BC CANCER
Provincial Health Services Authority

Surgery Network Newsletter

ISSUE 39, SEPTEMBER 2023 | www.bccancer.bc.ca/surgerynetwork

Wait Times & Access to Radiation Therapy for Rectal Cancer Surgery Patients

Dr. Tom Wallace, Chair, Clinical Practice & Quality Assurance

Dr. Chris Baliski, Regional Cancer Surgical Lead – Interior Health Region

Ensuring that BC Cancer Surgery patients receive excellent quality of care is inarguably of paramount importance. The Clinical Practice and Quality Assurance (CPQA) Committee of BC Cancer - Surgery is concerned with how we define, measure and improve that quality of care.

Surgeons who provide care to cancer patients are uniquely positioned to recognize opportunities for improvement within the structures, processes and outcomes important to cancer surgery patients. The CPQA is composed of the chairs of each of the 12 Surgical Tumour Groups (STG). Each STG is itself made up of surgeons from across the province who are experts in their fields. The STGs focus on quality issues related to their relevant tumour sites.

A useful construct to define and conceptualize quality of care is presented in the BC Health Quality Matrix. One of the dimensions of quality that has received significant attention recently is accessibility. This dimension of quality is of critical importance to multiple stakeholders including patients, clinicians, and payers (government). Accessibility can be defined as timely access to care.

Members of the Colorectal Surgical Tumour Group recognized that there may be opportunities for improvement within the accessibility dimension of quality for rectal cancer patients. The treatment paradigm for rectal cancer is representative of the complex, multidisciplinary care required by many cancer surgery patients. Rectal cancer patients require diagnostic procedures, specialized medical imaging, and multidisciplinary review by providers including radiology, pathology, surgery, medical oncology, and radiation oncology.

The rectal cancer patient journey typically begins with consultation by a rectal cancer surgeon specialist. This surgeon becomes a patient advocate and coordinator of the patient's cancer care. At the time of initial consultation, the surgeon maps out the anticipated patient journey including the multidisciplinary care that will be required, such as radiation and medical oncologic consultations and

IN THIS ISSUE

treatments. Invariably the patient will inquire about the relevant time posts of their journey such as: 'how long will each phase of treatment take' and 'when will these treatments begin'.

While having these patient conversations, the importance of accessibility and the potential opportunity for improvement in patients' access to radiation therapy was recognized. There was a perception amongst surgeons that patients' waiting times were more than established targets. A quality assurance project was initiated to determine the waiting times to initiation of radiation therapy.

Stakeholders including surgeons and radiation oncologists were engaged. The patient journey was mapped with special attention paid to the timestamps relevant to evaluating access to radiation therapy. The Data and Analytics team at BC Cancer helped to direct this process by guiding project leaders in identifying data points from existing sources. The process of identifying, abstracting, and reporting this wait time accessibility data is ongoing.

Once data reports are available to share with stakeholders they will have a better understanding of this dimension of quality for their patients and may be able to help design and implement quality improvement projects to address any identified opportunities for improvement.

Patient Reported Outcomes in Breast Cancer

Dr. Melina Deban, Surgical Oncologist, Providence Breast Centre

In the modern era of patient-centered care, patient reported outcomes (PROs) offer a unique opportunity to involve patients actively in their treatment plan. The combination of physician and patient perspectives delivers a more accurate and holistic report of clinical status [1]. It enables shared-decision making, benefitting both the patient and the provider.

Patient-reported outcomes are defined as any measure of health status reported directly by the patient, without the interference of a healthcare provider [2-4]. In breast cancer, PROs can target areas ranging from body image, surgical outcomes (reconstruction or lumpectomy) to general quality of life measures during adjuvant therapy. Breast cancer patients are already leading the way in PROs with up to 123 RCTs using them as primary or secondary outcome [5, 6]. The majority of PROs summarized have been elaborated based on expert opinion, with others incorporating literature review and patient interviews [3].

A limited number of these PRO tools are centered on surgical outcomes. There are four, namely: BIBCQ, BREAST-Q, MBROS-S and BCTOS. Other tools focus on outcomes and side effects of oncological interventions instead.

Summary of PRO tools used in breast cancer [2-4]

Name	Number of items	Main domain assessed
Body Image after Breast Cancer Questionnaire (BIBCQ)	53	Body image
Hopwood Body Image Scale (HBIS)	10	Body image
Polivy Body Image Scale (PBIS)	13	Body Image
Michigan Breast Reconstruction Outcomes Study (MBROS-S) Satisfaction Survey	7	Reconstruction (including implants, TRAM)
MBROS Body Image (MBROS-BI) Questionnaire	9	Reconstruction, body image
BREAST-Q	Variable	Breast surgery and oncological team
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-BR23)	23	General Breast Cancer
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-BR45)	45	As above, new items include psychological condition and satisfaction of patient
Functional Assessment for Cancer Therapy-Breast Cancer (FACT-B)	44	General breast cancer, focus on patient values
Breast Cancer Treatment Outcome Scale (BCTOS)	22	Lumpectomy outcomes
Mastectomy Attitude Scale (MAS)	33	Mastectomy outcomes

