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Surgical Oncology Network Newsletter

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Surgical Oncology Network

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MARK YOUR CALENDARS!

SON FALL UPDATE ON COLORECTAL CANCERS

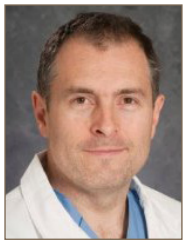
October 14, 2017
Four Seasons Hotel
Vancouver

HIGHLIGHTS FROM THE SON FALL UPDATE 2016

MANAGEMENT OF LIVER, PANCREAS, MELANOMA AND BREAST CANCERS

On October 22th of last year, the Surgical Oncology Network (SON), hosted the annual Fall Update on Surgical Oncology at the Four Seasons Hotel in downtown Vancouver. The day was focused on the management of Liver, Pancreas, Melanoma and Breast Cancers. It brought together surgeons and residents from across British Columbia. Presentations from the event are viewable on the Surgical Oncology Network website.

LEFT TO RIGHT: DR. CHRIS BALISKI, DR. ELAINE MCKEVITT, DR. GREG MCKINNON, DR. ALICE WEI, AND DR. SHAWN MACKENZIE



Management of Liver and Pancreas Cancers

Dr. Shawn MacKenzie, Hepato-Pancreatico-Biliary Surgeon , Royal Columbian Hospital

The morning session focused on liver and pancreas malignancies, with our keynote speaker, Dr. Alice Wei (Hepato-Pancreatico-Biliary Surgeon, Toronto General Hospital, Toronto), gave an excellent presentation reviewing the identification, workup and management of hepatic lesions. Dr. Wei covered the spectrum of liver lesions from benign lesions

Continued from Page 1

to primary hepatic malignancies - cholangiocarcinoma and hepatocellular carcinoma. Her presentation covering a large topic was both engaging and practical for the surgeons in attendance. Dr. Wei emphasized the team approach to the workup and management of liver tumours with early referral to a Hepatobiliary surgeon and discussion of the patient case at a multidisciplinary tumour conference for individual patient treatment planning. Dr. Wei also reviewed her work as the lead of quality and knowledge transfer for the Surgical Oncology Program at Cancer Care Ontario, and how regionalization of complex cancer is changing the surgical landscape in Ontario.

Conclusions:

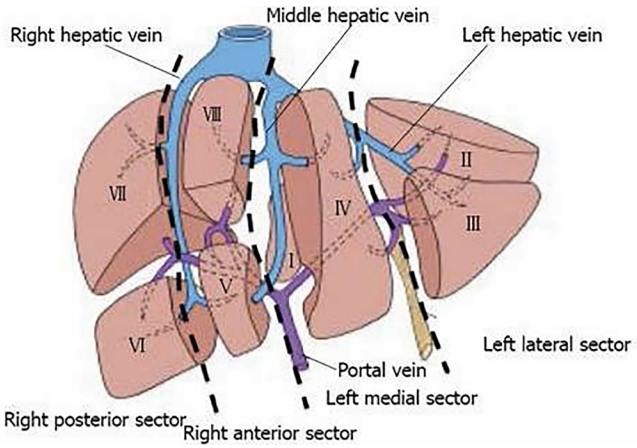
- **Liver masses are commonly identified**
- **Imaging usually distinguishes between benign/ malignant masses**
- **Selective biopsy for indeterminant lesions or when tissue is required for treatment**
- **Liver resection should be performed at an experienced centre**

Dr. Maja Segedi (transplant surgeon, Vancouver General Hospital) then reviewed the current management of colorectal liver metastases. She reviewed the change in practice related to resection of colorectal metastasis over the past two decades after the publication of the Fong Score in 1999. Dr. Fong identified increased recurrence of colorectal metastasis with:

1. **Node positive colorectal primary,**
2. **Disease free interval to identification of liver metastasis less than 1 year,**
3. **More than one hepatic tumour,**
4. **The largest hepatic lesion greater than 5 cm, and**
5. **A CEA level greater than 200 ng/ml.**

