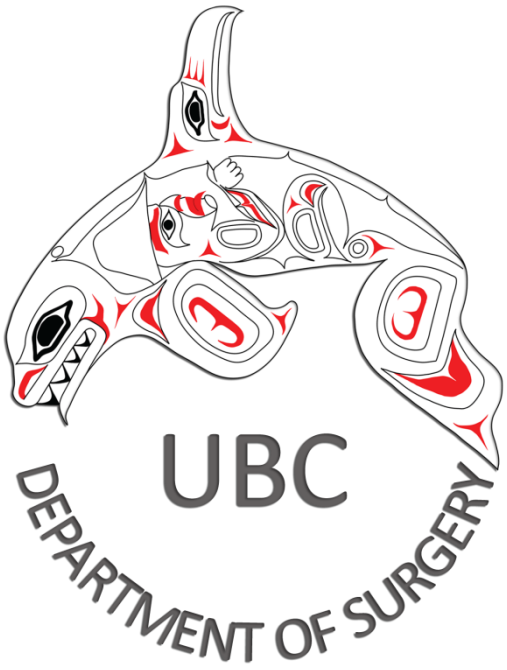
THE SURGICAL TIMES

UBC Department of Surgery November 2014



The 20th Annual

WB & MH Chung Lectureship and Research Day

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The Surgical Times is the Newsletter of the Dept of Surgery. The past editors were two distinguished emeriti professors: Dr. Phil Ashmore and Dr. John MacFarlane. With the advent of electronic communication the Surgical Times is now only printed in paper form once a year for Chung Research Day. Special thanks to *Jane Li* who put together this year's Surgical Times.

UNIVERSITY OF BRITISH COLUMBIA
Department of Surgery
Research Day

20TH ANNUAL W.B. & M.H. CHUNG LECTURESHIP 2014

Invited Lecturer

Dr. Thomas Waddell
Pearson-Ginsberg Chair, Division of Thoracic Surgery,
Head, Division of Thoracic Surgery
University of Toronto
Toronto, Ontario

VANCOUVER GENERAL HOSPITAL

Monday, November 17, 2014

CORDULA AND GÜNTER PAETZOLD HEALTH EDUCATION CENTRE
Main Floor
Jim Pattison Pavilion South

MORNING SESSION -1
Chair: Dr. Gary Redekop

**8 minute paper with 2 minute discussion*

0800 **WELCOME - Dr. Gary Redekop**

0805 **Dr. Sam Wiseman, General Surgery**
Whole Transcriptome Profiling of Thyroid Nodules For Accurate Preoperative Thyroid Cancer Diagnosis

0815 **Dr. Sarah Nicole Hamilton, Radiation Oncology**
Second malignancies after adjuvant radiotherapy for early stage breast cancer: Is there an increased risk with the addition of regional radiation to local radiation?

0825 **Dr. Alan Nichol, Radiation Oncology**
A phase II study of whole brain radiotherapy with simultaneous integrated boost using volumetric modulated arc therapy for one to ten brain metastase

0835 **Christopher Dickman, Otolaryngology**
Serum miRNAs and Their Role as Biomarkers for Oral Squamous Cell Carcinoma

0845 **Dr. Perry Gdalevitch, Plastic Surgery**
Effects of Nitroglycerin Ointment on Mastectomy Flap Necrosis in Immediate Breast Reconstruction: A Randomized Controlled-Trial

0855 **Dr. Karen Slater, Plastic Surgery**
Autologous Breast Reconstruction In Women Over vs. Under 65 Years of Age: A Multi-Centre Analysis

0905 **Dr. Ameen Amanian, Otolaryngology**
Identification of potential risk factors associated with development of synechiae following functional endoscopic sinus surgery: A retrospective review

0915 **Dr. Daniel Mendelsohn, Neurosurgery**
Patient and Surgeon Exposure to Radiation during Intraoperative CT-Based Spine Navigation

0925 **Dr. David Wilson, Engineer in Scrubs**

0935 ***REFRESHMENT BREAK***

MORNING SESSION - 2

1000 **Dr. Yasmin Halwani, General Surgery**
Transanal Minimally Invasive Surgery (TAMIS): Review of Initial Experience

1010 **Dr. Grace Chan, Pediatric General Surgery**
Audit of Emergent and Urgent Surgery for Acutely Ill Pediatric Patients: is Access Timely?

