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Highlights from the Fall Update 2018 Head & Neck Endocrine Tumours

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On Saturday October 13, 2018, the BC Cancer Surgery Network held our annual Fall Update on Head and Neck Endocrine Tumours. The day was attended by surgeons and residents from General Surgery and Otolaryngology, and we were fortunate to have Dr. David Terris and Dr. Eric Genden with us as guest speakers from the United States. A summary of the presentations from the day follows below.

THYROID ULTRASOUND REPORTING (TIRADS/ATA/ETC): WHAT DOES THE SURGEON REALLY NEED TO KNOW?

Dr. Patrick Vos, who is a radiologist at St. Paul's Hospital, spoke on the adoption of ultrasound (US) based risk stratification systems to direct selection of thyroid nodules that are appropriate for fine needle aspiration biopsy (FNAB).

There are many systems that have been developed by professional organizations (ACR TI-RADS, ATA, K TI-RADS, F TI-RADS, BTA, NCCN, and others) to determine which thyroid nodules warrant FNAB. Two of these systems that are most commonly utilized in North America are the American Thyroid Association (ATA) system and the American College of Radiology Thyroid Imaging, Reporting, and Data System (ACR TI-RADS), and both have been shown to provide effective cancer risk stratification for thyroid nodules.

The ACR TI-RADS system is a score based thyroid nodule cancer risk stratification reporting system that has recently been adopted at St. Paul's Hospital, and also by several other centres around BC. For each of five ultrasound characteristics (composition, echogenicity, shape, margin, echogenic foci) points are assigned and the overall scoring of the nodule, along with its size, dictates whether FNAB is recommended, and also determines follow up recommendations.

The ACR TI-RADS system provides clinicians with:

- **Standardized terminology for US reporting**
- **Specific definitions for growth**
- **Follow up recommendations**

Unlike the ATA system, the ACR TI-RADS system can classify all thyroid nodules. Even though it's early in our experience utilizing the ACR TI-RADS system in BC, it does seem to provide an evidence-based framework for thyroid nodule US reporting, FNAB, and patient follow up. This system improves communication between radiologists and clinicians, and allows for a more rationale application of FNAB. However, there are still many areas that warrant

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BC CANCER SURGERY NETWORK

IN THIS ISSUE

study, such as system applicability in the setting of patients who have risk factors for thyroid cancer (ie. family thyroid cancer history or head and neck radiation exposure history) and ongoing evaluation will be important.

RAPID UPDATE - THYROID CYTOPATHOLOGY/PATHOLOGY FOR THE SURGEON: CURRENT STATUS OF THE BETHESDA THYROID CYTOPATHOLOGY SYSTEM, AJCC STAGING SYSTEM & WHAT IS A NIFTP?

Dr. Blair Walker, a pathologist at St. Paul's Hospital who has been a provincial leader in the adoption of the Bethesda Thyroid Cytopathology System, gave an update on the Bethesda System, and reviewed the changes in the AJCC thyroid cancer staging system and the implications of a NIFTP diagnosis.

Noninvasive Follicular Thyroid Neoplasm with Papillary-like nuclear features (NIFTP) is a new pathological diagnostic term that has recently been introduced to replace encapsulated follicular variant of papillary carcinoma. Due to a very low risk of adverse outcomes from these tumours, the change in terminology aimed to reduce the emotional burden of a cancer diagnosis for patients, and to promote a more conservative management approach.

NIFTPs have an excellent prognosis, but should not be considered benign as a small number of individuals diagnosed with these tumours (2-3%) may go on to eventually develop metastatic disease.

It must be understood that while the pathological criteria for a NIFTP diagnosis have been clearly defined, these tumours cannot be definitively diagnosed based upon a preoperative FNAB. When a NIFTP undergoes an FNAB it usually yields an indeterminate diagnosis, and a small number of cases have a malignant cytopathological diagnoses (3-4%). Thus, NIFTPs do influence the cancer risk within the Bethesda Thyroid Cytopathology System's diagnostic categories (see below).

The Bethesda System for Reporting Thyroid Cytopathology provides six diagnostic categories for thyroid cytopathology; and each of these categories has an assigned cancer risk, and a recommended clinical action. These categories and their associated cancer risks, if NIFTP is not considered malignant, are shown in TABLE 1.

The primary aim of this system is to provide standardized terminology and definitions, and therefore improve communication between pathologists and other clinicians. Challenges pathologists face when reviewing thyroid cytopathology, and utilizing the Bethesda System, were also reviewed. As well, it is important that centres that adopt this system evaluate their own outcomes, as well as diagnostic category utilization.

Bethesda Thyroid Cytopathology System Diagnostic Category	Cancer Risk
Nondiagnostic / Unsatisfactory	5-10%
Benign	0-3%
Atypia of Undetermined Significance (AUS) / Follicular Lesion of Undetermined Significance (FLUS)	6-18%
Follicular Neoplasm (FN)/Suspicious For Follicular Neoplasm (SFN)	10-40%
Suspicious For Malignancy	45-60%
Malignancy	94-96%

TABLE 1. BETHESDA THYROID CYTOPATHOLOGY SYSTEM DIAGNOSTIC CATEGORIES (IF NIFTP NOT CONSIDERED MALIGNANT)

The Bethesda System for reporting thyroid cytopathology has been adopted by centres across the world, including most centres here in BC, and its utilization is recommended by the current ATA guidelines.