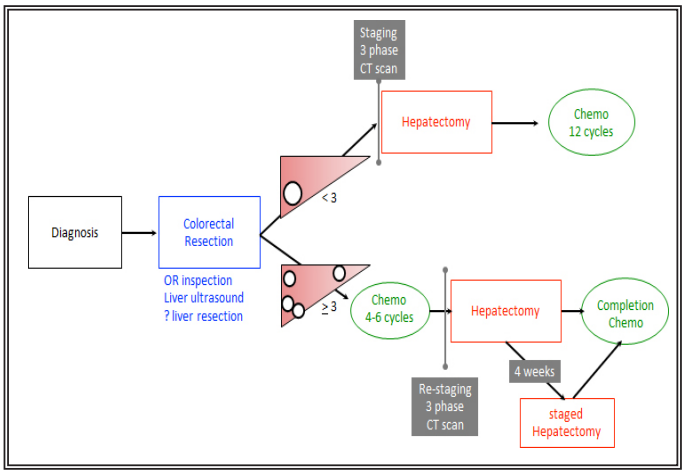
The Fong score was used to select patients as candidates for surgical resection of their liver metastases. With the advent of improved chemotherapy, new non-surgical liver directed therapies, and a more aggressive surgical approach, patient selection for treatment of colorectal liver metastases has broadened. Surgical treatment is now based on anatomy of the liver and the position of the tumours within the liver.

The liver surgeon must be able to remove the liver metastases with a negative margin, and preserve both in flow and drainage to at least two segments of liver, with a liver remnant greater that 30% of the original size. The biology of the tumour and the tumour's response to systemic chemotherapy, may be the most important factor in determining a patient's selection for hepatic resection. Systemic chemotherapy and surgical resection synergy again highlights the need for a multidisciplinary treatment plan for hepatic metastases in the setting of colorectal cancer.



Nomenclature for describing hepatic resectional surgery based on liver segmental and sectorial anatomy

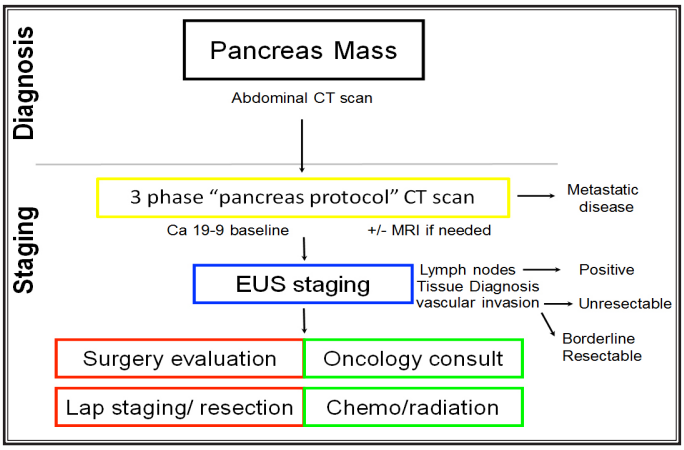
Dr. Shawn MacKenzie (Hepato-Pancreatico-Biliary Surgeon, Royal Columbian Hospital) led case presentations of liver malignancies, with the panel discussion focusing on a practical approach for the presented patient scenarios. The fluid panel discussion, with engaged audience participation, revealed the controversies and real life difficulties in diagnosing and managing liver lesions. The presentations were tailored to a practical approach for the community general surgeon. The panel was comprised of Dr. Wei, Dr. Segedi, and we welcomed Dr. Dan Renouf (B.C. Cancer Agency, Vancouver) to the stage for the panel discussion, where he provided the medical oncology perspective.



Management algorithm for colorectal cancer metastasis

After a short morning break, Dr. Wei presented a practical approach to the workup of the pancreas mass, focusing on the diagnosis and management of pancreas adenocarcinoma. She reviewed the workup for the incidentally discovered pancreatic mass and/or painless jaundice with a pancreas

specific protocolled CT scan and an endoscopic ultrasound +/- ERCP with stenting for control of biliary obstruction. She discussed resectability of pancreatic cancer and clarified borderline and unresectable tumours.



WORK UP OF PANCREATIC MASS

Afterwards, Dr. MacKenzie presented a series of pancreas case presentations to the panel of Dr. Wei, Dr. Segedi, and Dr. Renouf, who provided a robust discussion on the management of pancreatic cancers.

