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Fall Update 2014
Breast Cancer: Current Controversies
October 18, 2014

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In This Issue...

HIGHLIGHTS FROM THE FALL UPDATE 2013: *ENDOCRINE SURGICAL ONCOLOGY*

On November 2, 2013, the Surgical Oncology Network, with the UBC Department of Surgery, hosted the Annual Fall Update at the Four Seasons Hotel, downtown Vancouver. The day was focused on Endocrine tumors. Presentations from this event are posted on the Surgical Oncology Network's website at www.bcca.bc.ca/son.

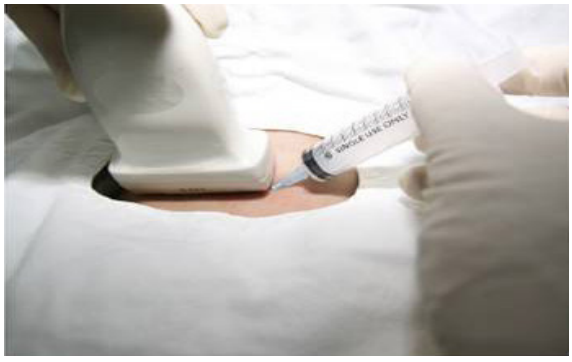
Dr. Sam Wiseman
Chair, Endocrine Tumor Group,
BC Surgical Oncology Network

We began the day with sessions focusing on the management of thyroid tumors.

Work Up & Evaluation of Thyroid Nodules in 2013: State of the Art

Dr. Todd McMullen, one of the visiting speakers, who is an Endocrine Surgeon and the Director of the Division of Surgical Oncology at the University of Alberta, spoke on the evaluation of thyroid nodules. He began by reviewing current literature that has reported a steadily rising incidence of thyroid cancer, mostly due to small papillary carcinomas, over the past 20 years. Much of this rising incidence has been attributed to the high prevalence of thyroid nodules and the increasing clinical utilization of neck ultrasound. In several large contemporary studies reporting on thyroid ultrasound, from a third to greater than a half of people were diagnosed with small thyroid nodules. A steady rise in performance of thyroid fine needle aspiration biopsy (FNAB) and thyroid surgery at several centers has also been observed.

Factors that increased patient thyroid cancer risk include familial adenomatous polyposis and a history of neck irradiation. Other factors that should trigger investigation of thyroid nodules include FDG-avid lesions on PET scans, uptake on MIBG and octreotide scans, and voice changes. Ultrasound has emerged as the most important tool for evaluation of thyroid nodules. While there are multiple nodule characteristics (microcalcifications, macrocalcifications, ill-defined margins, intranodular vascularity, taller–then-wide, solid, and echogenic) that have variable sensitivity and specificity for diagnosing cancer, ultrasound guided fine FNAB is really the critical diagnostic test. Nodules >1-1.5cm, or smaller nodules with suspicious features, are generally biopsied, and interestingly the false negative rate of 'benign' nodules >4cm is actually 10%. Several molecular based tests have been developed and are being utilized clinically in some centers to reduce the need for diagnostic thyroid surgery for individuals who have an indeterminate or suspicious FNAB diagnosis. For nodules diagnosed as benign by FNAB, a repeat biopsy may be required if they grow over time.



Ultrasound guided fine needle aspiration biopsy of a thyroid nodule

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Thyroid Cytopathology: Weighing In On The Bethesda System

Dr. Blair Walker, a senior pathologist at St. Paul's Hospital who has been a provincial leader in adoption of the Bethesda Thyroid Cytopathology System, continued the thyroid nodule work up theme by speaking about the Bethesda System.

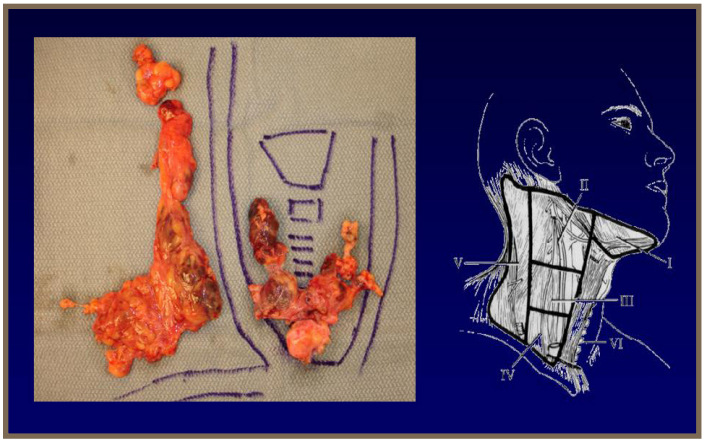
The Bethesda System for Reporting Thyroid Cytopathology was developed at the National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference held in October 2007 in Bethesda Maryland. This system provides 6 diagnostic categories for thyroid cytopathology and each of these categories has an assigned cancer risk, and a recommended clinical action. These categories and their associated cancer risks are: Nondiagnostic/Unsatisfactory (1-4%); Benign (0-3%); Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (5-15%); Follicular Neoplasm/Suspicious For Follicular Neoplasm (15-30%); Suspicious For Malignancy (50-75%); Malignancy (97-99%).

A major aim of this system is to provide standardized terminology and therefore improve communication between pathologists and other clinicians. Challenges facing the pathologist when reviewing thyroid cytopathology and utilizing the Bethesda System were discussed. As well, it is important that centers that adopt this system evaluate their own outcomes and diagnostic category utilization. The Bethesda System For Reporting Thyroid Cytopathology has been increasingly adopted by centers across the world, including here at home in British Columbia.

Thyroid Cancer: Resection, Dissection, Surveillance, and Recurrence

Dr. Cord Sturgeon, another visiting speaker, who is an Endocrine Surgeon and Director of Endocrine Surgery at Northwestern University Feinberg School of Medicine in Chicago, Illinois, then spoke on the management of thyroid cancer.

Total thyroidectomy, radioactive iodine ablation (in selected patients), TSH suppression, and ongoing surveillance have remained the cornerstones in the management of differentiated thyroid cancer. Total thyroidectomy with appropriate lymph node clearance, thyroid hormone replacement, and surveillance have remained the cornerstones of management of medullary carcinoma. The overall goals of initial surgery for thyroid cancer include: removal of the primary tumor and any extra-thyroidal disease, minimize disease recurrence and metastatic spread, minimize treatment and disease related morbidity, permit accurate staging and long term surveillance, and to facilitate postoperative treatment. For differentiated thyroid cancer, abnormal lymph nodes diagnosed either preoperatively or intraoperatively should be managed with a compartment oriented lymph node dissection (central +/- lateral selective neck dissection).



