

## Department of Otorhinolaryngology

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### General Summary

Our basic and clinical studies have examined: the pathogenesis of cholesteatoma, surgery for adhesive otitis media, navigation medicine, space motion sickness, nasal allergy, endoscopic endonasal sinus surgery, sleep apnea syndrome, phonosurgery, deglutition, and reconstructive surgery for head and neck tumors.

### Research Activities

#### *Research issues in otology*

Our research projects span experiments on the fundamental aspects of middle ear mucosa regeneration and its clinical application, research on gene therapy targeting epithelium with residual cholesteatoma, and the development of a navigation system utilizing virtual-reality technology to increase the safety of surgery. In addition, cases of cholesteatoma surgery performed at our hospital are recorded in our database, which is used to analyze the condition of patients, to select operative methods, and to review postoperative outcomes. In regard to research on hearing loss, we are studying the physiology of the inner ear in metabolic disorders using experimental animal models and collaborating with Shinshu University in the genetic analysis of deaf patients.

We perform approximately 200 middle ear surgeries annually at our hospital. Cochlear implantations performed every year have also yielded favorable results. We perform skull-base surgery, including that for cholesteatoma in the petrous part of the temporal bone, in conjunction with the Department of Neurosurgery, and have found that hearing and facial nerve function can be preserved in many cases. We also perform acoustic tumor surgery via the posterior cranial fossa approach, middle cranial fossa approach, or translabyrinthine approach, depending on the case.

For secretory otitis media we select the treatment method in individual patients depending on the degree of development of the mastoid air cells. With respect to the duration of placement of indwelling ventilatory tubes, we determine the timing of tube removal in each patient by measuring the changes in the middle ear total pressure caused by transmucosal gas exchange.

In the field of neuro-otology, we have introduced vestibular evoked myogenic potential (VEMP) testing to evaluate saccular function in patients with such conditions as vestibular neuritis, Meniere's disease, and dizziness of unknown cause to facilitate diagnosis and treatment. Moreover, we are examining the prevalence of abnormal saccules in various disorders as measured with VEMP testing, the ictal and nonictal phases of Meniere's dis-

ease, and the incidence of VEMP abnormalities according to disease stage. We also perform furosemide-loading VEMP as a test for patients suspected to have delayed endolymphatic hydrops. In addition, we are advancing research on the localization of the vestibular cortex and the projection from the vestibular system to the cerebral cortex by analyzing cerebral blood flow with single photon emission computed tomography in conjunction with the Department of Neurology.

For the selection of astronauts by the Japan Aerospace Exploration Agency, our neurotology team performed third-stage examinations at the Tsukuba Space Center. In this examination, the candidates' aptitude to be astronauts was tested by applying "Coriolis stimulation" with a rotating chair to provoke motion sickness.

#### *Research in rhinology*

We are involved in the analysis of data on factors related to the intractability of rhinosinusitis obtained from patients undergoing endoscopic sinus surgery (ESS) and from prospective studies of the postoperative course. In an attempt to expand the indications for ESS from paranasal sinus tumors to skull-base surgery, including that for spinal fluid leakage, skull-base tumors, and pituitary gland tumors, and to improve the safety of ESS, we have performed high-tech navigation surgery in which 3-dimensional endoscopic images and stereonavigation images are superimposed. We have identified problems and possible areas of improvement relevant to this operative method and are altering the device to improve its accuracy and performance.

This year, we began developing clinical studies and treatment methods for patients with a variety of olfactory disorders. Since last year we have offered anatomy training using fresh-frozen cadavers at skills laboratory, and went to skull-base surgery and ordinary endoscopic sinus surgery training. We reflected improvements in procedures under the endoscopic skull-base surgery and paranasal sinus tumorectomy in result. In addition, we started creating new methods of Internet access using telemedicine and a distance-training system.

#### *Research issues on head and neck tumors*

For common advanced cancers we perform radical surgery (e.g., total pharyngolaryngectomy combined with reconstruction by means of free intestinal flap transfer for hypopharyngeal cancer and total laryngectomy for laryngeal cancer); however, we perform larynx-preserving surgery (partial hypopharyngectomy combined with reconstruction by means of free-flap transfer and partial laryngectomy) to preserve function, especially vocal function, to the greatest extent possible. We have obtained favorable outcomes in terms of both laryngeal preservation and survival. For conservative therapy and postoperative treatment for advanced cancer, we perform radiotherapy, alone or with concurrent chemotherapy with cisplatin and 5-fluorouracil, and have obtained favorable results. We use narrow-band imaging endoscopy for diagnosis in routine practice and make good use of this technology for the diagnosis and treatment of early-stage superficial mesopharyngeal and hypopharyngeal cancers.

