

Saturday, Sept. 25, 2021

Biwako Hotel Ruri Hall 4

ARSR Symposium 1

9:00~10:00

Chairperson: Ruby Pawankar, Takaki Miwa

- ARSR-S1-1 **Keynote Lecture: COVID-19, Allergic rhinitis and asthma- epidemiology to molecular mechanisms**  
Ruby Pawankar<sup>1,2</sup> (<sup>1</sup>Department of Pediatrics Nippon Medical School, Tokyo, Japan, <sup>2</sup>Department of Otolaryngology, Showa University School of Medicine, Tokyo, Japan)
- ARSR-S1-2 **Keynote Lecture: The association between chronic rhinosinusitis and COVID-19**  
Zheng Liu (Department of Otolaryngology-Head and Neck Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China)
- ARSR-S1-3 **Keynote Lecture: Smell and taste dysfunctions of COVID-19**  
Takaki Miwa (Department of Otorhinolaryngology, Kanazawa Medical University, Japan)
- ARSR-S1-4 **ACE2 protein expression is unchanged by age, sex, smoking or sinus disease and is not affected by angiotensin II receptor blocker (ARBs)**  
Chun-Kang Liao (Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan)
- ARSR-S1-5 **Aspergillus antigen Asp1 identification and allergic inflammation in patients with CRSwNP.**  
Takechiyo Yamada (Department of Otorhinolaryngology, Head and Neck Surgery, Akita University, Graduate School of Medicine, Akita, Japan)
- ARSR-S1-6 **Fine particulate matter during pregnancy and infancy and incident of pediatric allergic rhinitis**  
Yu-Ting Lin (Department of Otolaryngology Head and Neck Surgery, China Medical University Hospital, Taichung, Taiwan)

Chairperson: Shigeharu Fujieda, Tsuguhisa Nakayama

- ARSR-S2-1 Keynote Lecture: Eosinophilic chronic rhinosinusitis**  
Shigeharu Fujieda (Department of Otorhinolaryngology-Head & Neck Surgery, University of Fukui, Japan)
- ARSR-S2-2 Keynote Lecture: Chronic rhinosinusitis with nasal polyps in asia**  
Luo Zhang (Department of Otolaryngology Head and Neck Surgery, Beijing Tongren Hospital, Beijing, China)
- ARSR-S2-3 Keynote Lecture: Endotypes of chronic rhinosinusitis in optimization of treatment: Are we there yet?**  
Baharudin Abdullah (Department of Otorhinolaryngology - Head and Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia.)
- ARSR-S2-4 Inflammatory molecular endotypic differences in nasal polyps derived from Japanese and caucasian chronic rhinosinusitis with nasal polyps**  
Tsuguhisa Nakayama<sup>1,2</sup> (<sup>1</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Jikei University School of Medicine, Tokyo, Japan, <sup>2</sup>Department of Otolaryngology-Head and Neck Surgery, Stanford University School of Medicine, Stanford, CA, USA)
- ARSR-S2-5 Clinical characteristics and cytokine profiles of central-compartment-type chronic rhinosinusitis**  
Yi-Tsen Lin<sup>1,2</sup> (<sup>1</sup>Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan, <sup>2</sup>Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan)
- ARSR-S2-6 Exposure to cigarette smoke enhances pneumococcal transmission among littermates in an infant mouse model**  
Daichi Murakami<sup>1,2</sup> (<sup>1</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan, <sup>2</sup>Department of Otorhinolaryngology, Kinan Hospital, Wakayama, Japan)

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Chairperson: Mitsuhiro Okano, Masayoshi Kobayashi

- ARSR-S3-1**    **Keynote Lecture: Mechanism of allergic rhinitis and allergen immunotherapy: Update**  
Mitsuhiro Okano (Otorhinolaryngology, International University of Health and Welfare, Narita, Japan)
- ARSR-S3-2**    **Keynote Lecture: How to treat allergic rhinitis with sublingual immunotherapy wisely: Experience in Korea**  
Chae-Seo Rhee (Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea)
- ARSR-S3-3**    **Keynote Lecture: Allergen immunotherapy: From subcutaneous to non-injection.**  
Pongsakorn Tantilipikorn (Mahidol University, Thailand)
- ARSR-S3-4**    **Local-nasal immunotherapy for allergic rhinitis: A systematic review and meta-analysis**  
Navarat Kasemsuk (Division of Rhinology and Allergy, Department of Otorhinolaryngology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand)
- ARSR-S3-5**    **Influences of CD8<sup>+</sup> Tregs on peripheral blood mononuclear cells from allergic rhinitis patients**  
Lin Lin (Department of Otorhinolaryngology-Head and Neck Surgery, Huashan Hospital of Fudan University, Shanghai, China)
- ARSR-S3-6**    **Endoscopic sinus surgery for olfactory dysfunction caused by eosinophilic chronic rhinosinusitis**  
Masayoshi Kobayashi (Otorhinolaryngology-Head and Neck Surgery, Mie University Graduate School of Medicine, Tsu, Japan)

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Chairperson: Yoshimasa Imoto

- ARSR-S4-1**    **Keynote Lecture: Recent advances of macrolide therapy for the treatment of chronic rhinosinusitis and other airway inflammation**  
Takeshi Shimizu (Otorhinolaryngology-Head and Neck Surgery, Shiga University of Medical Science, Otsu, Japan)
- ARSR-S4-2**    **The characteristics and surgical outcomes of CCAD in mid-taiwan**  
Chih-Jaan Tai<sup>1,2</sup> (<sup>1</sup>Department of Otorhinolaryngology, China Medical University Hospital, Taichung, Taiwan, <sup>2</sup>School of Medicine, China Medical University, Taichung, Taiwan)
- ARSR-S4-3**    **Keynote Lecture: Introduction of hands-on seminar on basic research for clinicians in the Japanese Rhinologic Society**  
Yoshimasa Imoto (Department of Otorhinolaryngology, Head and Neck Surgery, University of Fukui, Japan)

Chairperson: Shin-ichi Haruna, Nobuyoshi Otori

- ARSR-S5-1**     **Keynote Lecture: Concept and basic technique of endoscopic sinus surgery for chronic rhinosinusitis.**  
Nobuyoshi Otori (Otorhinolaryngology, Jikei University School of Medicine, Tokyo, Japan.)
- ARSR-S5-2**     **Keynote Lecture: Prelacrimal approach versus conventional surgery for inverted papilloma in the maxillary sinus**  
Shin-ichi Haruna (Department of Otorhinolaryngology – Head and Neck Surgery, Dokkyo Medical University, Tochigi, Japan.)
- ARSR-S5-3**     **Keynote Lecture: Endonasal approach for Meckel's cave and foramen rotundum**  
Boonsam Roongpuvapaht (Department of Otolaryngology Head and Neck Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand)
- ARSR-S5-4**     **Predictors of disease progression after endoscopic sinus surgery in patients with chronic rhinosinusitis**  
Kenzo Tsuzuki (Department of Otorhinolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Hyogo, Japan)
- ARSR-S5-5**     **Extent of endoscopic sinus surgery for eosinophilic chronic rhinosinusitis cases with asthma**  
Yasuyuki Hinohira (Department of Otolaryngology, Kamio Memorial Hospital, Tokyo, Japan)
- ARSR-S5-6**     **Effectiveness of budesonide irrigation after FESS**  
Teik Ying Ng (Department of Otorhinolaryngology, China Medical University Hospital, Taichung, Taiwan. College of Medicine, China Medical University, Taichung, Taiwan.)

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Chairperson: Muneki Hotomi, Kazuhiro Omura

- ARSR-S6-1**     **Keynote Lecture: Appropriate antimicrobial management of acute rhinosinusitis**  
Muneki Hotomi (Department of Otorhinolaryngology, Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan)
- ARSR-S6-2**     **Keynote Lecture: The clinical features of endoscopic treated isolated sphenoid sinus diseases**  
Te Huei Yeh (Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan)
- ARSR-S6-3**     **Keynote Lecture: Surgical success in obstructive sleep apnea**  
Sung Wan Kim (Department of ORL-HNS, Kyung Hee University, Seoul, Korea)
- ARSR-S6-4**     **Optimal multiple-layered anterior skull base reconstruction using a 360-degree suturing technique**  
Kazuhiro Omura (Department of Otolaryngology, Jikei University School of Medicine, Tokyo, Japan)
- ARSR-S6-5**     **The transseptal approach enhances nasal recovery without compromising resectability in endoscopic endonasal transsphenoidal adenomectomy**  
Yenhui Lee (Department of Otolaryngology, National Taiwan University Hospital, Taipei, Taiwan)
- ARSR-S6-6**     **Rhinosinusitis following endoscopic endonasal skull base surgery**  
Yu Wen Huang<sup>1,2</sup> (<sup>1</sup>Department of Otolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, <sup>2</sup>School of Medicine, National Yang Ming Chiao Tung University, Taiwan)

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Chairperson: Takeshi Shimizu, Kazuhiko Takeuchi

- ARSR-S7-1**     **Keynote Lecture: Differences and similarities between upper and lower airway focusing on innate immunity**  
Joo-Heon Yoon (Department of Otorhinolaryngology, Yonsei University College of Medicine, Seoul, Korea)
- ARSR-S7-2**     **Keynote Lecture: Role of zinc oxide and asian sand dust in the development of aspergillus fumigatus biofilm on nasal epithelial cells**  
Seung-Heon Shin (Department of Otolaryngology-Head and Neck Surgery, School of Medicine, Catholic University of Daegu, Daegu, Korea)
- ARSR-S7-3**     **Keynote Lecture: Copy number variation in DRC1 is the major cause of primary ciliary dyskinesia in Japan**  
Kazuhiko Takeuchi (Department of Otorhinolaryngology, Head & Neck Surgery, Mie University Graduate School of Medicine, Tsu, Japan)
- ARSR-S7-4**     **Polyethylene glycol-coated graphene oxide loaded with erlotinib as an effective therapeutic agent for treating nasopharyngeal cancer cells**  
Ming-Ying Lan<sup>1,2</sup> (<sup>1</sup>Department of Otolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, <sup>2</sup>School of Medicine, National Yang-Ming Chiao Tung University, Taipei, Taiwan)
- ARSR-S7-5**     **The paradigm shift in treating olfactory neuroblastoma: A 10-year analysis in taipei veterans general hospital**  
Yun-Ting Chao (Department of Otorhinolaryngology, Head-and-Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan)

## e-poster

- EP-1**      **Decreased expression of type I (IFN- $\beta$ ) and III interferon (IFN- $\lambda$ ) and IFN-stimulated genes in chronic rhinosinusitis with and without nasal polyps**  
Sang Hag Lee, MD, PhD (Department of Otorhinolaryngology-Head & Neck Surgery, College of Medicine, Korea University, Seoul, Korea)
- EP-2**      **PVP-I reduces LPS-induced airway inflammation by blocking TLR4 signaling in airway epithelial cells**  
Seung Hoon Lee, Sun-Hee Yeon, Seung-Hyeon Choi, Soo-Kyung Park, Mi-Ra Choi, Yong Min Kim\* (Department of Otorhinolaryngology-Head and Neck Surgery, Research Institute for Medical Science, Chungnam National University School of Medicine, Daejeon, Korea)
- EP-3**      **Two siblings with primary ciliary dyskinesia with the same homozygous variants**  
Guofei Feng<sup>1\*</sup>, Shun Saso<sup>2</sup>, Hajime Sasano<sup>3</sup>, Yifei Xu<sup>1</sup>, Kazuhiko Takeuchi<sup>1</sup> (<sup>1</sup>Department of Otorhinolaryngology - Head and Neck Surgery, Mie University Graduate School of Medicine, Tsu, Japan., <sup>2</sup>Faculty of Medicine, Mie University, Tsu, Japan., <sup>3</sup>Department of Respiratory MedicineI, Ise Red Cross Hospital, Ise, Mie, Japan.)
- EP-4**      **Using three-dimensional printed sinus models for assessing the performance of sinus ultrasound in diagnosis of sinusitis**  
Chih-Kai Hsu, MD<sup>1,2</sup>, Hung Chang, MD<sup>3</sup>, Wen-Chan Yu<sup>4</sup>, Yi-Chun Chen, PhD<sup>5</sup>, Ming-Ying Lan, MD, PhD<sup>1,3\*</sup> (<sup>1</sup>School of Medicine, National Yang-Ming University, <sup>2</sup>Department of Medical Education, Taipei Veterans General Hospital, <sup>3</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital, <sup>4</sup>3D Printing Technology and Resource Integration Center, Department of Rehabilitation and Technical Aid Center, <sup>5</sup>Department of Optics and Photonics, National Central University, Taiwan)
- EP-5**      **Using image J platform in analysis of sinus X-ray for assisting diagnosis of fungal sinusitis**  
Liting Hung<sup>1\*</sup>, Chingyin Ho<sup>2</sup>, Shengan Lee<sup>3</sup>, Chengjie Hsu<sup>1</sup>, Mingying Lan<sup>1,4</sup> (<sup>1</sup>Department of Otolaryngology, Taipei Veterans General Hospital, <sup>2</sup>Department of Otolaryngology, Cheng Hsin General Hospital, <sup>3</sup>Department of Health Management, Kainan University, <sup>4</sup>School of Medicine, National Yang Ming Chiao Tung University, Taiwan)
- EP-6**      **A novel scoring system of surgical findings at the sinus and olfactory cleft in patients with chronic rhinosinusitis**  
Ken Okazaki\*, Takahiro Saito, Katsuya Fushimi, Kenzo Tsuzuki (Department of Otorhinolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Hyogo, Japan)
- EP-7**      **Statistical analysis of eosinophilic chronic rhinosinusitis at Fukuyama city hospital**  
Takahisa Koyama\*, Youhei Noda, Kikuko Naka, Yasuhiko Yamashita (Fukuyama City Hospital, Fukuyama, Japan)
- EP-8**      **Therapeutic effects of sinonasal topical steroid treatment on postoperative eosinophilic chronic rhinosinusitis patients.**  
Takahiro Saito<sup>1\*</sup>, Ken Okazaki<sup>1</sup>, Katsuya Fushimi<sup>1</sup>, Kengo Hashimoto<sup>2</sup>, Kenzo Tsuzuki<sup>1</sup> (<sup>1</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Hyogo College of Medicine, <sup>2</sup>Department of Otorhinolaryngology, Kawanishi City Hospital, Japan)
- EP-9**      **Mepolizumab therapy on eosinophilic chronic rhinosinusitis associated with asthma**  
Isao Suzaki\*, Eriko Sekino, Sawa Kamimura, Shohei Matsuura, Kojiro Hirano, Hitome Kobayashi (Department of Otorhinolaryngology, Showa University School of Medicine, Tokyo, Japan)

- EP-10 Combination flap technique for choanal atresia**  
Takashi Ishino\*, Daisuke Takahara, Yuichiro Horibe, Kota Takemoto, Manabu Nishida, Takashi Oda, Sachio Takeno (Department of Otorhinolaryngology, Head and Neck surgery, Hiroshima University, Hiroshima, Japan)
- EP-11 A study of the efficacy on surgical treatment for allergic rhinitis**  
Satoko Hamada<sup>1,2\*</sup>, Yoshiki Kobayashi<sup>1,2</sup>, Masami Shimono<sup>1</sup>, Daiki Sakamoto<sup>1</sup>, Akihiro Shimamura<sup>1</sup>, Akira Kanda<sup>1,2</sup>, Mikiya Asako<sup>1,2</sup>, Hiroshi Iwai<sup>1</sup> (<sup>1</sup>Department of Otorhinolaryngology, Kansai Medical University, <sup>2</sup>Allergy Center, Kansai Medical University Hospital, Osaka, Japan)
- EP-12 Study of allergic rhinitis in atopic individuals and diagnostic significance of nasal eosinophilic count**  
Jaya Geeta Pydi\*, Syuji Yonekura, Toyoyuki Hanazawa (Dept. of Otolaryngology Head and Neck Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan)
- EP-13 Perspicuous treatment algorithm for pediatric blowout orbital fractures**  
Kosuke Takabayashi<sup>1\*</sup>, Yohei Maeda<sup>2</sup> (<sup>1</sup>Department of Otorhinolaryngology, Japanese Red Cross Asahikawa Hospital, Hokkaido, Japan, <sup>2</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Osaka University Graduate School of Medicine, Suita City, Osaka, Japan)
- EP-14 Pathophysiology of current odontogenic maxillary sinusitis and endoscopic sinus surgery preceding dental treatment**  
Kiminori Sato<sup>1,2\*</sup>, Shun-ichi Chitose<sup>2</sup>, Kiminobu Sato<sup>2</sup>, Fumihiko Sato<sup>2</sup>, Takeharu Ono<sup>2</sup>, Hirohito Umeno<sup>2</sup> (<sup>1</sup>Department of Otolaryngology-Head and Neck Surgery, Sato Clinic & Hospital, Oita, Japan., <sup>2</sup>Department of Otolaryngology-Head and Neck Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan)
- EP-15 Analysis of symptomatic frontal sinusitis after endoscopic sinus surgery**  
Wakako Nakanishi\*, Wayo Kawawaki, Ryosuke Sugito, Hiroko Monobe (Japanese red cross medical center, Japan)
- EP-16 Modified endoscopic medial maxillectomy to overcome absent or limited prelacrima recess**  
Huang Ching-Yuan<sup>1</sup>, Lin Yu-Hsuan<sup>1,2,3\*</sup> (<sup>1</sup>Department of Otolaryngology, Head and Neck Surgery, Kaohsiung Veterans General Hospital, Kaohsiung, <sup>2</sup>School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, <sup>3</sup>School of Medicine, Chung Shan Medical University, Taichung, Taiwan)
- EP-17 Endonasal endoscopic closure for oroantral fistula- report of 2 cases**  
Chen Po-Fu<sup>1\*</sup>, Lin Yu-Hsuan<sup>1,2,3</sup> (<sup>1</sup>Department of Otolaryngology, Head and Neck Surgery, Kaohsiung Veterans General Hospital, Kaohsiung, <sup>2</sup>School of Medicine, National Yang Ming Chiao Tung University, Taipei, <sup>3</sup>School of Medicine, Chung Shan Medical University, Taichung, Taiwan)
- EP-18 Olfactory dysfunction in an IgG4-related disease mice model**  
Misako Kaneda<sup>1,2\*</sup>, Sayaka Yagi-Nakanishi<sup>1</sup>, Fumi Ozaki<sup>1</sup>, Satoru Kondo<sup>1</sup>, Tomokazu Yoshizaki<sup>1</sup> (<sup>1</sup>Division of Otolaryngology, Head and Neck Surgery, Kanazawa University Graduate School of Medical Sciences, Ishikawa, Japan, <sup>2</sup>Public Central Hospital of Matto Ishikawa)