Neck dissection for papillary thyroid cancer

Thyroid cancer can recur locally, regionally, or distantly, and thyroid cancer mortality is largely dependent upon thyroid cancer histopathology (papillary < follicular < medullary). Multiple factors influence the risk of PTC recurrence and these include: cancer size, local invasion, histological subtype, maintenance of TSH suppression, utilization of radioactive iodine, presence of lymph node metastases, and the extent of the initial thyroid operation. Cervical lymph node metastases may be found in up to 80% of PTC patients who undergo a central neck dissection as part of their initial operation. For PTC, the presence of large nodal metastases, a large number of positive nodes, and the presence of extra-nodal cancer extension are risk factors for recurrence.

Though commonly performed for individuals undergoing operation for thyroid cancer, the performance of prophylactic central neck dissection is still considered controversial. Approximately 20 prophylactic central neck dissections need to be carried out in order to avoid a single reoperation for thyroid cancer nodal recurrence. Advantages of central neck dissection must be weighed against disadvantages, specifically increased risk of complications that include transient or permanent hypoparathyroidism or recurrent laryngeal nerve dysfunction.

Thyroid cancer patients must all undergo post-treatment surveillance, and guidelines from the NCCN and ATA provide algorithms for follow up of these patients. The treatment of thyroid cancer recurrence is complex and depends upon: the type of cancer, the site of recurrence, the tumor burden, and the type and response to prior treatment. If the thyroid cancer recurrence can be localized, and is resectable, surgery is generally an important part of its treatment. In addition to surgery and radioactive iodine therapy, external beam radiation therapy and newer targeted therapeutic drugs may be utilized to treat thyroid cancer recurrence.

Vessel Sealing Technology For Thyroid Surgery: Current Evidence

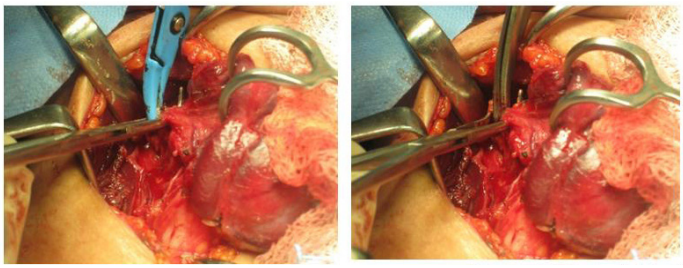
Dr. Sam Wiseman, Chair Endocrine Tumor Group, who is an Endocrine Surgeon based out of St. Paul's Hospital in Vancouver, and the Director of Research for the Department of Surgery, Providence Health, spoke about the utilization of vessel sealing technology for thyroid surgery.

Modern thyroid surgical technique was pioneered by Kocher in the 1880s and involved meticulous dissection and tying of named and smaller blood vessels. Clips, monopolar cautery, and bipolar cautery are all routinely applied to thyroid surgery today. Cautery is limited by its ability to reliably seal vessels 2-3mm in diameter and by unpredictable lateral thermal injury for a zone of 2-8mm.

Vessel sealing technologies include the harmonic scalpel (HS) that uses high frequency mechanical energy to seal and cut vessels. There is no electrical energy transferred to or through the patient. Vessels up to 5mm may be sealed and the thermal spread may be up to 2.2mm from the instrument. Greater then 80 published studies have evaluated the HS for thyroid surgery.

Electrothermal Bipolar Vessel Sealing Systems (Ligasure, Covidien) (LS) are computer controlled diathermy systems that utilize pressure and bipolar energy and incorporates impedance based feedback loops to modify bipolar energy to seal and then cut vessels. Vessels up to 7mm may be sealed and the thermal spread may be 1.2 to 3mm from the

instrument. Greater than 50 published studies have evaluated the LS for thyroid surgery.

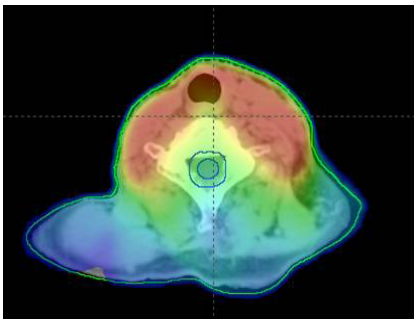


Electrothermal vessel sealing during thyroidectomy

Both systems have been reported to reduce: operative time, transient hypoparathyroidism, blood loss, drain output, hematoma, recurrent laryngeal nerve injury, incision length, hospital stay, and costs. Studies that have compered these 2 vessel sealing systems to each other have suggested they are similar in terms of time savings and postoperative complications, and they are safe and useful time saving alternatives to conventional surgical hemostasis techniques. The choice of device is really based upon surgeon preference. Vessel sealing technologies will continue to evolve and do represent an important technical advance for thyroid surgery.

Update On Adjuvant Therapy For Differentiated Thyroid Cancer

Dr. John Hay, Radiation Oncologist, British Columbia Cancer Agency then presented an update on recent trials of adjuvant treatment of thyroid cancer. These recent studies have helped identify the most appropriate dose of iodine for thyroid remnant ablation, utilized intensity modulated radiotherapy (IMRT) to reduce morbidity from external beam radiation therapy, confirmed the efficacy of thyrotropin-α, and focused on new drugs that increase the uptake of iodine by thyroid cancer and treat radioactive iodine refractory thyroid cancer. These drugs include antibodies against cell surface receptors (such as trastuzunab and bevacizumab) and small molecules that enter the cell and block upregulated pathways (such as imatinib, selunitinib, sorafenib, vandetanib). Fosbretabulin, a vascular disrupting agent, has also recently showed promise for treatment of anaplastic thyroid cancer. Vandetanib, an oral kinase inhibitor that targets VEGF, RET, and EGFR, has shown promise for treatment of locally advanced or metastatic medullary thyroid cancer. There are many new treatment options available for individuals with locally advanced or metastatic thyroid cancer.



Intensity Modulated Radiotherapy (IMRT) of thyroid cancer

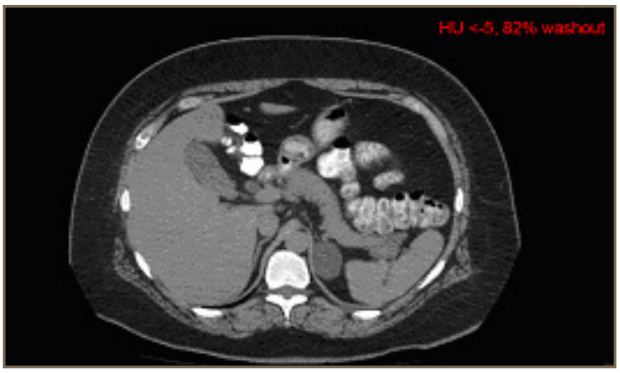
Panel 1: Thyroid Case Discussions

The morning lectures were followed by several thyroid cancer focused case-based panel discussions. Panels were multidisciplinary and members included: Dr. Chris Baliski (Surgical Oncology), Dr. Don Anderson (Otolaryngology), Dr. John Hay (Radiation Oncology), Dr. Todd McMullen (Endocrine Surgery), Dr. Cord Sturgeon (Endocrine Surgery), Dr. Blair Walker (Pathology) and Dr. Sam Wiseman (Endocrine Surgery).