BREAST-Q assesses the patient satisfaction with surgical outcomes in addition to the oncological team. The copyright belongs to Memorial Sloan Kettering Cancer Center and the University of British Columbia (version 2.0, 2017, available at: https://qportfolio.org/breast-q/breast-cancer/) [7]. Some general PROs, for example Short Form-36 (SF-36) or Patient-Reported Outcomes Measurement Information System (PROMIS-29), have not been included as they are not specific to breast cancer. Currently, the tool that is most often used to report outcomes and side-effects of therapies in cancer is Common Terminology Criteria for Adverse events (CTCAE version 4, available at: http://evs.nci.nih.gov/ftp1/CTCAE/About.html). There are limitations to the use of CTCAE, to which PROs can be complimentary. Symptoms are under-represented in CTCAE and all outcomes are reported by the clinician. A

notable benefit of including PROs in medical practice is to provide a better picture of patient health and functional status [1]. Moreover, use of PROs can allow earlier detection of adverse symptoms [1, 6]. Other benefits to the use of PROs include prediction of progression-free survival, as it contains prognostic information independent of that provided by Eastern Cooperative Oncology Group Performance Score (ECOG-PS). In patients with hormone-receptor positive/HER-2 negative advanced or metastatic breast cancer treated with abemaciclib, those with intermediate and high function derived a greater benefit from the agent compared to those with low physical function scores. [8]

In a different study including patients with advanced HER-2 positive breast cancer receiving contemporary systemic therapy, PROs were identified as independent prognostic factors for overall survival, progression-free survival and grade >= 3 adverse effects. On multivariate analysis, both physical well-being and ECOG-PS provided independent prognostic information, but physical well-being (PROs) discriminated better than ECOG-PS regarding overall survival outcomes. [9]

Overall, use of PROs enhances patient satisfaction, can be predictive of survival outcomes and offers the opportunity to improve quality of life through early detection of adverse symptoms and effects.

How do we translate this into practice? Basch and colleagues describe three potential approaches to bring together patient and provider perspectives: independent, merged and collaborative. The first includes completely separate collection, analysis and report of each party. In the second approach, data is collected separately and merged for analysis with a single output metric. In the latter, preferred by the authors, patients report symptoms to providers, who use it to inform their own report. Although ongoing research has yet to determine which of these approaches is most effective, the authors argue that the latter approach provides a better opportunity of communication between the patient and the provider to enable shared-decision making. [1]

Recognizing that progress has been made, the use of PROs is currently budding in the medical field. Registries such as PROMOTION [10] aim to collect information on all cancer RCTs that include PROs and review their PRO assessments. The CONSORT PRO extension to the CONSORT Statement [11] provides guidance in methodology and reporting of PROs. Future uses of PROs may include drug safety reporting, informing patient decisions, incorporation in development of drugs, regulators and payers in systems with alternate healthcare models. It is hoped that the next version of CTCAE (version 5) may include PROs. [1]

References for this article can be found on the BC Cancer Surgery Network Website.

Management of Colorectal Liver Metastases

Dr. Graziano Oldani, Hepatobiliary & Liver Transplant Surgeon, UBC Hospital & VGH. Assistant Professor, UBC.

The liver is the most common site for metastasis in colorectal cancer patients, with 25% developing colorectal liver metastases (CRLM). Management of patients with CRLM is multifaceted, involving various medical disciplines. The goal is to maximize resection, using techniques like downsizing chemotherapy, portal vein embolization, and liver partitioning. Laparoscopic, Robot-assisted, or open liver resection may be conducted after, with or before colorectal surgery. For unresectable patients, alternatives like chemotherapy, targeted agents, and radiotherapy improve survival and may lead to operability.

Current advancements include biomarker analysis, novel systemic agents, and possibly reintroducing liver transplantation, aimed at long-term survival and cure.

Surgical and other Invasive Management

Upfront Resection

Patients with technically simple disease and excellent oncologic profile should be evaluated for upfront resection. There has not been a proven oncologic advantage in delivering neo-adjuvant systemic therapy to this population [1]. On the other hand, chemotherapy-induced liver toxicity may lead to higher morbidity and surgical-related deaths. Identifying this population may be a challenge; that is why new AI tools may be helpful and could become the gold standard in the future [2].

Conversion Therapy

Initially, unresectable liver metastases convert to resectable disease in up to 50% of the cases, under FOLFOXIRI + bevacizumab regimen [3]. The constant improvements in systemic agents, along with the refinement of surgical strategies allowed to turn a terminal illness into chronic disease and eventually cure in a significant number of cases (at least 20%).Typically, patients have large metastases, bilobar disease, or relatively smaller nodules placed close to major vascular branches.

The purpose of neo-adjuvant systemic treatments is to reduce the size of the nodules, allowing for a radical and safe resection in terms of future liver remnant. More importantly, it allows to test the biology of the disease, before submitting the patient to potentially risky procedures.

Especially in these cases, a multidisciplinary approach is fundamental. Often these patients need multistage procedures and complex vascular embolizations to promote the growth of the liver remnant.

The surgical team must be familiar with multiple techniques, choosing the safest strategy case by case. Some patients, for example, may be anatomically resectable but the post-chemotherapy liver quality may not allow for extended parenchymal resections. In these cases targeted wedge resections eventually in combination with microwave ablations, usually done via open means, are more indicated. Other patients may cope well with more extensive resections and benefit more from a minimally invasive approach, either laparoscopic or robot-assisted, for example.