Recent updates to the system include:

- Cancer risk for each category being recalculated based on post-2010 data.
- Risks of cancer being presented with NIFTP either considered, or not considered, a malignancy.
- Molecular testing now considered an option for the management of cases diagnosed as AUS/FLUS or FN/SFN.
- The definition and diagnostic criteria for FN/SFN has been revised due to NIFTP and cases that exhibit mild nuclear changes associated with papillary carcinoma (PTC) are now included.
- The definition and diagnostic criteria for the PTC group within the malignant category has been modified so cases with classical PTC features are only included.
- Optional notes may be added for cases of FN/SFN and AUS with characteristics suggestive of follicular variant of PTC or NIFTP.
- Optional notes may also be added to cases with a malignant diagnosis that specifies a small number of cases may actually be a NIFTP.

The American Joint Commission on Cancer (AJCC) has recently released an update to the staging system for thyroid cancer (8th edition). Changes to the system include raising the threshold age to ≥55 years from ≥45 years, so differentiated thyroid cancer (DTC) patients with any T stage and any N stage and who are M0 and younger than

55 years, have Stage I disease, compared with those who are M1 who have Stage II disease. Patients ≥ 55 years with distant metastatic disease are Stage IVB, and cases without distant metastases are further categorized based upon the presence or absence of gross extrathyroidal extension, tumour size, and lymph node status. Patients ≥ 55 years, with ≤ 4cm (T1 or T2) tumours confined to their thyroid with no evidence of lymph node metastases (N1a or N1b) have Stage II disease. Patients ≥ 55 years with a tumour > 4cm that is confined to the thyroid have Stage II disease regardless of their lymph node status.

Minor extrathyroidal extension (microscopic) was removed from the definition of T3 disease. Patients that are ≥ 55 years with tumours that exhibit gross extrathyroidal extension have: Stage II disease if only strap muscles are invaded (T3b), Stage III disease if gross invasion of subcutaneous tissue, larynx, trachea, esophagus, or recurrent laryngeal nerve (T4a) and Stage IVA disease if there is gross invasion of prevertebral fascia or there is encasement of the carotid artery or internal jugular vein. Level VII lymph nodes were reclassified as being central neck (N1a) and not lateral neck (N1b) to improve anatomical consistency and ease of coding. Distant metastases in ≥ 55 year old patients are now classified as Stage IVB rather than Stage IVC disease.

In order to facilitate accurate staging of thyroid cancer patients, the surgeon needs to clearly communicate:

- **Whether gross extrathyroidal extension is present**
- **In cases of locally advanced disease, which structures are involved**
- **The location(s) of lymph nodes removed**

AVOIDING DISASTER IN THYROID SURGERY: 5 CRITICAL PRINCIPLES

Dr. David Terris, a visiting speaker, who is Regents Professor of Otolaryngology and Endocrinology and the Surgical Director of the Thyroid Center at Augusta University, then spoke about avoiding complications from thyroid operations. He defined these complications as being: airway obstruction, vascular injury, metabolic crisis, visceral injury, permanent hypocalcemia, recurrent laryngeal nerve (RLN) injury, poor cosmetic outcome, retained thyroid tissue, wound complications, and anesthesia complications. While many thyroid surgery related complications may be avoided intraoperatively, careful preoperative planning and postoperative management are also critical.

Preoperative anticipation of challenging thyroid surgery due to patient characteristics (ie. high BMI, kyphoscoliosis, pre-existing vocal cord dysfunction, medical comorbidities, etc.) and tumour characteristics (ie. large goiter, locally advanced cancer, etc.) can be evaluated preoperatively, and useful tests include: laryngoscopy, US, cross-sectional imaging (CT, MRI), and thorough medical work up. Airway obstruction during intubation can be avoided through preoperative recognition of patients who may be at increased risk, and employing techniques such as video assistance during intubation, and in some circumstances awake fiberoptic techniques may also be helpful. A hybrid technique utilizing both of these approaches concurrently, in extreme circumstances, was also discussed. The utility of RLN monitoring was also reviewed as an approach to avoid bilateral RLN injury, vocal cord paralysis and potentially fatal postoperative airway obstruction. Use of continuous vagal nerve monitoring was also discussed as another approach to avoid bilateral RLN injury.

Loss of signal from a nerve monitor when the first side of a bilateral thyroid operation is completed should, in most circumstances, lead the surgeon to change the operative plan, and stage the procedure, or defer removal of the contralateral side to a later time in order to avoid bilateral RLN injury. Preoperative discussion with the patient of this possible surgical scenario is also important.

Avoidance of postoperative hemorrhage and airway compromise is also important. Tips to reduce this uncommon but potentially fatal complication include: avoidance of strap muscle closure, employment of deep extubation techniques, and superior pole vessel ligation with electrothermal or ultrasonic vessel sealing instruments. Vascular injury during thyroid surgery is another uncommon complication and may occur due to anomalous vascular anatomy, such as a high-riding innominate artery, or trauma to the carotid artery(s). Carotid injury is especially a concern when operating on very large goiters that may distort normal anatomy. In such cases mobilization or division of the strap muscles, and clear visualization of the inferior thyroid artery may also be helpful maneuvers during surgery.

Avoidance of intraoperative metabolic crisis through adequate preoperative preparation of hyperthyroid patients, and ensuring patients being operated on for medullary carcinoma have been screened and treated for pheochromocytoma, is also important. Visceral injury, or injury to the trachea and/or esophagus may lead to mortality, and the surgeon must always be aware of the location of these structures during a thyroid procedure, as well as using caution to avoid thermal injury when using

advanced energy instruments and electrocautery. Finally, avoidance of postoperative permanent hypocalcemia/hypoparathyroidism is also extremely important and is only possible with careful identification, and meticulous dissection of normal parathyroids, and liberal autotransplantation of devitalized parathyroid glands. In the early postoperative period employment of a protocol that routinely supplements patients with a tapering dose of oral calcium is simple and cost-effective.