1020 **Dr. Michael Bleszynski, General Surgery**
Surgical Abdominal Sepsis: Insight Into Inflammatory Cytokines in Peritoneal Fluid and Serum During Initial Source Control Surgery

1030 **Romy Hoeppli, General Surgery**
Evaluation of Thymus as a Novel Source of T Regulatory Cells for Therapy after Transplantation

1040 **Ryan Hartwell, Plastic Surgery**
An in-situ forming, bio-hybrid skin substitute system as biological coverage for the fibrotic wound

1050 **Dr. Alison Wallace, General Surgery**
Assessment of Electronic-cigarettes in the Reduction of Postoperative Pulmonary Complications in Smokers Undergoing Thoracic Procedures

1100 ♦ **CHUNG LECTURE**

* **Dr. *Thomas Waddell***

The Role of Research Training in Surgical Education

1200 **Pick-up catered LUNCH**

1230 ♦ **LUNCH and LEARN (**Simultaneous Oral Presentations

Session A Chair – Dr. Fred Kozak

Session B Chair – Dr. Hannah Carolan

Session C Chair - Dr. Dan Luciani

AFTERNOON SESSION
Chair: Dr. Jock Reid

**8 minute paper; 2 minute discussion*

1330 **Dr. Ronak Rahmanian, Pediatric General Surgery**
Placing the port: Location matters

1340 **Dr. Nazgol Seyednejad, General Surgery**
Unplanned Admissions Following Daycare Laparoscopic Cholecystectomy

1350 **Dr. Paul Mick, Otolaryngology**
Hearing Loss is Associated with Poorer Ratings of Patient-Physician Communication and Healthcare Quality

1400 **Dr. Diana Song, Plastic Surgery**
What is the Best Way to Track Surgical Complications? Comparing ACS NSQIP versus Traditional M&M Rounds

1410 **Dr. Aaron Knox, Plastic Surgery**
If a picture is worth a thousand words, is a video worth a thousand pictures? Comparing Dynamic vs. Static Instructional Multimedia for Learning Complex Surgical Skills

1420 **Dr. Victoria Cheung, General Surgery**
Resident Attrition from Surgical Specialties in Canada

Reception and Dinner (RSVP required)

1830 Reception – Vancouver Aquarium

1900 - Presentation of Annual Faculty Awards and Research Day Awards in the Goldcorp Theatre

1930 Dinner among the fish

LEARNING OBJECTIVES

1. **Describe and evaluate the clinical, education and basic science research being conducted in the Department of Surgery.**

2. **Discover new and innovative research techniques.**

3. **Participate in the collaborative research environment within the Department of Surgery.**

Accredited by:

ACCREDITATION:

This event is an Accredited Group Learning Activity eligible for up to 6 Section 1 credits as defined by the Maintenance of Certification program of the Royal College of Physicians and Surgeons of Canada. This program has been reviewed and approved by UBC Division of Continuing Professional Development. Each physician should claim only those credits he/she actually spent in the activity.