- EP-19 Efficacy of combination therapy using olfactory training and medication for post-traumatic olfactory dysfunction**  
Kento Takeichi\*, Masayoshi Kobayashi, Kohei Nishida, Hiroyuki Morishita, Eisuke Ishigami, Kazuhiko Takeuchi (Department of Otorhinolaryngology-Head and Neck Surgery, Mie University Graduate School of Medicine, Japan)
- EP-20 Treatment with nasally administered adipose-derived stem cells from GFP transgenic mice in olfactory impaired mice**  
Tomoko Ishikura, MD<sup>1\*</sup>, Hideaki Shiga, MD, PhD<sup>1</sup>, Yuka Nakamura<sup>2</sup>, Takako Kanitani<sup>1</sup>, Yasuhito Ishigaki, PhD<sup>2</sup>, Takaki Miwa, MD, PhD<sup>1</sup> (<sup>1</sup>Department of Otorhinolaryngology, Kanazawa Medical University, <sup>2</sup>Medical Research Institute, Kanazawa Medical University, Ishikawa, Japan)
- EP-21 Comparison of magnetic resonance imaging and computed tomography in the evaluation of the olfactory cleft and ethmoidal cell**  
Tomotaka Hemmi MD<sup>1,2\*</sup>, Kazuhiro Nomura MD, PhD<sup>2</sup>, Jun Suzuki MD, PhD<sup>1</sup>, Yuta Kobayashi MD, PhD<sup>1,3</sup>, Risako Kakuta MD, PhD<sup>1</sup>, Mitsuru Sugawara MD, PhD<sup>2</sup>, Yukio Katori MD, Ph.D.<sup>1</sup> (<sup>1</sup>Department of Otolaryngology, Head and Neck Surgery, Tohoku University School of Medicine, Japan., <sup>2</sup>Department of Otolaryngology, Tohoku Kosai Hospital, Japan., <sup>3</sup>Department of Otolaryngology, Iwate Prefectural Iwai Hospital, Japan.)
- EP-22 Preoperative endovascular embolization in an easily bleeding respiratory epithelial adenomatoid hamartoma (REAH) of the olfactory cleft**  
Jun Suzuki<sup>1\*</sup>, Hiroki Tozuka<sup>1</sup>, Tomotaka Hemmi<sup>1</sup>, Hiroyuki Ikushima<sup>1</sup>, Tomohiko Ishikawa<sup>1</sup>, Kazuhiro Nomura<sup>2</sup>, Mitsuru Sugawara<sup>2</sup>, Yukio Katori<sup>1</sup> (<sup>1</sup>Department of Otolaryngology, Head and Neck Surgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan, <sup>2</sup>Department of Otolaryngology, Tohoku Kosai Hospital, Sendai, Miyagi, Japan)
- EP-23 Clinical study of tumors in the nasal septum**  
Tessei Kuruma<sup>1\*</sup>, Mariko Arimoto<sup>1</sup>, Kunihiro Nishimura<sup>1,2</sup>, Kinga You<sup>1</sup>, Yuka Kawade<sup>1</sup>, Akira Kondo<sup>1</sup>, Yasue Uchida<sup>1</sup>, Tetsuya Ogawa<sup>1</sup>, Yasushi Fujimoto<sup>1</sup> (<sup>1</sup>Department of Otorhinolaryngology, Head and Neck Surgery, Aichi Medical University, Aichi, Japan, <sup>2</sup>Nishimura ENT Clinic, Aichi, Japan)
- EP-24 Impact of prior cancer history on the overall survival of patients with nasopharyngeal carcinoma**  
Chien-Fu Yeh (Department of Otorhinolaryngology-Head & Neck Surgery, Taipei Veterans General Hospital, Taipei, Taiwan)
- EP-25 Accuracy of intraoperative frozen section diagnosis of laser assisted endoscopic nasopharyngectomy in recurrent nasopharyngeal carcinoma**  
Kai-Hsiang Shih<sup>1\*</sup>, Chih-Ying Wu<sup>2</sup>, Yu-Hsin Tsai<sup>2</sup>, Rong-San Jiang<sup>3</sup>, Chen-Chi Wang<sup>1</sup>, Kai-Li Liang<sup>1</sup> (<sup>1</sup>Department of Otolaryngology, <sup>2</sup>Department of Pathology and Medical Laboratory, and <sup>3</sup>Department of Medical Research, Taichung Veterans General Hospital, Taichung, Taiwan)
- EP-26 Extracranial trigeminal schwannoma in the pterygopalatine fossa successfully resected by endoscopic modified medial maxillectomy approach**  
Takuya Murao\*, Ichiro Tojima, Takeshi Shimizu (Department of Otorhinolaryngology Head and Neck Surgery, Shiga University of Medical Science, Shiga, Japan)



## ARSR Symposium 1


**ARSR-S1-1 Keynote Lecture: COVID-19, Allergic rhinitis and asthma- epidemiology to molecular mechanisms**

Ruby Pawankar, MD, Ph.D.<sup>1,2</sup>

<sup>1</sup>Department of Pediatrics Nippon Medical School, Tokyo, Japan

<sup>2</sup>Department of Otolaryngology, Showa University School of Medicine, Tokyo, Japan

The COVID-19 pandemic caused by SARS-CoV2 virus, has rampaged throughout the world. People with asthma and allergic rhinitis (AR) are usually at greater risk of more severe outcomes with viral infections. However, recent reports show that the prevalence of AR and asthma in patients with COVID-19 is low.

In COVID-19 infection, the spike protein of SARS-Cov2 virus binds to the angiotensin converting enzyme 2 (ACE2) and the transmembrane protease serine 2 (TMPRSS2) cleaves the docked spike protein for virus entry by membrane fusion. In SARS-CoV-2, ACE2 expression was significantly reduced not only in the lower airway epithelial cells but also in the nasal epithelial cells in both asthma and AR patients and IL-13 down regulates ACE2 expression. Moreover, in patients with AR and asthma, the innate immune response to COVID-19 infection may be impaired due to lower levels of IFN $\gamma$  in their bronchial epithelial cells, and may further reducing ACE2 expression, which is IFN $\gamma$  dependent. In addition, mannose binding lectin (MBL), and surfactant protein A (SP-A) and D (SP-D) that are produced by alveolar type 2 cells in the lung, found in higher concentrations in the BALF of patients with asthma and respiratory allergy bind the spike protein of SARS-CoV-2 virus, and inhibits its binding to the ACE2 receptor, thereby protecting the alveolar macrophages from virus-induced activation. Additionally, trained immunity in alveolar macrophages may provide anti-viral immunity in the airways. Thus the molecular mechanisms underlying allergic inflammation may have a protective effect in patients with AR and asthma against COVID-19.

#### Curriculum vitae

Prof. Ruby Pawankar, MD, Ph.D, Department of Pediatrics, Nippon Medical School, Tokyo, Japan and also a Visiting Professor at the Department of Otolaryngology, Showa University School of Medicine, Tokyo, Japan. Prof. Pawankar is President of the Asia-Pacific Association of Allergy Asthma and Clinical Immunology (APAAACI). She served as Board of Directors, World Allergy Organization (WAO) for 17 years and was President, WAO (2012 and 2013) She is also Secretary General of ARSR., a Board Member of the Collegium Internationale Allergologicum and InterASMA.

Prof. Pawankar is a Member/Fellow of several academic organizations and serves on committees including the Japanese Society of Allergology, American Academy of Allergy Asthma and Immunology, European Academy of Allergy and Clinical Immunology, ACAAI, World Universities Network and WHO-GARD.

Her research has focused on the cellular and molecular mechanisms of allergy, mast cells, T cells, epithelial cell- immune cell interaction, early life microbiome and allergy, food allergies, biomarkers of asthma. This has resulted in 562 publications with an h-index of 76 and 37297 citations. She is an Editor of several peer-reviewed journals and books including 'Allergy Frontiers' by Springer Nature, the WAO White Book on Allergy, Update on Respiratory Disorders, Monograph Series on Allergy (Springer Nature) and is a co-author of several guidelines/consensus documents.

Prof. Pawankar is a recipient of many academic awards to name a few, the WAO Gold Medal Award, the Pravasi Bharatiya Samman Award from the President of India, International Distinguished Fellow Award of ACAAI and Honorary Fellow of the Royal College of Physicians (UK).

ARSR Symposium 1



**ARSR-S1-2 Keynote Lecture: The association between chronic rhinosinusitis and COVID-19**

Zheng Liu MD, PhD

Department of Otolaryngology-Head and Neck Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Angiotensin-converting enzyme 2 (ACE2) is identified as a key cell entry receptor for SARS-CoV-2, the pathogen of Coronavirus disease 2019 (COVID-19). ACE2 expression is highly enriched in nasal epithelial cells, suggesting the importance of nasal cavity as the primary target site of SARS-CoV-2. The prevalence of chronic rhinosinusitis is high worldwide. Therefore, it is critical to understand whether there is an alerted expression of ACE2 in nasal mucosa of patients with chronic rhinosinusitis and whether the patients with chronic rhinosinusitis have increased risk of developing COVID-19. Our studies showed that although the ACE2 expression was downregulated in sinus mucosa, it was not changed in inferior turbinate mucosa in patients with chronic rhinosinusitis. ACE2 gene expression in nasal cavity is regulated at least in part, by the counter effect of type 2 and interferon inflammation. Our data showed that patients with chronic rhinosinusitis did not present increased risk to develop severe COVID-19.

Curriculum vitae

Zheng Liu currently serves as a professor of Otolaryngology Head and Neck Surgery, and vice president of Tongji Hospital affiliated to Tongji Medical College, Huazhong University of Science and Technology. He is an Associate Editor of *Clinical and Experimental Allergy*, and member of editorial board of several international journals including *Allergy*, *International Archives of Allergy and Immunology*, and *PLoS One*. He is also an International Member of The American Academy of Allergy Asthma and Immunology (AAAAI) and section member of AAAAI Rhinitis, Rhinosinusitis and Ocular allergy Committee.

After completing his training in Medicine in Tongji Medical College in Wuhan, Dr Liu got his training in Allergy and Clinical Immunology from 2002-2004 in Johns Hopkins Asthma and Allergy Centre, USA, as a visiting scientist. His research work has focused on the basic and translational research of chronic rhinosinusitis and allergic rhinitis, particularly the phenotype and endotype of chronic rhinosinusitis (CRS) in Chinese since 2004. Dr Liu's group found that over half of Chinese patients with CRS with nasal polyps present noneosinophilic inflammation, which is distinct from Caucasian patients. His continuous work contributes to understanding of the immune pathogenesis of CRS and endotype in Chinese. Dr Liu has published over 50 peer-reviewed articles as a corresponding author in prestigious medical professional journals including *Journal of Allergy and Clinical Immunology*, *Allergy*, and *American Journal of Respiratory and Critical Care Medicine*, and has been invited to give lectures at a number of international conferences.

## ARSR Symposium 1

**ARSR-S1-3 Keynote Lecture: Smell and taste dysfunctions of COVID-19**

Takaki Miwa

Department of Otorhinolaryngology, Kanazawa Medical University, Japan

Smell and taste dysfunctions are characteristic symptoms of the Corona virus disease 2019 (COVID-19). More than half of the patients with COVID-19 complains these symptoms. The clinical characteristics of olfactory dysfunction in COVID-19 are very different from those of other etiologies. Infected patients just present it without other significant complains such as nasal obstruction or discharge. Most of the patients improved their smell function in a few weeks. The pathophysiology of olfactory dysfunction has been clarified by basic research using human and animals. Virus-cell fusion is mediated by angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) with their organ expression pattern determining affinity of virus to human organs. Both ACE2 and TMPRSS2 are abundant in the nasal cavity and tongue, and are expressed markedly in supporting cells rather than olfactory neurons in the olfactory epithelium. These findings from basic research may be consisted with clinical characteristics of olfactory dysfunction by COVID-19. In this symposium, I would like to present the updated findings of smell and taste dysfunctions by COVID-19.

## Curriculum vitae

1977-1983: Toyama Medical &amp; Pharmaceutical University, MD

1985-1989: Kanazawa University, PhD

1997-2009: Associate Professor, Kanazawa University, Department Otorhinolaryngology

2009-present: Professor &amp; Chairman, Kanazawa Medical University, Department Otorhinolaryngology

2015-2017: Vice president, Kanazawa Medical University Hospital

2016-present: Vice president, Kanazawa Medical University

2018-2021: President, Japanese Association for the Study of Taste and Smell

2018-2021: President, Japanese society of Stomato-Pharyngology

ARSR Symposium 1

**ARSR-S1-4 ACE2 protein expression is unchanged by age, sex, smoking or sinus disease and is not affected by angiotensin II receptor blocker (ARBs)**

Chun-Kang Liao<sup>1\*</sup>, Ivan T. Lee<sup>2,3,4</sup>, Tsuguhisa Nakayama<sup>3,5</sup>, Chien-Ting Wu<sup>6</sup>, Yury Goltsev<sup>2</sup>, Sizun Jiang<sup>2</sup>, Yi-Tsen Lin<sup>1</sup>, Chih-Feng Lin<sup>1</sup>, Garry P. Nolan<sup>2</sup>, Jayakar V. Nayak<sup>3</sup>, Te-Huei Yeh<sup>1,7</sup>

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Angiotensin-converting enzyme 2 (ACE2), the initial attachment of SARS-CoV-2, is an entry point for COVID-19 infection. The expression of ACE2 has been proposed as a potential factor in COVID-19 infectivity. The effect of renin–angiotensin–aldosterone system (RAAS) inhibitors, including common antihypertensive medication angiotensin II receptor blockers (ARBs), on ACE2 levels is uncertain.

To further investigate whether ACE2 protein expression in the upper airway is influenced by patient demography, social habit(smoking), comorbidities (hypertension/sinus diseases, etc.) or medication use, we utilized previously collected human sino-nasal tissue bank for ACE2 protein expression analysis.

First, no significant differences in ACE2 expression based on age ( $\geq 65$  years), sex, smoking. Second, no observed differences in ACE2 expression were noted between healthy donor and patient with/without polyp (CRSwNP/CRSsNP) or between various anatomical regions within sinonasal cavity. Last but not least, ACE2 expression is not increased in patients taking ARBs.

Our result showed that host factor dose not significantly predispose the patient’s susceptibility to SARS-CoV-2 infection. The use of angiotensin II receptor blockers (ARBs) does not raise the risk of COVID-19 infection through enhancing the expression of ACE2 receptor. Patient with long-term usage of ARBs should be safely continued same medication, based on current molecular data. These findings are crucial to our understanding of the transmission of SARS-CoV-2 for prevention and control of this virulent pathogen.

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ARSR Symposium 1

**ARSR-S1-5 Aspergillus antigen Asp f1 identification and allergic inflammation in patients with CRSwNP.**

Takechiyo Yamada\*, Yui Miyabe, Hiroki Tomizawa

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

Background: In allergic inflammation, the cells existing in the mucosa take up antigens and present them to produce specific IgE, but there is no clinical study that quantifies antigens that cause allergies in local tissues.

Materials and Methods: Infiltration-type mycosis was excluded, and the nasal polyp tissue was thoroughly washed to remove the fungus in the nasal discharge and used as samples. The nasal polyp tissues were homogenized, and the levels of Asp f 1, Aspergillus-specific IgE, and galectin were measured using ELISA system.

Results: Eighteen samples (15.9%) tested positive for Asp f 1 and were divided into two groups based on Asp f 1 levels. Asp f 1 levels positively correlated with Aspergillus-specific IgE levels ( $r=0.89$ ,  $p<0.0001$ ). Aspergillus-specific IgE, IgG, and IgE levels in nasal polyps were significantly higher in the high Asp f 1 group than in the low Asp f 1 group. No significant differences were observed in IgA or IgM levels between these groups. Furthermore, Asp f 1 levels positively correlated with galectin-10 levels ( $r=0.89$ ,  $p<0.0001$ ), but not with tissue eosinophil counts ( $r=-0.27$ ,  $p=0.28$ ).

Conclusion: This is the first study to detect an Aspergillus fumigatus antigen in the nasal polyps of patients with CRSwNP. The presence of antigens in tissues may induce type 2 inflammation and be involved in local IgE increase, eosinophil activation, and atosis. It is thought to be useful for elucidating allergic inflammation.

## ARSR Symposium 1

**ARSR-S1-6 Fine particulate matter during pregnancy and infancy and incident of pediatric allergic rhinitis**

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**Background:** The effect of prenatal and postnatal exposure to fine particulate matter (PM<sub>2.5</sub>) on the development of allergic rhinitis (AR) remain unknown. We would like to identify the vulnerable period for AR development to reduce further adverse effects.

**Methods:** We used a large population-based birth cohort of 140,911 singleton live infants in Taichung, Taiwan with a highly temporal-resolution satellite-based hybrid model to evaluate the effects of prenatal and early postnatal exposure on the onset of AR.