The RLN must always be identified during thyroidectomy. Tips to avoid RLN injury include: employment of loupe magnification, headlight illumination, controlled retraction of the thyroid, and RLN monitoring. Incision cosmesis is also important and may be optimized through: preoperative marking the incision in the upright position, trimming skin edges at the end of the procedure, and utilization of skin adhesives.

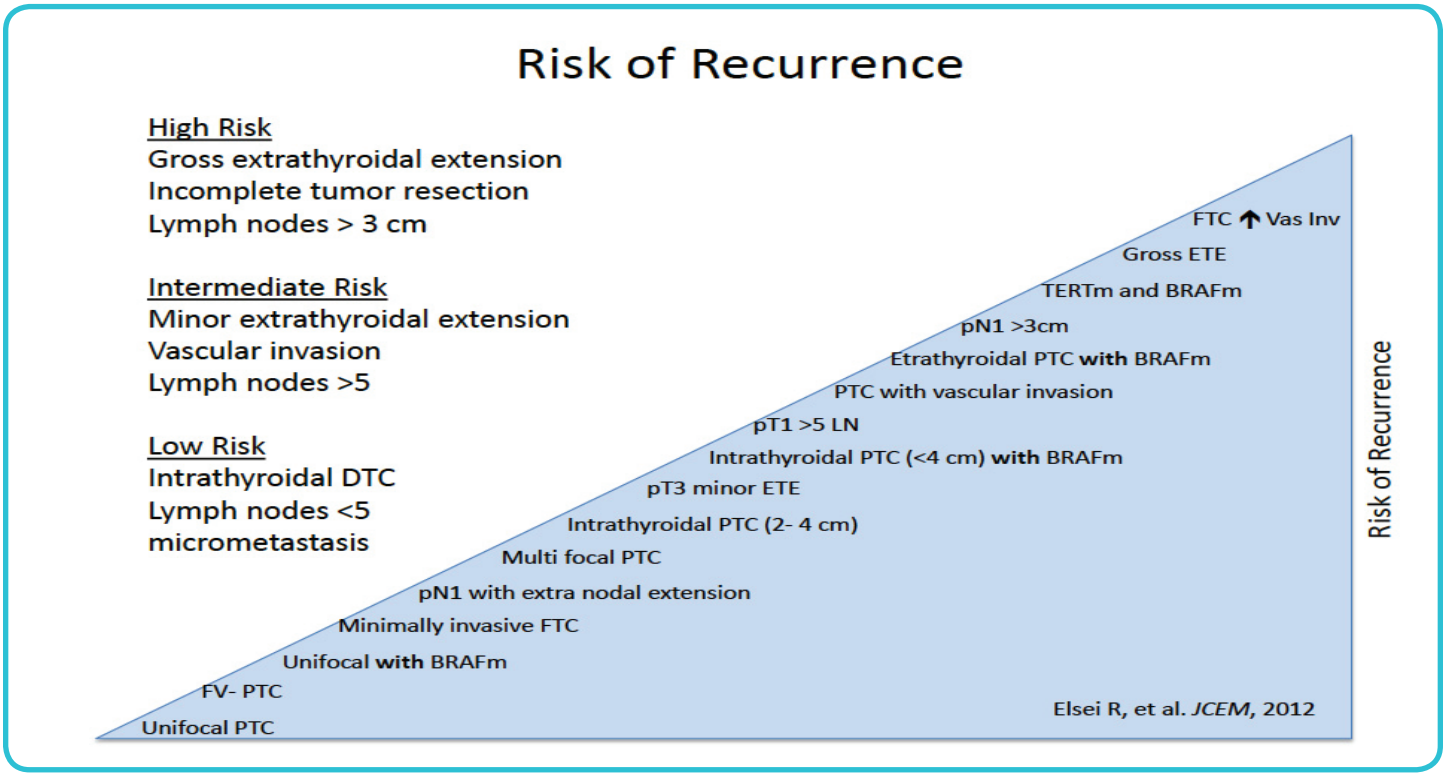
Avoidance of retained thyroid tissue may be facilitated by identification of Joll's space, ensuring the pyramidal lobe has been removed, meticulous dissection of the RLN at Berry's Ligament, and care to avoid a residual substernal goiter remnant. Incision complications may be avoided by not creating subplatysmal flaps, and observing small seromas. Finally, avoidance of anesthetic complications is also important and paramount in preventing postoperative nausea and vomiting and ensuring correct placement of the nerve monitoring endotracheal tube during intubation.

MANAGEMENT OF RECURRENT THYROID CANCER

Our other visiting professor, Dr. Eric Genden, the Isadore Freisner Endowed Professor and Chairman of the Department of Otolaryngology - Head and Neck Surgery at the Icahn School of Medicine at Mount Sinai, spoke next on the management of recurrent thyroid cancer. While preoperative thyroid cancer risk stratification systems and staging provide information regarding disease-specific mortality, they fail to adequately predict the risk of disease recurrence.