Lunch and Learn

Simultaneous Session A

Paetzold Multipurpose Room, 12:30 -13:30,
Chair – Dr. Fred Kozak

Abstract #	Division	First Author *Last Author*	Abstract title
A01	General surgery	Paul D'Alessandro *Gerri Frager*	Operating theatre: medical humanities increase empathy and inter-professionalism in first year surgical residents
A02	Plastic surgery	Aaron Knox *Dimitri Anastakis*	Challenges When Measuring Cognitive Load in Novice Medical Trainees Using Dynamic or Static Multimedia to Learn Surgical Skills
A03	Plastic surgery	Benjamin Chan *Aziz Ghahary*	Pre-clinical/manufacture validation of a novel biohybrid skin substitute
A04	Pediatric general surgery	Nick Zhygan *Geoffrey Blair*	Predictors of low APGAR score following emergency cesarean section and surgical care at a regional referral hospital in rural Uganda
A05	Plastic surgery	Mohammadreza Pakyari *Erin Brown*	Development of non-rejectable skin graft by induction of local immune tolerance
A06	Plastic surgery	Mohsen Khosravi-Maharlooei *Aziz Ghahary*	Intra peritoneal injection of IDO-expressing fibroblasts increases the survival of skin allografts through induction of tolerogenic dendritic cells and regulatory T cells
A07	Otolaryngology	Alykhan Rajwani *Amin Javer*	Omalizumab therapy for refractory allergic fungal rhinosinusitis patients with moderate or severe asthma
A08	Otolaryngology	Al-Rahim R. Habib *Amin Javer*	Sinonasal Outcome Test-22 as a Tool to Identify Chronic Rhinosinusitis in Adults with Cystic Fibrosis
A09	Plastic surgery	Krista Genoway *Anthony Papp*	The safety, efficacy and patient outcomes following new major burn clinical practice guideline implementation
A10	Otolaryngology	Joshua Gurberg *Jeffrey Ludemann*	Pediatric First Branchial Cleft Anomalies: Management of the Facial Mass and the Occasionally Novel Otologic Malformation
A11	Otolaryngology	Joshua Gurberg *Desmond Nunez*	The Canadian Contribution to the Otolaryngology Literature: a Five Year Bibliometric Analysis
A12	General surgery	Shahrzad Joharifard *Seyed Morad Hameed*	ACCESS: The Design of a Novel Tablet-Based Consultation, Elective Admission, and Patient Rounding List "App" for General Surgical Services at Vancouver General Hospital

Lunch and Learn

Simultaneous Session B

Paetzold Atrium, 12:30 -13:30,
Chair – Dr. Hannah Carolan

Abstract #	Division	First Author Last Author	Abstract title
B01	Radiation oncology	Robert Olson *John French*	Impact of a Multi-pronged Intervention to Improve the Use of Single Fraction Radiotherapy for Bone Metastases Across All BC Cancer Agency Centres
B02	Radiation oncology	J. Conway *R. Olson*	Comparison of Patient-Reported Outcomes with Single versus Multiple Fraction Palliative Radiotherapy for Bone Metastasis
B03	Radiation oncology	Jennifer Locke *Robert Bristow*	NKX3.1 Haploinsufficiency is Prognostic for Prostate Cancer Relapse Following Surgery or Image-Guided Radiotherapy
B04	Radiation oncology	Andrea Lo *Karen Goddard*	A Cross-sectional Cohort study of Cerebrovascular Disease after Radiation Therapy for Craniopharyngioma
B05	Otolaryngology	Charles Yu *Neil K Chadha*	Prevalence and ethnic variation of pre-auricular sinuses in children
B06	Neurosurgery	S. Makarenko *A. Brevner*	Suitability of suprasellar meningiomas for endoscopic endonasal surgery: anatomy and surgical outcomes
B07	Vascular surgery	Jonathan Misskey *York Hsiang*	Fistula Outcomes in Octogenarians: Is a Fistula First Approach Appropriate?
B08	Vascular surgery	Rollin Y. Yu *York N. Hsiang*	Determining the Toe-Brachial Index in Young Healthy Adults
B09	Pediatric general surgery	Phyllis Kisa *Sonia Butterworth*	Major Thrombotic Complications with Lower Limb PICCs in Surgical Neonates
B10	Plastic surgery	Morgan Evans *Anthony Papp*	Treatment of Toxic Epidermal Necrolysis by a Multidisciplinary Team. A Review.
B11	Plastic surgery	Adelyn L Ho *Peter A Lennox*	A Review of Post-mastectomy Irradiation in Two-stage Tissue Expander/Implant Immediate Breast Reconstruction with Acellular Dermal Matrix
B12	Plastic surgery	Layla Nabai *Aziz Ghahary*	Controlled delivery of anti-fibrosis agent, FS2, using biocompatible microspheres: A novel approach to prevention of fibrotic scar formation after surgery