Liver Transplantation

Patients that despite a good response to systemic treatment are still technically unresectable may qualify for liver transplantation. Long considered a non-indication to transplant, the Scandinavian SECA studies from 2013 on proved encouraging survivals of patients selected based on stringent criteria [4]. Such criteria include, along with proven radiological non-progression, the absence of BRAF mutation, a significant decrease in CEA during systemic treatment, and the absence of extrahepatic disease (mostly PET- and prior to transplant node biopsy-proven).

Microwave and Radiofrequency Ablation

In combination or complementation to surgery, or for patients that are not candidates for more radical treatment, ablative techniques are a valuable tool [5]. Smaller metastases within 3 cm can be treated this way. Depending on the situation, ablations can be performed percutaneously on local anesthesia or during a laparoscopy or laparotomy.

Systemic and other Non-invasive Management

Chemotherapy and Targeted Therapy

Chemotherapy is often the first-line treatment for patients with unresectable CRLM. Various combinations of chemotherapy drugs have been developed, targeting different pathways to stop or slow tumour growth. In addition, monoclonal antibodies that target specific molecular pathways are increasingly being used, either alone or in combination with chemotherapy.

The efficacy of these combinations has dramatically improved over the last decade. Oxaliplatin or irinotecan-based regimens have demonstrated response rates achieving 40-50%, and up to 70% when combined with Cetuximab, for example [6].

Immunotherapy

Although still in its infancy, immunotherapy has shown promise in some colorectal cancers, especially the ones with DNA mismatch repair deficit. Immunotherapies include immune checkpoint inhibitors, cancer vaccines, and other biotherapeutics such as chimeric antigen receptor (CAR) T cells. It is conceivable that, in the near future, this strategy may match the efficacy of surgery in selected cancer subtypes [7].

Stereotactic Body Radiotherapy (SBRT)

SBRT delivers high doses of radiation directly to the tumour, sparing surrounding healthy tissue. This approach can be particularly beneficial for patients with large inoperable tumours [8], non-responders to systemic treatments or very frail patients.

Conclusion

The management of colorectal liver metastases is a multifaceted process that necessitates a personalized approach, taking into consideration the individual characteristics of the tumour and the patient. The integration of surgery, systemic therapies, and ablative techniques provides a wide range of treatment options, maximizing the chances of survival and improving the quality of life. Since a large proportion of initially unresectable patients can be offered curative options when evaluated in a specialized high-volume center, these patients should never be labelled upfront and always referred to a reputed multidisciplinary team.

References for this article can be found on the BC Cancer Surgery Network Website.

Transforming Breast Cancer Care: The South Island Integrated Breast Cancer Program

Dr. Elaine Lam & Dr. Heather Emmerton-Coughlin, South Island Integrated Breast Cancer Program – Medical Directors

The South Island Integrated Breast Cancer Program was launched in April 2021. This initiative, championed by medical directors Dr. Heather Emmerton-Coughlin and Dr. Elaine Lam, was a collaboration between multiple medical specialists and brought forth with the support of Island Health and the Enhancing Access Initiative through Doctors of BC. The South Island Integrated Breast Cancer Program is not only revolutionizing breast cancer care but also setting a new standard for access to comprehensive, patient-centered healthcare. We would like to highlight key features of this new program.

Centralized Referral System: Enhancing Efficiency and Coordination

One of the cornerstones of the South Island Integrated Breast Cancer Program is its centralized referral system. By streamlining the referral process, healthcare providers ensure that breast cancer patients receive prompt attention from the moment they enter the healthcare system. This integrated approach eliminates unnecessary delays, enabling swift access to diagnostic procedures and expert opinions.

Reducing Wait Times: From Diagnosis to Surgical Treatment

The program's commitment to reducing wait times is reshaping the breast cancer journey. Through close collaboration between medical specialists, radiologists, and surgeons, the program has significantly shortened the time from diagnosis to surgical treatment. This not only eases the emotional burden on patients but also contributes to better treatment outcomes. Fast-tracking care without compromising quality is a testament to the program's dedication to excellence.

Integration of Specialized Breast Health Nurses: A Holistic Approach

Recognizing the multifaceted needs of breast cancer patients, the South Island Integrated Breast Cancer Program integrates a dedicated team of specialized breast health nurses. These compassionate professionals serve as invaluable guides throughout the patient's journey, offering expert medical advice, emotional support, and educational resources. Their presence ensures that patients have a comprehensive support system that addresses not only medical concerns but also emotional well-being.

Tracking Patient Satisfaction: Putting Patients First

Patient satisfaction is at the heart of the program's mission. Through proactive patient engagement and personalized care plans, the program actively seeks feedback from patients to continually improve services. By listening to patients' voices, the program adapts and refines its approach, ensuring that the care provided aligns with patients' expectations and needs.

Monitoring Quality Outcomes: A Commitment to Excellence

The South Island Integrated Breast Cancer Program is steadfast in its pursuit of excellence. Through rigorous monitoring of quality outcomes, the program holds itself accountable for delivering the highest standards of care. Continuous assessment, data analysis, and collaboration with medical experts help drive evidence-based improvements, resulting in optimized treatment plans and improved patient experiences.