The rate of reoperation for thyroid cancer has risen over the past 20 years, and reoperation is strongly and independently predictive of mortality from PTC. Recurrent disease occurs when thyroid cancer is diagnosed after at least one year of being disease-free. Recurrence is usually diagnosed during postoperative biochemical (thyroglobulin) and imaging (US and CT +/- MRI) surveillance. Surgery is generally not indicated in the absence of a structural disease recurrence. Approximately 95% of recurrent disease will occur within the neck. Cervical US is the first-line imaging test for evaluation of locoregional recurrence of thyroid cancer, and FNAB with cytology and thyroglobulin aspirate measurement are important for diagnosis confirmation. Most reoperations are carried out soon after thyroidectomy and most likely reflect disease persistence, and not recurrence. Persistent differentiated thyroid cancer (DTC) has a worse outcome than recurrent disease. It is also important to be aware

LEFT TO RIGHT: DR. ERIC GENDEN, DR. SAM WISEMAN, AND DR. DAVID TERRIS



RISK OF RECURRENCE - *ELSEI R, ET AL. JCEM, 2012*

of the characteristics of patients that are at increased risk for cancer recurrence and these include: the presence of metastatic disease, aggressive histological subtypes (ie. tall cell), and the presence of specific mutations (ie. BRAF, TERT).

Preoperatively the identification of such characteristics may influence the treatment plan and patient counseling. Postoperatively assessable cancer characteristics that predict an increased risk of disease recurrence include: gross extrathyroidal cancer extension, vascular invasion, and the presence of lymph node disease > 3cm.

The decision to operate or observe patients with recurrent small-volume thyroid cancer is complex. It is a shared decision between the patient and surgeon, and must be tailored to the individual case.

Tips for surgeons who reoperate on patients for thyroid cancer recurrence include:

- **Consideration of staging reoperative bilateral central compartment neck dissection**
- **Utilization of RLN monitoring**
- **Utilization of intraoperative PTH monitoring**
- **Shaving cancer from the trachea when it is not invaded**
- **Tracheal resection and even laryngectomy may be indicated for some highly select cases**

ADJUVANT THERAPY OF THYROID CANCER: rhTSH, RAI, EBRT AND TARGETED THERAPEUTICS

Dr. Jonn Wu, a radiation oncologist at BC Cancer, presented an update on adjuvant therapy of thyroid cancer.

Adjuvant therapy of thyroid cancer includes radioactive iodine (RAI) ablation of microscopic disease (therapy 150-200 mCi, remnant ablation 30 mCi), and less commonly external beam radiation therapy for treatment of macroscopic disease.

Individuals who warrant RAI therapy are those at highest risk of recurrence and death from disease. The ATA risk stratification system separates patients into low, intermediate, and high risk groups and allows for estimation of cancer recurrence, compared with the AJCC staging system and the AGES, AMES, and MACIS risk stratification systems that predict disease specific mortality.

Unfortunately, there are no prospective randomized trials that evaluate the utility of postoperative RAI in reducing disease specific recurrence and mortality in thyroid cancer patients.

BC Cancer uses the MACIS system and multidisciplanary conference review, to assist with decision-making regarding utilization of postoperative adjuvant RAI.

At BC Cancer, MACIS score > 6.0 or ATA high risk group patients are given therapeutic dose RAI. MACIS score 5.0–6.0 or ATA intermediate risk group patients are reviewed at the weekly provincial multidisciplinary thyroid cancer conference for adjuvant treatment decision making.

In general, during recent years, fewer patients are being given therapeutic dose adjuvant RAI treatment. Thyrotropin alpha (rhTSH) is utilized because it allows for TSH stimulation without thyroid hormone withdrawl and improved quality of life. Lower RAI doses are being utilized for ablation (30 mCi), and more cases are being treated as outpatients.

External beam radiotherapy (EBRT) is generally reserved for the treatment of gross unresectable disease that is not responsive to RAI. Thyroxine suppression of TSH is also important and reduces the risk of cancer recurrence. Targets for TSH suppression are influenced by several factors that include: patient characteristics, cancer characteristics (low, intermediate or high risk) and current guidelines. For thyroid cancer recurrence that is not resectable, RAI and EBRT may be utilized for treatment. In the setting of non-iodine avid DTC, a combination of EBRT and multikinase inhibitors (ie. lenvatinib) may be considered for treatment.

I131 SIALADENITIS: INCIDENCE & MANAGEMENT

Next Dr. Robert Irvine, a head and neck surgeon who practices at St. Paul's Hospital, presented on the incidence and management of RAI sialadenitis. Review of the current literature suggested that even though there is variation in its reported incidence, sialadenitis is a common morbidity that occurs after RAI therapy (observed in up to 46% of patients in one study) and symptoms tend to be more common with higher RAI doses. Prevention of RAI sialadenitis is important and most strategies include massage and early use of sialagogues. Management of RAI sialadenitis involves hydration, massage, sialagogues, and antibiotics. Therapeutic sialendoscopy is a technique that allows for salivary duct endoscopy, dilation, irrigation, stenting, and even steroid instillation. It may have a benefit for refractory cases.

THE 5-HOUR PARATHYROIDECTOMY: HOW IS THIS POSSIBLE?

Dr. David Terris, our visiting speaker, opened discussion of parathyroid surgery by reviewing the role of surgeon experience and how, as suggested by Malcolm Gladwell in his book Outliers, it takes 10,000 hours to achieve mastery of any skill, including surgery. Despite a growing literature that suggests improved patient outcomes for surgeons who perform high volume thyroid and parathyroid operations, 80% of endocrine surgical operations in the United States are currently performed by low volume (≤ 3 procedures/year) surgeons.

The five most common pitfalls of parathyroid surgery were reviewed and included: misdiagnosis, imaging misinterpretation, failure to recognize an overly descended superior parathyroid gland, inappropriate or inadequate access, and several other technical issues.

