GP IN-SYNC

A quarterly e-newsletter by NUH GP Liaison Centre

NUH National University Hospital

GP Appointment Hotline +65 6772 2000

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Featured Doctors of the Month

Dr Ng Li Shia

MBBS(S'pore), MRCS(Glasgow),
M Med(ORL)

Consultant
Division of Facial Plastics
and Reconstructive Surgery
Department of Otolaryngology – Head and Neck Surgery
National University Hospital (NUH)

Assistant Professor
Yong Loo Lin School of Medicine
National University of Singapore (NUS)

Dr Ng Li Shia underwent sub-specialty training in facial plastics and reconstruction.

Her clinical interests include reconstruction of ear deformities, correction of nasal obstruction and deformities, as well as skin malignancies in the head and neck.

Facial Plastics and Reconstructive Surgery

In this particular aspect of ENT (Ear, Nose, Throat) surgery, we aim to provide holistic care to patients suffering from both functional and aesthetic problems in the head and neck. Some of these examples include patients with hearing loss and ear deformity, as well as nasal obstruction with external nasal deformity.

Patients may present with congenital or acquired ear deformities, which vary from a mild protruding ear to severe complete absence of the ear. This may be associated with hearing loss due to a malformed external ear canal or middle ear. We aim to restore appearance as well as functional hearing to the patient.

Reconstruction of the ear usually precedes hearing restoration to ensure the viability of soft tissue. We will first assess the severity of the ear malformation and condition of the surrounding tissues, then advise the patient on the appropriate type of reconstruction. Reconstruction is more commonly performed using rib cartilage (Figure 1). However, if the patient does not wish to harvest his own rib, there is an option of using MEDPOR, which is a porous polyethylene that is implanted in the shape of a ear.

Thereafter, in favourable conditions of the middle ear, hearing is restored by re-creating the ear canal. If the patient is unsuitable for canal plasty, a semi-implantable hearing aid can be used.

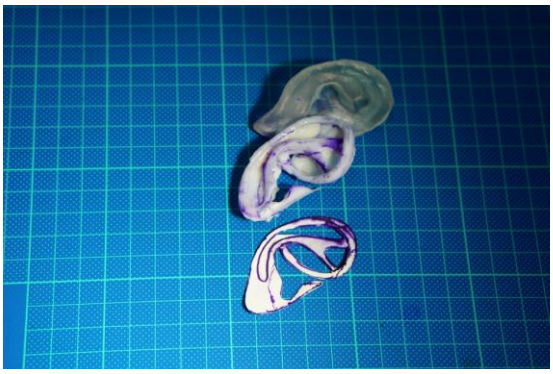
Patients who have allergic rhinitis or other causes of blocked nose may also have visible external nasal deviation. In cases whereby patients fail medical therapy or are keen to correct external deformity of the nose, nasal surgery can address both internal and external problems, which helps with improved nasal breathing and external appearance of the nose.

Excision of benign and malignant skin lesions of the head and neck may result in significant loss of skin, especially skin cancers, which require adequate clearance of margins.

The plan for reconstruction will have to consider function of the surrounding structures such as the eyes, nose and oral cavity. The aims of reconstruction will be to preserve function and minimise disruption to the appearance of the patient.

Trauma or prior surgery to the head and neck may produce undesirable hypertrophied scars and keloids. Management of such scars will not only involve scar removal but also the prevention of future recurrences.

In the management of ENT conditions, we no longer only focus on the functional aspect of the various structures of the face, but also the importance of enabling patients to present their best face forward.



