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What provider volume is appropriate for gastric cancer resection? Results of a RAND/UCLA expert panel. *Natalie Coburn,^{**†§} Matthew Dixon,^{*¶} Alyson Mahar,^{**††} Lawrence Paszat,^{‡§} Robin McLeod,[†] Calvin Law,^{**†§} Carol Swallow,[†] Lucy Helyer,^{**} Rajini Seevaratnam,^{*} Roberta Cardoso^{*} and the Gastric Cancer Processes of Care Expert Panel. From the ^{*}Sunnybrook Research Institute, the Departments of [†]Surgery and of [‡]Health Policy, Management and Evaluation, University of Toronto, the [§]Institute for Clinical Evaluative Sciences, Toronto, Ont., the Departments of Surgery, [¶]Maimonides Medical Center, Brooklyn, NY, and ^{**}Dalhousie University, Halifax, NS, and the ^{††}Department of Community Health and Epidemiology, Queen's University, Kingston, Ont.*

Background: Some studies suggest an inverse relationship between volume and mortality. Optimal provider volumes for gastric cancer (GC) are unclear. **Methods:** A multidisciplinary expert panel of 16 physicians from 6 countries scored 24 scenarios. Appropriateness was scored from 1 (highly inappropriate) to 9 (highly appropriate). Median appropriateness scores (AS) from 1 to 3 were considered inappropriate, 4 to 6 uncertain and 7 to 9 appropriate. Agreement was reached when 11 of 16 panelists scored the scenario similarly. If a scenario was agreed to be appropriate, it was given a necessity score in the same manner. The AS and necessity score are reported if agreement was met. **Results:** It is inappropriate for surgeons who perform fewer than 3 GC cases/year to perform multivisceral resection (MVR; AS 1.0–1.5), D2 lymph node dissection (D2 LND; AS 2.0), laparoscopic total gastrectomy (AS 2.0) or endoscopic mucosal resection (EMR; AS 2.0). It is appropriate for a surgeon to have an annual volume of 11–20 cases/year for open gastrectomy (AS 7.5–8.0) or D2 LND (AS 7.0), and 20–50 cases/year for MVR (AS 9.0), laparoscopic gastrectomy (AS 9.0) or EMR (AS 9.0). It is inappropriate for a hospital managing fewer than 5 cases/year to perform D2 LND (AS 2.0) or laparoscopic total gastrectomy (AS 2.0). It is inappropriate for a hospital managing 11–20 cases/year to perform an MVR involving a pancreaticoduodenectomy (MVR-PD; AS 2.0) or EMR (AS 2.5). At least 21 cases/year is an appropriate hospital volume for any GC procedure (AS 7.0–8.0). There was disagreement over the appropriateness of resection at hospitals with volumes of 5–20 cases/year. It is inappropriate for MVR to be performed in a hospital with no interventional radiology services (AS 2.5) and for MVR-PD to be performed at a hospital with no level 1 intensive care unit (AS 1.0). **Conclusion:** The expert panel felt that resection of gastric cancer by extremely low-volume providers was inappropriate for cases more complex than a distal gastrectomy.

Self-renewal as a therapeutic target in human colorectal cancer. *Antonija Kreso,^{**†} Peter van Galen,^{*} Thomas Davis,[‡] Liangxian Cao,[‡] Ramil Baiazitov,[‡] Wu Du,[‡] Nadiya Sydorenko,[‡] Young-Choon Moon,[‡] Eva Szentgyorgyi,[§] Steven Gallinger,^{¶**} Catherine A. O'Brien,^{*¶††} John E. Dick.^{*†}* From the ^{*}Division of Stem Cell and Developmental Biology, Campbell Family Institute for Cancer Research and Ontario Cancer Institute, the [†]Department of Molecular Genetics, University of Toronto, Toronto, Ont., [‡]PTC Therapeutics, South Plainfield, NJ, the Departments of [§]Pathology and [¶]Surgery, Toronto General Hospital, the ^{**}Fred A. Litwin Centre for Cancer Genetics, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, and the ^{††}Institute of Medical Sciences, University of Toronto, Toronto, Ont.