**Results:** Among 140,911 children, 47,276 (33.55%) were cases of incident AR. The mean age of the children with AR at initial diagnosis was  $2.97 \pm 1.78$  years. We identified a significant association of AR with an interquartile range (IQR): 17.98  $\mu\text{g}/\text{m}^3$  increase in PM<sub>2.5</sub> from 30 gestational weeks to 52 weeks after birth. The exposure-response relationship revealed that AR had a significant positive association between PM<sub>2.5</sub> of 25-79  $\mu\text{g}/\text{m}^3$  (adjusted hazard ratios ranged from 1.01 to 1.05).

**Conclusion:** Our study provides evidence that both prenatal and postnatal exposures to PM<sub>2.5</sub> are associated with later development of AR. The vulnerable time window may be within late-gestation and the first year of life. Our findings suggest that children should remain indoors or avoid outdoor activities during the early postnatal period to reduce their risk of developing rhinitis as a result of exposure to particulate matter.

ARSR Symposium 2

ARSR-S2-1 Keynote Lecture: Eosinophilic chronic rhinosinusitis



Shigeharu Fujieda

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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 pathogenesis of ECRS has not been clear, some microorganism might be involved in stimulating the type 2 inflammation to promote IgE production and eosinophil infiltration through various pathways. We performed RNAseq and proteomics of nasal polyp of ECRS to find the specific cellular and molecular factor contributing to the pathogenesis of nasal polyp. Several factors were found and investigated for the function of them. While, the coagulation system is activated and the fibrinolytic system is suppressed, leading to deposition of fibrinous networks in nasal polyps. A fibrin-degrading agent could be a one of candidate for the 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-4R $\alpha$  chain Ab (dupilumab), have been performed for large nasal polyps of CRSwNP (nasal polyp score  $\geq$  5). Dupilumab improved nasal polyp score, CT score by Lund-Mackay score, QOL scores and the olfactory test score. We also examined these effects by Dupilumab according to the Japanese Epidemiological Survey of Refractory Eosinophilic Rhinosinusitis algorithm. Dupilumab produced consistent improvement in symptoms of severe CRSwNP irrespective of ECRS status. Therefore, blood eosinophil level may not be a suitable biomarker for dupilumab efficacy in CRSwNP.

Curriculum vitae

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1980.4-1986.3 University of Fukui, School of Medicine

1986.4-1990.3 Post graduate course, University of Fukui

1990.4-1991.3 Otolaryngologist, Sabae Hospital

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1993.12-1995.12 Visiting Researcher at Clinical Immunology & Allergy, University of California, Los Angeles (UCLA): Prof. Andrew Saxon

1996.3-2002.4 Associate Professor at Department of Otorhino - laryngology Head & Neck Surgery, University of Fukui

2002.5- present Chairman, Professor: Department of Otorhino - laryngology Head & Neck Surgery, University of Fukui

2021.4- present Dean, Faculty of Medical Science, University of Fukui

**Subspecialty:**

1) Rhinology and Allergy:

2) Head and neck surgery:

**Patent:**

“Immunoglobulin trans-spliced transcripts and uses thereof”

United state of America Patent No. 6,030,830

6 Japanese patents.



## ARSR Symposium 2

## ARSR-S2-2 Keynote Lecture: Chronic rhinosinusitis with nasal polyps in asia



Luo Zhang MD, PhD

Department of Otolaryngology Head and Neck Surgery, Beijing Tongren Hospital, Beijing, China

Sinonasal tissue eosinophilia is present in a majority of CRSwNP patients but is currently more common in the West than in the East. Although in the Western world about 80% of nasal polyps carry a type 2 signature, this might be between 20% and 60% in Asian countries. There are accumulating evidences showing that the percentage of type 2 signature disease in patients with CRSwNP is dramatically increasing in several Asian countries (China, Korea, and Thailand) over the last 20-30 years. A huge challenge has already appeared due to the eosinophilic CRSwNP was extremely easy to relapse. In the recent years, the prognosis studies about CRSwNP are rising rapidly with the development of endoscopic sinus surgery. CRSwNP with asthma is a systemic disease that inevitably recurs. Radical surgery prolongs recurrence time and improves olfaction, rhinorrhea, and quality of life in the short-term. Ongoing research is focused on improving biomarkers for diagnosis, prognosis, and personalized optimal therapy.

Chinese CRSwNP patients may be classified into five phenotypes with different polyp recurrence rates, based on the presence of predominantly plasma cells, lymphocytes, neutrophils, eosinophils or mixed inflammatory cells in polyps. Tissue eosinophils are characteristic of inflammation in most but not all patients with CRSwNP and may be useful for defining subgroups and making treatment choices. It will be important to identify validated eosinophil-related biomarkers in different continents/countries for future research and for the introduction of precision medicine.

## Curriculum vitae

Professor ZHANG, Luo is Chang Jiang Scholars Program Professor, Capital Medical University (Beijing), China. He is President of Beijing TongRen Hospital.

Over the last decade his work has focused on the pathophysiology of chronic rhinosinusitis; the regulation of airway ciliary activity; mechanisms of specific-allergen immunotherapy of allergic rhinitis; and surgical techniques of endoscopic sinus surgery. His work has resulted in more than 260 peer reviewed publications.

He is Treasure of Asia Pacific Association of Allergy Asthma and Clinical Immunology. He is also the immediate past-president of the Chinese Allergy Society and President of International Society of Inflammation and Allergy of the Nose (ISIAN). He takes part in the editorial boards of Allergy (Associate Editor), International Forum of Allergy and Rhinology (Associate Editor), Laryngoscope, Expert Review of Clinical Immunology, Allergy Asthma & Immunology Research, and PLoS ONE. From 2016 to 2019, he was a director member of World Allergy Organization.



ARSR Symposium 2



**ARSR-S2-3 Keynote Lecture: Endotypes of chronic rhinosinusitis in optimization of treatment: Are we there yet?**

Professor Dr Baharudin Abdullah

Department of Otorhinolaryngology - Head and Neck Surgery, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia.

Despite recent advances, the optimal management of chronic rhinosinusitis (CRS) remains elusive. The goals of treating CRS are to improve quality of life, control inflammation and disease progression, and avoid complications. The goals are mostly achieved using pharmacotherapy with surgery performed in recalcitrant cases. Even though the phenotypic classification is expedient, it is inadequate to address the complexities and differences among the heterogeneous CRS subtypes which highlights the significance of CRS endotypes. Endotyping of CRS enables the prediction of the natural course of the disease, improves the understanding of the involved mechanism and thus helps to determine the appropriate modality from pharmacotherapy to surgery. The impact of endotyping can be clearly seen in the use of biologics. For the subgroup of CRS patients with persistent disease following pharmacotherapy and surgery, the use of biologics provides a valuable option. The differentiation of CRS into type 2 and non-type 2 endotypes, outlined the role of inflammatory markers in the disease process. The cytokines involved in type 2 inflammation such as IL-4, IL-5, IL-13 and IgE are important target of biologics. However, question still remain of the pertinent timing to initiate treatment, whether there is any difference to use it at preoperative or postoperative stage. Moreover, as the use of biologics is costly, the majority of CRS patients still depend on standard medical therapy and surgical intervention which need to be personalized according to individual patient.

Curriculum vitae

Professor Dr Baharudin Abdullah

Professor Baharudin Abdullah is a Senior Consultant in the Department of Otorhinolaryngology-Head & Neck Surgery in Universiti Sains Malaysia. He graduated with MBBS of Medicine and Surgery from Universiti Malaya (1994) and Master of Medicine (MMED) in Otorhinolaryngology-Head & Neck Surgery from Universiti Sains Malaysia (2002). He was an Honorary Visiting Scholar at Chinese University of Hong Kong, Hong Kong (2006) and Asian Surgical Association Clinical Fellow (Head and Neck Surgery), University of Hong Kong, Hong Kong (2006). He was a Fellow in Rhinology and Endoscopic Sinus Surgery at University of Graz, Austria (2014).

He is on the editorial board of several international medical journals. He has published widely in allergy, rhinology and head and neck surgery in several international and national journals and presented many scientific studies and papers both at the national and international level. He has contributed significantly to the successes of symposiums and workshops in Universiti Sains Malaysia (USM), and other symposiums, congresses and workshops both at national and international level. He is currently the President of Malaysian Society of Allergy and Immunology (MSAI).

## ARSR Symposium 2

**ARSR-S2-4 Inflammatory molecular endotypic differences in nasal polyps derived from Japanese and caucasian chronic rhinosinusitis with nasal polyps**

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Yasuhiro Tsunemi<sup>4</sup>, Peter H. Hwang<sup>2</sup>, Vijay R. Ramakrishnan<sup>5</sup>,  
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<sup>4</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Dokkyo University School of Medicine, Tochigi, Japan

<sup>5</sup>Department of Otolaryngology-Head and Neck Surgery, University of Colorado, Aurora, CO, USA

**Background:** There is emerging evidence on the heterogeneity of chronic rhinosinusitis with nasal polyps (CRSwNP) from population having disparate racial and geographic backgrounds. To better clarify these differences, we analyzed gene expression profiles of NPs derived from Japan and United States.

**Methods:** We performed whole transcriptome RNA sequencing and compared the gene expression profiles and analyzed the endotypes.

**Results:** Comparison of the transcriptome between Japanese and Caucasian NPs showed no apparent significant difference. Unsupervised cluster analysis identified two endotypes present with each NPs cohort: 1) type 2 endotype with higher expression of the C-C motif chemokine ligand 26 (*CCL26*), *CCL18*, cystatin SN (*CSTI*), collagen type IV alpha 5 chain (*COL6A5*), and *CCL13*, and 2) a non-type 2 endotype with high expression of the cysteine rich secretory protein 3 (*CRISP3*), statherin (*STATH*), cadherin 19 (*CDH19*), lactoperoxidase (*LPO*), and BPI fold containing family B member 2 (*BPIFB2*).

**Conclusions:** The gene expression profiles of Japanese and Caucasian were largely similar rather than heterogenous as expected. NPs from both racial groups is composed of the same two endotype, which we determine are present in differing ratios between each cohort with CRSwNP.

## ARSR Symposium 2

**ARSR-S2-5 Clinical characteristics and cytokine profiles of central-compartment-type chronic rhinosinusitis**

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**Background:** The clinical characteristics of central-compartment-type chronic rhinosinusitis (CRS) in East Asian individuals are not clear. We sought to investigate the clinical features and the cytokine profiles of central-compartment-type CRS in our patient group.

**Methods:** Adult patients diagnosed with bilateral CRS were recruited, and patients who had previously undergone sinus surgery and pansinusitis (the Lund-Mackay scores greater than 23) were excluded. Central-compartment-type CRS was defined by radiological pattern. The symptoms, inhalant allergen sensitization status, endoscopic findings, and radiological assessments were recorded and compared between the central-compartment-type CRS and other types of CRS. We also examined the extent of tissue eosinophilia and specific cytokine protein levels (eosinophil cationic protein [ECP], myeloperoxidase [MPO], immunoglobulin E [IgE], interleukin [IL]-4, IL-5, and IL-13) in the sinonasal tissues.

**Results:** Central-compartment-type CRS was found in 16 (23.9%) patients, and noncentral-compartment-type CRS was found in 51 (76.1%) patients. Hyposmia or anosmia as the major symptom was more common in the central-compartment-type CRS group. The numbers of eosinophils in tissue and serum were significantly higher in the central-compartment-type CRS patients. The presence of allergen sensitization was not significantly different between groups. The levels of IL-5 and IL-13 were increased in middle turbinate tissues of patients with central-compartment-type CRS.

**Conclusions:** Central-compartment-type CRS was associated with hyposmia or anosmia, eosinophilic subtypes, and elevated levels of IL-5 and IL-13 in middle turbinate tissues but not allergy status in our patients.

## ARSR Symposium 2

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### **ARSR-S2-6 Exposure to cigarette smoke enhances pneumococcal transmission among littermates in an infant mouse model**

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*Streptococcus pneumoniae*, one of the most common commensal pathogens among children, is spread by close contact in daycare centers or within a family. Host innate immune responses and bacterial virulence factors promote pneumococcal transmission. However, investigations into the effects of environmental factors on transmission have been limited. Passive smoking, a great concern for children's health, has been reported to exacerbate pneumococcal diseases. Here, we describe the effect of cigarette smoke exposure on an infant mouse model of pneumococcal transmission. Our findings reveal that the effect of cigarette smoke exposure significantly promotes pneumococcal transmission by enhancing bacterial shedding from the colonized host and by increasing susceptibility to pneumococcal colonization in the new host, both of which are critical steps of transmission. Local inflammation, followed by mucosal changes (such as mucus hypersecretion and disruption of the mucosal barrier), are important underlying mechanisms for promotion of transmission by smoke exposure. These effects were attributable to the constituents of cigarette smoke rather than smoke itself. These findings provide the first experimental evidence of the impact of environmental factors on pneumococcal transmission and the mechanism of pathogenesis.

## ARSR Symposium 3

**ARSR-S3-1 Keynote Lecture: Mechanism of allergic rhinitis and allergen immunotherapy: Update**

Mitsuhiro Okano\*, Kengo Kanai, Aiko Oka, Maki Akamatsu

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The Practical Guideline for the Management of Allergic Rhinitis in Japan is the standard guideline in Japan. The first edition was published in 1993, and the 9<sup>th</sup> edition was released in 2020. In this latest edition, the figure showing the mechanism of allergic rhinitis was revised in which type 2 immune response has a crucial role. Type 2 immune response is characterized by the production of type 2 cytokines including IL-4, IL-5, IL-13 and IL-31. For example, we showed that approximately two thirds of peripheral blood mononuclear cells from patients with Japanese cedar and cypress pollinosis (JCCP) produced IL-31 in response to allergen suggesting that IL-31 is not essential for the onset of JCCP. On the other hand, patients positive for IL-31 production showed higher symptom and QOL scores during pollen dispersal, and the levels of IL-31 was positively correlated with the scores suggesting that IL-31 is associated with the exacerbation. Th2 cells and ILC2 cells are the major source for type 2 cytokines. ILC2 cells in nasal mucosa are increased in patients with allergic rhinitis, and they produced IL-5 and IL-13 in response to PGD<sub>2</sub> and leukotrienes. In addition, regulatory mechanism for type 2 responses has been clarified in allergen immunotherapy. The immunotherapy can lead to a suppression of type 2 cytokine production and/or an induction of IL-10 via promoting regulatory cells including regulatory T cells and regulatory B cells. In addition, microenvironment especially microbiome in oral cavity affects the efficacy of sublingual immunotherapy.

## Curriculum vitae

1989: Kagawa Medical School (MD)

1993: Okayama University Graduate School of Medicine (PhD)

1995-1998: Visiting Researcher (Postdoctoral fellow)

Department of Immunology and Infectious Diseases

Harvard School of Public Health

1998-2003: Research Associate

2003-2004: Assistant Professor

2004-2017: Associate Professor

Department of Otolaryngology – Head & Neck Surgery

Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences

2017-present: Professor, Department of Otorhinolaryngology,

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ARSR Symposium 3



**ARSR-S3-2 Keynote Lecture: How to treat allergic rhinitis with sublingual immunotherapy wisely: Experience in korea**

Chae-Seo Rhee

Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

The prevalence of allergic rhinitis (AR) in the general population is increasing, and prevalence rates are reported to be between 2.9% to 54.1% across various regions and age groups. AR can have a considerable effect on a patient’s quality of life, and can be a cause of substantial socioeconomic burden. Among the current treatment options for AR, specific allergen immunotherapy is the only medical intervention that modifies fundamental immunologic mechanisms by inducing tolerance, and changes the natural course of the disease.

Sublingual immunotherapy (SLIT) for treatment of AR is now widely used, and its efficacy and safety have been established by many clinical trials, studies, and meta-analyses. Studies on the long-term effects of SLIT on AR treatment have shown its efficacy and safety not only in the adult population but also in the pediatric population though the two groups exhibit different levels of immunological factors at baseline. Furthermore, immunologic parameters have been suggested to better predict patient satisfaction with the treatment. However, factors such as new sensitization during SLIT and early adverse events are not correlated with the treatment outcome. As clinicians we should be able to select appropriate patients for SLIT treatment and if necessary, reassure patients to continue with the treatment depending on early parameters.

In this session, I will review about the SLIT with our reported experiences in Seoul National University Hospital, Seoul, Korea, and focus on the changes in immunologic parameters and adverse effects.

Curriculum vitae

Professor and Chair of Dept. of Otorhinolaryngology-Head and Neck Surgery, Seoul National University Hospital, Seoul National University College of Medicine,

- 1986 M.D. degree from Seoul Nat’l Univ. College of Medicine, Korea
- 1997 Ph.D degree from Seoul Nat’l Univ. Graduate School of Medicine, Korea
- 1987-1990 Served in Korean Army as an Army Physician
- 1990-1994 Residency of ORL at Seoul National University Hospital (SNUH)
- 1994-1998 Faculty at Seoul City Boramae Hospital Affiliated SNUH
- 1998-present Faculty of ORL-HNS at SNUH
- 1996.12-1997.02 Visiting scholar at Mie University, Department of Otorhinolaryngology, Japan
- 2000.3-2002.2 Visiting scholar at Dennis A Carson’s Immunology lab, and Eyal Raz’s Allergy Lab, Department of Internal Medicine, UCSD, CA, USA
- 2008.4-present Tenured Professor at SNU College of Medicin
- 2010.09-2014.03 Chair, Department of ORL-HNS at Seoul National University Bundng Hospital
- 2018.07.16-present Chair, Department of Otorhinolaryngology at SNUH and Seoul National University College of Medicine

## ARSR Symposium 3

**ARSR-S3-3 Keynote Lecture: Allergen immunotherapy: From subcutaneous to non-injection.**

Pongsakorn Tantilipikorn, MD PhD

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Allergic rhinitis is one of the most common health problems globally. The prevalence in Europe ranged from 17% to 28.5%. Whereas, the prevalence in Asia ranged from 6.9% to 36% and tend to increase every year. There are many treatment options for allergic rhinitis symptom control including allergen avoidance and environmental control, various choices of pharmacotherapy; e.g. topical steroids and oral antihistamines, immunotherapy and others; e.g. inferior turbinate reduction, acupuncture and herbal therapy.