A Vision for the Future

Looking ahead, the South Island Integrated Breast Cancer Program remains committed to innovation and progress. With the adoption of new technologies such as wireless seed localization and point of care specimen mammography, the program will increase surgical capacity as well as access to specialist care in satellite and community centres. These advances will help to ensure timely access to treatment for all patients, and often closer to home. By nurturing a patient-centered culture, and fostering collaboration among medical professionals, the program envisions a future where breast cancer is met with swift, effective, and compassionate care.

As we celebrate the milestones achieved in the first two years of the South Island Integrated Breast Cancer Program, we would like acknowledge the women and men who have contributed to the success of the program so far, and reaffirm our commitment to excellence in care and

empowerment for our patients throughout their breast cancer journey.

Criteria for Adjuvant Therapy for Stage II Melanoma

Dr. Sita O. Ollek, Surgical Oncologist – Kelowna General Hospital

The incidence of invasive cutaneous melanoma is rising worldwide, and in Canada melanoma accounts for 80% of all skin cancer related mortality.[1, 2] The majority of patients will present with stage I or II disease.[3] These node negative patients are considered to have early stage melanoma. However, so called early stage melanoma in fact encompasses a heterogeneous group of patients with significantly different prognoses. This heterogeneity is particularly evident when looking at patients with stage II disease.[3–5]

By definition, stage II melanoma patients are node negative. However, this group includes a wide range of Breslow depths, which is a key independent prognostic factor (Figure 1).[6] As a result, stage II patients can be subdivided into low risk (stage IIA) or high risk (stage IIB/IIC) categories. The relevance of this is reflected in the vastly different outcomes; stage IIA patients have a 10 year melanoma specific survival (MSS) of 94% compared to 75% for stage IIC patients.[5] These high risk stage II patients in fact have outcomes inferior to stage IIIA patients, and similar to stage IIIB patients.[4] Despite surgery traditionally being the only treatment for node negative patients, high risk stage II patients remain at risk for recurrence after surgery.

Figure 1. Stage II melanoma based on AJCC 8th edition

	Stage	T	N	M
'Low risk'	IIA	T2b	0	0
		T3a	0	0
'High risk'	IIB	T3b	0	0
		T4a	0	0
	IIC	T4b	0	0

The landscape of systemic therapy in melanoma has significantly changed over the past several years. Adjuvant systemic therapy with either immunotherapy (pembrolizumab or nivolumab) or targeted therapy (dabrafenib and trametinib) for 12 months is now the standard of care for patients with completely resected stage III melanoma.[7] This is as a result of several key trials that have consistently shown improved outcomes with these systemic agents, including improved recurrence free survival (RFS), distant metastatic free survival (DMFS) and overall survival (OS).[8–10] With these improved outcomes and often sustained responses in stage III disease, there has been a natural shift towards evaluating the use of these agents in earlier stage disease.[7]

Despite patients with high risk stage II disease being at risk for recurrence, the data on adjuvant therapy in this setting is limited and these patients were not included in the majority of previous trials.[4] However, more recent data does support a benefit in these patients. The KEYNOTE-716 trial is a randomized controlled trial that compared 12 months of adjuvant pembrolizumab versus placebo in patients with completely resected stage IIB or IIC melanoma.[11] Overall, patients who received pembrolizumab had significantly improved RFS (18 month RFS 86% vs 77%). DMFS was also improved with an approximately 50% reduction in the risk of distant recurrence (12% placebo vs 6% pembrolizumab). Similarly, the CheckMate76K trial compared 12 months adjuvant nivolumab with placebo in patients with resected high risk stage II melanoma.[12] The use of nivolumab significantly improved RFS at 12 months (89% vs 79%) and DFMS (92% vs 87%). Ongoing trials continue to investigate the role of adjuvant systemic therapy in high risk stage II disease, including the use of targeted therapy for *BRAFV600* mutated melanoma.[7] Interestingly, data from both KEYNOTE-716 and CheckMate76K demonstrate that amongst patients who developed recurrence, distant metastatic disease was more common than regional recurrence.[11, 12] This supports that despite being node negative, these patients are at high risk of recurrence. This may also highlight the importance of systemic, rather than only locoregional, therapy. Finally, patients were required to have a sentinel lymph node biopsy performed, emphasizing the importance of accurate staging in these patients. Despite these improved outcomes, adjuvant systemic therapy is not without risk.

This may be particularly important to consider as we shift towards using systemic therapy in patients who have traditionally been treated with surgery alone.[7] Treatment related toxicity, which may be lifelong, needs to be considered.[11] In addition, the impact of previous immunotherapy exposure on patients who go on later to develop metastatic disease is not yet clear.[7]

Overall, we have seen significant improvements in our understanding and management of patients with high-risk stage II melanoma. At this time, patients in British Columbia with resected stage IIB or IIC melanoma are now eligible for adjuvant immunotherapy with pembrolizumab. After surgery, including a sentinel lymph node biopsy, confirms stage II disease these high-risk patients should be referred to BC Cancer for discussion and consideration of this.