Background: Tumour recurrence following treatment remains a major clinical challenge. Evidence from xenograft models and human trials indicates selective enrichment of cancer-initiating cells (C-ICs) in tumours that survive therapy. Together with recent reports showing that C-IC gene signatures influence patient survival, these studies predict that targeting self-renewal, the key stemness property unique to C-ICs, may represent a new paradigm in cancer therapy. **Methods:** Using primary human colorectal cancer tissue and xenografts, levels of the self-renewal gene *BMI-1* were downregulated through lentivirus-mediated RNA interference, and BMI-1 protein was impaired with BMI-1 inhibitors. **Results:** Here we demonstrate that tumour formation and, more specifically, human colorectal C-IC function are dependent on the canonical self-renewal regulator BMI-1. Downregulation of BMI-1 inhibits the ability of colorectal C-ICs to self-renew, resulting in the abrogation of their tumourigenic potential. Treatment of primary colorectal cancer xenografts with small molecule BMI-1 inhibitors resulted in colorectal C-IC loss with long-term and irreversible impairment of tumour growth. **Conclusion:** Inhibiting a recognized regulator of self-renewal is an effective approach to control tumour growth, providing the first evidence that self-renewal is a clinically relevant target. Thus, targeting the BMI-1 related self-renewal machinery provides the basis for a new therapeutic approach in the treatment of colorectal cancer.

A novel hepatic parenchymal preserving technique in the management of neuroendocrine tumour liver metastases: a feasible approach. *Ashlie Nadler,^{*} Moises Cukier,^{*} Simron Singh,[†] Laurent Milot,[†] Calvin Law.^{**†}* From the ^{*}Division of General Surgery, University of Toronto, and the [†]Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ont.

Background: Aggressive surgical resection of neuroendocrine tumour liver metastases (NET-LM) is associated with symptomatic relief. Debulking up to 90% of tumour burden, even with positive margins, has been shown to be beneficial. However, patients with diffuse hepatic metastases may not qualify for resection owing to associated insufficient remnant liver parenchyma. The purpose of this study is to describe our early experience with a novel hepatic parenchymal preserving (HPP) approach. **Methods:** We retrospectively reviewed our institutional neuroendocrine tumours database (Oct. 2008 to July 2011), identifying 9 patients with NET-LM, including symptomatic patients with extensive bilobar involvement, who underwent perioperative virtual volumetric assessment combined with HPP resection. Clinical and biochemical outcomes were analyzed. **Results:** The jejunum/ileum was the most common primary NET site (78%). Preoperative virtual volumetric assessment revealed liver replacement up to 36%. Patients had from 4 to 50 lesions resected, with positive microscopic margins in all cases. Postoperative virtual volumetric assessment demonstrated more than 70% of normal parenchymal preservation and revealed no residual disease in 78%. Symptomatic improvement was observed in 100% of patients. Postoperative normalization of chromogranin A occurred in 67% and 88% of patients with previously elevated 5-HIAA 24-hour urine levels. Four patients had postoperative complications, with no 90-day mortality. **Conclusion:** The described HPP approach is feasible and safe. Relief of symptoms and decreased biochemical parameters were observed in the majority of cases. This reproducible approach could expand surgical resection options for patients with NET-LM, even with diffuse bilobar involvement.

Inflammatory markers predict survival in liver metastases from colorectal cancer. *Trevor Hamilton,* Derek Leuger,† Karen Kopachuk,† Elijah Dixon,* Francis Sutherland,* Oliver Bathe.** From the Departments of *Surgery and †Statistics, University of Calgary, Calgary, Alta.

Background: The inflammatory state is postulated to contribute to cancer progression. Complex interactions between tumour and the host are still not well understood. Inflammatory cytokines may provide an avenue for determining prognosis in patients with hepatic resection for colorectal cancer (CRC) liver metastases. **Methods:** Data from 70 patients with CRC liver metastases were collected prospectively between 2006 and 2011. Serum samples were tested for concentrations of 42 different inflammatory markers. Survival data were obtained by Kaplan–Meier analysis. Markers were examined with SAM and COX analysis. **Results:** The median patient age was 61, and the majority (66%) were men. A total of 53% had synchronous hepatic metastases at presentation. Elevated C-reactive protein was associated with decreased survival ($p = 0.02$). Five cytokines (GM-CSF, IL-1 β , IL-6, IL-12, IL-15) were associated with an increased inflammatory state. An additional 5 cytokines (IL-3, IL-9, MCP-1, PDGF-AB/BB, TGF- α) were predictive of survival. **Conclusion:** The inflammatory state, which reflects tumour biology and the host response to a given tumour, may influence survival outcomes in patients undergoing hepatic resections for CRC liver metastases.