Management of Melanoma

Dr. Chris Baliski, Chair SON and SON Melanoma Surgical Tumour Group

We were very fortunate to have one of the opinion leaders in the field of melanoma surgery, Dr. Greg McKinnon (Surgical Oncologist, Calgary), as one of the two invited speakers at this year's meeting. Dr. McKinnon's presentation focused on three areas pertaining to the use of sentinel lymph node biopsy (SLNB) in patients with melanoma, and the future of systemic treatment. The questions he addressed were:

1. WHAT ARE THE BENEFITS AND INDICATIONS FOR SLNB?
2. IS A COMPLETION LYMPH NODE DISSECTION NECESSARY AFTER A POSITIVE SLNB?
3. WHAT IS THE ROLE OF NEWER IMMUNOMODULATORS, AND HOW WILL THIS INFLUENCE SURGICAL MANAGEMENT?

Currently the NCCN guidelines suggest that SLNB be "discussed and offered" in all patients with melanomas greater than one millimeter thickness. These same guidelines also state that it "may be considered" in patients with thin melanomas (0.76 - 1.0 mm) with "high risk features" (ulcerated, greater than one mitosis per mm2, and LVI).

Further review was then presented about the evidence for this later suggestion in thin melanoma. The background manual utilized for the NCCN guideline, identified that SLN pathological positivity (ppSLN) is influenced by depth of melanoma, with ppSLN's in 2.9% of those with melanomas less than 0.75 mm, while 7.1% of deeper melanomas (0.75 - 1.0 mm) were ppSLN's. There is some concern though, that this may not be broadly generalizable, as there would be selection bias in patients chosen for SLNB in these studies.

Further discussion occurred about whether there would be any "high risk" factors that would predict a higher risk of ppSLN's. The depth of the primary and presence of ulceration were shown in multivariate analysis to influence ppSLN's. The influence of mitotic rate is controversial, with presentation of one study showing no correlation with pathologically involved SLN's. This contradicted at least one other study which suggests that mitotic features may be predictive of SLN status. Ultimately Dr. McKinnon concluded that the indications for SLNB in thin melanomas are questionable, and should be the exception rather than the rule.

What about patients with thick melanomas? This is also controversial, with some suggesting the chance of systemic disease is quite high in these patients, and the results of the SLNB being unlikely to influence outcome. Others suggest that SLNB provides valuable prognostic information that may be beneficial to the patient. He then reviewed subgroup information from MSLT-I, which is a seminal trial of patients with melanoma, randomized to SLNB vs observation. This study showed no difference in overall survival, nor melanoma specific survival, thus questioning the therapeutic benefits.

Although a five percent greater survival was found in those undergoing SLNB, it did not reach statistical significance and was not powered to distinguish a difference. It has been suggested that there is therapeutic value to SLNB, improving loco-regional control. Dr. McKinnon presented a hypothetical scenario based on patients in MSLT-I that suggested that locoregional control would likely be a benefit in only one in a hundred patients with thick melanomas, further questioning the value. It was acknowledged that more aggressive treatment may ultimately be required in these patients in the form of repeat lymph node dissections, or the use of adjuvant XRT, which would not necessarily be the case in those undergoing SLNB.

A brief discussion of the use of SLNB in patients with intermediate thickness melanomas also occurred. It is likely a benefit in these patients, as those with ppSLN's have a better survival rate than those in the observation group eventually developing clinically positive lymph nodes.

This is also controversial as well, with no overall survival benefit in those undergoing SLNB, only in those in the subgroup analysis. He suggested that SLNB in intermediate thickness melanomas is highly prognostic, may improve regional control and survival, and help guide early adjuvant treatment.

