH15* and *PJVK* might be associated with unfavorable CI performance. The unfavorable CI performance associated with these specific mutations, as evidenced in our recently-generated CRISPR mouse models, might result from pathologies in the auditory neural pathway. Of note, children with *PCDH15* or *PJVK* mutations might exhibit clinical features indistinguishable from those of other typical pediatric CI candidates. As such, comprehensive genetic examination is indicated in all CI candidates prior to operation and should be included into the pre-CI evaluation battery.

In addition to outcome prediction, genetic testing might also help in the clinical decision making. For instance, auditory neuropathy patients with *OTOF*, *WFS1*, and *OPA1* mutations do not experience spontaneous recovery of auditory phenotypes with age, but they usually demonstrate favorable outcomes with CIs. Therefore, cochlear implantation should be performed in these patients whenever indicated, without unnecessary delay. Patients with *MYO15A* or *TMPRSS3* mutations might present severe-to-profound SNHI with low-tone residual hearing initially, but the residual hearing could deteriorate gradually. Special considerations in the electrode selection are thus necessary for these patients. Our experience with regards to the application of genetic examination in cochlear implantation will be presented.

SY4-6

## Hearing Protective Effect of Dextromethorphan on Military Gun-Shooting Practice and Noise-Induced Hearing Loss Animal Models

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Noise-induced hearing loss (NIHL) remains a public health problem in the factory, construction, farming, entertainment, and military sectors. In a military perspective, hearing loss and tinnitus are the most prevalent military service-connected disability. NIHL continues to be the focus of research aiming to develop preventive and therapeutic management strategies.

The etiopathology of NIHL comprises ischemia, oxidative stress with reactive oxygen species, and inflammation and cell death caused by noise. Currently, another mechanism of hearing loss is noise-induced cochlear synaptopathy, which causes hidden or permanent hearing loss. This mechanism may contribute to glutamate excitotoxicity involving N-methyl-D-aspartate (NMDA) receptor activation and related auditory nerve excitation. NMDA receptor inhibition has been proposed as a pharmacologic approach for the treatment of NIHL.

Dextromethorphan (DXM), an uncompetitive and low-affinity NMDA receptor antagonist, has been widely used as a non-opioid, nonnarcotic, and over-the-counter antitussive for over 50 years. DXM has demonstrated considerable neuroprotective properties in numerous in vitro and in vivo models of central nervous system injury and neurodegenerative diseases. This study aimed to evaluate the potential effect of DXM on military gun-shooting practice clinical trial and elucidate the mechanisms using noise-induced animal models.

In clinical trial, DXM was given to subjects who perform gun-shooting practice for the first time after joined the army aged between 20 and 30 years old. Our data revealed subjects in DXM group had significantly less hearing loss and hearing threshold shift than control group. Fewer subjects in DXM group developed tinnitus after shooting. DXM may attenuate hearing loss through maintaining more synaptic complexes co-localized with ribbons (inner hair cells) and postsynaptic receptors (spiral ganglion neurons) in the DXM group in CBA/J mice. DXM also preserved more serotonin transporter (SERT) expression by using 4-[18F]-ADAM/micro-PET and restored the NMDA-inhibited neurite length of serotonergic neurons in SD rat.

In conclusion, DXM may provide a protective effect on hidden hearing loss and tinnitus during military gun-shooting practice. DXM may attenuate noise-induced hearing loss through maintaining synaptic connection in cochleae and SERT density and against neurite degeneration of serotonergic neurons in brain.



## Symposium 5 Audiology

## SY5-1

## Effects on middle ear muscle reflex on middle to high frequency sounds in human - A doubt on current assessing method for olivo-cochlear reflex-

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### Introduction

In mammals, it has been known that there are two different types of acoustic reflex, middle ear muscle reflex (MEMR) and medial olivo-cochlear reflex (MOCR), which play roles to protect the inner ear from high intensity sounds and to adjust the input sound in adequate range for inner ear, and it is also known that the former mainly act to lower frequency sound and latter to higher frequency. However, recent study using wide frequency impedance measurement revealed that middle ear might affect high frequency sound in human. Therefore, it is required to clarify whether role-sharing of two acoustic reflex is also applied in human or not.

### Subject and Method

At present, a normal ear subject was measured. ER10C miniature microphone with receiver for otoacoustic emission (Etymotic Research, USA) was placed in one side of the ear. A 250Hz tone and from 1000 to 6000Hz tones with 500Hz interval were simultaneously presented from the receiver for 2.62 seconds, and those sound in the ear canal was measured with the microphone. One seconds after the onset of the tones, the opposite ear was stimulated with reflex-eliciting tone, which was 1000Hz tone with 70, 80, or 90dBHL. From the measured sound, time courses of instantaneous sound level and phase of each stimulus frequency were calculated. After then, the level and phase were translated into reflectance.

### Results and Conclusion

The time-course of reflectance of 1000 to 6000Hz tones showed increasing or decreasing during contralateral stimulation of eliciting tone. The polarity (increasing or decreasing) changed according to the frequency. In several frequencies, the time course showed dual peaks, which were synchronized to the onset and end of contralateral tone. This could be seen only when the amount of reflectance change was large with large contralateral tone, and the polarity of reflectance change was always the same to continuous change during the contralateral tone.

This result indicates that mechanism of sound level change measured in the ear is single regardless of measured frequency or eliciting sound level. This leads to a conclusion that MEMR plays a major role in acoustic reflex in human, which is different from small mammals.

## SY5-2

## Genetic polymorphisms and susceptibility to inner ear diseases

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The etiologies of inner ear diseases such as idiopathic sudden sensorineural hearing loss (SSNHL) and Ménière's disease remain unclear. Recently, accumulating evidence has demonstrated that free radicals are related to the pathology of inner ear disease. Because genetic factors may contribute partly to the etiologies of SSNHL and Ménière's disease, we investigated the association between genetic polymorphisms located in genes related to the free-radical process and susceptibility to SSNHL and Ménière's disease. We compared 83 patients affected by SSNHL and 83 patients affected by Ménière's disease with 2048 adults (for SSNHL) and 1946 adults (for Ménière's disease) who participated in the National Institute for Longevity Sciences, Longitudinal Study of Aging. Multiple logistic regression was used to calculate odds ratios (ORs) for SSNHL and Ménière's disease in individuals with polymorphisms in the genes: methionine synthase (*MTR*; rs1805087); methionine-synthase reductase (*MTRR*; rs1801394); nitric oxide synthase 3 (*NOS3*; rs1799983); caveolin 1 (*Cav1*; rs3840634); melatonin receptor 1B (*MTNR1B*; rs1387153); NAD(P)H oxidase p22(phox) subunit (*NADH/NADPHp22phox*; rs4673); and mitochondria 5178 (*MT5178*; rs28357984). The *NOS3* polymorphism was significantly associated with a risk of SSNHL; in addition, the OR for the *NOS3* polymorphism and SSNHL risk was 2.108 (CI: 1.343–3.309) with adjustment for age and sex. The *Cav1* polymorphism was significantly associated with a risk of Ménière's disease; moreover, the OR for the *Cav1* polymorphism and Ménière's disease risk was 1.849 (CI: 1.033–3.310) with adjustment for age and sex. In conclusion, the *NOS3* and *Cav1* polymorphisms were significantly associated with the risk of SSNHL and Ménière's disease, respectively.



SY5-3

## **NLRP3 mutation and cochlear autoinflammation cause syndromic and nonsyndromic hearing loss DFNA34**

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Sensorineural hearing loss can result from dysfunction of the inner ear, auditory nerve or auditory pathway in the central nervous system. Sensorineural hearing loss includes a wide variety of disorders such as idiopathic sudden sensorineural hearing loss, age-related hearing loss, noise-induced hearing loss and almost all of genetic hearing loss. Although these disorders are mainly caused by dysfunction of the inner ear, little of the pathophysiology in sensorineural hearing loss is known due to inaccessibility of the living human inner ear for biopsy and pathological analysis. The inner ear has previously been thought of as an immune-privileged organ due to the existence of its tight junction-based blood-labyrinth barrier. We recently showed that a missense mutation of the *NLRP3* gene causes autosomal-dominant sensorineural hearing loss with cochlear autoinflammation in two unrelated families. *NLRP3* encodes the NLRP3 protein, a key and eponymous component of the NLRP3 inflammasome. The NLRP3 inflammasome is an intracellular innate immune sensor that is expressed in immune cells, including monocytes and macrophages. Gain-of-function mutations of *NLRP3* cause abnormal activation of the NLRP3 inflammasome leading to IL-1 $\beta$  secretion in a spectrum of autosomal dominant systemic autoinflammatory diseases termed cryopyrin-associated periodic syndromes. The affected subjects of our two families demonstrated atypical phenotypes compared with those reported for subjects with cryopyrin-associated periodic syndromes. These observations led us to explore the possibility that macrophage/monocyte-like cells in the cochlea can mediate local autoinflammation via activation of the NLRP3 inflammasome. Indeed, the inflammasome can be activated in macrophage/monocyte-like cells in the mouse cochlea, resulting in secretion of IL-1 $\beta$ . This pathway could underlie treatable sensorineural hearing loss in DFNA34, CAPS, and possibly in a wide variety of hearing loss disorders, such as sudden sensorineural hearing loss and Meniere's disease that are elicited by pathogens and processes that stimulate innate immune responses within the cochlea.

SY5-4

## **The effect of electroacupuncture for noise induced hearing loss in animals**

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Noise is one of the major causes of acquired hearing loss, resulting temporary or permanent auditory injury with or without annoying tinnitus. Several treatment strategies have been suggested for the management of acute noise trauma, including steroid, hyperbaric oxygen, hemorheologic agent, vitamins, antioxidants. The results are still controversial. Acupuncture has its role in management of inner ear disorders. The purpose of this study is to investigate the effect of electro-acupuncture (EA) on noise induced hearing loss in animals. Sprague Dawley rats were used for this study. The animals were divided into five groups: control, EA only, noise only, pre-EA then noise, noise then post-EA. The noise exposure was 121 dB white noise for 2 hours. The animals had the EA at the acupoint of right Zhongzhu (SJ3) with 2mA for 1 hour under sedation. Serial hearing tests with auditory brainstem responses were measure up to 4 weeks. The cochlea and brain tissue was removed for immunohistochemical examinations. The animals pre-treated or post-treated with EA had significant hearing recovery from noise trauma, compared with the noise only group. Massive superoxide formation was found in the cochlea after noise exposure. However, EA could reduce the superoxide formation. Similar changes were found in the central auditory tract. In conclusion, EA may prevent or ameliorate the acute noise injury through the reduction of oxidative stress in the cochlea and central auditory tract.

## SY5-5

## Transuterine inner ear gene delivery by a synthetic adeno-associated virus

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Hereditary deafness is one of the most common sensory disorder worldwide. Adeno-associated virus (AAVs) has been used to investigate the gene therapy in the inner ear lately. The transduction efficiency of AAVs in inner ear hair cells is critical for the success of gene therapy, yet until now, limited types of AAV discovered are applicable in inner ears.

In this study, we deliver a synthetic AAV, which has been claimed for its high expression in neonatal and adult mice's inner ears, into the embryonic otocysts to test the feasibility of prenatal gene therapy for deafness. Unlike other AAVs only infect inner hair cells, we found that this synthetic AAV can target both cochlear inner and outer hair cells in high transduction rate. In addition to cochlea, the transduction ability also performs well in other inner ear cell types, including the vestibular hair cells and neuronal cells of spiral ganglion. Those advantages indicate the potential use of AAV in prenatal inner ear gene therapy.

## SY5-6

## Statistical analysis of hearing screening tools for referral newborns

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**Background:** According to current studies, the prevalence of congenital moderate-severe hearing impairment are around 1 to 2 in every 1000 newborns. These deaf and hearing-impaired children often experience delayed development of speech, language and cognitive skills, which may result in slow learning and difficulty progressing in school. Therefore, early detection is a important element in providing appropriate support for deaf and hearing-impaired babies that will help them enjoy equal opportunities in society alongside all other children. In Taiwan, current gold standard for newborn's hearing screening tool is aABR due to its high sensitivity and specificity. For referral newborns in CMUH, routine hearing screening tools are Tympanometry, aABR (automated Auditory Brainstem Response), OAE (Otoacoustic Emission) and ART (Acoustic Reflex Thresholds). In this studies, we try to compare current hearing screening tools (aABR/OAE/ART) from these referral newborns.

**Materials and methods:** This was a retrospective study of 461 referral newborns who failed to initial hearing screening examinations at birth and were referred to CMUH ENT outpatient department between April 2014 and April 2018. Our exclusion criteria are microtia and incomplete ABR threshold data. After selection, there are 454 referral newborns (908 ears) who are enrolled in our study. Our hearing screening tools are aABR, OAE and ART. We defined final diagnosis as hearing impairment by ABR thresholds determination.

**Results:** In 454 referral newborns, there are 262 male neonates and 192 female neonates respectively. There is a total of 908 ears enrolled in our study, which 870 ears receive aABR (548 ears pass, 322 ears refer), 736 ears receive OAE (644 ears pass, 92 ears refer) and 862 ears receive ART (421 ears pass, 441 ears refer). After statistical analysis of these three hearing screening tools, the sensitivity / specificity are as follows respectively: aABR (93.0% / 78.7%), OAE (81.2% / 50.3%) and ART (46.3% / 95.9%).

**Conclusion:** aABR is still the gold standard of hearing screening tools for referral newborns due to its good sensitivity (93.0%) and specificity (78.7%). In our study, ACT has good specificity (95.9%) and combination with aABR for referral newborns may be suggested in the future.

**Symposium 6** Head and Neck Oncology

**SY6-1**

**Controversies in relation to neck management in N0 early oral tongue cancer**

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**Pros and cons of prophylactic neck dissection for early oral tongue cancer**

The standard local treatment for early-stage tongue cancer with no clinical lymph node metastases is partial glossectomy. The frequency of occult lymph node metastasis is roughly 20%–30%. As such, whether prophylactic neck dissection with glossectomy or glossectomy alone should be performed has been a controversial issue since the 1980s. Both treatments have advantages and disadvantages; however, especially in cases involving prophylactic neck dissection, surgical invasion and complications, including the cosmetic drawback of a neck skin incision, accessory or facial nerve (mandibular marginal branch) paralysis, stiffness of the shoulder or neck and a feeling of neck tightness have been considered issues that may be resolved by providing less-invasive treatment to the 70%–80% of patients without occult lymph node metastasis. A more accurate preoperative diagnosis and strict follow-up are required to provide minimally invasive treatment while ensuring a therapeutic effect. It is also necessary to narrow down the target based on the risk–benefit balance.

**Will the new TNM classification change the rate of occult metastases and prognosis?**

In the 8th edition of the UICC-TNM staging system, the depth of invasion (DOI) was added as a factor that determines the T-category. In our retrospective study, the cut-off value of the DOI for predicting occult lymph node metastasis in the receiver operating characteristics analysis was 5 mm. The cut-off value of DOI for predicting deterioration of the disease-free/overall survival was 10 mm in both cases. There is therefore a difference between the cut-off value for predicting occult metastasis and that for predicting a worsening prognosis. The rate of occult neck lymph node metastasis of early tongue cancer has been reported to be about 20%–30%, and indications for prophylactic neck dissection have been discussed. However, with this TNM classification revision, tongue cancer with a DOI >10 mm is now classified as T3, thus meaning that the DOI values more closely associated with occult metastasis and a poor prognosis now fall outside of the T1–2N0 tongue cancer category.

**SY6-2**

**Present status of endoscopic surgery for malignant sinonasal tumors in Japan**

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(Introduction) The endoscopic approach has become the standard of care as a minimally invasive approach, not only for inflammatory sinonasal diseases, but also for benign sinonasal tumors. However, use of this approach for malignant tumors is still controversial. This study was aimed at determining the present status of endoscopic surgery for sinonasal malignancies. (Materials and Methods) In the current study, we conducted a questionnaire-based survey and investigated the present status of the surgical treatment for sinonasal tumors and future issues, particularly in relation to endoscopic surgery in Japan. In addition, we retrospectively reviewed the clinical data in this research group. (Results) The questionnaire was sent to 633 institutions accredited by the Oto-Rhino-Laryngological Society of Japan, and 428 of these facilities (67.6%) returned valid responses to the questionnaires. In 385 of these facilities (90.0%), the endoscopic approach was used for the resection of inverted papillomas in the nasal cavity and sinuses, while the open surgical approach was adopted for tumors of the maxillary and frontal sinuses. In 91 of the facilities (21.2%), skull base surgery was performed for malignant sinonasal tumors; a purely endoscopic approach or the endoscopic approach in combination with the craniofacial approach was used for the surgery in 82 of these facilities (86.3%).

We reviewed the data of 110 patients with sinonasal malignancies from 10 hospitals who were treated by endoscopic surgery. A histopathological survey revealed squamous cell carcinoma and olfactory neuroblastoma in 29% and 24% of patients, respectively. In regard to the distribution of the T classes, T1, T2, T3, T4a and T4b accounted for 29%, 26%, 15%, 13% and 17% of cases, respectively. At our research institutions, which are high-volume centers for endoscopic skull base surgery, a purely endoscopic approach was adopted for 71 patients (65%), a combined approach for 27 patients (25%), and pure open skull base surgery was performed in 11 patients (10%). The combined approach was used for cases with intracranial invasion or intraorbital invasion. Among the patients in whom a pure endoscopic approach or a combined endoscopic plus open approach was used, there were several complications, including blindness, diplopia in one case, and cerebrospinal fluid leakage in two cases. (Discussion) Endoscopic skull base surgery for malignancies is becoming popular in Japan, and is especially useful for some types of tumors. However, the indications are limited and a high skill level is needed for this surgery. It is important to carefully identify the surgical indications and to accumulate experience with skilled surgeons.

## SY6-3

## A clinical analysis of sinonasal squamous cell carcinoma: A comparison of *de novo* squamous cell carcinoma and that arising from inverted papillomas

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**BACKGROUND:** Sinonasal squamous cell carcinoma (SCC) is a rare tumor arising either *de novo* or in association with inverted papillomas (IPs). The incidence of SCC arising from IPs ranges from 2% to 27% in the literature. However, the clinical features of SCC arising from IP versus those of *de novo* SCC remain unclear, with substantial debate persisting. The aim of this study was to investigate and compare the oncological features and prognosis of patients with sinonasal SCCs based on their etiology. In addition, we evaluated the role of high-risk human papillomavirus (HPV) in the pathogenesis of SCCs arising from IPs.

**METHODS:** The medical records of 117 patients who had been diagnosed with sinonasal SCCs (*de novo* SCC) or those arising from IP (IP-SCC) were retrospectively reviewed. Out of 117 patients, 23 were diagnosed with IP-SCC. The clinical characteristics and survival outcomes of the patients were analyzed. *In situ* hybridization analyses for high-risk HPV and p16 immunohistochemistry were also performed in 10 cases with IP-SCC.

**RESULTS:** The average ages of *de novo* SCC and IP-SCC patients were 63.8 and 60.5 years old, respectively. There were no significant differences in the age, gender or tumor origin between patients with *de novo* SCC and those with IP-SCC. Regardless of tumor etiology, the maxillary sinus was the most common site of origin (89% *de novo* SCC and 74% IP-SCC), followed by the nasal cavity. The three-year disease-specific survival rate was higher in cases with T1, 2 and 3 than in cases with T4 in both tumor groups. T4 cases with *de novo* SCC had a better disease-specific survival than those with IP-SCCs. HPV16/18 was not detected in any of the 10 IP-SCCs.

**CONCLUSION:** There was no significant difference in the overall survival rate between the two tumor groups. However, T4 cases with *de novo* SCC tended to have a better disease-specific survival than those with IP-SCC. Some T4 patients with IP-SCC were found to have a highly aggressive disease. Careful treatment planning should be performed. High-risk HPV may not play a vital role in the carcinomatous transformation of most IP-SCC cases.

## SY6-4

## Ubiquitin Conjugating Enzyme 2C is a Poor Prognostic Factor of Tongue Squamous Cell Carcinoma

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Ubiquitin-conjugating enzyme 2C (UBE2C) is required for cell-cycle transition from metaphase to anaphase. Overexpression of UBE2C has been demonstrated in many types of human malignancies. We studied the role of UBE2C in oral squamous cell carcinoma (OSCC). Firstly, UBE2C protein expression was examined by immunohistochemistry on tissue microarray of 507 OSCC and 387 corresponding tumor adjacent normal (CTAN) tissues. The association of UBE2C expression with patient clinicopathologic characteristics was analyzed. The UBE2C protein level was significantly elevated in OSCC comparing to the CTAN. A higher UBE2C expression was associated with a poorer disease-specific survival. Subgroup analysis showed that the adverse impact of high UBE2C expression on disease-specific survival was evident in tongue cancer patients, especially in male patients, and patients with moderate/ poor differentiated tumor, advanced pathological stage, positive nodal metastasis, as well as patients received postoperative radiation therapy. In the second part of the study, OSCC cell lines including SAS and CA922 were used to examine the role of UBE2C. Silencing RNA was used to knock down expression of UBE2C. In both cell lines, the viability, cell migration/invasion, and colony formation were all significantly reduced when UBE2C expression was knocked down. UBE2C knockdown also caused an increased susceptibility of OSCC cell lines to radiation treatment. These results suggested that UBE2C may contribute to OSCC cell survival and aggressiveness, and its over-expression may be associated with increased resistance to radiation therapy. It may serve as a poor prognostic factor for patients with tongue squamous cell carcinoma.



SY6-5

## The influence of marginal vs segmental mandibulectomy on local recurrence and survival in oral squamous cell carcinoma

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**Purpose:** In order to identify the different mandibular surgical methods whether affect the prognosis of patients with oral squamous cell carcinoma (OSCC) including local recurrence and survival rate.

**Materials and Methods:** We carry on a retrospective cohort study of 474 patients with OSCC who received either marginal mandibulectomy (MG) or segmental mandibulectomy (SG) at our hospital from January 2008 through December 2017. The local recurrence rate and survival rate after these 2 treatment modalities were analyzed using Kaplan-Meier survival analysis. Besides, we also compare the difference of two groups for local recurrence rate and survival rate, included mandibular involvement, adjuvant chemotherapy and/or radiotherapy only. At univariate and multivariate analyses, the Cox regression model was used to screen risk factors for local recurrence, included pathological T stage (pT), pathological N stage (pN), perineural invasion (PNI), lymphovascular invasion (LVI), mandibular invasion, extranodal extension (ENE), and methods of mandibulectomy. Statistical significance was considered when P values was less than .05.

**Results:** Of the 474 patients, 354 underwent MG and 120 underwent SG. According to statistical analysis, the disease free survival (DFS) rate (MG vs SG = 74.2% vs 58.0% in 3-year,  $P = .001$ ; 65.3% vs 54.2% in 5-year,  $P = .008$ ) and overall survival (OS) rate (MG vs SG = 80.7% vs 69.8% in 3-year,  $P = .01$ ; 75.8% vs 64.4% in 5-year,  $P = .01$ ) were significantly different between the 2 groups. However, the local recurrence rate did not have significant difference (MG vs SG = 18.1% vs 27.6%,  $P > .05$ ). Also, the 3- and 5-year DFS rates, OS rate and local recurrence rates of mandible involvement with adjuvant chemoradiotherapy have no significant difference between the 2 groups ( $P > .05$ ). Besides, the univariate analysis disclosed the impact factors for local recurrence rate of OSCC included pN stage, PNI, LVI and ENE. The pN stage is the only independent factor about local recurrence rate at multivariate analysis.

**Conclusion:** The results suggest that MG is safe for selected OSCC patients with limited mandibular invasion, and not jeopardize local control rate and OS rate. The 3- and 5-year DFS rate, OS rate and local recurrence rate of both groups with limited mandibular invasion have no significant difference.

SY6-6

## Adequate Pathological Surgical Margin in Oral Cancer

Yi-Shing Leu

Department of ENT of MacKay Memorial Hospital, Taipei, Taiwan

Margin is correlated further local recurrence. Tumor margin shrinks significantly after formalin fixation by 25%. Principle: resection margin  $> 10\text{mm}$ . Aim: pathological margin  $> 5\text{mm}$ , clear

Transoral eHNS (including TORS) can facilitate de-intensified (reduced dose) postoperative radiation therapy (RT) and maintain loco-regional disease control, while improving swallowing function. The primary objective is to evaluate progression-free survival in "intermediate-risk" patients, comparing two postoperative RT doses: 50 Gy versus a standard dose of 60 Gy. Intermediate risk as those with close margins ( $< 3\text{mm}$ ), the presence of 2-4 metastatic lymph nodes or extracapsular extension (ECE) of tumour outside any of these nodes of  $< 1\text{mm}$ .

Specimen 4 surfaces: esp deep margin

Our total data in Taiwan (2011-2014,  $n = 9456$ ). 30% cases with margin  $> 5\text{mm}$  4-yrs survival: OS: 82.4%, CSS: 85.3%. OS  $> 80\%$ , margin 2.1-3.0mm is enough. (OS: 81.4%, CSS: 84.4%). CSS  $> 80\%$ , margin 1.1-2.0mm is enough (OS: 77.1%, CSS: 80.8%). MTTR (Margin to tumor thickness ratio) (MTTR), MTTR  $< 0.1$ , 5-yrs survival: 49.3%, MTTR = 0.1-0.3, 5-yrs survival: 65.4%, MTTR  $> 0.3$ , 5-yrs survival: 81.6%, so MTTR may be the better indicator than a simple value of surgical margin.

## Symposium 7 Voice

## SY7-1

**Vocal fold injection of basic fibroblast growth factor in patient with vocal fold scar, atrophy, and sulcus vocalis**

Shintaro Sueyoshi, Hirohito Umeno, Takashi Kurita, Shun-ichi Chitose

*Department of Otolaryngology-Head and Neck Surgery, Kurume University School of Medicine, Japan*

**(Introduction)**

Patient with vocal fold scar, atrophy and sulcus vocalis are supposed to have voice disorder because of property change in vocal fold. The change is caused by histologic alternation of the lamina propria of the vocal fold mucosa. Regeneration of the extracellular matrix (ECM) in the lamina propria leads to excessive deposition of disorganized collagen, reduction of elastic fiber and hyaluronic acid (HA). These histologic alternations result in fibrotic change in the mucosa. So far, there is no reliable treatment for these property change. Dr. Hirano's group has been studying about the treatment effect of basic fibroblast growth factor (bFGF) on aged vocal fold. They reported that bFGF stimulates growth and proliferation of fibroblasts in lamina propria and found that it stimulates cells to produce more HA and reduce collagen production. The vocal fold injection with bFGF has been performed, as well, in Kurume University hospital referring to their study. In the present study, we examined voice outcome following bFGF injection into vocal fold.

**(Material and Method)**

The bFGF injection was performed in nine patients (five men and four women, mean age 70 years) from January 2016 to November 2016 in Kurume University hospital. There were vocal fold scar in six patients, vocal fold atrophy in two patients and sulcus vocalis in one patient. Ten micrograms of bFGF was injected into superficial layer of lamina propria in each vocal fold. The injection was performed unilaterally or bilaterally and repeated four times with an interval of one week between each injection. Laryngomicrosurgery was performed for first injection and percutaneous injection was performed in second time or later. Aerodynamic, acoustic and stroboscopic examination were performed in each time point after surgery (1 month, 3 months, 6 months, 1 year, 2years). Fundamental frequency, maximum phonation time (MPT), mean flow rate (MFR), amplitude perturbation quotient (APQ), and pitch perturbation quotient were examined and compared between pretreatment and posttreatment.

**(Result)**

Voice quality has improved after treatment in most patient. Aerodynamic assessment, MPT and MFR, improved from early, 1 month after treatment. On the other hand, acoustic assessment, APQ and PPQ, improved from 6 months after treatment.

**(Discussion)**

It took longer time to find acoustic improvement than aerodynamic improvement in the present study. That indicated that it took longer time to achieve the improvement of vocal fold vibration than to find mere volume change of vocal fold. Additionally, we might have to consider about re-exacerbation of voice quality and necessity of re-treatment in the future.

## SY7-2

**Real-world treatment procedure of laryngeal disease for elderly patients with serious complications**

Hiromitsu Hatakeyama

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The elderly population in Japan is in a rapid growth, and it is predicted to exceed 30% of the total population in 2035. In laryngeal disease, most of standard treatment procedure has been available even for elderly patients due to the development of techniques and devices for micro or endoscopic minimally invasive surgery. We investigated the treatment procedure and prognosis of laryngeal cancer in elderly patients over 65 years old (range: 65-94 median: 74). Standard therapy according to the guideline was available to 80% of the patients with laryngeal cancer. However, 33% of the patients with laryngeal cancer could not be received standard dose of radiation or chemoradiation. On the other hand, surgery was done in 95% of the patients successfully. In terms of treatment outcome, 3-years survival rate in standard treatment group is more than 90%, whereas the rate in non-standard treatment group was very low. The risk with platinum-based chemotherapy for the elderly patients with laryngeal cancer is high, irradiation to larynx often caused swallowing disorder. Endoscopic excision of early laryngeal cancer was possible for the elderly patients, and total laryngectomy was also possible in most cases even in advanced cases. It is important not to hesitate in standard surgical procedure in the treatment of laryngeal cancer in the elderly patients. Furthermore, office-based surgical procedure with local anesthesia could be treatment option in high-risk cases of general anesthesia in elderly patients with serious complication. Some successfully treated cases with local anesthesia will be shown.



SY7-3

## Angiolytic laser treatment for laryngeal lesions

Yo Kishimoto

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The damages on the vocal fold mucosa sometimes result in fibrotic alterations. It decreases the viscoelasticity of the mucosa, which results in the persistent, intractable dysphonia. Dysphonia can deteriorate the quality of life of the patient, and thus, it is crucial not to damage the surrounding tissues in the vocal fold mucosa during the surgical treatments for laryngeal lesions.

The lasers with wavelength of 532 to 595 nm are called as angiolytic lasers, and because their wavelengths are close to the absorption peak of hemoglobin, these lasers are preferentially absorbed by hemoglobin in the vessels. Based on these characteristics, angiolytic lasers allow the selective angiolysis and photocoagulation of vascular structures with minimal thermal damages to surrounding tissues. After the introduction of these angiolytic lasers to the clinical practice, they are applied to the vascular lesions in the vocal folds such as venous malformation and hemorrhagic polyps. And many previous studies have reported that angiolytic lasers can photocoagulate vascular lesions beneath the vocal fold mucosa with minimal damages to the epithelium, when they are delivered at a low power.

Although, they were initially used for the treatment of vascular lesions of vocal folds, indications have been expanded gradually to include some epithelial lesions such as papillomatosis, leukoplakia, carcinoma in situ (CIS) and Reinke's edema. Angiolytic laser treatment photocoagulate microvascular structures beneath these epithelial lesions, and effectively induce a delayed regression or elimination of the lesions.

Basically, the photocoagulation using angiolytic lasers can be performed as an office procedure using flexible endoscopy under topical anesthesia, and the procedure is very simple, safe and easy. We have applied this procedure against various laryngeal lesions over the past decade, and it results in the good control of the lesions in most cases without any major complications.

Photocoagulation using the angiolytic laser seems to be a feasible and safe treatment for laryngeal lesions, and our experiences will be introduced with the representative cases in this symposium.

SY7-4

## Voice from nerves: what does LEMG tell us when nerve being injured?

Tuan-Jen Fang

*Department of Otolaryngology Head and Neck Surgery, Chang Gung Memorial Hospital at Linkou, Chang Gung University, Taoyuan, Taiwan*

Laryngeal electromyography (LEMG) was first described in 1944 by Weddell et al. Conventional LEMG examination can tell the impairment of neuromuscular control from the abnormal neural signals but is hard to add more clinical information. Recently, the progressing of the technique of LEMG analysis extends the field of research on laryngeal neuropathies. However, clinical physicians are not familiar with the principle and value of LEMG. The diagnostic criteria of nerve injury are not consistent among different labs. The knowledge of neurophysiology of the vocal fold is helpful for the management plans. In some recent reports, the correlation of clinical presentations, prognosis and findings of LEMG has been established. The development of quantified LEMG (QLEMG) further extend the field of its utilization. Turn frequency as an objective parameter, determined the controversies between modern concepts and traditional theories. Some gold standard lasting over decades has been challenged. From applying the data, evidence-based decision making became possible. The lecture will concentrate on the electrophysiology of laryngeal nerve injury and introduce the updating results from modern QLEMG evaluation. We wish the audience, after the talk, can realize the principle and clinical applications of laryngeal EMG.

## SY7-5

## The development and applications of office-based laryngeal surgery

Yen-Bin Hsu

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Traditionally, laryngeal surgeries are performed in the operating room under general anesthesia. Since the development of flexible endoscope in 1970s and distal chip endoscope in 1999, laryngologists can see the vocal fold clearly and office-based laryngeal surgery has become more and more popular. This technique only requires local anesthesia without the need of monitoring vital signs or an intravenous line. It can be an extremely useful treatment method for a variety of voice or laryngeal disorders.

There are many different indications for this kind of technique. Foreign body can be removed under endoscopic guidance. Laryngeal or hypopharyngeal tumors can be sampled by using curved forceps or instrument through the working channel. Phonosurgery may also be performed in some selected cases. Injection laryngoplasty can be performed to improve glottal closure by pushing vocal fold toward the midline. In addition, a substantial number of patients with benign laryngeal lesions may spare surgical intervention after the injection of corticosteroid into the vocal fold. Some neurologic disorders affecting the larynx can also be treated by injection of botulinum toxin into the glottis.

In our experience, there are some distinct advantages of office-based surgery when compared with traditional methods. It is a practical procedure with low invasiveness and minimal morbidity. The risk of general anesthesia is avoided. The patients can save valuable time and cost of admission as well. There is no absolute contraindication for this technique, and age is not a major concern if patient performance is acceptable. For patients with poor medical status and a higher surgical risk, this technique is a good alternative to direct microlaryngoscopic surgery. It provides a simple and cost-effective alternative to conventional procedures.

## SY7-6

## Pre- and Posttreatment Voice and Nasality Changes in Patients With Nasopharyngeal Carcinoma Treated With (Chemo) radiotherapy: A preliminary report

Ting-Shou Chang

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### Objectives:

To investigate voice and nasality changes in patients following the (chemo)radiotherapy for nasopharyngeal carcinoma

### Design:

Prospective study

### Materials and Methods:

We collected the newly diagnosed nasopharyngeal carcinoma patients in the Department of Otolaryngology-Head and Neck Surgery of Kaohsiung Veterans General Hospital or referred from other hospital during Aug. 2017 to Sep. 2018. Basic data will be studied, including age, sex, smoking history, tumor histology, cancer stage, treatment modality and radiation dosage. Vocal function and nasality degree also assess in a comprehensive manner and compared at different treatment timing (pre-treatment baseline, post-RT 1 months, post-RT 3 months, post-RT 6 months and post-RT 12 months). The voice assessment includes (1)Voice Handicap Index-10 (VHI-10) (2)acoustic analyses(3)aerodynamic measurement(4) nasality severity index.

### Results:

Forty-seven patients were enrolled into the study. Twelve patients dropped out the study due to their request or treatment at the other hospitals. Now, thirty-five patients were regularly follow-up at our study. Twenty-two patients were regularly follow-up for 1 year and their data were available for data analysis. The 22 patients' mean age was  $51.18 \pm 13.52$  y/o, including 19 males and 3 females. Four patients were early stage (stage 1&2) and eighteen patients were late stage (stage 3&4). VHI-10 worsened postradiotherapy gradually. A statistically significant deterioration was seen between pre- and post-RT 3 months, pre- and post-RT 6 months, pre- and post-RT 1 year in total score, functional domain score, physical domain and emotional domain ( $p < 0.05$ , respectively). Aerodynamic measures were no statistically significant difference between pre- and post-RT. Acoustic assessment revealed statistically significant deterioration on fundamental frequency(F0), jitter, relative average perturbation, pitch perturbation quotient and voice turbulence index, which significant higher by post-RT 3 months to 6 months and returned by 1 year ( $p < 0.05$ , respectively). Nasality severity index score showed statistically significant lower at post-RT 1 year ( $p < 0.001$ ).

### Conclusion:

By 1-year follow-up, patient-reported VHI-10 questionnaire, acoustic outcomes and nasality severity for nasopharyngeal cancer patients treated by IMRT showed statistically significant deterioration compared to pretreatment function. Long term follow-up assessment is required to investigate the voice and nasality changes following chemoradiotherapy.

**Symposium 8**    **Dysphagia**

**SY8-1**

**Surgical Treatment of Dysphagia  
Caused by Neuromuscular  
Diseases**

Yurika Kimura

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“Neuromuscular disease” is a general term for diseases in which the central or peripheral nervous system, neuromuscular junction, or muscles are impaired. Various diseases cause dysphagia, and their mechanisms are diverse. Among these diseases are amyotrophic lateral sclerosis (ALS) and multiple system atrophy (MSA).

ALS is a rare disease in which selected primary motor neurons and secondary motor neurons progressively degenerate and disappear. The bulbar paralysis type, manifested mainly by bulbar symptoms such as dysarthria and dysphagia, progresses swiftly, and may affected patients die within 3 months of onset. In some cases, a patient whose chief initial complaint, difficulty in swallowing or speaking, is first seen in the otolaryngology department. In ALS, weight loss is rapid in the early stages, and disease-specific hypermetabolism is present. The prognosis is significantly worse in patients with severe weight loss. Malnutrition caused by the progression of dysphagia also promotes weight loss; therefore, early intervention for dysphagia is important. In general, oral disorders (difficulty swallowing solid or viscous foods) appear in the early phase of the disease. Pathologic evaluation with VE and VF can help affected patients make appropriate dietary choices. For patients who experience repeated aspiration, preventive surgery against aspiration is recommended in the Japanese Clinical Practice Guideline for ALS. For patients desiring tracheotomy with positive-pressure ventilation, preventive surgery against aspiration may be performed with the aims of maintaining oral intake, preventing pneumonia, and reducing the burden of suction.