Resection of multisite metastases from colorectal cancer:

feasibility and interim results of a multicentre prospective phase II study. *Alice C. Wei,* Natalie G. Coburn,† Katharine S. Devitt,* Carol-anne Moulton,* Sean P. Cleary,* Calvin Law,† Paul D. Greig,* Steven Gallinger.** From the *Toronto General Research Institute, University Health Network, University of Toronto, and the †Sunnybrook Research Institute, Sunnybrook Health Sciences Centre, Toronto, Ont.

Background: Resection of intrahepatic metastases (IHM) from colorectal cancer (CRC) is associated with an excellent 5-year survival of up to 60%. But as many as 80% of patients are ineligible for liver resection, many owing to the presence of extrahepatic metastases (EHM). The objective of this study was to evaluate the results of metastasectomy for patients with multisite CRC metastases. **Methods:** A phase II study of metastasectomy for both IHM and EHM from CRC was conducted at 2 high-volume hepato-pancreatic-biliary centres. Eligible patients with IHM and up to 3 foci of EHM, resectable with R0 intent, were identified prospectively and offered metastasectomy. Clinical and survival data were collected and analyzed using standard statistical methods. **Results:** In all, 23 patients were enrolled, with a median age of 56 (32–84) years. Most patients presented with synchronous disease (12 of 23, 52%). The median numbers of IHM, EHM and combined sites were 2, 1 and 3, respectively. The lung was the most common EHM (12 of 23, 52%). Prior to enrollment, 21 of 23 (91%) patients received chemotherapy. Protocol surgery was completed in 18 of 23 (74%) cases, including 12 of 23 (52%) planned sequential resections. Perioperative morbidity and mortality were 9 of 23 (40%) and 1 of 23 (4%), respectively. At last follow-up, 19 of 23 (83%) had developed recurrent disease, with a median disease-free survival of 4 months. **Conclusion:** Complete metastasectomy of multisite CRC is feasible and safe. But for the vast majority of patients, disease will recur quickly. Thus, metastasectomy for multisite CRC metastases should still be considered experimental, and these procedures should be performed in the context of a clinical trial.

Is fine-needle aspiration cytology in symptomatic breast lesions still an important diagnostic modality? *Myles J. Smith,* Cynthia C. Heffron,† Jane R. Rothwell,* Barbara M. Loftus,† Michael Jeffers,† James G. Geraghty.** From the *Department of Surgery, Adelaide and Meath incorporating the National Children's Hospital (AMNCH), and the †Department of Histopathology, AMNCH, Tallaght, Dublin, Ireland

Background: Controversy surrounds the optimal tissue biopsy methodology for the diagnosis of symptomatic breast cancer and the identification of benign disease. Fine-needle aspiration cytology (FNAC) in the context of a rapid assessment breast clinic (RABC) allows same-day diagnosis and early treatment of breast cancer, with the immediate reassurance and discharge of those who have benign disease. We aimed to assess the utility of FNAC in a “one-stop” symptomatic breast triple assessment clinic. **Methods:** We analyzed prospective data accrued from 2004 to 2007. All patients were triple assessed, with FNAC performed on site by 2 consultant cytopathologists. Investigations were reported immediately, and clinical data were captured via a bespoke electronic patient record with closed field data entry. **Results:** There

were 4487 attendances at our RABC, with 1572 FNACs performed. The positive predictive value of FNAC with a C5 cancer diagnosis was 100%, 95.6% for a C4 report, with a complete sensitivity of 94%. The full specificity of correctly identified benign lesions was 77.4%, with a false-negative rate of 3.85%. This enabled 66% of patients attending the RABC to receive a same-day diagnosis of benign disease and discharge. **Conclusion:** Fine-needle aspiration cytology is highly accurate in the diagnosis of symptomatic breast cancer in an RABC; FNAC allows accurate diagnosis of benign disease and immediate discharge of the majority of patients. In this era when the large majority of patients have benign disease, we believe that FNAC provides an equivalent, if not better, method of evaluation of patients in a triple assessment RABC.

The effect of surgery on recurrence and survival of young women with breast cancer. Pamela Hebbard,* Nancy Baxter,^{†‡} Lingsong Yun,[†] Eileen Rakovitch,[§] Frances Wright,[¶] Ellen Warner, David McCready,^{††} Nicole Hodgson,^{‡‡} May Lynn Quan.*** From the *Department of Surgery, Foothills Medical Centre, University of Calgary, Alta., the †Institute for Clinical Evaluative Sciences, University of Toronto, the ‡Department of Surgery and Keenan Research Centre, St. Michael's Hospital, University of Toronto, and Department of Health Policy Management Evaluations, University of Toronto, the §Department of Radiation Oncology, the ¶Division of Surgical Oncology and the **Department of Medical Oncology, Sunnybrook Health Sciences Centre, University of Toronto, the ††Department of Surgical Oncology, University Health Network, University of Toronto, Toronto, and the ‡‡Department of Surgery, Juravinski Cancer Centre, McMaster University, Hamilton, Ont.