Recommendations for SLNB in melanoma

- **< 1mm thick melanoma:** rarely requires SLNB
- **1-4mm:** prognostic, improves regional control, helps avoid CLND, allows adjuvant therapy, and may improve survival
- **> 4mm:** improved regional control, and potential avoidance of radical surgery and radiation

An area of ongoing study is the need for completion lymph node dissection (CLND) in patients with a ppSLNB. While this has traditionally been the preferred management, this is not necessarily practiced. In Alberta, CLND is common after a ppSLN is identified, which is not always the case elsewhere. There are concerns regarding the morbidity of the procedure, and that only a minority of patients will have further lymph nodes with pathological involvement (15%), suggesting the number of patients benefitting is low. While we are awaiting results from a seminal trial (MSLT-2) comparing observation vs CLND in patients with ppSLN's, a similar study has also been performed in Germany. The DeCOG-SLT accrued a similar patient cohort. In this study, patients were followed with serial physical exams, ultrasound surveillance, along with CT, MRI, or PET-CT. At a median follow-up of 35 months, there appears to be no difference in overall survival, disease specific survival, or recurrence outside of loco-regional control. In those without CLND only seven percent have recurred in the absence of systemic disease (3% in CLND), suggesting a low overall impact on loco-regional control.

Conclusions for CLND:

- Completion node dissection is no longer mandatory
- If no CLND, patient should be followed closely for nodal recurrence
- SNB alone provides good regional control

A review of the potential impact of new novel directed treatments (BRAF inhibitors) and immunomodulators (PD-1 and CTLA-4 inhibitors) was also reviewed. These have been found to improve survival in the metastatic setting. There are also a number of trials of adjuvant treatment currently occurring, with anticipated completion dates between 2018 to 2023. One completed trial (EORTC18071) using adjuvant Ipilimumab, revealed an 11% absolute five year survival rate. These research results suggest a new age in the treatment of melanoma, which is likely to have an impact on the clinical care of melanoma patients.

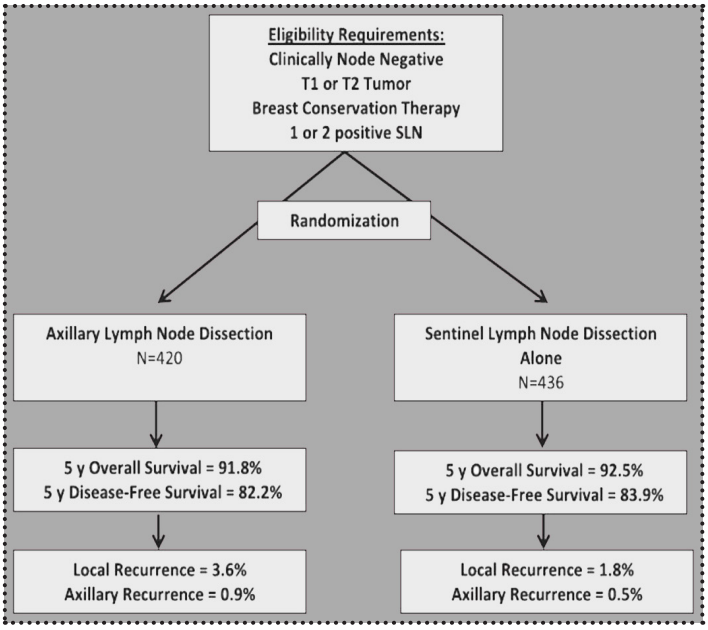
Management of Breast Cancers

Dr. Elaine McKevitt, Chair SON CPD-KT Committee and SON Breast Surgical Tumour Group

The afternoon of the 2016 Fall Update focussed on breast cancer; looking at management of the axilla, surgical management of breast cancer in the setting of neoadjuvant chemotherapy, and nipple sparing mastectomy.

Dr. Greg McKinnon, our guest speaker from Calgary, reviewed the topic of management of the axilla in 2016. He emphasized that management has evolved into a team effort and involves medical and radiation oncologists, as well as surgeons. He looked at the question of "who needs an axillary lymph node dissection?" (ALND) and the evidence behind current recommendations.

The NSABP B32 study showed that sentinel node biopsy (SNBx) is accurate in 97.2% of patients. Of those patients that have positive sentinel lymph nodes, the sentinel node is the only positive node in 61% of patients. This means that there were other positive nodes in 39% of patients. There was a false negative rate in the study of 9.8%. There was no difference in overall survival, disease free survival, or local recurrence rate in those patients with a negative SNBx only compared to those with a SLNBx and ALND. However, those with a SNBx only had a decreased rate of lymph edema and arm parasthesias.