To avoid a misdiagnosis of primary hyperparathyroidism, and an unnecessary surgical exploration, several diagnoses should first be ruled out including:

- **Vitamin D deficiency (can elevate PTH)**
- **Familial hypercalcemic hypocalcuria (24-hour urine collection calcium level will be low)**
- **Non-PTH mediated hypercalcemia (PTH is appropriately suppressed due to hypercalcemia having a different etiology such as bone metastases or a paraneoplastic syndrome)**

Patients with normocalcemic hyperparathyroidism (normal calcium level and elevated PTH level) and a normal (nonsuppressed) PTH in the setting of hypercalcemia do have distinctive forms of primary hyperparathyroidism, and often benefit from parathyroidectomy.

Another common pitfall of parathyroid surgery is imaging misinterpretation. This problem may be overcome if the surgeon spends time reviewing their own sestamibi scans, considers repeating the scan at a high volume centre, and performs their own US.

An important pitfall of parathyroid surgery, and a common reason for needing reoperation, is the missed overly descended superior parathyroid adenoma.

Planar imaging may diagnose a "lower pole" adenoma that is presumed to be an inferior gland. At exploration the inferior gland, which appears morphologically normal, may be encountered and inappropriately removed. If this clinical scenario is encountered the surgeon should dissect dorsal to the RLN and expose the esophagus, and the overly descended adenoma will often be found in the

retroesophageal location. An inappropriate or inadequate skin incision is another pitfall that should be avoided during parathyroid operations. Incisions placed laterally are inhibitory to bilateral exploration and should be avoided. Similarly, a transverse incision that is well centred, but too small or poorly positioned to allow for safe removal of the adenoma should also be avoided.

There are several other technical issues that must be considered when carrying out parathyroidectomy, that help to improve patient outcomes, and these include: maintaining a bloodless field for clear operative exposure, having a low threshold for identifying the RLN, avoiding removal of normal parathyroid glands, using ballottement of surrounding tissues to help reveal the adenoma, and having a low threshold for dividing the superior thyroid vascular pedicle (especially if the superior parathyroid cannot be identified).

Remember, for a missing superior parathyroid look inferior to the inferior gland, and for a missing inferior parathyroid look superior to the superior gland.

Finally, for surgeons who perform parathyroidectomy, it must be remembered that speed does not necessarily equate with success, rather success is achieved when the normal parathyroid glands and RLNs are preserved during an operation, and the pathological gland(s) are removed.

QUALITY INDICATORS FOR THYROID/THYROID CANCER AND PARATHYROID OPERATIONS: WHAT THE SURGEON SHOULD KNOW

Dr. Sam Wiseman, chair of the BC Cancer Surgery Network's Thyroid Surgical Tumour Group, and a head and neck surgeon who practices at St. Paul's Hospital, spoke about thyroidectomy and thyroid cancer surgical quality indicators (QIs).

Thyroid cancer surgical QIs pose a unique challenge because thyroid cancer generally has an excellent prognosis with mortality being uncommon, may recur over decades, and if considered "low risk" a total thyroidectomy, central neck dissection, and RAI therapy may not be necessary.

Currently, thyroid cancer surgical QIs are based upon the completeness of the thyroid cancer operation, and none are currently considered standard of care.

Further study of thyroid cancer surgical QIs is needed.

Surgeons who perform thyroid operations should be aware of:

- **Patient morbidity and mortality in their practice**
- **Recurrence risk in their practice**
- **Cancer surgical QIs (postop RAI uptake, thyroglobulin level and metastatic lymph node ration)**
- **Their own surgical volumes**

MANAGEMENT OF THE NECK MASS: DO'S & DON'TS

Dr. Eric Genden, our visiting speaker, presented an approach to the workup and evaluation of the neck mass.

Thorough examination of the head and neck, especially sites at highest risk given the specific presentation of the neck mass, is important, and will usually direct further investigation.

Imaging including US, CT, and MRI will assist the surgeon establish a diagnosis. Upper aerodigestive tract squamous cell carcinoma, HPV-associated oropharyngeal carcinoma, metastatic thyroid cancer, lymphoma, and infectious causes such as tuberculosis, must all be considered in the differential diagnosis of a neck mass. FNAB and/or core-needle biopsy may be carried out, with or without image guidance, to allow for a definitive pathological diagnosis.

Open biopsy may be required for some cases. Cytomorphology, immunocytochemistry or immunohistochemistry (including thyroglobulin staining), invader chemistry, PCR, flow cytometry, and culture may all also assist in establishing a specific pathological diagnosis.

Other less common diagnoses that may present with a neck mass, and should be considered in its differential diagnosis include: actinomycosis, a reaction to injectable fillers, and IgG4-related disease.

Detailed knowledge of the lymphatic drainage patterns of the head and neck is critical for a surgeon who is evaluating patients that present with a neck mass.

WHAT DOES THE PATHOLOGIST EXACTLY NEED FROM THE SURGEON WHEN CARRYING OUT A LYMPH NODE BIOPSY?

The final presentation of the day was given by Dr. Brian

Skinnider, a pathologist based out of BC Cancer and Vancouver General Hospital.

The diagnosis of lymphoma involves an approach that evaluates morphology (architecture and cytology), immunophenotype (flow cytometry and immunohistochemistry), lymphoid clonality (PCR), and chromosomal translocations (FISH analysis). Analytical techniques have evolved since the 1990s and currently fresh tissue is only required for flow cytometry.

Flow cytometry requires a $1cm^3$ piece of tissue that should be processed as soon as possible. While it is not essential for every case, flow cytometry is especially useful for differentiating reactive lymph nodes from low-grade lymphomas (facilitated by staining for kappa and lambda), and for distinguishing low-grade B cell lymphomas.