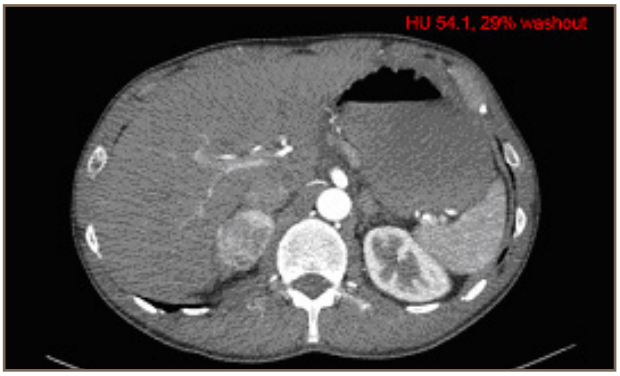
Adrenal Incidentaloma: Evidence Based Management

Dr. Adrienne Melck, Endocrine Surgeon based out of St. Paul's Hospital Vancouver spoke about the management of adrenal incidentalomas.

Adrenal incidentalomas (AI) are inapparent adrenal masses detected incidentally with imaging studies conducted for other reasons. The prevalence of AI increases with age and their incidence has been increasing. The AACE/AAES have published guidelines for management of AI that are an excellent resource for managing this problem. AI > 1cm warrant evaluation and may be defined as being benign or malignant and functional or nonfunctional. The majority (>80%) of AIs are benign and nonfunctional. Key characteristics to consider when evaluating these patients are tumor size and patient history of malignancy. 25% Of AI > 6cm will be adrenocortical carcinoma. Individuals with an AI and a history of lung cancer, melanoma, renal cell carcinoma, breast or colon cancer have a 25-72% risk of the tumor being a metastasis.



Benign Adrenal Adenoma



Atypical adrenal imaging

Initially it is important to evaluate AI patients for findings that suggest functionality by history and physical examination (ie. hypertension, hypokalemia, flushing, weight loss, weight gain, fatigue, etc.). The critical laboratory workup includes biochemical screening for pheochromocytoma (24 hour urine metanephrines and catecholamines, plasma free metanephrines) and Cushing's Syndrome (low dose dexamethasone suppression test, 24 hour urine free cortisol, late night salivary cortisol, serum ACTH measurement) as well as screening for Conn's (plasma aldosterone and renin, saline suppression test, adrenal venous sampling) in the presence of hypertension.

Dedicated adrenal imaging with either CT or MRI should also be carried out as benign AI's have different imaging characteristics compared to AI's that are atypical or cancer. Biopsy of AIs is rarely required, may precipitate crisis in an undiagnosed pheochromocytoma and will not diagnose adrenocortical carcinoma. AIs that are functional or suspicious

for malignancy should undergo surgery. Benign nonfunctional AIs should be followed with repeat imaging in 3-6 months and then every 1-2 years, as well as an annual functional biochemical workup. With the exception of adrenocortical carcinoma minimally invasive surgical approaches have become standard.

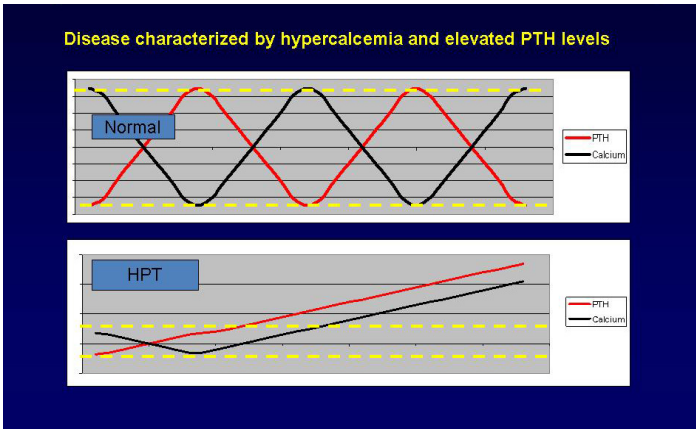
Indications For Surgery In Primary Hyperparathyroidism: Do Guidelines Make a Difference?

Dr. Cord Sturgeon, our visiting speaker, opened discussion of parathyroid disease with a review of indications and rationale for surgery.

Women aged 50-60 years are most commonly diagnosed with primary hyperparathyroidism (PHP), and most will present with asymptomatic disease detected by biochemical testing. Classically PHP is described as a disease of renal STONES, painful BONES, abdominal GROANS, psychogenic MOANS, and fatigue OVERTONES. Risk factors for PHP include a history of neck irradiation, prolonged lithium use, MEN1 and 2A, Familial Isolated Hyperparathyroidism, and Hyperparathyroidism Jaw Tumor Syndrome.

The majority of PHP cases are sporadic and individuals will be found at surgery to have a solitary adenoma most commonly (80-85%). Four gland hyperplasia will be found in 15% of cases, other multi-gland disease in 15% of cases, and parathyroid carcinoma in < 1% of cases. All individuals diagnosed with symptomatic PHP should be offered surgery.

The National Institute of Health initially reported guidelines for surgical management of asymptomatic PHP patients initially in 1990, and these were revised in 2002 and 2008. Asymptomatic patients account for the majority (50-75%) of individuals diagnosed with PHP. These guidelines define levels of serum calcium, 24 hour urine calcium clearance, creatinine clearance, bone mineral density, and patient age that can assist with surgical decision making. Individuals who do not specifically meet the guidelines for parathyroidectomy may still be operated on.



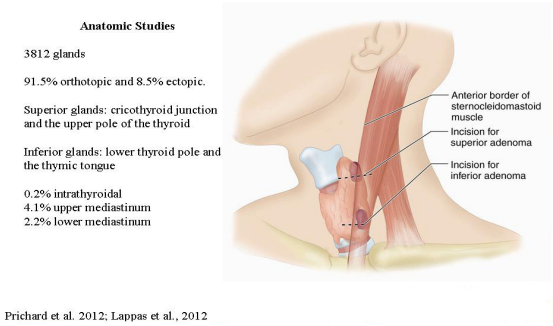
Biochemical presentation of normal versus primary hyperparathyroidism

Surgical parathyroidectomy allows for rapid, durable, and cost effective treatment of PHP. It is generally a low physiological risk procedure that is often carried out in an outpatient setting on the elderly and has a cure rate that is greater than 95%. Surprisingly, several studies have reported that only 20-25% of individuals with PHP who met criteria for surgery underwent parathyroidectomy. Identifying the barriers that prohibit surgical referral, as well as educating patients and care providers, is critical for PHP patients to receive appropriate surgical management in the future.