Multiple system atrophy is an intractable neurological disease in which three neurological systems—the cerebellar brainstem, extrapyramidal system, and autonomic nervous system—degenerate. In advanced stages, dysphagia and vocal cord abduction disorder appear. In MSA-P in particular, reflecting the progression of extrapyramidal disorders, vocal abduction disorder and dysphagia tend to progress simultaneously. In some cases, tracheostomy for vocal cord abduction disorder exacerbates dysphagia and makes it difficult to prevent aspiration of saliva. Many cases with vocal cord abduction disorder are accompanied by disorders of articulation. In addition to tracheotomy, preventive surgery against aspiration may be performed when airway maintenance is needed after vocal fold ablation.

In this symposium, I will talk about the optimal time for a surgical approach to dysphagia and the effects of the surgery on patients with these two diseases.

**SY8-2**

**Swallowing function after  
hypopharyngeal cancer surgery  
involving vocal function  
preservation**

Mariko Hiramatsu

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School of Medicine, Japan*

**<Introduction>**

Laryngeal function preservation is essential in terms of quality of life (QOL) in patients with hypopharyngeal cancer and remains challenging. Surgical procedures for laryngeal preservation are mainly classified into two types: the transoral method and the external incision approach. Transoral procedures include transoral videolaryngoscopic surgery, endoscopic laryngopharyngeal surgery (ELPS), and transoral robotic surgery.

**<Subjects>**

The aim of this study is to evaluate the surgical procedures for laryngeal function preservation in patients with hypopharyngeal cancer who underwent surgical resection by assessing food intake ratio after surgery.

**<Results>**

Patients comprised 82 men and 9 women with a mean age at the time of surgery of 67.5 years (range, 41-90 years). In a total of 91 patients, 58 patients were received ELPS and 15 were free flap, 10 were Pearson's Near Total Laryngectomy (NTLP) and 8 were one-step plication suture,. In 58 ELPS patients, 39 patients (67.2%) could start to food intake orally on postoperative day 1 and 50 patients (86.2%) within postoperative day 3. At three months postoperatively, oral consumption was feasible for ELPS is 57/58(98.2%) , forearm flap is 87.5%(7/8) and one-step plication suture is 100%(10/10). One patient with ELPS developed severe dysphagia immediately after surgery and required further surgical procedures (laryngeal suspension and cricopharyngeal myotomy) The other patient of forearm flap and one patient with a NTLP developed dysphagia more than ten years after the surgery. These two cases are presented, and how aspiration that was difficult to treat was managed is reported.

**<Discussion>**

The patient who developed dysphagia after ELPS underwent extensive resection of bilateral hypopharyngeal piriform sinuses, and excessive resection may have led to prolonged dysphagia. Aging was suggested to contribute to worsened swallowing function in patients indicating the necessity for long-term observation.

## SY8-3

**Swallowing function after segmental mandibulectomy and reconstruction using a CAD/CAM system**

Ayako Nakanome<sup>1</sup>, Takenori Ogawa<sup>1</sup>,  
Akira Ohkoshi<sup>1</sup>, Koreyuki Kurosawa<sup>2</sup>,  
Takuya Yoshida<sup>1</sup>, Yukio Katori<sup>1</sup>

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Surgery for locally advanced lower gingival cancer often requires wide resections with submandibular bone. It makes many problems including swallowing disorders and change in facial image.

After segmental mandibulectomy, reconstruction using a free flap with bony tissue has many benefits, such as; decrease a risk of destructions of reconstruction plate, possible bite-reconstruction using dental prosthesis and implant materials, cosmetic improvement, and better functional outcome in terms of biting and swallowing.

For the efficiency of the process and better outcomes, we have used a virtual operation planning, and model and surgical guide for reconstruction using CAD/CAM (computer aided sign and computer aided manufacturing) system. The DICOM data obtained from preoperative CT are translated into STL (standard triangulated language), adapted by the CAD software, and used for creating a virtual model with a 3D printer. The surgeon was able to use this model for planning the surgical margin and collection of the most appropriate osteocutaneous flap, which was finally applied for the surgical procedure.

From Dec. 2015 to Mar. 2019, we experienced 15 cases underwent mandibulectomy with reconstruction using CAD/CAM system. Before and after surgery, we evaluate swallowing function using video endoscopic and video fluoroscopic examinations. Those information lead important suggestions for the rehabilitation.

We think that the surgery using CAD/CAM system could facilitate the precise reconstruction, thus aiding rehabilitation of biting and swallowing function and improving the cosmetic outcome. It will improve quality of life for some oral cancer patients.

## SY8-4

**Changing Paradigm of Conservation Surgery of Hypopharyngeal Cancer from Open to Endoscopic: Oncologic and Functional Outcomes**

Pen-Yuan Chu

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Hypopharyngeal cancer usually presented at advanced stage and has the poorest prognosis in the head and neck cancer. Traditionally, radical surgery and postoperative adjuvant therapy is the standard treatment in the past several decades. Radical surgery usually included total laryngectomy and partial or total pharyngectomy, and reconstruction. The quality of life is poor after surgery.

Organ preservation therapy has become more popular in the treatment of hypopharyngeal cancer in recent years. Chemoradiotherapy is one of the most important organ preservation therapies, however, acute and late toxicity are high after treatment. Conservation surgery is an alternative of organ preservation therapy. In our experience, there is also a trend of conservation surgery shifting from open to endoscopic for early T1, T2, and selected T3 diseases. Transoral laser microsurgery has been popularly used in our institute. This presentation will show the oncologic results and functional outcomes, esp. the speech and swallowing functions, as well as quality of life after treatment.

SY8-5

## Speech and Swallowing Function Preservation Difference in T1/2 Tongue Cancer Patients Received Partial Glossectomy with Flap or Non-flap Reconstruction

Chien-Jen Chiu

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Tongue is an important structure during deglutition and speech. Patients with tongue cancer would loss some tongue volume which impairs deglutition and speech function to some extent. Our study included total 31 patients with T1/T2 tongue cancer. We allocated these patients into different groups and compared post-op deglutition and speech function.

Treatment of oral cancer is critical for survival. How to conserve patient's life quality is also an important work that we should pay attention to.

SY8-6

## Risk Factors and Clinical Impact of PPI non-responsive Laryngopharyngeal Reflux- related Symptoms A High-resolution Impedance Manometry Study

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**Introduction:** Laryngopharyngeal reflux (LPR)-related symptoms (hoarseness, throat clearing, throat pain, globus, and chronic cough) are common, but definite diagnosis and risk factors remain elusive.

**Objective:** To explore the risk factors and clinical impact of LPR in terms of esophageal motility, gastroesophageal reflux, and psychiatric profile.

**Method:** This is a prospective, case-control study conducted during November 2014 and March 2018 in single tertiary medical center. Consecutive patients who had exhibited at least one LPR symptom for  $\geq 4$  weeks after 2-month proton pump inhibitor treatment were enrolled. Healthy volunteers were also recruited. validated symptom questionnaires, esophagogastroduodenoscopy, and high-resolution impedance manometry (HRIM) were performed. Scores of symptom questionnaires were evaluated and HRIM parameters were compared between patients and volunteers.

**Results:** Eighty-nine LPR patients underwent comprehensive work-up; 63 healthy volunteers were also recruited for comparison of esophageal parameters on HRIM. Of the patients, 48.3% reported a high GerdQ score, indicative of gastroesophageal reflux disease, 69.3% had psychological distress, and 84.3% were poor sleepers. Compared with healthy volunteers, the patients had significantly shorter upper and lower esophageal sphincters (UES and LES), a shorter intraabdominal esophagus ( $P < 0.01$  for the three), higher four-second integrated relaxation pressures (IRP-4s) ( $P = 0.01$ ) of the LES. After adjusted for age, sex, body weight, body height and alcohol consumption, multiple regression analysis showed that LES IRP-4s, the lengths of the UES, LES, and intraabdominal esophagus were independent risk factors for LPR symptoms (OR 1.107, 95% CI 1.004–1.222; OR 0.432, 95% CI 0.254–0.736; OR 0.336, 95% CI 0.175–0.646; OR 0.100, 95% CI 0.025–0.399, respectively).

**Conclusions:** The etiology of LPR symptoms appears to be multifactorial. Our study suggests that a high proportion of patients have typical reflux symptoms, higher psychological stress than normal, and poor sleep. Esophageal structural factors and LES IRP-4s may contribute to the occurrence of LPR symptoms.



## Symposium 9

## OSAS Beyond CPAP –Not only CPAP but also personalized medicine

## SY9-1

**ALLERGIC RHINITIS AND SLEEP**

Shintaro Chiba

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Allergic rhinitis is a type 1 hypersensitivity reaction of the nasal mucosa mediated by immunoglobulin (Ig)E and T helper 2 (TH2) cells in response to inhaled environmental allergens. Rhinitis is a common problem that causes disabilities worldwide. In industrialized countries, AR affects approximately 10% to 30% of the population with various prevalence rates. The most commonly reported symptom of AR is nasal obstruction. Nasal obstruction also has been shown to increase upper airway resistance and play a role in OSA. In addition to nasal obstruction, systemic release of mediators of AR such as inflammatory cytokines and histamine may lead to decreased cognition and arousal, as well as daytime somnolence. A recent article showed that AR influences sleep more than expected, and a sleep disorder due to AR may influence symptoms in the daytime function including daytime sleepiness. However, details of the association between AR and sleep disorders are still unclear. These 3 following hypotheses are presented: 1. Nasal obstruction due to AR causes OSA, and, as a result, a sleep disorder causes sleepiness. 2. Directly, nasal obstruction is related to daytime sleepiness by disturbing the quality of the sleep (regardless of OSA). 3. Allergic disease by itself influences the sleep/wake center (through an inflammatory mediator) and causes a sleep disorder and sleepiness. All these hypotheses may further be affected by changes in brain chemistry due to circadian rhythm. Clearly, the relationship among nasal obstruction, allergic disease, sleep disorders, OSA, inflammatory mediators, and the sleep/wake(center) regulation is not yet clear. We should consider not only influence of nasal obstruction on OSA, but also the impact of specific allergic pathophysiology on sleep/wake regulation.

## SY9-2

**Drug-induced sleep endoscopy (DISE) for adults and children; A new generation**

Masaaki Suzuki

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Drug-induced sleep endoscopy (DISE) is performed to examine the obstructive site, obstructive pattern, and collapsibility by direct observation of pharyngeal collapse during sleep. DISE examinations are performed on adults and children over 10 years of age who are considered as surgical indication in our laboratory. We perform the DISE examination using propofol anesthesia under target controlled infusion (TCI) with monitoring of bispectral index (BIS) by anesthesiologists in the operation room. To understand the obstructive site, pattern, and collapsibility, the direct observation of pharyngeal collapse during sleep seems to be better than any other examinations such as cephalometry, 3DMRI reconstruction, multi-level pressure sensor. Although there might be differences in mechanism of arousability between each sleep stage and drug-induced sleep, obstructive sites, patterns, and collapsibility would not change in the same patient. In addition, the BIS monitor can distinguish between shallow and deep sleep roughly. Other strength is that the DISE video is very persuasive for patients and families to understand their surgical indication. There is a position paper on DISE in Europe describing technical equipment, staffing, local anesthesia, medications, patient position, drugs, scoring and classification systems, and so on. Hypoglossal nerve stimulation (HNS) has been approved by Japanese PMDA in 2018 for adult patients with OSA. DISE examination has been recommended as a tool in assessment of eligibility and a more detailed understanding of mechanisms for an HNS effects. The importance of the DISE has increased the world over, therefore, otolaryngologists need to perform this examination more and more.

Our comparative study between the DISE and computational fluid dynamics (CFD) in children with OSA will be presented at this symposium.



SY9-3

## Relationship between Ménière's disease and sleep dynamics

Takenao Mihara

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Several recent reports have described the relationship between sleep disorders and Ménière's disease. Many clinicians may also have had the experience of patients who say their dizziness are less noticeable when they sleep well. Therefore, sleep disorders might be one of stressor for Ménière's disease. Obstructive sleep apnea (OSA) is one that can affect a patient's quality of sleep. As a mechanism of these phenomena, we focused on brain activity and examined how changes in sleep dynamics led to improvement in dizziness symptoms after improving OSA in patients with Ménière's disease.

We analyzed 23 patients with Ménière's disease (male: female = 16: 7, median age = 68.5 years old) who visited our department from January 2010 to December 2017 and were diagnosed with OSA by polysomnography (PSG). The results of PSG (respiratory events, sleep stages) and self-administered questionnaires (Epworth Sleepiness Scale: ESS, Pittsburgh Sleep Quality Index: PSQI, Dizziness Handicap Inventory: DHI, Hospital Anxiety and Depression Scale: HADS) were evaluated retrospectively, before and after treatment of continuous positive airway pressure (CPAP). In the PSG, CPAP treatment improved all the respiratory events due to sleep apnea ( $p < 0.001$ ). In Non-REM sleep stages, N1 decreased significantly ( $p < 0.001$ ), N2 increased significantly ( $p < 0.001$ ), and N3 was tend to increase ( $p = 0.049$ ), suggesting a shift to deeper sleep. REM sleep also increased significantly ( $p < 0.025$ ). In the self-administered questionnaires, all subjective symptoms such as sleep disorder (ESS:  $p = 0.039$ , PSQI:  $p = 0.020$ ), dizziness disorder (DHI:  $p = 0.005$ ), and anxiety/depression (HADS:  $p = 0.009$ ) were significantly improved. In conclusion, the improvement of respiratory events due to OSA in Meniere's disease patients might lead to reduce the arousal response and smooth brain activity during sleep, contributing to QOL of patients. We will present these results with literature review at this symposium.

SY9-4

## How to manage continuous positive airway pressure (CPAP) failure -hybrid surgery and integrated treatment

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Obstructive sleep apnea (OSA) is a prevalent disease, which influences social relations and quality of life with major health impact. The etiology of OSA is multi-factorial involving both anatomical obstruction and physiological collapse of the upper airway during sleep with different proportion in individual patients. Continuous positive airway pressure (CPAP) is the gold standard and first-line treatment for OSA patients. The mechanism of CPAP is acting as air splint to avoid principal *pharyngeal collapse* during sleep. Consequently, extrapharyngeal collapse and significant pharyngeal obstructions can lower its compliance and lead to its failure. Adequate mask and pressure with thorough survey to eliminate side effects of CPAP from nasal, mask and flow-related problems are the prerequisite to improve CPAP compliance. For CPAP failure patients, multi-dimensional surgery is an alternative and salvage treatment that involves soft tissue surgery, skeletal surgery, and bariatric surgery. OSA patients with craniofacial anomaly are suggested to skeletal surgery. By contrast, OSA patients with pathological obesity are referred to bariatric surgery. Soft tissue surgery targets at the nose, soft palate, lateral pharyngeal wall, tongue and epiglottis that can be implemented by *multi-level surgery with hybrid technique* (mucosa- preservation, fat-ablation, muscle-suspension, tonsil-excision, cartilage-reconstruction) to maximize surgical outcomes and minimize complications. Some evolution in surgical concept and technique are noteworthy that include mini-invasive septoturbinoplasty, palatal suspension instead of excision, whole tongue treatment, and two-dimensional supraglottoplasty. Postoperative *integrated treatment* including myofunctional, positional therapy and body weight control reduces relapse of OSA and improves long-term treatment outcomes.

## SY9-5

## Pediatric obstructive sleep apnea: the associations of obesity and inflammatory biomarkers on surgical outcome

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**Background:** Obstructive sleep apnea (OSA) and obesity in children have been associated with inflammation. The present study aimed to evaluate the presence of inflammatory alterations among children with OSA, with and without obesity, and the impact of treatment of OSA on inflammatory profiles.

**Methods:** A cross-sectional, prospective, single-center study of Taiwanese children aged 5-12 years with an apnea-hypopnea index (AHI)  $\geq 1$  events/hour were randomly selected in the first phase. Obesity was defined by body mass index (BMI) Z-score  $\geq 1.645$  for age and sex. All the participants undergo adenotonsillectomy in the treatment of OSA. Standard in-lab polysomnography and fasting blood tests were performed at baseline and at least three months after adenotonsillectomy. Surgical response was defined as a  $\geq 50\%$  reduction in the AHI and AHI reduced to  $< 5$  event/hour.

**Results:** A total of 60 OSA children (14 girls and 46 boys) with a mean age of  $7.5 \pm 2.2$  years completed follow-up assessments. The mean follow-up period was  $4.8 \pm 2.0$  months. Baseline levels of interleukin (IL)-5, IL-6, and interferon- $\gamma$  significantly differed among inflammatory parameters in children with severe OSA and without severe OSA (all  $p < 0.05$ ). Baseline levels of IL-1 receptor antagonist (IL-1ra), IL-2, IL-4, IL-8, IL-9, basic fibroblast growth factor, platelet-derived growth factor BB (PDGFBB), and regulated on activation, normal T cell expressed and secreted (RANTES) significantly differed in OSA children with obesity and without obesity (all  $p < 0.05$ ). After adenotonsillectomy, mean AHI significantly reduced from  $15.2 \pm 17.2$  to  $3.4 \pm 3.2$  ( $p < 0.001$ ). The rate of surgical success was 63% (38/60). Their mean BMI z-score increased from  $0.582 \pm 2.050$  to  $0.849 \pm 1.547$  ( $p = 0.08$ ). There were significant differences in the levels of IL-1 $\beta$ , IL-1ra, IL-2, IL-4, IL-5, IL-8, IL-10, IL-15, IL-17, eotaxin, granulocyte-macrophage colony-stimulating factor, interferon- $\gamma$ -induced protein 10 (IP-10), monocyte chemoattractant protein-1, macrophage inflammatory proteins (MIP)-1 $\alpha$  (MIP-1 $\alpha$ ), MIP-1 $\beta$ , PDGFBB, and RANTES between baseline and follow-up. Using receiver operating characteristic curves, the optimal cut-off values of baseline age ( $< 7$  years), AHI ( $> 8$  events/hour), and IP-10 ( $< 825$  pg/mL) were determined to predict surgical response. Using binary logistic regression modeling, age  $< 7$  years (odds ratio = 4.2,  $p = 0.003$ ), AHI  $> 8$  events/hour (odds ratio = 6.0,  $p < 0.001$ ), and IP-10  $< 825$  pg/mL (odds ratio = 4.2,  $p = 0.003$ ) could independently significantly predict surgical response.

**Conclusion:** Concurrent OSA and obesity could promote inflammatory alterations, and the inflammatory biomarkers appeared to sensitive to OSA treatment. Furthermore, IP-10 is a potential biomarker to predict surgical response in children with OSA.

## SY9-6

## A safe and precise tongue base surgery for OSA: Real-time Intraoperative Ultrasound-Assisted TORS

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Obstructive sleep apnea is a health issue that has been gradually recognized by people in recent years. Continuous positive airway pressure (CPAP) is the standard of care for medical treatment of OSA. While generally not as effective as CPAP, upper airway surgery is an option as salvage therapy in CPAP failures.

Obstructions can occur at many areas along the upper airway, and 58% to 87% of patients with OSA have multilevel collapse. Residual obstructions along the tongue base account for 17% to 33% of upper airway collapse and are especially prominent in the obese and severe OSA populations.

Transoral robotic surgery (TORS) provides a novel technique for surgical resection of the base-of-tongue (BOT) and lingual tonsil. TORS was initially used for resection of BOT neoplasms in 2006. The concept of TORS as a treatment of OSA was first introduced in 2009 by Vicini et al. in their feasibility report for the treatment of BOT hypertrophy. Since then, TORS has been shown to be an effective treatment option for both isolated retrolingual obstruction and when combined with other techniques in cases of multilevel obstruction.

Despite the many advantages of TORS, such as enhanced visualization, current robotic surgical systems do not provide haptic feedback to the surgeon. Haptic feedback allows the surgeon to palpate vascular structures within the operative field. One of the most devastating complications that may occur during TORS is massive hemorrhage from inadvertent injury to the vasculature. Although the excellent 3D visualization provided by the robotic system is helpful in locating these vessels, the absence of haptic feedback does place the surgeon at a disadvantage.

Since 2016, ENT department, NCKUH, uses intraoperative imaging with real-time ultrasound to augment the 3D visualization of the robotic system. Ultrasound imaging may allow for identification of the vascular structure (esp. lingual artery) within the BOT, thereby extending the tissue resection and reducing morbidity. In this speech, we will provide our experience of the intraoperative ultrasound assisted TORS for OSA.

SY9-7

## Insights of Drug-Induced Sleep Endoscopy in Adults with Obstructive Sleep Apnea

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Obstructive sleep apnea (OSA) becomes a burden in high-income countries. It is oriented with the collapsing effect of negative pressure arising from pulmonary system. Although continuous positive airway pressure (CPAP) device could deal with it perfectly, there are half patients cannot tolerate this solution. Surgery may play a role to help these patients fix the problem. Clearly the aim of surgery is to make the upper aerodigestive tract remain patent during asleep. Therefore, how to identify the obstruction sites is very important.

Clinically, patients are assessed with Friedman's scoring system, which is composed by tonsil size, tongue position and body mass index. It helps to predict success rate of uvulopalatopharyngoplasty (UPPP). But there exists insufficiency of this system; especially it only checks awake people at the front door of airway. The anatomy of OSA patients is heterogeneous, and the airway collapsibility may change obviously from awake to asleep. It mainly is owing to weakening of muscle tone. For such issue, drug-induced sleep endoscopy (DISE) provides direct vision to observe the dynamic change of upper aerodigestive tract in a mimic sleep manner. There are various scoring systems used to report the findings of DISE. The most popular one is VOTE classification, which indicates the inspecting levels at Velum, Oropharynx, Tongue base and Epiglottis. Through recording the degree and the configuration (anteroposterior, lateral or concentric) at each level, the patterns and sites of collapse are presented. DISE shows potential to guide treatment decisions for individual patients with OSA.

In our practice, patients are evaluated with DISE before surgery. About 95% patients have severe collapse at velum level in our series, which are good candidates treated with UPPP. Multiple-site collapse could be observed in half patients. Multi-level surgery may be indicated for such cases. Obstruction may not only happen at tongue base or epiglottis level. Collapse over arytenoid level is noticed, which is about 15% in our case series. Laryngomalacia is a neuromuscular disorder and presents with obstruction over supraglottic structures. Since the collapse happened at epiglottis or arytenoid level with severe obstruction, we call such DISE findings as laryngomalacia sign.

After UPPP performed, our patients follow up with polysomnography (PSG). About 40% non-responders are noticed. Having severe collapse at epiglottis or arytenoid level is highly correlated with the failure. On the contrary, "absence of laryngomalacia sign" is strong indicator to rule out non-responder of UPPP.

The Friedman's staging system involves tonsil size and tongue position. The VOTE system only records the level above epiglottis. Both systems ignore the possible collapse at the gate of larynx. There will be lack of full information to the surgeon in such case. We advocate that DISE should be done before surgery, and the investigation should include laryngomalacia sign.

## Symposium 10 Dizziness

## SY10-1

**Changes in vertigo frequency and endolymphatic volumes after endolymphatic sac drainage surgery**

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Meniere's disease is a common inner ear disease, that presents with recurrent vertigo and fluctuating/progressive cochlear symptoms. The pathology of Meniere's disease was first reported to involve endolymphatic hydrops in 1938. The endolymphatic sac is thought to have a role to keep the hydrostatic pressure and endolymph homeostasis for the inner ear. We usually take endolymphatic sac surgery with intra-endolymphatic sac application of large doses of steroids for intractable Meniere's disease to control hydrops and preserve or improve inner ear function. In the present study, to observe the effect of this surgery, we calculated the endolymphatic space size using 3-Tesla magnetic resonance imaging (MRI) 4 hours after intravenous injection of gadolinium enhancement at two time points: just before and two years after surgery. To reveal the condition of the endolymphatic space, we constructed 3D MR images semi-automatically and fused the 3D images of the total fluid space of inner ear and the endolymphatic space. After fusing the images, we calculated the volume of the total fluid space and endolymphatic space.

Two years after surgery, 16 of 20 patients showed complete relief from vertigo attacks and reductions in the ratio of the volume of the endolymphatic size to the total fluid space especially in the cochlea and vestibule using 3D analysis of inner ear MRI. These results indicate that endolymphatic sac surgery with intra-endolymphatic sac steroids is a good treatment option for patients with intractable Meniere's disease to control hydrops, resulting in free from vertigo/dizziness.

The 3D analysis of inner ear MRI could be helpful for the detection of volumetric changes in endolymphatic space. The localization of hydrops might be important for understanding of mechanisms of vertigo attacks in Meniere's disease. Further developments both in inner ear MRI and analyzing software will give us reasonable answers for unsolved issues in this field.

## SY10-2

**Changes in cognitive function in patients with intractable dizziness following vestibular rehabilitation**

Fumiyuki Goto

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Previous studies have reported an association between vestibular dysfunction and various forms of cognitive impairments, including visuospatial ability, attention, executive function, and memory. The purpose of the present study was to investigate changes in cognitive functions, including visuospatial ability, attention, and executive function in patients with intractable dizziness following vestibular rehabilitation, and the correlation between improvements of cognitive function, dizziness-related variables, and emotional distress.

During hospitalization for 5 days, participants were trained on a vestibular rehabilitation program. Participants completed questionnaires including the Dizziness Handicap Inventory (DHI), Hospital Anxiety and Depression Scale (HADS), and Trail Making Test (TMT), which were used to assess cognitive function. The center of gravity fluctuation measurement and timed up and go test (TUG), which were objective dizziness severity indexes, were performed before, 1 month after, and 4 months after hospitalization. Following vestibular rehabilitation, participants exhibited a significant improvement in the TMT, DHI, HADS, and TUG scores. Correlation analysis between the variables at each time point indicated that TMT scores positively correlated with TUG at baseline.

In the present study, we demonstrated that patients with intractable dizziness exhibited a significant improvement in cognitive functions including visuospatial ability, attention, and executive function as evidenced by the TMT. These changes also coincided with improvement in dizziness-related indexes and psychological distress following vestibular rehabilitation.

SY10-3

## Persistent Postural-Perceptual Dizziness (PPPD): ICD-11-cited chronic vestibular syndrome

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Persistent postural-perceptual dizziness (PPPD) is characterized by persistent chronic vestibular syndrome lasting >3 months that is typically preceded by acute vestibular disorders. The core vestibular symptoms of PPPD are dizziness, unsteadiness, or non-spinning vertigo and are exacerbated by upright posture/walking, active or passive movement, and exposure to moving or complex visual stimuli. Diagnostic criteria of PPPD <sup>1)</sup> was established by Barany Society at 2017 and this entity was cited as one of diseases showing chronic vestibular syndrome in International Classification of Diseases-11 (ICD-11) by World Health Organization (WHO) at 2018. PPPD is classified as a functional disorder but is not a structural or psychiatric condition. No specific laboratory test for PPPD is available, and the precise assessment of symptoms, exacerbating factors, and medical history is important for PPPD diagnosis. In the present study, we developed a questionnaire named the Niigata PPPD Questionnaire (NPQ) <sup>2)</sup> to aid the diagnosis or assessment of PPPD severity. Fifty PPPD patients and 50 consecutive control patients with other vestibular disorder answered questions on three exacerbating factors of PPPD (upright posture/walking, movement, and visual stimulation), and each factor was evaluated using four questions scoring the severity from 0 (none) to 6 (unbearable). Cronbach's alpha, a marker for questionnaire's reliability, was >0.8 for all factors except the movement factor, indicating high reliability of the NPQ. Regarding the validity, the combined and individual questionnaire scores for each factor were higher in PPPD patients than in controls, indicating the questionnaire's high validity. The area under the curve (AUC) of the receiver operating characteristic curve was widest for the visual stimulation factor (0.830), and a score of 9 (total full score 24) had the best sensitivity (82%) and specificity (74%) for discriminating PPPD patients from controls. In conclusions, the NPQ exhibited high reliability and validity in diagnosing and evaluating PPPD severity. The visual stimulation factor may be the most characteristic discriminatory among the three exacerbating factors.

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SY10-4

## Vestibular Dysfunction in Patients with Idiopathic Sudden Sensorineural Hearing Loss

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Sudden sensorineural hearing loss (SSNHL) has been the healthy burden for about 5-20 persons in annual incidence. Approximately 20-60% patients with SSNHL suffered from concurrent vestibular symptoms, and previous literature revealed less hearing recovery in this group. Several vestibular diagnostic methods were developed in the past decades to discover objective evaluation in vestibular organs, such as the caloric test, cervical vestibular-evoked myogenic potential (cVEMP), ocular vestibular-evoked myogenic potential (oVEMP), and video head impulse test (vHIT). For patients with SSNHL, the affected zone in audiovestibular system was discussed with these tools recently. For this session, we analyzed the vestibular laboratory data and hearing outcome for patients with SSNHL in our tertiary center and discussed the current controversy in vestibulocochlear lesion patterns.



## SY10-5

**Inner migraine and vertigo**

Jen-Tsung Lai

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Migraine plays an important role in clinical management of vertigo. Inner ear migraine" a migraine variant, is often encounter in our neurological practice. Inner ear migraine presented as well known vestibular migraine (VM) and a new proposed diagnosis cochlear migraine (CM).

CM often confused in the clinical practice as acute low tone hearing loss (ALHL), sudden hearing loss and cochlear Meniere's disease (MD). Migraine might damage the hearing and balance through a neuroinflammation mechanism. The neuroinflammation resulted from migraine is a possible cause of vestibular symptoms and cochlear symptoms.

In large-scale cohort study, we found that patients with a history of migraine had a tendency to develop cochlear disorder and tinnitus. People with migraine had almost three times increased risk of cochlear disorder especially tinnitus, compared with people without migraine.

In our clinical observation, there is a group of patients had symptoms overlapping between VM and CM. We proposed them as vestibular-cochlear migraine (VCM) or cochlear-vestibular migraine (CVM), depend on vestibular or cochlear symptoms developing at first. In fact, VCM and CVM often diagnosed as MD before. Estimation of CVM and VCM are 5~10 times more than MD patients in epidemiology. In some cases Migraine related Meniere disease (MrMD) is a great imitator of Primary Meniere disease. (PrMD)

## SY10-6

**Idol worship and reflection in vertiginous diseases**

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Diseases were often named by symptoms, signs, anatomical abnormalities, pathophysiological changes, genetic variations, or some notable persons' name. In vertiginous field, Meniere's disease (MD) was the most well-known and the only one described by a name. Initially, the so-called MD was mainly an anatomical and pathologic diagnosis. But, later, it was shifted to a symptomatic diagnosis by some arbitrary criteriae. In fact, many etiologies may contribute to MD. And, the diagnostic criteriae for MD were non-specific and altered with time.

With many advances on disease mechanisms, more and more diseases in all medical fields were named by pathophysiological findings and/or underlying mechanisms, but not by notable person's name.

Similarly, some new tools/findings were reported in the vertiginous field, for example, electrocochleography, MRI, vestibular migraine, cochlear migraine, and cochleovestibular migraine, etc. Therefore, it may be the time to reflect idol worship in vertiginous diseases in the view of modern precision medicine.



**Symposium 11** Head and Neck Benign

**SY11-1**

**Percutaneous ethanol injection therapy in the treatment of thyroid cyst**

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The thyroid cyst is an ultrasonically common finding and considered to be caused by hemorrhage and subsequent degeneration of nodules. Although most cysts are too small to treat, there were several methods for treating benign large thyroid cysts, such as fine-needle aspiration, thyroid hormone suppression therapy, and sclerotherapy. In this session, the safety and the effectiveness of percutaneous ethanol injection therapy (PEIT), which is a method of sclerotherapy, is introduced.

In our study, 11 patients with fine-needle aspiration cytology-proven benign cysts underwent PEIT. Four patients were male, the median age was 58 years old (range: 35 - 95 years). Thyroid cyst fluid was aspirated, and less than 4 mL of sterile 95% ethanol was injected. The cyst volume converted for pretreatment ranged from 3 to 164 mL (average 44 mL). PEIT was carried out one to four times (median, once). Cyst volume after treatment ranged from 0 to 92 mL (average 8 mL), and the volume reduction rate ranged from 22 to 100% (average 89%). Three patients without subcutaneous anesthesia complained of a local burning sensation at the injection site while the remaining eight patients with subcutaneous anesthesia did not. Another complain were not occurred in undergoing PEIT.

One of 11 patients with a huge thyroid left lobe cyst is presented; a 58-year-old man had noticed swelling in the neck one year previously, and experienced dyspnea five days before visiting our clinic. Computed tomography revealed a 88×57×53 mm-sized low density mass located in the left lobe of the thyroid, extending to the superior mediastinum. Furthermore, the trachea was deviated to the right. Fine needle aspiration was performed to examine the aspirate and reduce the mass effect. The aspirate was approximately 150 mL of dark brown sticky liquid, composed of histiocytes and blood components, and the patient was diagnosed cytologically as having cyst fluid with no malignancy. After aspiration, the patient's dyspnea improved and 4 mL of dehydrated ethanol was infused into the cyst four times over 19 months. The cyst was gradually reduced to 14 mm in size. PEIT with subcutaneous anesthesia is safe and avoid burning sensation and effective in reducing the volume of benign large thyroid cysts.

**SY11-2**

**The current status of cervical schwannoma surgery and the attempt of reduction in postoperative neurological deficit**

Toshikazu Shimane

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While there has been a debate to select follow-up or surgery for dealing with cervical schwannoma, various views or opinions are still available when selecting surgery. At our center, we perform inter-capsular resection as basic surgical procedures in reference to patient's age, a growth rate of tumor, and an increasing rate for incidence of neurological deficit. In addition, we consider it is important to appropriately perform inter-capsular resection for reducing postoperative neurological deficit. In this study, we report our attempts to reduce postoperative neurological deficit at our center.

Firstly, it needs to understand a tumor structure by using a schwannoma model. Since schwannoma is originally derived from Schwann cells, tumor-derived nerve fibers and other nerve fibers are mixed in the epineurium. In order to preserve a postoperative nerve function, a surgeon must remove nerve fibers with preserving non tumor-derived nerve fibers as much as possible. In this model, it reproduces that a surgeon only can remove those nerve fibers in the true tumor capsule layer.

Secondly, it is inter-capsular resection with use of narrow band imaging (NBI). In NBI, the running of nerve fibers and fibrous tissues can be clearly and three-dimensionally observed with contrast. It is difficult to observe fibrous tissues on the tumor capsule by naked eyes or normal light due to the transparent color, but the tissues can be observed in NBI. If there is no residual fibrous tissues on the tumor, it confirms as reaching into true tumor capsule. Thus, we consider that such procedure will be useful to reduce postoperative neurological deficit.

In addition to the above description, we also report the treatment results of 100 cases with inter-capsular resection performed at our center.

## SY11-3

**Fukui-style retro-auricular approach of Endoscopic thyroid surgery without robot**

Masafumi Kanno

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In Japan, robotic thyroid surgery is not approved. Endoscopic-assisted thyroid surgery is called VANS (Video Assisted Neck Surgery), and otolaryngologists approach the thyroid mainly from the chest below the clavicle. In our department, we have approached from below the clavicle, but recently we are approaching from retro-auricle more aesthetically. To get started, we visited several hospitals in Korea and received advice. Our unique methods include the following points. To reduce the difficulty of surgery; a camera port is created in the neck to ensure a sufficient field of view. The upper side of the operation monitor should be the foot side and the lower side should be the head side. For safety; the superior thyroid artery is detached and ligated with silk, and the NIM monitor is used to confirm the superior laryngeal nerve and recurrent laryngeal nerve. Aesthetic ingenuity; the incision line is hidden in the hair. We believe that this method is aesthetic, with no surgical wounds in the exposed areas, can be operated at low cost, and is not inferior to robotic surgery in all aspects. In our department, multiple doctors can perform VANS. Based on the data of 10 cases, about 3 hours of surgery time was required for hemithyroidectomy. The amount of bleeding was insignificant, and there was no change in the surgical method such as external incision. Although no recurrent nerve palsy was observed as a complication, there was one case requiring reoperation due to postoperative bleeding. The patient bled from the inferior thyroid artery when she began walking the day after surgery. The drain was inserted, but suction was insufficient. There were factors such as hypertension in the patient's background, but it was also due to insufficient excision with the energy device. The patient is allowed to leave the hospital on the fifth day after the operation, but is considered to be possible on the third day after the drain is removed. In this session, we will introduce our surgical method with surgical videos.

## SY11-4

**Application of multi-arm or single-port robotic surgical systems for the trans-hairline approach of submandibular gland resection**

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Conventional surgery is associated with significant esthetic morbidity in clinical practice of treating head and neck diseases by the open approach. The possibility of leaving obvious scars on the neck that has significantly reduced since the introduction of the techniques of robotic and endoscopic surgery. Furthermore, cosmetic outcome after surgery has greatly improved since the development of robotic surgery through a trans-hairline approach. However, the bulky sizes of robotic arms and the rigid design of camera and instruments in the current multi-arm robotic systems increased the surgical difficulty. With the launch of the flexible single-port (SP) robotic system, the surgical procedures of trans-hairline approach for robotic neck surgery could be successfully performed. The unique features include an easy docking procedure, different viewing angles, the use of the third arm, and coordination of instrument positions without a bedside assistant, which are unavailable in current multi-arm robotic systems. All advantages of applying the flexible, SP robotic system in robotic neck surgery through the trans-hairline approach pose the significant impact on the improvement of surgical technique and outcomes.

SY11-5

## Ultrasound-Guided Fine-Needle Aspiration Drainage and Percutaneous Ethanol Injection for Benign Neck Cysts

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**Background:** Ultrasound-guided fine needle aspiration drainage (US-FNAD) and percutaneous ethanol injection (US-PEI) have been widely used in the management of benign neck cysts. However, the long-term results of US-FNAD and US-PEI are not well elucidated.

**Materials and Methods:** We retrospectively collated patients under neck US exams from March 2007 to Dec. 2017 and investigated the recurrence after US-FNAD and US-PEI. Univariate and multivariate Cox regression analyses were used to assess significant risk factors for recurrence after US-FNAD.