Lunch and Learn

Simultaneous Session C

Paetzold Lecture Theatre, 12:20 -13:30

Chair – Dr. Dan Luciani

Abstract #	Division	First Author Last Author	Abstract title
C01	General surgery	Stephanie Campbell *Brad Hoffman*	The Core Trithorax Group Protein Wdr5 is Essential for Pancreas Progenitor Differentiation
C02	Radiation oncology	Pier-Luc Clermont *Cheryl D. Helgason*	Polycomb-Mediated Silencing in Neuroendocrine Prostate Cancer
C03	General surgery	Nicholas AJ Dawson *Megan K Levings*	Development of high-dimensional mass cytometry for immune monitoring in hematopoietic stem cell transplant patients
C04	General surgery	Nicole A. J. Krentz *Francis C. Lynn*	Increasing G1 Length During Pancreatic Progenitor Cell Differentiation
C05	Otolaryngology	James Lawson *Cathie Garnis*	Mechanisms and Impacts of Exosomal microRNAs on Lung Adenocarcinoma Tumorigenesis
C06	General surgery	Dominika Nackiewicz *Jan A. Ehses*	Resident islet macrophages are M2 skewed in models of islet inflammation and type 2 diabetes in an effort to limit inflammation and beta cell damage
C07	General surgery	Yoo Jin Park *Lucy Marzban*	Blocking IL-1 Receptor Signaling Restores Impaired Processing of Pro-Islet Amyloid Polypeptide and Reduces Amyloid Formation in Human Islets: Implications in Clinical Islet Transplantation
C08	General surgery	Alexis Shih *Dan S. Luciani*	Bcl-xL Regulates Pancreatic Beta-cell Function and Dysfunction during Glucotoxic Stress
C09	General surgery	Thilo Speckmann *Francis Lynn*	Regulation Of Npas4 Expression And Stability In Pancreatic Beta Cells
C10	Thoracic surgery	Annika C *Garth L. Warnock*	Novel roles of the negative co-stimulatory molecule B7-H4 in ?-cell function and ER stress signaling
C11	General surgery	Bryan R. Tennant *Brad G. Hoffman*	Myt3 mediates ECM induced islet migration via regulation of Tgfbi
C12	General surgery	Dan Wu *Megan Levings*	Investigating the function of tribbles proteins in regulatory T cells
C13	General surgery	Eric E Xu *Francis C Lynn*	Sox4 cooperates with Neurogenin3 to regulate endocrine pancreas formation
C14	General surgery	Yun Zhang *Lucy Marzban*	Amyloid Formation Reduces Phospho-PKB Levels in Islet Beta Cells via IL-1 Beta Signaling Pathway

Message from the Chair, Dr. Gary Redekop

The WB & MH Chung Research Day provides an opportunity for our large and diverse Department of Surgery to highlight the wide range of basic and clinical research conducted by our faculty and trainees. The program includes topics ranging from pure basic science to translational research and clinical outcome studies.

We are honored to have Dr. Thomas Waddell as our visiting Chung lecturer. Dr. Waddell is the Pearson-Ginsberg Chair, Division of Thoracic Surgery, University of Toronto and Head of the Division of Thoracic Surgery at University Health Network. His laboratory focuses on alternative approaches to the chronic shortage of donor lungs, especially stem cell and regenerative medicine. His clinical interests include lung transplantation and lung volume reduction surgery, lung cancer and minimally invasive and robotic thoracic surgery.

Our day will conclude with an awards reception and dinner at the Vancouver Aquarium. This venue will provide an outstanding setting in which to celebrate our Department's success in the creation of new health knowledge through research, and an opportunity to foster an atmosphere of collaborative research and interaction.

I would like to recognize the energy and creativity that Dr. Alice Mui has once again contributed to the success of the Chung Research Day. Alice and her organizing committee have carefully reviewed many abstracts and submissions and selected a cross section of high quality representative projects, which will be presented in a variety of formats. Thank you Alice!

I would also like to acknowledge the outstanding accomplishments of the many faculty, residents, fellows, and graduate students in the Department of Surgery, and sincerely hope that you will share with me a deep satisfaction that comes from noting our Department's many research activities.

Gary Redekop

Head, Department of Surgery

November 2014

The Benefactors

FOUNDERS OF THE W.B. AND M.H. CHUNG LECTURESHIP

Prior to the establishment of the W.B. and M.H. Chung Research Day, the Dept of Surgery only had Division specific research days. In 1995, the Dr. W.B. and M.H. Chung created an endowment that allows us to hold an annual research day that has become the premier, department-wide event at which we recognize our research achievements

Wallace B. Chung, MDCM, FRCSC, DSc '94

Dr. Chung was born and raised in Victoria, British Columbia. After pre-medical education at Victoria College and UBC, he attended the McGill University medical school and received his M.D. in 1953. Following internship and surgical residency training at VGH and UBC, Dr. Chung was appointed to the Dept of Surgery at UBC as an Instructor in 1960. After being appointed to an Assistant Professor in 1961, Dr. Chung rose quickly through the ranks to become a full Professor in 1972. For his many professional and community contributions, Dr. Chung has received many awards, including being appointed to the Order of Canada in 2005.