Allergen immunotherapy is a repeated allergen administration in order to modulate immune response. Major mechanisms are immune deviation in favor of Th1 deviation and induction of regulatory T cells. Current evidences show that immunotherapy can reduce allergic symptoms, minimize medication usage and prevent new sensitization. Common injectable route of immunotherapy administration is subcutaneous immunotherapy (SCIT) and non-injectable route is sublingual immunotherapy (SLIT). The standardized mean difference of nasal symptom score for SLIT is  $-0.33[-0.54, -0.13]$ (1) and for SCIT is  $-2.17[-3.50, -0.84]$  as compared to placebo. There is no significant difference for symptom score between SLIT and SCIT. Actually, there are many alternatives of non-injectable immunotherapy such as epicutaneous immunotherapy, intradermal immunotherapy, oral immunotherapy, bronchial immunotherapy, intra-lymphatic immunotherapy and local nasal immunotherapy.

Local nasal immunotherapy (LNIT) is an immunotolerance induction in the nasal cavity. It was first introduced in the 1970s. Nasal dendritic cells in the nasal associated lymphoid tissue (NALT) play an important role for the induction of vaccine-induced priming and disseminating immune response. The network of dendritic cells around nostrils facilitates allergen molecules uptake and initiates the adaptive immune response. This may be the benefit of an immunotolerance induction directly in the nasal cavity which is a shock organ as compare to other non-injectable routes such as SLIT. Evidence demonstrates that LNIT and SCIT provide similar clinical efficacy. Murine model also shows that LNIT is able to induce IL-10 release and desensitization in allergen challenge. LNIT becomes less popular shortly after then because of several reasons; the dosage control difficulty and the compliance matter due to the frequent local side effects and the specific administration techniques needed in order to avoid allergen spillage into lower airway. The most recent randomized controlled trial of LNIT published in 2009.

Non-injectable immunotherapy repossesses attention lately. It is an easy route of administration which can be done by the patient at their home. It is less expensive, less time consuming and less invasive as compare to injection immunotherapy. Moreover, it is less likely to induce systemic reaction. Nasal route could be considered as an another option for non-injectable immunotherapy.

**Curriculum vitae**

*Head of Center of Research Excellent in Allergy & Immunology, Faculty of Medicine Siriraj Hospital, Mahidol University, THAILAND.*

*Assistant President for Research & Academic Affairs, Mahidol University, THAILAND.*

Associate Professor Dr. Pongsakorn Tantilipikorn completed his MD degree in 1992, and ENT training in Thailand in 1997. He was a rhinology fellow with Prof David Kennedy in University of Pennsylvania during 1997-1999. From 1999, he worked as an assistant professor in Chiang Mai University till 2004. During 2008-2010, he went to study with Prof Jean Silvain Lacroix at University of Geneva under the topic involved with basic science research in nasal inflammation. He got his PhD of Biostatistic & Epidemiology, under the thesis (with excellent result of defending thesis) title "Nasal Allergy: Diagnostic Criteria and Its Co-morbidities".

He currently is an Associate Professor and Chief of Center of Research Excellence in Allergy & Immunology of Faculty of Medicine and Assistant President in Research and Academic Affairs, Mahidol University. After being a fellow in American Rhinologic Society and European Rhinologic Society for more than 20 years, he was elected to be a board member of the International Society of Infection and Allergy of the Nose (ISIAN) since 2016. His special interests are : allergen immunotherapy, nasal inflammation, minimally invasive rhinologic procedures, mucosal immunity of nose & paranasal sinuses and pathophysiology of rhinosinusitis.



ARSR Symposium 3

**ARSR-S3-4 Local-nasal immunotherapy for allergic rhinitis: A systematic review and meta-analysis**

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**Rationale:** Non-injectable immunotherapy repossesses attention lately. It is an easy route of administration which can be done by the patient at their home, less expensive, less time consuming and less invasive as compare to injection immunotherapy. Moreover, it is less likely to induce systemic reaction. Nasal route could be considered as an appropriate option for non-injectable immunotherapy.

**Methods:** A systematic search was done using OVID Medline and EMBASE as main databases. We included all RCT comparing LNIT and placebo published in English language, up to 19 December, 2020. Data were pooled for meta-analysis. The heterogeneity measurement and sensitivity analysis were done.

**Results:** 20 studies with 698 participants were included. The LNIT group had greater post-treatment improvement of TNSS than the control group (SMD -1.37; 95% CI: [-2.04, -0.69]). All the individual symptom scores favour LNIT. SMD and 95%CI of SMS and medication score were -1.55; 95% CI: [-2.83, -0.28] and -1.09; 95% CI: [-1.35, -0.83]. No significant difference for serum specific IgE, nasal IgE and nasal ECP was observed between two groups. Only serum IgG showed significant increase (MD 0.45; 95% CI: [0.20, 0.70]) in LNIT group. The nasal provocation threshold changes obviously favoured LNIT (MD 27.30; 95% CI: [10.13, 44.46]). No significant adverse event was reported.

**Conclusion:** LNIT improves clinical symptoms, lessen medication usage and increase nasal provocation threshold in allergic rhinitis patients. No severe adverse event for LNIT application was reported. Although there is no difference for serum specific IgE, nasal IgE and nasal ECP, LNIT is still a route of choice for non-injection immunotherapy administration.

ARSR Symposium 3

**ARSR-S3-5 Influences of CD8<sup>+</sup> Tregs on peripheral blood mononuclear cells from allergic rhinitis patients**

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Department of Otorhinolaryngology-Head and Neck Surgery, Huashan Hospital of Fudan University, Shanghai, China

**Objectives—**CD8<sup>+</sup>(or CD4<sup>+</sup>) CD25<sup>+</sup>fork-head box transcription factor (Foxp3)<sup>+</sup> regulatory T cells (CD8<sup>+</sup> or CD4<sup>+</sup> Tregs) all play a significant role in immune homeostasis and tolerance. However, the role of CD8<sup>+</sup> Tregs in allergic rhinitis (AR) have not been clearly elucidated. The present study was aimed to assess the influence of CD8<sup>+</sup> Tregs on peripheral blood mononuclear cells (PBMCs) from AR patients.

**Methods—**Patients with AR were enrolled. PBMCs were obtained, and CD4<sup>+</sup> and CD8<sup>+</sup> Tregs were separated from PBMCs and cultured in vitro. We examined percentages of these Tregs in total CD4<sup>+</sup> or CD8<sup>+</sup> T cells, respectively. After that, we evaluated levels of interleukin (IL)-10 and transforming growth factor (TGF)-β in Tregs cultures. Finally, we administered CD4<sup>+</sup> and CD8<sup>+</sup> Tregs from AR patients into PBMCs cultures and examined contents of IL-4 and IL-5.

**Results—**The percentages of CD4<sup>+</sup> or CD8<sup>+</sup> Tregs in the total CD4<sup>+</sup> or CD8<sup>+</sup> T cells from PBMCs in AR patients were reduced compared to normal subjects. However, IL-10 and TGF-β and their mRNAs were increased in CD4<sup>+</sup> and CD8<sup>+</sup> Tregs cultures from AR patients, and there were no significant differences in their levels between these two Tregs cultures. IL-4 and IL-5 were increased in AR subjects PBMCs compared to normal ones and decreased after the AR CD4<sup>+</sup> or CD8<sup>+</sup> Tregs administration. However, there were no statistical differences in IL-4 and IL-5 concentrations between these two Tregs treatments.

**Conclusions—**The findings demonstrate that CD8<sup>+</sup> Tregs may alleviate inflammatory responses in AR condition.

**Keywords**

CD4<sup>+</sup> Tregs; CD8<sup>+</sup> Tregs; allergic rhinitis; PBMCs

## ARSR Symposium 3

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### ARSR-S3-6 Endoscopic sinus surgery for olfactory dysfunction caused by eosinophilic chronic rhinosinusitis

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#### I. Introduction

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

#### II. Methodology

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

#### III. Results

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

#### IV. Conclusion

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



ARSR Symposium 4

**ARSR-S4-1 Keynote Lecture: Recent advances of macrolide therapy for the treatment of chronic rhinosinusitis and other airway inflammation**



Takeshi Shimizu

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In 1984, the effectiveness of low-dose, long-term erythromycin treatment (macrolide therapy) for diffuse panbronchiolitis (DPB) was first reported in Japan. The 5-year survival rate for DPB improved from 62.9 to 91.4% after implementation of macrolide therapy. The usefulness of this treatment has since been demonstrated in patients with other chronic airway diseases, such as chronic bronchitis, cystic fibrosis, bronchiectasis, and chronic rhinosinusitis (CRS). The new 14-membered macrolides clarithromycin and roxithromycin and the 15-membered macrolide azithromycin are also effective for treating these inflammatory diseases. The mechanism of action of the 14- and 15-membered macrolides may involve anti-inflammatory rather than anti-bacterial activities.

Macrolide therapy is now widely used for the treatment of CRS in Japan; it is particularly effective for treating neutrophil-associated CRS and is useful for suppressing mucus hypersecretion. However, macrolide therapy is not effective for eosinophil-predominant CRS, which is characterized by serum and tissue eosinophilia, high serum IgE levels, multiple polyposis, and bronchial asthma. Recent reports have described new antiviral activities and the clinical efficacy of macrolides in treating chronic obstructive pulmonary disease (COPD), influenza virus infection and severe pneumonia.

We demonstrated that orally administered CAM attenuates the severity of avian influenza A virus (H5N1, H7N9) infection in monkeys by inhibiting the infection and reproduction of viruses and by suppressing the cytokines responses of infected lung. The therapeutic value of macrolides in treating severe airway inflammation may be caused by inhibition of the “cytokine storm” associated with the dysregulation of host immune responses, which causes respiratory distress in severe pneumonia.

Curriculum vitae

Takeshi Shimizu  
 Professor and Chairman  
 Department of Otorhinolaryngology-Head and Neck Surgery,  
 Shiga University of Medical Science, Otsu, Japan

Prof. Shimizu graduated from Mie University School of Medicine in 1983 and spent his fellowship at the Department of Otorhinolaryngology, Mie University (Prof. Yasuo Sakakura). He worked at the Department of Pulmonary Pathobiology (Prof. Paul Nettesheim), National Institutes of Environmental Health Science, U.S.A. in 1988-1991. Prof. Shimizu has been a chairman of Department of Otorhinolaryngology-Head and Neck Surgery, Shiga University of Medical Science, Otsu, Japan, since 2004. Prof. Shimizu’s major research interest is airway inflammation (Allergy and Immunology) in Rhinology, and he received the award of Japan Rhinologic Society in 1996.

## ARSR Symposium 4

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### ARSR-S4-2 The characteristics and surgical outcomes of CCAD in mid-taiwan

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Central compartment atopic disease (CCAD) is one of the phenotypes of the chronic rhinosinusitis with nasal polyp recently discovered by John M. DelGaudio in 2017. However, the mechanism and possible risks factors of CCAD has not yet been fully understood. The aim of this study is to unveil the clinical presentations and risk factors of CCAD in mid-Taiwan.

We retrospectively collect patients with CRS who underwent FESS in China Medical University Hospital from September, 2015 to September, 2020. Based on pre-operation CT and sinoscopy, the patients were divided into: “CCAD”, “non-CCAD” and “Equivocal” groups. Patients’ demographics, systemic disorders and comorbidity (hypertension, diabetes mellitus, allergic rhinitis, ectopic dermatitis, aspirin-exacerbated respiratory disease and asthma), preop and postop 3 month SNOT-22, surgical outcomes were analysed.

784 patients with CRS underwent FESS were included. 133 was excluded due to previous FESS or incomplete data. 73 were classified into CCAD group and 496 into non-CCAD group. There was a strong relationship between asthma and CCAD (19% versus 4%,  $p < .00001$ ), but relatively weak relationship between allergic rhinitis (37% versus 28%,  $p = 0.06$ ) and CCAD. Furthermore, more 2nd look FESS could be found in CCAD group. (29% versus 20%,  $p = 0.04$ )

CCAD is related to particular types of allergic diseases. The prevalence of allergic comorbidities might exist racial or regional difference. The prevalence of asthma was higher in our CCAD patients. Clinical symptoms of CCAD were more severe than other types of chronic rhinosinusitis with nasal polyps and the symptoms relieved well after surgical intervention.

ARSR Symposium 4



**ARSR-S4-3 Keynote Lecture: Introduction of hands-on seminar on basic research for clinicians in the Japanese Rhinologic Society**

Yoshimasa Imoto

Department of Otorhinolaryngology, Head and Neck Surgery, University of Fukui, Japan

As both clinical and basic research have been revealing the precise mechanisms about rhinologic disorders in this decades, it is important for otorhinolaryngologists to understand the disease from the point of both clinical and basic research. However, clinicians may encounter some problems when they start up and continue the basic research.

The Japanese Rhinologic Society has launched “Hands-on Seminar on Basic Research for Clinicians” since 2014. The aims of the seminar are to raise the motivation and research skills of basic research for all clinical otorhinolaryngologists, and to encourage inter-disciplinary collaboration through research with universities. So far, the seminar had been held by showing several basic experiments such as isolation of single cells from nasal samples, ELISA, Western blot, PCR, immunohistochemistry, cell culture, CRISPER-Cas9, and so on. Based on the questionnaire from the participants, they had a high need and satisfaction of these research seminars. Because this seminar has a great opportunity for all otorhinolaryngologists to find new idea to expand the avenue of basic understanding of rhinologic disorders, we believe this seminar should be continued as long as possible.

In this session, we would like to introduce about this seminar and show some experimental method including the isolation of mononuclear cells from peripheral blood, nasal polyps, and tonsils.

Curriculum vitae

2003 University of Fukui Faculty of Medical Sciences

2013 Post graduate course, University of Fukui Faculty of Medical Sciences

04/2003-03/2006 Resident, Division of Otorhinolaryngology Head & Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Science, University of Fukui

04/2011-10/2012 Medical Staff, Division of Otorhinolaryngology Head & Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Science, University of Fukui

11/2012-3/2015 Assistant Professor, Division of Otorhinolaryngology Head & Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Science, University of Fukui

4/2015-3/2017 Visiting scholar, Division of Allergy and Immunology, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois

4/2017- Assistant Professor, Division of Otorhinolaryngology Head & Neck Surgery, Department of Sensory and Locomotor Medicine, Faculty of Medical Science, University of Fukui

## ARSR Symposium 5


**ARSR-S5-1 Keynote Lecture: Concept and basic technique of endoscopic sinus surgery for chronic rhinosinusitis.**

Nobuyoshi Otori

Otorhinolaryngology, Jikei University School of Medicine, Tokyo, Japan.

Endoscopic sinus surgery (ESS) has become widespread as a standard surgical method for chronic rhinosininitis (CRS). Radical and thorough as well as appropriate removal of the sinus pathology leads the patient recovery from the disease. On the other hand, inappropriate and rough manipulation during the surgery may cause major complications such as orbital injury and CSF leakage. Especially, prevalence of orbital injury which resulted in permanent orbital dysfunction has been increasing.

Key points for safer and proper surgery are as follows,

1. Understand anatomy, especially anatomical relations of basal lamellas and ethmoidal air cells.
2. Examine pre-op CT, then image “3D” structure.
3. Keep a clear and proper field of endoscopic view.
4. Suitable choice of instruments.
5. Use microdebrider properly.
6. Know about the complications which actually occurred, and then learn how to prevent it.

The choice of instruments is important not only for a safe and accurate operation but also for smooth post-op healing process. There are many types of forceps, but through-cutting forceps are primarily used. They are preferred for effective preservation of mucosa and for prevention of injury. Microdebrider is very useful tools for smooth mucosal healing. OR time becomes shorter, and the stress for the patients are less. However, this “powered instrument” always have some risk of orbital and cranial complications. Moreover, these complication tend to progress rapid.

In this lecture, concept and techniques of our ESS is presented.

Curriculum vitae

Professor of Otorhinolaryngology, The Jikei University School of Medicine, Tokyo, Japan.

Nobuyoshi Otori received both his M.D. and Ph.D. from The Jikei University School of Medicine in Tokyo, Japan. His specialty in rhinology lies in the surgical management for nasal and sinus disease and skull-base disease. Computer assisted surgery, development of high-tech device and development of surgical training system are also the topics of his recent research work.

ARSR Symposium 5



**ARSR-S5-2 Keynote Lecture: Prelacrimal approach versus conventional surgery for inverted papilloma in the maxillary sinus**

Shin-ichi Haruna<sup>1\*</sup>, Tsuguhisa Nakayama<sup>2</sup>, Nobuyoshi Otori<sup>2</sup>

<sup>1</sup>Department of Otorhinolaryngology – Head and Neck Surgery, Dokkyo Medical University, Tochigi, Japan.

<sup>2</sup>Department of Otorhinolaryngology, Jikei University School of Medicine, Tokyo, Japan

**Objectives:** Prelacrimal approach has recently been applied for inverted papilloma (IP) in the maxillary sinus. We previously reported one of the prelacrimal approaches, endoscopic modified medial maxillectomy (EMMM). EMMM provides access to the maxillary sinus identically to conventional EMM, despite preservation of the inferior turbinate and nasolacrimal duct.

**Methods:** We retrospectively reviewed the patients with IP in the maxillary sinus to compare the surgical results by ESS and/or Caldwell-Luc (conventional approach) vs EMMM at different timepoint.

**Results:** Eighteen patients were performed conventional approach, and 28 performed EMMM. The clinical characteristics in both groups were similar. All the patients belong to T3 based on Krouse staging system and the average follow-up time were 45.5 months. Of the 18 patients with conventional group, recurrence was seen in 3 patients (16.6%). Whereas, no recurrence was seen in 28 patients with EMMM. No postoperative complication was seen in EMMM group.