Unlike flow cytometry, immunohistochemistry is performed on formalin-fixed paraffin-embedded tissue, and expression of different markers can be correlated with morphology. There are a wide variety of antibodies available for immunohistochemistry. Unfortunately, kappa and lambda do not work well by immunohistochemistry.

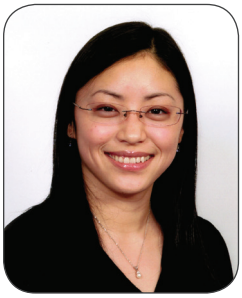
Even though a lymph node biopsy can be performed as a core, an incisional or excisional procedure is preferred. The pathologist also prefers to evaluate the largest intact lymph node that has been sampled.

Reasons for this include: difficulty in assessing architecture in small biopsies, lymphoid tissue may easily be crushed especially in core biopsies, and the capsule of an intact lymph node helps to keep morphology intact. The quality and quantity of lymphoid tissue available to be assessed by core biopsy is also quite variable. When carrying out a lymph node biopsy (although ideally the specimen should be processed by pathology as soon as possible) nodal tissue can remain viable for several hours if refrigerated (preferably on saline-soaked gauze and not floating in saline). Finally, even though pathologists would prefer not to perform frozen sections if lymphoma is the probable diagnosis, it may be carried out if required to confirm that lesional tissue is present.

Q&A PANEL SESSION (LEFT TO RIGHT) DR. ADRIENNE MELCK (MODERATOR), DR. SAM WISEMAN, DR. CHRIS BALISKI, DR. ERIC GENDEN, DR. DAVID TERRIS, DR. JONN WU, DR. VANCE TSAI, DR. NADINE CARON, AND DR. SABRINA GILL.

Evidence-Based Management of Epithelial Lacrimal Gland Malignancies

DR. VIVIAN T. YIN, DEPARTMENT OF OPHTHALMOLOGY AND VISUAL SCIENCES, UBC



DR. VIVIAN T. YIN

Approximately 30% of all lacrimal gland (LG) tumours are malignant, with a population incidence of 0.7 per 1,000,000 people per year according to the Danish cancer registry.[1] Among the malignant tumours, over half are epithelial tumour with half of which as adenoid cystic carcinoma (ACC).[1]

Although extremely rare, especially when compared to breast cancer at 124.7 per 100,000 population[2], there is a high 5-year mortality rate of 50% despite aggressive local treatment with exenteration.[3] Furthermore, aggressive local treament does not improve survival as seen in a retrospective review of 79 patients over 40 years.[4]

In an attempt to improve survival, *Tse et al.*[5] treated patients with neoadjuvant intraartieral chemotherapy followed by chemoradiation with concurrent weekly cisplatin and 4-cycles of cisplatin and doxorubicin.

The rigour of the protocol led to only five (23%) of 21 patients completing the treatment as planned; however, overall survival was 76.1% (16/21) and disease-specific survival was 84.2%, at a median of 10-years.

At the same time, others pushed for saving the eye with globe-sparing surgery followed by radiation, especially when aggressive treatment does not improve survival.

A combined review of 37 patients showed 5-year survival of 87.4% and disease-free survival of 72.9%[6] (Table 1.). The study also showed the possibility of a good visual function after orbital RT, with 68% of patients having good vision, better than 20/40 (Table 2).

			5-year			10-year		
	N	Median Age (y)	OS	DFS	RFS	OS	DFS	RFS
Woo 2018	37	43	87.4%	72.9%	44.8%			
Tse 2006	9	36	83.3%					
Tse 2013	21	42				76.1%	71.4%	61.9%

TABLE 1. COMPARISON OF NEOADJUVANT INTRAARTERIAL CHEMOTHERAPY (TSE 2006 & 2013) VS. GLOBE-SPARING SURGERY AND RT (WOO 2018) FOR LACRIMAL GLAND TUMOURS.[5,6,13]

Ocular SE	Gore et al.	Woo et al.
Corneal epitheliopathy/Dry eye	100%	59%
Filamentary keratitis	22%	
Chronic corneal epithelial defect	54%	
Corneal perforation	13%	
Retinopathy		38%
Cataracts		16%
Enucleation		2.7%

TABLE 2. OCULAR SIDE EFFECTS FROM RADIATION OF 50-60Gy DELIVERED IN 2Gy FRACTION FOR LACRIMAL GLAND TUMOURS.[6,14]

AJCC T stage 3 or greater is associated with worse 5-year disease-free survival but not recurrence free survival.[4,6] The presence of gross residual disease is associated with both worsened progression-free survival and overall survival.[7] The significance of basaloid or solid histological subtype as prognosticator is less consistent in the literature.

With an increase in the development of targeted therapy, there is new interest in mutational drivers for LG tumours. Despite some similarity with parotid and salivary gland tumours, miRNA expression for LG ACC has shown it to be distinct.[8] Studies have implicated three possible distinct mutational pathways for LG ACC, including MYB rearrangements,[9,10], KRAS/NRAS[11] and NOTCH[12] mutations.

Further understanding of the contribution of mutational profile to clinical phenotypes and risk of metastasis is needed for designing clinical trials for targeted therapy in epithelial tumours of the lacrimal gland.