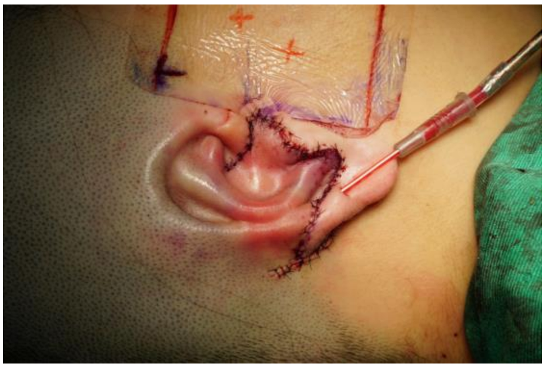
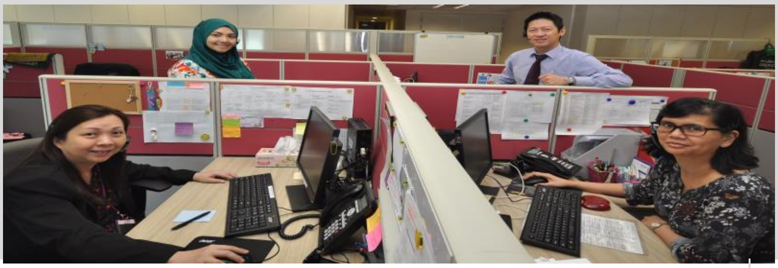


Figure 1: Reconstruction of the right ear using rib cartilage.



Dr Lim Chwee Ming

MBBS(S'pore), MRCS(Edin), M Med (ORL)

Senior Consultant
Department of Otolaryngology – Head and Neck Surgery, National University Hospital (NUH)

Division of Surgical Oncology (Head and Neck Surgery)
National University Cancer Institute Singapore(NCIS)

Assistant Professor
Yong Loo Lin School of Medicine
National University of Singapore (NUS)

Dr Lim did a two-year Head and Neck Oncologic Fellowship at the University of Pittsburgh Medical Centre. During his time there, he conducted translational bench work research in immunotherapy in head and neck cancer, focusing of immunological mechanisms in monoclonal antibody based therapy in cancer and identifying novel immune modifiers in cancer therapy. In his clinical training, he was trained in transoral robotic surgery (TORS), minimally invasive video assisted thyroidectomy (MIVAT) and minimally invasive approaches in head and neck surgery, in addition to the major head and neck resections.

Dr Lim Chwee Ming's clinical expertise spans across robotic assisted head and neck surgery, thyroidectomy, head and neck surgery, MIVAT, cancer immunotherapy and therapy, across the following clinical conditions/procedures:

- Head and Neck cancer – nasopharyngeal cancer oropharyngeal cancer, head and neck squamous cell cancer, thyroid cancer/nodules, salivary gland cancers
- Transoral robotic surgery (TORS) for oropharyngeal cancer
- Robotic assisted thyroidectomy, neck dissection and parapharyngeal space tumours
- Transoral laser microsurgery for early laryngeal cancers

Cancer Immunotherapy

Harnessing the immune cells against virally driven cancer like nasopharyngeal cancer (NPC) is feasible given the expression of viral oncoproteins which are potential targets for immunotherapy. In this regard, NCIS has opened several trials using autologous expanded natural killer cells (pioneered by Prof Dario Campana's group at NUS). In NPC, we have established a protocol using autologous natural killer cells with cetuximab (a monoclonal antibody targeting the epidermal growth factor receptor) in patients with refractory NPC. (clinical trial NCT02507154).

Clinical Highlights

Robotic assisted head and neck surgery

Robotic assisted surgery has established itself as an accepted approach in many surgical specialty, including head and neck surgery. The advantages of using the robotic system include its enhanced magnification, 3-dimensional optics as well as increased degree of movements with the "wristed" robotic arms which have allowed surgeons to navigate and resect tumour in "tight-cavities" such as the pelvis and oropharynx/larynx in head and neck region.

Furthermore, with the aid of robotic system, remote access surgery is made possible since the robotic arms can allow the surgeon to operate from a distance. For example, performing thyroidectomy can be safely achieved through an axillary incision or facelift incision with the robotic system (Figure 1).

This article serves to highlight the indication(s) of using this novel technology in head and neck surgery and present the current and future development in robotic assisted head and neck surgery.