**Results:** A total of 1,075 patients were recruited, and their age was  $50 \pm 15$  (mean $\pm$ SD) years old. A total of 862 patients had thyroid cysts, 118 patients had thyroglossal duct cysts (TGDC), 20 patients had branchial cleft cysts, 64 patients had parotid sialocysts and 11 patients had plunging ranulas. Most patients (97%, 1037/1075) reported significant symptom improvement immediately. However, 38% of patients had recurrence with a median 3-year follow-up period. In a multivariate Cox-regression analysis with adjustment for age and gender, plunging ranula [HR 2.44, 95% confidence interval (CI) 1.19-4.99] and lateral dimension size  $\geq 0.8$  cm (HR 1.32, 95% CI 1.04-1.67) after US-FNAD were independent risk factors for recurrence. There were 15 male and 19 female patients who received US-PEI therapy after repeated US-FNAD, of whom 23 patients had thyroid cysts, 6 had plunging ranulas, 4 had TGDC and one had a branchial cleft cyst. The overall successful rate was 94% (32/34) with a median follow-up period of 1.6 years. Two recurrent symptomatic patients both had plunging ranulas. Some patients stated mild pain (21%, 7/34) and swelling sensation (26%, 9/34) after the injection. No major complications, such as vocal fold paresis or airway compression, were found.

**Conclusion:** US-FNAD was an effective management of benign neck cysts with a 38% recurrent rate. Plunging ranulas had the highest rate of recurrence after FNAD. US-PEI was effective for most recurrent neck cysts after repeated US-FNAD.

SY11-6

## The role of ultrasound of Pediatric head and neck

Ming-Yu Hsieh

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Pediatric ultrasonography has emerged as the first-line imaging modality for the evaluation of pediatric head and neck masses. Without utilizing radiation, iodinated contrast material, or sedation and/or anesthesia, US provides a means for quick and cost-effective acquisition of information, including the location, size, shape, internal content, and vascularity of the mass. Benign and malignant entities have been specifically chosen for discussion: neonatal scalp hematoma, dermoid and epidermoid cysts, lymph nodes and their complications, thyroglossal duct cyst (TDC), branchial cleft cyst (BCC), cervical thymus, congenital goiter, thyroid papillary carcinoma, parathyroid adenoma, hemangioma, lymphangioma, internal jugular vein phlebectasia...etc. Ultrasound can be adopted by otolaryngologists for use within the clinic and the operating room. Ultrasound offers several advantages to the pediatric patient : low-cost, non-invasive, inexpensive, easily accessible. It is well tolerated and adds a degree of precision to the physical examination. It can be done repeatedly as lesions evolve and treatment is performed. Fine-needle aspiration biopsy is a minimal invasive method used for the diagnosis of neoplastic and non-neoplastic lesions in the head and neck region. The procedure is generally without complication and it is safe, and well-tolerable by patients. It usually does not require anesthesia and the results are obtained rapidly. FNAB can be used in pediatric cases with head-neck mass because it can decrease the number of surgical interventions planned to be performed for diagnosis owing to its high predictive value in the establishment of diagnosis. In conclusion, ultrasonography is useful for the diagnostic workup of a pediatric neck mass.

## Symposium 12 Pediatrics

## SY12-1

## Treatment of congenital cholesteatomas: Endoscopic ear surgery and the emergence of the exoscope

Tsukasa Ito

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**Introduction** The microscope has long been the only option for visualizing the surgical field in ear surgery, but it now shares the stage with the endoscope and exoscope. Transcanal endoscopic ear surgery (TEES) offers advantages over traditional microscopic ear surgery (MES) such as a wide field of view, higher magnification, and less invasiveness, while the exoscope allows for an ergonomic, heads-up posture which can alleviate strain on the surgeon. The exoscope also facilitates communication and education because the surgical field is visible on a high-quality 3D display which can be viewed by the surgical team and student observers. This presentation shall demonstrate the use of TEES and its efficacy in the treatment of congenital cholesteatomas (CC) and introduce our experience using exoscopes in ear surgery.

**Patients and Intervention** Thirty-two patients with CCs who underwent surgery by TEES and/or MES from December 2011 to December 2017 (mean age/range: 7 yr/2–16 yr; 20 males/12 females; mean follow-up/range: 3 yr/0.6–6.7 yr). TEES was performed with a 2.7-mm endoscope coupled to a full HD system. Some TEES procedures included a transcanal attico-antrostomy using an ultrasonic aspirator if the cholesteatoma extended into the antrum in a procedure called “Powered TEES”. A dual approach using both TEES and MES was performed for patients with cholesteatomas extending beyond the antrum into mastoid cells. TEES was performed to remove any part of the CC in the tympanic cavity and a microscopic transcortical mastoidectomy was performed for CC located in the mastoid.

**Results** Twenty-six patients (81%) underwent TEES and 6 patients (19%) underwent a dual procedure. Twenty-five patients with a Patsic grade III or lower cholesteatoma underwent TEES. Twenty patients underwent a one-stage operation, while the remaining 12 patients required a two-stage operation due to the risk of a residual cholesteatoma when the cholesteatoma could not be removed en-bloc. Six patients (19%) had residual cholesteatomas out of which 5 were an open-type congenital cholesteatoma treated by a one-stage operation. Postoperative evaluation revealed that 26 of all 32 patients (81%) with CCs and 23 of 26 patients (88%) in the TEES group achieved good air-bone gap results of less than or equal to 20 dB HL.

**Conclusions** An endoscope can be used to safely and effectively treat CCs with a resulting improvement in hearing. Furthermore, additional advances should be reaped with a new dual approach using both an endoscope and exoscope in both surgical outcomes and surgeon comfort.

## SY12-2

## Evaluation of Airway problems for surgeries in patients with Mucopolysaccharidosis

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Mucopolysaccharidosis (MPS) is a lysosomal storage disorder caused by a lysosomal enzyme deficiency that leads to systemic accumulation of glycosaminoglycans (GAGs). Accumulation of GAGs in the upper airway causes respiratory tract narrower, resulting in respiratory problems due to thickening of the supraglottic region, and diffuse thickening of the tracheobronchial tree.

Children with Hunter syndrome (MPSII) are prone to obstructive sleep apnea and often require adenoidectomy and tonsillectomy. When adenoidectomy and tonsillectomy are performed under general anesthesia, these airway risks should be noted as perioperative management. For example, tracheal stenosis is one of the major risk factors for intubation failure under general anesthesia. In addition, the chest is stiff and difficult to ventilate, and intraoperative airway management can be difficult for professional anesthesiologists.

We have previously evaluated tracheal CT images and endoscopic findings of larynx in patients with MPS. The tracheal morphology was found to be abnormal in 50-60%, and in particular, the tracheal cross section was deformed laterally. In addition, we reported that edematous changes in the laryngeal mucosa were observed in 20%. Therefore, in this presentation, we will describe the relation between progression of upper airway stenosis respiratory disorders. Periodic CT and endoscopic assessment can predict respiratory problems during anesthesia, which is useful for perioperative management of upper airway problems.

SY12-3

## **The new strategy for the pediatric severe allergic rhinitis: submucosal turbinectomy and selective posterior nasal neurectomy combined with rush immunotherapy**

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Allergic diseases, including allergic rhinitis, are an important health problem, and their prevalence has been increasing considerably in the past few decades. Immunotherapy and surgical treatment is one of the therapeutic option for sever allergic rhinitis.

In traditional immunotherapy, patients come in every week for a shot, then once a month until 3-5years. Each time, patients have to wait 30 minutes after receiving the shot to make sure they're not going to have an allergic reaction. Rush immunotherapy's main benefit is shortening the buildup phase of allergy shots.

On the other hand, the most effective types of surgery are submucosal turbinectomy and selective posterior nasal neurectomy. The inferior turbinate bone has 3 or 4 canal-like structures including a cord-like structure with vessels and the most peripheral palatine nerve. After the surgery patient needs to stay hospital in a few days.

We establish the new strategy for sever allergic rhinitis RUSH Immunotherapy in the perioperative period. This technique arrows us the shortening the buildup phase of SCIT using the perioperative period after the surgical treatment.

### **CASE:**

13 YO male patient with sever perennial allergic rhinitis, shows low response for any conventional therapy. The patient always has sever headache and abdominal pain, tends to be absent from school. We plan the combination therapy of rush immunotherapy and submucosal turbinectomy with selective posterior nasal neurectomy. The surgical treatment was performed under general anesthesia with 7days admission. Rush immunotherapy was started on post operative 2nd days. Give 4 or 5 times allergy shots per day during perioperative admission period. After admission keep increasing the SCIT once week until booster dose. Adverse events were not seen during built-up period of SCIT. After keep the boost dose around 1.5 Y, now AIT was changed SCIT to SLIT. Symptom of the patient is stable and the quality of school life is improved after the therapy. Multimodal allergy therapy was suit for sever allergy patient especially for the modern busy generation.

SY12-4

## **Pearls and Pitfalls in Transhairline Da Vinci Robot-Assisted Excision of Cervical Lymphangioma**

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Robotic surgeries of the head and neck have gained popularity in the past two decades with improved functional and cosmetic surgical outcomes. Majority of the robotic surgeries in the pediatric head and neck area were performed via the transoral approach. The transhairline robot-assisted surgical approach to cervical lymphangiomas in the pediatric population takes into consideration not only in cosmesis, but also the future functional outcomes. Complicated by scar contracture and soft tissue fibrosis frequently encountered especially in those patients have been treated with sclerosing agents and limited by the very narrow working space in the pediatric population, the magnified and 3-D surgical view offers the advantage of addressing the anatomical issues posed by airway obstruction and potential injuries to great vessels and nerves. Through videos of robotic surgeries, pearls and pitfalls in transhairline robot-assisted excision of cervical lymphangiomas will be presented and discussed.



## SY12-5

## Investigation and Management of Tracheal Deformity in Type IVA Mucopolysaccharidosis (Morquio-A Syndrome)

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**Background:** Mucopolysaccharidosis(MPS) is an inherited metabolic disorder with lysosomal enzyme deficiency and result in glycosaminoglycans(GAGs) accumulate in the connective tissue of whole body including: skin, hair, bone, cartilage, joint, brain, and other organs. Patients with MPS type IVA usually have short stature, hypoplasia of cervical spine, flaccid soft tissue and subluxation of joints. They usually develop in airway obstruction because of anatomical change include: collapsed spine, and deformity of thoracic cage and crowding intrathoracic structures, leading the trachea compressed by crossing tortuous innominate artery. The GAGs deposit may thicken the tracheal wall and damage the framework of cartilage. The average life span is between 20-30 years. The most common cause of death of MPS type IVA was airway obstruction.

**Objective:** The objective of this presentation is to investigate morphology of the entire airway deformity by the images of fiberbronchoscopy(FB), CT scan, and pathology, and try to analysis the etiology of tracheal stenosis. I also offered the method of airway reconstruction with T-tube stent in MPS type IVA patients.

**Materials and Methods:** The airway of type IVA MPS patients was evaluated by FB and CT scan. All the images were recorded to demonstrate the site, severity, models of tracheal stenosis and morphology of lumen collapse. Make use of colloidal iron stain in pathological studies to detect the GAGs deposit in the tracheal cartilage. LTR and T-tube stent was used in three severe patients weak phonation, prolong feeding and needed to hyperextend the neck for breathing.

**Results:** Nine type IVA MPS patients had complete CT and FB examination at the same time. Eight of the nine patients have airway problems. Tracheal narrowing may increase in severity with age. The eldest three patients (age 26~31years old) had severe tracheal deformity with external compression by innominate artery and need airway intervention. IN pathological study with colloidal iron stain, they all revealed GAGs deposit in the tracheal cartilage. The morphology of tracheal deformity included worm, U, triangular shape, kinking/bending shape, GAGs deposit leading tracheal deposit nodule or thickening of cricoid ring.

**Conclusions:** MPS type IVA patients usually have multifactorial obstructive airway. T-tube stent may provide patent airway and preserve the laryngeal function, including phonation, respiratory and swallowing. We should take special concerns for pre-operation planning, including the type, the size and the position (below or above the cord) of the T-tube. Y-shaped Montgomery® pediatric T-tube is more suitable for MPS type IVA patients.

## SY12-6

## Autoimmune Diseases Represent a Comorbidity of Chronic Rhinosinusitis

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**Background** Chronic rhinosinusitis (CRS) is characterized by inflammation of the sinus mucosa. Prior studies on the association between CRS and autoimmune diseases have been inconclusive. Since lacking of an overall and systemic population-based analysis of CRS comorbid with common autoimmune diseases, we endeavor to clarify the relation between these two by a cross-sectional study. Moreover, whether subdivisions of CRS are involved is also discussed in this article.

**Methods** This is a cross-sectional study utilizing data from Longitudinal Health Insurance Database 2000. The 13,173 CRS patients were defined by ICD-9-CM code 473 in both inpatient and outpatient visits between January 1, 2012 and December 31, 2013. Patients are investigated in two aging groups, with aged under 18 as pediatric group and aged between 18 to 80 as adult group. Logistic regression analysis was utilized for risk assessment of comorbidities for the CRS and comparison groups, and results were presented using Odds Ratios.

**Results** In adult, asthma, systemic lupus erythematosus, rheumatoid arthritis, sjogren's syndrome, vasculitis, ankylosing spondylitis, autoimmune hepatitis, Crohn's disease, atopic dermatitis, urticaria, and psoriatic arthritis all show significant relation with CRS. (OR: 3.65, 2.44, 2.77, 2.17, 1.96, 1.88, 1.81, 1.79, 1.63, 1.61, 1.36) (p value < 0.01). Furthermore, analyzing subdivision among these, those autoimmune diseases mentioned above mostly have higher risk to have CRSsNP, except for Crohn's disease, which is more related with CRSwNP. There are four diseases only significantly associated with CRSsNP, rather than CRSwNP, including rheumatoid arthritis, Hashimoto's disease, vasculitis, and psoriatic arthritis. (OR: 2.47, 2.11, 2.10, 1.43) (p value < 0.01).

Regarding to pediatric results, compared to the control, patients with CRSsNP have higher risk of having Crohn's disease, asthma, urticaria, and ulcerative colitis as comorbid diseases. (OR: 4.61, 2.63, 2.08, 2.08) (p value < 0.01). Besides, patients with CRSwNP are predisposed to asthma, autoimmune hepatitis, ulcerative colitis, urticaria, atopic dermatitis, and Crohn's disease. (OR: 3.27, 1.88, 1.68, 1.68, 1.52, 1.40) (p value < 0.01). Noted that atopic dermatitis and autoimmune hepatitis only showed significant relation with CRSwNP, rather than CRSsNP in our study.

**Conclusion** Patients with CRS are predisposed to various systemic and autoimmune diseases. We believe that they should be explained by multi-immune mechanism, more than Th1 pathway and Th2 pathway. Further studies should be done to clarify these complex interactions.

**Key Words** Autoimmune disease, chronic rhinosinusitis (CRS), CRSwNP, CRSsNP

# Paper

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15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery

## Paper 1 Laryngology 1

O01-01

### Predictive Factor Analysis for Successful Decannulation after Glottis-dilating Surgery in Patients with Bilateral Vocal Fold Immobility

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**Introduction:** A number of surgical procedures for glottic widening and decannulation after tracheotomy in patients with bilateral vocal fold immobility (BVFI) have been reported: laterofixation, arytenoidectomy and laser transverse cordectomy. However, none of these techniques have been necessarily able to achieve airway sufficiency, and preoperative prediction of their success/failure has been difficult. The aim of the present study was to identify preoperative factors for affecting the success/failure of glottic widening surgery.

**Materials and Methods:** We retrospectively studied a total of 15 patients (9 male and 6 female; median age, 63 years; age range, 14 to 76 years) who underwent glottic dilatation surgery between 2005 and 2018 in Osaka University Hospital. By reviewing clinical records, the following information was investigated: gender, age, a period from the onset of BVFI to the first visit and tracheotomy, the vocal fold motions during repetitive inspiration and phonation, the surgical procedures used and outcomes of decannulation in each surgery, and the presence of ankylosis of the cricoarytenoid joint. In particular, the degree of maximal opening of the vocal folds was evaluated by measuring the angle between the bilateral vocal folds (VFs).

**Results:** The following surgical procedures were selected in the initial surgery of the 15 BVFI patients (arytenoidectomy, 7; laser transverse cordectomy, 1; Ejnell's laterofixation surgery, 7). After the initial surgery, decannulation was achieved in 9 of the 15 patients, (arytenoidectomy, 3/7; laser transverse cordectomy, 1/1; Ejnell's laterofixation 5/7). As the reason for the failed decannulation, the cricoarytenoid joint ankylosis (3/6) were found. In the 3 of the 6 patients who failed glottal widening, the second surgery achieved decannulation. A significant difference in the successful decannulation rate was found between the patients showing more and less than 10 degree of the preoperative maximal VF angle, although other factors than the VF angle were not associated with the successful decannulation rate.

**Conclusion:** The present results demonstrate that only the preoperative maximal VF angle contributes to the success/failure of glottic dilatation surgery, and suggest that the presence of narrow maximal VF angles implies the existence of cricoarytenoid joint ankylosis, leading to insufficient widening of the glottal space.

O01-02

### Our experience in the treatment of bilateral vocal fold immobility

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**Objectives:** The primary goal is to present our experience in the treatment of the bilateral vocal fold immobility (BVFI).

**Background:** The neurological BVFI usually presented respiratory problem as chief complaint in clinic and various related treatments had been provided. However, the mechanical BVFI still challenged not only the lateralization but also the medialization of the vocal folds in patients with dyspnea and dysphonia respectively.

**Materials and Methods:** From 1994 to 2018, 113 patients with BVFI, resulted by various causes, were treated for breath in 87 patients and for voice in 26 patients. Among 87 patients with chiefly presenting with dyspnea or tracheostomy, 43 neurological patients underwent suture lateralization (SL), 4 mechanical BVFI needed arytenoid release (Ar) and then SL, and 40 patients received conservative treatment. Among 26 patients chiefly presenting with breathy hoarseness or aphonia, 4 patients underwent modified arytenoid adduction (mAA) procedure for aphonia, 2 patients were treated inappropriately with one laryngeal reinnervation (LR) and one implantation laryngoplasty (IL) respectively, and 20 patients were treated conservatively.

**Results:** A total of 43 patients (8 males and 35 female, aged from 18 to 82) with BVFI underwent 46 SL. Improvement of dyspnea or decannulation were obtained in 40 patients with 3 decannulation failure. The causes of failure were one infection, one mechanical BVFI and one threatening aspiration due to old age. Four mechanical BVFI treated by Ar plus SL had one decannulation and 3 improvements of dyspnea. In voice treatment, four mechanical BVFI (three females and one male, aged from 18 to 73) were treated with mAA procedures. Three mAA procedures were augmented with silicone block and one mAA was not. The acoustic analysis showed detectable jitter and shimmer from preoperatively undetectable status. Pulmonary function test showed increased midvital capacity flow ratio but in the St George's Respiratory Questionnaire, the respiratory function was recognized as adequate in three patients after the operation for daily routine activities. The mean follow up time was 48.3 months (from 9 to 120 months).

**Conclusion:** The outcomes illustrate that the SL provides improvement of dyspnea or decannulation in neurological BVFI. Arytenoid release is definitively required in mechanical BVFI no matter lateralization or medialization are attempted. Lateral positioned vocal folds in patients with mechanical BVFI seems to offer the mAA procedure an adequate space to achieve a compromise between the respiratory and phonatory performance.

O01-03

## The Etiologies and Treatments for Patients with Bilateral Vocal Paralysis

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**Objectives:** To evaluate the etiologies of bilateral vocal palsy and to characterize the different clinical treatments.

**Methods:** A retrospective case series study was conducted from 2009-2019 at the Tri-Service General Hospital, Taiwan. Patients who had experienced bilateral vocal palsy and underwent treatments were enrolled. Data pertaining to basic characteristics, laboratory profiles, image studies, and treatments were also collected.

**Results:** A total of 41 patients (16 females and 25 males) were included. The average age is 64.1 years old. The bilateral vocal palsy was diagnosed by laryngoscope. The etiologies in our patient's included thyroid neoplasm status post total thyroidectomy, post endotracheal tube insertion, stroke, mediastinum cancer, brain tumor, head and neck cancer status post chemoradiation therapy, and idiopathic causes, etc. We performed tracheostomy, cordectomy or laryngoplasty to these patients. The symptoms improved after treatments.

**Conclusions:** Patients with bilateral vocal palsy underwent either cordectomy or tracheostomy can have respiratory improvements. There is little difference between post-operative swallowing and pronunciation. However, which surgical intervention we choose depends on the patient's clinical conditions.

O01-04

## A Novel Adjustable Device for Laryngeal Framework Surgery: An Animal Study

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**OBJECTIVE:** To describe the method of inserting an adjustable balloon implant (ABI) for medialization thyroplasty and evaluate its effect using porcine larynges.

**METHODS:** A prototype ABI was inserted respectively in eight porcine larynges of various sizes through laryngeal framework surgery type I and then filled with saline. Several parameters (Södersten and Lindestad Classification for area of glottic closure, etc.) were measured for the following conditions: vocal fold paralysis and paralysis with the ABI.

**RESULTS:** The glottic closure area was significantly lower for ABI compared to paralysis trials. The ABI was stable and the glottic closure of the larynges remained the same after being followed up for 1.5 years.

**CONCLUSIONS:** Effective vocal fold medialization was observed with ABI in this preliminary porcine larynges. The ABI offers the potential for a minimally invasive insertion in addition to postoperative adjustability. Further studies in humans are warranted to evaluate clinical utility.

## Paper 2 Laryngology 2

O02-01

### Disease Control and Voice Outcome after KTP Laser for Recurrent Laryngeal Papillomatosis

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#### Introduction:

Recurrent respiratory papilloma (RRP) is caused by human papillomavirus virus (HPV) type 6 and 11. According to the size and the position of the lesion, clinical manifestation may range from dysphonia to airway compromise. Because there is no definite cure for RRP presently; clinical management of RRP mainly relies on repeated surgical debulking with careful preservation of healthy tissue. To date, only a few studies had reported the voice quality after multiple procedures for RRP.

#### Subjects and Methods:

This study retrospectively enrolled 16 patients diagnosed with RRP and treated at a voice clinic of a tertiary teaching hospital from 2013 to 2019. Most of the patients received their first KTP laser surgery in the operation suite to confirm the diagnosis on histopathological examination. In case of recurring lesions, subsequent KTP laser procedures were conducted either in the office or return to OR, depending on the tolerance of the patient, lesion size and location. All the patients were regularly follow-up in the clinic. Disease control was investigated by videolaryngostroboscopic (VLS) exams. Voice outcome was evaluated regularly using 10-item voice handicap index (VHI-10), acoustic, and perceptual analyses of voice quality.

#### Results:

Among these 16 patients (6 women, 10 men; mean age, 38.5 years [range, 23-73 years]), 7 patients received KTP laser once, 5 patients received twice to 5 times, and 4 patients received more than 10 procedures, with a decreasing frequency of procedures over time. Three patients developed anterior commissure web because of bilateral vocal fold involvement. VLS showed mild fibrotic change of vocal folds in 4 patients, without significant dysphonia. VHI-10, CPPs, MPT, and GRB scores all showed statistically significant improvement after KTP laser procedures and maintained stationary even after 12 repeated procedures.

#### Conclusion:

Our experience revealed that KTP laser is a handy tool for managing RRP of the larynx. By peeling of papilloma and preserving lamina propria, KTP laser procedures can effectively control RRP and preserve phonatory function in the meantime. Staged unilateral procedures may help to reduce postoperative sequels in the future.

O02-02

### Application of machine learning for the screening, detection, and classification of voice disorders

Chi-Te Wang, Po-Wen Cheng

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With recent advancements of machine learning technology, many studies had applied different algorithms, e.g. support vector machine (SVM) and Gaussian mixture model (GMM), to detect abnormal voice samples. Our research group started to use modern deep neural networks (DNN) in the task of automatic differentiation between normal and abnormal voice samples since 2016. We extracted mel frequency cepstrum coefficients from 3-seconds of voice samples of continuous vowel “ah”. The experimental results demonstrated that DNN outperforms SVM and GMM. Its accuracy in detecting voice pathologies reached 94.26% and 90.52% in male and female subjects. When applied to the MEEI voice disorder database for validation, DNN also achieved a higher accuracy (99.32%) than previous literatures.

We subsequently proceeded to the automatic classification of voice disorders into different distinct categories, which had never been published before. Because different vocal lesions might present with similar voice qualities, we alternatively use demographics and symptomatic features to classify three common type of voice disorders, e.g. phonotraumatic lesion, vocal palsy, and glottic neoplasm. Decision tree analyses revealed that sex, age, smoking status, sudden onset of dysphonia, and 10-item voice handicap index scores were significant characteristics for classification. When combining these demographic and symptomatic variables, artificial neural network achieved the highest accuracy of  $83 \pm 1.58\%$ .

Recently, we investigated whether acoustic signals and medical records can be combined for better prediction and classification of voice disorders. We developed a multi-modal approach, using two stage DNN structure to handle complex data in sequence. The overall accuracy achieved  $87.26 \pm 2.23\%$ . Our works may be applied in the future for the early detection of voice changes, for dysphonic patients without a readily access to medical facilities, and for patients presenting with recurring symptoms after previous treatments.



O02-03

## Morphometric Analysis of Larynx under Computerized Tomography Image

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Morphometrics of larynx are very essential for surgeons planning to perform laryngeal framework surgery and affected surgical landmarks. Computerized tomography (CT) scan is a common tool for surgeons to evaluate anatomy and structure of larynx before surgery such as thyroplasty. There were studies comparing morphometrics of larynx between different ethnics, gender and age. Distinct differences were reported in different gender and ethnics. We studied CT scan from human laryngeal cadavers from Medical University of Vienna, and obtained CT images of neck from patients in Taiwan. Osiri X MD computer software was used to analyze CT-Scan images and measurements of human larynx. Length of thyroid lamina, width of laryngeal box, the angle at which thyroid lamina from both sides converge at the midline were obtained under analysis of the software. The result can be used for developing new thyroplasty device in future.

O02-04

## Continuous and Simultaneous Evaluation of Glottal Contact and Expiratory Effort during Phonation Using Electroglottography and Manometry

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**Introduction** Excessive use of loud voice has been considered to lead to the onset of both organic and functional voice disorders. The prerequisite for loud voice production is an increase in subglottic pressure, which is regulated by laryngeal resistance (dependent on the degree of glottic adduction) and/or intra-abdominal/-thoracic pressures (enhanced by contraction of expiratory muscles). Generally, it has been considered that increased laryngeal resistance is hygienically inappropriate, whereas phonation dependent on the contraction of abdominal-muscles is ideal. However, no medical examination has been able to judge whether loud voice production depends on these two factors. The aim of the present study was to develop a method to monitor the degrees of glottal contact and expiratory effort during phonation continuously using electroglottography (EGG) and manometry.

**Materials and methods** Each participant were inserted the probe of a 4ch manometer via the nasal cavity so as to place the 4 pressure sensors at the intra-stomach, intra-thoracic/cervical esophagus and hypopharynx. The EGG electrodes and an accelerometer as a contact microphone (CM) were attached on the neck surface skin. He/she was asked to increase the vocal loudness gradually during phonation of a sustained vowel /e:/ or production of a hum /m:/, while the four-site pressures, EGG signals and CM signals were simultaneously recorded. The contact quotient (CQ) of the EGG signals and acoustic energy of the CM signals were calculated. The time-dependent changes of these measures/parameters were compared between the tasks.

**Results** Both of intra-gastric/intra-thoracic-esophageal pressures and the CQ values showed an increasing tendency with an increase in the acoustic energy during both two tasks. The gradual loudness increase during humming production showed a greater increase in both intra-gastric and intra-thoracic-esophageal pressures and a lesser increase in the CQ value than that during normal vowel phonation.

**Conclusion** We have succeeded in continuous and simultaneous monitoring of the changes in the laryngeal and respiratory dynamics during a gradual increase in vocal loudness. In addition, the present results demonstrate that humming can help alleviate the increase in the degree of glottal contact and facilitate hygienic loud voice phonation dependent on expiratory effort.

## Paper 3 Others

O03-01

## Comparison of the Response for Aspiration Injury Evoked by Two Type of Jelly Products; In Vivo Animal Study

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### 【Background】

Aspiration pneumonia, caused by aspirated materials, including food and/or oral bacteria, is an important etiology for serious illness and death. So far, several therapeutic interventions have been developed and performed for patients with aspiration pneumonia.

The modified texture of foods is an effective intervention for the patients. Specifically, jelly products can be safely ingested orally and adopted for evaluating patients' swallowing ability before the determination of rehabilitation programs.

Today, many commercial jelly-type food products are being developed for patients with dysphagia. These products each contain varying ingredients and nutritional values. It is possible that the inflammatory response varies upon aspiration of each jelly product, but these details remain unclear.

### 【Objective】

This study aimed to determine differences in the elicited injury response after aspiration of varying jelly products.

### 【Method】

Two jelly products were used for this study (Isocal jelly KURIN™ and Isocal jelly HC™; Nestle Japan Ltd., Japan). Ten Sprague-Dawley rats were enrolled and randomly divided into two groups (KURIN group n=5, HC group n=5).

Intratracheal injections with two different jelly products were performed. The lungs were harvested 24 hours post-injection.

Sections of the left lung were stained with hematoxylin-eosin and used to perform a pathological evaluation for each group. The average of Acute Lung Injury (ALI) score for each group was recorded and compared.

Statistical analysis was performed using a *t*-test, and a value of *p* < 0.05 was considered as a statistically significant difference.

### 【Result】

The average ALI score of the HC group was statistically higher than that of the KURIN group (*p* < 0.05).

At 24 hours post-aspiration injury, Isocal jelly HC (containing carbohydrate, protein, and fat) injured the lungs more severely than Isocal jelly KURIN™ (containing carbohydrate only).

### 【Conclusion】

The jelly product consisting of carbohydrate, protein, and fat exerted greater pulmonary toxicity than that of carbohydrate only. The result of this study should be taken into consideration in the management of food modification against patients with dysphagia.

O03-02

## Locating Lingual Artery with Intraoperative Ultrasound for Safety in Performing Transoral Robotic Surgery for Obstructive Sleep Apnea

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**Background:** Injury of lingual artery (LA) is a devastating complication during transoral tongue base resection. Our study aimed to investigate the feasibility of using intraoperative ultrasound imaging to accurately locate the position of LA when performing tongue base reduction in obstructive sleep apnea (OSA) operation with transoral robotic surgery (TORS).

**Methods:** Adult obstructive sleep apnea (OSA) patients who received TORS for base of tongue (BOT) resection were recruited in this study. All patients received pre-operative over-night hospital polysomnography (PSG) examination and anatomy-based Friedman Staging. During TORS procedure, intraoral ultrasound imaging was utilized to locate the accurate position, and to measure the anatomic parameters of LA within BOT, which included horizontal distance to midline, depth to mucosal surface and the diameter of LA.

**Results:** From November 2016 to September 2018, 66 OSA patients (56 male, 84.8%) were included. The mean age was 42.4±9.9 years old, with their mean body mass index (BMI) being 29.0±4.5 kg/m<sup>2</sup>. Average apnea hypopnea index (AHI) was 57.2±20.6 events/hour. There were 41 (62.1%) patients in Friedman stages I and II. The position of lingual artery was successfully detected intraoperatively in all patients (100.0%). The average horizontal distance of LA to midline was 16.5±2.8 mm. The average depth of LA to mucosal surface was 5.4±2.1 mm. The average diameter of LA was 2.9±0.7 mm. BMI (*p*=0.012), AHI-REM (Apnea-Hypopnea Index during Rapid Eye Movement sleep) (*p* < 0.001), tonsil size (*p*=0.002) and Friedman tongue position (*p*=0.036) were found to be significantly correlated with the depth of LA. Postoperative bleeding occurred in 4 patients (6.1%). But none of these patients had bleeding related to LA injury (3 at tonsillar fossa, 1 at surface of tongue base).

**Conclusion:** Intraoperative ultrasound can accurately locate the position of lingual artery when performing tongue base reduction in OSA surgery with TORS. The catastrophic injury of lingual artery can thus be minimized.

**Keywords:** obstructive sleep apnea, intraoperative ultrasound, transoral robotic surgery (TORS), tongue base reduction, lingual artery (LA).

O03-03

## Suppression of CD82 reduces resistance to cisplatin and paclitaxel in 3D culture model of head and neck cancer cell

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Micro cell aggregates including circulating tumor cell cluster (CTC cluster) or micro metastases of head and neck squamous cell carcinoma putatively cause later recurrence or metastasis. Induction chemotherapy has not been reported to reduce later distant metastasis in spite of its intensity, suggesting that micro cell aggregates have resistance to chemotherapeutic agents. In this study, cancer spheroids (multicellular tumor spheroid, MCTS) were obtained from human oropharyngeal cancer cell line, T3M-1 through 3D culture to analyze resistance against chemoradiotherapy in an *in vitro* model of micro cancer cell aggregates. Observations demonstrated that T3M-1 MCTS have significant resistance to cisplatin, paclitaxel, and radiation. The monolayer cell line T3M-1SMO was established with single cells separated from T3M-1 MCTS. T3M-1SMO was proven to lose resistance, suggesting that resistance of the MCTS is not irreversible. PCR array analysis demonstrated that expression of CD82 was increased in MCTS compared to monolayer T3M-1. Real-time PCR confirmed that the expression of CD82 was increased only in MCTS: not in T3M-1SMO cells. Suppression of CD82 by RNAi reduced resistance of MCTS against cisplatin and paclitaxel. CD82 is a feasible target to overcome chemoresistance of micro cancer cell aggregates including CTC cluster or micro metastasis. Induction chemotherapy with CD82 suppression can be a novel strategy to repress later metastasis in head and neck cancers.

O03-04

## A case of fibrous dysplasia of clivus

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Fibrous dysplasia is a benign process in which medullary bone is replaced by fibro-osseous tissue. Most cases are asymptomatic and can be managed conservatively through observation rather than active treatment. Patients with intracranial fibrous dysplasia however may report symptoms of cranial nerves compression, and in such cases decompressive surgery is often preferred.

In this report we describe the case of a 27 year-old male who presented with facial paresis and dysgeusia. He scored 18/40 on the Yanagihara Facial Nerve Grading System (i.e. moderate impairment). Suspecting facial nerve paresis, he was initially managed conservatively however CT scanning later revealed hypertrophy of the clivus. Gadolinium contrast-enhanced MRI (T1 weighted) images further characterized the hyper-intense mass, demonstrating homogenous enhancement. The patient subsequently underwent endoscopic sinus surgery via trans-sphenoidal approach, and biopsies were taken. Pathology confirmed his diagnosis as clival fibrous dysplasia.

Fibrous dysplasia generally affects younger populations, with new cases rare post-puberty. It can be classed as monostotic (70-80% of cases, as was that of our gentleman), polyostotic (15-20% of cases) or McCune-Albright syndrome (3% of cases), the latter a polyostotic form with associated endocrine manifestations. Often asymptomatic and found incidentally through cranial imaging, the condition is mostly benign, but rarely malignant cases are reported thus observation and routine monitoring is advised.

## Paper 4 Otolology 1

O04-01

**Morphological changes of otolith in estrogen deficiency mice by  $\mu$ CT.**

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Benign paroxysmal positional vertigo (BPPV) is one of the most common peripheral vestibular diseases. BPPV can occur in all age groups and both sex, however, the prevalence of BPPV is common in middle-aged and elderly female. In addition, it is reported that the occurrence and/or recurrence of BPPV is associated with osteopenia/osteoporosis. Therefore, it is suggested that peri-menopause condition which causes the deterioration of serum level of estrogen leads the disturbance of calcium metabolism and may induce the changes of otolith organs. In animal stude, it is reported that bilateral ovariectomy (OVX), which causes the deterioration of estrogen, leads to the morphological changes of otoconia. Honda et al reported that otoconial layer could be visualized using micro computed tomography ( $\mu$ CT) with minimal artifacts, however, it is unknown whether  $\mu$ CT is useful to detect the morphological changes of otoconial layer after OVX. Therefore, we investigated the morphological changes of otoconial layer after bilateral OVX and whether  $\mu$ CT is useful for evaluating the changes of otoconial layer after OVX.

Female C57BL/6J (C57) mice were used in this study. Bilateral OVX was performed at 8 weeks of ages. Sham operated mice were used as control. The animals were sacrificed for radiological and histological study at 2, 4, and 8 weeks after OVX. The volume of utricle otoconial layer was measured from the histological serial sections and  $\mu$ CT scan images.

The volume of utricle otoconial layers in OVX group was increased 4 weeks after OVX, and there was significantly differences between that in OVX group and that in sham group at 4 weeks after OVX. The results from  $\mu$ CT scan images were similar to the results from histological study.

This study suggested that the volume of the utricular otoconial layer increased 4 weeks after OVX, and that the changes of the otoconial layer could be detected using  $\mu$ CT.

O04-02

**Systematic quantification of the anion transport function of pendrin and its disease-associated variants**Koichiro Wasano<sup>1</sup>, Takashi Kojima<sup>2</sup>, Tatsuo Matsunaga<sup>1</sup>, Kazuaki Homma<sup>2</sup>, Kaoru Ogawa<sup>3</sup><sup>1</sup>National Hospital Organization Tokyo Medical Center,<sup>2</sup>Northwestern University, <sup>3</sup>Keio University School of Medicine, Japan

**Background:** Thanks to the advent of rapid DNA sequencing technology and its prevalence, many disease-associated genetic variants are rapidly identified in many genes from patient samples. However, the subsequent effort to experimentally validate and define their pathological roles is extremely slow. Consequently, the pathogenicity of most disease-associated genetic variants is solely speculated in silico, which is no longer deemed compelling. We established a systematic experimental approach to efficiently quantify the pathogenic effects of disease-associated genetic variants with a focus on *SLC26A4*, which encodes an anion transporter, pendrin, essential for normal development and maintenance of the inner ear. Alterations of this gene are associated with both syndromic and nonsyndromic hereditary hearing loss with various severity.

**Methods:** We established stable cell lines that express pendrin missense variants in a doxycycline-dependent manner, and systematically determined their anion transport activities with high accuracy in a 96-well plate format using a high throughput plate reader. We also performed *in vitro* splicing assay to examine whether exonic single nucleotide variants affects pre-mRNA splicing.