Surgical Management of Hyperparathyroidism In 2013: Is There An Ideal Approach?

Dr. Todd McMullen, our visiting speaker, continued with a discussion of the management of PHP.

The true incidence of multigland parathyroid disease (MGD) is central to the surgical management of PHP, and whether a focused or multigland exploration is necessary for cure. A review of 12 studies that described >4000 PHP cases reported MGD was present 11-25% of the time. Preoperatively sestamibi (SPECT-CT) scanning (sensitivity 87-95%, specificity 83-95%) and ultrasound (sensitivity 82-90%, specificity 90-98%) are commonly both performed at most institutions as part of preoperative localization. For imaging recurrent or persistent disease other localization studies may include MRI, CT, PET, and Venous Sampling.



Anatomical location of parathyroid adenomas

There are many different criteria that are used intra-operatively when measuring PTH to allow for a focused procedure. The Miami Criteria, or cure determined by a 50% fall from the highest pre-excision value at 10 minutes post parathyroid removal, is commonly utilized. Large case series have reported approximately 8.5% of parathyroid adenomas may be located at an ectopic site which may include the superior mediastinum, lower mediastinum, intrathymic, retroesophageal, undescended, within the carotid sheath, and intrathyroidal. Despite this observation, less than 1% of parathyroids are not accessible through a cervical incision.

Multiple factors impact the operative approach for parathyroid disease (focused parathyroidectomy versus 4 gland exploration) and must be considered when making surgical decisions and tailoring a surgical approach. These patient and disease factors include: suspicion of multigland disease, patient size/BMI, concern regarding the presence of possible parathyroid carcinoma, and the presence of a goiter or other thyroid disease.

Complications of Thyroid & Parathyroid Surgery: Approach & Treatment

Dr. Nadine Caron, Endocrine Surgeon based out of Prince George Regional Hospital spoke about complications of thyroid and parathyroid surgery.

Postoperative hemorrhage is an uncommon event after thyroid or parathyroid surgery and requires emergent management. Other major complications of concern, though uncommon, include recurrent laryngeal nerve dysfunction (either temporary of permanent) and superior laryngeal nerve dysfunction (either temporary or permanent) that effect vocal cord function and voice. If persistent, referral to an Otolaryngologist with expertise in laryngology/voice is appropriate. Options for management of persistent voice disability include local injection therapy or thyroplasty. The utilization of recurrent laryngeal nerve monitoring to reduce risk of postoperative nerve dysfunction is currently viewed as controversial.

Temporary or permanent hypoparathyroidism is another troublesome complication of thyroid and parathyroid surgery. There are a variety of approaches that have been utilized to treat/follow parathyroid function postoperatively and minimize its morbidity. Measurement of PTH after total thyroidectomy has been shown in many studies to be useful for predicting risk of postoperative hypoparathyroidism, need for supplementation, and appropriateness for early hospital discharge. Current literature suggests operator experience/case volume has a relationship with morbidity for individuals undergoing thyroid and parathyroid operations.

Panel 2: Parathyroid and Adrenal Case Discussions

The afternoon lectures were followed by several parathyroid and adrenal focused case-based panel discussions. Panels were multidisciplinary and members included: Dr. Andy McFadden (Surgical Oncology), Dr. Nadine Caron (Endocrine Surgery), Dr. Noelle Davis (Surgical Oncology), Dr. Todd McMullen (Endocrine Surgery), Dr. Cord Sturgeon (Endocrine Surgery), Dr. Adrienne Melck (Endocrine Surgery), Dr. Ehud Ur (Endocrinology), and Dr. Sam Wiseman (Endocrine Surgery).

Thyroid & Parathyroid Surgery Operative Checklist Project: SON Update

The final session was focused on synoptic reporting of thyroid and parathyroid operations, referred to as operative checklists. Operative checklists improve communication with other health care providers, increase awareness amongst surgeons of elements of the operative procedure that need reporting because they may influence adjuvant treatment and disease prognostication as well as be indicators of quality of care. Such checklists also are important for outcomes data collection. Such checklists have already been developed by other SON tumor groups for breast and colorectal surgery. Dr. Wiseman, St. Paul's Hospital Vancouver, presented the operative checklists that had been developed and piloted by the SON Endocrine Tumor Group. All attendees present at the meeting, including the expert visiting speakers, were solicited for input. The parathyroid and thyroid checklists will next be mailed out to surgeons and multidisciplinary experts province–wide before being finalized and adopted.

Dr. Elaine McKevitt, new Chair of the SON Continuing Professional Development and Knowledge Translation Committee

Dr. Elaine McKevitt

The Surgical Oncology Network is very pleased to announce that Dr. Elaine McKevitt has agreed to serve as the chair of the Surgical Oncology Network Continuing Professional Development and Knowledge Translation committee. Dr. McKevitt, an active and long-time member of the CPD-KT committee, is replacing Dr. Rona Cheifetz in this role.

As member of the SON CPD-KT committee and Breast Surgical Tumour Group, Dr. McKevitt was a Lead on the SON Breast Cancer Synoptic Operative Report initiative. She is also playing an essential planning role in this year's Fall Update and is preparing several exciting case studies to be presented at the event.

Dr. McKevitt is a General Surgeon at Providence Health Care in Vancouver. She did her medical training and general surgery residency in British Columbia. She also holds a Masters degree in Education, UBC. Her practice is focused at Mt St. Joseph Hospital and she is part of the Mount St. Joseph Breast Program and Rapid Access Breast Clinic. SON members and staff are delighted to welcome her to her new position.

Dr. Elaine McKevitt, (L) assisted by Dr. Anne Wachsmuth during a lumpectomy at Mount Saint Joseph Hospital in Vancouver September 22, 2010. Photo courtesy of John Lehmann/ The Globe and Mail

The Bethesda System for Reporting Thyroid Cytopathology

BS Sheffield, B Walker, SM Wiseman

Thyroid nodules are incredibly common in the general population and carry a small but significant risk of malignancy. Fine-needle aspiration biopsy (FNAB) is the best option available to clinicians in determining which nodules are high-risk for malignancy, requiring surgery. Over the past decades, technological advances have led to improved quality of FNAB. These advances are exemplified by the widespread use of ultrasound-guidance as well as the advent of liquid-based cytology fixative (reducing the number of obscuring artifacts for the pathologist). Currently, FNAB can arrive at a definitive conclusion (either benign or malignant) for about two thirds of all thyroid nodules.

Fine-needle aspirates diagnosed as either benign or malignant are incredibly reproducible and accurate. The remaining third of all FNABs comprise a heterogeneous group of entities, problematic for both clinicians and pathologists, the so-called 'indeterminate' nodules. These lesions may be diagnosed with a highly variable terminology, and carry a spectrum of risk, ranging from very close to benign, to almost certain (but not diagnostic of) malignancy.