SCHEMA AND RESULTS FOR THE ACOSOG Z11 TRIAL

The ACOSOG Z11 trial looked at survival and local recurrence in patients with one or two positive sentinel lymph nodes

with the breast primary treated with partial mastectomy and whole breast radiotherapy randomizing patients with one or two positive nodes to a completion ALND. Patients with three or more positive lymph nodes, matted nodes, or having neoadjuvant chemotherapy were excluded from the trial.

At five and ten years of follow up there was no difference in local regional recurrence or survival between the groups. Similarly, the IBCSG 23-01 randomized patients with sentinel node micrometastases to completion ALND and found no difference in local regional recurrence or survival.

The EORTC-AMAROS trial randomized patients to either a completion ALND or axillary radiation (RT) and included patients that had total mastectomy (18% of study population). Following up after 6.1 years found there was no difference in survival. There was a higher rate of lymphedema in patients having ALND compared to those having axillary RT (23% vs 13%). There was no difference in range of motion or quality of life.

The Early Breast Cancer Trialist's Collaborative Group published a meta-analysis in 2014 looking at the effect of axillary RT following mastectomy and axillary surgery for patients treated before 2000. This meta-analysis found decreased local recurrence and improved survival with axillary RT in patients with one to three positive nodes as well as four or more positive nodes. The MA 20 trial looked at axillary RT after axillary dissection for one to three positive lymph nodes, and showed a five percent improved disease free survival with the addition of axillary RT, but no improvement in overall survival.

To further look at this question, two trials (POSNOC and BOOG 2013-07) are recruiting patients and randomizing them to either ALND or axillary RT compared to adjuvant therapy alone. In September 2016 the American Societies of Clinical Oncology, Radiation Oncology, and Surgical Oncology published new guidelines for post mastectomy radiotherapy, and acknowledge that clinical judgement is necessary to identify those patients that will benefit from ALND and axillary RT, and those with a sufficiently low risk that additional axillary treatment may not be justified.

The benefit of completion ALND was also looked at in "high risk" patients (<50, Her 2+ve, triple negative) compared to "average risk" patients with positive sentinel nodes. There was no difference found between these groups for residual axillary disease and local recurrence at 31 months follow up. They concluded that completion ALND was not indicated based on sub-type or age.

To help put all of these trials into perspective we also have the 25 year follow up results of the NSABP-B04 study that was published in 2002. This trial had randomized patients with operable breast cancer to total mastectomy alone, total mastectomy and radiation, or radical mastectomy for both clinically node positive and node negative patients. There was no significant difference between those patients receiving ALND, axillary RT or no axillary treatment in that trial.

The second breast presentation was given by Dr Rebecca Warburton, from Mount Saint Joseph Hospital in Vancouver, looking at surgical management of breast cancer in the setting of Neoadjuvant Chemotherapy (NAT). NAT has traditionally been used in the setting of inflammatory breast cancer or treatment of inoperable or locally advance breast cancer. The NSABP B18 trial demonstrated equivalency to adjuvant and neoadjuvant chemotherapy in patients with operable breast cancer. Advantages to giving NAT include converting a patient from having a traditional mastectomy to a post NAT skin sparing mastectomy with breast reconstruction, a large lumpectomy to a post NAT smaller lumpectomy, and prognostic information for the patient from the response to NAT as patients achieving a complete pathologic response have improved overall survival.

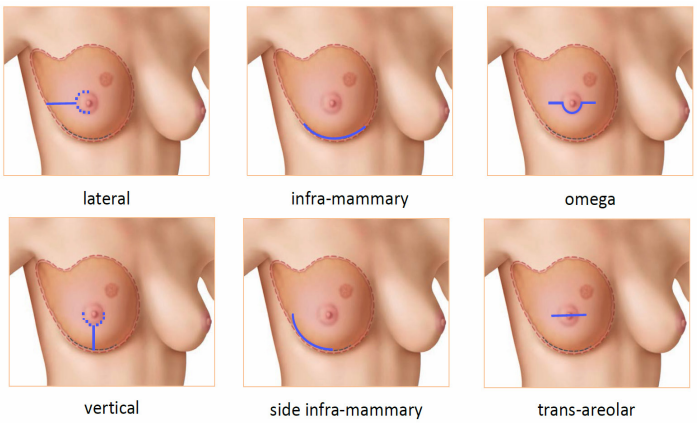
It is also thought that NAT may allow us to decrease axillary surgery for patients that convert from having positive nodes pre NAT to negative nodes post NAT. However this is currently controversial and trials are currently addressing this question. Patients with triple negative tumours and Her 2 positive tumors are more likely to have a complete pathologic response to NAT. Patients considered for NAT should have imaging of the breast and axilla and FNA of any suspicious nodes and a clip placed into the tumor (regardless of the type of surgery initially planned).