Transoral Robotic Surgery (TORS)

TORS is approved by the Federal Drug Authority (FDA) in the surgical management of T1-T2 oropharyngeal cancer (Figure 2). Traditionally, transoral resection of oropharyngeal tumor is challenging as the surgeon has difficulty visualising the deep aspect of the tongue base resection which precludes safe and oncologic resection. In many cases, a traditional lip-split, midline mandibulotomy approach is necessary.

With the use of TORS, oropharyngeal tumour can be effectively and safely removed and this technology is gaining widespread acceptance among head and neck surgeons . Numerous clinical studies in tertiary centres in the USA have shown favourable clinical outcome in patients treated surgically using TORS. Furthermore, improved swallowing outcome is evident from these studies.

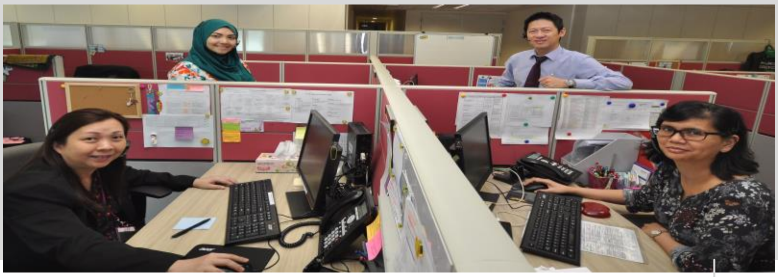
Particularly relevant is the increased prevalence of human papillomavirus (HPV) associated oropharyngeal cancer (HPV-OPC) which typically presents with a small primary tumour (T1-T2) and relatively larger nodal metastasis. This has clinical implications as the robotic system can be used to resect these small tumours transorally without the conventional open approaches. In the USA, the prevalence of HPV-OPC has reached epidemic proportions with nearly 90% of all OPC being HPV positive. Locally, our NUH data has shown a prevalence of approximately 42% of HPV-OPC.

Beside oncologic head and neck surgery, tongue base reduction surgery for obstructive sleep apnea (OSA) can been safely performed on OSA patients with tongue base obstruction. Prior to the advent of robotic system, there are a myriad of tongue base procedures for OSA with mixed results. Using the robotic system, a more précise reduction of the tongue base can be achieved to increase the airway without compromising on swallowing function. A recent published study showed that TORS for OSA has improved clinical outcome compared to radiofrequency procedures on the tongue base area. However, the long-term result of TORS tongue base reduction is still unknown and we are eagerly waiting for more data on this aspect.

Remote access surgery

Thyroidectomy is a common head and neck surgery for management of both benign and malignant thyroid nodules. The standard midline neck crease incision is gradually frowned upon by patients who are concerned about the visibly midline neck scar.

With this concern in mind, head and neck surgeons have started performing thyroidectomy from a remote access area (eg axilla or hairline). The initial experience with endoscopic assisted thyroidectomy via an axillary approach was first popularised by the Koreans. With the robotic system, surgeons are increasingly utilising robotic assisted thyroidectomy via the axillary or modified facelift approach, given the excellent magnified visualisation of the surgical field (Figure 3).



Outcome data from Korea has shown that this approach is associated with equivalent results with respect to complication rate and oncologic resection (depicted by the post-operative radio-iodine scan) compared to the standard midline neck approach.

Training for robotic head and neck surgery

With the increasingly use of robotic head and neck surgery, there needs to be a re-look in surgical training for residents and head and neck surgeons wanting to adopt this new technology.

First, the anatomy of the relevant area needs to be re-learned. The traditional “lateral to medial” anatomy needs to be relooked from a“medial to lateral” perspective. The transoral anatomy is important to understand the 3-dimensional perspective for oncologic resection and to identify landmarks necessary to prevent inadvertent neurovascular injury.

Second, the training of using of the robot needs to be systematically addressed. Currently, there are dry-lab training available for surgeons to be acquainted with the function of the robotic system. Further training is also available in the form of didactic lectures and live dissection using animal model or cadaveric dissection. Proctorship is also available to allow adequate clinical experience to be attained with supervision from more experienced head and neck surgeons.