Looking forward, molecular studies will likely be able to parse out nodules with indeterminate cytology, and effectively triage those with a high cancer risk towards surgical management. Currently accurate molecular diagnostic tests are costly and limited to research use. While we await the next technological advance to facilitate a breakthrough in the efficacy of FNAB, we must do the best with what we have.

The terminology used to diagnose indeterminate lesions tends to be varied, which can be confusing and lead to suboptimal patient management.

Previous surveys have clearly demonstrated that the thoughts of the pathologist are poorly translated into the actions of surgeons through thyroid cytopathology reports. The Bethesda system for reporting thyroid cytopathology provides a framework of diagnostic terminology for thyroid FNAB, dividing lesions into 6 categories, and ascribing each category a risk of malignancy and a recommended clinical action. The system is specifically designed to standardize, and thereby reduce miscommunication in, thyroid cytology reporting.

The benefits of such a system are many, and span from clinical care to basic research. For the surgical oncologist, patients are triaged into tiers, each with a unique and reproducible cancer risk, fitted to an appropriate treatment algorithm. For the clinician, variable terminology is removed, creating a clear-cut decision as to which patients need surgical referral, versus re-biopsy and monitoring versus clinical follow-up. For the pathologist, this system greatly reduces the ambiguity associated with communicating uncertainty, fostering an environment where diagnostic uncertainty is acceptable and linked to a predefined management strategy. Not to be overlooked are the benefits to thyroid cancer research, the groups created by the Bethesda system are reproducible in multiple centres, standardizing many aspects of the study of thyroid cancer. Furthermore, the diagnostic value of ancillary molecular studies is greatly aided by a standardized cytopathology nomenclature.

A similar cytopathology nomenclature, the Bethesda system for reporting cervical cytology was introduced over a decade ago, and is now virtually a gold standard, and used in the diagnostic terminology for all cervical smears interpreted in the province of British Columbia. It has been 7 years since the National Cancer Institute revealed its analogous thyroid cytopathology nomenclature, but in 2014 the terminology is found in only a minority of reports. Possible reasons for this may include conservatism of pathologists and surgeons unwilling to embrace change, a lack of information regarding the benefits of standardized nomenclature, a lack of awareness of the confusion caused by ambiguous terminology, or incredulity surrounding the cancer risks published along with the Bethesda system descriptions.

Recently our group completed a review and meta-analysis of the Bethesda system for reporting thyroid cytopathology. We searched the medical literature for published experiences using the system, extracted the raw data, and compared their pooled experience to the cancer risks published with the system. We found that the Bethesda system, and its associated cancer risks, were highly reproducible in a variety of medical centres located around the globe. The Bethesda system was implemented at St. Paul's Hospital in 2010 and has been widely accepted by the cytopathology staff as well as the dedicated endocrine surgery group. A preliminary validation of the implementation of the Bethesda system at St. Paul's Hospital has, again, confirmed that this set of diagnostic terminology can be reliably and reproducibly associated with stratified risks of malignancy.

Problems with the system do exist, and critical reports are numerous in the literature. Most concerns are controversies regarding the reflex management of some of the indeterminate categories. Others focus on where the boundaries have been drawn separating one risk group from the next. Regardless, it seems clear that despite minor details that should be worked out with time, large-scale validations of the system such as the one recently performed by our group have demonstrated the systems robustness.

Ultimately, the Bethesda system for reporting thyroid cytopathology represents a major advance in the diagnosis, treatment, and understanding of thyroid nodules. The use of this system simply requires trading in bulky and awkward verbiage for a streamlined set of diagnostic terminology. It is now the time for additional centres in British Columbia to consider adopting the Bethesda system– a cheap and simple intervention to improve patient care, easily implemented at any hospital laboratory.

Selected References:

1. Sheffield BS, Madoudi H, et al. Preoperative diagnosis of thyroid nodules using the Bethesda system for reporting thyroid cytopathology: a comprehensive review and meta-analysis. Expert Rev Endocrinol Metab. 2014; Early online, 1-14 10.1586/17446651.2014.887435.

2. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009; 19(11): 1159-65.

Commentary on "Current Thyroid Cancer Trends in the United States"

recently published by Davies and Welch in the Journal of the American Medical Association

Eitan Prisman MD MA FRCSC

Davies and Welch compare the incidence of thyroid cancer in 2009 versus 1975, and report a near 3 and 2.2 fold increase in the incidence of thyroid cancer in women and men respectively, the vast majority (87%) of which are less then 2 cm in size. Despite this increase, the mortality rate has remained stable and therefore they propose an epidemic of over diagnosis rather then an epidemic of disease and suggest a de-escalation in treatment and potentially an active surveillance tract. (1)

While mortality has remained stable, it is not the only variable indicative of carrying the burden of the disease, and other variables, such as disease free survival and recurrence, may reveal a positive relationship with the increased incidence. Nevertheless, there has been a striking increase in the rate of incidental findings of papillary carcinoma that otherwise may not have surfaced clinically. This is in keeping with reports of papillary carcinoma on autopsy ranging from 0.5 – 5.2%. The data acquisition for this publication is limited to the SEER database and therefore data regarding how these carcinomas were truly detected is lacking.

The authors reference the active surveillance experience in Japan,(2) and discuss the growing body of literature supporting active surveillance in the prostate arena. In the study by *Ito et. al*, they carefully restrict the surveillance cohort to sub centimeter, well differentiated thyroid cancer that are in a favorable anatomic location. Of the 340 patients in the observational cohort, 15.9% had their primary tumor increase by more then 3mm, and 3.3% had novel nodal metastases at 10 year follow up. However, there were no variables predictive of tumor progression or development of nodal metastases in this cohort. In contrast, in the prostate arena, the Gleason scoring system combined with prostate specific antigen levels, provides a more sensitive risk stratification process that can more accurately predict aggressive malignancies and those more likely to metastasize. In thyroid cancer, this type of histologic scoring and blood test is still outstanding.

While ultrasonographic characterizations of papillary thyroid carcinoma nodules are easily measurable and reproducible, the sizes of these lesions have inconsistently been associated with the presence of occult lymph node disease and disease free survival. Molecular markers, such as BRAF mutations, are not yet predictive of disease progression.(3) Certainly routine thyroid ultrasonography as a screening investigation

should be discouraged, however palpable thyroid nodules should be investigated according to the American Thyroid Association guidelines. Until a biologic marker is developed to better predict aggressive disease, even in an incidentally found thyroid papillary carcinoma, it will be difficult for patients to consider active surveillance with a lack of information predicting their true risk of progression and metastases.