Breast conserving surgery (BCS) after NAT gives acceptable rates of local control. Predictors of failure of BCS are multicentric disease, a poor clinical response to NAT, diffuse calcification, and lobular cancer, and mastectomy may need to be considered in these circumstances or if margins are positive. Imaging after NAT can be considered but there are currently no specific guidelines.

Although early studies (2000-2005) showed unacceptable results with sentinel node biopsy following NAT, Hunt in 2009 showed that SNBx following NAT was as accurate as SNBx prior to chemotherapy in patients presenting with negative lymph nodes. This has been confirmed in other studies and now most surgeons are comfortable in performing SNBx following NAT in the setting of a pre NAT negative axilla.

Studies of SNBx following NAT in node positive disease initially showed that SNBx was feasible but there was an

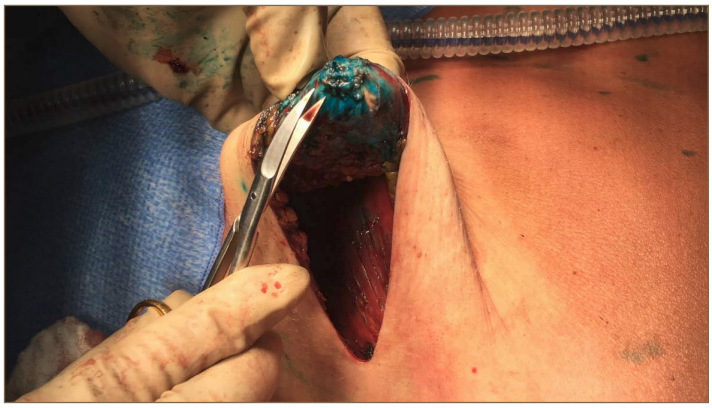
unacceptably high false negative rate. Efforts are underway to define a group of patients that may be able to be spared an ALND following NAT. When considering the Sentina, Z-1071, and FN ANSC trials there is a decreased false negative rate when two tracers are used for the SNBx and more than two nodes are removed. Some centres are offering SNBx to patients that are clinically N0 following NAT with completion ALND for any residual disease (including isolated tumor cells) but this is still controversial. Current trials are looking at ALND and axillary RT following conversion from N1 to N0 with NAT and these results will help inform patient management in the near future.



PLANNING THE INCISION FOR NIPPLE SPARING MASTECTOMY

The last session of the meeting looked at nipple sparing mastectomy (NSM), with tips and tricks from general surgery and plastic surgery, and was presented by Dr. Rebecca Nelson (Plastic Surgeon, Burnaby) Esta Bovill (Plastic Surgeon, Mount Saint Joseph Hospital and UBC) Connie Chiu (General Surgery, Royal Columbian Hospital) and Elaine McKevitt (General Surgery Mount Saint Joseph Hospital).

NSM is an extension of a skin sparing mastectomy in which the nipple areolar complex (NAC) is preserved after removal of all visible breast tissue. Preservation of the NAC enhances the cosmetic outcome and "normal" anatomy and studies have shown improved coping, psychosocial, and sexual wellbeing with NSM compared to skin sparing mastectomy (SSM). Traditionally the NAC was removed with mastectomy due to concerns about local recurrence and central lymphatic spread, but meta-analysis and systematic reviews have shown a low (<3%) local regional recurrence rate with NSM in selected patients. Absolute contraindications to NSM are T4 tumors, inflammatory breast cancer, pathologic nipple discharge, and Paget's disease. Relative contraindications are tumors <2 cm of the NAC, DCIS, multi-centric tumors, positive nodes, large or ptotic breasts, smoking, prior breast surgery or radiation, and obesity.