**Results:** Our doxycycline dosage-dependent transport assay objectively distinguishes missense variants that indeed impair the function of pendrin from those that do not (functional variants). We also found that some of these putative missense variants disrupt normal mRNA splicing.

**Conclusions:** We rigorously quantified the functional consequences of 51 disease-associated missense variants found in the pendrin gene, which is the key to understanding the pathology underlying the large phenotypic spectrum of pendrin-associated hereditary hearing loss.

O04-03

## Hearing Impairment in Xeroderma Pigmentosum: Clinical characteristics and animal model

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Xeroderma pigmentosum (XP) is an autosomal recessive hereditary disease characterized by increased susceptibility to freckle-like pigmentation and skin cancers at sun-exposed body sites. Furthermore, some patients display neurological manifestations, including hearing impairment. There are eight subtypes of XP: XP-A-XP-G and XP variant. XP occurs at a higher frequency in Japan (1:22,000) than in the United States (1:250,000). Approximately 50% of all Japanese patients with XP are assigned to the XP-A, and most patients with XP-A exhibit severe neurological manifestations.

While its pathogenesis of skin symptoms have been well-studied, that of neurological symptoms, including sensorineural hearing loss (SNHL) remains unknown. In a recent temporal bone study of XP-A patients, diffuse and severe atrophy of the organ of Corti and SGNs was evident.

We have conducted a study to characterize the mechanisms of neurological dysfunction and hearing impairment in patients with XP through evaluation of hearing loss in *Xpa*-deficient mice. We found that these mice exhibited SNHL, with significantly higher hearing thresholds at frequencies of 4, 8, and 16 kHz, relative to those in wild type (WT) mice. We also observed lower numbers of SGNs in these mice, providing important insights into the pathogenesis of SNHL in patients with XP-A.

O04-04

## Nestin may be a candidate for regeneration of cochlear hair cells in the mouse organ of Corti

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Sensorineural hearing loss (SNHL) is mostly due to loss of cochlear hair cells, and has a highly negative impact on living in human. Regenerative approach is necessary for fundamental treatment for SNHL because lost hair cells never regenerate in adult in mammals.

Nestin, type VI intermediate filament, is thought to be a neural stem cell marker in the central nervous system, and recently some reports have shown that Nestin expresses in the organ of Corti and auditory neuron in mice. However, the role of Nestin in the cochlea is poorly known so far. Accordingly, we set out to elucidate the role of Nestin in the organ of Corti in mice. Herein, we report normal distribution and expression pattern after hair cell injury of NESTIN protein using Nestin-EGFP transgenic mice.

Nestin-EGFP signal was seen in the cochlear hair cells and supporting cells in the postnatal day 0-1, and gradually downregulated to the inner phalangeal cells and inner boarder cells. Next, inner ear hair cells were selectively ablated with diphtheria toxin administration using double transgenic mice (NESTIN-EGFP X Pou4f3-DTR mice). We found triple (Myo7a, Sox2 and Nestin)-positive cells in the ablated cochlea at early postnatal days, which implies that postnatal Nestin-positive supporting cells can generate new hair cells in the mouse cochlea in a specific condition.

Here we shows possibility of regeneration of cochlear hair cells in Nestin-positive cells in the early postnatal mice.



## Paper 5 Otolology 2

O05-01

**Cryopreservation of human nasal mucosal tissue for fabricating transplantable cell sheet**

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**Introduction.** Epithelial cell sheet made by temperature responsive cell culture dish has been used to regenerate many kinds of tissues in regenerative medicine. We succeeded on fabricating autologous nasal mucosa (NM) cell sheet and transplanting the cell sheet into middle ear cavity after cholesteatoma surgery in 15 cases. However, for cholesteatoma or other middle ear lesion, sometimes stage surgery or second operation is needed. Patient would be burdened by the twice biopsies of NM as a cell source of cell sheet. If we could cryopreserve NM as a living tissue, repeated cell sheet culture would be possible. In this study, we compared the quality of NM cell sheet before and after cryopreservation.

**Methods.** NM tissue was harvested via nasal endoscopy, and primary explant culture was performed with keratinocyte culture medium. The outgrown cells were collected with trypsin and seeded on a temperature-responsive cell culture dish as subculture for cell sheet fabrication. Another group of NM tissue was immersed with cryoprotectant medium STEM-CELLBANKER and kept frozen under -80°C over one week. The frozen tissue was thawed, and same cell sheet culture procedures were performed. Cell number, viability, immunohistology of the cell sheet were analyzed.

**Results.** Epithelial cells outgrew from both fresh and frozen-thawed NM tissue. The frozen-thawed NM tissue possesses comparable ability to be fabricated into cell sheet as fresh ones. Moreover, we confirmed that the immunohistological characteristics of the cell sheet made from frozen-thawed NM tissue such as cytokeratin expression patterns and cell-cell adhesion proteins are without significant differences after cryopreservation.

**Conclusion.** NM tissue can be cryopreserved with this simple method while keeping its proliferative ability and histologic features equivalent to fresh nasal tissue. This study will contribute to further study for middle ear mucosa regeneration with NM cell sheet.

O05-02

**Association of the Quantitative Analysis on 3D-FLAIR MRI and the Hearing Outcome in Patients with Sudden Sensorineural Hearing Loss**

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**Objective:** We evaluated the hearing outcome and signal intensity of the cochlea on 3 Tesla T2-weighted three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging (3D-FLAIR MRI) in patients with sudden sensorineural hearing loss.

**Materials and methods:** A total of 28 patients with sudden sensorineural hearing loss were included in this study. All patients underwent intravenous gadolinium 3D-FLAIR MRI and pure tone audiometry (PTA) at presentation and three months later. MRI was performed with a 3 Tesla scanner using a 32-channel array head coil. The hearing loss was classified into grades 1–4 on PTA at presentation based on the criteria of the Research Committee of the Ministry of Health and Welfare for Acute Profound Deafness in Japan. Using the signal value of the cerebellar hemisphere as a control, we measured the signal intensity ratio (SIR) of the basal and apical turns in the cochlea on 3D-FLAIR MRI. A statistical analysis was performed between SIR and the average hearing levels at low- (125, 250, and 500 Hz) and high-tone frequencies (2, 4, and 8 kHz) in four groups. Patients were mainly treated with oral or intravenous systemic steroid therapy. In cases of insufficient hearing recovery, intratympanic steroid administrations were added. Patients with uncontrolled diabetes or a poor general condition were treated only with intratympanic steroids.

**Results:** There was a significant association between a low hearing improvement rate at high-tone frequencies and increment in SIR of the basal and apical turns on pre-contrast 3D-FLAIR MRI and of the basal turn on post-contrast 3D-FLAIR MRI in patients with grade 3 or 4 hearing loss. There was also a significant association between a low hearing improvement rate at low-tone frequencies and increment in SIR of the apical turn on post-contrast 3D-FLAIR MRI. In patients with grade 1 or 2 hearing loss, there were no associations between the hearing prognosis and SIR on 3D-FLAIR MRI.

**Conclusion:** Several studies have found an association between MRI and sensorineural hearing loss. In this study, MRI was performed with higher sensitivity than earlier, and the high SIR of the basal and apical turns of the cochlea on 3D-FLAIR MRI might reflect a poor hearing prognosis at high- and low-tone frequencies in severe sudden sensorineural hearing loss. It might be possible to quantitatively analyze each turn of the cochlea and predict the hearing outcome on MRI of patients with sudden sensorineural hearing loss in the future.

O05-03

## The difficulty of determining Eustachian tube function using Eustachian tube function tests alone

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Masataka Ogawa<sup>1</sup>, Yasuhiro Hamanoue<sup>1</sup>,  
Shuhei Ono<sup>1</sup>, Tsubasa Mogi<sup>1</sup>, Ryutaro Sakamoto<sup>1</sup>,  
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**[Objective]** When an otological doctor sees a patient who complains of aural fullness and/or voice autophony but without extremely abnormal findings of the tympanic membrane, the doctor may try to rule out Eustachian tube (E-tube) dysfunction. In Japan, doctors can conduct sonotubometry and tubo-tympano-aerodynamic-graphy consisting of four maneuvers; Valsalva maneuver, deep breathing through the nostril, nasal sniffing, and Toynbee's maneuver, i.e., a total of five tests, using one commercially available instrument. However, it seems to be difficult for young doctors to reach the right diagnosis from multiple E-tube function tests. We analyzed how much confusion of diagnosis is created when a doctor judges E-tube function from only a single test without a comprehensive analysis of multiple tests, clinical history, and clinical findings. **[Methods]** Thirty patients with acute sensorineural hearing loss (SNHL) were included in the study. Finally, subjects were 30 ears with acute SNHL and 19 contra-lateral ears. A total of five E-tube tests mentioned above were conducted. Each ear was classified normal-, stenotic-, patulous-, or undeterminable-type at each test. The undeterminable-type means that the test might be conducted incorrectly or that the external auditory pressure waveform was too untypical to determine the exact type of E-tube function. **[Results]** Results of E-tube function tests were not always consistent between those five tests. For example, an ear was diagnosed as normal-type with sonotubometry, as undeterminable-type with Valsalva maneuver, as patulous-type with deep breathing, as normal- or stenotic-type with nasal sniffing, and as normal-type with Toynbee's maneuver. Ears of which test results were consistent between five tests were 9/49 ears (18%), i.e., the concordance rate of results was 18%. An external auditory pressure waveform of Toynbee's maneuver was ambiguous, and then the diagnosis was very subjective. Therefore, we analyzed how much the concordance rate changes after excluding the results of Toynbee's maneuver. The rate became 47%. With Valsalva maneuver, 16/49 ears (33%) were classified as undeterminable-type. When the results of undeterminable-type with Valsalva maneuver were ignored from the analysis of the concordance rate, the concordance rate increased to 69%. **[Conclusion]** We should not forget that E-tube function will not be determined with E-tube tests alone. Comprehensive analysis of clinical information is critical for the exact diagnosis of E-tube dysfunction. There is room for the further development of E-tube tests for detecting the cause of the various and subtle auditory abnormal sensation.

O05-04

## Experience with middle ear implant for unilateral profound conductive hearing loss by meatal atresia

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Vibrant Soundbridge (VSB) is one of active middle ear implant and VSB with RW and OW approach for conductive or mixed hearing loss was approved by Japanese government at 2015. National insurance has been approved at 2016. Indication criteria of VSB is as follows; 1, Implanted ear in the patients with bilateral hearing loss is conductive or mixed hearing loss. 2, Conductive or mixed hearing loss could not be improved by conventional otosurgery and hearing aid. Investigative clinical study for effectiveness of VSB to unilateral conductive or mixed hearing loss was performed at 2019 for 3 patients with unilateral congenital meatal atresia. We could conclude that VSB is effective for improvement of speech discrimination in noise and sound localization in the patients with unilateral conductive hearing loss induced by meatal atresia.

## Paper 6 Otolaryngology 3

O06-01

### Simple Input for the IOOG SAMEO-ATO Framework and the EAONO/JOS System

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The IOOG SAMEO-ATO framework has been proposed as an international classification for tympanomastoid surgery. EAONO / JOS system has also been proposed as an international classification for middle ear cholesteatoma. The challenge now lies in how to spread these two classifications throughout the world for daily clinical use. Database entry should be as easy as possible when the surgeon is exhausted after the surgery. There are two A's and two O's in the SAMEO-ATO framework, which is confusing and hard to remember. In the EAONO-JOS system, the cholesteatoma classification and the STAM system are partially linked, and the staging judgment also changes depending on the complications. To solve this problem, an Excel document has been devised that could complete the input in a few minutes. The option buttons and checkboxes are arranged on the summary figures. It is possible to comply with the above two international classifications simply by selecting them. Staging is an automatic calculation. For instance, Pars tensa cholesteatoma with a check in T and S2 with no complications will be classified as stage II. The calculation can also detect unlogical inputs, such as an error message "why no A? " will be returned if there is no check in A despite selecting Pars flaccida cholesteatoma. Because it is an Excel document, it naturally supports all electronic medical record systems in all facilities in the world. The Excel document creates a string for pasting into electronic medical records. It also helps to paste as multiple cells to the existing databases. Saving the Excel document is another good option.

O06-02

### The development of a safe method of canal wall down technique, using the medical image processing system

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**Objectives:** The purpose of this study is to develop a safe method for ones (to remove the bridge and to lower the facial ridge) of the most dangerous procedures in canal wall down using the medical imaging processing system. The medical image processing system is useful for the evaluation of ear diseases and the planning, education, simulation, and navigation of ear surgery. Here, we introduce a safe method of canal wall down technique using the medical imaging processing system.

**Materials and Methods:** 0.25 mm, 1024 matrix ultra-high resolution CT (Aquilion Precision, Canon Medical Systems, Tokyo, Japan) images of the temporal bone with ear

Three dimensional reconstructive images (3DRIs) of ultra-high resolution temporal bone CT were made using a medical image processing system (Synapse Vincent, Fuji Film, Tokyo, Japan).

**Results:** 3DRIs showed that the lateral wall of the attic (bridge) has two slopes (anterior-inferior and posterior-superior). The deepest point is the anteroinferior point of the bridge, being equivalent of the anterosuperior point of the tympanic ring. One of the safest sequences of resecting the bridge is shown to make a slope parallel to the lateral wall of the attic, subsequently to resect the bridge as anteriorly as possible, and finally to remove the bridge by cutting the overhanging bone from anterior. In advancing the resection of the bridge, the posterior buttress is clearly formed and develops into the facial ridge and the posterior wall of the external auditory canal as the facial recess is opened. Lowering the facial ridge sometimes causes damages to the facial nerve and the lateral semicircular canal. 3DRIs showed that the second genu of the facial nerve is located most laterally in the temporal bone and the lateral semicircular canal is located in the posterior superior part of the facial ridge. The facial ridge also has a curved longitudinal axis and the transversal axis. 3DRIs showed that one of the safest ways of lowering the facial ridge is to remove the overhanging bone of the ridge at the extension of resection of the bridge after identifying the horizontal segment of the facial nerve as a landmark. The posterior ligament of the incus is attached to bone protruding from the horizontal segment of the facial nerve canal. This should be taken into consideration in lowering the facial ridge.

**Conclusions:** The medical imaging processing system is a useful tool to develop a novel canal wall down technique.

006-03

## Tympanoplasties based on assessments of middle ear aeration by staged surgery in treatment of cholesteatomas

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**Objective:** Given unclear middle ear aeration function, recurrent cholesteatoma may be encountered when optimal reconstruction is not performed. Thus, we have selected a reconstructive procedure of second surgery based on the grade of middle ear aeration or the condition of reconstructed external auditory canal during second surgery.

**Methods:** From 1995 to 2011, 155 ears undergoing our modified staged canal wall up tympanoplasty (CWUT), were included in our study. In the first-stage operation, the tympanic scutum defect was closed with bone pate via initial scutum plasty. The defective mastoid cortex was reconstructed by mastoid cortex plasty (MCP). In the second-stage operation, one of three reconstructive procedures was selected; MCP with second scutum plasty using a sliced cartilage for well aerated ears (MCP group), bony mastoid obliteration (BOT) with the second scutum plasty for poorly aerated ears (BOT group) or canal wall down tympanoplasty (CWDT), in which a large sliced cartilage was used for myringoplasty and a smaller tympanic cavity than that afforded by CWDT was reconstructed, for ears in which the reconstruction was absorbed or deteriorated (CWD group).

**Results:** The modified staged CWUT was completed in 145 of these ears (94%) ; 74 ears in the MCP group, 71 ears in the BOT group, and 10 ears in the CWDT group. In Kaplan–Meier survival analysis, recurrence rates for ears with deep retraction pocket formation were 0% for MCP group after 10 years, 5.0% after 5 years, and 9.5% after 10 years for BOT group, 0% for CWD group after 10 years

**Discussion:** For well aerated ears, only MCP was enough to prevent the formation of a deep retraction pocket because deep retraction pockets formed by soft tissue ingrowths were evident in our previous study before MCP. In addition, BOT may exclude possibility of a better hearing outcome in which the patients' middle ear aeration function is maintained. For poorly aerated ears, BOT is both necessary and sufficient; however, BOT is unnecessary for well aerated ears, and unsatisfactory for very poorly aerated ears. For very poorly aerated ears, a large, sliced-cartilage graft can be useful to reconstruct an eardrum with a smooth surface and no gaps. Additionally, the reconstructed tympanic cavity was thought to be small enough to prevent the recurrence.

**Conclusion:** The staging was meaningful and beneficial for selecting appropriate surgical procedures and ruling out very poorly aerated ears which are not cured by CWUT.

006-04

## Meatotympanoplasty for external auditory canal stenosis and lateralized tympanic membrane

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**Objectives:** The aim of the present study was to evaluate the postoperative hearing levels and other outcomes of 10 cases with external auditory canal stenosis (EACS) and lateralized tympanic membrane (LTM).

**Materials and Methods:** This was a retrospective case review of patients with EACS and LTM who underwent meatotympanoplasty from 2008 to 2018. Their mean age at surgery was 31.6 years. The surgeries were performed taking into consideration the following: 1) creating a large EAC and functioning tympanic membrane (TM); and 2) avoiding complete mastoidectomy to prevent postoperative cavity problems.

**Main outcome measures:** 1) Changes in air-bone gaps (ABGs); 2) changes in air conduction (AC) and bone conduction (BC); and 3) postoperative complications

**Results:** Ten cases were treated with unilateral EACS and LTM. Their mean follow-up period was 3 years 10 months. The average preoperative and postoperative ABGs were 40.4 dB and 23.0 dB, respectively, and there was a significant difference. A postoperative ABG less than 30 dB was achieved in 80% (8/10) of patients. Four cases had postoperative complications (re-stenosis of the EAC and/or re-lateralization of the TM). Re-operations were performed in two cases, and they have shown good outcomes so far.

**Conclusion:** These results indicated that our surgical procedure was a useful technique for EACS and LTM. However, further development is needed to prevent re-lateralization of the TM after surgery.



## Paper 7 Head and Neck 1

O07-01

### Indications and Surgical Outcomes of Enucleation for Benign Parotid Tumors

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**BACKGROUNDS:** Benign parotid tumors including Warthin tumor (WT) and pleomorphic adenoma (PA) has been conventionally treated with partial parotidectomy. Partial parotidectomy involves the resection of parotid tissue with exposure of the facial nerve, which may cause facial nerve injury and the loss of parotid function compared with enucleation of the tumor. Based on characteristics of WT with multifocal pattern and the low rate of malignant transformation, the indications for enucleation in our institution needed the preoperative cytological diagnosis of WT. In the diagnosis of benign parotid tumors or cysts excluding PA, the clinical features of tumors were also considered for the indications for enucleation, such as the tumor mobility and softness, the tumor location in the tail of the parotid gland, and solid or simply cystic images on CT or MRI.

**MATERIALS AND METHODS:** Patients with the parotid gland tumor who underwent both preoperative fine needle aspiration cytology (FNAC) and surgical resection were included in this study. Among a total of patients, 117 receiving enucleation for benign parotid tumors were enrolled to verify indications of enucleation for benign parotid tumors; 146 with the definitive histology of WT were enrolled to compare surgical outcomes between enucleation and partial parotidectomy.

**RESULTS:** Among 117 patients receiving enucleation, the preoperative diagnosis of WT with FNAC was observed in 98 patients, among whom 96 had the definitive histology of WT. Thus, the accuracy of cytological typing for WT was 98.0%. The preoperative cytological diagnosis of others without WT was observed in 19 patients, among whom 16 had the definitive histology of WT. Among 117 patients receiving enucleation, 112 had the definitive histology of WT and the remaining 5 had other definitive histology excluding PA or malignant tumors. The incidence rates of postoperative temporary facial nerve palsy, numbness around the earlobe and salivary fistula were significantly lower in 112 patients treated with enucleation than in 34 with partial parotidectomy. The operative time and blood loss were also significantly decreased.

**CONCLUSION:** Indications of enucleation for benign parotid tumors in our institution were successfully validated and surgical outcomes of enucleation were superior to those of partial parotidectomy. Considering the high accuracy of cytological typing for WT, enucleation is encouraged for treatment of the parotid gland tumor in cases with the preoperative cytological diagnosis of WT.

O07-02

### Effective preoperative embolization of the feeding arteries just before carotid body tumor resection

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Carotid body tumor (CBT) is a rare tumor derived from carotid body paraganglion cells. It is well known that this tumor has a rich vascular network in its contents and capsules supplied by many feeding arteries. When head and neck surgeons intend to resect this tumor, they sometimes experience much blood loss or injuries of carotid arteries' wall. In some cases reconstruction surgeries are required to repair or replace the damage of carotid arteries. To save blood loss during surgery of CBT, preoperative embolization of the feeding arteries is sometimes carried out. However, this procedure has been controversial about its effectiveness for the surgery so far.

We planned to try embolization of the feeding arteries just before surgery and performed the surgery at the same day.

From March 2013 to August 2019, 16 patients with CBT were referred to our hospital and 17 CBT were resected. They were 9 female and 7 male patients and their mean age was 46.3 years old ranging from 20 to 62 years old. Four patients had family history of paragangliomas. The patients underwent embolization of the feeding arteries under local anesthesia in the morning. They underwent resection of the tumor under general anesthesia just after the embolization of the feeding arteries in the afternoon of the day. The average time of surgery was 158 min. and the average blood loss was 35.8 ml. When the two patients who underwent resection and reconstruction of carotid arteries were omitted, the average time of surgery and the average blood loss were 126 min. and 8.5ml, respectively. The tumor volume after embolization was markedly reduced and the mean reduction rate was approximately 50%. Complications of surgery in our series of patients were first bite syndrome in 3 patients, recurrent nerve palsy in 5, glossopharyngeal nerve palsy in 1, hypoglossal nerve palsy in 4 and Horner syndrome in 2 and they were recovered within several months after surgery.

Our "same-day procedure" resulted in obvious reduction of blood loss and operation time. We concluded that this method is superior to other procedures for the safety of CBT surgery.



O07-03

## Transoral laser microsurgery in the management of T3 glottic cancer- Experience of Taipei Veterans General Hospital

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### Purpose

In tradition, total laryngectomy with or without postoperative concurrent chemoradiation was the main treatment modality for advanced glottis cancer, though it could not preserve the larynx and had a severe impact on the patient's quality of life. Over the years, as the concept of organ preservation was becoming more prevalent, concurrent chemoradiation was becoming more frequent application in advanced glottic cancer with adverse effects of prolonged duration of therapy, radiation effects, and sometimes it could not completely preserve the throat function. Transoral laser microsurgery (TLM) had used to treat the early stage glottis cancer. With advancement of treatment concepts and the accumulation of experience, we tried to use this treatment modality on T3 glottic cancer and hope to achieve the goals of tumor control and organ preservation. This study was focused on analyzing of the oncologic and functional results in patients with T3 glottic cancer treated with TLM.

### Methods

From 2006 to 2018, we evaluated the effect on tumor control and larynx preservation in patients with stage T3 glottic squamous cell carcinomas underwent TLM in our department. Patients who received treatment previously, or who did not have histologically confirmed SCC were excluded from data analysis.

### Results

Fifty patients who underwent TLM were included. The patients were predominantly male (48 male, 2 female) with median age of 63 years (range, 42 to 89 years). 1 patient underwent modified type III cordectomy, 5 underwent type IV cordectomy, 36 underwent type V cordectomy, and 9 underwent type VI cordectomy. There were no postoperative complications such as bleeding or aspiration pneumonia, only one case (2%) of subcutaneous emphysema. Twenty-two patients (44%) received postoperative radiotherapy. With a median follow-up of 46 months for all patients, 13 patients (26%) were found tumor recurrence, including 11 local recurrence (22%), and 2 neck recurrence (4%). After salvage surgery, 6 of them could preserve larynx and lived without disease. The overall laryngeal preservation rate was 86% (43/50). The five-year overall and disease-specific survival rates were 92% and 86%, respectively.

### Conclusion

Among patient with T3 glottic SCC, TLM was one of treatment modality for organ preservation other than concomitant chemoradiation, with advantage of less amount of blood loss intraoperatively, reduced postoperative complications, and shorter recovery time. If we could selective T3 cases properly, it could lead to good local control rate and laryngeal preservation rate.

O07-04

## Systematic review and meta-analysis of the complications of salvage total laryngectomy

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**BACKGROUND AND OBJECTIVES:** Management paradigms in laryngeal cancer have shifted to "organ preservation" chemoradiotherapy protocols. In the event of treatment failure, salvage total laryngectomy remains the only curative treatment option. However a comprehensive review of the complications of this procedure has not been reported.

**METHODS:** A systematic review of the literature was performed using keywords "salvage laryngectomy" to retrieve relevant publications between January 2000 and August 2015.

**RESULTS:** Of the 407 articles retrieved from the literature search, 50 studies encompassing 3292 patients were included. Forty-nine studies reported pharyngocutaneous fistula which occurred in 859 patients (pooled incidence 28.9%; 95% confidence intervals 25.5-32.5%). Twenty-four studies reported complications in addition to PCF and these included wound complications (infection, dehiscence and necrosis), dysphagia, bleeding, and pharyngeal and stomal stenosis.

**CONCLUSIONS:** Overall complication rate was 67.5%, Pharyngocutaneous fistula was the commonest complication with a pooled incidence of 28.9%.

## Paper 8 Head and Neck 2

O08-01

### Improvement of cervical retrieved lymph node number during neck dissection in oral cancer patient

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#### Background

Previously, several lymph node (LN) feature, such as number of positive LN, LN yield, and log odds of positive LN (LODDS) had been explored for prognostic significance in oral cancer. LODDS outperformed other features in several studies. However, the index of neck dissection quality remained unanswered. Recently, LN yield was one of most acceptable indices for the quality of neck dissection.

This study was aim to explore the different strategy to improve LN yield in oral cancer surgery.

#### Materials and methods

Using the cancer registry data in our hospital, newly diagnosed oral cancer treated with primary tumor resection and neck dissection between 2007-2019 Jun were included. In our institute, a check list was introduced between 2015 Oct-2018 Sep to remind healthcare providers of LN yield when neck dissection was performed. Since 2018 Oct, a dashboard system has been applied to ensure enough LN yield. Main outcomes included adequate neck dissection rate, LN yield, positive LN number and log odds of positive lymph nodes (LODDS).

#### Results

Between 2007 and 2019 Jun, 333 oral cancer patients were included. The mean age was 55±11 years, and 89.7% were male. The adequate neck dissection rate increased over time from 79.4% to 100% ( $p < 0.001$ ). The mean LN yield increased from 22±13 to 39±13 ( $p < 0.001$ ). LODDS decreased from -1.3±0.5 to -1.7±0.4 ( $p < 0.001$ ).

#### Conclusions

LN yield can be used as a quality index for neck dissection. Use of a checklist and dashboard-based strategy may improve the LN yield.

O08-02

### The prognostic value of pretreatment C-reactive protein-to-albumin ratio in oral cavity cancer

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**Purpose:** Although previous studies demonstrated that elevated C-reactive protein to albumin ratio (CAR) predicted poor prognosis in various tumors, little was known about the prognostic value of CAR in patients with oral cavity squamous cell carcinoma (OSCC). The present study was designed to retrospectively evaluate the prognostic value of the C-reactive protein/albumin (CRP/albumin) ratio in OSCC.

**Methods:** Three hundred and twenty-six newly diagnosed OSCC patients admitted between May 2013 and October 2017 were retrospectively reviewed. Their serum CRP and albumin levels were quantified preoperatively. The relationship between the CRP/albumin ratio and the clinicopathologic features was analyzed. Receiver operating characteristic curve was used to calculate the prognostic value of the CRP/albumin ratio. Then, the Cox proportional hazards model was used in univariate and multivariate analyses to identify significant prognostic factors associated with overall survival and disease-free survival.

**Results:** The cutoff value for CRP/ALB ratio was 0.195. An elevated CRP/ALB ratio was significantly associated with nodal metastasis with extra-nodal extension, advanced T classification, tumor depth more than 10mm, need adjuvant therapy, and less survival months. High values of CRP/albumin ratio were also significant predictors for poor overall survival and disease-free survival on multivariate analysis.

**Conclusion:** Pretreatment CRP/albumin ratio may have significant prognostic value in patients with OSCC.

O08-03

## Surgery for Oral Cancer with Infratemporal Fossa Invasion

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**Introduction:** The infratemporal fossa is an anatomical location which consisted of 1. bony landmarks: maxilla tuberosity, coronoid process of mandible, medial and lateral pterygoid plates, 2. four masticator muscles: masseter, medial pterygoid, lateral pterygoid, temporalis muscle, 3. blood vessels: pterygoid venous plexus, internal maxillary artery, 4. V3 mandibular nerve. Surgery of infratemporal fossa is technique-challenging for head neck surgeon. The aim of this study is to collect patients who received surgery for oral cancer with infratemporal fossa invasion in our department.

**Method:** Patients who diagnosed with oral cancer with infratemporal fossa invasion between 2011 and 2019 and received surgery in Tri-Service General Hospital were included. Both primary and recurrent oral cancer were included. Only masseter muscle involvement or initial oropharynx cancer with recurrence over infratemporal fossa were excluded. The age, type of surgery, flap choices, complications, disease status were analysed.

**Result:** 20 patients who received surgery for oral cancer with infratemporal fossa invasion were included. 10 were primary cancer and 10 were recurrent cancer. All patients were male with mean age 55.1 (43-72). The surgery included composite resection or segmental/marginal mandibulectomy or total/partial maxillectomy. The flap choices were: anterolateral thigh flap 11, pectoralis major myocutaneous flap 10, rectus abdominis myocutaneous flap 2, submental island flap 1. Major surgical complications included: total loss of flap 2, partial loss of flap 3, flap dehiscence 1. Disease status were: alive/no evidence of disease 7, alive with disease 2, die of disease 10, die of other cause 1.

**Conclusion:** Surgery for oral cancer with infratemporal fossa invasion is feasible with acceptable surgery risks. Care should be taken to avoid injury of vital structures, especially the internal carotid artery.

O08-04

## Factors affecting conversation and swallowing function following tumor resection and reconstruction in patients with tongue cancer

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### <Introduction>

In the resection of tongue cancer and subsequent reconstruction, the preservation of the postoperative function of the upper aerodigestive tract has been considered to affect the quality of life. In the present study, we attempted to assess the degrees of conversation and swallowing function and identify factors associated with the incidence of disturbance of these function after radical surgery and reconstruction in patients with tongue cancer.

### <Patients and methods>

62 patients with tongue cancer were enrolled (median age: 59, range: 16-88). Conversational function was evaluated according to Conversation score (CS) of Clinical practice guideline for Head and Neck Cancer of the Japan Society for Head and Neck Cancer. Swallowing function was evaluated using the Method of intake, Time of intake, and Food score (MTFS), and Functional Outcome Swallowing Scale (FOSS).

### <Results>

The median of the CS, MTFS and FOSS was 9, 12, and 1, respectively. In 53 (86%) of the 62 patients, the CS was more than 8 (compatible with Excellent), and only one (2%) showed 4 of the CS reflecting poor social language activity. We divided the patients into two groups; the younger group (< 65 years of age, 42 patients) and the older group (≥65 years of age, 20 patients). The proportion of patients showing more than 8 of the CS in the younger and older groups was respectively 93% and 70%, with a significant difference (p=0.01). Patients who were resected more than 50% of the tongue showed a significant CS decrease compared with those who were resected no more than 50% (p=0.01). With regard to the MTFS and FOSS, in the younger group, 79% were scored no less than 12 of the MTFS and 67% showed 1 or less of the FOSS. In the older group, 30% showed no less than 12 of the MTFS and 35% exhibited 1 or less in FOSS score. The comparison between the two group showed significant differences (MTFS: p<0.01, FOSS: p=0.04). Patients who were resected more than 50% of the base of tongue showed a significant FOSS decrease compared with those who were resected no more than 50% (p=0.04). However, the performance of postoperative radiation therapy affected none of the scores.

### <Conclusion>

These results demonstrate that conversation and swallowing function after complete resection of tongue cancer followed by reconstruction are affected by patients' age and the extent of resection.

## Paper 9 Head and Neck 3

009-01

### Real-world outcomes and prognostic factors in patients receiving nivolumab therapy for recurrent or metastatic head and neck carcinoma

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**Background:** Recently, a global phase III study demonstrated that nivolumab remarkably improved patient outcomes in recurrent or metastatic head and neck carcinoma (RMHNC). However, the efficacy of nivolumab in patients who are ineligible for clinical trials is unknown. We investigated nivolumab efficacy in real-world patients and prognostic factors associated with the response to nivolumab.

**Methods:** This study was conducted in 11 institutes associated with the Kyoto University and its Affiliated Hospitals - Head and Neck Oncology Group. A total of 95 patients with RMHNC who received nivolumab between May 2017 and May 2018 were retrospectively reviewed. Objective response rate (ORR), overall survival, and progression-free survival (PFS) were evaluated. Univariate and multivariate analyses were performed to identify prognostic factors.

**Results:** The ORRs in patients with squamous cell carcinoma (SCC) and non-SCC were 17.9% and 0%, respectively. In patients with SCC and non-SCC, the 1-year PFS rates were 28.0% and 10.0%, respectively. The hazard ratio (HR) for risk of PFS events (SCC vs. non-SCC) was 2.17 (95% CI: 1.17–4.03; log-rank  $p=0.01$ ). Univariate and multivariate analyses revealed radiotherapy history, platinum-refractory carcinoma, and treatment-related adverse events (TRAEs) as important prognostic factors associated with PFS in patients with SCC.

**Conclusion:** In a real-world setting, non-SCC and platinum-refractory carcinoma were associated with a poorer prognosis, and history of radiotherapy to the primary site and TRAEs were associated with a better prognosis. These findings could be useful for clinicians and patients when selecting a treatment strategy.

009-02

### Short-term outcome of 47 external auditory canal cancer treated at a single institution

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External auditory canal cancer is an extremely rare disease entity, with an annual incidence of 1 per million populations. Due to its rarity and surgical difficulty caused from complex anatomy of the temporal bone, general consensus for treatment protocol isn't achieved yet. In this paper, we discuss about our short-term outcome of external auditory canal cancer. Forty-seven cases managed from July 2015 to April 2019 were participated: 39 cases were treated with surgery, and 8 cases without surgery. Surgical procedures consisted of 26 lateral temporal bone resections, 11 subtotal temporal bone resections, and 2 partial resections. Pathology comprised 33 SCC, 3 ACC, and 3 adenocarcinomas. Non-surgical treatment consisted of 6 CRT with TPF, 1 CRT with CDDP, and 1 heavy particle therapy. Pathology included 7 SCC and 1 ACC. Survival analysis for the events of OS or DFS revealed no significant difference between surgically managed and conservatively managed cases, though we had small number of cases with conservative management group. In surgically-managed cases, ACC and adenocarcinoma demonstrated better short-term post-operative performance, compared to SCC. In surgically-managed cases with SCC, post-operative recurrences occurred relatively early on, within half a year, with averaged 3-year DFS of about 80%. Uni-variate and subsequent multi-variate analysis revealed that, aged patients and recurrent cases after conservative treatment showed significantly poor DFS outcome. On the other hand, disease staging failed to demonstrate significant contribution to DFS. Group with post-operative recurrence consisted of 3 cases after conservative treatment, 2 with pre-operative rapid progression, and 3 with recurrences on neck lymph node metastasis. In conservatively-managed cases, we couldn't identify any contributing parameters to DFS, though with relatively small number of cases. Further evaluation for long term OS and DFS will provide evidence to establish standardized treatment protocol for external auditory canal cancer.

O09-03

## How to measure velopharyngeal function after treatment of head and neck cancer?

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### Introduction

For head and neck cancer (HNC) patients, swallowing function could be impaired due to the treatment. Endoscopic and fluoroscopic examinations are useful but qualitative, so quantitative evaluation method is strongly desired. In 2010, we proposed a blowing ratio as a simple quantitative method for measuring velopharyngeal function. Nine years have passed and now HRM is positioned as the most accurate quantitative test. However, there is few research reporting changes after surgery or chemoradiotherapy of HNC.

### Materials and Method

A retrospective chart review was conducted for 10 patients who underwent Blowing ratio and HRM after treatment of HNC at our hospital. 6 patients received surgery of oral cancer and 4 patients received chemoradiotherapy of oropharyngeal cancer are included. The blowing ratio was measured by dividing the blowing time with the open nose by the blowing time with the closed nose. HRM data was measured by the starlet®, and the maximum pressure and DCI of velopharynx and oropharynx were compared with Blowing ratio.

### Results

Blowing ratio showed significant correlation with maximum pressure and DCI of oropharynx, but not with the velopharynx. (Spearman's rank correlation coefficient).

### Discussion and Conclusion

Bowing ratio was significantly correlated with HRM and reconfirmed as a simple and accurate quantitative test. However, the correlative site was not the expected velopharynx, but oropharynx, so it is necessary to examine the physiological meaning by increasing the number of cases and comparing with other swallowing examinations.



## Paper 10 Otology / Vestibulology

### O10-01

#### Development of a Validated Questionnaire for Persistent Postural-Perceptual Dizziness (PPPD) and Investigation of the Subtypes of PPPD

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Persistent postural-perceptual dizziness (PPPD) is characterized by persistent chronic vestibular syndrome lasting >3 months that is typically preceded by acute vestibular disorders. The core vestibular symptoms of PPPD are dizziness, unsteadiness, and/or non-spinning vertigo and are exacerbated by upright posture/walking, active or passive movement, and exposure to moving or complex visual stimuli. No specific laboratory test for PPPD is available, and the precise assessment of symptoms, exacerbating factors, and medical history is important for diagnosing PPPD. We developed a 12-item questionnaire evaluating the three exacerbating factors of PPPD and tested its reliability and validity to diagnose PPPD. Furthermore, we investigated the subtypes of PPPD.

Fifty PPPD patients and 50 consecutive control patients with other vestibular disorders were enrolled in the study. Patients answered questions on three exacerbating factors of PPPD (upright posture/walking, movement, and visual stimulation), and each factor was evaluated using four questions scoring the severity from 0 (none) to 6 (unbearable). The questionnaire's reliability was tested by Cronbach's alpha, and it was validated by examining the differences in the questionnaire's scores between PPPD patients and controls. The area under the curve (AUC) of the receiver operating characteristic curve for each factor was calculated. Existence of subtypes of PPPD was tested by factor analysis and cluster analysis.

