

## Department of Otorhinolaryngology

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### General Summary

We have 5 research areas, which are otology, rhinology, laryngology, head and neck surgery, and sleep science. The researchers in these areas worked on developing safe and effective surgical techniques. They also do basic research in their specialized fields and have achieved excellent results.

### 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. We perform approximately 300 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. For secretory otitis media we select the treatment method in individual patients depending on the degree of development of the mastoid air cells. 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 disease, and the incidence of VEMP abnormalities according to disease stage. We also adopted the video head impulse test (vHIT) for examining the function of the semicircular canal.

#### *Research in rhinology*

We are analyzing 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. We perform special care for skull-base diseases, such as pituitary tumors and cerebrospinal fluid leak, with a good relationship with the Department of Neurosurgery. 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-technology navigation surgery in which 3-dimensional endoscopic images and stereonavigation images are superimposed. We have planned clinical studies and developed treatment methods for patients with a variety of olfactory disorders. To clarify the pathogenesises of eosinophilic chronic rhinosinusitis and allergic fungal rhinosinusitis, we investigate how environment fungi and bacteria induce activation and degranulation of human eosinophils and the airway epithelium.

#### *Research 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 fluorouracil, and have obtained favorable results. 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, the evaluation of epidermal growth factor receptor expression, and targets for molecularly targeted agents, such as the expression of human papilloma virus, which has been implicated in the development of mesopharyngeal cancer and oral cancer.

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

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. For many years we have performed injections of atelocollagen into the vocal folds 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.

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.

### Research on sleep apnea syndrome

To verify whether allergic rhinitis is involved in sleep disorders, research for patients with pollinosis has been performed. 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 of surgical treatment are still unknown. We will be able to present the adaptation of surgical treatment for sleep disorders. Long-distance sleep examinations have been performed since 2009. These research studies are joint projects with the Ota Sleep Science Center.

### Publications

**Takaishi S, Saito S, Kamada M, Otori N, Kojima H, Ozawa K, Takaiwa F.** Evaluation of basophil activation caused by transgenic rice seeds expressing whole T cell epitopes of the major Japanese cedar pollen allergens. *Clin Transl Allergy.* 2019; **20**: 11.

**Omura K, Nomura K, Aoki S, Tochigi K, Miyashita K, Tanaka Y, Otori N, Kojima H.** Effect of a Superior Lateral Anterior Pedicle Flap for Druf Procedures. *J Craniofac Surg.* Epub 2019 Feb 25.

**Komori M, Tada T, Koizumi H, Takahashi M, Sanpei S, Morino T, Motegi M, Miura M, Yamamoto K, Sakurai Y, Yaguchi Y, Yamamoto Y, Kojima H.** Practical analysis of pars flaccida cholesteatoma with classification and staging system proposed by Japan Otological Society: a comparative study. *Acta Otolaryngol.* 2018; **138**: 977-80.

**Morino T, Takagi R, Yamamoto K, Kojima H, Yamato M.** Explant culture of oral mucosal epithelial cells for fabricating transplantable epithelial cell sheet. *Regen Ther.* 2018; **17**: 36-45.

**Nakayama T, Sugimoto N, Okada N, Tsurumoto T, Mitsuyoshi R, Takaishi S, Asaka D, Kojima H, Yoshikawa M, Tanaka Y, Haruna SI.** JESREC score and mucosal eosinophilia can predict endotypes of chronic rhinosinusitis with nasal polyps. *Auris Nasus Larynx.* 2019; **46**: 374-83. Epub 2018 Sep 19.

**Sugimoto N, Nakayama T, Kasai Y, Asaka D, Mitsuyoshi R, Tsurumoto T, Takaishi S, Omae S, Kojima H, Tanaka Y, Haruna SI.** The role of ADAM-like decysin 1 in non-eosinophilic chronic rhinosinusitis with nasal polyps. *Acta Otolaryngol.* 2018; **138**: 830-6. Epub 2018 Jun 23.

**Kuboki A, Kikuchi S, Asaka D, Onda N, Na-**

**kayama T, Kojima H, Otori N.** Nasal silicone splints and quilting sutures using a septum stitch device following septoplasty: a prospective comparative study. *Eur Arch Otorhinolaryngol.* 2018; **275**: 1803-9. Epub 2018 May 23.

**Nakayama T, Asaka D, Kuboki A, Okushi T, Kojima H.** Impact of residual frontal recess cells on frontal sinusitis after endoscopic sinus surgery. *Eur Arch Otorhinolaryngol.* 2018; **275**: 1795-801. Epub 2018 May 18.

**Urashima M, Asaka D, Endo T, Omae S, Sugimoto N, Takaishi S, Mitsuyoshi R, Nakayama T, Nagakura H, Endo T, Akutsu T, Tachimoto H, Kojima H.** Japanese cedar pollinosis in Tokyo residents born after massive national afforestation policy. *Allergy.* 2018; **73**: 2395-7. Epub 2018 Aug 16.

**Rikitake M, Sampei S, Komori M, Sakurai Y, Kojima H.** Bilateral Deafness as a Complication of the Vaccination-A Case Report. *Int Tinnitus J.* 2018 **1**; **22**: 19-22.

### Reviews and Books

**Morita Y<sup>1</sup>, Tono T<sup>2</sup>, Sakagami M<sup>3</sup>, Yamamoto Y, Matsuda K<sup>2</sup>, Komori M, Hato N<sup>4</sup>, Hashimoto S<sup>5</sup>, Takahashi H<sup>6</sup>, Kojima H (Niigata Univ Graduate Sch Medical and Dental Sciences, <sup>2</sup>Univ Miyazaki, <sup>3</sup>Hyogo Coll Med, <sup>4</sup>Ehime Univ, <sup>5</sup>Natl Sendai Medical Center, <sup>6</sup>Nagasaki Harbor Medical Center).** Nationwide survey of congenital cholesteatoma using staging and classification criteria for middle ear cholesteatoma proposed by the Japan Otological Society. *Auris Nasus Larynx.* 2019; **46**: 346-52. Epub 2018 Nov 8.