- **Aggressive local therapy does not improve survival for malignant epithelial tumours of the lacrimal gland.**
- **Tumour stage T3 or greater is associated with significant worse survival.**
- **Ocular side effects from orbital radiation is variable by centre and technique.**
- **Mutational profile of epithelial lacrimal gland malignancies is not the same as parotid and salivary gland.**

References for this article are posted on the BC Cancer Surgery Network website at www.bccancer.bc.ca/health-professionals/networks/surgery-network/newsletter

Is Microductectomy Still Necessary to Diagnose Breast Cancer: A Ten-Year Study on the Effectiveness of Duct Excision and Galactography

DR. DANIEL LUSTIG (BC CANCER SURGERY NETWORK 2018 TRAVEL AWARD RECIPIENT)
SUPERVISORS: DR. REBECCA WARBURTON, DR. CAROL DINGEE, DR. URVE KUUSK, DR. JIN-SI PAO, AND DR. ELAINE MCKEVITT

Breast cancer presents exclusively with nipple discharge in approximately 10% of patients. Traditionally, women with discharge who have neither clinically palpable masses nor evidence of disease with mammography and ultrasound go on to have surgery to rule out cancer.

However, the majority of nipple discharge is caused by benign causes leading many women to undergo surgery to prevent missing a diagnosis of cancer.

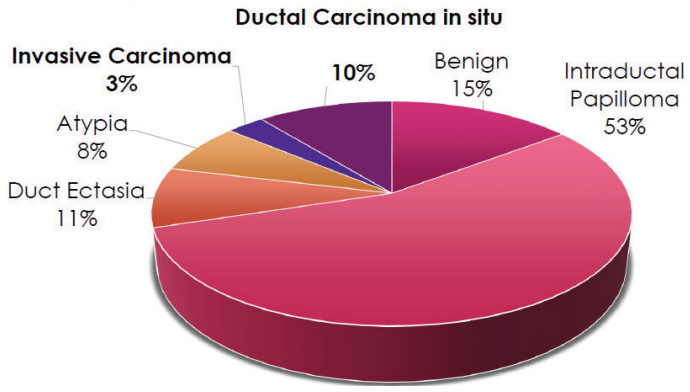


FIGURE 1: INCIDENCE OF BENIGN AND MALIGNANT DISEASE IN CLINICALLY AND RADIOGRAPHICALLY NEGATIVE PATIENTS

As breast imaging improves, it has raised the question whether microductectomy (surgical removal of the duct) is still necessary. The purpose of our study was to determine the incidence of malignancy in patients presenting nipple discharge who underwent a duct excision.

We determined that 13% of women with nipple discharge and no evidence of disease on initial work up were diagnosed with invasive or pre-invasive cancer. Thus, duct excision should continue to be performed within this patient population to prevent missing a diagnosis of cancer.

Recommendations:

- **Microductectomy should continue to be performed in women presenting with spontaneous nipple discharge equivocal work up to avoid missing a malignancy.**
- **We do not recommend performing routine galactograms owing to poor sensitivity and specificity, though it may be useful in pre-operative planning.**

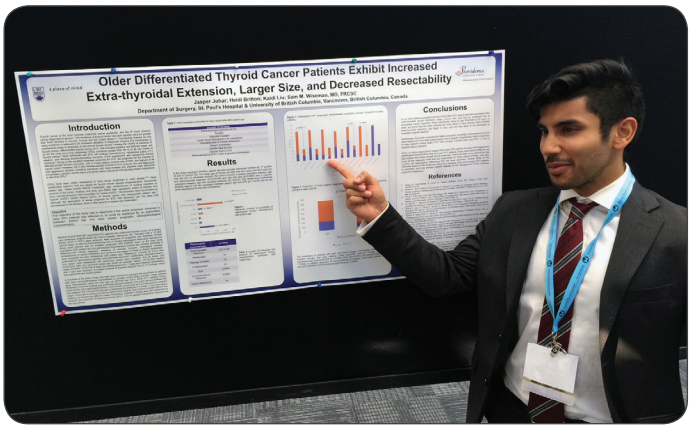
Presented at the American College of Surgeons Clinical Congress, October 2018, Boston.

OLDER DIFFERENTIATED THYROID CANCER PATIENTS EXHIBIT INCREASED EXTRA-THYROIDAL EXTENSION, LARGER SIZE, AND DECREASED RESECTABILITY

DR. JASPER JOHAR (BC CANCER SURGERY NETWORK 2017 TRAVEL AWARD RECIPIENT)
SUPERVISOR: DR. SAM WISEMAN

I was honoured to present our poster at the annual meeting of the American Thyroid Association on October 20th, 2017 in Victoria, BC. My research project focused on differentiated thyroid cancer (DTC) and why age is associated with a worse disease prognosis. For the last three decades, the incidence of DTC has been steadily rising and it is currently the most commonly diagnosed endocrine cancer, and is the fifth most common cancer diagnosed in women.

Age is an important disease prognosticator for DTC and is included in the current American Joint Committee on Cancer's (AJCC) thyroid cancer staging system. Despite age being important for cancer prognostication, it is not currently understood why older patient age is associated with a worse cancer prognosis.



DR. JASPER JOHAR PRESENTING AT THE AMERICAN THYROID ASSOCIATION MEETING

For my research project I evaluated 941 thyroid cancers that were treated at St. Paul's Hospital in Vancouver. Of the cases, 601 tumours were primary DTC and ≥1cm in size, which we were interested in because most DTCs < 1cm in size do extremely well and often are an incidental finding. I found that larger cancer size, the presence of extra-thyroidal cancer extension (ETE), and reduced cancer resectability were all correlated with older patient age.

There are likely many alterations that occur at the molecular level that contribute to the importance of age as a prognosticator in DTC patients, and also underlies the pathological differences that we observe. The hope is that by bringing the pathological characteristics of older DTCs to light, our results will help inform the search for molecular markers that correlate with age and cancer prognosis.