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Breast Cancer Risk Reduction in High Risk Patients

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Women with a diagnosis of atypical breast cell proliferation, such as atypical ductal and lobular hyperplasia, in-situ disease, or hereditary gene mutations (BRCA 1 and 2), or invasive breast cancers and breast cancer recurrences all face the prospect of an increased future risk of breast cancer. Most are interested in advice regarding what they can do to reduce their risk.

The Surgical Oncology Breast Program at the BCCA Vancouver Centre sees an average of 500 new patients annually, the majority of whom have biopsy proven breast cancer or are at high risk for developing breast cancer. Along with definitive surgical intervention, the program focuses on risk reduction for both primary and recurrent breast cancer through lifestyle modifications and chemoprevention.

Based on the literature, risk reduction recommendations for both primary and recurrent breast cancer are mostly consistent and focus on body weight, diet, exercise, alcohol consumption, smoking and hormone therapy. While evidence related to modifiable lifestyle factors has not always shown a clear relationship to breast cancer prevention and / or recurrence, they are important in chronic disease risk reduction and management. The recommendations and rationale for each address the global health of women. Surgeons who provide care to these women, may find the following information useful as a basis for counseling their patients.

BODY WEIGHT

Maintain a healthy body weight with a BMI under 25, and waist circumference less than 88 cm (35 inches).

Overweight (BMI 25 to 29) and obese (BMI 30 and over) women are at higher risk of developing breast cancer after menopause and having a recurrence. According to a prospective study by the American Cancer Society of 900,000 men and women published in 2003, being overweight can increase your risk of cancer death in multiple sites, including breast cancer by up to 50% (1). This study followed 900,000 initially cancer free men and women for 16 years and found that those with a BMI of 40 or more had increased death rates of cancer by 52% in men and 62% in women over normal weight men and women.

This study was the first to be touted as a definitive link between obesity and cancer risk. Specific to breast and other cancers of the female reproductive system, an increase in body fat increases blood levels of estrogen and insulin which can stimulate cancer cell growth. In terms of breast cancer recurrence, there have been over 50 studies examining the relationship of body weight and breast cancer prognosis. A meta analysis of 45 studies prior to 2005 demonstrated that women who are obese at diagnosis have a 30% increased risk of breast cancer related and overall mortality compared to leaner women (2). Other studies have not shown a consistent relationship between weight gain and breast cancer outcomes, though some have shown an increased risk of recurrence in women who gained weight after diagnosis of early breast cancer.

DIET

Limit fat intake to less than 20 to 30% of total calories i.e. 35 to 45 gms (based on a 1,600 to 2,000 calorie diet) and choose lower fat options whenever possible.

Many studies have looked at the link to diet and breast cancer focusing on dietary fat, intake of fruits and vegetables and meat. The results to date are conflicting. Most studies have found that breast cancer is less common in countries where diets are typically low in total fat. Fat is calorie dense and high intakes are linked to obesity, which is a risk for breast cancer. To date there are only two large randomized controlled trials (RCT) that have assessed the impact of dietary modification on disease free and overall survival in women diagnosed with early stage breast cancer.

The WIN study, which followed 2,437 post menopausal women from 1994 to 2001, was the first large scale trial to show that diet can improve breast cancer outcomes in early stage breast cancer. After a median of five years follow up, women randomized to the lower dietary fat group that led to a 6 pound weight loss, had a 24% overall risk reduction (RR) in breast cancer recurrence over the control group. Of note, this study found a 42% RR in women with estrogen negative breast cancer, and a 15% RR in women with estrogen positive breast cancers (3).

The WHEL study randomized 3,088 women to a low fat diet with increased fruit and vegetables. This cohort did not lose weight, and results showed no difference in the rates of recurrence between the intervention and the control groups (4).

PHYSICAL ACTIVITY

To reduce risk of breast cancer, moderate to vigorous exercise for 4 to 7 hours weekly is recommended. To reduce risk of recurrence, exercise 3 to 5 hours weekly.

Exercise may lower a woman's risk of breast cancer by reducing insulin growth factor which can stimulate cell growth. Exercise also reduces circulating estrogen which is produced and stored in body fat, especially in the abdominal area of post menopausal women. Approximately 80%

of breast cancers are estrogen sensitive. Results from the Nurses Health Study (NHS) in 2008 showed that vigorous exercise, defined as brisk walking (3 to 4 mph) for a weekly total of 7 hours was associated with a 20 % reduced incidence of breast cancer in post menopausal women (5).

Observational data also suggest that physical activity may yield beneficial effects on breast cancer outcomes. The NHS looked at 2,987 women with Stage 1 to 3 breast cancers diagnosed between 1984 and 1998. In an 8 year follow up, risk of recurrence and death from breast cancer was reduced 19% in those who walked (2 to 3 mph) or did similar exercise for 1 to 3 hours weekly, 54% in those who did 3 to5 hours weekly and 29% who did more than 5 hours weekly (6).

In terms of premenopausal women, the NHS11 examined physical activity in 64,777 females ages 12 to 35 and found a 23% reduction in risk for pre menopausal breast cancer in those who exercised vigorously (running) on average 3.5 hours weekly or walking 13 hours weekly in their adolescence compared to inactive women. Higher levels of activity between the ages of 12 and 22 contributed most strongly to this reduction (7).

ALCOHOL

For women who consume alcohol, the current recommendation for primary prevention is to consume 1 or less alcoholic beverages daily. For prevention of recurrence, consume no more than 3 to 4 alcoholic beverages weekly.

There is strong evidence that alcohol consumption is a risk for breast cancer. Based on an analysis of over 180,000 women in the NIH-AARP Diet and Health Study, women who consumed 3 or more alcoholic beverages a day had more than a 50% (from 1% to 1.5%) increase risk of hormone sensitive breast cancers (8). A large prospective study of 1,897 women in the LACE study found that alcohol intake of 3 to 4 drinks weekly increased risk of recurrence by 30%, particularly in post menopausal and obese women (9).

SMOKING

While there is limited evidence that smoking tobacco causes breast cancer, smoking is a risk factor for many chronic diseases. There is some data to support a link to increased risk of breast cancer in smokers.

In 13 years of follow up of 73,388 women in the American Cancer Society Prevention Study, the rate of new breast cancers was increased by 24% in smokers and 13% in former smokers compared to non smokers. Women who started smoking before menarche had a 61% increased risk, and women who started smoking after menarche and 11 years before their first child had a 45% increased risk over non smokers. Within 10 years of quitting smoking, risk for breast cancer goes back to a non smoker level (10). In terms of second hand smoke as a risk factor, research continues on the link between heavy second hand smoke exposure and postmenopausal breast cancer.

HORMONE THERAPY

The current North American Menopause Society Guidelines recommend taking combined estrogen and progesterone for no longer than 3 to 5 years, or estrogen alone for no longer than 7 years (11).