Cronbach's alpha coefficient was >0.8 for all factors, except the movement factor. Combined and individual questionnaire scores for each factor were higher in PPPD patients than in controls. The AUC was widest for the visual stimulation factor (0.830), and a score of 9 (full score 24) had the best sensitivity (82%) and specificity (74%) for discriminating PPPD patients from controls. Three factors (perceptual factor, movement factor, posture factor) were extracted by factor analysis. Cluster analysis revealed that there were three clusters in PPPD patients. The first cluster had high score of the movement factor, the second cluster had high score of the perceptual and posture factors, and the third cluster had low score of all the three factors.

In conclusion, we developed a questionnaire that exhibited high reliability and validity in evaluating PPPD severity (The Niigata PPPD Questionnaire, NPQ) (Yagi C et al. *Otol Neurotol* 2019). The visual stimulation factor may be the most characteristic among the three exacerbating factors. There were three subtypes in PPPD: movement-induced subtype, perception-and posture-induced subtype, and mild symptoms subtype.

### O10-02

#### Cervical Vestibular evoked myogenic potential and Caloric test responses in obstructive sleep apnea patients with vertigo

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**Objective:** To investigate the response of cervical vestibular evoked myoelectric potential (cVEMP) and Caloric test in patients with obstructive sleep apnea (OSA) with vertigo.

**Methods:** In this study, we retrospectively collected the cVEMP and Caloric test result of patients who were diagnosed of idiopathic vertigo in Shuang Ho hospital ENT department from March 2018 to May 2019. After exclusion of any other history of hearing impairment, tinnitus, cervical spine injury, or a history of migraine, 169 patients without snore and 49 patients with OSA were enrolled. We try to explore any different response in the cVEMP or Caloric test between the two groups. In order to avoid the error of the examiner, we select the cVEMP and Caloric test performed by the same senior audiologist.

**Results:** After adjusting for age and gender, there was no significant difference in P1 and N1 latency, P1N1 interpeak latency, or VEMP Asymmetric Ratio and bithermal caloric test between the two groups, but the P1N1 amplitude of the two ears was weaker in the OSA group ( $P < 0.05$ ).

**Conclusion:** This study showed that the sacculocollic reflex was impaired partially in OSA patients with vertigo. The possibility may due to intermittent nocturnal hypoxia, but its clinical significance remains to be confirmed.

O10-03

## Novel evaluation method for cVEMP

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### Introduction

Vestibular evoked cervical myogenic potential (cVEMP) has established status as a functional test of the otolith-inferior vestibular nerve. Although asymmetry ratio (AR) has been usually used for the evaluation cVEMP, it is difficult to diagnose in the case with bilateral dysfunction. The aim of this study was to evaluate the usefulness of normalize amplitude (NA) to diagnose bilateral vestibular dysfunction.

### Subjects and methods

Subjects were 18 cases with Meniere's disease, 7 cases with vestibular neuritis and 6 cases with acoustic neurinoma. For the control, 20 normal healthy volunteers were used. All were under 65 years old. For these, the cVEMP were and evaluated using both NA and AR. When the value was exceeded normal range (mean + 2 SD), we defined as abnormal in two evaluation methods.

### Results

In Meniere's disease, abnormal results were observed in 6 cases (33%) of AR and 13 cases (72%) of NA. In the vestibular neuritis, 4 cases (57%) of AR and 5 cases (71%) of NA. In the cases with acoustic neurinoma, abnormal results were shown in 5 cases (83%) of NA and AR.

### Discussion

The abnormalities in two methods were almost same in the cases with vestibular neuritis and acoustic neurinoma. Therefore, NA was as useful as AR in diagnosing unilateral vestibular nerve dysfunction. On the other hand, in the cases with Meniere's disease, the results of NA showed a higher abnormality than those of AR. It was known that there are occulta endolymphatic hydrops in the cases with unilateral Meniere's disease. Abnormalities of AR may have been concealed due to the reduced bilateral response. NA is useful for evaluating the dysfunction of otolith-inferior vestibular nerve in the cases with bilateral involvement.

O10-04

## Prediction of short-term prognosis of hearing impairment in patients with unilateral Meniere's disease by the results of Head-shaking test

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In Meniere's disease (MD), generally hearing loss gradually worsens with repeated attacks. While many studies have discussed the long-term prognosis of hearing loss in MD, few have investigated short-term hearing outcomes. Most patients would like to know the short-term prognosis of hearing loss and whether their hearing may recover.

We investigated the relationship between head-shaking nystagmus (HSN) patterns using the head-shaking test (HST) before treatment and short-term hearing results in patients with unilateral MD. The medical records of 157 patients with hearing loss who were diagnosed with unilateral MD were retrospectively reviewed. The hearing level when hearing loss was first detected was compared with the best score within 6 months. HSN was observed under conventional Frenzel's light goggles (non CCD), and the first phase of HSN was evaluated before treatment.

As results, HSN was present in 57 cases (36%) and absent in 100 (64%). Ipsilesional HSN (i-HSN) was observed in 28 cases and contralesional HSN (c-HSN) in 29. The outcomes of hearing loss after treatment were "recovery" in 25, 23, and 95 cases and "no change" in 3, 6, and 5 cases in the i-HSN, c-HSN, and no-HSN groups, respectively. A statistical evaluation showed more patients with "no change" in the c-HSN group compared to the no-HSN group but no significant difference between i-HSN and c-HSN or i-HSN and no-HSN.

In conclusion, the HST may be useful in MD patients to predict the short-term prognosis of hearing impairment. Hearing recovery may be poorer in patients with c-HSN compared to no-HSN.

## Paper 11 Head and Neck 4

O11-01

### Nicotinic acetylcholine receptor subunit alpha-5 promotes radioresistance via recruiting E2F activity in oral squamous cell carcinoma

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Radiotherapy is commonly used to treat patients with oral squamous cell carcinoma (OSCC), but a subpopulation of OSCC patients shows a poor response to irradiation treatment. Therefore, identifying a biomarker to predict the effectiveness of radiotherapy in OSCC patients is urgently needed. *In silico* analysis of public databases revealed that upregulation of *CHRNA5*, the gene encoding nicotinic acetylcholine receptor subunit alpha-5, is extensively detected in primary tumors compared to normal tissues and predicts poor prognosis in OSCC patients. Moreover, the *CHRNA5* transcript level was causally associated with the effective dose of irradiation in a panel of OSCC cell lines. Artificial silencing of *CHRNA5* expression enhanced but nicotine treatment reduced the radiosensitivity of OSCC cells. Gene set enrichment analysis demonstrated that the E2F signaling pathway is highly activated in OSCC tissues with high levels of *CHRNA5* and those derived from patients with cancer recurrence after radiotherapy. *CHRNA5* knockdown predominantly suppressed E2F activity and decreased the phosphorylation of the Rb protein; however, nicotine treatment dramatically promoted E2F activity and increased Rb phosphorylation, which was mitigated after *CHRNA5* knockdown in OSCC cells. Notably, the signature combining increased mRNA levels of *CHRNA5* and the E2F signaling gene set was associated with worse recurrence-free survival probability in OSCC patients recorded to be receiving radiotherapy. Our findings suggest that *CHRNA5* is not only as a useful biomarker for predicting the effectiveness of radiotherapy but also a druggable target to enhance the cancericidal effect of irradiation on OSCC.

[Ed1]Please ensure that the intended meaning has been maintained in this edit. Please note that similar changes have been made throughout the manuscript and cover letter.

Alternatively, please consider whether “to have received” would better convey the intended meaning here and elsewhere in the manuscript and cover letter.

O11-02

### PLAG1 expression proved a carcinoma ex pleomorphic adenoma with lung metastasis: a diagnostic dilemma

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Carcinoma ex pleomorphic adenoma (CXPA) is an aggressive but poorly understood malignancy which usually arises from salivary gland as a primary or recurrent benign pleomorphic adenoma(PA). It often poses a diagnostic challenge to clinicians and pathologist. It is supposed maintenance of PLAG1 expression from PA to CXPA. We present a case of 59-year-old man with a right submandibular mass sized 12 cm in maximal diameter that had been slowly growth for 10 years. Fine needle aspiration cytology showed cellular change conclusive for malignancy. PET-CT revealed a small faintly FDG-avid ground glass opacity in the superior segment of left lower lung. He received radical surgery of right submandibular gland with neck dissection and sequential lung segmentectomy was done. The pathology reported an intracapsular CXPA of right submandibular gland with 3mm closest margin distance from the tumor and no lymph node metastasis was noted. Chronic inflammation of left lower lung lesion with no malignancy and no lymph node metastasis were also showed in pathology report. Because of the intracapsular tumor feature, the patient did not receive adjuvant treatment after tumor board discussion. However, recurrence of right submandibular tumor was found for 3 months later and followed PET-CT showed multiple increased uptake nodules in the bilateral lungs and hilum. Neck sonography revealed cellular change conclusive for malignancy and CT guided biopsy of lung lesion disclosed a metastatic malignancy. Tracing back to his pathology, PLAG1 was positive in right submandibular gland and previous left lower lung specimen. The diagnosis of CXPA with lung metastasis was finally made. Given that the experience of misdiagnosis pathology, a more accurate pathological diagnosis by immunohistochemistry for PLAG1 should be advocated in suspicious CXPA metastasis patients and which may help discriminate CXPA from its de novo carcinoma counterpart.

O11-03

## The Geriatric Nutritional Risk Index as a prognostic factor in patients with advanced head and neck cancer

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**Objective.** The Geriatric Nutritional Risk Index (GNRI) is a simple and well-established nutritional assessment tool and is a significant prognostic factor in various cancers. However, the role of the GNRI in predicting clinical outcomes in patients with advanced head and neck cancer (AHNC) has not been investigated. The aim of the present study was to examine the association between the GNRI and prognosis in patients with AHNC.

**Methods.** Data collected between 2002 and 2013 from Tsukuba University Hospital (Tsukuba, Ibaraki, Japan) were reviewed. The GNRI was calculated according to the equation,  $1.489 \times \text{serum albumin (g/l)} + 41.7 \times (\text{body weight/ideal body weight})$ . The ratio of body weight to ideal body weight was set to 1 when the patient's body weight exceeded the ideal body weight. Characteristics and prognosis were compared among three risk groups: high (GNRI < 82); intermediate (GNRI 82–98); and normal (GNRI > 98). The primary endpoint was overall survival.

**Results.** A total of 248 AHNC patients was enrolled, among whom 134 (54%) exhibited no nutritional risk, 53 (21%) had an intermediate risk for malnutrition, and 61 (25%) exhibited a high risk for malnutrition. Three-year survival rates according to the three-group GNRI scores for normal, intermediate, and high risk were 76.6%, 56.3% and 19.5%, respectively. As the three-group GNRI score increased, the risk for mortality significantly increased (adjusted hazard ratio [HR] for intermediate to normal, 1.73 [95% CI 1.02 to 2.92]; adjusted HR for high to normal, 4.31 [95% CI 2.71 to 6.84]).

**Conclusions.** The GNRI could be considered a useful prognostic factor in patients with AHNC.

O11-04

## Nutritional indexes as a predictor of serious complications of reconstruction surgery for head and neck cancer patients

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**Objective:** To examine a role of preoperative nutritional indexes in predicting major surgical complications of reconstruction surgery for patients with advanced head and neck cancer.

**Methods:** The study enrolled 55 patients with head and neck cancer who received reconstruction surgery involving oral cavity or pharynx from 2014 to 2018. Demographic and clinical characteristics of the patients are as follows; median age was 65 years (42–85 years), sex was 48 of male and seven of female, median body mass index was 21.7 (14.9–32.6). Primary tumor sites were as follows; 29 cases of oral cavity, 13 of hypopharynx, six of oropharynx, four of maxillary sinus, and three of larynx. T classification was 10 of T2, 18 of T3, and 27 of T4. N classification was 18 of N0, 10 of N1, 26 of N2, and one of N3. Eight cases had previous neck surgery and 10 cases had previous neck irradiation. As nutritional indexes, AGR (Albumin-Globulin Ratio), NLR (Neutrophile-Lymphocyte Ratio), O-PNI (Onodera's Prognostic Nutrition Index), CONUT (Controlling Nutritional Status), and GPS (Glasgow Prognostic Score) were calculated using blood biochemical data before surgery. The relationship between each nutritional indexes and the occurrence of major complications based on Clavien-Dindo classification Grade 3a or higher was analyzed.

**Results:** Nutritional indexes were as follows; median AGR was 1.15 (0.55–2.42), median NLR was 2.29 (0.58–9.03), median O-PNI was 45.6 (31.6–56.8), median CONUT was 2 (0–9), and median GPS was 0 (0–2). Major complications occurred in 21 cases (32%), and the breakdown was as follows; 11 cases of wound infection, five of orocutaneous or pharyngocutaneous fistula, three of flap necrosis, two of wound dehiscence, two of lymphatic leakage, one each of suture failure, postoperative bleeding, and respiratory failure. In univariate analysis, there was a significant difference in the previous neck surgery, low AGR, high NLR, and high GPS ( $p < 0.05$ ). In multivariate analysis using these four factors, the previous neck surgery and low AGR were independent risk factors of major complications ( $p < 0.05$ ). In the receiver operating characteristic curve predicting the occurrence of serious complications, the area under the curve of AGR was 0.758, with a sensitivity of 65% and a specificity of 76% at a cut-off value of 1.165.

**Conclusion:** AGR was an independent risk factor for the occurrence of major complications of reconstruction surgery for head and neck cancer patients.

## Paper 12 Head and Neck 5

O12-01

### Our preliminary experience of the shear wave elastography for the major salivary gland tumors

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#### Objectives

The aim of the study was to evaluate the shear wave elastography of the major salivary gland tumors

#### Methods

We reviewed 236 patients who received the neck ultrasound with fine needle aspirations for the major salivary gland tumors from Jan, 2015 to May, 2018. Among the 236 patients, 75 patients who received further operation or core needle biopsy were included. The shear wave elastography was recorded in kPa. The mean and standard deviation of elasticity was compared according to the pathological reports.

#### Results

Among the 75 included patients, there were 66 benign tumors (23 Warthin tumors, 23 pleomorphic adenomas and 20 other benign tumors) and 9 malignant tumors. Comparing the mean of elasticity, there were no significant difference between benign tumors and malignant tumors (mean±SD, 57±25 vs 67±13 kPa,  $p=0.32$ ). However, there were significant difference between Warthin tumors and pleomorphic adenomas (mean±SD, 50±25 vs 65±19 kPa,  $p=0.04$ ). Comparing the standard deviation of elasticity, which representing the heterogeneity of elasticity, there were significant difference between benign tumors and malignant tumors (mean±SD, 31±15 vs 43±6,  $p=0.04$ ). The standard deviation of elasticity of Warthin tumors, pleomorphic adenomas, other benign tumors, and malignant tumors also showed significant difference under Kruskal-Wallis test (mean±SD, 26±13, 36±14, 30±17, and 43±6 (mean±SD),  $p=0.03$ ). However, for differentiating malignancy, the area under the ROC curve for standard deviation of elasticity is only 0.75.

#### Conclusion

The malignant tumors and pleomorphic adenomas tend to have higher elasticity than Warthin tumors and other benign tumors. However, the clinical use is still limited due to the lower differentiating ability for malignancy.

O12-02

### Head and Neck Ultrasound Examination by Otolaryngologists - Five-Year Experience

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Head and neck ultrasound has gained popularity among otolaryngologists worldwide for several reasons. First, high-resolution images of anatomical details in head and neck region can be easily provided under sonography for surgical guidance or disease follow-up. Second, compared with traditional image modalities (such as CT scan), the ultrasound exam can be a radiation-free and contrast-free alternative. Third, real-time images are beneficial for tissue manipulation (aspiration, injection, ablation ...) in a portable or office-based setting. Therefore, for better medical service, the otolaryngology ultrasound team of Cathay General Hospital was established since 2014. At first, there was only one clinician performing the exam. Until this day, at least five ENT doctors participated and over 5500 cases were done throughout these years. Our current instrument is BK Medical Ultrasound system with a 7-14Hz linear transducer. After analyzing the previous cases, we found that our majority cases were thyroid disorders and lymphadenopathy evaluation. However, there were increasing number of applications in accessing major salivary gland and other miscellaneous complaints in recent years. We would like to share the collected data and discuss the discrepancies between the image and intra-operative findings in hopes of improving the quality of our current exam.



O12-03

## Detection of Human Papillomavirus and Epstein-Barr virus in Saliva and Blood of Head and Neck Cancer Patients

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### Introduction

In addition to traditional risk factors such as smoking, alcohol consumption, and betel nut use, most research providing evidence for the role of oncogenic viruses in head and neck squamous cell carcinoma (HNSCC) development. This study aimed to analyze the prevalence of human papillomavirus (HPV), and Epstein-Barr virus (EBV) in HNSCC.

### Methods:

We prospectively enrolled patients with primary HNSCC who receive treatment in our hospital since 2016. Patient's blood and saliva were collected before treatment for virus detection. Detail personal history of tobacco, alcohol and betel nut, personal medical history, tumor stage, and pathological features of initial therapy were recorded.

### Results:

We investigated 197 patients with newly diagnosed HNSCC in our hospital. The majority of patients of the present study were male (185/197,94%), and the mean age at the time of diagnosis was 60 years (range 34-86). Immunohistochemistry for p16 was performed on 212 tumor samples. Tumor specimens from 10 of 197 patients were classified as p16 positive (cytoplasm and nuclear diffuse staining more than 70% of tumor cells) and p16 negative based on IHC analysis for p16 protein by pathologists. Of the 155 saliva samples tested, 30(19.4%) were positive for HPV16 DNA, and 96(61.9%) were positive for EBV DNA. Of the 158 plasma samples tested, 34(21.5%) were positive for HPV16 DNA. However, only one patient with positive plasma EBV DNA(0.6%).

### Conclusion:

Early detection and prevention of HPV and EBV infection may be the new targeting treatment in HNSCC patients.

O12-04

## Effectiveness of image-enhanced endoscopy for detection of second primary esophageal neoplasm in patients with hypopharyngeal cancer

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### Introduction:

Esophageal squamous cell neoplasm (ESCN) is common in hypopharyngeal squamous cell carcinoma patients. We aimed to evaluate the effectiveness of image-enhanced endoscopy in patients with hypopharyngeal squamous cell carcinoma.

### Material and methods:

We retrospectively recruited patients with squamous cell carcinoma in hypopharynx at Taipei Veterans General Hospital, Taiwan. Endoscopy with white-light imaging, narrow-band imaging (NBI) with magnifying endoscopy (ME), and chromoendoscopy with 2 % Lugol's solution was used for detection of esophageal squamous cell neoplasm (ESCN).

### Results:

The study included 99 patients. The patients included in the study were divided into 2 categories (newly diagnosis group, or follow-up group ) based on the timing of endoscopic examination. 30 patients of newly diagnosis group (ND group) underwent image-enhanced endoscopy before definite treatment, and 69 patients of follow-up group (FU group) underwent image-enhanced endoscopy for post-treatment routine follow-up. 8 (27%) and 23 (33%) patients had second primary ESCN in the "ND group" and "FU group" respectively. In the "FU group", patients with previous second primary SCC in upper aerodigestive tract had a higher incidence developing secondary primary ESCN (35% vs 13%,  $p=0.0343$ ). In the "FU group", 7 patients had symptoms (dysphagia, choking, foreign body sensation), and 16 patients had no symptoms while receiving endoscopic examination; among patients without symptoms, less-advanced T stage (56% vs 100%,  $p=0.0359$ ) of ESCNs were found and more patients could be treated with minimal invasive therapy (75% vs 0%,  $p=0.0013$ ) compared with patients with symptoms complaints.

### Conclusions:

Second primary esophageal squamous cell neoplasm (ESCN) is common in patients with hypopharyngeal squamous cell carcinoma. Patients in the "FU group" may benefit from routine esophageal screening due to the detection of early stage of second primary ESCNs and the therapy of minimal invasive procedures.

## Paper 13 Rhinology 1

O13-01

### Is serum total Immunoglobulin E levels as a good predictor for post-operative corticosteroid response in chronic rhinosinusitis with nasal polyps?

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#### Introduction:

Chronic rhinosinusitis(CRS) is a clinical disorder characterized by persistent inflammation of the nasal mucosa and sinus. Recent research had focus on that the coexistence of allergy in 25% to 58% CRS patients. An elevation in serum Immunoglobulin E(IgE) levels and local tissue eosinophils, as markers of allergic inflammation, contributes to allergic rhinitis and is considered a potent predictor of the development of CRSwNP. However, no useful biomarker is available for predict the outcome with postoperative corticosteroid use. The present study aim the potential benefits of postoperative corticosteroids on surgical outcomes in terms of visual analogue scale (VAS), Sino-Nasal Outcome Test 22 (SNOT-22) score, and Lund-Kennedy Endoscopic Score (LKES). To determine whether serum total IgE levels have any relationship with the response to postoperative corticosteroid treatment in patients with CRSwNP.

#### Methods:

From December 2016 to June 2019, patients with bilateral CRSwNP who failed medical therapy and underwent bilateral ESS were enrolled. The patients were randomized to receive Mometasone furoate nasal spray(Group A) or Mometasone furoate nasal spray plus oral prednisolone after surgery (Group B). The patients were divided into two categories: high IgE (>100 IU/mL) and low IgE (<100 IU/mL) in each group. We compared the two categories between baseline values and final values for the following parameters: VAS and SNOT-22 scores at and Lund-Kennedy Endoscopic Score were measure postoperatively in each group.

#### Results:

A total of 101 patients underwent ESS for bilateral CRSwNP were consecutively enrolled after giving informed consent. 53 patients were enrolled in group A and 48 patients in group B. There were no statistically significant differences between high serum IgE and low serum total IgE levels regarding the change of VAS, SNOT-22, LKES.

#### Conclusions:

On the basis of these findings, we cannot conclude that serum total IgE levels may predict the response to the post-operatively corticosteroid treatment of patients with chronic rhinosinusitis with nasal polyps.

O13-02

### Phenotype of Eosinophilic Rhinosinusitis

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Eosinophilic rhinosinusitis (ERS) is refractory and easily recurrent type sinusitis characterized by bilateral multiple polyps in nasal cavities and a frequent complication of asthma. The diagnostic and severity criteria were established in 2015 after the nationwide clinical survey of JESREC study. The pathophysiological relationship between chronic rhinosinusitis with nasal polyp (CRSwNP) in European and American guidelines and ERS after JESREC study are still under debate. On the other hand, clinical trials of antibody therapy for the refractory rhinosinusitis become quite global recently, and subjects registered in each trial should be consistent beyond nations. Refractory rhinosinusitis needs to be analyzed and classified from the view point of precision medicine consisting of phenotype, endotype and genotype analyses. In this study, in order to analyze the phenotype of ERS cases epidemiologically, we reviewed 91 chronic rhinosinusitis cases operated in Nippon Medical School, Musashikosugi Hospital from January in 2017 to July in 2018. Among 91 cases, according to the JESREC, 39 cases were classified into ERS (43%) and others non-ERS (57%). Asthma was found in 16 (41%) in 39 ERS cases and in 5 (10%) in 47 non-ERS cases, respectively. Aspirin intolerant asthma was in 4 cases only in ERS cases. Forced expiratory volume 1 second (FEV1/FVC) was significantly ( $p < .05$ ) lower in ERS than non-ERS cases before operation. Allergic and other backgrounds are also studied, and very interesting results were obtained. ERS was considered to be a very characteristic entity in chronic rhinosinusitis through this phenotype analysis. Further analysis about the phenotype of ERS is necessary in order to contribute to improve the precision medicine for CRSwCP cases.

O13-03

## The Association of PM 2.5 and Allergic Rhinitis and Non-allergic rhinitis

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### Background

Fine suspended particulates (PM2.5) is a growing concern in Taiwan as well as other Asian countries. It's impact on lower airway and cardiovascular systems have been studied and identified. However, few studies focused on upper airway. The study aims to understand whether rhinitis was influenced by PM2.5.

### Objectives

To explore the relationship between the exposure of fine particulate matter (PM2.5) and the prevalence of rhinitis in Taiwan.

### Material and Methods

This study is a retrospective case-control study. We used the National Health Insurance Database to defined case group and used propensity score matching (1:4) based on the demographic characteristics of the case group and the proportion of comorbidities to defined control group. This study was divided into two analysis methods, including the Kriging method for fine particulate matter exposure assessment with geographic information system software arcGIS10.2. Correlation analysis for the case group and control group, Chi-square test and Logistic regression analysis are included.

### Results

The total number of study population was 30718, including 15359 in the case group and 15359 in the control group. These cases were correlated according to the level of exposure to PM 2.5 (mild, moderate and severe). Every 1-unit increase of PM2.5 was significantly associated with an increased risk of rhinitis ( $p < 0.001$ ).

### Conclusions

In our study, PM2.5 was significantly correlated with the prevalence of rhinitis. Enviromental protection regarding PM2.5 is critical in order to reduce the disease burden of rhinitis in Taiwan.

## Paper 14 Rhinology 2

### O14-01

#### Factors associated with Lose to follow-up after Functional Endoscopic Sinus Surgery

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**Background and aim:** Functional endoscopic sinus surgery (FESS) is a minimally invasive technique which can restore sinus ventilation and normal function. Postoperative care is critical for the long-term success. However, lost to follow-up remains a common problem. The aim of this study was to identify the factors associated with loss to follow-up after FESS.

**Materials & Methods:** A retrospective analysis was conducted of 221 (129 men/92 women) patients with chronic rhinosinusitis underwent FESS. The average age was 45.10 years. All patients were well instructed about the post-operative care before surgery arrangement. The postoperative clinic follow-up appointments were made after surgery (1 week, 2 weeks, 1 month and 3 months post-operation). According the compliance of follow-up at 2 weeks, 1 month and 3 months, the patients were categorized into three groups. Group 1 is the patients who had no more than once follow-up after surgery, which defined as “loss follow-up”. Group 2 is the patients who had twice follow-ups and is defined as “partially regular follow-up”. Group 3 is the patients who had all three follow-ups and is defined as “regular follow-up”.

**Results:** From January 2017 to May 2018, a total of 221 (129 men/92 women) patients with chronic rhinosinusitis underwent FESS were included in this study. Only 88 patients (39.8%) had regular follow-up. A logistic regression showed younger age is a significant risk factors for lose to follow-up post-operation ( $p < 0.05$ ).

**Conclusions:** Loss to follow-up is a common problem in patients after FESS in Taiwan. In our study, the only risk factor for lose to follow-up post-operation was patients with younger age. Regular follow-up after FESS should be as important as the operation itself and could increase the efficacy in improving outcomes. For younger patients, we shall educate them and more emphasize the importance of post-op follow-up before the operation. More attentions are needed for their post-operative follow-up.

### O14-02

#### Plasma Galectin-10 and mucosal eosinophil infiltration in chronic rhinosinusitis

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The Charcot-Leyden crystal protein, galectin-10 is a predominant protein present within the cytoplasm of eosinophils. We examined the levels of galectin-10 and other molecules in the plasma of patients and compared the number of infiltrating eosinophils in the nasal mucosa with chronic rhinosinusitis. The plasma level of galectin-10 was significantly higher in the high-eosinophil mucosal infiltration group. The number of infiltrating eosinophils in the mucosa was significantly higher in the group with the higher galectin-10 level. The levels of IP-10, eotaxin-2, and eotaxin-3 were significantly higher in the high-level galectin-10 group. This is the first report suggesting galectin-10 as a plasma biomarker for mucosal eosinophil infiltration.

O14-03

## Nasal Irrigation Therapy in patients with allergic patients

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The popular treatment of allergic rhinitis is Anti-Histamine. However, the patients sometimes complain daytime sleepiness in spite of using 2<sup>nd</sup> generation of medicines. Nasal topical therapy is recommended as a supplement of oral medicine. A new hypertonic saline aerosol has recently been introduced in Japan. The present study aimed to determine the effect of this aerosol in patients with allergic rhinitis. The patients with perennial allergic rhinitis were randomly assigned to a hypertonic saline (2.7% sodium solution) group or normal saline group. They were applied the aerosol for one second to each nostril twice daily for two weeks. The effects on nasal symptoms, nasal patency were compared between the groups. All patients in the hypertonic saline group completed the aerosol therapy without complaint or adverse events. Nasal symptoms in hypertonic saline group statistically improved in comparison with normal saline group. The results suggest that allergic rhinitis can be effectively managed by daily nasal irrigation with the new saline aerosol. This device is also effective in patients with seasonal allergic rhinitis and day time activity will be improved. However a nasal irrigation device should be selected considering nasal cavity stimulation and aerosol particle size.

O14-04

## Successful treatment of eosinophilic chronic rhinosinusitis with an anti-IL-5 receptor monoclonal antibody, benralizumab

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**Introduction:** Eosinophilic chronic rhinosinusitis (ECRS) known as refractory chronic sinusitis is characterized by the presence of nasal polyps, dominant ethmoid shadows on computed tomography (CT) images, and eosinophil infiltration into nasal polyps and peripheral blood. Many patients with ECRS have severe asthma which is difficult to control. Recently, the development of monoclonal antibody-based biologics including benralizumab represents potentially effective treatments for asthma and allergic diseases. Because both asthma and ECRS are closely associated and occur as a single airway disease, benralizumab may be useful for managing ECRS with severe asthma. Here, we describe a patient with severe asthma, ECRS and eosinophilic otitis media (EOM) who developed hyper eosinophilia and exhibited a rapid response to benralizumab treatment.

**Case presentation:** We treated a 47-year-old female patient with severe asthma, ECRS and EOM. She visited our department complaining of nasal discharge, nasal obstruction and hearing impairment. Nasal endoscopy findings showed filling of polyps in the bilateral middle nasal meatus. Otolaryngoscopic findings showed the effusion in bilateral tympanic cavity. The sinus and temporal CT images showed dominant ethmoid sinus shadows and tympanic cavity shadows, respectively. Biopsy of nasal polyps revealed a large number of eosinophils, leading to the diagnosis of ECRS. Because of poor control of severe asthma despite regular use of high dose inhaled and systemic corticosteroids, respiratory physician in our hospital started benralizumab (30 mg/body, subcutaneous, every 4 weeks) for the treatment of refractory asthma. One month after the start of benralizumab, peripheral blood eosinophil ratio dramatically decreased from 14.7% to 0.0%. Continuing benralizumab led to improve asthma symptoms. Biopsy of nasal polyps 3 months after the start of benralizumab revealed no evidence of eosinophils. The remarkable reduction of bilateral middle nasal polyps was recognized 5 months after the start of benralizumab and CT images showed remission of soft tissue filling. As for otitis media, aeration of the tympanic cavity improved based on CT images and otoscopic findings, resulting hearing improvement.

**Discussion and Conclusion:** In the current case, benralizumab improved not only symptoms of severe asthma but also those of ECRS and EOM. The elimination of eosinophils by benralizumab might be important role in improvement of ECRS and EOM. Benralizumab administration may be useful for the treatment of ECRS and EOM with severe asthma.



## Paper 15 Rhinology 3

O15-01

### Free mucosal grafting of the inferior turbinate facilitates drainage pathways after extended frontal sinus surgeries

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**Background:** The success of extended frontal sinus surgery for refractory sinusitis largely depends on the patency of drainage pathways by mucosal covering of the exposed bone surface. We consider that free inferior turbinate grafts with silastic sheet scaffolds provide both free positioning and good stability to cover the bony surface of the neo-ostium. We have undertaken a case-control study to demonstrate clinical efficacy and post-operative results of this technique combined with extended frontal sinus surgeries including the modified Lothrop procedure (Draf type III).

**Patients and methods:** Nineteen consecutive patients with refractory chronic sinusitis were enrolled between October 2015 and June 2018. The mucosal free flap technique was applied to 10 patients (FF group). For this purpose, the lateral side of the inferior turbinate mucosa was removed with turbinate scissors. They were thinned to 1 to 2 mm thickness and placed over exposed bone of the nasofrontal area. Silastic sheet stents with 0.5 mm thickness were then inserted to support the mucosal grafts. We evaluated viability of the mucosal free flap and the degree of preservation of the neo-ostium.

#### Results:

The average age of the patients was 56.9 years and the mean follow-up period was 19.6 months. Six out of 19 patients were diagnosed as eosinophilic chronic rhinosinusitis (ECRS). The mucosal grafts were viable and well-integrated in the neo-ostium in all patients of the FF group. The patency of the neo-ostium in this group was well-preserved showing a horseshoe shape. In contrast, post-operative stenosis occurred in 6 patients of the control group.

**Conclusion:** We found that free mucosal grafting of the inferior turbinate for extended frontal surgeries was effective to preserve the patency of neo-ostia by preventing scar formation and osteogenesis. The procedure is simple and useful similar to other grafts or pedicle flap techniques.

O15-02

### Add-on Effect of Clarithromycin to Oral Steroids as Post-ESS Medical Therapy for CRSwNP—A Randomized Controlled Trial

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**Background:** Evidence is lacking regarding the efficacy of macrolides and oral corticosteroids in chronic rhinosinusitis with nasal polyps (CRSwNP) after endoscopic sinus surgery (ESS). The aim of this study was to examine the benefit of adding on clarithromycin to oral prednisolone as post-ESS medical therapy in CRSwNP patients.

**Methods:** This study was a randomized double-blind, placebo-controlled trial. Patients enrolled were allocated to three study groups receiving different post-ESS medical therapy: group A (placebo for 14 weeks), group B (oral prednisolone 15mg twice daily for 2 weeks, followed by placebo for 12 weeks), and group C (oral prednisolone 15mg twice daily for 2 weeks, followed by clarithromycin 500mg daily for 12 weeks). Baseline and postoperative visual analogue score (VAS), Sino-Nasal Outcome Test (SNOT-22), and Lund-Kennedy endoscopic scores (LKES) were collected as the primary outcomes.

**Results:** 126 patients who received ESS for bilateral CRSwNP were randomized into group A (n=43), group B (n=42), and group C (n=41). Compared to group A and B, group C had greater VAS and SNOT-22 improvement at 12 weeks post-ESS. Group C had significantly better LKES than group A and B at 8, 12, 24 weeks post-ESS. After we stratified LKES results with presence/absence of tissue eosinophilia, greater macrolides effects was observed in subgroup of patients without tissue eosinophilia.

**Conclusions:** Combination of short-term moderate-dose oral corticosteroids and long-term low-dose macrolides presented to be a well-tolerated and effective therapy that provides benefits in subjective and objective outcomes in post-ESS CRSwNP patients.

Dec. 6

Dec. 7

O15-03

## Combined usage of sinus ultrasound and sinus plain film for diagnosis of maxillary fungal sinusitis

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**Background:** Early diagnosis and surgical intervention are crucial in the management of fungal sinusitis, to avoid progression of disease and devastating complications. Although A-mode sinus ultrasound and sinus plain film are widely used in daily practice for the diagnosis or follow-up of maxillary bacterial sinusitis, there was no study addressing their usage in fungal sinusitis. In our clinical observation, there were a high percentage of patients with maxillary fungal sinusitis presented with a false negative sinus ultrasound and a positive sinus plain film. Hence, we propose a potential screening method for diagnosis of maxillary fungal sinusitis using combination of sinus ultrasound and sinus plain film.

**Methods:** We retrospectively reviewed data of patients with pathologically-proved maxillary fungal sinusitis that had pre-operative sinus ultrasound from May 2013 to May 2019 in our hospital. Data regarding demographics, pathology, sinus plain film and sinus computed tomography (CT) scan were retrieved. Screening criteria for fungal sinusitis was defined as a false negative sinus ultrasound and a positive sinus plain film.

**Results:** A total of 36 patients with maxillary fungal sinusitis (14 men, 22 women) were evaluated. The average age was 62 years old. There were 6 cases (16.6%) diagnosed with invasive fungal sinusitis. 26 patients (72.2%) presented with false negative sinus ultrasound. There were 21 patients who also underwent pre-operative sinus plain films and had positive findings. Among them, 15 patients (71.4%) met our screening criteria for fungal sinusitis (false negative sinus ultrasound).

**Conclusion:** False negative sinus ultrasound combined with positive sinus plain film, as diagnostic criteria for maxillary fungal sinusitis, can potentially become an easy and cost-effective screening tool before using relatively expensive CT examination.

O15-04

## Management of invasive aspergillosis in paranasal sinus

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Invasive aspergillosis in paranasal sinuses is not a common disease, in comparison with non-invasive type aspergillosis in paranasal sinuses. This disease entity usually coincides with the immunocompromised hosts such as immunodeficiency patients, the aged patient, and patients with diabetes mellitus. Clinical outcome of these patients is not satisfactory. The prognosis varies in each case, depending on the effects of multidisciplinary treatments such as medication of anti-fungal agents and/or surgical intervention. We have recently experienced 11 different cases of paranasal sinus aspergillosis invading to the orbit and skull base. Therefore, clinicopathological feature of this disease entity and clinical course are introduced herein.

Our clinical experience indicates that as invasive aspergillosis in paranasal sinuses can be often fatal, so an earliest diagnosis is warranted for aiming a better prognosis. Therefore, clinical course in each patient should be exactly considered, by employing CT scan and MRI with monitoring beta-D-glucan or CRP in sera. In immunocompromised hosts, such as an aged person, diabetes mellitus, or leukemia/lymphoma patients, a desirable radical surgical intervention is not always permitted, because of poor general condition. Taking these into consideration, very much careful attention should be paid for patient's prognosis, even though the minimally invasive surgical removal of fungal lesion under ESS can be considered to be advantageous as well as a pharmaceutical treatment with antifungal agents.