Future directions

The future of robotic assisted head and neck surgery looks promising as more research, both clinical and preclinical, are embarked to expand its clinical indications as well as to further develop a more versatile robotic system.

Robotic neck dissection is currently performed and initial clinical experience has demonstrated good safety and oncologic outcome. Moreover, robotic-assisted nasopharyngectomy is being performed in some centres with positive early experience.

With evolution of surgical technology, there is also intense research to design smaller robotic system to allow an even more flexible system to be employed in “tight- cavity” such as the oropharynx/larynx. Additional haptic (tactile) feedback system is also being actively explored by biomedical engineers to allow real-time tactile feedback currently not available with the present robotic system.

Figure 1 : Modified facelift approach (Hairline) in robotic thyroidectomy

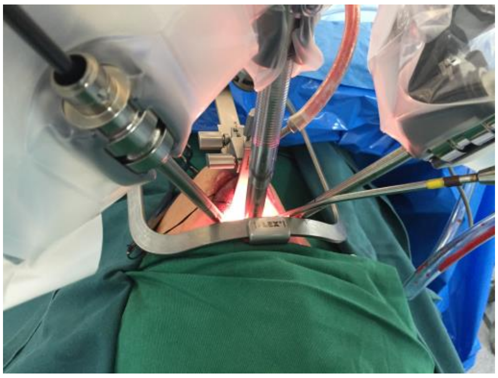


Figure 2: Transoral robotic surgery (TORS) using the Da Vinci robot

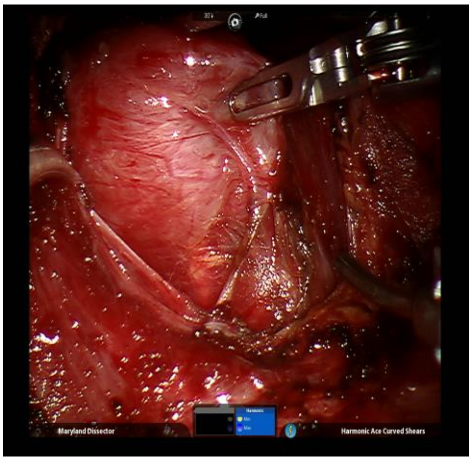
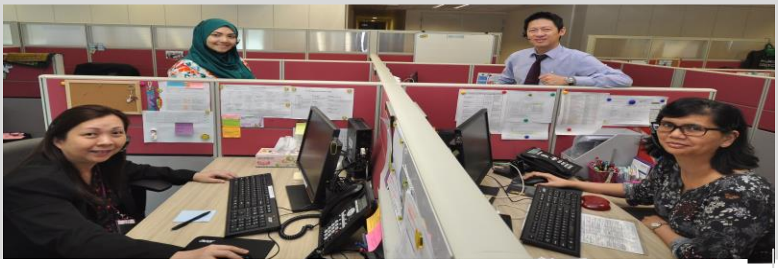


Figure 3: Excellent visualisation of thyroid gland seen during robotic assisted thyroidectomy

Raman spectroscopy for improving diagnosis and detection of nasopharyngeal cancer

Raman Spectroscopy (RS) is an optical analytic technique which uses the principle of inelastic scattering of light that allows characterisation of biochemical molecules such as proteins, lipids and amino acids in the tissue. Therefore, the technology may potentially be exploited for real-time tissue analysis which is invaluable for screening and surveillance of cancer. This system has been miniaturised and developed for clinical applications by Associate Professor Huang Zhiwei from the Department of Engineering, National University of Singapore (NUS).

In the last few years, clinicians from the National University Cancer Institute, Singapore (NCIS) have investigated the utility of this system in cancer surveillance. Unsurprisingly, this system appears to bridge the gap in the surveillance of nasopharyngeal cancer (NPC), which is the most common head and neck cancer seen locally. Due to its deep anatomical location, detecting early recurrence of nasopharyngeal cancer can be challenging; and more often than not, local recurrences are detected late, precluding surgical salvage due to the close proximity of the tumour to critical neurovascular structures in the skull base.