In regard to research on cancer, we are performing basic studies and applying their findings to future studies and to clinical practice; such fundamental studies include extraction

of DNA from specimens obtained during surgery and evaluation of epidermal growth factor receptor expression, a target for molecularly targeted agents. In the future, we hope to perform clinical research on the expression of human papilloma virus, which has been implicated in the development of mesopharyngeal cancer and oral cancer, and to investigate treatments, such as vaccine therapy, for various cancers.

#### *Research on vocal and swallowing functions*

1. Phonosurgery: We are performing outpatient day surgery using a flexible fiberoptic laryngoscope and performing laryngomicrosurgery using the microflap method under general anesthesia for vocal fold polyps, vocal cord nodules, and vocal cord cysts. To determine the optimal surgical indications and operative methods, we compare potential operative methods by means of fiberoptic laryngoscopy, stroboscopy, acoustic analysis, aerodynamic testing, and assessment using the Voice Handicap Index before and after surgery.

For many years we have performed intra-vocal-fold injection of atelocollagen as outpatient day surgery for unilateral recurrent nerve paralysis; however, we are also performing laryngeal framework surgery for patients who are considered poor candidates for atelocollagen injection.

2. Diagnosis and treatment of spasmodic dysphonia: Since December 2004 we have performed botulinum toxin treatment as a first-line therapy for spasmodic dysphonia with the approval of the ethics committee of the university. The prevalence of this disorder has been increasing; therefore, evaluating methods for diagnosis and treatment is of clinical importance. An important future task in this context is developing surgical treatment methods for patients who do not respond to botulinum toxin treatment.

3. Evaluation and treatment of dysphagia: We collaborate with other departments, such as the departments of neurology and rehabilitation, and include co-medical staff, such as nurses, in our treatment team. We consider therapeutic strategies by evaluating patients by means of video endoscopy and video fluorographic tests and are promoting swallowing training.

#### *Research on sleep apnea syndrome*

To verify whether allergic rhinitis is involved in sleep disorders, research for patients with pollinosis has been performed since last year at the Ota Sleep Science Center.

Continuous positive airway pressure treatment will be the first choice for patients with obstructive sleep apnea syndrome of greater than moderate severity. On the other hand, the effectiveness and safety questioned surgical treatment. Therefore, we analyzed about the adaption of surgical treatment for sleep disorders such an uvulopalatopharyngoplasty representatively.

Long-distance sleep examinations have been performed since 2009 at the Ota Sleep Science Center.

## Publications

**Wada K, Matsuwaki Y, Yoon J, Benson LM, Checkel JL, Bingemann TA, Kita H.** Inflammatory responses of human eosinophils to cockroach are mediated through protease-dependent pathways. *J Allergy Clin Immunol* 2010; **126**: 169-72. e2.

**Wong WK, Matsuwaki Y, Omura K, Moriyama H.** Role of intraoperative CT-updates during image-guided endoscopic sinus surgery for sino-nasal fibro-osseous lesions. *Auris Nasus Larynx* 2011; **38**: 628-31. Epub 2011 Jan 11.

**Okushi T, Tonogi M, Arisaka T, Kobayashi S, Tsukamoto Y, Morishita H, Sato K, Sano C, Chiba S, Yamane GY, Nakajima T.** Effect of maxillomandibular advancement on morphology of velopharyngeal space. *J Oral Maxillofac Surg* 2011; **69**: 877-84.

**Sakurai Y, Suzuki R, Yoshida R, Kojima H, Watanabe M, Manome Y, Ohashi T, Eto Y, Moriyama H.** Inner ear pathology of alpha-galactosidase A deficient mice, a model of Fabry

disease. *Auris Nasus Larynx* 2010; **37**: 274-80.

**Tahara M, Araki K, Okano S, Kiyota N, Fuse N, Minashi K, Yoshino T, Doi T, Zenda S, Kawashima M, Ogino T, Hayashi R, Minami H, Ohtsu A.** Phase I trial of combination chemotherapy with docetaxel, cisplatin and S-1 (TPS) in patients with locally advanced or recurrent/metastatic head and neck cancer. *Ann Oncol* 2011; **22**: 175-80.

**Sano H, Matsuwaki Y, Kaito N, Joki T, Okushi T, Moriyama H.** A case of sphenoid sinus meningoencephalocele repaired by an image-guided endoscopic endonasal approach. *Auris Nasus Larynx* 2011; **38**: 632-7. Epub 2011 Mar 9.

## Reviews and Books

**Matsuwaki Y, Moriyama H.** Progress in endoscopic sinus surgery (in Japanese). *Nippon Rinsho* 2010; **68**: 1360-5.