**Conclusions:** EMMM is an effective surgical approach and reduces the recurrence for inverted papilloma in the maxillary sinus. In addition, EMMM is a less complicated method than other prelacrimal approaches.

Curriculum vitae

Education: Graduated at jikei Medical university in 1985.

Became Prof and Chairman of Dokkyo Medical University in 2006.

Professional Experience: Training of Endoscopic sinus surgery was made in Jikei University Hospital for more than 20 years.

During 1990-1992, the research of middle ear mucosa similar to sinus mucosa was studied in Minnesota University.

Professional Society: Japan Otorhinolaryngologic Society : Board member

Japan Rhinologic society: President

Major Interest: Pathological condition of the upper airway, specially eosinophilia and Endoscopic sinus surgery

## ARSR Symposium 5

**ARSR-S5-3 Keynote Lecture: Endonasal approach for Meckel's cave and foramen rotundum**

Boonsam Roongpuvapaht

Department of Otolaryngology Head and Neck Surgery, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Meckel's Cave located in petrous apex and surround by temporal lobe meningeal, trigeminal nerve and intercavernous carotid artery. This area had very complex anatomy and had surgical challenge. This area can approach by many routes eg. Endonasal approach, Transorbital approach, frontotemporal approach, orbitozygomatic approach, Subtemporal transpetrosal-transtentorial approach with anterior petrosectomy (Kawase-Shiobara approach). Endoscopic endonasal approach is more feasible from surgical knowledge, instruments and surgeon's expertise, this technique had less brain manipulation and no external incision. The Foramen Rotundum is one of landmark for approach to the Meckel's cave and use for define infratemporal fossa, middle cranial fossa and pteryopalatine fossa. There are few cases reports of spontaneous CSF leak from Foramen Rotundum which requires surgical management. Some case of tumor can spread from these compartments. This session we would like to share our experience in surgical of Meckel's cave and Foramen Rotundum.

## Curriculum vitae

## Education

MD. Faculty of Medicine, Ramathibodi Hospital, Mahidol University Otolaryngology Head and Neck Surgery  
 Department of Otolaryngology Head and Neck Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University

## Affiliations/Memberships

- Member of the Royal College of Otolaryngology head and neck surgeons of Thailand
- Executive committee of Thai Rhinologic Society
- Honorary Member of Thai Endocrine Surgeons Society

## Interests

- Advance Sinus Surgery and anterior skull base surgery
- Advance Head and Neck Surgery
- Endoscopic thyroidectomy
- Robotic Surgery
- Sialendoscopy

## ARSR Symposium 5

### ARSR-S5-4 Predictors of disease progression after endoscopic sinus surgery in patients with chronic rhinosinusitis

Kenzo Tsuzuki\*, Ken Okazaki, Takahiro Saito, Katsuya Fushimi, Kengo Hashimoto

Department of Otorhinolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Japan

**Objective:** This study aimed to determine adverse predictors after endoscopic sinus surgery (ESS) in patients with chronic rhinosinusitis (CRS), using our proposed operating (OP) scoring and postoperative endoscopic appearance (PEA) scoring systems.

**Patients and Methods:** Between 2007 and 2017, 281 adult patients with bilateral CRS undergoing primary ESS, who could be endoscopically evaluated after 12 months or more, were retrospectively analyzed. Patients were divided into eosinophilic CRS (E CRS, n = 205) and non-E CRS groups (n = 76). To determine postoperative exacerbation factors in sinonasal condition, the PEA score was clinically analyzed in relation to the pre- and intra-operative findings by multiple regression analyses.

**Results:** In analysis of changes of the PEA scores, the postoperative courses of E CRS showing similar to the early period (< 12 months) for non-E CRS significantly deteriorated over time after 12 months (p < 0.001). Especially, frontal sinus polyps recurred in the early period in E CRS. Young adult, asthma, high CT score, and frontal sinus polyps were shown as significant adverse predictors in multivariate analyses in E CRS.

**Conclusion:** This study suggests that complete pneumatization of the frontal sinus drainage pathway without any residual cells could be important for the maintenance of sinonasal condition, especially in younger adult patients with E CRS accompanying asthma. Early appropriate estimation of sinonasal condition appears to be important for the successful surgical management in CRS.

## ARSR Symposium 5

### ARSR-S5-5 Extent of endoscopic sinus surgery for eosinophilic chronic rhinosinusitis cases with asthma

Yasuyuki Hinohira, MD<sup>1\*</sup>, So Watanabe, MD<sup>2</sup>, Tomoaki Mori, MD<sup>3</sup>, Kenji Ishii, MD, Tetsuya Monden, MD, Koshiro Miura, MD, Taishin Motooka, MD, Tomonobu Kamio, MD, PhD<sup>1</sup>

<sup>1</sup>Department of Otolaryngology, Kamio Memorial Hospital, Tokyo, Japan

<sup>2</sup>Department of Otolaryngology, Khonodai Hospital, National Center for Global Health and Medicine, Ichikawa, Japan

<sup>3</sup>Department of Otolaryngology, Showa University Kotoh-Toyosu Hospital, Tokyo, Japan

**Introduction:** Eosinophilic chronic rhinosinusitis (E CRS) is known as refractory sinusitis with nasal polyps showing remarkable eosinophil infiltration. E CRS cases with bronchial asthma including aspirin exacerbated respiratory disease (AERD) are classified as severe type, and multiple ESS may be required. We have applied extended ESS to severe E CRS cases to overcome conventional ESS. The surgical procedures and the outcome are demonstrated in this study.

**Cases & methods:**

Extended ESS of both the frontal and the ethmoid sinuses was performed on 27 severe E CRS cases. 9 AERD cases were included.

All operations were performed under general anesthesia in Kamio Memorial Hospital. Submucous resection of the nasal septum cartilage and the inferior turbinate bone were done. Thick and edematous medial inferior turbinate mucosa was sacrificed because of severe allergic reaction. Extended ethmoid surgery as a new approach we advocated aims to extend the middle nasal meatus laterally. From the lateral to the anterior part of the middle nasal meatus was punched and/or drilled out up to the nasolacrimal duct to clearly open the lateral ethmoid and frontal recess cells. Draf I/IIb surgery was then performed to obtain postoperative pathway to the frontal sinus. The first branch of the olfactory nerve was identified if necessary.

**Outcomes and conclusion:**

Postoperative CT and endoscopic scores 1 year after surgery remarkably reduced from 60.2 to 14.6 and 14.0% respectively although long-term follow-up study is necessary. Our extended ESS is acceptable for severe E CRS.

## ARSR Symposium 5

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### ARSR-S5-6 Effectiveness of budesonide irrigation after FESS

Teik-Ying Ng\*, Liang-Chun Shih, Chih-Jaan Tai

Department of Otorhinolaryngology, China Medical University Hospital, Taichung, Taiwan.  
College of Medicine, China Medical University, Taichung, Taiwan.

**Introduction:** Chronic rhinosinusitis is a common inflammatory disease of the nasal mucosa. Successful rate of Functional Endoscopic Sinus Surgery (FESS) is about 85%. Current mainstay of medical therapy for chronic rhinosinusitis after surgery is sinus irrigation, topical or systemic steroid, systemic antibiotics. Budesonide nasal irrigation was introduced for postoperative management of patients with chronic rhinosinusitis.

**Objective:** Our study investigated effectiveness of budesonide irrigation in patients with chronic rhinosinusitis after FESS.

**Materials and Methods:** This is a prospective case-control study. We included patients with bilateral chronic rhinosinusitis post FESS, Lund-Mackay score >6 each side, complete 12 weeks Budesonide to large-volume, low-pressure saline sinus irrigation and complete SNOT-22 special sheet. We matched control group for age, gender, smoking condition, deviated nasal septum, Lund-Mackay score, allergic rhinitis and hypertension history. Study group used Budesonide 1mg add into Sodium Chloride & Sodium Bicarbonate mixture in 240cc distilled water or boil tap water for sinus irrigation. Control group used Sodium Chloride & Sodium Bicarbonate mixture in 240cc distilled water or boil tap water for sinus irrigation. We used t-test for outcome analysis.

**Results:** Our study included total 28 patients. SNOT-22 of two groups showed significant difference for thick nasal discharge.

**Conclusions:** Budesonide group saline irrigation significantly different in efficacy than saline controls on SNOT-22 thick nasal discharge outcome. Large, double-blinded, randomized controlled trials needed to clarify the effectiveness of budesonide nasal irrigation in chronic rhinosinusitis patients.



ARSR Symposium 6

**ARSR-S6-1 Keynote Lecture: Appropriate antimicrobial management of acute rhinosinusitis**



Muneki Hotomi

Department of Otorhinolaryngology, Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan

Acute rhinosinusitis is defined as “A disease that presents with respiratory symptoms such as nasal congestion, rhinorrhea, post-nasal drip, and cough, and is accompanied by headache, cheek pain, and facial tightness.” The Japanese Rhinologic Society has advocated Practical guideline for management of acute rhinosinusitis in Japan. It has been recommended to do antimicrobial treatment in consideration of the pathophysiology and antimicrobial resistance.

Diagnosis of severity of acute rhinosinusitis

Acute rhinosinusitis is mostly based on viral infection. Acute viral rhinosinusitis is thought to improve spontaneously within 10 days. Acute bacterial rhinosinusitis is diagnosed if purulent nasal discharge persists for more than 10 days or if the condition worsens after 5-7 days. For the diagnosis of acute rhinosinusitis, it is important to evaluate the severity of the disease.

Fundamentals of antimicrobial treatment for acute rhinoinusitis

Antimicrobial treatment should be considered based on the severity of the disease. In mild cases, viral infection is considered to be the main pathological condition, and follow-up without administration of antibacterial agents is recommended. On the other hand, in moderate to severe cases, treatment with amoxicillin is recommended.

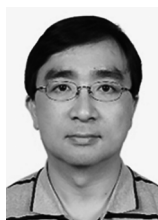
Intractable and/or prolonged pathogenesis

The biofilm formed by causative pathogens, interaction between the causative microorganisms, and the intra- and intracellular infections are involved in the pathogenesis of acute rhinosinusitis. Appropriate antimicrobial treatment guideline based on amoxicillin have been established in consideration of drug resistance. It is necessary to develop a treatment strategy that does not make it intractable or prolonged based on the evaluation of the host-pathogen interaction.

Curriculum vitae

1988-1993 M.D.	Wakayama Medical University
1993-1994	Resident in Department of Otolaryngology-Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan
1994-1998	Post graduate school of medicine, Wakayama Medical University, Wakayama, Japan
1998-2002	Chief of Department of Otolaryngology-Head and Neck Surgery, Arita Municipal Hospital, Wakayama, Japan
2002-	Assistant Professor of Department of Otolaryngology-Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan
2003-2005	Visiting Scientist, Department of Microbiology, University of Alabama at Birmingham (Prof. David E. Briles)
2009-2010	Visiting fellow, Department of Head and Neck, Cancer Institute Hospital (Dr. Kazuyoshi Kawabata)
2010-	Assistant Professor of Department of Otolaryngology-Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan
2016-	Professor and Chairman of Department of Otolaryngology-Head and Neck Surgery, Wakayama Medical University, Wakayama, Japan

## ARSR Symposium 6


**ARSR-S6-2 Keynote Lecture: The clinical features of endoscopic treated isolated sphenoid sinus diseases**

Te Huei Yeh

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

**Background:** Isolated sphenoid sinus disease (ISSD) is a rare clinical entity with potentially serious complications. The etiological distribution of ISSD varies among different areas and ethnicities. We aimed to investigate the clinical features of patients with endoscopic treated ISSD.

**Methods:** We retrospectively reviewed all patients with ISSD who had undergone endoscopic surgery between April 2013 and May 2019. The patient records were reviewed for demographic data, clinical presentations, endoscopic and imaging study findings, surgical outcomes and complications.

**Results:** A total of 37 patients with ISSD who underwent surgery were recruited. We divided patients into three groups according to etiology, including inflammatory diseases (78.4%), neoplasms (13.5%) and spontaneous cerebrospinal fluid (CSF) leaks (8.1%); fungal ball (62.2%) constituted the major cause of ISSD. Overall, the most common presenting symptom was headache or facial pain (65.5%). The endoscopic findings of bloody discharge and tumor lesions were mainly from the neoplasm group. Bony defects were more obvious on computed tomography in the neoplasm and CSF leak groups. Magnetic resonance imaging revealed a higher rate of involvement of the cavernous sinus (40.0%) and intracranial extensions (40.0%) in the neoplasm group. To summarize the surgical outcomes, the success rate was 97.1%, and the major complication rate was 5.4%.

**Conclusion:** ISSD represents a variety of etiologies, mostly comprising fungal ball in our area, while there is still a considerable proportion of ISSDs attributed to neoplasm and CSF leak. Untreated ISSD can result in serious complications. We recommend early surgical intervention for all patients with ISSD.

**Keywords:** sphenoid sinus, sinusitis, fungal infection, sinonasal neoplasm, cerebrospinal fluid leak

## Curriculum vitae

9/1977~6/1984	M.D.	Department of Medicine, National Taiwan University, College of Medicine
9/1993~6/1997	Ph.D.	Graduate Institute of Pharmacology, National Taiwan University, College of Medicine
Since 1990	Visiting Staff	Otolaryngology Department, National Taiwan University Hospital
10/1999~7/2000	Chairman	Otolaryngology Department, Lo-Tung Po-Ai Hospital
8/2010~	Associate Professor	Otolaryngology Department, National, Taiwan University, College of Medicine
11/1990~11/1991		
6/1997~10/1997	Research Fellow	Hospital of Lariboisiere, University of Paris VII
4/1998~5/1998	Clinical Fellow	Department of Otolaryngology, Hospital of University of Pennsylvania,
Since 1990	Member	Taiwan Society of Otolaryngology Head and Neck Surgery
Since 1990	Member	Formosan Medical Association
Since 1999	Member	Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum (CORLAS)
Since 2007	General secretary Executive director	Taiwan Society of Otolaryngology Head and Neck Surgery
Since 2019	Vice President	
Since 2020	President	Taiwan Rhinology Society

ARSR Symposium 6

ARSR-S6-3 Keynote Lecture: Surgical success in obstructive sleep apnea



Sung Wan Kim

Department of ORL-HNS, Kyung Hee University, Seoul, Korea

Surgical treatment in OSA patients is an important treatment method for failing positive-pressure treatment or first line treatment option depending on the patient’s condition. The most important limitation of surgical treatment is that it cannot be expected to work in many patients, such as positive pressure therapy, and it is not clear whether surgical treatment is successful postoperatively.

Criterion of surgical success is used in a variety of ways. However, there is no evidence of a reduction in long-term complications of sleep apnea, and whether or not to succeed in surgery is determined by AHI in many cases, but it is also true that AHI itself has many limitations. Therefore, it is thought that the success of the operation needs to be evaluated by many factors other than reducing AHI.

Various polysomnographic parameters other than AHI should be considered for the success criteria. And anatomical parameters such as objective widening of airway compared to preoperative state, change of Pcrit, are also important. The improvement of symptoms should not be overlooked. The timing of postoperative evaluation is also important. Patients differ a lot depending on the timing of the postoperative evaluation.

Surgeons will, therefore, need the formation of a new consensus for the criteria for surgical success and I would like to introduce a new tool for evaluation of OSA patients and the criteria for surgical success.

Curriculum vitae

Kyung Hee University, Korea

2003 PhD. Graduate School (Medicine, Otorhinolaryngology)-Ph. D

1998 Master, Graduate School (Medicine, Otorhinolaryngology)

1987 Undergraduate School (Medicine)

1999-2000 Visiting Scientist, Children’s Hospital Research Center, UTMB, USA

2005 Visiting Professor, Sleep Surgery Center, Stanford University, CA, USA

Professor, Dept. of ORL-HNS, Kyung Hee University Hospital, Seoul, Korea

Director, Department of Future Strategy, Kyung Hee Healthcare System, Seoul, Korea

2001- Member, Board of Directors, Korean Rhinologic Society

2009- Member, International Surgical Sleep Society

2009- Sleep Technology Special Interest Group, Advisory board member

2011- Member of Advisory Council, Korean Academy of Asthma, Allergy and Immunology

2011- Member of Advisory Council, Korean Society of Sleep Medicine

2014- Editorial board, Auris Nasus Larynx

Reviewer of Laryngoscope, JAMA Otolaryngology-Head and Neck Surgery, Clinical and Experimental Otolaryngology, Auris Nasus Larynx, etc

## ARSR Symposium 6

**ARSR-S6-4 Optimal multiple-layered anterior skull base reconstruction using a 360-degree suturing technique**

Kazuhiro Omura, MD, PhD<sup>1\*</sup>, Kazuhiro Nomura, MD, PhD<sup>2</sup>, Nobuyoshi Otori, MD, PhD<sup>1</sup>

<sup>1</sup>Department of Otolaryngology, Jikei University School of Medicine, Tokyo, Japan

<sup>2</sup>Department of Otolaryngology, Tohoku Kosai Hospital, Miyagi, Japan

**Background:** Advances in technique and instrumentation have improved outcomes after resection of anterior skull base tumors. However, cerebrospinal fluid (CSF) leak occurs in 4%–20% of patients. To reduce the risk of CSF leak, we have developed a novel reconstruction technique that consists of a four-layered graft with patchwork suturing and hard material.

**Objective:** The aim of this study was to evaluate the effectiveness of this reconstruction technique when used for resection of anterior skull base tumors.

**Methods:** This case series included 59 patients with anterior skull base tumors in whom a four-layered closure technique was used. The main outcome measures were complications, including CSF leak, meningitis, postoperative bleeding, and infection.

**Results:** There were no cases of CSF leak or serious complications after closure of the anterior skull base using the four-layered technique.

**Conclusion:** Closure of the anterior skull base in four layers prevented CSF leak and was not associated with any serious complications. However, further studies in larger numbers of patients are needed to confirm our outcomes using this closure method.