References for this article can be found on the BC Cancer Surgery Network Website

Surgery Network Travel Award Recipients

Anna Black, 3rd Year Urology Resident - UBC

Multicenter evaluation of neoadjuvant and induction gemcitabine-carboplatin versus gemicitabine-cisplatin followed by radical cystectomy for muscle-invasive bladder cancer

Cisplatin-based induction and neoadjuvant chemotherapy (NAIC) is the standard of care for muscle invasive bladder cancer with and without lymph node metastasis, respectively. However, up to 50% of patients are cisplatin-ineligible. Gemcitabine-carboplatin (GCa) represents an alternative chemotherapy regimen for these patients, although it is thought to be less effective than gemcitabine-cisplatin (GC). Therefore, we performed a retrospective review to compare pathological response and survival between NAIC with GC and GCa.

Table 1. Cox Regression looking at risk factors for cancer specific and overall survival

		Cancer Specific Survival		Overall Survival	
		HR (95% CI)	p-value	HR (95% CI)	p-value
NAIC regimen	GC				
	GCa	1.38 (0.96-1.997)	0.085	1.25 (0.88-1.76)	0.210
Age (years)		1.02 (0.998-1.04)	0.073	1.02 (1.00-1.04)	0.020
CCI	0-2				
	3-5	0.82 (0.56-1.20)	0.32	0.94 (0.67-1.33)	0.73
	≥6	1.66 (0.995-2.74)	0.052	1.029 (1.05-2.69)	0.029
cT stage	≤T2				
	≥T3	1.55 (1.11-2.15)	0.009	1.44 (1.07-1.94)	0.017
cN stage	0				
	1-3	1.25 (0.86-1.82)	0.251	1.01 (0.77-1.53)	0.607

Methods

We included all patients who received at least three cycles of NAIC followed by radical cystectomy (RC) as one of 19 centers between 2000 and 2013. Demographic and clinical parameters were compared using Student's t test, chi-squared, or Fisher's exact test. Putative risk factors for cancer-specific and overall survival were analyzed using Cox regression, while predictors of pathological response were investigated using logistic regression.

Results

Data were available for 747 (147 GCa and 600 GC) patients. Patients treated with GCa were significantly older (67 vs 65 years; p<0.001), had a higher Charlson Comorbidity Index (p=0.016) and had a higher rate of clinical node-positive disease (32% vs 20%; p=0.013) than patients treated with GC.

Conclusion

The rate of complete pathological response (pCR; ypT0N0) did not significantly differ between GCa and GC groups (20.7% vs 22.1% respectively; p=0.73). Chemotherapy regimen was not associated with pCR in the multivariable analysis, and as seen in table 1, was not a predictor of overall or cancer-specific survival.

Next-Steps

This suggests that cisplatin-ineligible patients may benefit from GCa chemotherapy prior to RC, which warrants further investigation.

Sahej Dhak, 3rd Year Medical Student - UBC

Inadequate pathologic margins and re-excision rates following breast conserving surgery for ductal carcinoma in-situ

Breast cancer is the most common malignancy affecting Canadian females. Re-excisions following breast conserving surgery (BCS) are common, occurring more frequently in ductal carcinoma in-situ (DCIS) than its malignant counterpart. Although one quarter of patients with breast cancer will have DCIS, there is limited information available regarding factors predisposing to suboptimal pathologic margins, and the need for re-excision.

Methods

Retrospective review of patients treated for DCIS at BC Cancer SAH-CSI (Kelowna) between the years 2010 to 2016 was conducted.

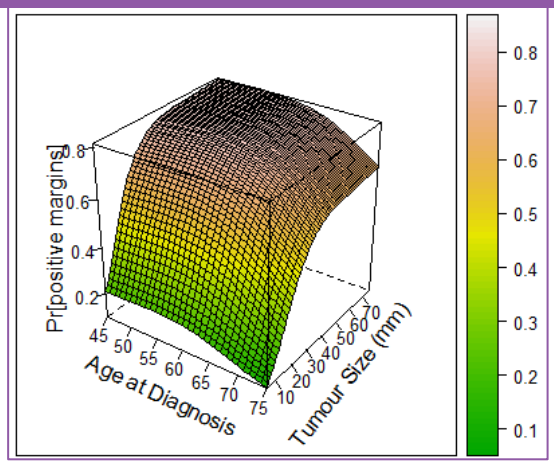
Patients with DCIS undergoing BCS were identified and evaluated for demographic and pathologic factors associated with suboptimal pathologic margins and re-excision.

Results

241 patients underwent BCS, and we found that 51.7% had suboptimal pathologic margins and 27.8% had undergone re-excision. Tumour size was the most influential variable, with larger tumour size associated with margins involvement (Figure 1) and re-excision. Younger patient age at diagnosis was also associated with suboptimal margins (Figure 1) and subsequent re-excisions. Low tumour grade was associated with re-excision, while estrogen receptor negative disease was associated with suboptimal margins. Inadequate pathologic margins following BCS, and subsequent re-excision rates are common in patients with DCIS, and consistent with the literature. Tumour size is the dominant factor driving this occurrence, with patient age and tumour grade also impacting outcomes.

Further research with larger sample sizes is needed to more effectively examine which variables affect suboptimal margins and re-excision for DCIS. We hope these findings can help guide changes in clinical practice that can reduce re-excision rates for DCIS, as undergoing repeat operations incurs financial, emotional, and cosmetic risks for patients as well as increased resource consumption on the healthcare system.

Figure 1. 3D heat map showing association of age at diagnosis and primary tumour size with probability of positive margins, with colour from green to red indicating increasing probability.