## Paper 16 Laryngology 3

O16-01

### Vocal fold steroid injection for benign vocal lesions in stage performers

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**Purpose:** Stage performers (i.e. singers, actor/actress, host/presenter) represent a unique subgroup among voice clinic. They usually demand intensive use of voice, higher voice quality. Because of busy performance schedule with limited time for voice rest, these patients may not cooperate with vocal therapy. Meanwhile, microsurgery may had some uncertainty of surgical outcome, with a long postoperative rest from performance. How to provide timely symptom relief within limited periods of voice rest remains a great challenge for phonosurgeons. Vocal fold steroid injection (VFSI) has been reported as an effective alternative to manage benign vocal fold lesions such as polyps, nodules or cysts in the last decades. This study investigated whether VFSI can be applied in stage performers.

**Materials and methods:** This study retrospectively enroll stage performers (i.e. singers, actor/actress, host/presenter) visiting our voice clinic from 2014-2018. The diagnosis of vocal lesions is based on videolaryngostroboscopy (VLS). The patients with diagnoses of benign vocal fold lesions and received VFSI as their primary treatment were included.

All the procedures were conducted in the office under local anesthesia. We prescribe complete voice rest for 3 days postoperatively, with at least 7 days before stage performance. Videolaryngostroboscopy (VLS), 10-item voice handicap index (VHI-10), maximum phonation time (MPT), perceptual analysis (GRB score) and acoustic analysis using smoothed cepstral peak prominence (CPPs) were applied to evaluate the treatment outcome before and one month after VFSI.

**Results:** 236 stage performers visited our voice clinic, 52 of them received VFSI for benign structural lesions, including cysts, nodules, polyps and Reinke's edema. Fourteen patients dropped out postoperatively. The remaining 38 patients were enrolled.

VLS showed significantly decreased lesion size in 30 patients (79%), with only one case of postoperative vocal fold hematoma. No other remarkable complication was noted. VHI-10 decreased from 21.4 to 13.7 points ( $p < 0.01$ ). GRB scores improved significantly from 3.9 to 2 points ( $p < 0.01$ ). Other acoustic analysis also showed significant improvement.

**Conclusion:** This study demonstrated that VFSI can be an effective treatment option with minimal complications, rapid recovery period and great safety profile for stage performers featured with limited time for voice rest. For larger vocal lesions, poor therapeutic efficacy or recurrent cases, laryngomicrosurgery remains the gold standard. How to improve the compliance of these patients for vocal therapy and regular follow-up remains challenging for phonosurgeons.

O16-02

### Negative Pressure Pulmonary Edema after Vocal Augmentation

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#### Case Presentation

A 74-year-old retired teacher without systemic disease came to our clinic with vocal fatigue for years. Examination showed left vocal atrophy. Vocal augmentation with autologous fat injection under general anesthesia was performed successfully. Stridor was noted on the way to post-anesthesia care unit. The fiberoptic laryngoscope showed vocal paresis. Within several minutes, the patient became agitated with oxygen desaturation to 50%. Auscultation showed breathing sound crackles. Treatment began with high-flow oxygen through a reservoir mask. Propofol was given for sedation. The chest X ray confirmed acute pulmonary edema. Under impression of negative pressure pulmonary edema (NPPE), diuretics were given. The patient stabilized within 30 minutes. He was discharged on postoperative day 2 with normal chest X ray and vocal movement.

#### Discussion

This case well illustrated the clinical scenario of NPPE type I: acute onset of pulmonary edema with the initial laryngospasm that triggers increased intra-thoracic pressures after forced inspiration followed by plasma flow into the interstitial space. Rapid resolve of pulmonary edema within one day after relief of laryngospasm supported the diagnosis of NPPE type I.

Vocal augmentation is the mainstay surgery for vocal atrophy and using autologous fat greatly reduces the inflammation and rejection reactions.<sup>1</sup> During the surgery, manipulation of the larynx can irritate the internal (sensory) branch of the superior laryngeal nerve, which can then stimulate prolonged motor activity in the intrinsic laryngeal muscle innervated by recurrent laryngeal nerve, leading to laryngospasm.<sup>2</sup> The external (motor) branch of superior laryngeal nerve which innervated the cricothyroid muscle showed no significant effect on the glottal configuration and aerodynamic functions.<sup>3</sup> Restated, laryngospasm is the main cause of airway obstruction leading to NPPE type I, not vocal augmentation.

Since NPPE type I often followed in the context of post-intubation laryngospasm in adults with the incidence ranged from 0.1% to 3%,<sup>4</sup> avoid the laryngospasm might be the first step to preventing NPPE type I. Careful oropharyngeal suctioning and fully awake before extubation was reasonable to reduce the risk. If signs and symptoms has occurred, prompt management might be beneficial because failure to recognize the problem can result in a prolonged recovery. Diuretics may hasten the resolution of pulmonary edema and rescue therapies should be considered in refractory hypoxemia.<sup>5</sup>

To conclude, in patients with more laryngeal irritation caused by surgery, post-intubation laryngospasm deserved careful consideration to prevent a potentially fatal sequela, NPPE type I. Early recognition and treatment are essential for rapid recovery.

O16-03

## **A case of Relapsing Polychondritis presenting with acute respiratory distress**

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Relapsing Polychondritis (RPC) is an autoimmune disease repeating inflammation and destruction of cartilage and connective tissue throughout the body. It is characterized clinically by chondritis of the ear, nose, larynx, trachea, and peripheral joints, and by inflammation of eyes, heart, kidney, and skin. Most common symptom is auricular perichondritis, which appears 40% of RPC patients as primary symptom and ends up with almost 80% of RPC patients. Laryngotracheal inflammation which cause of respiratory failure has been reported half of RPC patients and it is a major cause of death.

The variability of clinical symptoms, a lack of familiarity with the disease among clinicians, repeating acute onset and natural disappearance make difficult to diagnose of RPC and result in diagnostic delay. Also there is no evidence-based treatment for RPC. Therefore it makes therapeutic delay for the inflammatory exacerbation and the respiratory crisis.

In this report we describes a 40-year-old female presenting with acute respiratory compromise. She visited our hospital with sore throat. Laryngoscopic examination showed slight vocal cord edema at first visit and gradually worsened. Although earache is occurred in the course of visit, there is no auricular perichondritis. Moreover, she has saddle nose in appearance. Her past medical history is significant for joint pain, uveitis, dermatitis, sensorineural hearing loss, and Aortic regurgitation. RPC were diagnosed by physical symptoms (joint pain, uveitis, sensorineural hearing loss) and has started oral corticosteroid. 5 months after the first visit, she had stridor at night and acute airway distress. She had intubation on emergency. Laryngoscopic view revealed extensive edema of the vocal cord and the tracheostomy was performed. Pulses of methylprednisolone followed by oral steroids with immunosuppressant were administered. Antibody test for collagen diseases showed negative except an Antigenic presentation of type 2 collagen.

## Paper 17 Head and Neck 6

O17-01

### The buccal space: a review of anatomy and pathology

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#### Objective

To review the available literature as it pertains to the buccal space with a specific focus on the pathologies encountered within this space. Clinical presentation, investigations, and surgical approaches to the region are also reviewed. The review is supplemented with a case series and anatomical dissection on cadaveric heads

#### Methods

A systematic review of the available literature was performed on buccal space tumours from 1980 to 2017. Data was extracted on clinical presentation, investigations and surgical approaches to the buccal space. The pathologies encountered in the buccal space were reviewed and presented.

#### Results

Forty-nine unique articles were reviewed, with a total 217 patients. The age of the patients ranged from 0 to 83 with a mean age of 45.8. A total of 51 pathologies were reported. The majority of these were vascular and salivary gland pathologies. The majority of salivary gland neoplasms were malignant. However a wide variety of benign and malignant soft tissue tumours were also reported to occur in this region.

#### Conclusions

The buccal space is a small and complex region with a variety of pathologies occurring within it. This review clarifies the differential diagnosis of a mass which presents in this area and the pathologies which occur within it.

O17-02

### The running pattern of cervical transverse arteries can be estimated using computed tomography imaging

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#### Background

The cervical transverse artery (CTA) is a common trunk of the superficial cervical artery and dorsal scapular artery. The CTA is a surgical landmark in the lower part of the neck. Generally, the CTA originates from the thyrocervical trunk at the medial side of the anterior scalene muscle. However, sometimes the CTA directly originates from the subclavian artery at the lateral side of the anterior scalene muscle; in such cases, we cannot use the CTA as a surgical landmark. It has been reported that the CTA directly originates from the subclavian artery in 15% of Japanese. Previous studies have evaluated the CTA running pattern in cadaver dissections. However, in many cases, the CTA can be detected using computed tomography (CT) imaging.

#### Objective

The study aimed to assess whether presurgical CT imaging is an appropriate technique to evaluate the running pattern of CTAs.

#### Methods

We assessed patients (n=94) who underwent oral, pharynx, larynx, salivary gland, or other neck surgery in our hospital from April to December 2018. We included patients that either underwent plain or contrast CT. We excluded three patients who did not undergo presurgical CT. Thus, the total number of eligible patients was 91 (182 sides).

We divided CTA running patterns into two groups according to the presurgical CT findings. CTAs were either detected in the superficial layer of the anterior scalene muscle or were not detected in the superficial layer of the anterior scalene muscle and were determined to directly originate from the subclavian artery. When arteries were not detected in the posterior part of the neck, we concluded that CTAs were not visible in the CT images.

#### Results

We detected the CTA in 163 sides (90%) of all eligible patients. We assessed that the CTA was not visible in 19 sides (10%). CTAs were detected in the superficial layer of the anterior scalene muscle in 131 sides (80%) and were not detected in the superficial layer of the anterior scalene muscle in 32 sides (20%). The thickness of all CT slices was  $\leq 5$  mm. CTAs were detected in 97% of the contrast CT images with a slice thickness  $< 5$  mm.

#### Conclusions

We could estimate CTA running patterns in 90% of presurgical CT images. Our results suggest that the evaluation of CTA running patterns with presurgical CT imaging improves the safety and efficacy of surgery.



O17-03

## Drainless Thyroidectomy: Our Preliminary Experience

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Drains are placed during thyroid surgery to prevent complications such as hematoma and seroma formation postoperatively, and the most worrisome risk of postoperative hematoma formation with airway compromised is life-threatening.

However the literature lacks any candid data to support this concept. The incidence rates of hematomas requiring surgical intervention are low, reportedly at around 0–1.5%. A meta-analysis of 25 randomized trials involving 2,939 patients found no difference in seroma formation between the groups who underwent the procedures with and without a drain.

Placement of drainage tubes may increase patient discomfort, prolongs days of hospitalization and post-operative recovery. There is difference of opinion about the placement of the drain in thyroid surgeries, and to the best of our knowledge, the efficacy of drainless thyroidectomy regarding various parameters of thyroid lesions has not been well-established and should be taken into careful considerations.

We performed a comprehensive analysis of drainless thyroidectomy with or without the use of tissue glue (Tissel) by a single surgeon. Preoperative parameters such as tumor sizes and extent of invasion are carefully reviewed and outcomes regarding operation time, days of hospitalization, and final pathology analyzed deliberately. Out of the cases without drain, no postoperative complication such as local hematoma, recurrent laryngeal nerve injury or seroma formation was observed. We advocate that drainless thyroidectomy with the use of tissue glue provide a safe and efficient technique in managing patients with thyroid neoplasm.

O17-04

## Facial nerve monitoring during partial parotidectomy; Anterograde and retrograde facial nerve dissection approach

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The treatment of choice for most parotid lesions is surgical excision. Surgical procedures on the parotid gland are sometimes challenging for head and neck surgeons. Especially preservation of the facial nerve in these operations is essential, because about 80% of parotid gland tumors are benign. Most common approach to the facial nerve in parotid gland operations is to find its main trunk (standard antegrade approach). However, in some situations, a retrograde dissection (retrograde approach) can become necessary or preferable. Intraoperative monitoring (IOM) of the facial nerve during parotidectomy is increasingly used and it is helpful for use of IOM to identify the branches of the facial nerve. However, there are controversies with its effectiveness in reducing the occurrence of facial nerve dysfunction and other outcomes. We performed retrospective analysis of all patients with benign parotid tumors who underwent partial parotidectomy (Standard antegrade and retrograde approach) at our department between 2006 and 2017. The study analyzed 234 patients undergoing partial parotidectomy without monitoring (unmonitored group) from 2006 to 2013, and 159 patients undergoing partial parotidectomy with monitoring from 2013 to 2016 (facial nerve monitoring; FNM group), subdivided in standard antegrade (95 cases) and retrograde approach (54 cases). In standard antegrade approach, Operation Time were 156.8 ( $\pm$ 41.7) and 155.8 (40.3) min in the Facial nerve monitoring (FNM) and Unmonitored group ( $p$ 0.44). Blood loss were 44.6 ( $\pm$ 29.3), and 54.5 ( $\pm$ 58.2) ml in FNM and Unmonitored group, respectively ( $p$ 0.18). Transient facial nerve dysfunction were 9/95 (9.47%) and 42/184 (22.8%) in FNM and Unmonitored group, respectively ( $p$ 0.025). In retrograde marginal mandibular branch approach, operation Time were 109.2 ( $\pm$ 32.7) and 99.1 (29.6) min in the FNM and Unmonitored group ( $p$ 0.77). Blood loss were 26.9 ( $\pm$ 23.2), and 30.3 ( $\pm$ 28.3) ml in FNM and Unmonitored group, respectively ( $p$ 0.56). Transient facial nerve dysfunction were 3/54 (5.5%) and 10/47 (21.3%) in FNM and Unmonitored group, respectively ( $p$ 0.021). In this study, use of intraoperative facial nerve monitoring significantly diminishes the incidence of postoperative transient facial weakness compared to the unmonitored parotidectomy in both standard antegrade and retrograde approaches. Use of intraoperative facial nerve monitoring had no significant effect on duration of surgery and blood loss during partial parotidectomy.

**Paper 18** Head and Neck 7

O18-01

**Primary Sarcoma of the Larynx: A Rare Cause of Out-of-Hospital Cardiac Arrest**

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A 73-year-old male was brought to our emergency room under out-of-hospital cardiac arrest state. After successful cardiopulmonary cerebral resuscitation, he was sent to intensive care unit. The patient had a history of chronic obstructive pulmonary disease and had been receiving long-acting  $\beta_2$  sympathomimetic agonist (LABA) as well as long-acting muscarinic antagonist (LAMA) intermittently for several years. In recent three months, he had presented to our pulmonary clinic with history of worsening dry cough and exertional dyspnea.

During intensive care unit stay, several attempts of weaning failure from mechanical ventilation were observed. Finding on nasopharyngoscopy was notable for one exophytic tumor obscured supraglottic inlet which causing total upper airway obstruction. Elective tracheostomy and laryngomicroscopic biopsy were arranged. Pathology reported atypical spindle cell proliferation. Head and neck magnetic resonance imaging revealed a 2cm enhancing polypoid lesion at larynx and glottic level without cervical lymphadenopathy. The patient underwent transoral carbon dioxide laser-assisted supraglottic tumor excision and reported complete abatement of his symptoms with uneventful tracheostomy tube decannulation. The final pathology diagnosis was unclassified pleomorphic spindle cell sarcoma, pT4acN0M0 (American Joint Committee on Cancer, 8<sup>th</sup> Edition). On follow-up 12 months later, the patient had no relapsing symptoms or locoregional recurrence during regular outpatient clinic visit.

O18-02

**Right Thyroid Hemiagenesis with Lingual Thyroid Ectopia - a Case Report**

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Ectopic thyroid gland is a rare embryologic anomaly that occurs in the process of thyroid migration. Thyroid hemiagenesis, defined as absence of one thyroid lobe, is also a rare congenital abnormality. We reported a case of 32-year-old female patient complaining foreign body sensation in the throat for one month. Ultrasound examination disclosed a hypoechoic tongue base mass and absence of right thyroid gland. Further Tc-99m thyroid scan showed non-visualization of the right thyroid lobe, increasing left thyroid uptake and focal uptake at the tongue base. The diagnosis of lingual thyroid ectopia with right thyroid hemiagenesis was then confirmed.

O18-03

## A case of parotid salivary duct stenosis treated by sialendoscopy

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**Introduction:** Sialendoscopy is a recently developing technique allowing diagnosis and treatment of the major salivary glands pathology. Sialendoscopy is superior to imaging study especially for treatment of obstructive diseases. Ductal strictures cause 15% to 25% of obstructive sialadenitis. We report a case of chronic parotiditis caused by salivary duct strictures which have been successfully treated with sialendoscopy.

**Case report:** A 35 year-old woman presented with a lump of left side of face. Neck ultrasonography (US) detected distal stenosis and massive proximal dilation (10.5mm) of the left Stenon duct. Computed tomography (CT) revealed no abnormalities including stones but chronic inflammation. Laboratory testing revealed normal anti SS-A and SS-B antibody. A diagnostic and therapeutic sialendoscopy was performed. A ductal stricture was encountered in the mid-portion of the Stenon duct occupied with fibrous tissues. After removing the fibrous tissues using grasping forceps and dilatation of a stricture, stenting was done in order to prevent recurrence of the stenosis. It was sutured to the buccal mucosa, using 5/0 nylon\*. No recurrence of the symptom was observed for two months after the surgery.

**Discussion and Conclusion:** Duct stenosis of parotid glands can be associated with autoimmune diseases, radioiodine therapy, allergy, juvenile recurrent parotiditis, or may be idiopathic. In this case, chronic inflammation of the ducts were suspected, of which the causes were unclear. Sialendoscopy is a useful way to directly visualize and treat the stenosis of parotid ducts no matter what causes the pathology. Stenting after dilatation is mandatory to prevent the recurrence of the stenosis.

## Paper 19 Otolaryngology 4

O19-01

### Surgical indication for the inner ear malformation associated with bacterial meningitis

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**Introduction:** Childhood bacterial meningitis is a life-threatening infection with high mortality. Especially recurrent bacterial meningitis is mostly associated with inner ear malformations and cerebrospinal fluid (CSF) leaks. Inflammation in bacterial meningitis can spread to the healthy ears and cause bilateral deafness in some cases. In recent years, newborn hearing screening made it possible to detect the congenital hearing loss. With the help of further imaging inspections, inner ear malformations have been increasingly diagnosed without any signs of meningitis. Early diagnosis of the underlying pathology is vital to prevent the occurrence of bacterial meningitis.

**Objectives:** We would like to discuss the surgical indications to prevent the bacterial meningitis secondary to malformation of the inner ear.

**Methods:** We present two cases of congenital inner ear malformations wherein surgical repair of the CSF leak was performed.

**Results:** Case 1 was a bilateral case of hearing impairment due to inner ear malformations, while Case 2 was a unilateral case (both TP-I). Case 1 was diagnosed as having an inner ear malformation on CT at 2 years of age, and a CSF leak in the right ear was suspected. The patient developed bacterial meningitis at 5 years and 4 months. He underwent surgical repair of the CSF leak of the right inner ear by stapedectomy. The CSF leak stopped after surgery, but unfortunately, hearing loss of the good hearing ear due to bacterial meningitis was observed, and cochlear implant surgery was performed. On the other hand, in Case 2, an inner ear malformation (TP-I) was diagnosed during examination for unilateral hearing loss. There was no history of meningitis or any findings of CSF leak on preoperative CT, but the patient underwent exploratory surgery. Since there was a small hole in the stapes footplate, surgical repair of the CSF leak was performed in Case 2.

**Conclusions:** Early identification of the specific types of inner ear malformations and determining the associated risk of meningitis are very important. In cases of inner ear malformations with a high risk of CSF leakage and bacterial meningitis, surgical repair of the CSF leak should be considered before bacterial meningitis develops.

O19-02

### Round window vs cochleostomy approach for Cochlear Implant. The ongoing debate: a literature review

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**Aim:** Cochlear Implant (CI) recipients with residual acoustic hearing show improved speech perception and music appreciation. The challenge is to develop atraumatic surgical techniques to preserve residual hearing. In view of the ongoing debate about the optimal access routes to scala tympani for cochlear implantation, a review of the evidence on round window intervention (RWI) and cochleostomy insertion techniques is presented and comparison made of their effects on postoperative residual hearing. Progress/limitations of each procedure is also reviewed.

**Methods:** Literature review. Electronic databases were systematically searched through Ovid, Medline and Pubmed of studies published until February 2019. Studies included if preoperative and postoperative hearing thresholds were reported. Studies with only one electrode array insertion technique were excluded because no comparisons between techniques could be made. All clinical/experimental studies reporting on residual hearing preservation in CI surgery were studied to draw conclusions of improving each technique outcome.

**Results/Discussion:** Reviewing seventeen single-centre human studies, with a total of 190 patients, only one study directly compared both surgical insertion techniques. The methodologic quality of the studies was varied and has high risk of bias and inter-surgeon variance in CI surgery. The data shows postoperative low-frequency hearing loss of 10-30 dB at 125/250/500 Hz, regardless of surgical technique. Postoperative complete hearing preservation ranged from 0-40% in cochleostomy group and from 13-59% in the RWI group.

Factors impacting on the success of each insertion method were explored. In RWI accurate, slow insertion, electrode array type and navigating the hook region, have been shown to minimise the risk of trauma (Briggs et al., 2006). In comparison, cochleostomy provides an insertion vector better aligned to the longitudinal axis of scala tympani (Breinbauer and Praetorius, 2015, Adunka and Buchman, 2007). It has been found to successfully accommodate a variety of electrode designs (Briggs et al., 2005), but requires accurate placement of the cochleostomy to achieve direct entry into scala tympani (Briggs et al., 2005, Li et al., 2007) and prevent immediate intracochlear damage (Breinbauer, 2015, Atturo et al., 2014). Anatomical modelling (Li et al., 2007, Guo et al., 2016) and implantation studies (Briggs et al., 2005, Adunka et al., 2007) have shown that the cochleostomy has to be drilled antero-inferiorly to the RWM to open into scala tympani.

**Conclusion:** Overall studies demonstrate both approaches effectively achieve hearing preservation with no clear evidence showing one to be more beneficial. Electrode type and accurate insertion, post-surgery intra-cochlear tissue response and clot remodelling all impact in the outcomes of each technique.

O19-03

## The prevalence of endolymphatic hydrops following cochlear implantation

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**Aim:** To explore evidence for the presence of endolymphatic hydrops (EH) in guinea pig cochleae in the first 3 months after cochlear implantation.

**Methods:** Dummy silastic electrodes were implanted atraumatically into the basal turn of scala tympani via a cochleostomy. Round window electrocochleography (ECoChG) was undertaken prior to and after implantation. Animals survived for 1, 7, 28 or 72 days prior to a terminal experiment, when ECoChG was repeated. The cochleae were imaged using micro-CT after post-fixing with osmium tetroxide to reveal the inner ear soft tissue structure. EH was assessed by visual inspection at a series of frequency specific places along the length of the cochlea, and the extent to which Reissner's membrane departed from its neutral position was quantified. Tissue response volumes were calculated. Using ECoChG, the ratio of the summing potential to the action potential (SP/AP ratio) was calculated in response to frequencies between 2 and 32 kHz.

**Results:** There was minimal evidence of electrode trauma from cochlear implantation on micro-CT imaging. Tissue response volumes did not change over time. EH was most prevalent 7 days after surgery in implanted ears, as determined by visual inspection. Scala media areas were increased, as expected in cases of EH, over the first month after cochlear implantation. SP/AP ratios decreased immediately after surgery, but were elevated 1 and 7 days after implantation.

**Conclusions:** EH is prevalent in the first weeks after implant surgery, even in the absence of significant electrode insertion trauma.

O19-04

## Clinical feasibility of auditory processing tests in Japanese older adults: a pilot study

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**Background:** Difficulty in listening comprehension is a major audiological complaint of older adults. Behavioural auditory processing tests (APTs) may evaluate it.

**Aims/Objectives:** The aim was to assess the feasibility of administering Japanese APTs to older adults at otolaryngology clinics.

**Material and Methods:** Using computer programs interfaced with an audiometer, APTs (dichotic listening test; fast speech test, FST; gap detection test, GDT; speech in noise test; rapidly alternating speech perception test) were administered to 20 older adults (65–84 years old; mean 75.3 years) and 20 young adults at the 40 dB sensation level. Monosyllable speech perception (MSP) and the Mini-Mental State Examination (MMSE) were evaluated.

**Results:** APT results except for GDT were significantly correlated with MSP. The performance on each APT was worse in older adults than in young adults ( $p < .01$ ). The older adults with good MSP  $\geq 80\%$  ( $n=13$ ) or excellent cognitive function (MMSE  $\geq 28$ ;  $n=11$ ) also did worse on APTs ( $p < .05$ ). A ceiling effect was noted in the APT data, with FST showing a minimum ceiling effect and reflecting interindividual variations of data.

**Conclusions and Significance:** It is feasible to administer APTs to older adults who visit otolaryngology clinics. Among our Japanese APTs, FST may be suitable for further large-scale clinical studies.



## Paper 20 Otolaryngology

### O20-01

#### Psychiatric comorbidity in patients with tinnitus or auditory hallucination and sound therapy

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[OBJECTIVE] We reported psychiatric (Psy) comorbidity (818/1183, 69.1%) in patients with dizziness. In this study, we investigated about tinnitus or auditory hallucination.

[METHODS] The subjects were 243 patients (99 men, 144 women) with tinnitus and 12 patients (4 men, 8 women) with auditory hallucination. Patients were diagnosed using ICD-10.

[RESULTS] Psy comorbidity was revealed in 189 (77.8%) with tinnitus. Of 189 patients, various types of Psy disorders (D) were found, such as anxiety or panic D (F41) in 89 (47.0%), mood D (F3) in 43 (22.8%), adjustment D or post-traumatic stress D (F43) in 8 (4.2%), other neurotic D (F48) in 10 (5.3%), But in addition organic mental D (F0) in 17 (9.0%) and schizophrenia (F2) in 9 (4.8%). Twelve patients with auditory hallucination suffered from schizophrenia in 10 cases and dementia in 2 cases.

[CONCLUSIONS] We believe that collaboration between psychiatrists and otolaryngologists and doctors in the hospital and/or doctors in local area can improve the mental condition and the quality of life of patients who are suffering from tinnitus or dizziness with psychiatric comorbidity.

### O20-02

#### Risk factors for the development of pars tensa cholesteatoma from adhesive otitis media in children

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Objectives: Atelectasis and adhesive otitis media in children are related to otitis media with effusion and Eustachian tube dysfunction in infancy, or infection and immunodeficiency. But its pathogenesis is not fully understood. Some cases progress to pars tensa cholesteatoma. It is debatable when and for which cases tympanoplasty should be performed. Therefore, we studied the risk factors involved in the development of pars tensa cholesteatoma from adhesive otitis media.

Methods: Eleven children (thirteen ears) with adhesive otitis media (pars tensa cholesteatoma Ia) and thirteen children (14 ears) with pars tensa cholesteatoma (Ib or worse) were included in the study, they were 16 years old or less and underwent tympanoplasty between 2011 and 2019. For each patient, information regarding life history, medical history, and nose symptoms was obtained using a questionnaire. A temporal bone CT was taken to evaluate the mastoid air cells, and presence of sinusitis, adenoid, or tonsillar hypertrophy. Blood tests were done to evaluate allergic rhinitis. A hearing test was performed, and the condition of the opposite ear was also studied.

Results: There were significantly more male patients in the both groups, and all patients had a history of acute otitis media or otitis media with effusion. There was a high rate of complication with allergic rhinitis, but the rate of sinusitis or sniffing was low. For complications, four of the thirteen patients with pars tensa cholesteatoma had Down syndrome. Development of mastoid air cells were MC0:1 ear, MC1:8 ears, MC2:4 ears in adhesive otitis media group, and MC0:9 ears, MC1:4 ears, MC2:1 ear in pars tensa cholesteatoma group. Development of temporal bone in the diseased ear was significantly worse and aeration in the middle ear was significantly less in pars tensa cholesteatoma group.

Discussion and conclusion: Risk factors for progression from adhesive otitis media to pars tensa cholesteatoma were MC0 poor mastoid pneumatization, aeration in the middle ear, and the complication of Down syndrome. Allergic rhinitis might decrease Eustachian tube function, so attention should be paid to this point. An exact test of the Eustachian tube is difficult in children, but it must be included in the evaluation thereafter. Strict observation is necessary in children with risk factors, and the appropriate timing of surgery is important.

O20-03

## Persistent stapedial artery with stapes ankylosis

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The persistent stapedial artery (PSA) is a very rare, congenital, vascular anomaly. It presents as a pulsatile middle ear mass and sometimes causes conductive hearing loss. The diagnosis of the presence of a PSA is always accidental, because it is so rare and difficult to predict. CT findings include the absence of the foramen spinosum and a soft-tissue prominence in the region of the tympanic segment of the facial nerve. The risks of surgery include facial palsy, hemiplegia caused by coagulation of the PSA, and bleeding due to injury of the carotid artery during surgery in cases of aberrant internal carotid. In this article we report a case of PSA with stapes ankylosis for which we performed malleusstapedotomy using a Teflon wire piston. We didn't coagulate the PSA. Nevertheless the PSA attached to the prosthesis, the patient presented significant improvement in hearing level and had no complaint of pulsating tinnitus. Thus, we have shown that attachment of the prosthesis to the PSA does not necessarily disturb improvement of hearing level after malleus-stapedotomy for otosclerosis with PSA. Based on our experience, many cases can be treated by stapedotomy using a prosthesis and without coagulating the PSA.

O20-04

## A case of nasopharynx carcinoma with ocular flutter

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Ocular flutter is characterized by intermittent bursts of horizontal saccades lacking an interval. Similar saccadic bursts are called opsoclonus when they were directed not only horizontally, but also vertically. Ocular flutter is often observed in cerebellar and/or brainstem lesions, but the precise mechanisms are not well known. We report a case of nasopharynx cancer with ocular flutter. A 59 year-old man visited our hospital for examination of neck swelling. A mass was detected in the nasopharynx and biopsy was performed to diagnose squamous cell carcinoma. At the same time, he began to complain of swaying vision and gait disturbance, and ocular flutter was recognized. No abnormalities were observed in the head MRI and in the cerebrospinal fluid examination. Paraneoplastic neurological syndrome was diagnosed. Steroid pulse therapy was performed, followed by radiation chemotherapy, and ocular flutter disappeared.

# Poster

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15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery

## Poster

## Head and Neck

P01

# HPV-status determines the efficacy of an oral fluoropyrimidine, S-1, in oropharyngeal carcinoma

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## Introduction

The rising incidence of OPCs is because of the increase of these cancers occurring in young to middle-aged adults and in people with limited tobacco and alcohol exposure. A subgroup of these patients is caused by infection with HPV type 16 (HPV16). It is clear from retrospective studies that HPV-positive OPC has a significantly improved prognosis compared to HPV-negative counterparts. The drug S-1 is an orally active combination of tegafur (an oral 5-FU prodrug), gimeracil (5-chloro-2,4-dihydroxypyrimidine dehydrogenase, a DPD inhibitor), and oteracil (which inhibits the phosphorylation of fluorouracil in the gastrointestinal tract, thereby reducing the gastrointestinal toxic effects of fluorouracil) in a molar ratio of 1 to 0.4 to 1.

## Patients and Methods

In this study, all patients had histologically proven OPC of stage III or IV with no evidence of distant metastases. In our hospital, sixty-four patients with OPC received curative treatment, such as surgery and/or radiotherapy with or without chemotherapy from December 1998 to June 2008. Only patients who were confirmed tumor-free at both primary site and regional lymph node were analyzed in this study. Among 38 cases analyzed, HPV was positive in 19 cases, in which only HPV16 were detected. Before 2003, none of the patients received S-1 adjuvant chemotherapy after curative therapy [S-1(-)-group]. After 2003, all patients who were eligible for S-1 administration received adjuvant chemotherapy within 3 months after curative treatment [S-1(+)-group]. The starting dose of S-1 administration was 50 mg twice a day (100 mg/d) for patients with a BSA of at least 1.5. The survivals of HPV-positive and HPV-negative OPCs were evaluated according to S-1 adjuvant chemotherapy. We considered *p* values less than 0.1 to indicate significance.

## Results

For HPV-negative patients, the three-year overall survival rate and the three-year disease-free survival rate were 80.0 and 60.0% in S-1 (+)-group and 42.9 and 35.7% in the S-1 (-)-group, respectively. The two groups had significantly different overall and disease-free survival rates (*p* = 0.065 and *p* = 0.082), respectively. For the HPV-positive patients, the three-year overall survival rate and the three-year disease-free survival rates were 100.0 and 90.9% in S-1 (+)-group and 100.0 and 87.5% in S-1 (-)-group, respectively. Kaplan-Meier calculation did not show any significant influence on survivals by administration of S-1 as adjuvant chemotherapy for HPV-positive OPCs.

## Conclusion

We conclude here that adjuvant chemotherapy with S-1 is useful choice for HPV-negative OPCs. However, the adjuvant chemotherapy is not recommended for HPV-positive patients.

P02

# Significance of basaloid squamous cell carcinoma component in HPV-related oropharyngeal carcinoma

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## [Background]

HPV-related oropharyngeal cancer (HPV-OPC) is known to have a relatively good prognosis compared to non-HPV-related oropharyngeal cancer, while the reports on the mechanisms of tumor formation and progression of HPV-OPC are limited. Although peculiar histological subtypes of squamous cell carcinoma (SCC), such as basaloid SCC, papillary SCC, lymph epithelial carcinoma, are often seen in HPV-OPC, it is unclear how these histological differences affect clinical aspect. Basaloid SCC (bSCC) is also seen in the other organs such as esophagus and the presence of bSCC has been reported to suggest a poorer prognosis. However, studies on its impact on oropharyngeal carcinoma are unsatisfactory, so far. Therefore, we aimed to clarify the clinicopathological significance of bSCC components in HPV-OPC.

## [Methods]

Among HPV-OPC cases surgically resected at Juntendo University Hospital between 2010 and 2017, 8 cases with histology of bSCC (bSCC group) were studied. Seven HPV-OPC cases with squamous cell carcinomas and without bSCC (non-bSCC group) were used as controls. The existence of comedo central necrosis, peripheral palisading, and solid growth in a lobular configuration was given special importance in making pathological diagnosis of bSCC. Clinical information such as sex, age, tumor diameter, TNM classification, smoking history, and alcohol consumption history were compared between the bSCC and non-bSCC groups. Immunohistochemical staining of CK14, 34 βE12, β-catenin, Bcl-2, p53, EGFR, Ki-67, IgG4 and FoxP3 was performed for both groups, based on the previous reports of esophageal bSCC.

## [Results]

There were no statistically significant difference in clinical parameters of patients between bSCC and non-bSCC groups. Immunohistochemical differences of CK14, 34 βE12, and EGFR were seen between the 2 groups; CK14 was positive for 0% (0/8 cases) / 91.7% (11/12 cases) for bSCC/non-bSCC groups, 34 βE12 was more weakly stained for bSCC group than non-bSCC group, and EGFR was more weakly stained or negative for bSCC component compared to SCC component.

## [Conclusions]

Although there were no significant differences in clinicopathological data, there was significant differences in immunohistochemical data between bSCC and non-bSCC groups. Since, the EGFR expression may relate to the effect of anti-EGFR drugs, it may be important information for the selection of chemotherapy. Authors add the data of molecular status of EGFR in our cohort and will report the results in upcoming conference.

P03

## Comprehensive analysis of HLA-presented peptides in head and neck cancer tissues

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### Aim:

The correlation between the therapeutic effect of the immune checkpoint inhibitor and the amount of oncogene mutation was clarified. Recently, mutation-derived neoantigens have attracted attention as immunotherapeutic targets. Identification of cancer antigens that serve as patient T cell targets and understanding of the immune response are major issues leading to therapeutic and biomarker establishment. However, the number of HLA-presented peptides on the surface of cancer cells is enormous, and it is not easy to grasp their repertoire and totality. We established an HLA ligandome analysis technology that combines HLA immunoprecipitation and mass spectrometry analysis. Unlike the conventional reverse immunology method using the HLA binding prediction algorithm, it is possible to decipher the sequence of peptides naturally presented in cancer tissue directly and comprehensively. In addition, analysis using HLA antibody columns simultaneously detects HLA class I and class II peptides.

### Materials and Methods:

We analyzed four head and neck cancer tissues obtained by surgery (2 cases of hypopharyngeal cancer, 1 case of tongue cancer, 1 case of cervical cancer of unknown primary site). We identified HLA-presented peptide sequences on the head and neck cancer cell surface using HLA ligandome analysis technology.

### Results:

We identified over 3000 peptide sequences that were HLA presented to 4 head and neck cancer tissues.

### Conclusion:

It was possible to identify neoantigens by HLA-presenting peptideome analysis using clinical samples. Currently, we are working on neoantigen data acquisition including cancer whole exome gene mutation analysis.

P04

## Experience of a Nivolumab use against our 32 cases of head and neck cancer

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### Introduction

The notable extension of overall survival rate in the patients who is received medical treatment using Nivolumab was verified in the international collaborative phase III (CheckMate141). However, the special side effects (immune-related adverse event: irAE) that is different from conventional it by anti-tumor drugs become important and undeniable point. Then, it is important to cooperate with several medical departments to cope with convoluted complications.

From use of Nivolumab was formal approved against the patients with unresectable head and neck cancer in March 2017 in Japan, we administered Nivolumab to the patients with recurrent/metastatic head and neck cancer in our institution.

### Materials

We picked up thirty-two patients with head and neck cancer who received medical treatment with Nivolumab in our institution for the duration from April first 2017 to July 31 2019.

### Result

There were 27 males and 5 females among total 32 cases, average age was 58.9 years old. There were squamous cell carcinoma of 22 cases, others of 10 cases (2 cases of olfactory neuroblastoma, 2 cases of adenoid cystic carcinoma at the submandibular gland, 2 cases of undifferentiated carcinoma in the rhino-paranasal cavities, 1 case of spindle cell carcinoma in the hypopharynx, 1 case of Lymphoepithelial carcinoma in the nasopharynx, 1 case of pleomorphic adenoma in the maxillary sinus, and a case of sebaceous cancer at the eyelid) in pathological statement. It was eight times in average number of medication, maximum number of medication was 37 times. It was difficult to continue in 7 cases for severe irAE. Interstitial Pneumonia occurred in 5 cases, autoimmune hepatitis and encephalitis occurred in each one. Therefore, All of irAE were grade3 (CTCAE v4.0) or higher. Moreover, medication was finished halfway in 2 cases for patients' own request, and was stopped or changed to other treatment in 16 cases due to progression of disease. Finally, medication is being receiving in only 7 cases now.