- ***Professional Career***

Dr. Chung was noted as a technically gifted surgeon who pioneered Vascular Surgery in Western Canada. In particular, Dr. Chung was known for his excellent surgical results for carotid artery surgery for transient ischemic attacks. He established Vascular Surgery as a new specialty in BC, and as a separate division of surgery at VGH and UBC. He was one of founders of the Canadian Society for Vascular Surgery, and served as its president in 1982. Throughout his academic career, Dr. Chung has taken positions of responsibility (appointed University Head of the Division of General Surgery in 1970, Head of the University Division of General and Vascular Surgery in 1978, Head of the Department of Surgery at the University Hospital in 1981). During his nine year tenure he built the University Hospital Dept of Surgery into an excellent academic unit with international recognition for vascular surgery and gastrointestinal surgery. He was also the Governor of the American College of Surgeons from 1980 to 1986. Dr. Chung has received many awards for his teaching and service, including being honoured by the vascular surgeons of British Columbia with a named day – The Wallace B. Chung Clinical Day.

- ***Community Service***

Dr. Chung has also been an effective and tireless pillar of the community. He has used his extraordinary gifts of wisdom and diplomacy to help advance the integration of the Chinese Community. He was one of the founding executives of the Chinese Cultural Centre of Vancouver serving as Chair from 1983-87. Under Dr. Chung's leadership, the Centre has become a model for other multicultural programs in Canada. Among his other community activities, Dr. Chung is a founding member and patron of the Sun Yat-Sen Gardens, served on the Board of Directors International Dragon Boat Festival Society, and Vice Chair of the Canadian Multiculturalism Council. Dr. Chung's contributions have been recognized by awards (Chinese Cultural Centre Outstanding Achievement Award in 1989 and Chinese Benevolent Association Outstanding Citizen Award in 1990) and his appointment to the B.C. Heritage Trust in 1993.

- ***History Scholar***

An avid reader and collector of first edition rare books, Dr. Chung became a renowned authority and collector of one of Canada's best libraries on the history of the Pacific Northwest exploration and Chinese Canadian immigration. Due to his interest in the Canadian Pacific Steamship Company, Dr. Chung was a guest curator of the Vancouver Maritime Museum for the "Empress to the Orient Exhibition" in 1991. In recognition of this interest, the Vancouver Maritime Museum has named its library, the W.B. and M.H. Chung Library. In 1999 he made a gift of more than 25,000 rare and unique items to the University of British Columbia. The Chung Collection is housed in the Ike Barber Learning Centre (http://chung.library.ubc.ca/) and attracts scholars and visitors from around the world.

Madeline Chung, MD, FRCSC

Dr. Madeline Chung was born in Shanghai, China. Her medical education took place at the Yale Medical College of China. She did her internship in Victoria, B.C. followed by specialty training in Obstetrics and Gynecology in Montreal and at the Mayo Clinic in Rochester, Minnesota. Upon coming to Vancouver in the late 1950's, she was the first female and first Chinese-Canadian specialist in Obstetrics and Gynecology in British Columbia. She was appointed as a Clinical Instructor at the University of British Columbia and by the time of her retirement she had delivered over 6,500 babies over a 40 year career, and held the rank of Clinical Professor. Shortly after her retirement from clinical practice she was made an Honorary Life Member of the College of Physicians & Surgeons of British Columbia. Dr. Madeline Chung is also a Clinical Professor Emeritus of the Dept of Obstetrics and Gynecology in the Faculty of Medicine at the University of British Columbia.

- ***Physician***

She was known as a compassionate and empathic physician who gave freely and willingly of her time to her patients, often acting as a counselor to her patients and mentor to the children and adults who she had previously delivered. Frequently, the children she delivered would return to see Madeline years later when it was time for them to have their own babies.

- ***Community Service***

Dr. Madeline Chung extended her philosophy of volunteerism and service to the community in all aspects of her life. Not only was this evident in her professional life but was active in her church and community as well. She served on boards of the Chinese United Church, the Vancouver Academy of Music, and was the founding Executive Director of the True Light Chinese School in Vancouver. Well into her eighties, she was given an honorary graduation certificate from York House School in recognition of her contributions to the school.