## ARSR Symposium 6

**ARSR-S6-5 The transseptal approach enhances nasal recovery without compromising resectability in endoscopic endonasal transsphenoidal adenomectomy**

Yen-Hui Lee<sup>1†</sup>, Huan-Chih Wang<sup>2†</sup>, Yi-Tsen Lin<sup>1</sup>, Shih-Hung Yang<sup>2</sup>, Chih-Feng Lin<sup>1</sup>, Po-Hao Huang<sup>2</sup>, Kuo-Chuan Wang<sup>2</sup>, Dar-Ming Lai<sup>2</sup>, Ham-Min Tseng<sup>2</sup>, Te-Huei Yeh<sup>1\*</sup>

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<sup>†</sup>Equal contributions

**Introduction:** Endoscopic endonasal transsphenoidal adenomectomy (TSA) is now the most frequently performed skull base surgery, and rhinological outcomes can be affected by different surgical corridors of TSA. We conducted this study to determine whether the endoscopic transseptal TSA could reduce nasal morbidities with comparable neurosurgical outcomes to those with the endoscopic transnasal approach.

**Method:** We retrospectively reviewed 62 consecutive patients who were aged 20 years old or older and received endoscopic endonasal TSA for pituitary adenoma from January, 2019 to June, 2020. We collected detailed data from radiological studies, endocrine studies, postoperative endoscopic evaluations, and smell tests for comparison.

**Results:** A total of 46 patients were enrolled in the analysis. The operation time and blood loss in the transseptal group were significantly less than those in the transnasal group (108 [69 – 143] minutes versus 170 [92 – 240] minutes,  $p < 0.05$ ; 50 [50 – 100] ml versus 100 [50 – 100] ml,  $p < 0.05$ ). The gross total resection rate was comparable between the two groups (63.0% versus 52.6%,  $p = 0.69$ ). Postoperative Lund-Kennedy endoscopic scores for crusting, discharge, edema and scarring were significantly lower in the transseptal group than in the transnasal group ( $p < 0.05$ ) while the smell test scores were not significantly different. The rates of complications were not significantly different.

**Conclusions:** The transseptal approach provides less operative time, less blood loss, and better recovery of nasal mucosa without compromising neurosurgical outcomes or increasing the rate of complications; thus, it could be considered when performing endoscopic endonasal TSA.

## ARSR Symposium 6

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### ARSR-S6-6 Rhinosinusitis following endoscopic endonasal skull base surgery

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The Endoscopic endonasal approach (EEA) has emerged as an alternative choice for skull base surgery. However, there is still limited data regarding postoperative sinusitis after EEA for skull base surgery. This study provided insight into the incidence and the possible risk factors of post-EEA sinusitis.

Patients undergoing EEA for skull base pathologies in a single institute from 2015 to 2019 were retrospectively recruited. Postoperatively, all patients were followed and checked with an endoscope weekly until nasal crusting or sinusitis subsided and then monthly. Demographic data, the site of the tumor, the type of reconstruction, and several outcomes including the incidence of sinusitis, culture reports were analyzed.

A total of 305 patients (119 males, 186 females) were recruited, with a mean age of 52.3 years. Over half of the tumors (77%) were located at sellar, parasellar or suprasellar region. 46.2 % of the cohort received a middle turbinate graft for reconstruction of the skull base. The incidence of sinusitis was 59.6%. Among them, only one case had chronic sinusitis. The most common culture report is *S. aureus*. Patients who had a prior history of radiation therapy in the head and neck region, or a history of prior endoscopic sinus surgery had a higher risk of postoperative acute sinusitis.

In conclusion, acute sinusitis following endoscopic endonasal skull base surgery is common but is usually transient and could subside with adequate local debridement and antibiotics treatment.

## ARSR Symposium 7


**ARSR-S7-1 Keynote Lecture: Differences and similarities between upper and lower airway focusing on innate immunity**

Joo-Heon Yoon, MD, PhD

Department of Otorhinolaryngology, Yonsei University College of Medicine, Seoul, Korea

The nose is the first respiratory barrier to external pathogens, allergens, pollutant or cigarette smoke, and vigorous immune responses are triggered when external pathogens contact the nasal epithelium. The mucosal epithelial cells of the nose are essential to the innate immune response against external pathogens and transmit signals that modulate the adaptive immune response. The upper and lower airways share many physiological and immunological features, but there are also numerous differences. It is crucial to understand these differences and their contribution to pathophysiology in order to optimize treatments for inflammatory diseases of the respiratory tract. This review summarizes important differences in the embryological development, histological features, microbiota, immune responses, and cellular subtypes of mucosal epithelial cells of the nose and lungs.

**Curriculum vitae**

1989~1991	Research Fellow, Department of Otorhinolaryngology, Yonsei University College of Medicine
1992~1997	Assistant Professor, Department of Otorhinolaryngology, Yonsei University College of Medicine
1998~2002	Associate Professor, Department of Otorhinolaryngology, Yonsei University College of Medicine
2003~present	Professor (tenured), Department of Otorhinolaryngology, Yonsei University College of Medicine
1999~2001	Associate Editor, Korean J of Otolaryngology, Head and Neck Surgery
2000~2010	Editorial board, J Korean Med Sci
2001~2003	Editor, Korean J of Skull Base Surgery
2004~2012	Director, The Airway Mucus Institute
2005~2008	Director of Medical Science Research Affairs, Yonsei University Health System
2005~2008	Director of Korean Otolaryngologic Board Examination
2008~2010	Vice Dean of Academic Affairs
2010~2014	Dean, Yonsei University College of Medicine
2011~2013	President, Korean Rhinologic Society
2009~2016	Editorial Board, Am J Respir Cell Mol Biol
2017~2018	Council member, Korean Society for Molecular and Cellular Biology
2021. 4.23-25	President, International Congress of Otorhinolaryngology-Head & Neck Surgery 2021
2003~present	Member of Collegium Otorhinolaryngologicum Amicitiae Sacrum (CORLAS)
2005~present	Member, The Korean Academy of Science and Technology
2009~present	Member, National Academy of Medicine of Korea

ARSR Symposium 7



**ARSR-S7-2 Keynote Lecture: Role of zinc oxide and asian sand dust in the development of aspergillus fumigatus biofilm on nasal epithelial cells**

Seung-Heon Shin\*, Mi-Kyung Ye, Dong-Won Lee, Mi-Hyun Chae

Department of Otolaryngology-Head and Neck Surgery, School of Medicine, Catholic University of Daegu, Daegu, Korea

**Background:** Over the past 10 years, there has been an increased prevalence of fungus ball (FB) in paranasal sinuses. Previous endodontic maxillary teeth treatments have increased FB development in the maxillary sinus. Asian sand dust (ASD) aggravate the inflammatory response of respiratory epithelial cells. We sought to evaluate the effects of zinc oxide (ZnO), the main component of endodontic sealers, and ASD on developing *Aspergillus fumigatus* biofilms on primary human nasal epithelial cells.

**Methods:** Primary nasal epithelial cells were cultured with *A. fumigatus* spores ( $1 \times 10^5$ /ml) with 1 µg/ml and 3 µg/ml of ZnO or 50 µg/ml and 100 µg/ml of ASD for 72 h. Supernatant and cellular interleukin (IL)-6, IL-8, and transforming growth factor (TGF)-β1 levels were determined by ELISA and RT-PCR. *A. fumigatus* biofilm formation were determined using crystal violet, concanavalin A, safranin staining, and confocal scanning laser microscopy.

**Results:** IL-6 and IL-8 mRNA expression levels and IL-6, IL-8 and TGF-β1 protein levels in nasal epithelial cells increased significantly by *A. fumigatus* exposure. When nasal epithelial cells were cultured with *A. fumigatus*, biofilm dry weight, crystal violet, safranin, and concanavalin A staining intensity increased in a time-dependent manner. 50 µg/ml of ASD significantly enhanced biofilm formation after 24 h. However, ZnO did not influence *A. fumigatus* biofilm formation.

**Conclusion:** *A. fumigatus* biofilm formation increased the presence of nasal epithelial cells and ASD enhanced biofilm formation. However, ZnO alone did not influence or aggravate biofilm formation in sinonasal mucosa.

Curriculum vitae

Name : Seung Heon Shin, M.D., PhD

Present Academic and Hospital Appointments: Professor of Otorhinolaryngology at Daegu Catholic University, School of Medicine, Rhinology & Allergy Division.

EDUCATION

1997-2001 Ph. D. Course, Kyung Pook National University, School of Medicine

1989-1991 M.S., Kyung Pook National University, School of Medicine

1982-1988 M.D., Kyung Pook National University, School of Medicine

1989-1992 Residency of Otorhinolaryngology, Kyung Pook National University Hospital, Daegu, Korea

2006. 10 -2007. 3 Visiting Scientist, Mayo Clinic, MN

1999. 8 – 2001. 3 Research Fellow, Mayo Clinic MN

2021.04 - President of Korean Rhinologic Society

## ARSR Symposium 7


**ARSR-S7-3 Keynote Lecture: Copy number variation in *DRC1* is the major cause of primary ciliary dyskinesia in Japan**

Kazuhiko Takeuchi

Department of Otorhinolaryngology, Head &amp; Neck Surgery, Mie University Graduate School of Medicine, Tsu, Japan

**Background:** Primary ciliary dyskinesia (PCD) is a rare genetic disorder caused by functional impairment of cilia throughout the body. It is known that major disease-causing genes differ from one population to another. The major genetic cause in the Japanese population remains unknown. Moreover, the involvement of copy number variation (CNV) in the development of PCD is largely unknown.

**Methods:** We examined 93 Japanese patients with clinically suspected PCD from 84 unrelated families. CNV was examined either by exome sequencing of a PCD gene panel or by whole-exome sequencing (WES). The identified alterations were validated by PCR and Sanger sequencing. Nasal ciliary ultrastructure was examined by electron microscopy.

**Results:** Analysis of CNV by the panel or WES revealed a biallelic deletion in the dynein regulatory complex subunit 1 (*DRC1*) gene in 21 patients, which accounted for 49% of the PCD patients in whom a disease-causing gene was found. Sanger sequencing of the PCR product revealed a 27,748-bp biallelic deletion including exons 1–4 of *DRC1* with identical breakpoints in all 21 patients. The ciliary ultrastructure of the patients with this CNV showed axonemal disorganization and the loss or gain of central microtubules.

**Conclusion:** The deletion of *DRC1* is the major cause of PCD in Japan and this alteration can cause various ciliary ultrastructural abnormalities.

## Curriculum vitae

Kazuhiko Takeuchi

1984	Graduated from School of Medicine, Mie University
1988	Graduated from Graduate School of Medicine, Mie University
1988	Staff of Department of Otorhinolaryngology, Mie University Hospital
1009~1992	Research fellow at University of California, San Francisco (Department of Anatomy)
2002	Associate Professor, Department of Otorhinolaryngology, Head & Neck Surgery, Mie University
2008	Professor and Chairman, Department of Otorhinolaryngology, Head & Neck Surgery, Mie University



ARSR Symposium 7

**ARSR-S7-4 Polyethylene glycol-coated graphene oxide loaded with erlotinib as an effective therapeutic agent for treating nasopharyngeal cancer cells**

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<sup>3</sup>Department of Chemical and Materials Engineering, Chang Gung University, Taoyuan, Taiwan.

<sup>4</sup>Department of Neurosurgery, Chang Gung Memorial Hospital Linkuo Medical Center and College of Medicine, Chang Gung University, Taoyuan, Taiwan

**Introduction:** Nasopharyngeal carcinoma (NPC) is a common cancer in southern China and Taiwan, and radiation therapy combined with or without chemotherapy is its mainstay treatment. Although it is highly sensitive to radiotherapy, local recurrence and distant metastasis remain difficult unsolved problems. In recent years, graphene oxide (GO) has been found to be a promising novel anti-cancer drug carrier. Here, we present our designed functionalized GO, polyethylene glycol-coated GO (GO-PEG), as a drug carrier, which was loaded with erlotinib and showed promising anticancer effects on NPC cells.

**Methods:** The effects of GO-PEG-erlotinib on the proliferation, migration, and invasion of NPC cells were investigated by WST-8 assay, wound healing assay, and invasion assay respectively. RNA sequencing was conducted and analyzed to determine the molecular mechanisms by which GO-PEG-erlotinib affects NPC cells.

**Results:** Our results showed that GO-PEG-erlotinib reduced NPC cell viability in a dose-dependent manner, and also inhibited the migration and invasion of NPC cells. The RNA sequencing revealed several related molecular mechanisms.

**Conclusions:** GO-PEG-erlotinib effectively suppressed NPC cell proliferation, migration, and invasion, likely by several mechanisms. GO-PEG-erlotinib may be a potential therapeutic agent for treating NPC in the future.

ARSR Symposium 7

**ARSR-S7-5 The paradigm shift in treating olfactory neuroblastoma: A 10-year analysis in taipei veterans general hospital**

Yun-Ting Chao<sup>1\*</sup>, Wei-Hsin Wang<sup>2</sup>, Ching-Yin Ho<sup>3</sup>, Chih-Hung Shu<sup>4</sup>, Ming-Ying Lan<sup>1</sup>

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<sup>3</sup>Department of Otorhinolaryngology, Cheng Hsin General Hospital, Taipei, Taiwan

**Purpose:** Olfactory neuroblastoma (ONB) is a rare sinonasal tumor arising from the neuro-epithelium of the cribriform plate, superior turbinate, and superior nasal septum. The ONB is prone to invade the dura, anterior cranial fossa, olfactory bulbs, and even frontal lobe of the cerebrum, making it challenging in treating such tumors. Traditionally, the surgical approach often involved open craniofacial resection. Nevertheless, the endoscopic endonasal approach (EEA) and skull base reconstruction techniques have been exploited to improve surgical outcomes, to reduce hospital stay and patient morbidity. In the current study, we aim to present the paradigm shift in treating ONB in a tertiary referral center and to analyze its impact on disease control, patient survival and complications.

**Methods:** We retrospectively included ONB patients who were treated in a single institute (Taipei Veterans General Hospital) during the past ten years (2011-2020). The shifting treatment strategies in different periods were observed. We collected data regarding clinical/histological staging and treatment modalities, and looked into their effects on the local recurrence, patient survival and complications.

**Results:** A total of 16 patients were included (9 females and 7 males, mean age: 50.9 ± 11.9 years old, mean follow-up time: 47.3 months). Eight (50%) patients were recurrent cases having been treated in other hospitals. The distribution in the modified Kadish staging system was 1 (6.3%) stage B; 13 (81.2%) stage C and 2 (31.3%) stage D. In Hyams histological staging, 2 (12.5%) cases were grade 1; 5 (31.3%) grade 2; 8 (50%) grade 3 and 1 case undetermined. Before 2015, 6 patients were included: three of them underwent craniotomy, only 2 received transnasal surgery (autologous fat or inferior turbinate mucosal graft reconstruction), and only 1 case received primary concurrent chemoradiation therapy. After

the year 2015 when we extensively implemented EEA, by which a total of 9 patients was treated. The skull bases were reconstructed in a multilayer fashion (1 with fascia lata and 8 with fascia lata plus pedicled nasoseptal flaps). Postoperatively, 8 patients received adjuvant radiotherapy with/without chemotherapy. There was no significant difference in disease-free survival between patient groups treated before and after 2015 (40.0% vs.68.6%;  $p=0.736$ ). As for the surgical complication, 1 patient suffered from cerebrospinal fluid leakage before 2015, while no leakage occurred after 2015 except for sphenoid sinus outflow tract obstruction by the nasoseptal flap in 1 case.

**Conclusion:** The composite EEA tumor resection and multilayer skull base reconstruction have become the mainstay of surgical treatment for ONB. The bi-nostril bi-manual technique through two-surgeon four-hand teamwork provides a wide surgical field for better hemostasis and tumor margin control. Furthermore, the advances of skull base reconstruction promise a radical resection of the tumor. Although no significant benefit in prognosis was observed compared to the traditional ways of surgical approach, the EEA still provides shorter recovery time, fewer complications, and a scar-free cosmetic outcome.

**EP-1 Decreased expression of type I (IFN- $\beta$ ) and III interferon (IFN- $\lambda$ ) and IFN-stimulated genes in chronic rhinosinusitis with and without nasal polyps**

Sang Hag Lee, MD, PhD

Department of Otorhinolaryngology-Head & Neck Surgery, College of Medicine, Korea University, Seoul, Korea

**Background:** Little is known about the antiviral responses in the sinonasal mucosa of patients with chronic rhinosinusitis (CRS).

**Objective:** we investigated the presence of virus, the expression of TLR3 and TLR7, and interferon (IFN) and IFN-stimulated genes (ISGs) in healthy mucosa of control and inflammatory sinus mucosa of CRS patients, and evaluated whether the levels of IFN and ISGs may be affected by CRS-related cytokines and by the treatment with macrolides, dexamethasone, or TLR3 and TLR7 agonists.

**Methods:** The presence of virus in sinonasal mucosa was evaluated with real time PCR. The expression of IFN and ISGs in sinonasal mucosa and in cultured epithelial cells treated with Th1 and Th2 cytokines, macrolides, dexamethasone, or TLR3 and TLR7 agonists were evaluated with real time PCR and western blot. The expression of TLR3 and TLR7 in sinonasal mucosa were evaluated with immunohistochemistry.

**Results:** Respiratory viruses was detected in 15 % of samples. IFN and ISGs are expressed in normal mucosa, but their levels were decreased in CRS patients. IFN and ISGs were up-regulated in cells treated with macrolides, dexamethasone, or TLR3 agonist, but a part of them was decreased in cytokine-treated cells. TLR3 and TLR7 levels showed no significant difference between normal and inflammatory sinus mucosa.