I would like to thank the BC Cancer Surgery Network for this travel award, and for giving me the opportunity to attend and learn at the conference. Presenting our results and listening to world-renowned experts in thyroid cancer at the American Thyroid Association meeting was a privilege. This experience has also inspired my interest in oncology and has also led me to consider making research an important part of my future medical career.

Shared Care/Communications Key For Primary Care Providers

DR. CATHERINE CLELLAND, PROVINCIAL LEAD, PRIMARY CARE PROGRAM, BC CANCER

DR. CATHY CLELLAND

BC Cancer established the Family Practice Oncology Network (FPON) in 2002 as a means to enhance family physicians' abilities to care for cancer patients. Efforts began with the General Practitioner in Oncology (GPO) Education Program designed to provide rural family physicians (FPs) with the skills and knowledge to administer systemic therapy and provide supportive care to cancer patients in their communities. The provision of continuing medical education and cancer care practice tools to support the broader primary care community followed thereafter.

In 2017, BC Cancer established its Provincial Primary Care Program to build on the success of FPON, to provide more effective integration of primary care within the continuum of cancer care, and to ensure greater support for FPs. To support this development, FPON conducted a province-wide primary care oncology needs assessment to gain current information on the needs of FPs providing cancer care.

Key results from this assessment published September 2018:

- **Shared care and team-based care are viewed by FPs as key to the sustainability of high quality cancer care. Effective communication and sharing of patient information between providers is pivotal.**
- **FPs often experience challenges related to geographic isolation and lack of resources. These are amplified when specialist advice is needed on 'what to do next' for a cancer patient and appropriate contact information is not at hand. Clear, accurate contact information with all documentation is of core importance to FPs including referrals to different specialists or supportive care services. (On a 5-point scale, surgeons ranked the easiest to communicate with at 3.8. BC Cancer specialists ranked 3.6, followed by GPOs at 3.5).**
- **FPs recommend adding cancer care to existing well utilized, highly accessible communication tools including the RACE (Rapid Access to Consultative Expertise) line and the Pathways referral website (pathwaysbc.ca). Ensuring accurate, current cancer surgery information via Pathways, for example, will help FPs significantly in planning patient care.**
- **Real-time communication tools, such as secure text messaging and direct phone access for urgent needs, and asynchronous tools such as secure email or provincial electronic medical records for non-urgent needs, are much sought after by FPs.**
- **Quality Improvement projects are viewed as a key method for relationship building among FPs, specialists, nurses, and allied health professionals.**

Finally, the landscape of primary care is evolving to include the establishment of Patient Medical Homes and Primary Care Networks led by local Divisions of Family Practice. Connecting with respective Divisions will be an important step for surgeons and other cancer specialists to support the development of a more integrated and seamless journey for patients with cancer and their families.

To learn more, please connect with Dr. Cathy Clelland at *cathy.clelland@bccancer.bc.ca* or go to *fpon.ca*.

BC Cancer Surgery Network News

DR. MALCOLM MOORE

Dr. Malcolm Moore will be leaving BC Cancer to return to Ontario, to be closer to friends and family at the end of April. During his 3.5 years with us, he led the creation of the provincial cancer care strategy and assembled a strong and experienced team of provincial and regional leaders, clinicians, staff and researchers.

Dr. Moore's decision comes at a time when PHSA is aligning the executive leadership structure and strategic objectives around a refreshed provincial mandate. This will create increased opportunities for collaboration across PHSA and all the other BC health authorities in the areas of clinical policy, clinical service delivery, commercial services, and digital and information services.

The recruitment plan for new leadership at BC Cancer will focus primarily on internal candidates within PHSA, and aims to have new leadership in place as soon as possible.

We thank Dr. Moore for his efforts during his tenure and wish him well in his future endeavours. In particular we acknowledge his support of cancer surgery. Our strategic plan, with its goals to reduce surgery wait times and improve patient outcomes, will continue to be supported as we roll out the plan this year.

SAVE THE DATE!
BC CANCER SURGERY NETWORK FALL UPDATE 2019 WILL BE HELD ON OCTOBER 5TH IN VANCOUVER

Upcoming Conferences

BC Surgical Society Annual Meeting, Penticton BC
May 9-11, 2019, www.bcss.ca

BC Cancer Surgery Network Annual Fall Update, Vancouver BC
October 5, 2019, www.bccancer.bc.ca/surgerynetwork

American College of Surgeons Clinical Congress, San Francisco CA
October 27-31, 2019, www.facs.org

Ontario Association of General Surgeons Annual Meeting, Toronto ON
November 2, 2019, www.oags.org

Western Surgical Association Annual Meeting, Las Vegas NV
November 2-5, 2019, www.westernsurg.org

North Pacific Surgical Associatation Annual Meeting, Victoria BC
November 8-9, 2019, www.northpacificsurgical.org

BC Cancer Summit, Vancouver BC
November 21-23, 2019, www.bccancer.bc.ca

BC CANCER SURGERY NETWORK NEWSLETTER

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VISIT THE SURGERY NETWORK WEBSITE:
www.bccancer.bc.ca/surgerynetwork

The BC Cancer Surgery Network exists to promote and advance quality cancer surgery throughout the province, enable the integration of quality surgical oncology services into the formal cancer care system, and ensure that patients have the best possible outcomes through consistent access to high quality multidisciplinary care. To enhance appropriate, equitable and timely access to surgical services for cancer patients as close to home as possible, the Network supports communication and sharing of knowledge between subspecialty and community surgeons, their respective hospitals and BC Cancer.