Surgical Oncology & Gynecologic Oncology Fellows Introductions

Dr. Erika Schmitz – 1st Year Surgical Oncology Fellow

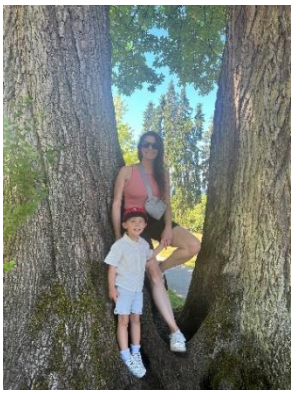
Dr. Schmitz completed Medical School and General Surgery Residency at the University of Ottawa. She is thrilled to continue her training in complex general surgical oncology at the University of British Columbia. She completed the New investigators Clinical Trials course with the Canadian Cancer Trials Group. She has special interest in resource utilization and clinical outcomes in cancer research. Dr. Schmitz can be reached at erika.schmitz1@vch.ca.

Dr. Lior Flor – 2nd Year Surgical Oncology Fellow

Dr. Flor is originally from the Greater Toronto Area. He went to undergrad at Western University and completed medical school and general surgery residency at the University of Toronto. He is currently in his first-year of fellowship in complex surgical oncology at The University of British Columbia. When not working he enjoys spending time with his wife Jesse, playing with his dog, biking, and exploring Vancouver and British Columbia. Dr. Flor can be reached at lior.flor@vch.ca.

Dr. Kathryn McCrae – 2nd Year Gynecologic Oncology Fellow

Dr. Katie McRae grew up in Halifax Nova Scotia and went to medical school at the University of Toronto. She continued her voyage west and completed residency in obstetrics and gynecology at the University of British Columbia. She is currently a second year fellow in gynecologic oncology at VGH. Her research interest is endometriosis-associated cancer. Her favourite meal is pizza and she love to ski and swim. She really enjoys collaborating with other surgical specialties in the OR. Dr. McCrae can be reached at kathryn.mcrae@vch.ca.

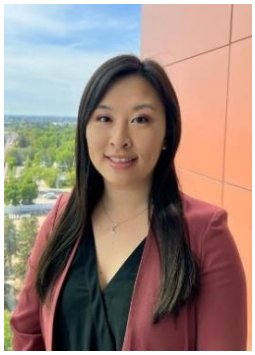


Dr. Elizabeth Clement – 2nd Year Colorectal Fellow

Dr. Elizabeth Clement is currently the clinical colorectal surgery fellow at St. Paul's Hospital. She received her medical degree from Queen's University in Kingston, Ontario, and then completed her residency in general surgery at the University of Alberta in Edmonton. She is thrilled to now be finishing her training in Vancouver. Dr. Clement's academic focus is on communication. Her research includes exploring the benefits of multidisciplinary rounds for both patients and doctors, as well as novel methods to explain operative and perioperative processes to patients. She recently received a grant that is helping to fund a study on the use of a graphic narrative – also known as a comic – to help consent patients for surgery. Outside of the hospital, Dr. Clement enjoys running along the seawall and spending time with her husband, Matt, and three-year-old son, Hugh. Dr. Clement can be reached at eclement1@providencehealth.bc.ca.

Dr. Gurdial Dhillon – 1st Year Gynecologic Oncology Fellow

Dr. Gurdial Dhillon grew up in India until his family immigrated to Canada when he was teenager. His medical education took him around the world and he did medical school in Newcastle, United Kingdom. He then moved to Philadelphia for residency in obstetrics and gynecology. He finally came home to BC and is currently a first year fellow in gynecologic oncology. He is interested in translational research and hopes to have a career as a clinician investigator. He loves meeting new people, reading fiction, running, and hiking with his dog Bodhi. Dr. Dhillon can be reached at gurdial.dhillon@ubc.ca.



Dr. Christine Li – 1st Year Colorectal Fellow

Dr. Christine Li completed her undergraduate and medical school training at McMaster University in Hamilton, Ontario. She then went on to complete general surgery residency at the University of Alberta. She has been slowly moving further west and is now rounding off her training in colorectal surgery. Dr. Li will also be concurrently completing the Master of Health Administration program while here at The University of British Columbia. Her research interests include surgical innovation, medical education, and addressing areas of need in surgery with a systems-based approach. She places a priority on mentorship within surgery and has been extremely lucky to work with many strong personal and professional mentors through her training. Dr. Li can be reached at ccl@ualberta.ca.

Mismatch Repair Testing in Gastrointestinal Cancers: An Essential Insight

Dr. Erika Schmitz, 1st Year Surgical Oncology Fellow

Microsatellites (MS), or Short Tandem Repeats (STR), are repeated simple sequences of 2-10 nucleotides that are naturally distributed across the genome. Microsatellites are especially prone to slippage by DNA polymerases during DNA replication, resulting in a mismatch between strands. Typically, these replication errors are repaired by the mismatch repair (MMR) mechanism. Epigenic modifications (MLH1 hypermethylation by pathogenic BRAFV600E variant) or mutations to the genes of the

MMR pathway (MLH1, PMS1, PMS2, MSH2) cause a deficient mismatch repair (dMMR) system, and consequently, unregulated DNA replication. This process yields highly polymorphic microsatellites, also known as microsatellite instability (MSI) that may promote further gene mutations relevant in oncogenesis.