**Conclusion:** These results suggest that decreased levels of IFN and ISGs in CRS may contribute to the impairment of the antiviral innate response in inflammatory sinonasal epithelial cells. Macrolides and glucocorticoids may provide the positive effects on the treatment of CRS by upregulating IFN and ISGs.

**EP-2 PVP-I reduces LPS-induced airway inflammation by blocking TLR4 signaling in airway epithelial cells**

Seung Hoon Lee, Sun-Hee Yeon, Seung-Hyeon Choi, Soo-Kyung Park, Mi-Ra Choi, Yong Min Kim\*

Department of Otorhinolaryngology-Head and Neck Surgery, Research Institute for Medical Science, Chungnam National University School of Medicine, Daejeon, Korea

**Background:** Povidone-iodine (PVP-I) is an antiseptic and a disinfectant with broad-spectrum antimicrobial activity against various pathogens. However, it is unclear whether PVP-I nasal instillation can suppress mucosal inflammation in non-eosinophilic chronic rhinosinusitis mice. **Objective:** The aim of the study was to explore the anti-inflammatory effects and the underlying molecular mechanism of PVP-I on LPS-stimulated airway epithelial cells and to investigate whether nasal instillation of PVP-I can suppress mucosal inflammation in non-eosinophilic CRS mice.

**Methods:** Analyses of the inflammation related molecules were measured by ELISA, western blotting, qRT-PCR, immunoprecipitation and histopathology (hematoxylin and eosin, immunohistochemistry, and periodic acid-schiff staining) stain assay in the nasal epithelial cells or non-eosinophilic CRS mice.

**Results:** PVP-I blocked expressions of the inflammation-related molecules, such as NLRP3, NF- $\kappa$ B-p65, caspase-1, and IL-1 $\beta$ , translocation of the NF- $\kappa$ B to the nucleus, and assembly of NLRP3/ASC complexes in the nasal epithelial cells or non-eosinophilic CRS mice. Notably, PVP-I strongly blocked the receptor interaction of TLR4 and MyD88 in the epithelial cell of nasal mucosa.

**Conclusion:** We demonstrated that PVP-I significantly attenuated inflammatory molecules and cytokines via blocking the formation of TLR4 and MyD88 complexes in the LPS-induced mucosal inflammation in non-eosinophilic CRS.

### EP-3 Two siblings with primary ciliary dyskinesia with the same homozygous variants

Guofei Feng<sup>1\*</sup>, Shun Saso<sup>2</sup>, Hajime Sasano<sup>3</sup>, Yifei Xu<sup>1</sup>, Kazuhiko Takeuchi<sup>1</sup>

<sup>1</sup>Department of Otorhinolaryngology - Head and Neck Surgery, Mie University Graduate School of Medicine, Tsu, Japan.

<sup>2</sup>Faculty of Medicine, Mie University, Tsu, Mie, Japan.

<sup>3</sup>Department of Respiratory MedicineI, Ise Red Cross Hospital, Ise, Japan.

Primary ciliary dyskinesia (PCD) is a rare genetic disorder with impaired function of motile cilia, which causes failure of mucociliary clearance. Mutations in PCD genes usually cause ciliary ultrastructural defects. Nevertheless, approximately 30% of PCD cases have normal ciliary ultrastructure. In the current study, we report two sisters in their twenties suspected of PCD with similar symptoms. They were born term and did not have situs inversus. The elder sister had chronic lower respiratory tract infections and bronchiectasis with wet cough when she was referred. She had asthma and allergic rhinitis. Ear endoscopic showed right eardrum with calcified plaque and left eardrum reflex was shortened. Paranasal sinus CT showed opacification of right maxillary sinuses. Chest CT showed bronchiectasis in both lower fields. The younger sister had sinusitis, allergic rhinitis, and asthma with a productive cough and rhinorrhea. Ear endoscopic showed bilateral eardrums were retracted and the light reflex was missing. Chest CT showed similar bronchiectasis with her sister. Electron microscopy of the nasal mucosa from elder sister showed a normal ciliary axoneme structure. The whole-exome sequencing of both siblings revealed a homozygous variant of a PCD-causing gene, and Sanger sequencing confirmed that the parents had heterozygous variants. This is the first report of Japanese siblings with PCD caused by a missense homozygous mutation of this gene.

### EP-4 Using three-dimensional printed sinus models for assessing the performance of sinus ultrasound in diagnosis of sinusitis

Chih-Kai Hsu, MD<sup>1,2</sup>, Hung Chang, MD<sup>3</sup>, Wen-Chan Yu<sup>4</sup>, Yi-Chun Chen, PhD<sup>5</sup>, Ming-Ying Lan, MD, PhD<sup>1,3\*</sup>

<sup>1</sup>School of Medicine, National Yang-Ming University

<sup>2</sup>Department of Medical Education, Taipei Veterans General Hospital

<sup>3</sup>Department of Otorhinolaryngology-Head and Neck Surgery, Taipei Veterans General Hospital

<sup>4</sup>3D Printing Technology and Resource Integration Center, Department of Rehabilitation and Technical Aid Center

<sup>5</sup>Department of Optics and Photonics, National Central University, Taiwan

**Background:** There is still limited research regarding using A-mode ultrasound (A-US) in the diagnosis of sinusitis. In this study, we designed a three-dimensional (3D) printed sinus model to simulate the clinical condition of using A-US in patients with rhinosinusitis.

**Methods:** Computed tomography images of three different sizes of normal maxillary sinuses were utilized to fabricate 3D printed sinus models. Water and different concentration of glycerol solutions were used for mimicking various sinus mucus with different viscosity. The depth and amplitude of back wall echo (BWE) in A-US were recorded and analyzed under different experimental parameters, such as fluid volume, the viscosity of the solution, and transducer measuring position.

**Results:** The amplitude of BWE was positively correlated to the anterior-posterior (AP) dimension of the sinus ( $p < 0.001$ ). On the other hand, the depth of BWE was negatively correlated to the concentrations of glycerol solution ( $p < 0.001$ ).

**Conclusion:** A 3D printed sinus model is an ideal tool to analyze A-US in various simulated clinical conditions of sinusitis. In our study, we found A-US is a convenient tool to diagnose sinusitis. Moreover, the AP dimension of the maxillary sinus and the viscosity of the sinus fluid were found to be highly related to the amplitude and the depth of BWE respectively.

**EP-5 Using image J platform in analysis of sinus X-ray for assisting diagnosis of fungal sinusitis**

Liting Hung<sup>1\*</sup>, Chingyin Ho<sup>2</sup>, Shengan Lee<sup>3</sup>, Chengjie Hsu<sup>1</sup>, Mingying Lan<sup>1,4</sup>

<sup>1</sup>Department of Otolaryngology, Taipei Veterans General Hospital

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<sup>3</sup>Department of Health Management, Kainan University

<sup>4</sup>School of Medicine, National Yang Ming Chiao Tung University, Taiwan

**Background:** Early identification of fungal sinusitis remains a challenge. This study aims to assist diagnosis of fungal maxillary sinusitis using sinus plain film and free software ImageJ platform.

**Material and methods:** We retrospectively collected patients with unilateral chronic bacterial rhinosinusitis, and fungal rhinosinusitis from Mar, 2015 to Jan, 2019. All the patients should have received endoscopic examination, sinus X-ray, and computed tomography of paranasal sinus. We used ImageJ software to mark bilateral maxillary sinuses to calculate and compared the integrated density.

**Result:** Forty patients were included. 32, 42, and 6 sides were diagnosed with normal sinus, bacterial sinusitis, and fungal rhinosinusitis, respectively. The integrated density was significantly different between fungal rhinosinusitis group and normal sinus, bacterial sinusitis group, respectively.

**Conclusion:** Using the integrated density of ImageJ software is a promising tool to assist diagnosis of fungal rhinosinusitis.

**EP-6 A novel scoring system of surgical findings at the sinus and olfactory cleft in patients with chronic rhinosinusitis**

Ken Okazaki\*, Takahiro Saito, Katsuya Fushimi, Kenzo Tsuzuki

Department of Otorhinolaryngology-Head and Neck Surgery, Hyogo College of Medicine, Hyogo, Japan

**Outcome Objective:** This study aimed to propose a surgical scoring system at endoscopic sinus surgery (ESS) and to evaluate recurrence in patients with chronic rhinosinusitis (CRS).

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

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

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

**EP-7 Statistical analysis of eosinophilic chronic rhinosinusitis at Fukuyama city hospital**

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**Introduction:** Eosinophilic Chronic Rhinosinusitis(=ECRS) often cause the recurrence of the nasal polyps after the operation and to suffer from treatment.

**Purpose:** We are characteristic in the chronic rhinosinusitis 127 cases with the history of treatment in each group of non-ECRS and ECRS at our hospital or analyze it.

**Result:** Non-ECRS were 37 cases among 127 CRS, There are ECRS 90 cases, of which 7 were mild ECRS,32 were moderate ECRS, 51 were severe ECRS in 127 CRS cases. In addition, there was significant difference between serum eosinophils level and, the total IgE level in each group .But there was not significant difference to the number of eosinophil in nasal polyp tissue in each group. Dupilumab uses 1case non-ECRS and 5 cases severe ECRS. Among them,5 severe ECRS cases were treated effectively.

**Conclusion:** This time, there was a significant difference in serum eosinophil level and the total IgE levels in each group. In addition, the control was also good in cases using the biological preparation. In the future, we would like to continue to analyze appropriate treatment including biological preparation and want to accumulate more cases.

**EP-8 Therapeutic effects of sinonasal topical steroid treatment on postoperative eosinophilic chronic rhinosinusitis patients.**

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**Objective.** Postoperative treatment is required for eosinophilic chronic rhinosinusitis (ECRS) to maintain the respiratory and olfactory function. Although available biotics have been recently reported to have therapeutically effects on the refractory ECRS and/or asthma, corticosteroids (steroids) still play an important role in the postoperative recurrence of nasal polyposis. The purpose of this study was to clarify the indications for sinonasal topical steroid treatments, and to evaluate its therapeutic effects in postoperative ECRS patients.

**Method.** Between January 2016 and February 2020, 30 adult patients (22 men and 8 women; median age: 48 years, age range 28-75 years) with ECRS who underwent bilateral primary functional endoscopic sinus surgery (FESS) were retrospectively enrolled in this study. We investigated postoperative courses in two groups: group A, patients who underwent sinonasal topical steroid treatment; and group B, control patients who did not.

**Results.** Group A was significantly younger than group B ( $p < 0.01$ ), and the preoperative CT score was significantly higher in group A than in group B ( $p < 0.05$ ). In the postoperative stage, the nasal symptoms questionnaire component of olfactory loss and the postoperative endoscopic appearance score were significantly worse in group A than in group B ( $p < 0.01$ ).

**Conclusion.** These data suggest that younger adult, more severe rhinosinusitis in the pretreatment stage, and postoperative olfactory loss led to the need for sinonasal topical steroid treatment to prevent relapsing inflammation after FESS in ECRS patients.

**EP-9 Mepolizumab therapy on eosinophilic chronic rhinosinusitis associated with asthma**

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**Background:** Eosinophilic chronic rhinosinusitis (ECRS), which is characterized by the accumulation of eosinophils in nasal polyps, is a refractory rhinosinusitis that is often associated with asthma. Although appropriate operation and post-operative management are necessary, there are currently no well-established treatments for this condition. The optimized asthma treatment is critical for management of ECRS. In Japan, an anti-IL-5 monoclonal antibody, mepolizumab, was approved for the treatment of severe asthma in 2016, and there are increasing numbers of evidence about its efficacy on eosinophilic asthma. However, there are only a few previous reports that show the efficacy of mepolizumab on ECRS associated with severe asthma.

**Method:** 12 patients with ECRS associated with severe asthma received mepolizumab therapy for at least 16 weeks. They were evaluated by nasal symptom VAS scale, nasal polyp score (NPS), Lund-Mackay system score (LMS), and number of peripheral blood eosinophils before and after receiving mepolizumab.

**Results:** NPS, LMS and the number of peripheral blood eosinophils were significantly improved after the initiation of mepolizumab. Some cases showed the dramatic improvement of nasal symptom VAS scale, but significant improvement was not recognized in all cases.

**Conclusions:** Anti-IL-5 therapy might be an additional treatment choice for ECRS associated with severe asthma.

**EP-10 Combination flap technique for choanal atresia**

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Choanal atresia is a congenital malformation showing obliteration or narrowing of nasal choanae. Recommended therapeutic options are suggested to perform surgical treatments using endoscopic technique: transnasal puncture or endoscopic resection with flap technique, but there is no clear consensus in the choice of above two surgical methods, as long-term outcomes including complication rate of restenosis should be affected by growth of patients. On the contrary, restenosis of created hole in sinus surgery is also suggested to be induced by scarring and/or synechia formation in surgical area, especially in exposed bone. Therefore, covering flap technique for exposed bone is well-recommended to reduce scarring and/or synechia formation in sinus surgery such as modified Lothrop procedure and nasoantral window formation etc. In the endoscopic resection of choanal atresia, there are mainly two flap techniques: 1) cross-over flap technique, which covers exposed septal bone surface located in vertical area, 2) single side-hinged flap technique, which covers horizontal surface of punctured choanal mucosa. We performed endoscopic resection with novel combination flap technique modifying above two techniques to cover exposed bone and mucosa in two choanal atresia cases, and experienced long-term good results. The combination flap technique would pave the way for good patency of atresia as reducing scarring and/or synechia formation.



**EP-11 A study of the efficacy on surgical treatment for allergic rhinitis**

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**Objective:** Allergic rhinitis (AR) is an endemic disease affecting a large proportion of Japan's population. According to the Japanese Guidelines for AR, surgical treatment is recommended for severe AR with nasal obstruction. The aim of this study was to evaluate the indications for surgical treatment in AR patients.

**Methods:** This retrospective cohort study involved 43 patients who underwent submucosal inferior turbinectomy combined with selective posterior nasal neurectomy and nasal septoplasty between 2013 and 2018. We evaluated the patients' nasal/eye symptoms, quality of life (according to guidelines), and nasal cavity volume by acoustic rhinometry and fractional exhaled nitric oxide as indications of eosinophilic airway inflammation. We compared the data before and after surgery. In addition, during the Japanese Cedar Pollen (JCP) dispersal season of 2019, in which large amounts of pollen were dispersed, the postoperative group was compared with a control group who received preseasonal prophylactic treatment, a group treated with sublingual immunotherapy (SLIT) with JCP for 1 year (SLIT1), and a group treated with SLIT for 5 years (SLIT5).

**Results:** Nasal symptoms and quality of life were improved significantly after surgery. In the JCP dispersal season of 2019, symptoms in the postoperative group were significantly decreased compared with those in the initial therapy group and SLIT1 group; however, they were equivalent to those in the SLIT5 group.

**Conclusion:** This study suggested that surgical treatment is suitable for patients with severe allergic rhinitis who have perennial nasal obstruction and need to improve symptoms early.

**EP-12 Study of allergic rhinitis in atopic individuals and diagnostic significance of nasal eosinophilic count**

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**Background:** Recently, increasing prevalence of allergic rhinitis in children has been the major health concern in Japan. Present study mainly emphasizes the changing sensitization in atopic paediatric group and their subsequent development of allergic rhinitis. This study also analyses the significance of nasal eosinophil count as a routine diagnostic tool for allergic rhinitis.

**Methods:** This study was conducted for a group of 264 atopic paediatric individuals whose parents had some allergic diseases. All of them were examined by an otolaryngologist and a paediatrician in Chiba University. Serum concentrations of specific-IgE were analysed at the ages of 1, 2, 5 and 7 years and their sensitization patterns were evaluated. Nasal eosinophil counts of all the above ages were analysed for their sensitivity and specificity in diagnosis of allergic rhinitis.

**Results:** It was observed that mites s-IgE was increasing from 7% to 57% at 1 and 7 years, respectively. The development rate of allergic rhinitis induced by mites has also shown increase from 2% (1yr) to 36% (7yr). Sensitivity and specificity of nasal eosinophil counts for diagnosing allergic rhinitis were 96% and 17% respectively at 1 and 2 years. Accuracy of these eosinophil counts as a predictive for diagnosis of allergic rhinitis was almost same in 7 years.

**Conclusion:** Sensitisation to mites and development rate of allergic rhinitis were significantly increasing with age. Nasal eosinophilic counts certainly had a significant role in diagnosing allergic rhinitis, however, the specificity was low.



### EP-13 Perspicuous treatment algorithm for pediatric blowout orbital fractures

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**Aim:** Pediatric blowout orbital fractures occasionally include cases that require urgent treatment to prevent serious sequelae. Sometimes physicians cannot confirm findings because pediatric patients may not be cooperative with examinations. Hence, we advocate for a simple, practical treatment algorithm for pediatric blowout orbital fractures. The oculocardiac reflex and missing rectus sign are especially emphasized as signs of an emergency. According to the algorithm, patients with these signs should undergo urgent release, even without a Hess screen test.

**Methods:** This retrospective cohort study included patients with pediatric blowout orbital fractures treated at Japanese Red Cross Asahikawa Hospital from April 2000 to August 2020 based on the algorithm. At follow-up, ocular movements were evaluated based on percentage of Hess area ratio (HAR%) and subjective diplopia. Patients were divided into two age groups: 0–12 years and 13–18 years. Differences in the frequency of urgent cases and HAR% were compared across groups.

**Results:** There were 9 patients who underwent urgent release, 16 who underwent repair, and 36 who underwent conservative treatment. Mean age was  $13.10 \pm 3.72$  years. HAR% on follow-up was  $98.0\% \pm 4.7\%$  (range, 77.6%–100%). Postoperative diplopia was observed in 4% of patients. More patients aged 0–12 years had urgent needs than those aged 13–18 years ( $p=0.0051$ ). There were no differences in HAR% between the groups.

**Conclusion:** The algorithm is suitable for pediatric blowout orbital fractures.

### EP-14 Pathophysiology of current odontogenic maxillary sinusitis and endoscopic sinus surgery preceding dental treatment

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**Objective:** The purpose of this study is to retrospectively investigate the pathophysiology of current intractable odontogenic maxillary sinusitis (OMS) and the role ESS, especially ESS preceding dental treatment, plays in its pathophysiology.