### Discussion

There were a lot of cases which medication is stopped for severe irAE against our plan compared with other reports. This tendency was remarkable in 2017. As a reason of early stopping of medication, it was thought of poor performance status or other complications like pneumonia. On the other hand, long-term survivor existed because of changing treatment.

It was important for us to detect in the early and cope with irAE quickly and properly.



## P05

## A study of prophylactic antibiotics in head and neck reconstruction surgery

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The head and neck region is frequently contaminated by resident bacteria, and radical resection of head and neck cancer including reconstruction is known to have a high risk of infection. In this study, we examined outcomes of postoperative antimicrobial treatment in 71 patients who underwent head and neck reconstructive surgery between 2010 and 2018 in Wakayama Medical University, Japan.

The cases were 71 patients from 43 to 84 years old, 57 males and 14 females. There were 16 lingual cancers, 20 oropharyngeal cancers, 22 hypopharyngeal cancers, 9 oral cancers, 2 maxillary cancers, and 2 cervical esophageal cancers. Reconstructions were done by 19 free forearm flaps, 10 free rectus abdominal flaps, 21 free jejunum, 10 pectoral pectoral flaps, 2 groin flaps, and 5 anterolateral thigh flaps. Two cases were reconstructed by gastric tube. The preoperative chemotherapy was done in 69 patients (TPF regimen was done in 65 patients). The initial selection of postoperative prophylactic antibacterial drugs was 25 cases for CEZ, 25 cases for ABPC/STB+MNZ, 11 cases for ABPC/STB, 2 cases for TAZ/PIPC, 1 case for CMZ, and 1 case for STB/ABPC+CLDM. Antibiotics were changed in 32 out of 71 cases. The second choice of antimicrobial agents were MEPM (28 cases), STB/ABPC (2 cases), MEPM+LZD (1 case), TAZ/PIPC (1 case). The reasons for changing antibiotics were 19 cases due to worsening of inflammatory findings such as increase of fever and CRP, 3 cases of suspicious fistula/abscess formation, 4 cases due to flap necrosis, and 1 case with aspiration pneumonia.

We evaluated the risk for surgical site infection. The practical guidelines recommend ASBT/ABPC, CEZ+MNZ or CLDM, or CMZ for the appropriate antimicrobial agents to prevent postoperative infection.

## P06

## A clinical study of oropharyngeal squamous cell carcinoma

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After it was clarified that human papilloma virus (HPV)-related oropharyngeal cancer has a favorable prognosis, the cancer was clearly classified as HPV-related oropharyngeal cancer with Positive reaction and non-HPV-related oropharyngeal cancer with Negative reaction determined by p16 immunostaining according to the 2017 newly-revised tumor-node-metastasis (TMM) classification (UICC/AJCC\* the 8<sup>th</sup> edition). Since then, various facilities have actively been conducting p16 detection and also discussing personalized treatment and low invasive procedure for positive case of p16. In this study, we carried out a clinical study through p16 immunostaining for total 40 oropharyngeal cancer cases with radical treatment at our center during the period from 2014 to 2019. The breakdown of the cases was male-to-female ratio (3:1) and median value/average of age (63.0/64.1 years old). We examined Side wall (23 cases), Upper wall (11 cases), Anterior wall (3 cases), and Posterior wall (3 cases) for subsite, and Positive reaction (17 cases) and Negative reaction (23 cases) for p16 immunostaining. The primary treatment was surgical resection (14 cases), cetuximab-combined radiation therapy (10 cases), and cisplatin-combined radiation therapy (16 cases). When making a comparison between the classification of UICC/AJCC the 7<sup>th</sup> edition (Stage I: 6 cases, Stage II: 2 cases, Stage III: 8 cases, and Stage IV: 24 cases) and the 8<sup>th</sup> edition (Stage I: 12 cases, Stage II: 6 cases, Stage III: 11 cases, and Stage IV: 11 cases), it indicates downstaging as a whole. For the 3-year survival rate, p16-positive oropharyngeal cancer was 70%, but p16-negative oropharyngeal cancer was 56.5% with no significant difference but a poor prognosis tendency.

P07

## A clinical study of lower gingival carcinoma

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Oral cancer accounts for approximately 1-2% of all cancers, and gingival squamous cell carcinoma is oral cancer with the second highest occurrence rate after tongue cancer. However, since it is often treated with dental surgery in Japan, there would be fewer opportunities to actually encounter such case in clinical practice as an otolaryngologist. Head and Neck Oncology Center of Showa University was established in 2014 for a joint treatment by otolaryngologist/head and neck surgeon and dental surgeon. Because the number of oral cancer cases dramatically increased, we report our examination of age distribution, gender, tumor-node-metastasis (TNM) classification, stage classification, proper diagnosis rate of preoperative/postoperative diagnosis, survival rate, and recurrence rate for 27 cases of gingival squamous cell carcinoma of lower jaw surgically treated at our center during the period from October 2014 to August 2019. We found there was a similarity to reports by other researchers such as more males in gender difference and relatively-average distribution in stage classification. We basically could not recognize a diagnostic difference when making a comparison between preoperative imaging findings and postoperative histopathological findings, but since preoperative imaging findings tend to have an overestimated invasion depth, we considered that it could be involved with inflammatory diseases such as periodontitis and osteomyelitis. Furthermore, we did not find recurrence from the bone stump after resection, but since the recurrence site was located at masticatory space and deep infratemporal fossa, it would be difficult to be treated by the secondary treatment and the primary site control might possibly be important in the primary treatment.

P08

## Will Radiotherapy increase cardiovascular complication in Patients with Head and Neck Cancer? : A Nationwide Population-Based Cohort Study

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### Background:

Long-term cardiovascular risk increases after radiotherapy (RT) in patients with breast cancer. However, whether RT is a risk factor for cardiovascular disease in patients with head and neck cancer remains unclear. This study investigated the association, if any, between cardiovascular disease and RT in patients with head and neck cancer.

### Methods:

This retrospective cohort study included the data of patients newly diagnosed as having head and neck cancer between January 1, 2000, and December 31, 2015, from the 2000 Longitudinal Health Insurance Database. Patients were categorized into the following groups according to the treatment regimens received: RT alone (RT-alone), RT combined with other treatments (any-RT), and treatments without RT (no-RT). The outcome was the occurrence of cardiovascular disease (angina, acute myocardial infarction or chronic heart disease) after treatment.

### Results:

Of the 8340 patients with head and neck cancer, the incidence of cardiovascular disease was 1.36 (per 1000 person months). According to subgrouping related to different treatment policies, RT-alone group, any-RT group and no-RT group have cardiovascular disease incidence as 1.73, 0.90 and 1.41. After multiple Cox regression analysis, the patients in RT-alone and any-RT groups did not have higher cardiovascular disease risk compared with patients in the no-RT group after adjusted with confounding factors(hazard ratio: 1.03 and 0.55; 95% confidence interval: 0.78–1.35 and 0.44–0.68, respectively).

### Conclusions:

This is the first nationwide population-based cohort study to evaluate the risk of cardiovascular disease in patients with head and neck cancer. Our results showed no significant association between radiotherapy and cardiovascular disease in patients with head and neck cancer.

P09

## Results of the Multidisciplinary Approach for Patients with T4b Malignant Tumors observed Middle Cranial Fossa Invasion of Maxillary Sinus

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The prognosis of patients with malignant tumors of maxillary sinus is still poor. Because of almost patients with advanced stages, the prognosis is poor and the quality of life of patients after treatment is diminished. The NCCN guidelines treatment strategy of T4b cases is written as three options consisted of clinical trial, definitive radiation, or systemic therapy/radiation. Background of the poor prognosis of T4b patients, the other treatment strategy is needed, and we have had efforts to break those issues. Among category T4b cases, patients were diagnosed as T4b due to middle cranial fossa invasion in our hospital. We have a surgical treatment strategy for T4b patients with middle cranial fossa invasion, and we have performed the multidisciplinary approach for T4b malignant tumors of maxillary sinus. The multidisciplinary approach was consisted of surgery, irradiation, and intra-arterial infusion of 5-fluorouracil. (Nishino, Cancer, 2000; Nishino, Head Neck, 2013) The resection with narrow safety surgical margins and 20Gy of irradiation with 1250mg of intra-arterial infusion of 5-fluorouracil was performed. The indication of our multidisciplinary approach was thought for patients without orbital apex invasion, dura invasion, or nasopharyngeal invasion. Due to the narrow safety surgical margins and low dose irradiation, we could have the preservation of orbital content and orbital function. Since 1980, we have treated 23 T4b patients with middle cranial fossa invasion by our multidisciplinary approach. Median age was 54 years old, 12 were female and 11 were male. Only two patients were diagnosed as neck lymph-nodes metastasis. On pathology of malignant tumors, 16 were diagnosed as SCC and 7 were as non-SCC. Median follow periods were 731 days (176~11505days). 5-year over-all survival rate was 56%. Based on the results of the other treatment strategies, 5-year over-all survival rates of LADPLAT were reported 57% (Homma: BJC, 2013) and 33.3% (Ono: J Craniomaxillofac Surg, 2017). At least the prognosis of our multidisciplinary approach was not inferior compared to LADPLAT.

P10

## Poorly differentiated clusters are prognostic factors for T1 or T2 squamous cell carcinoma of the external auditory canal

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[Objective] Squamous cell carcinoma of the external auditory canal (SCC-EAC) is rare and carries a poor prognosis. A revised University of Pittsburgh staging system is commonly used for prognosis and treatment decisions in patients with SCC-EAC. We demonstrated that tumor budding (TB) is associated with shorter survival in advanced stage SCC-EAC (T3–T4). Unfortunately, there are some patients with tumors that recur despite their categorization as early stage SCC-EAC (T1–T2). Histopathologically, TB refers to the presence of less than 5 invading cancer cells, although clusters composed of more than 5 invading cancer cells and lacking a gland-like structure [known as poorly differentiated clusters (PDCs)], may also be found in cancer stroma. Notably, PDCs are an established negative prognostic factor in colorectal cancer. In this study, we examined the association of PDCs with prognoses for early stage SCC-EAC.

[Methods] Clinicopathological data from 10 patients, who received a partial temporal bone resection, with T1 or T2 SCC-EAC were reviewed. Pretreatment biopsy specimens were also available. SCC-EAC biopsy specimens were fixed in formalin and processed into paraffin blocks. TB and PDCs were counted in cytokeratin stained immunohistochemistry sections. In SCC-EAC, clusters surrounded by stroma and composed of more than 5 cancer cells were defined as PDCs. To quantify PDCs, the whole tumor was first scanned under low magnification to identify the area with most PDCs. Next, the clusters were counted within the microscopic field of a 20x objective lens. Tumors with less than or more than 5 PDCs were classified as low-grade and high-grade, respectively.

[Results] Of the 10 patients studied, 4 had high-grade PDCs that were all recurrences, whereas the remaining 6 had low-grade PDCs that were all non-recurrences. Patients with high-grade PDCs had significantly shorter survival times than those with low-grade PDCs.

[Conclusion] Poorly differentiated clusters grade is a prognostic factor that can selectively identify recurrent cases in T1 or T2 squamous cell carcinoma of the external auditory canal.

P11

## Prediction for facial nerve paralysis after parotidectomy using intraoperative facial nerve monitoring

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**Introduction:** Complete tumor resection and reliable preservation of the facial nerve is required in the operation of the parotid tumor. Even if the facial nerve is preserved during surgery, it may cause temporary facial paralysis after surgery.

**Objective:** To predict the postoperative facial nerve paralysis during the operation by using intraoperative facial nerve monitoring.

**Patients and Methods:** We prospectively examined 113 patients who underwent partial parotidectomy for parotid tumors at the Department of Otorhinolaryngology Head and Neck Surgery of Osaka Medical College from 2015 to 2018. Patients were 48 male and 65 female. Mean age was 54 years old (15-81). Tumor site were 67 in superficial lobe, 18 in deep lobe and 28 in lower pole. After identifying main trunk of the facial nerve, we underwent partial parotidectomy for all the patients. Intraoperative electromyographic at 1mA stimulated facial nerve during surgery. After the tumor removal, we measured amplitude responses in the condition with 1mA stimulation of the facial nerve in the main trunk, temporal, zygomatic, buccal muscle, and mandibular marginal branches using intraoperative facial nerve monitoring. Postoperative facial nerve dysfunction was assessed at next day of operation. Moreover, the cases with facial nerve dysfunction were followed to check the recovery period from dysfunction.

**Results:** 20 (17.7%) among 113 cases was detected postoperative facial nerve dysfunction. 16 cases were one branch paralysis, 3 cases were three branches paralysis, and only 1 case was in all branches paralysis. In the cases with normal facial nerve function, amplitude responses were not significant differences between main trunk and each branch. On the other hand, in the cases with facial nerve dysfunction, amplitude response of main trunk were significantly lower than branch ( $p < 0.001$ ). The recovery period from paralysis is 98 days (30-150 days) for temporal branch ( $n = 4$ ), 7 days (4-70) for zygomatic branch ( $n = 7$ ), 20 days for buccal muscle branch ( $n = 5$ ) (4-30), mandibular marginal branch ( $n = 13$ ) was 60 days (3-180). The zygomatic and buccal muscle branches had significantly longer recovery times than the temporal and mandibular branches ( $p < 0.005$ ). Paralysis recovered 50% in 1 month, 80% in 3 months, and 100% in 6 months. To predict the recovery period from postoperative facial nerve dysfunction is difficult by intraoperative electromyographic ( $R^2=0.15$ ).

**Conclusion:** Postoperative facial nerve paralysis after parotidectomy can be predicted by using intraoperative electromyographic at the end of the operation.

P12

## Incorporation of shear wave elastography into a prediction model in the assessment of cervical lymph nodes

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**Rationale and Objectives:** To assess the performance of shear wave elastography (SWE) and an extended model in predicting malignant cervical lymph nodes (LNs).

**Materials and Methods:** 109 patients who underwent ultrasound (US) and SWE before needle biopsy were enrolled. The optimal cutoff value of elasticity indices (EIs) was determined by receiver operating characteristic (ROC) curves. The c-statistic, net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were used to compare extended model and traditional one.

**Results:** Malignant LNs had higher EIs than benign nodes ( $p < 0.001$ ). The optimal cutoff point was 42 kilopascal, corresponding to 83.3 % sensitivity, 64.7% specificity, and 68.8% overall accuracy. A multivariable logistic regression analysis confirmed that EI was an independent predictor for malignancy. The new extended prediction model had a positive NRI (0.96) and IDI (0.10) for predicting malignant neck LNs. Nevertheless, the c-statistic was not significantly different between the two models.

**Conclusion:** The parameter of SWE theoretically improve the model performance. However, its real clinical impact is minor, as the parameters of US-based model is already very robust. SWE can be considered as an adjunctive quantitative tool beyond conventional US examination.

## P13

## Seven cases of small cell carcinoma of the head and neck

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Small cell carcinoma of the head and neck is a rare disease and highly malignant with poor prognosis. We experienced seven patients with small cell carcinoma of the head and neck in our hospital from 2011 to 2019.

One patient was diagnosed as stage III, four patients as stage IVA and two patients as stage IVC. The primary anatomic sites of the tumors were oropharynx in two, hypopharynx in two and paranasal sinus in three. The patients age ranged from 38 to 85 years old, averaged 56.

Our treatment choice was mainly concurrent chemoradiotherapy with cisplatin and etoposide. But two patients who were over 80 years old underwent radiotherapy alone, and one patient with multiple distant metastases underwent chemotherapy alone.

The two patients who underwent radiotherapy alone died of distant metastases within nine months after treatment. Among four patients who underwent concurrent chemoradiotherapy, one patient died of local recurrence, and other three patients survive without disease over three years, one year, and eight months respectively. But one patient was diagnosed therapy-related myelodysplastic syndrome two years after chemoradiotherapy.

Small cell carcinoma has poor prognosis because of distant metastasis, so not only local treatment but also systemic chemotherapy is very important. Chemotherapy with cisplatin and etoposide could be an effective regimen for small cell carcinoma of the head and neck as well as pulmonary small cell carcinoma, but we should be careful of the severe adverse events such as hematotoxicity.

## P14

## Two cases of carcinoma at sites of old maxillary fractures

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Malignant changes occasionally arise in the scar tissue that forms following injury. These changes are frequently detected on previously traumatized skin, most commonly appearing as squamous cell carcinoma (SCC) developing in burn scars. On the other hand, few reports have described malignancies other than skin cancers developing in the head and neck area. One hypothesis involves prolonged overactivation of tissue repair systems due to chronic inflammation and irritation, although the pathogenesis of cancers occurring in scars is not fully understood. We report two cases with histories of maxillary fractures at the site of subsequent squamous cell carcinoma development.

The first patient developed SCC 7 years after right maxillary fractures resulting from a traffic accident. He underwent chemoradiotherapy (70 Gy in 35 fractions) and maintained complete response (CR) for 15 months. The second patient developed SCC three years after sustaining right maxillary fractures in an ice hockey game. Radiotherapy and total maxillectomy were performed, but local recurrence arose and he has since been receiving chemotherapy.



P15

## Advanced malignancy found incidentally with internal jugular venous thrombosis: a report of 2 cases

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Internal jugular venous thrombosis (IJVT) is a rare disease detected during ordinary otorhinolaryngological examination. IJVT has various causes, including deep neck abscess, malignancy, and iatrogenic trauma.

We encountered 2 cases of IJVT caused by malignancy. Case 1 involved a 68-year-old man who presented with a 2-week history of swelling and pain in the right neck. Computed tomography (CT) revealed thrombosis in the right internal jugular vein from the clavicle level to the hyoid bone level. In addition, CT revealed multiple cervical lymphadenopathies. Thrombolytic therapy with warfarin was not effective. Open biopsy of the right lymph node was performed. Pathological examination revealed squamous cell carcinoma. Examination of the original lesion showed unclear results. We diagnosed cancer of unknown origin (cervical, mediastinal, and axillary lymph nodes) and performed chemoradiotherapy (carboplatin + paclitaxel, 1 course; radiotherapy + cisplatin [CDDP] + S1, 4 courses). He achieved completion remission (CR) after 5 months. CR was maintained until he died due to another disease 14 months after starting chemotherapy.

Case 2 involved a 61-year-old man who presented with a 1-week history of swelling and pain in the right neck. CT revealed thromboses in the right internal jugular vein and left subclavian vein. In addition, CT revealed multiple cervical and mediastinal lymphadenopathies. Open biopsy of the right lymph node was performed. Pathological examination revealed adenocarcinoma. On <sup>18</sup>F-fluoro-deoxy-d-glucose positron emission tomography, right lung cancer was detected as the original lesion. We consulted a respiratory physician, and they prescribed chemotherapy and thrombolytic therapy with rivaroxaban. He received 7 courses of pembrolizumab as first-line chemotherapy, but tumor progression was observed. Second-line chemotherapy involved 4 courses of CDDP + pemetrexed, followed by 3 courses of pemetrexed. Thirteen months after the first visit, he died of complications from lung cancer.

Various underlying diseases may present as IJVT. Therefore, when IJVT is suspected, appropriate tests should be performed as soon as possible, followed by selection of the best treatment approach.

In these 2 cases, advanced malignancy presented with IJVT. In such cases, we should select multidisciplinary treatment for malignancy. However, resolution of thrombi in IJVT is associated with a risk of serious complications, such as pulmonary embolism. Sufficient attention should be paid to this issue.

P16

## A case of papillary mucinous neoplasm occurred in sublingual gland

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It is said that salivary gland cancer would account for 3-5% of head and neck cancers, and the occurrence frequency of sublingual gland tumor could be rare or approximately 2-3% among the salivary gland cancers. In this study, we report our experience of newly-proposed and relatively-favorable prognostic cases for papillary mucinous neoplasm among the sublingual gland malignant tumors, along with some literature reviews.

The case was for female at the age of 76 who was already aware of tumor in the right floor of the mouth from a few years ago. Because the symptom progressed slowly at an increasing rate, she visited a local doctor and then she was referred to our center for the detailed examination. With visual inspection, we found a highly-mobile tumor (size:30cm) with smooth surface in the right floor of the mouth. Since we did not reach a definitive diagnosis even after a tissue biopsy due to no sign of cervical lymph node metastasis or distant metastasis on a CT scan, intraoral excision of the sublingual gland including its tumor was performed for covering both diagnosis and treatment. Surgical margin was set to approximately 10mm, but we performed combined resection due to invasion of Wharton's duct and lingual nerve. Later, we diagnose it as papillary mucinous neoplasm after the histopathological examination. Papillary mucinous neoplasm is widely known as intraductal papillary mucinous tumor. In addition to pancreas, it is reported that the cancer also occurred in stomach, large bowel, liver, lung, and prostate gland, but there are only 4 reported overseas cases for cancer occurred in salivary gland even after extensive research. Because AKT1 gene mutation was found in all of these 4 cases, it is pointed out that papillary mucinous neoplasm can be a specific gene mutation.

P17

## A rare sinonasal tract carcinomas - Human Papillomavirus-Related Multiphenotypic Sinonasal Carcinoma

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Human papilloma-virus(HPV)-related multiphenotypic sinonasal carcinoma (HMSC) is the sinonasal tract carcinomas with an established etiological role of HPV infection, especially with type 33. It is a rare sinonasal neoplasm with relatively indolent behavior. To date, only a few case series have been published in English literature.

HMSC bears a distinctive clinicopathologic profile characterized by high-risk HPV association, sinonasal tract localization, salivary gland tumor-like appearance and high-grade histologic appearance. This kind of tumor exacerbated by a lack of awareness of this entity by pathologists and oncologists make this entity susceptible to misdiagnosis, erroneous management and eventual skewing of clinical and epidemiologic data. Not much is known about the optimal treatment of this newly recognized tumor. Herein, we illustrate a case of nasal HMSC.

P18

## Small cell neuroendocrine carcinoma of nasopharynx in an adult: a case report

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Small cell neuroendocrine carcinoma is extremely rare in head and neck region and presented aggressive characteristics with a poor prognosis. Due to the rarity of these tumors, no specific treatment exists at present. To our best knowledge, only 7 cases of primary nasopharyngeal small cell carcinoma have been reported in English literature. We report a case of 47-year-old man with a progressive left neck tumor for 1 month with progression. He also presented repeated episodes of blood-tinged sputum. A 2.5 cm hard fixed tumor was noted at left neck level II. Head and neck magnetic resonance imaging showed an extensive tumor of bilateral nasopharynx, with the invasion to bilateral parapharynx, prevertebral muscle, left medial pterygoid muscle, clivus and metastases to left retropharyngeal space and left neck level II-III-V with extranodal extension. Biopsy of nasopharyngeal tumor was performed and pathology showed malignancy and immunohistochemically positive for CK, TTF-1 and synaptophysin, and negative for chromogranin-A and p16. EBV in situ hybridization (EBER) is negative. Small cell neuroendocrine of nasopharynx was confirmed. The patient received induction chemotherapy and concurrent chemoradiotherapy. No local recurrence or distant metastasis was noted during 10 months of follow-up.

P48

## Early mobilization after microvascular free-flap reconstruction for head and neck cancer

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**Objectives:** Large defect after head and neck cancer resection are usually reconstructed with microvascular free flap. Postoperative mobilization is recommended to decrease pulmonary complications and overall length of stay. But many microsurgeons hesitate about the mobilization protocols due to the risk of flap failure. The aim of this study was to determine whether early postoperative mobilization affected microvascular flap outcome and post operation complications.

**Methods:** 88 consecutive patients were enrolled in the study from November 2015 to December 2016. All patients were treated with head and neck cancer resection and microvascular free flap reconstruction. The microvascular reconstructions were all performed by the same surgeon. We changed the postoperative mobilization protocol from post-operation day 7 to day 4 on July 2016. The post-operative complications, length of hospital stay and flap condition were compared between early and late mobilization.

**Results:** The flap failure was no significant difference between early mobilization group (1/45) and late mobilization group (2/43). The incidence of pulmonary complications and the length of hospital stay were both increased in late mobilization group.

**Conclusion:** Early mobilization (before 4 days post-operation) does not increase flap failure rates. Besides, it can reduce pulmonary complications and hospital stay.

P49

## Perivascular epithelioid cell tumor (PEComa) of major salivary gland

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Perivascular epithelioid cell tumors (PEComa) are defined by the “mesenchymal tumors composed of histologically and immunohistochemically distinctive perivascular epithelioid cells” that coexpress muscle (actin and/or desmin) and melanocytic markers (HMB-45 and/or melan-A). The family includes angiomyolipoma (AML), clear cell sugar tumor of the lung (CCST), lymphangiomyomatosis (LAM), and very rare tumors in other locations. The most common reported anatomic site of involvement of PEComa-not otherwise specified (PEComa-NOS) is the uterus, followed by the Gastrointestinal tract (GI) tract. It is proved to be women predominant, occasionally associated with tuberous sclerosis complex (TSC). Few cases of PEComas behave in a malignant potential and the main strategy is to complete resection. We report the case of a 31-year-old woman, who presented with left infra-auricular mass rapid growth in 3 weeks. Imaging studies demonstrated a relatively well-demarcated mass, measuring approximately 27 mm in diameter, located in the left parotid gland. We performed tumor excision, Endoscopic assisted. Due to the frozen section showed malignancy during operation, she underwent left total parotidectomy. The final pathology diagnosis showed Left Parotid gland, TFE3-rearranged Perivascular epithelioid cell tumor (PEComa). To the best of our knowledge, this is the first case of PEComa which has been reported in the literature in the world located in major salivary gland.

**Poster**    Laryngology

P19

**Laryngopharyngeal reflux image quantization and analysis of its severity**

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Laryngopharyngeal reflux (LPR) is a prevalent disease affecting a high proportion of patients seeking laryngology consultation. Diagnosis is made subjectively based on history, symptoms, and endoscopic assessment. The results depend on the examiner's interpretation of endoscopic images. There are still no consistent objective diagnostic methods. The aim of this study is to use image processing techniques to quantize the laryngeal variation caused by LPR, to judge and analyze its severity. This study proposed methods of screening sharp images automatically from laryngeal endoscopic images and using throat eigenstructure for automatic region segmentation. The proposed image compensation improved the illumination problems from the use of laryngoscope lens. Fisher linear discriminant was used to find out features and classification performance while support vector machine was used as the classifier for judging LPR. Evaluation results were 97.16% accuracy, 98.11% sensitivity, and 3.77% false positive rate. To evaluate the severity, quantized data of the laryngeal variation was used. LPR images were combined with reflux symptom index score chart, and severity was graded using a neural network. The results indicated 96.08% accuracy. The experiment indicated that laryngeal variation induced by LPR could be quantized by using image processing techniques to assist in diagnosing and treating LPR.

P20

**Two case of bilateral vocal cord paralysis as an early manifestation of multiple system atrophy**
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Multiple system atrophy (MSA) is a neurodegenerative disease with cerebellar, autonomic symptoms and parkinsonism as three significant signs. The prevalence of MSA is 7-10 per 100,000 population, which is not a rare disease among neurodegenerative diseases.

MSA is known to be associated with vocal cord paralysis, and its onset often occurs during the progression of the disease and rare in the early stage of the disease. Here, we report two cases of MSA whose initial symptoms was bilateral vocal cord paralysis (BVP).

Case 1: A 67-year-old woman presented to our hospital with a chief complaint of stridor and respiratory distress. Laryngeal fiberscope revealed BVP. She had no symptoms other than stridor and respiratory distress. Considering the possibility of central BVP, we consulted with the neurology department. Examinations at the neurology department determined autonomic neuropathy, followed by the diagnosis of MSA. Four months later, she received tracheotomy because of exacerbation of respiratory distress.

Case 2: A 77-year-old man presented to our hospital with a chief complaint of stridor. Laryngeal fiberscope revealed bilateral vocal cord paralysis. A detailed examination was performed at the neurology department, but no obvious abnormality was observed. One year later, he underwent Elnell's Operation at another hospital. Three years after surgery, he complained of symptoms suspected of autonomic dysfunction. He was examined again by the neurology department and diagnosed as MSA.

As shown in these 2 cases, it is noteworthy that bilateral vocal cord paralysis can be the FIRST clinical sign of MSA. The acute exacerbation of by BVP can cause the sudden death of MSA patients. An otolaryngologist needs to have MSA as the differential diagnosis of solo BVP without any other neurological symptoms. So if BVP exacerbates, a tracheotomy can increase their QOL and avoid sudden asphyxia. We should perform tracheotomy at an appropriate time for patients with BVP. Also, early diagnosis of MSA can give patients a chance to treat their cerebellar symptoms by Taltirelin Hydrate.

Poster Oral / Pharyngeal

P21

## Associations between age and postoperative complications following tonsillectomy, Histopathological study

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**Background:** Tonsillectomy is one of the most commonly performed surgical procedure for otolaryngologists. There is a significant literature on complication rates from a tonsillectomy in the pediatric patients but not adults. In the previous report of about associations between age and postoperative complications in Taiwan, the rates of readmission for any reason was positively correlated with age. By contrast, the rates of bleeding-related readmission and re-operation for bleeding were inversely correlated with age. However, in the previous US reports, the adult tonsillectomy patients have a higher bleeding rate than pediatric patients after the surgery. In the previous Japanese reports, male, obesity, age, surgeon's skill level (beginner), and use of epinephrine during the surgery were risk factors of post-operative hemorrhage.

**Objective:** The aim of this study is to investigate the associations between age and postoperative complications, including post-operative bleeding following tonsillectomy.

**Material and methods:** A retrospective study of 295 patients who underwent a tonsillectomy in our Hospital from 2016 to April 2019 was conducted. The obtained data were statistically analyzed using the Excel and Stat Mate III. We also examined the effects of aging on tonsillectomy using the surgical specimens.

**Results and Conclusion:** All operated patients were admitted, with a postoperative average length of stay in-hospital stay (LOS) of seven days. No statistically significant differences were detected associating ages and the LOS. The surgical time tended to longer with age, but it was not statistically significant. Post-operative bleeding, including minimal hemorrhage was observed 29 of 295 (9.8%) patients performed tonsillectomy. Nine bleeding cases (3%) needed for the re-operation under the general anesthesia. Among the 115 case of tonsillectomy for chronic tonsillitis, post-operative bleeding, including minimal hemorrhage was observed 23 patients (20%). Nine bleeding cases (8%) needed for the re-operation under the general anesthesia. The results showed chronic tonsillitis patients have a higher post-operative bleeding rate than other patients after the tonsillectomy. These results suggest that the adhesion of the Palatine tonsil and the surrounding tissue might be the cause of post-operative complications including post-operative bleeding. Therefore, we hypothesized that the reason for post-operative complications and post-operative bleeding could be found in surgical specimens. We examined the relationship between age and the factors such as adhesion of muscle tissue and inclusion minor salivary gland in the surgical specimens. Although no useful results were obtained, the findings of the surgical specimens might be related to the skill level of the operator.

P22

## A case of SAPHO syndrome: tonsillectomy as an effective treatment for arthralgia

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### Introduction:

SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) syndrome was proposed in 1987 to describe a clinicoradiological entity manifesting in the joints, skin, and bones. SAPHO syndrome is characterized by (a) hyperostosis or chronic recurrent multifocal osteomyelitis or (b) other osteo-articular symptoms associated with dermatologic conditions, such as acne or palmoplantar pustulosis (PPP).

We describe the case of a patient with SAPHO syndrome for whom bilateral tonsillectomy was effective for the treatment of arthralgia, which was quantified using multiple pain scales such as the visual analog scale (VAS), the revised version of Short-Form McGill Pain Questionnaire (SF-MPQ-2), and the pain disability assessment scale (PDAS).

### Case report:

A-75-year old woman presented with arthralgia in both wrists, shoulders, upper limbs, and ankles and complained of having difficulty in walking and housework. A diagnosis of SAPHO syndrome was made based on dermatological manifestation and thickened sternoclavicular joints. Symptoms did not respond to celecoxib, methotrexate, and adalimumab, an anti-TNF drug. After bilateral tonsillectomy, her arthralgia and skin symptoms were dramatically improved. Prior to the tonsillectomy, the VAS, SF-MPQ-2, and PDAS scores were 30, 37, and 28, respectively. At 3 months after tonsillectomy, the methotrexate dose could be reduced, and the patient showed significant improvement of skin symptoms. The postoperative VAS, SF-MPQ-2, and PDAS scores were 20, 7, and 19, respectively. At 6 months after tonsillectomy, the patient no longer needed celecoxib. The VAS, SF-MPQ-2 and PDAS scores were 10, 4, and 14, respectively.



P23

## Expression of interleukin-33 is correlated with poor prognosis in patients with squamous cell carcinoma of the tongue

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Inflammation plays a crucial role in cancer development and progression. Release of interleukin-33 (IL-33) results due to inflammation and IL-33 can affect various inflammatory cells that express its receptor ST2 including mast cells. The aim of this study was to clarify the role of IL-33 in tumour progression. Surgical specimens from 81 patients with tongue squamous cell carcinoma (SCC) were studied by immunohistochemistry. Primary tumour sections were examined for the expression of IL-33 and ST2. To examine the influence of IL-33 on the microenvironment of the tumour, stromas were examined for the mast cell density (MCD) and microvessel density. The high IL-33 group had significantly worse prognosis ( $p = 0.004$ ). IL-33 expression was significantly elevated in the cases with local recurrence and nodal recurrence ( $p = 0.014$  and  $p = 0.019$ ). ST2 expression was also associated with worse prognosis ( $p = 0.024$ ) and significantly elevated in the cases with nodal recurrence ( $p = 0.004$ ). MCD was associated with worse prognosis ( $p = 0.038$ ), and IL-33 expression was significantly correlated with MCD ( $r = 0.626$ ,  $p < 0.001$ ). Microvessels in the stroma were significantly increased in the high IL-33 group ( $p < 0.001$ ). These data suggest that IL-33/ST2 axis contributes to tumour aggressiveness through not only affecting tumour itself but also microenvironment of tumour. The evaluation of IL-33 and ST2 expression by immunohistochemistry is useful for identifying those patients at a high risk for a poor prognosis.

P24

## The effects of HBXIP on the Biological Functions of TSCCa Cell Line

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Oral cancer is one of the 10 most common cancer with high mortality rate in the world, and TSCC (Tongue squamous cell carcinoma) is most malignant in oral cancer. TSCCa cells were transfected with HBXIP plasmid. The cells were divided into an experimental group (transfected with pEGFP-N1-HBXIP plasmid), a control group (untransfected group) and a vector control group (vector group, pEGFP-N1). The effects of HBXIP overexpression on the proliferation, migration, and invasion of TSCCa cells were measured by MTT assay, transwell assay and scratch test, respectively, and the effects of HBXIP mRNA overexpression on the protein expression levels of AKT, p-AKT, PI3K, p-PI3K and S100A4 were detected by western blotting. The results of the MTT assay showed that there were significantly more cells that proliferation in the experimental group than in the control groups ( $P < 0.05$ ). Based on the results of the scratch test, the migration rate was remarkably greater in the experimental group than in the control groups ( $P < 0.01$ ). As shown by the results of the transwell assay, the number of invading cells in the experimental group was clearly higher than that in the control groups ( $P < 0.001$ ). The results of western blotting revealed that the expression levels of p-AKT, p-PI3K and S100A4 were increased in the experimental group after HBXIP overexpression. HBXIP mRNA overexpression can influence the proliferation, invasion, and migration of TSCCa cells and promote their proliferation and migration by increasing the protein expression levels of p-AKT, p-PI3K and S100A4.

P25

## Analysis of AEBP1 in the microenvironment of head and neck squamous cell carcinoma

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We have identified AEBP1 as a novel cancer stroma-related gene in colorectal carcinoma and found that AEBP1 may play an important role in tumor development. In this study, we aimed to unravel the role of AEBP1 in head and neck squamous cell carcinoma (HNSCC). Analysis using The Cancer Genome Atlas (TCGA) datasets of primary HNSCC (n = 559) revealed that higher expression of AEBP1 is associated with worse overall survival. Immunohistochemistry in primary HNSCC tissues showed that AEBP1 is strongly expressed in CAFs than in normal fibroblasts in non-cancerous regions. We isolated cancer associated fibroblasts (CAFs) from surgically resected HNSCC tissues. Treatment of CAFs with tumor conditioned medium (TCM) derived from a HNSCC cell line upregulated AEBP1 transcript, suggesting that HNSCC cells could activate AEBP1 expression in CAFs. Gel contraction assay revealed that knock down of AEBP1 in CAFs suppressed gel contraction potency, suggesting that AEBP1 is associated with the activity of CAFs. Our results suggest that AEBP1 may play an important in HNSCC via activating CAFs, and that it could be a potential therapeutic target.

Poster Others

P26

# Sublingual immunization with phosphorylcholine reduces antigen specific IgE levels and nasal symptoms in allergic rhinitis model mice

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**Aims:** Phosphorylcholine (PC) is a structural component of a wide variety of pathogens. Recently, we showed that intranasal or sublingual immunization of mice with PC induced PC-specific mucosal as well as systemic immune responses in upper respiratory tract, suggesting that intranasal or sublingual immunization with PC might be effective to prevent upper airway bacterial infections. Moreover, Th1-type immune responses such as IFN-gamma production were predominant in sublingual immunization compared to intranasal immunization, indicating that sublingual immunization might be effective to reduce type I allergic reaction such as allergic rhinitis which is concerned in mucosal immunization. In fact, sublingual immune therapy has been used for the treatment of allergic rhinitis. However, the mechanism how sublingual immunization with PC reduces type I allergic rhinitis is not yet clarified. The purpose of this study is to investigate the influence of sublingual immunization with PC on ovalbumin-induced allergic rhinitis model in mice.

**Methods:** Female BALB/c mice were sublingually immunized with PC-keyhole limpet hemocyanin (KLH) or phosphate-buffered saline as control once a week for three consecutive weeks. After the final immunization, samples of serum were collected. Following sublingual immunization with PC, each group mice were sensitized with OVA conjugated with alum by intraperitoneal inoculation with OVA and challenged by intranasal administration with OVA. Five minutes after the last challenge, the number of nasal symptoms was counted to evaluate the severity of allergic rhinitis. Antigen-specific antibody titers including IgE in serum were measured by ELISA. The number of eosinophils infiltrating into nasal mucosa and epithelial damages on nasal mucosa were determined. The production of antigen-specific cytokine on CD4 positive T cells collected from cervical lymph node and spleen was measured by ELISA.