GP Liaison Centre (GPLC)

GP Appointment Hotline: +65 6772 2000

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Through an Institutional Review Board (IRB) approved protocol, our team at the Department of Otolaryngology (Head and Neck Surgery) has sought to investigate the utility of near infra-red Raman Spectroscopy in the surveillance of nasopharyngeal cancer patients. Our system comprises the following equipment which is summarised in Table 1.

Table 1: Summary of equipment used in surveillance of NPC

Materials	Description
Near-Infra Red Laser Source	Fixed wavelength of 758nm
Fibre Optic probe	1.8mm probe with optic fibres for transmitting laser for excitation and collection of scattered light
Thermo–electrically cooled Charged-Coupled Device (CCD) Camera	Filtering and differentiation of collected scattered light intensity into wave peaks according to biomolecules
Computer	Data acquiring and analysis using Matlab software for diagnostic prediction

Since the initiation of this study in 2015, we have collected the Raman Spectroscopy information for 135 data-points on 79 patients with either newly diagnosed NPC (N=12) (Figure 1), post-irradiated nasopharynx (N=37) and healthy normal nasopharynx (N=30) (Figure 2). In this surveillance system, a near infra-red laser of 758 nm is emitted from the 1.8 mm fiberoptic probe. As the laser is emitted onto the nasopharyngeal tissue, the differential light waves which are scattered back to the device is collected and filtered to remove the auto-fluorescent background. This final filtered signal (Raman signal) is then funnelled through the air cooled CCD (Charged Coupled Device) camera which differentiates and displays the different wavelengths' spectral peaks. Each of these spectral peaks represents a specific tissue composition which can be compared to specific amino acids/lipids or proteins based on previously published databases. Therefore, depending on the tissue composition among healthy nasopharyngeal tissue, post-irradiated tissue and nasopharyngeal cancer tissue, differential expression of these spectral peaks will be obtained.

Data Processing

Data processing of this dataset will largely be based on using exiting mathematical algorithm in the analysis. A multi-variate statistical analysis will be performed by constructing a PCA-LDA (Principal Component Analysis- Linear Discrimination Analysis) model. The PCA is carried out to retain the information which is significant for classification of the tissue by reducing the dimensionality of the Raman data obtained.

This significant information is then used as input for constructing the LDA algorithm for predicting and classifying the tissues between normal versus cancer, cancer versus post-treatment and post-treatment versus normal. In order to differentiate the "correct" and "incorrect" classification of tissue, the Receiver Operating Characteristic (ROC) curve is generated for analysis.

Using this model, we have shown that there was good specificity of differentiating nasopharyngeal cancer from either post-irradiated nasopharyngeal tissue or healthy normal nasopharyngeal tissue. Therefore, we believe that this preliminary result can be expanded to validate the utility of near infra-red Raman Spectroscopy in the surveillance of nasopharyngeal cancer. Hopefully, in the near future, when the clinician encounters a normal looking nasopharynx during the follow-up of a nasopharyngeal cancer patient, a "benign" Raman Spectroscopy signal will increase confidence of post-irradiated tissue; and a "malignant" Raman Spectroscopy signal should be pursued with Raman-directed biopsy to exclude a local cancer recurrence.

Figure 1

Figure 2

Figures 1 and 2 : Cancerous nasopharynx versus healthy nasopharynx

Upcoming CME Event

Date	Topic	Venue
18 Nov	Primary Eye Care - The Future of Ophthalmology Practice	NUHS Tower Block, Level 7, Rooms: T07 -01 to T07-05 1E Kent Ridge Road, Singapore 119228

For more information and registration, you may contact the GP Liaison Centre at **gp@nuhs.edu.sg**

Registration & lunch will start at 1.00 pm

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