**Methods:** Ninety-seven adults who underwent ESS for intractable OMS were retrospectively examined.

**Results:** In 85 cases (87.6%), causative teeth were periapical lesions after root canal treatment (endodontics). The root canal procedures were not sufficient; hence, the root-canal-treated teeth had periapical lesions causing OMS. The ciliated columnar epithelium with intractable OMS was not severely damaged and not irreversibly injured. In postoperative nasal endoscopy and CT scans for all patients, the natural ostiums and the membranous portions of the maxillary sinuses were enlarged and the ostiomeatal complexes remained widely open. Temporary acute sinusitis recurrence after primary ESS was observed in 10 cases (11.8%). However, since the ostiums were enlarged and the ostiomeatal complexes remained widely open, antibiotic administration alone without dental treatment cured the acute sinusitis. Regarding the causative endodontic treated teeth, 97.6% of them were able to be preserved with only antibiotic treatment and without dental retreatment. In two cases, extraction of the teeth was necessary because the teeth became mobile.

**Conclusion:** ESS is highly indicated for OMS requiring surgery. The treatment results are exceptionally good once the ventilation and drainage of the maxillary sinus is successfully restored after surgery. Consequently, ESS can be considered the first-line therapy for intractable OMS caused by root canal treatment (endodontics), followed by close dental follow-up and dental treatment when necessary.

### EP-15 Analysis of symptomatic frontal sinusitis after endoscopic sinus surgery

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(background) The frontal recess is made up of ethmoid cells and has a very narrow and complicated drainage route. Occasionally, patients experience symptomatic frontal sinusitis after endoscopic sinus surgery (ESS) because of the obstruction of its drainage route. In this study, we addressed the cause of frontal sinusitis.

(methods) We retrospectively evaluated patients who underwent ESS between May 2020 and April 2021. Five patients presented with symptomatic frontal sinusitis after ESS. We compared the preoperative and postoperative computed tomography (CT) images.

(results) A total of seven sides showed evidence of frontal sinusitis in five patients. Two patients had bilateral frontal sinusitis. In postoperative CT images, an anterior wall of supra bulla cells remained of 2 sides, of supra bulla frontal cells did in 3 sides, and of supra agger frontal cells (T3) did in 1 case. One patient developed frontal sinusitis because of middle turbinate lateralization.

(conclusion) Incomplete resection of the anterior walls of supra bulla cells or supra bulla frontal cells caused frontal sinusitis after surgery. Hence, the size and localization of these cells should be determined before the operation.

### EP-16 Modified endoscopic medial maxillectomy to overcome absent or limited prelacrima recess

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Background: Endoscopic prelacrima recess approach can be widely used in maxillary sinus lesion, orbit, and infratemporal fossa because it provides adequate access to the maxillary sinus. However, it is reported not feasible in cases with type I (<3mm) and absent prelacrima recess (PLR). To overcome the limit, we proposed a modified endoscopic medial maxillectomy (MEMM) for these cases by preserving the function of inferior turbinate (IT) and nasolacrimal duct (NLD)

Material and Methods: Six consecutive patients (9 lesions) undergoing MEMMs were recruited. Categorization of PLR is based on the methodology proposed by Simmen. Pre- and post-surgical SNOT-22 and 10-point visual analog scales (VAS) were collected to assess the impact of MEMM on quality-of-life.

Results: Three out of 6 patients (4 males; mean age:  $51.3 \pm 9.4$  year) had absent PLR, and the averaged AP diameter for the three type I PLR was  $2.1 \pm 0.7$ mm. We had nine lesions (7 MEMMs) because two patients had concurrent 2 pathologies and one had bilateral sinusitis. Three lesions (33.3%) were recurrent sinusitis, two lesions were inverted papilloma, and four lesions were mycetoma, cholesterol granuloma, fibrous dysplasia, and orbital tumor, respectively. After MEMMs, we found significant improvements in VAS ratings (from  $6 \pm 4.69$  to  $0.4 \pm 0.55$ ), nasal domain of SNOT-22 ( $18.4 \pm 14.77$  to  $1.80 \pm 1.92$ ), and total SNOT-22 scores (from  $33.2 \pm 23.38$  to  $10 \pm 15.49$ ). There were no neurologic deficits and alar collapse.

Conclusion: We concluded that MEMM is an effective method in cases with limited or absent PLR. When short-term life-quality improvements were promising, future large-scale studies with longer follow-up periods are warranted to strengthen our findings.

Keywords: Prelacrima recess, Endoscopy, Modified medial maxillectomy, VAS, SNOT-22

**EP-17 Endonasal endoscopic closure for oroantral fistula- report of 2 cases**

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Oroantral fistula (OAF) is not uncommonly seen after extraction of upper molar tooth. Though several promising techniques were proposed, combined procedures are usually necessary to close fistula as well as to treat sinusitis. However, when most of them mainly focus on transoral approaches with OAF repair, very few studies address single endonasal endoscopic surgery (EES). In this investigation, we report our successful experience using ESS for two OAF cases who had uncontrolled sinusitis and persistent fistula after transoral repairments. The average size of OAF is 7.1mm (7.5mm and 6.7mm, respectively). We address the defects through modified endoscopic medial maxillectomy (MEMM) by preserving naso-lacrimal duct and inferior turbinate. After removing the diseased maxillary sinus mucosa, the fistulas were repaired by a free bone graft and a mucoso-osteal graft harvested from medial maxillary wall. Successful closures after a single procedure were achieved in both cases. No complication or recurrence was observed after 4-month follow-up. To conclude, we found single ESS through MEMM is feasible to salvage patients who have small-to-median sized OAF failed prior trans-oral repairs.

Keywords: Oro-antral fistula, dental extraction, endoscope, modified medial maxillectomy, graft

**EP-18 Olfactory dysfunction in an IgG4-related disease mice model**

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IgG4-related disease is a systemic illness that is characterized by extensive infiltration of lymphocytes and IgG4-positive plasma cells, with fibrosis of various affected organs and elevated serum IgG4 concentrations. Our previous study revealed patients with IgG4-related disease experience olfactory dysfunction. LATY136F knock-in mice have been established as an IgG4-related disease model for pancreatic, kidney, and salivary gland lesions. This study examined whether LATY136F knock-in mice is an applicable IgG4-related model for the olfactory system. Behavioral tests to evaluate olfactory function showed that the LATY136F knock-in mice had a statistically significant level of olfactory dysfunction. Histological analysis showed that the thickness of the olfactory epithelium in these mice was thinner than that in the age-matched wild-type mice. Olfactory marker protein and growth-associated protein 43 expressions in the olfactory epithelium of the LATY136F knock-in mice were markedly lesser than those in the wild-type mice. In the olfactory epithelium of the LATY136F knock-in mice, the function of both newly differentiated and mature olfactory nerve cells were impaired.

**EP-19 Efficacy of combination therapy using olfactory training and medication for post-traumatic olfactory dysfunction**

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Post-traumatic olfactory dysfunction is a refractory disease and efficacious treatment is limited. Recently, olfactory training has been reported to be efficacious for sensorineural olfactory dysfunction. We previously reported that combination of olfactory training and medication using Tokishakuyakusan, zinc preparation and vitamin B12 had improved post-infectious olfactory dysfunction better than the medication alone. The present study was designed to investigate if the combination therapy is efficacious for post-traumatic olfactory dysfunction. A total of 47 patients with post-traumatic olfactory dysfunction were treated with either the combination therapy or medication alone. Olfactory function was assessed by Japanese standard olfactory function test using T&T olfactometry before and after the treatments. Curative ratio was 43% (6 of 14 patients) in the combination therapy group and 21% (7 of 33) in medication group although there is no significant difference between these two groups in all generations ( $p = 0.12$ ). In young generation 35 years old and under, however, the combination therapy cured all patients' olfactory dysfunction (100%, 4 of 4), which is significantly better than the medication group (26%, 5 of 19,  $p = 0.01$ ). These results indicate that olfactory training can potentiate therapeutic efficacy of medication for post-traumatic olfactory dysfunction at least in young patients.

**EP-20 Treatment with nasally administered adipose-derived stem cells from GFP transgenic mice in olfactory impaired mice**

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Adipose-derived stem cells (ADSCs) express neurotrophic factors. In this study, we determined whether nasal administration of ADSCs from GFP transgenic mice increases recovery of odor aversion behavior and olfactory epithelium regeneration with increased neurotrophic signaling in olfactory impaired mice treated with methimazole, a toxic agent for olfactory epithelium.

The intrinsic odor aversion behavior to butyric acid was assessed before and after the methimazole intraperitoneal injection in C57BL/6J mice (male, 8W). The ADSCs or vehicle control (phosphate-buffered saline) were nasally administered to the left nostril of mice 7d after the methimazole injection. Markers for olfactory neural cells and GFP were assessed by immunohistochemical staining in the epithelium of nasal septum.

The treatment with nasal administration of ADSCs significantly increased a recovery of odor aversion behavior to butyric acid in compared with the treatment of vehicle control at 7d and at 14d after the nasal administration of ADSCs or vehicle control. The OMP expressions in nasal epithelium were significantly increased in the mice treated with ADSCs than the control mice 14d after the nasal administration. The expressions of Ki-67, MASH-1 or P-TrkA Tyr490 were significantly increased in nasal epithelium of mice treated with ADSCs, as compared to controls 24h after the nasal administration. GFP positive cells were shown in the treated-side nasal cavity of the mice 24h after nasal administration of ADSCs.

Nasal administration of ADSCs increases recovery of odor aversion behavior and olfactory epithelium regeneration with activation of TrkA signaling and increased globose basal cells in the olfactory impaired mice.

**EP-21 Comparison of magnetic resonance imaging and computed tomography in the evaluation of the olfactory cleft and ethmoidal cell**

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No study has examined whether magnetic resonance imaging (MRI) alone can be used for evaluating olfactory cleft and ethmoidal sinus in patients with olfactory disorders. Therefore, we analyzed the discrepancies between computed tomography (CT) and MRI in the imaging of the olfactory cleft and ethmoidal sinus. Patients who underwent CT and MRI within 30 days were evaluated. Age, sex, diagnosis, presence of bronchial asthma (BA), peripheral blood eosinophil percentage, and CT and MRI findings were retrospectively reviewed, and the sinuses were assessed on a scale of 0-3. Overall, 146 patients with 292 sinuses were enrolled. The ethmoid sinus score and the olfactory cleft score had 77.1% and 72.6% image similarity in CT and MRI. Sex and BA status were not associated with olfactory cleft score discrepancies (sex:  $p=0.52$ , BA:  $p=0.41$ ). MRI scores tended to be rated higher than the CT scores as age increased, although this difference was not statistically significant ( $p = 0.09$ ). The higher the peripheral blood eosinophil percentage, the more the magnitude by which the CT score tended to exceed the MRI score; however, this finding was also not statistically significant ( $p = 0.11$ ). MRI scans should be limited to the evaluation of intracranial regions. Scans of olfactory cleft and ethmoid cells are not accurate for the assessment of olfactory dysfunction.

**EP-22 Preoperative endovascular embolization in an easily bleeding respiratory epithelial adenomatoid hamartoma (REAH) of the olfactory cleft**

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Respiratory epithelial adenomatoid hamartoma (REAH) was first described in 1995 by Wenig and Heffner and is a relatively recently established disease. REAHs are uncommon tumors occurring in the nasal cavity and sinuses, and their etiology is still unknown. The endoscopic diagnosis of REAH is difficult because of the frequent coexistence of common inflammatory polyps, and REAH is often misdiagnosed as nasal polyposis or other tumors. Preoperative endovascular embolization for sinonasal tumors is now widely recognized as an effective method to decrease blood loss, soften the tumor, and facilitate surgical procedures. However, to the best of our knowledge, there are no clinical reports of the requirement for preoperative endovascular embolization in the treatment of REAH. Here, we report a 70-year-old male with an easily bleeding REAH of the olfactory cleft, vascularized by branches of the bilateral internal and external carotid arteries. We removed the tumor endoscopically after preoperative endovascular embolization of the bilateral sphenopalatine arteries. Histological investigation showed an intratumoral hemorrhage accompanying the REAH, with no evidence of a residual or recurrent tumor during the last follow-up at 6 months. In conclusion, some REAHs may receive an abundant blood flow. Correct preoperative diagnosis and proper preoperative interventions such as endovascular embolization are needed for safe and sufficient treatment of REAHs with an abundant blood flow.

**EP-23 Clinical study of tumors in the nasal septum**

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Nasal septal tumors are rare diseases. We have experienced 56 cases of septal tumors in the last 10 years. The breakdown was 41 (73%) benign tumors and 15 (27%) malignant tumors, with many benign diseases. Pathological diagnosis was benign tumor (cavernous hemangioma 18 cases, papillary type 9 cases, polyp 5 cases, fibrous type 4 cases, polymorphic adenocarcinoma 2 cases, schwannoma 2 cases, inflammatory granuloma 1 case), malignant tumor (squamous epithelial cancer 7 cases, malignant melanoma 3 cases, hemangiopericytoma 2 cases, adenocarcinoma 1 case, adenoid cystic carcinoma 1 case, rhabdomyosarcoma 1 case). The chief complaint was epistaxis in 33 cases. Thirty-nine benign tumors were resected by endoscopic surgery. For squamous cell carcinoma, combined chemoradiationtherapy was performed in 3 cases, resection by external incision was performed in 2 cases, and endoscopic resection was performed in 2 cases. Two cases of malignant melanoma underwent heavy ion radiotherapy. Endoscopic resection was performed in 1 case of adenocarcinoma, 1 case of adenoid cystic carcinoma, and 2 cases of hemangiopericytoma.

Endoscopic surgery was effective for benign tumors, and it was considered that there was no recurrence because the tumor could be resected with a secure margin.

SCC was found in some cases with a significantly advanced primary lesion, but the response to treatment was good. However, in some cases, diseases such as rhabdomyosarcoma and malignant melanoma died due to distant metastasis even if the primary lesion could be controlled.

**EP-24 Impact of prior cancer history on the overall survival of patients with nasopharyngeal carcinoma**

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**Objective:** Nasopharyngeal carcinoma (NPC) is a common cancer and the mainstay treatment is radiotherapy and chemotherapy. If a prior cancer history can affect the survival of NPC patients is still unclear.

**Methods:** We retrospectively collected 666 patients with NPC from 2006 to 2018. Patients in this study were divided into two groups: those patients with a prior cancer history and those without a prior cancer history. We then analyzed the demographic data and survival of these two groups.

**Results:** We identified 25 NPC patients with a prior cancer history in our case series. In univariate analysis, NPC patients with a prior cancer history had older age ( $P < 0.05$ ), compared with those without a prior cancer history. In patients with stage III NPC, having a prior cancer history leads to a poor prognosis. In cox regression analysis, old age and a prior cancer history were independent predictors of poor prognosis.

**Conclusion:** We found that prior cancer history could lead to poor prognosis in stage III NPC.



**EP-25 Accuracy of intraoperative frozen section diagnosis of laser assisted endoscopic nasopharyngectomy in recurrent nasopharyngeal carcinoma**

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**Background:** The treatment options of locally recurrent nasopharyngeal carcinoma (rNPC) include re-radiation and salvage nasopharyngectomy. Intraoperative consultation with frozen section is important in evaluation of adequate surgical margins of H&N tumor excision. Nevertheless, it is believed that frozen section analysis is less accurate in recurrent NPC compared to other H&N tumors. In addition, laser and electrocoagulation assisted resection increases the difficulty of accurate intraoperative diagnosis.

**Methods:** Patients with rNPC who had underwent endoscopic laser assistant nasopharyngectomy were enrolled from year 2010 to 2021. Results of intraoperative consultation of resection margins were reviewed and analyzed.

**Results:** A total of 32 NPC patients were enrolled for this study. Four patients were excluded from this study due to no intraoperative consultation. A total of 151 comparative sets of frozen section and permanent results were used for analyses. The accuracy of intraoperative consultation was 94.03%. The sensitivity, specificity, positive predictive value, and negative predictive value were 36.36%, 99.19%, 80%, and 94.57%, respectively.

**Discussions:** Only one study from Hong Kong investigated the efficacy of frozen section analysis for nasopharyngectomy of rNPC. Current study demonstrates a comparable accuracy with a high negative predictive value of intraoperative consultation. Challenges of intraoperative consultation of nasopharyngectomy are radiation effects, crush and coagulation artifacts, and lymphoid infiltration of current tumor entity. **Conclusion:** Our study provided evidence of value in frozen section consultation for nasopharyngectomy. The high negative predictive value of frozen section provides surgeons helpful information in determining adequate margins intraoperatively.

**EP-26 Extracranial trigeminal schwannoma in the pterygopalatine fossa successfully resected by endoscopic modified medial maxillectomy approach**

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Tumors in the pterygopalatine fossa (PPF) are rare, and the most common cases are benign neurogenic tumors such as schwannoma. We report a rare case of schwannoma arising from the extracranial trigeminal nerve (the greater palatine nerve) in the left PPF. Endoscopic medial maxillectomy (EMM) had been used as endoscopic surgical approach for the tumor in the maxillary sinus. However, this procedure sacrifices the inferior turbinate and the nasolacrimal duct. Recently, endoscopic modified medial maxillectomy (EMMM) was newly developed to preserve inferior turbinate and nasolacrimal duct. We applied EMMM approach for the resection of PPF schwannoma. Preoperative transcatheter embolization of the left sphenopalatine artery and intraoperative CT-guided navigation system were useful for the safe and complete resection. Postoperative hypoesthesia was found around his left hard palate, but no other complications were observed. No local recurrence has been observed in 3 years follow-up period. EMMM approach with a CT-guided navigation system is useful for the surgical resection of benign PPF tumors.