Background: Breast-conserving therapy (BCT) and mastectomy are equivalent treatments for breast cancer, but outcomes have not been specifically studied in very young patients. Because guidelines, such as those by the National Comprehensive Cancer Network, recommend mastectomy over BCT in young women without good evidence, we sought to study surgical treatment and outcomes in young women with breast cancer in the population. **Methods:** This is a retrospective cohort study including all women ages 18–35 diagnosed with invasive breast cancer in Ontario from 1994 to 2003, identified through the Ontario Cancer Registry. Demographic, tumour, treatment and outcome (recurrence and survival) variables were obtained through primary chart abstraction. Data on death were determined using the Ontario Registered Persons Database. **Results:** In all, 1556 young women with a diagnosis of breast cancer were included in our cohort; 1415 had surgery (759 [54%] BCT and 656 [46%] mastectomy). Median follow-up was 12 years. Locoregional recurrence occurred in 120 (16%) BCT patients and 120 (18%) mastectomy patients. When controlling for known confounding variables, there was no difference in overall survival between BCT and mastectomy groups (hazard ratio 1.2, $p < 0.08$). **Conclusion:** We have demonstrated that young breast cancer patients selected for BCT do not have worse survival than those undergoing mastectomy. Locoregional recurrence is high in both groups. Further research is needed to accurately predict the best surgical treatment in individual patients in this high-risk population.

Survival and selection criteria for cytoreductive surgery in patients with peritoneal carcinomatosis from colorectal cancer: results from a prospective Canadian cohort. Yarrow J. McConnell, Lloyd A. Mack, Walley J. Temple. From the Tom Baker Cancer Centre, University of Calgary, Calgary, Alta.

Background: Peritoneal carcinomatosis from colorectal cancer (CRC) has an historical median survival of 6–12 months. In the literature, cytoreductive surgery (CS) with hyperthermic intraperitoneal chemotherapy (HIPEC), combined with systemic chemotherapy, is achieving median survivals of 30–63 months, with a 5-year overall survival of 25%–51%. Disease-free survival and selection criteria are not widely reported. **Methods:** The prospective database of patients undergoing CS+HIPEC at the University of Calgary was searched for those with peritoneal carcinomatosis from CRC. Demographic, clinical and follow-up data were extracted. Statistical analysis included χ^2 and Fisher exact testing for descriptive parameters, Kaplan–Meier survival analysis with log-rank testing for univariate factors and Cox proportional hazard modelling for multivariate analysis. **Results:** Between January 2003 and May 2011, 83 patients underwent exploration for intended CS+HIPEC. Thirteen (15.7%) were unresectable. For the resectable patients, systemic chemotherapy was received by 60.2% preoperatively and 57.7% postoperatively. The peritoneal cancer index (PCI) was less than 10 in 29 patients, 10–20 in 21 patients and greater than 20 in 20 patients. Symptoms (pain, ascites, weight loss, bowel obstruction) were present in 14 patients. The perioperative morbidity (grade III/IV) and mortality were 25.7% and 1.4%, respectively. Median follow-up was 22 months. Median overall and disease-free survival were 30.8 and 11.0 months, respectively; 5-year overall and disease-free survival were 20.2% and 15.0%, respectively. A PCI less than 10 and the absence of symptoms were associated with improved outcomes on multivariate analysis. **Conclusion:** Cytoreductive surgery with HIPEC, combined with systemic chemotherapy, improves long-term survival in select patients with peritoneal spread of colorectal cancer.

How often do level 3 nodes bear melanoma metastases, and does it affect patient outcomes? Carolyn Nessim,* Calvin Law,* Yarrow McConnell,[†] Shachar Sade,* Gregory McKinnon,[†] Frances Wright.* From the *Sunnybrook Health Sciences Centre, the Odette Cancer Centre, University of Toronto, Toronto, Ont., and †Alberta Health Services, the Tom Baker Cancer Centre, University of Calgary, Calgary, Alta.