In 2022, the College of American Pathologists consensus guidelines reported testing by immunohistochemistry (IHC) for MMR, Polymerase Chain Reaction (PCR) for MSI and validated Next-Generation Sequencing (NGS) for MSI [1]. Detecting MSI/dMMR in tumours flags a possible underlying Lynch Syndrome (LS) [2] or Constitutional Mismatch Repair Deficiency (CMMRD) syndrome, and triggers germline testing, genetic counselling, treatment recommendations and surveillance protocols. The high prevalence of MSI found in 15% of colorectal and 20% of endometrial cancers supports reflex testing for MSI/dMMR in these tumour types as a screen for underlying LS [3]. In an analysis of over 15,000 samples of 50 tumour subtypes, 16% of patients with microsatellite unstable tumour were found to have an underlying germline mutation. Notably, 50% of these MSI tumours were not of endometrial nor colorectal origin, of which only 46% did not meet germline testing criteria [2]. The NCCN has since recommended that MSI/dMMR testing be completed regardless of age for small bowel, ovarian, gastric, pancreatic, biliary tract, brain, bladder, urothelial and adrenocortical cancers. Recent advances in cancer immunology have demonstrated immunogenic neoantigens in these hypermutated tumours that can be targeted by immune checkpoint inhibitor therapy, more specifically anti-PD1 therapy [4, 5]. The efficacy of pembrolizumab in MSI/dMMR tumours was demonstrated in the landmark phase 2 KEYNOTE-016, KEYNOTE-164, KEYNOTE-012, KEYNOTE-028, and KEYNOTE-158 trials. The evidence supported accelerated FDA approval for pembrolizumab in advanced solid MSI/dMMR tumours in 2017, followed by an overwhelming drive to support pan-cancer testing, trials and development of Cancer Immunotherapy Guidelines by the Society for Immunotherapy of Cancer [6]. For the general surgeon and surgical oncologist, a summary of clinical implications of MSI/dMMR positivity in gastrointestinal cancers is outlined in Table 1.

Table 1. Clinical Implications of MSI/dMMR positivity in gastrointestinal cancers

Gastric	• MSI is present in 10-22% of all gastric cancers, and is associated with earlier stage of presentation, and Lauren intestinal phenotype [7] • Reflex MSI/MMR should be considered on all localized or metastatic malignant endoscopic biopsies as results may inform need for germline testing. • Patients with advanced gastric cancer often have a poor response to neo-adjuvant chemotherapy with unchanged overall survival[8]. Further evidence is required for immunotherapy in the neo-adjuvant setting. • In unresectable and stage IV gastric cancer, initiation of immunotherapy with chemotherapy or targeted therapy should be considered as first line therapy. • Strong consideration should be made for review of all patients with gastric cancer at multidisciplinary tumor conference to individualize treatment and facilitate possible clinical trial enrolment
Small bowel	• Consider MSI/MMR testing in all patients with small bowel cancer • Consider review at multidisciplinary tumor conference and/or clinical trial enrolment
Colon	• MSI is present in 15-20% of stage II, 8-12% of stage III and 5% of stage IV CRC and is associated with improved overall survival compared to MSS tumors. • Reflex MSI/MMR should be performed on all malignant endoscopic biopsies as results may inform need for germline testing, and influence extent of surgical resection (i.e. total abdominal colectomy) [9] • Consider multi-gene panel germline testing for all early onset colorectal cancer patients (age <50 years) [10] • In MSI/dMMR colon cancer, there is limited response to 5-FU-based chemotherapy [11, 12] Consideration should be made for oxaliplatin-based therapy. • In unresectable or stage IV colon cancer, consider initiation of pembrolizumab as first line of therapy. • Consider review at multidisciplinary tumor conference and/or clinical trial enrolment
Rectum	• Reflex MSI/MMR testing should be performed on endoscopic biopsies as results may inform need for germline testing, and findings may regress after neo-adjuvant radiotherapy [13] • Consider multi-gene panel germline testing for all early onset colorectal cancer patients [10] • Neo-adjuvant immunotherapy may be considered for locally advanced rectal cancer as part of clinical trial. • Strongly consider review of all patients with rectal cancer at multidisciplinary tumor conference to individualize treatment and facilitate possible clinical trial enrolment.

Advances in cancer genomics and immunotherapy is expected to dramatically change the landscape of cancer care. Ongoing and further trials are expected to address many clinical questions, including the role of immunotherapy in the neo-adjuvant and adjuvant settings for gastrointestinal cancers, use as curative intent therapy and pathways for resistance to treatment. Until then, testing for MSI is an important tool at our disposal that can dramatically improve oncologic care and is recommended in all gastrointestinal and Lynch-related cancers.

References for this article can be found on the BC Cancer Surgery Network Website.