In the WHI randomized placebo-controlled trial of 16,608 women, combined hormone therapy increased invasive breast cancer incidence (395 vs 285) of all tumour sub types, and more often involved lymph nodes (81 vs 43) according to an 11 year follow up. There were more deaths attributed to breast cancer (2.6 vs 1.3) and all causes following a diagnosis of breast cancer (5.3 vs 3.4 per 10,000 women) (12).

Long term use of hormone therapy (HT) in women over 60 is associated with increased risk compared to women age 50 to 59. In a prospective review of 60,000 post menopausal women in the NHS from 1980 to 2008, researchers found an increase in breast cancer incidence of 88% in women who took combined therapy for 10 to 15 years compared to non users. The risk doubled if taken for 15 to 20 years. Estrogen use alone for 10 to 15 years resulted in a 22% increase in risk and 43% increase if taken 15 to 20 years. This study also found that the risk did not plateau and continued to increase with duration of use (13).

CHEMOPREVENTION

Women at high risk for breast cancer, including strong family history, previous diagnosis of a pre-malignant lesion and breast density on mammogram, may want to consider taking Tamoxifen or an alternative medication for 5 years to reduce their risk.

The SERM drugs Tamoxifen and Raloxifene are currently offered. The NSABP Breast Cancer Prevention Trial (P-1) randomized 13,388 to Tamoxifen or placebo for 69 months from 1992 to 1998. The results showed an overall 50 % decreased risk for both invasive and non invasive cancer and a 69% decrease in estrogen sensitive breast cancers (14). The 1999 to 2006 NSABP STAR Trial (P-2) randomized 19,747 post menopausal women to Tamoxifen or Raloxifene for 5 years.

A follow up analysis compared the initial results at 5 years to 81 months and found that the risk ratio (RR) widened for invasive, and narrowed for noninvasive cancer at 81 months. Raloxifene retained 76% of the effectiveness of Tamoxifen in preventing invasive disease which represents a 38% reduction compared to the untreated group. Raloxifene was 78% as effective as Tamoxifen over time in preventing noninvasive disease with less toxicity in terms of risk of developing endometrial cancer (0.55 vs 0.83) and thromboembolitic events (0.75 vs 0.93). There were no significant differences in mortality (15).

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New Orthotumor Website

WWW.ORTHOTUMOURS.CA

Dr. Paul Clarkson, Orthopaedic Oncology Surgeon and Chair of the Musculokeletal Tumour Group at the BC Cancer Agency has spearheaded the development of a new website, www.orthotumours.ca.

The website provides information and practice cases about musculoskeletal oncology for medical students, orthopaedic residents and family physicians. Bone and soft tissue tumours are very challenging malignancies, and this website is designed to help non-specialists understand these tumours better.

"The website encourages multidisciplinary management to improve patient outcomes" states Dr. Paul Clarkson.

The website was developed in partnership with numerous colleagues and collaborators including an orthopaedic oncologist, a multidisciplinary specialist and fellows, residents, students and many others. The project was in the works for 18 months and was launched in mid-2013

"This was truly a collaborative project. The content was developed and reviewed by many different experts in the field" said Clarkson. "Each of the collaborators generously donated their time to the project, while the user friendly design and production was funded by a generous grant from the Teaching and Learning Enhancement Fund (TLEF) through the University of British Columbia".

While there are many other excellent websites with sarcoma information, this website focuses on case presentations and an interactive format. The website aims to educate visitors regarding basic science, epidemiology, pathology, and management of musculoskeletal tumours. It offers comprehensive case studies which feature differential diagnostic screens as well as links to relevant information.

While the website is not intended to be a how-to guide for individual patients, it does contain patient-appropriate information that physicians can use for patient-education purposes. Students can complete a short test which will provide them with a certificate of completion.

It is envisaged that more cases of varying levels of complexity will be added over time, to make the website useful for surgical residents preparing for exams. The website is already proving popular and providing high quality information to the community.

On the SON website in the Fall of 2014: HIPEC Lecture

Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis

The SON will be video-recording a lecture by VGH Surgical Oncologist Dr. Yarrow McConnell and making it accessible through the SON website by November 2014 for educational purposes. The title of Dr. McConnell's lecture will be: *Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis.*

The cytoreductive surgery/HIPEC procedure is new to British Columbia. Prior to Dr. McConnell establishing the Peritoneal Malignancy program in the last year, patients had to travel to Alberta or US for the procedure. The one hour lecture is expected to provide a balanced review of the procedure including patient selection, outcomes, surgical videos, and patient referral process in BC.

This project is consistent with the SON's vision to ensure the best possible outcomes for all cancer surgery patients in British Columbia. The primary target audience includes SON members - all providers of surgical oncology services from surgeons in remote areas to sub-specialists - as well as other medical professionals including gastroenterologists and community surgeons, community oncologists and medical oncologists.

The SON thanks Sanofi for supporting this video project through an educational grant.

SURGICAL ONCOLOGY NETWORK NEWS

SON Resident Travel Award for BC Surgery Residents/Fellows and Medical Students

This is a competitive award intended to motivate physicians and medical students early in their training, to pursue an interest in surgical oncology and to allow them to present research findings at conferences. Approved applications may be funded up to a maximum of $1000. Forms and guidelines are available online at www.bccancer.bc.ca/son.

2014 Recipients:

- **Dr. Leah Jutzi, Gynecologic Oncology of Canada 35th Annual Meeting, June 13, 2014, Niagara Falls, Ontario**
  The Role of Palliative Colorectal Stents in Gynecologic Malignancy
- **Dr. Magdalena Recsky, Tripartite Colorectal Meeting, June 30 – July 3, 2014, Brimingham UK**
  Comparing Outcomes of TEM vs. TME for Treatment of Stage T1 Rectal Cancer

SON/UBC Summer Student Research Program

The SON/UBC Summer Student Research Program provides undergraduate students with an opportunity to explore their interest in medical research by undertaking a project over the summer under the supervision of a principal investigator with an appointment in the Faculty of Medicine. For more information and to apply please visit http://med.ubc.ca/research/md_undergrad/funding/summer-student-research-program

2014 Recipient:

- **Golden Gao. Supervisor: Dr. Peter Lennox**
  Project Title: Post-mastectomy irradiation in two-stage tissue expander/implant immediate breast reconstruction with acellular dermal matrix (ADM).

SURGICAL ONCOLOGY NETWORK NEWSLETTER

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VISIT THE SURGICAL ONCOLOGY WEBSITE
www.bccancer.bc.ca/son

The BC Surgical Oncology 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 the BC Cancer Agency.

The Council Executive oversees the implementation of the Network's mandate and is comprised of surgeons and senior health administrators representing all the health regions across the province. The three committees - Clinical Practice, Continuing Professional Development & Knowledge Transfer and Research & Outcomes Evaluation-assist with the planning, implementation and promotion of the Network's goals and priorities. The thirteen Surgical Tumour Groups advise on the issues and challenges in the surgical management of patients within each tumour site to improve the surgical management of cancer patients.