**Results:** PC-specific IgG in serum were significantly increased in PC-treated group. Nasal symptoms, the number of eosinophils infiltration, mucosal damages and OVA-specific IgE production in PC-treated group was significantly decreased compared with PBS-treated group. Antigen-specific TGF- $\beta$ 1 production from cervical lymph nodes and spleen was significantly enhanced.

**Conclusion:** Sublingual immunization with PC might be useful to prevent the occurrence of allergic rhinitis as well as bacterial upper respiratory infection.

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# Unique profiles of lesional B cell subsets underlie the pathogenesis of IgG4 related disease

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**Rationale:** IgG4-related disease (IgG4-RD) is a chronic fibro-inflammatory disease characterized by elevation of serum IgG4 level and infiltration of IgG4<sup>+</sup> plasma cells in various affected organs. However, the underlying immunological mechanisms involved in IgG4-RD remain unclear. In this study, we examined B cell subsets in lesions of IgG4-RD to address this issue.

**Methods:** B cells subsets in tissues of submandibular glands (SMGs) from patients with IgG4-RD and tonsils from patients with tonsillar hypertrophy were characterized by flow cytometry, and their results were compared. Correlations between results obtained by flow cytometry and clinical parameters related to IgG4-RD were also analyzed.

**Results:** The percentages of naive B cells (CD3<sup>-</sup>CD19<sup>+</sup>CD27<sup>-</sup>IgD<sup>+</sup>) and germinal center B cells (CD3<sup>-</sup>CD19<sup>+</sup>CD20<sup>+</sup>CD38<sup>+</sup>) in SMG from patients with IgG4-RD were significantly larger than those in tonsils from patients with tonsillar hypertrophy. In contrast, the percentage of memory B cells (CD3<sup>-</sup>CD19<sup>+</sup>CD27<sup>+</sup>IgD<sup>-</sup>) in IgG4-RD SMGs decreased compared with that in tonsils. Further analysis showed that there were marked positive correlations of the percentage of plasmablasts (CD3<sup>-</sup>CD19<sup>+</sup>CD24<sup>lo</sup>CD38<sup>hi</sup>) with number of involved organs. Moreover, the percentage of CD20<sup>+</sup> cells (CD3<sup>-</sup>CD19<sup>+</sup>CD20<sup>+</sup>) was positively correlated with number of involved organs, serum IgG level, serum IgG4 level and serum IgG4/IgG ratio, respectively.

**Conclusions:** Unique patterns of B cell subset population were observed in lesions of IgG4-RD. Plasmablasts and CD20<sup>+</sup> cells are increased in IgG4-RD SMGs, and their percentages are correlated with clinical manifestations of IgG4-RD. Further analysis of lesional plasmablasts and CD20<sup>+</sup> cells in IgG4-RD may lead to a deeper understanding of the pathogenesis of persistent inflammation and aberrant activation of humoral immune responses in IgG4-RD.

P28

## CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea have similar effect as uvulopalatopharyngoplasty

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**Objective:** Obstructive sleep apnea (OSA) is a risk factor of cardiovascular diseases. The continuous positive airway pressure (CPAP) could be the main treatment for OSA and the sleep surgery such as uvulopalatopharyngoplasty (UPPP) could be an alternative solution. In this study, we aim to compare the difference of preventing cardiovascular events for OSA patients between CPAP and UPPP treatment.

**Methods:** This study is retrospective cohort study of cardiovascular events of OSA. The 413 patients (age $\geq$ 35 years) who received treatments either CPAP or UPPP in Shuang Ho Hospital between 2009 to 2016 were enrolled. Data of characteristics, comorbidities, PSG reports were also collected. The CPAP group (n=199) and the UPPP group (n=91) divided into two groups based on whether major adverse cardiovascular events (MACEs) occurred before treatment, respectively. The primary end points of this study were all-cause death or newly diagnosis of myocardial infarction, stroke, heart failure, atrial fibrillation, ventricular fibrillation and coronary artery bypass graft.

**Results:** Of 290 OSA patients, most were male and the patients in CPAP group were significantly older (mean: 51.7 v.s. 45.8), had significantly higher proportion of DM, HTN and CVD, longer follow-up time (1542.5 v.s. 1052.4), higher BMI (29.8 v.s. 27.7), higher RDI (53.0 v.s. 44.0), higher NONREMAHI (52.7 v.s. 43.9), higher AI (157.6 v.s. 91.6), lower sleep latency (18.1 v.s. 31.1), lower MeanSAT (92.9 v.s. 94.7) and higher event rate (41.0 v.s. 26.7 person-years) than those in UPPP group. In Kaplan-Meier analysis, there was no difference in cumulative survival rate between the CPAP group and the UPPP group. Further, we divided two groups into four groups based on whether MACEs occurred before treatment, and the cumulative survival rate were no significant difference across these four groups.

**Conclusion:** Therapy with CPAP, as compared with UPPP, had similar effect for preventing cardiovascular events in patients with obstructive sleep apnea.

**Keywords:** obstructive sleep apnea (OSA); continuous positive airway pressure (CPAP); uvulopalatopharyngoplasty (UPPP); cardiovascular disease.

P29

## OSA patient with Vertigo have higher risk of REM OSA

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### OBJECTIVES

In recent population-based case-control studies, sleep apnea was significantly associated with a higher incidence (hazard ratio, 1.71) of vertigo. The purpose of this study was to investigate the difference between OSA patient with vertigo and without vertigo.

### METHODS

The collected data among patients from May 1st, 2018 to October 31st, 2018 at Shuang Ho Hospital. Eligibility criteria included an age older than 20 years, a diagnosis of obstructive sleep apnea. The diagnosis of OSA was defined as an respiratory disturbance index of at least 5, was established with the use of PSG at hospital. Patients who had idiopathic vertigo were labeled as vertigo group. In the other hand, patients who had no vertigo were labeled as control group. 58 patients were in the vertigo group, and 113 were in the control group.

### RESULTS

171 OSA patients were included, 58 patients who had idiopathic vertigo (29 males, average age=57.07 years old, BMI= 26.64, RDI=24.69, N3=2.78%, ESS=8.65), and 24 patients of them (41.3%) were REM OSA (REM RDI/NREM RDI >2 and NREM RDI <15). In the control group, 113 patients had no vertigo (92male, average age=49.66 years old, BMI= 26.06, RDI=35.19, N3=4.34%, ESS=11.43), and 18 patients of them (15.9%) were REM OSA. In our study, OSA patient who had idiopathic vertigo would have higher proportion of REM OSA (P <0.001).

### CONCLUSIONS

The OSA patient with vertigo have higher rate of REM OSA, and the acceptance rate to continuous positive airway pressure (CPAP) in REM OSA is low (3.4% vs 40.7%). Further research is needed to explore novel therapeutic approaches, or combination of currently available non-CPAP therapies, especially in patients with REM OSA. Besides, female OSA with vertigo and no daytime sleepiness (Epworth Sleepiness Scale <10) have the odds ratio of 35 to REM OSA.

## P30

## Omni-suspension of the Soft Palate with Coblation Ablation of the Tongue (OSCA) for Obstructive Sleep Apnea

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**Background:** Omni-suspension of the soft palate with coblation ablation of the tongue (OSCA) was designed to treat obstructive sleep apnea (OSA) patients with the concentric collapse of the velopharynx and anterior-posterior collapse of the tongue during durg-induced sleep endoscopy.

**Objective:** The objective of this study was to investigate the feasibility, safety and effectiveness of OSCA in a specific group of OSA patients.

**Method:** This case series study included 30 consecutive adults OSA patients. Key techniques of OSCA are tonsillectomy with preservation of pillar mucosa, full layer (palatopharyngeus, superior pharyngeus constrictor, palatoglossus muscles) sutures of tonsillar fossa with lateralization from inferior pole, suspension of palatopharyngeus muscle to pterygomandibular raphe via through and through figure of eight fixation model at upper, middle and lower raphe, coblation ablation of the middle tongue anterior to circumvallate papilla for 12 points.

**Results:** No patient experienced postoperative bleeding, airway compromise and persistent nasal regurgitation or hypernasality following OSCA. Postoperative pain profile showed average mild pain and odynophagia scores. Perioperative snoring severity (visual analogue scale) and daytime sleepiness (Epworth Sleepiness Scale) improved significantly. Polysomnography showed that apnea-hypnea index and minimal saturation improved significantly. Cephalometry revealed significant increase of posterior air space at the retropalatal area and retroglossal areas. Thickness and length of the tongue decreased significantly.

**Conclusion:** Our preliminary findings show that OSCA seems to be feasible, safe and effective in treating OSA patients with both palate and tongue obstruction. However, further studies including a large number of patients and control group are warrant to clarify the individual role in this combined surgery.

## P31

## Applications of Portable Ultrasound in Remote Medical Care- Cathay Medical Mission Team in Fiji

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Portable ultrasound machines are typically used in situations where space is limited, mobility is important, or the scanning must be done in the field. Currently portable ultrasound machines are used in Cardiac, Vascular, Radiology, Endocrinology, Pediatric and OB/GYN applications. Handheld ultrasound (US) machines are also increasingly being used in the diagnostic utility for trauma encountered in the battlefield. Furthermore, US guidance may assist in the performance of some procedures performed in battlefield medical care. In addition, EMS(emergency medical services) personnel from several countries have used portable ultrasound evaluations in the field. Our Cathay medical mission team started from 2014 and there had been 11 times of our medical services in Fiji. Portable Ultrasound Applications were used in otorhinolaryngology (ENT), radiology and anesthesiology and pain clinic section. In ENT field, we used it for thyroid surgeries pre-operative evaluation. The radiologist also used it for diagnosis and neural and general intervention. For anesthesiologist, it is helpful with portable ultrasound assisting in pain clinic evaluation.



P32

## Influence of vascular risk factors on balance function in a community-dwelling population in Japan

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**Background and Objectives:** Balance function deteriorates with age, and postural balance disorders in older people lead to falls. Moreover, falls are the leading cause of hospital admission or accidental death, and can lead to decline in activities of daily living (ADL) and quality of life (QOL). Therefore, in an aging society, balance function is important in maintenance of the ADL and QOL in older people. The mechanisms of balance dysfunction are complex and multifactorial. Recently it has been suggested that increased vascular risk factors are associated with dizziness and falls, but it has not been fully elucidated. The purpose of this study was to examine the relationships between balance function and vascular risk factors.

**Materials and Methods:** We included volunteers who had participated in the Iwaki Health Promotion Project. In total, 1,051 subjects (404 men, 647 women) were included in the analysis. We evaluated balance function by using static posturography. We conducted the examination twice, first with the subjects' eyes open and then with their eyes closed. We used sway length (the total length determined from the sway path) for analysis. And we evaluated vascular risk factors such as blood pressure, lipid values, haemoglobin A1c (HbA1c), and brachial-ankle pulse wave velocity (baPWV). Multiple linear regression analysis was used to examine the effects of vascular risk factors on the sway length.

**Results:** In both men and women, age and HbA1c were significantly related to sway length. Only in women, baPWV was also significantly associated with sway length.

**Conclusions:** The results of this study suggested that diabetes affected the balance function in both men and women. Postural instability in diabetic patients is assumed to be attributed to the absence of accurate peripheral sensory information from the feet. Furthermore, only in women, it was suggested that progression of arteriosclerosis causes balance dysfunction. Arteriosclerosis are expected to cause impaired blood flow not only in the central nervous system but also in peripheral blood vessels such as the vestibule, which leads to balance dysfunction.

P33

## A patient with intractable dizziness during psychiatric hospitalization whose condition improved with eperisone hydrochloride: a case report

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Eperisone hydrochloride is a drug that has been developed as a central muscle relaxant, but also has analgesic and vasodilatory effects.

We report a case in which eperisone hydrochloride was administered to an intractable dizziness patient with headache and stiff shoulders admitted to a psychiatric department with a diagnosis of anxiety disorder.

The patient was a 39-year-old woman. She experienced dizziness and breathlessness, which appeared due to the stress of human relationships in the workplace since two years prior to presentation at our clinic. Medication began at a nearby doctor's mental clinic. An increase in dizziness and anxiety occurred since 5 months ago. She was diagnosed with anxiety disorder and psychiatrically hospitalized. At the hospital, she was treated with anti-anxiety drugs and antipsychotic drugs. However, her condition did not improve. During hospitalization she was referred to our department. She had dizziness, bilateral tinnitus and headache, but neurological examination was completely unremarkable. Nystagmus was absent.

The Dizziness Handicap Inventory (DHI) score was 84 points and the Hospital Anxiety and Depression Scale (HADS) was 37 points.

Differentiating diagnosis revealed inner ear dizziness or vestibular migraine. She was treated with betahistine mesylate, isosorbide, and ATP. Treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) was started, but was unsuccessful with no change in symptoms.

She was strongly complaining of stiff shoulders, and when eperisone hydrochloride was prescribed at 150 mg/day, dizziness significantly reduced and tinnitus disappeared. DHI and HADS scores also improved.

Currently, prescription is continued in the psychiatric department where she was hospitalized.

In this case, the cause of dizziness is thought to be due to the cervical circulatory disturbance due to the tension caused by mental stress, and the stiff shoulders were getting worse.

Eperisone has been reported to improve vertebral artery blood flow and to suppress vestibular nucleus neurons, and is effective in dizziness patients with stiff shoulders.

## Poster

## Otology

P34

**vHIT usefulness in the patients with unstable vestibular compensation**

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If a unilateral semicircular canal function is highly impaired, not only the semicircular canal function of the affected side, but the function of the healthy side is also decreased temporarily. This phenomenon is known as a vestibular compensation. Vestibular compensation is one of the important reaction to relieve the unpleasant symptoms in the acute phase of the vestibular dysfunction. However, it is not well known that the vestibular compensation may be unstable due to the “overcompensation” or “decompensation” in some patients. One of the reasons is that the caloric test, a general semicircular canal function test, is a time consuming and difficult to perform repeatedly.

video Head Impulse Test (vHIT) is one of the semicircular canal function test that is easy to perform, and takes only a few minutes. Here, we report two cases of Hunt syndrome who had complicated clinical courses because of the unstable vestibular compensation. To measure the vestibular function using vHIT, the findings of vHIT were dramatically changed with clinical course. As a result, we could understand the complicated clinical course with the unstable vestibular compensation in detail. We consider that vHIT is a useful tool for understanding temporal changes in the vestibular function.

P35

**Immunohistological analysis of myeloid dendritic cell in the model animals of eosinophilic otitis media**

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Background: Eosinophilic otitis media (EOM) is known as an intractable otitis media characterized by eosinophil enriched highly viscous middle ear effusion. EOM shares many aspects of pathophysiology with bronchial asthma (BA) which is known as Th2-type allergic inflammatory disease. Recent studies have been revealed that epithelial derived cytokines such as thymic stromal lymphopoietin (TSLP) act as an initiator of Th2-type allergic reaction. However, the pathway how TSLP initiates Th2-type allergic reaction in EOM remains unknown. Myeloid dendritic cells (mDCs) has been highlighted as one of the essentials in the cascade of Th2 allergic inflammation. It has been reported that CD11c+mDCs are activated by TSLP and induce an immune response by producing Th2-related cytokines. However, it is unknown whether CD11c+mDCs are involving in allergic reaction in EOM. In the present study, we investigated the immunoreactivity of CD11c and TSLP receptor (TSLPR), exploring the distribution and co-localization of TSLPR and mDCs in animal model of EOM.

Methods: After three times weekly intraperitoneal injection of OVA to Hartley guinea pigs as general sensitization, daily application of intratympanic OVA stimulation to the right ear was performed for 7 days and for 14 days. Saline was injected to the left ear which was used as control. Immunostaining and double immunofluorescent staining for CD11c and TSLPR were performed. The sections were observed to detect the immunopositive cells and their distribution.

Results: We found CD11c immunopositive cells in the submucosal area of the middle ear epithelium, particularly in the submucosal area around eustachian tube. The number of CD11c positive cells was significantly larger than control side. Immunopositive cells for TSLPR showed similar distribution with CD11c positive cells.

Conclusion: We speculate that CD11c and TSLPR positive cells observed in this study are DCs. The result of the present study suggests that TSLP stimulates CD11c + DCs in the submucosal area of the middle ear epithelium and DCs in turn induce Th2-type immunoreaction in animal model of EOM.

P36

## Cochlear implantation in a case of POU4F3 gene mutation

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### Introduction

The *POU4F3* gene encodes in a transcription factor specifically expressed in inner hair cells, and it is responsible for autosomal dominant nonsyndromic hereditary hearing loss (HL). In Japan, 12 types of variants have been reported in 15 families and 24 cases by Kitano et al.(2017). However, the onset age and progression of deafness vary, and there are few reports about detailed clinical features of patients. Here we describe the case of a 51-year-old male suffering from bilateral progressive HL caused by a *POU4F3* mutation.

### Case report

The patient has never indicated HL on medical examination, but he has been aware of bilateral HL since 40 years old. At the age of 47, on his first visit to the Tokyo Medical University Hospital, the pure-tone average was 83.8 dB for the right ear and 85 dB for the left ear. He has a family history of HL. His mother has been experiencing HL since her 30s, and his brother has been experiencing since his 10s. However, his two daughters have normal hearing. After the first visit, HL gradually progressed to 90dB for the right ear and 92dB for the left ear over a period of two and a half years and left cochlear implant (CI) surgery was performed at the age of 51 years. The hearing threshold with CI was 25 dB, and maximum speech discrimination score was 75% at 65 dB SPL. The residual hearing has been preserved completely till 6 months post-operatively, but residual hearing was suddenly lost.

### Conclusion

Although mutations in the *POU4F3* gene are known to cause progressive HL, there are few reports about the rate of progression. Pauw et al. (2008) reported that the mean rate of HL progression was 0.8 dB / year and that HL progressed relatively slowly. However, in this case, this patient became profound HL gradually within about 10 years after becoming aware of HL with relatively quick progression. In addition, conditions indicative of rapid HL, such as sudden deafness, were recognized. Thus, the pattern of HL progression is diverse. *POU4F3* is expressed specifically in the inner ear. Patients with HL due to *POU4F3* mutation are considered good candidates for CI. However, there is no detailed report on the outcome after CI surgery for HL due to *POU4F3* mutations. The hearing result with CI surgery in the present case support the usefulness of CI surgery for HL due to *POU4F3* mutation.

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## Cochlear implantation with local anesthesia

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Due to the aging society, cochlear implant surgery for the elderly is increasing. For this reason, sometimes we have to suspend the surgery due to the risk of general anesthesia associated with aging and complications. We report on an elderly patient with profound hearing loss and respiratory dysfunction underwent cochlear implantation under conscious sedation with local anesthesia. The operation was performed with a cervical plexus block and conscious sedation with dexmedetomidine. No complications were observed. The postoperative audiological tests showed a significant improvement in the hearing perception. The perioperative course was augmented by the ability to communicate closely with the patient and surgical team. Further experience with cases and establishment of anesthesia is expected.

Key words: elderly, cochlear implantation, local anesthesia

P38

## Hyperbaric oxygen with steroid and prostaglandin E1 for idiopathic sudden sensorineural hearing loss

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### Objective:

The pathogenesis of ISSNHL is not distinct; thus, various treatments have been attempted. The efficacy of hyperbaric oxygen therapy (HBOT), systemic corticosteroids, and prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) has been assessed. However, little is known about the efficacy of HBOT combined with systemic corticosteroids and PGE<sub>1</sub>. Consequently, we aimed to investigate the efficacy of the combination HBOT with conventional corticosteroid and PGE<sub>1</sub> treatment in patients with severe ISSNHL.

### Methods:

We recruited 35 patients with ISSNHL who had been treated with systemic corticosteroid and PGE<sub>1</sub>, either with HBOT (n=24) or without HBOT (n=11). The systemic corticosteroid prescribed was prednisolone. The dose of prednisolone was tapered over 7 days as follows: 60mg/day (30mg twice daily) for the first 3 days, followed by 30mg/day (15mg twice daily) for 2 days, and 15mg/day (15mg once daily) for the last 2 days. PGE<sub>1</sub> (40μg for 7 days) was dissolved in 200mL of saline and administered by intravenous drip infusion. HBOT was administered at a pressure of 2 atmosphere absolute (ATA) for 60min once daily for 10 days. Inclusion criteria were 15 years old or older, ISSNHL diagnosed within 14 days of onset, with severe hearing loss (arithmetic mean hearing of 250, 500, 1000, 2000, and 4000Hz ≥ 60dB), and clinical follow-up of at least 1 month. Patients' hearing level was evaluated 1 month after hearing loss onset. The main outcome was hearing improvement, assessed with pure tone audiometry. We also evaluated patients' sex, age, date of birth, affected side, the interval between onset and treatment, incidence of vertigo, presence of diabetes mellitus, and presence of hypertension.

### Results:

There were no significant differences in the initial pure tone hearing level and pure tone hearing levels at every frequency between the two groups. However, the patients were significantly younger ( $p < 0.05$ ) in the HBOT group ( $56.3 \pm 3.0$  years) than those in the No-HBOT group ( $71.0 \pm 4.0$  years).

The hearing improvement for patients treated with systemic corticosteroid therapy and PGE<sub>1</sub> therapy combined with HBOT ( $41.5 \pm 4.5$  dB) was significantly greater ( $p < 0.05$ ) than for those without HBOT ( $24.7 \pm 6.3$  dB), especially at the low frequencies (125Hz and 250Hz). (mean  $\pm$  1SEM)

### Conclusion:

These findings suggest that HBOT conferred a significant additional therapeutic benefit for severe ISSNHL when combined with systemic corticosteroid therapy and PGE<sub>1</sub> therapy, especially at the low frequencies.

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## Degradation and modification of cochlear gap junction proteins are crucial in early development of age-related hearing loss

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**BACKGROUND:** AHL (Age-related hearing loss) is defined as a progressive, bilateral, high-frequency hearing loss in elderly people. Connexin (CX)26 is one of the major protein subunits to form gap junctions in the cochlea. Mutations in CX26 are one of the most common causes of inherited nonsyndromic deafness. The relationships between CX26 and AHL are not fully understood. Here, we investigated the CX26 quantitative change and molecular pathology of AHL.

**METHODS:** C57BL/6J mice were used as a representative model of AHL. The hearing levels were evaluated by ABR (auditory brainstem responses). We investigated the formation of gap junction plaques in cochlear inner sulcus cells and hair cell morphology by confocal microscopy and the cochlear gap junction proteins such as CX26 and CX30 by western blotting and compared 4- and 32-week mice. Moreover, we used a biochemical approach to separate the hydrophobic and hydrophilic microdomains of cochlear membrane proteins and then quantified CX26 and CX30 in these fractions by western blotting to investigate the relationship between connexins and lipid rafts.

**RESULTS:** ABR thresholds gradually increased to 32 weeks and rapidly elevated at 36 weeks. It was suggested that the pathological progression of hearing loss in early stage accelerated between 32 weeks and 36 weeks. Therefore, 32-week-old mice were investigated as initial stage model of AHL. In immunohistochemical analysis of the cochlea in 4-week-old mice, gap junctions showed linear plaques along the cell-cell junction sites with adjacent cells. In contrast, gap junction plaques in 32-week-old mice did not show the normal linear structure but instead formed small spots around the cell-cell junction sites and gap junction lengths were significantly shorter than in 4-week-old mice. Hair cell loss were also compared between 4- and 32-week-old mice. However, their differences were not significant. In western blotting, CX26 and CX30 protein level were significantly decreased in 32-week-old mice compared with 4-week-old mice. Moreover, CX26 was more significantly enriched in the hydrophilic fraction at 4 weeks but was more significantly enriched in the hydrophobic fraction at 32 weeks, indicating an age-related conversion of this biochemical property.

**CONCLUSIONS:** These results indicated that the disruption of GJPs and hydrophobic conversion of CX26 were crucial pathogenesis of AHL occurring before the hair cell degenerations. Moreover, disruption of the gap junction plaques and decreased gap junction proteins might contribute to the onset and progression of AHL. Furthermore, the treatment targeting CX26 such as GJB2 gene therapy may be effective for AHL.



P40

## Cortical responses to the sensory conflict between visual and rotary stimuli by fNIRS

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Sensory conflict among visual and vestibular inputs elicited vertiginous sensation. In this study, the cortical hemodynamic responses to the sensory conflict between visual and horizontal rotatory stimuli were measured by fNIRS. We controlled the rotatory chair speeds and directions. The accelerated/decelerated speed in starting/ending stimulation was  $3^\circ/\text{sec}^2$  in 20 sec (rotate to the right or left) and the subject looked on the white stripe which was projected on the screen surrounding the chair during this 2 periods, the stable speed was  $60^\circ/\text{sec}$  in 80 seconds between 2 modes. After rest time, the opposite moving direction of the chair was applied. We used 2 visual stimuli: the first was the “congruent” stimulation (i.e. natural visual stimulation: the white stripes rotated contrariwise direction of the chair) and the second was the “incongruent” one (i.e. conflicted visual stimulation: the white stripe and chair rotated the same direction). The cortical responses were measured from bilateral temporal-parietal regions. Statistical analyses using NIRS-SPM software indicated that bilateral temporal-parietal junctions (TPJ) and MST area were activated in the incongruent condition.

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## Epidemiology and risk factors of mortality in hospitalised patients with sudden sensorineural hearing loss: a 14-year nationwide population-based study

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**Objective:** To conduct a 14-year nationwide study on the epidemiologic incidence in patients with sudden sensorineural hearing loss (SSNHL) and risk factors and comorbidities of its relevant inpatient mortality.

**Design:** Retrospective cross-sectional design.

**Study sample:** Data of patients hospitalized with the diagnosis of SSNHL from 2000 to 2013, extracted from the Taiwan National Health Insurance Research Database.

**Results:** In total, 31,258 patients were included. The mean age was  $50.30 \pm 16.70$  years. Males (53.5%) were more commonly diagnosed with SSNHL than females (46.5%). The patients most commonly presented with SSNHL were in the age group of 45–64 years. The crude incidence of SSNHL from 2000 to 2013 was 9.76 per 100,000 people per year. The annual incidence rate shows a steady increased from 5.15 in 2000 to 13.97 per 100,000 people in 2013 with a statistical significance ( $p < 0.001$ ). A total of 16 patients exhibited mortality with a percentage of 0.05% in patients with SSNHL and an incidence of less than 0.01 per 100,000 people per year. The risk of inpatient mortality of SSNHL is associated with older age (adjusted OR: 1.042, 95% CI: 1.009-1.077), and the presence of catastrophic illness (adjusted OR: 4.949, 95% CI: 1.290-18.996).

**Conclusion:** This 14-year nationwide study indicated an increased incidence rate of SSNHL. This study showed that inpatient mortality rate was relatively rare, but we still should be aware of its existence in patients with SSNHL. We necessitate to develop additional treatment modalities to enhance the prognosis and the clarification of the underlying mechanism of this enigmatic disease.



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## **A case of cholesteatoma associated with traumatic ear canal closure discovered 50 years after injury**

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A 79 years old woman. About one year before her coming to our department, she felt dizziness after finishing 105 days of cruising, and 6 months later, her symptoms became stronger when she got up at night. She had a history of right-sided head injury (traffic accident) 50 years ago and cerebral infarction 10 years ago. At the first visit, right ear canal obstruction, right facial palsy (30/40 in Yanagihara scale), and right conductive hearing loss were found. There were no gaze nystagmus, spontaneous nystagmus, or head positional nystagmus. In temporal bone CT findings, there was a low-density shadow filling from the external auditory canal to the tympanic cavity and the ossicular chain was eroded, but the otic capsule was intact. In diffusion-weighted MRI findings, the diffusion was suppressed remarkably at the area samed as low-density shadow area of CT. Thus, the patient was diagnosed as the cholesteatoma associated with traumatic ear canal closure, and the ear canaloplasty and tympanoplasty in the right ear were performed.

Acquired ear canal closure can be caused by trauma or inflammation, postoperative scar formation, or tumor. When the ear canal is closed, there is a risk of cholesteatoma formation due to keratinized deposits in the closed space as well as a reduction in quality of life due to conductive hearing loss. Since this case was 50 years after the trauma, cholesteatoma grew up and was developed from the external auditory canal to the tympanic cavity. A cholesteatoma grown in a closed external auditory canal is not easy to find because of the invisibility and the original hearing loss due to ear canal closure.

We experienced a case of cholesteatoma that was fortunately discovered by dizziness after disembarking. It is important to properly observe patients with traumatic ear canal closure.

Dec. 6

Poster

Rhinology

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Withdrawn

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**A case report of respiratory epithelial adenomatoid hamartoma without rhinosinusitis with improved olfaction after endoscopic sinus surgery**

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**Backgrounds:** Respiratory epithelial adenomatoid hamartoma (REAH) is a benign tumor which occurs in one or both sides of nasal septum, and the REAH is likely to be complicated with rhinosinusitis. It has been reported that olfactory dysfunction with REAH is improved after endoscopic sinus surgery (ESS), however, it is not clear whether ESS is useful in patients with REAH without rhinosinusitis. We show a case with REAH without rhinosinusitis treated with ESS to determine whether the ESS was useful for the treatment of olfactory dysfunction in the patients with REAH.

**Subjects:** A 52 years old male with REAH without rhinosinusitis was treated with the ESS at Kanazawa Medical University Hospital. T&T olfactometry, a standard olfaction test in our country, was performed before and after the surgery.

**Results:** Both of the odor detection and recognition thresholds examined with T&T olfactometry showed improvement 6 months after ESS in the patient.

**Conclusions:** The tip of surgery to improve olfactory function is not to damage olfactory epithelium using the microdebrider system.

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## Rotenone nasal exposure may increase the risk of neurodegenerative diseases via enhanced olfactory transport of metals to the olfactory bulb

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In this study, we assessed whether a decreased number of dopaminergic interneurons in the olfactory bulb would alter thallium-201 olfactory transport to the olfactory bulb in rodents by using rotenone, a mitochondrial respiratory chain complex I inhibitor that has been used as a pesticide in agriculture. For this assessment, we nasally administered rotenone + thallium-201 in the animals' left nasal passage. Using imaging (e.g., SPECT/CT) and immunostaining techniques, we evaluated the thallium-201 migration rate to the olfactory bulb, tyrosine hydroxylase expression in the olfactory bulb (to ascertain the location of dopaminergic interneurons in the olfactory bulb), and the action potentials of olfactory sensory neurons in rodents (i.e., mice and rats). We found that rotenone treatment significantly increased the migration rate of thallium-201 to the olfactory bulb; decreased tyrosine hydroxylase expression in the glomerular layer of the olfactory bulb; and significantly reduced the number of action potentials in the olfactory sensory neurons. Rotenone nasal exposure may increase the risk of neurodegenerative diseases, including Alzheimer's disease, via enhanced olfactory transport of metals to the olfactory bulb. In Alzheimer's disease, high levels of manganese participate in the formation  $\alpha$ -synuclein aggregates in intracellular inclusions, called Lewy bodies that cause synaptic dysfunction and interrupt axonal transport. Manganese, as well as thallium, migrates to the olfactory bulb in mice via olfactory transport. Therefore, thallium-based olfactory imaging as called "Olfactory Scintigraphy" that could be used to detect enhanced olfactory transport of metals could potentially allow clinicians to begin treatment sooner and prevent or lessen symptoms of a neurodegenerative disease. This work was supported, in part, by the Japan Society for the Promotion of Science KAKENHI, Tokyo, Japan [grant number JP17K11369], which was awarded to HS.

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## Clinical features and treatment results of the patients with olfactory disorders

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### Objective:

To report the clinical features and treatment outcomes of patients with olfactory dysfunction since the smell clinic has been launched at our hospital on June 2009 to May 2019.

### Patients and Methods:

The clinical records of twenty-one hundred and thirty-seven patients who consulted the smell clinic at Kanazawa Medical University Hospital from June 2009 to May 2019 were retrospectively reviewed in this study. Both the odor detection and recognition thresholds has been assessed in all of subjects with using T&T olfactometry, which is a standard means of measuring olfactory thresholds in our country. The improvement in the odor recognition threshold was judged according to the criteria of the Japanese Rhinologic Society.

### Results:

The causes of olfactory dysfunction were as follows, chronic sinusitis, 42%; upper respiratory tract infection, 21%; head trauma, 6%; allergic rhinitis, 5%; congenital, 1%; toxic agent, 1% and idiopathic, 20%, which were similar to the previous reports. The ratio of female to male was approximately 1:1 in all of subjects, in other side, the female patients with olfactory dysfunction after upper respiratory tract infection clearly showed a larger population of the subjects 2.5 times, compared to that in males. The mean of age was as follows, chronic sinusitis, 54.4 years; upper respiratory tract infection, 55.5 years; head trauma, 44.6 years; allergic rhinitis, 39.5 years; congenital, 24.6 years; toxic agent, 60 years and idiopathic, 61.9 years.

In treatment outcomes, more than 70% of patients with olfactory dysfunction after upper respiratory tract infection showed improvement 3 months after the first visit. In addition, thirty-five percent of patients with head trauma recovered 3 months after the first visit.

### Conclusions:

In general, olfactory dysfunction is regarded as poor prognostic disease. Our results showing good outcomes in a part of subjects suggests that the prognosis is not always poor in patients with olfactory dysfunction.

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## Clinical indication of nasal surgery for the CPAP intolerance in obstructive sleep apnea with nasal obstruction

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**Objective:** The role of isolated nasal surgery for obstructive sleep apnea (OSA) patients with nasal obstruction, especially for an intolerance for continuous positive airway pressure (CPAP), is unclear. The aim of this study was to assess the effects of surgery for OSA patients with symptomatic nasal obstruction and CPAP intolerance.

**Design:** retrospective study.

**Setting:** Tertiary care center & Affiliated sleep laboratory.

**Patients:** 1063 OSA patients with apnea-hypopnea index (AHI)  $\geq 20$  were enrolled.

**Main Outcome Measures:** Case-control study was performed between the male apnea patients undergoing nasal surgery: surgery group (n=44) and the pair-matched apnea patients for age, sex, body mass index, and race: control group (n=44). The surgery group suffering from nasal obstruction could not use continuous positive airway pressure, and the CPAP group free from nasal obstruction could use it successfully.

**Results:** In surgery group, surgery significantly decreased the nasal resistance and Epworth sleepiness scale scores without changing the AHI. Surgery significantly increased the nadir of oxygen saturation and shortened the apnea-hypopnea duration. Although all of the surgery group failed to use positive airway pressure preoperatively, the 41 patients of the 44 CPAP intolerance patients were able to use CPAP postoperatively. The resting three patients were cured OSA. For both groups, the cutoff nasal resistance for differentiating the failure of positive airway pressure and its success was 0.33 Pa/cm<sup>3</sup>/s.

**Conclusion:** Isolated nasal surgery is effective for an intolerance of positive airway pressure in sleep apnea with nasal obstruction presumably by decreasing nasal resistance.

# Luncheon Seminar

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15th Japan-Taiwan Conference on Otolaryngology-Head and Neck Surgery



**Luncheon Seminar 1** Precision Medicine for Head and Neck Cancer**LS1****The latest update of Immune check point inhibitors therapy for head and neck squamous cell carcinoma**

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Immune check point inhibitors have shown their efficacy for various cancer types, including head and neck squamous cell carcinoma (HNSCC). In August 2017, Nivolumab was approved in Taiwan for patients with recurrent or metastatic squamous cell carcinoma of the head and neck based on the result of a phase III trial of CheckMate141 for platinum refractory HNSCC, nivolumab significantly improved overall survival compared with investigator's choice. With minimum follow-up of 24.2 months, median OS was 12.1 months in Nivolumab group and 6.2 months in investigator's choice group (HR 0.41, 95%CI: 0.19-0.88). 2-year OS rate was 22.7% in Nivolumab group and 0% in IC group. Median PFS was 1.9 months in Nivolumab group and 1.8 months in investigator's choice group (HR 0.56, 95%CI: 0.24-1.29), 2-year PFS rate was 12.7% in Nivolumab group and 0% in investigator's choice group respectively. Another important study KEYNOTE-048, which is a randomized phase 3 trial of pembrolizumab monotherapy vs. pembrolizumab plus chemotherapy vs. the EXTREME regimen as first line treatment of recurrent or metastatic SCCHN, was reported. In this session, I would like to introduce the latest update of Immune check point inhibitors therapy for recurrent or metastatic HNSCC.

## Luncheon Seminar 2

### LS2

## Intervention and treatment for chronic sensorineural hearing loss

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Japan faces the super-aging society, and the relationship between hearing loss and dementia which are both common among elderly people has been attended. The attention on the age-related hearing loss (ARHL) has been growing, not only from the view points of clinical practice, but from the social and political problems. The results from a number of epidemiological studies have demonstrated a significant link between ARHL and cognitive function. The Lancet International Commission on Dementia, Prevention, Intervention, and Care has estimated that mid-life hearing loss is the most important factor which might decrease the risk of dementia by 9% out of 35%, since hearing loss is a modifiable age-associated condition linked to dementia. The relationship between ARHL and dementia remains to be established, however, the hypotheses of etiological mechanisms between ARHL and cognitive decline has been proposed: (1) cognitive load hypothesis; (2) common cause hypothesis; (3) cascade hypothesis; and (4) over-diagnosis or harbinger hypothesis. In this seminar, I would like to summarize the relationship between ARHL and cognitive function and also the effects of hearing aids on this issue.

In addition, we have to think about the novel therapeutic strategies for chronic sensorineural hearing loss including ARHL. Spontaneous auditory hair cell regeneration was reported in birds and fish during the 1980s~1990s. Now, we know that the mammalian hair cell can be regenerated by some interventions of Notch signals or by using iPS cells. These findings suggested the potential for a novel therapy to treat human chronic sensorineural hearing loss. In this presentation, we would like to show our novel therapeutic trials for chronic sensorineural hearing loss.