PRRT for Small Bowel Neuroendocrine Tumours

Dr. Lior Flor, 2nd year Surgical Oncology Fellow

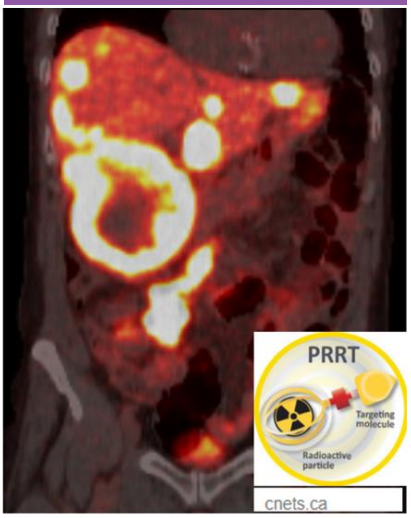
PRRT is a molecular targeted internal radiotherapy used in the management of metastatic gastrointestinal neuroendocrine tumours (NETs). It exploits the fact that many NETs overexpress somatostatin receptors. Radioactive isotopes, such as lutetium-177, are coupled with somatostatin analogs, such as octreotide or DOTATATE. Once injected, these peptides bind to receptors on tumour cells, delivering a targeted dose of radiation and minimizing damage to healthy tissues. [1, 2]

Landmark Trial: The NETTER-1 study is a landmark phase 3 trial published in the New England Journal of Medicine in 2017 by Strosberg et.al. demonstrating the efficacy of PRRT. The trial compared Lutathera (lutetium-177 dotatate) versus long-acting octreotide in the treatment of patients with well-differentiated metastatic midgut NETs. There was a significant improvement in progression-free survival (65% vs 11% at 20 months) and response rate (18% vs 3%) in patients treated with PRRT. This landmark trial secured regulatory approval for PRRT. [3]

Indications for PRRT: Eligible patients are those with unresectable well differentiated midgut NETs that demonstrate avidity on DOTATOC PET/CT and have progressed on somatostatin analogue. Patients are discussed at BC Cancer GI tumour conference to assess for candidacy. Currently in BC, PRRT is funded for midgut NETs and not yet for pancreatic, lung, or hindgut NETs. Pregnant patients, or patients with poor renal, cardiac or hepatic function are excluded. Caution is advised in patients with significant peritoneal disease due to the concern that concentrated radioactivity to adjacent bowel may increase risk of reactive peritonitis or perforation. [4, 5]

Side Effects: PRRT is given intravenously and is generally well tolerated. Some patients may experience nausea and vomiting so all are pre-medicated with antiemetics and a renoprotective amino acid infusion. PRRT can trigger carcinoid crisis so patients are monitored for flushing, hypotension, or bronchoconstriction and octreotide may be required for treatment. Post infusion, patients are monitored for bone marrow suppression, hepatotoxicity, and renal toxicity. PRRT can be repeated every 6-12 weeks often for a total of 4 doses. [6, 7]

68Ga-DOTATOC PET Scan



Radiation Precautions: During and following PRRT administration patients are considered a radiation hazard due to gamma emissions of lutetium-177. PRRT must be performed in a facility with qualified personnel, valid nuclear safety licensing, and an appropriately shielded room. Patients are isolated for 4-5 hours following treatment and have a measured discharge dose rate of less than 25 mSv/hr at 1 meter distance. Specific contact restrictions are guided by local regulations and providers, while general recommendations aim to minimize exposure to children, family, and the public. Typically, external radioactivity is negligible after about 48 hours.

Ideally, elective surgery should be deferred while receiving PRRT. In the event a patient requires an emergency procedure within 48 hours of PRRT administration, healthcare teams should adhere to established radiation safety protocols. Protective equipment such as lead aprons, gloves, and thyroid shields should be employed, especially by team members within 1 meter of the patient or bodily fluids. Pregnant team members should avoid exposure altogether when feasible. A local radiation safety officer or nuclear medicine expert should be consulted to ensure adherence to best safety practices. The overall radiation dosing and associated risk is low, but recommendations exist to minimize exposure. [7, 8, 9]

References for this article can be found on the BC Cancer Surgery Network Website.

Spring Update Summary 2022/2023

In April 2023, BC Cancer – Surgery's Continuing Professional Development & Knowledge Translation Committee (CPD-KT) held its annual Spring Update, a fully accredited MOC event designed to profile specific areas in cancer surgery and care. This year's event focussed on palliative oncology and geriatric care, being conducted in hybrid format, including speakers from across BC and Ontario, with backgrounds ranging from surgical and radiation oncology to physiotherapy and geriatric care. Topics included delivering patient-centred care in the era of MAID, surgical oncology considerations in the geriatric population, pre and post-surgical rehabilitation in the geriatric population, palliative surgery for rectal cancer, palliative gastrectomy for gastric cancer, considerations for palliative radiation, mastectomy in metastatic breast cancer, medical and frailty considerations in older adults undergoing surgery, alongside case presentations and panelist discussions. This event was well attended by multiple disciplines and providers from across the province, both in-person and virtually, and as a mechanism to improve surgical oncology practice knowledge by providing the most current information in the field, the CPD-KT looks forward to hosting its next Update in spring 2024. Please stay apprised of planning developments for the next Update here, where further information will be posted/can be found.

BC CANCER SURGERY NETWORK NEWSLETTER

Executive Editor: Dr. Heather Stuart, Chair - CPD-KT
Managing Editor: Amol Gill, Manager – Provincial Programs

Design and Layout: Pilar Rodriguez, Project Coordinator – Provincial Programs

To submit article ideas or for information, please contact: SurgeryNetwork@bccancer.bc.ca

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. In enhancing 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.