NIPPLE CORE BIOPSY WITH NIPPLE SPARING MASTECTOMY (NSM)

Advantages to NSM include a single stage procedure which is easier for the patient and less costly to the health care system as well as improved cosmetic results. Disadvantages include decreased access to parts of the breast with some of the incisions, the learning curve for the procedure and possible increased operative time, and the possibility of non-viability of the NAC requiring removal. With increasing experience with NSM the eligibility criteria and reconstructive options are expanding.

Out with the wash in endometrial cancer

Dr. Janice Kwon
Gynecologic Oncologist
Vancouver General Hospital

There is uncertainty about the utility of peritoneal cytology from washings obtained during endometrial cancer surgery. The status of washings was removed from the most recent staging guidelines[1], as it did not appear to be an independent determinant of outcome. However, a large retrospective study using SEER data in 2013 concluded that positive peritoneal cytology was a significant risk factor in early stage endometrial cancer[2].

However, this study did not adjust for known covariates in endometrial cancer such as myometrial invasion, lympho-vascular space invasion (LVSI) and adjuvant chemotherapy.

We conducted a retrospective population-based cohort study of women who had surgery with peritoneal washings for Type 1 (endometrioid) endometrial cancer in British Columbia from 2003 through 2009. We focused specifically on

those with low and intermediate risk endometrial cancer for whom treatment decisions could change if positive peritoneal cytology was found to be independently associated with worse outcome. A Cox proportional regression was used to model disease-free and overall survival rates.

There were 370 and 298 women with low-risk and intermediate risk endometrial cancer, respectively, for a total of 668 patients. Positive cytology rate was 2.2%.

After adjustment for known covariates, positive cytology was not independently associated with disease-free survival (HR 3.17, 95% CI 0.91-11.03) or overall survival (HR 1.32, 95% CI 0.47-3.76). Only age, LVSI, and chemotherapy were significantly associated with inferior overall survival.

The strength of this study is the large sample size and the details on known covariates. The limitation is that we were unable to evaluate the association between peritoneal cytology and outcome in Type 2 (high-risk) cancers. However, the majority of women with endometrial cancer have Type 1 low or intermediate risk disease, and the positive cytology rate is very low. While it is easy to obtain peritoneal washings during surgery, it does cost approximately $150 per case, and in the absence of proven clinical benefit, it is difficult to justify this practice. Therefore in British Columbia, we have recommended "out with the wash" (no assessment of peritoneal washings for cytology) in Type 1 endometrial cancer.

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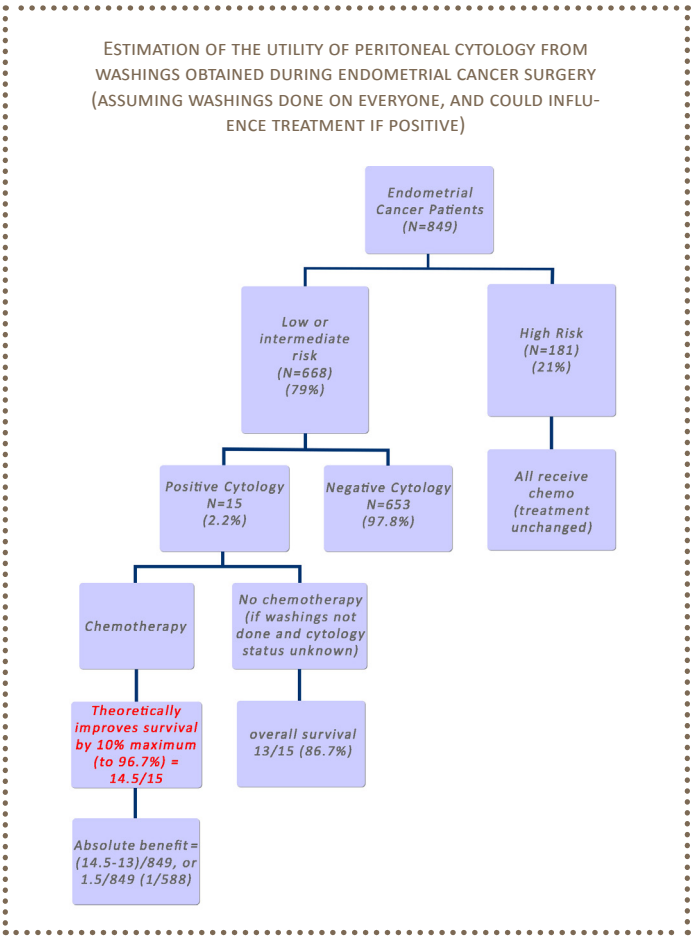
2. Garg G, Gao F, Wright JD, Hagemann AR, Mutch DG, Powell MA. Positive peritoneal cytology is an independent risk-factor in early stage endometrial cancer. Gynecologic oncology 2013;128:77-82.