Background: Limited data exist regarding the necessity of resecting level 3 lymph nodes as part of an axillary dissection for melanoma. The objective of this study was to determine how often the level 3 nodes have metastases in patients with sentinel lymph node (SLN)-positive, palpable and bulky axillary disease and to determine patient outcomes. **Methods:** A retrospective chart review was completed at 2 tertiary care centres of patients with melanoma who had a level 3 axillary dissection. At the time of surgery, the level 3 nodes were sent as a separate specimen. Bulky disease was defined as a large mass in all 3 levels that could not be separated. **Results:** We identified 117 patients: 3%, 18% and 100% of patients with SLN-positive, palpable and bulky

disease, respectively, had further disease in their level 3 nodes. Those with level 3 nodal disease had a worse 3-year overall survival than those who did not (15.2% v. 61.1%, $p < 0.001$). In SLN-positive patients, the 18-month systemic recurrence rate (SRR) was 27%. For patients with palpable and bulky disease, the 18-month SRRs were 65% and 88%, with a median time to metastasis of 13.6 and 2 months, respectively. **Conclusion:** Patients with SLN-positive disease rarely have positive level 3 nodes, and a level 1/2 dissection may be adequate. In light of the rapidity of the development of metastases after surgery, for patients with palpable/bulky disease, the risks and benefits of surgery should be weighed in order to provide patients with appropriate care.

Predicting outcomes of thyroid cancer. *K. Alok Pathak, Andrea Mazurat, Pascal Lambert, Thomas C. Klonsch, Richard W. Nason.* From the Department of Surgery and Anatomy, University of Manitoba, Winnipeg, Man.

Background: Thyroid cancers represent a conglomerate of diverse histological types with equally diverse prognosis. There is no valid prognostic scoring system for the different histological types of thyroid cancer. **Methods:** We built a prognostic nomogram based on the individual patient information from a population-based historical thyroid cancer cohort (1970–2005) with a median follow-up of 152 months. **Results:** Our cohort included 423 (24.9%) male and 1279 (75.1%) female patients with 1550 (91.1%) differentiated thyroid cancers, 66 (3.9%) medullary carcinoma and 69 (4.0%) anaplastic carcinoma. After excluding 17 (1%) unclassified and 55 (3.2%) autopsy-diagnosed thyroid cancers, the disease-specific survival for the remaining 1628 patients was 89.1% at 10 years and 86.1% at 20 years. On multivariate analysis, age, histological type, distant metastasis and extrathyroidal extension were independent determinants of disease-specific survival. The individualized 10-year disease-specific survival was predicted by totalling their weighed scores in the nomogram. On internal cross-validation, the concordance index was 0.83, and the calibration curve was very close to the

diagonal. **Conclusion:** A successful prognostic nomogram was developed to predict outcomes of thyroid cancer.

Long-term outcomes of stenting as a bridge to surgery for acute left-sided malignant colonic obstruction. *Fayez A. Quereshy,* Jensen T.C. Poon,† W.L. Law.†* From the *Department of Surgical Oncology, University of Toronto, Toronto, Ont., and the †Department of Surgery, Queen Mary Hospital, University of Hong Kong, Pokfulam, Hong Kong

Background: Stenting as a bridge to surgery has been increasingly applied in cases of acute left-sided colonic obstruction. This study aims to evaluate both the short- and long-term outcomes associated with colonic stenting as a bridge to surgery in patients with obstructing adenocarcinoma of the colon. **Methods:** Patients with potentially curable acute left-sided colonic obstruction treated with stenting as a bridge to surgery (28) or with emergency surgical resection (39) from January 1998 to December 2008 were identified using a prospectively maintained database. Short-term data on postoperative mortality, morbidity, necessity of intensive care and length of hospital stay were compared. Disease-free and overall survival data were also analyzed. **Results:** Patients within the 2 study arms had similar demographic profiles. Patients receiving preoperative stenting had a higher likelihood of a laparoscopic resection ($p < 0.001$). Further, the emergency surgery group had a higher rate of postoperative complications ($p = 0.024$), rate of intensive care unit admission ($p = 0.013$) and longer total length of stay (9 v. 12 d, $p = 0.001$). With a median follow-up of 26.5 and 31.3 months for the stenting and surgical resection groups, respectively, there was no difference in overall and disease-free survival (overall survival 30 v. 31 mo, $p = 0.858$; disease-free survival 13 v. 12 mo, $p = 0.989$). As well, there was no difference in the rate of systemic recurrences (8 v. 13, $p = 0.991$). **Conclusion:** Stenting as a bridge to surgery is a safe treatment strategy in the management of patients with acute left-sided colonic obstruction, with improved short-term outcomes and comparable long-term oncologic results.