Recent Publications

The role of palliative colorectal stents in gynaecologic malignancy
Jutzi L, Russell D, Ho S, Kwon JS.
Gynecologic Oncology, 2014. In Press.

Influence of nurse navigation on wait times for breast cancer care in a Canadian regional cancer center
Baliski C, McGahan CE, Liberto CM, Broughton S, Ellard S, Taylor M, Bates J, Lai A.
Am J Surg. 2014 May;207(5):686-91; discussion 691-2.

The Significance of Combination Chemotherapy in Epithelial Ovarian Cancer
Kwon JS, McGahan C, Dehaeck U, Santos J, Swenerton K, Carey MS.
Int J Gynecol Cancer. 2014 Feb;24(2):226-32.

Upcoming Conferences

2014 Canadian Surgery Forum, Vancouver, BC, Fairmont Waterfront Hotel
September 17-21, 2014, http://www.cags-accg.ca

European Society for Medical Oncology, Madrid Spain, IFEMA – Feria de Madrid
September 26–30, 2014, http://www.esmo.org/Conferences/ESMO-2014-Congress

Surgical Oncology Network Breast Cancer Fall Update, Vancouver, BC, Four Seasons Hotel
October 18, 2014, http://www.bccancer.bc.ca/HPI/SON

18th SIS World Congress on Breast Healthcare, Orlando Florida, Walt Disney World Swan Hotel
October 16-19 2014, http://www2.kenes.com/sis/info/Pages/GeneralInformation.aspx

American College of Surgeons Clinical Congress, San Francisco, CA
October 26-30 2014, http://www.facs.org/clincon2014/index.html

European Society of Surgical Oncology (ESSO), Arena and Convention Centre Liverpool (ACC Liverpool)
Oct 29-31 2014, http://www.ecco-org.eu/ESSO34

North Pacific Surgical Association (NPSA), Seattle, WA
Nov 14-15, 2014, http://www.nopacsurg.org/

SSO Annual Cancer Symposium, Houston, Texas, George R. Brown Convention Center
March 25-28, 2015 http://www.surgonc.org

BC Surgical Society Annual Spring Meeting, Whistler, BC
April 30-May 2, 2015, http://bcss.ca/

American Society of Clinical Oncology, Chicago, IL, USA, McCormick Place
May 29–June 2, 2015, http://am.asco.org/

Saturday – October 18, 2014, Vancouver, BC

SON Breast Cancer Update: Current Controversies 2014

The BC Cancer Agency's Surgical Oncology Network invites you to take part in its 2014 Annual Fall Update at the Vancouver Four Seasons Hotel. This year's event will focus on Breast Cancer: Current Controversies. This event is an Accredited Group Learning Activity eligible for up to 7.25 Section 1 credits as defined by the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada. This program has been reviewed and approved by UBC Division of Continuing Professional Development.

This one day conference features topics on surgical techniques, breast cancer pathology, quality indicators, adjuvant therapy, imaging, radiation and reconstruction that relate to breast cancer. The event will be chaired by Dr. Laurence Turner (Chair, SON Breast Surgical Tumour Group) and is a must-attend for surgical oncologists, general surgeons, plastic surgeons, medical oncologists, radiation oncologists, residents and other related specialists. Accreditation for this event is currently being applied for by the Royal College of Physicians and Surgeons of Canada and by the UBC Division of Continuing Professional Development.

Time	Topic	Speaker
7:30 - 8:00 am	*Registration and Continental Breakfast*	
8:00 - 8:05 am	Welcome and Introduction	Dr. Laurence Turner
SESSION 1	**BIOLOGY AND PATHOLOGY OF BREAST CANCER Moderator: Dr. Laurence Turner**	
8:05 - 8:25 am	The genetic and biological basis of breast malignancy (including DCIS) – a basic primer for surgeons	Dr. Sam Aparicio
8:25 - 8:45 am	The pathological basis of breast malignancy and its subtypes (including DCIS) - a basic primer for surgeons.	Dr. Malcolm Hayes
8:45 - 9:05 am	Margins – oncological and practical considerations	Dr. Rebecca Warburton
9:05 - 10:05 am	Panel discussion: Do we need to change our guidelines? Moderator: Dr. Chris Baliski	Dr. J.F. Boileau. Dr. Malcolm Hayes, Dr. Scott Tyldesley, Dr. Rebecca Warburton, Dr. Frances Wright
10:05 -10:30 am	Coffee Break	
SESSION 2	**BREAST CANCER QUALITY OF CARE Moderator: Dr. Rebecca Nelson**	
10:30 –11:00 am	From Screening to Diagnostics: Some of the Controversies	Dr. Christine Wilson
11:00 – 11:30 am	Let's get it right: Quality in Breast Cancer Care	Dr. Elaine McKevitt and Dr. Michelle Goecke
11:30 - 12:00 pm	Reconstruction: State of the Art	Dr. Sheina Macadam
12:00 – 12:30 pm	Case Discussions. Moderated by Dr. Rebecca Nelson, case presentations by Dr. Elaine McKevitt	Dr. J.F. Boileau, Dr. Michelle Goecke, Dr. Sheina Macadam, Dr. Christine Wilson, Dr. Frances Wright
12:30 - 1:30 pm	Networking Lunch	
SESSION 3	**PRACTICAL ISSUES Moderator: Dr. Elaine McKevitt**	
1:30 - 2:00 pm	Surgical management of the axilla	Dr. J.F. Boileau
2:00 - 2:30 pm	Guidelines for neoadjuvant therapy	Dr. Christine Simmons
2:30 - 3:00 pm	Surgical management in the setting of neoadjuvant therapy	Dr. Frances Wright
3:00 – 3:30 pm	Who should we radiate and why?	Dr. Lorna Weir
3:30 - 3:45 pm	Coffee Break	
3:45 - 4:45 pm	Case Discussions Panel Chairs: Dr. Chris Baliski and Dr. Rebecca Warburton	Dr. J.F. Boileau, Dr. Christine Simmons, Dr. Frances Wright, Dr. Lorna Weir
4:45 - 5:00 pm	Course Evaluation/ Wrap Up	Dr. Laurence Turner

Early-bird registration is $300 for those who register before October 3, and $325 for those who register by the October 10, 2014 deadline. There is a special $75 registration rate for residents. Special accommodation rates are available at the Four Seasons Hotel, 791 W Georgia, Vancouver, tel. 604-689-9333, please use confirmation code **CI1014BCCA** when you register.

For more information or to register contact Chrystal Palaty at Chrystal.Palaty@bccancer.bc.ca, tel. 604-877-6000 ext. 673269 or visit our website, www.bccancer.bc.ca/HPI/SON.

Surgical Oncology Network