POEM: OVER-READING OF BREAST BIOPSY SAMPLES IS COMMON

Dr. Michelle Goecke
General Surgeon
Fraser Health Authority

In September 2016 the Canadian Medical Association released a POEM (Patient Oriented Evidence-based Management) entitled "Over-reading of breast biopsy samples is common".[1] The clinical question asked was "How accurate are breast biopsy interpretations and can they be improved?" The paper chosen to answer this question was a simulation study by Joann Elmore et al. entitled, "Evaluation of 12 strategies for obtaining second opinions to improve interpretation of breast histopathology: simulation study". This study "compared the effect of different criteria for triggering procurement of a second opinion on the accuracy of interpretation of breast disease" and was designed "to assess improvements in accuracy in a controlled test situation".[2] It should be noted that the chosen study does not fully address the specific clinical question asked in the POEM.

Through simulation, Elmore et al. found that a second opinion decreased over-and under-interpretation of breast pathology and this was the most notable for cases of atypia and ductal carcinoma in situ (DCIS). Their finding supports the belief already held by many pathologists that second opinions in breast pathology improve diagnostic accuracy. This study did not address the impact of the second opinion on patient outcome.

While this POEM has drawn significant criticism, the SON Breast Tumour Group felt this POEM should be brought to the attention of surgeons in British Columbia in the event that

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there is an increase in patient requests for second opinions of their pathology.

Breast core biopsy specimens read by pathologists at larger, high volume centres in British Columbia often receive an unofficial second opinion by other members of the department.[3] Furthermore, radiology-pathology correlation is to be documented for every core biopsy this is an important step validating the biopsy result.[4]

The SON Breast Tumour Group recommends that surgeons receiving pathology reports from lower volume centres should be familiar with their local pathologists' comfort with interpreting breast core biopsy specimens. If there are any concerns with the diagnosis, in particular for reports of atypia or DCIS, additional opinions should be considered to help ensure proper patient management.

The surgical breast tumour group feels that quality assurance of core biopsy pathology is not the direct responsibility of the surgeon. Surgeons, however, may be faced with requests for second opinions from patients following this POEM. We have forwarded this matter to the provincial breast tumour group for their consideration.

References:

1. POEMs by Essential Evidence Plus. CMA. September 21, 2016. Over-reading of breast biopsy samples is common

2. Elmore JG, Tosteson AN, Pepe MS, et al. Evaluation of 12 strategies for obtaining second opinions to improve interpretation of breast histopathology: simulation study. BMJ 2016;353:i3069.

3. Personal communication from pathologists, Royal Columbian Hospital.

4. Canadian Association of Radiologists Practice Guidelines and Technical Standards for Breast Imaging and Intervention, 2012. http://www.car.ca/uploads/standards%20guidelines/20131024_en_breast_imaging_practice_guidelines.pdf. Accessed March 28, 2017.

Upcoming Conferences

BC Surgical Society Annual Meeting, Parksville BC
May 4-6, 2017, www.bcss.ca

BC Surgical Oncology Network Annual Fall Update, Vancouver BC
October 14, 2017, www.bccancer.bc.ca/health-professionals/networks/surgical-oncology-network

American College of Surgeons Clinical Congress, San Diego CA
October 22-26, 2017, www.facs.org

North Pacific Surgical Annual Meeting, Hyatt Regency, Vancouver, BC
November 10-11, 2017, www.northpacificsurgical.org

Western Surgical Annual Meeting, Mesa AZ
November 4-7, www.westernsurg.org

SURGICAL ONCOLOGY NETWORK NEWSLETTER

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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.