- ***Family***

Despite her tireless devotion and dedication to her patients she was still able to balance a healthy family life providing endless support to her husband, Wally, while raising two children who felt inspired enough by their home life to pursue careers in medicine. Their daughter Dr. Maria Chung is in the Division of Geriatric Medicine at the University of British Columbia. Their son Dr. Stephen Chung is the past University of British Columbia Head of the Division of General Surgery and the current Vancouver General Hospital Head of Hepatobiliary & Pancreatic Surgery. Late in her career, she experienced a life-threatening illness but was able to return to full-time work. At the same time, she was the primary caregiver to her elderly mother whom she looked after in her home.

Currently, Dr. Madeline Chung's most enjoyable role is that of a busy grandmother chasing after five active grandchildren.

Chung Lecture 2014

The role of research training in surgical education

Dr. Thomas Waddell

Chair, Division of Thoracic Surgery, University of Toronto
Professor, Department of Surgery, University of Toronto
Head, Division of Thoracic Surgery, UHN
Senior Scientist, Toronto General Research Institute, UHN

Dr. Waddell is the Pearson-Ginsberg Chair, Division of Thoracic Surgery, University of Toronto and Head of the Division of Thoracic Surgery at University Health Network. His laboratory focuses on alternative approaches to the chronic shortage of donor lungs, especially stem cell and regenerative medicine approaches to lung disease. His clinical interests include lung transplantation and lung volume reduction surgery, lung cancer and especially minimally invasive and robotic thoracic surgery.

Plenary Presentations

P01 **Sam Wiseman,** General Surgery

Title: Whole Transcriptome Profiling of Thyroid Nodules For Accurate Preoperative Thyroid Cancer Diagnosis

Sam Wiseman BSc, MD, FRCSC, FACS Department of Surgery, Division of General Surgery, St. Paul's Hospital & University of British Columbia

Background: Due to the limitations of fine-needle aspiration biopsy (FNAB) cytopathology, many individuals who present with thyroid nodules eventually undergo thyroid surgery to diagnose thyroid cancer.

Objective: The objective of this study was to use whole-transcriptome profiling to develop and validate a genomic classifier that significantly improves the accuracy of preoperative thyroid cancer diagnosis.

Methods: Nucleic acids were extracted and amplified for microarray expression analysis on the Affymetrix Human Exon 1.0 ST GeneChips from 1-mm-diameter formalin-fixed and paraffin-embedded thyroid tumor tissue cores. A training group of 60 thyroidectomy specimens (30 cancers and 30 benign lesions) were used to assess differential expression and for subsequent generation of a genomic classifier. The classifier was validated in a blinded fashion on a group of 31 formalin-fixed and paraffin-embedded thyroid FNAB specimens.

Results: Expression profiles of the 57 thyroidectomy training and 31 FNAB validation specimens that passed a series of quality control steps were analyzed. A genomic classifier composed of 249 markers that corresponded to 154 genes, had an overall validated accuracy of 90.0% in the 31 patient FNAB specimens and had positive and negative predictive values of 100% and 85.7%, respectively. The majority of the identified markers that made up the classifier represented nonprotein-encoding RNAs.

Conclusions: Whole-transcriptome profiling of thyroid nodule surgical specimens allowed for the development of a genomic classifier that improved the accuracy of preoperative thyroid cancer FNAB diagnosis.

P02 **Sarah Nicole Hamilton,** Radiation Oncology

Title: Second malignancies after adjuvant radiotherapy for early stage breast cancer: Is there an increased risk with the addition of regional radiation to local radiation?

Sarah Nicole Hamilton, MD,[1,2] Scott Tyldesley, MD,[1,2] Dongdong Li MSc[3], Robert Olson MD[4], Mary McBride MSc[3; 1]Department of Surgery, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia; [2]Department of Radiation Oncology, British Columbia Cancer Agency – Vancouver Centre, Vancouver, British Columbia; [3]Cancer Control Research Department, British Columbia Cancer Agency – Vancouver Centre, Vancouver, British Columbia; [4]Department of Radiation Oncology, British Columbia Cancer Agency – Centre for the North, Prince George, British Columbia

Purpose: To determine if there is an increased risk of second malignancies (SM), particularly lung cancer, in early stage breast cancer patients (pts) treated with the addition of nodal fields to breast/chest wall radiotherapy (RT).

Materials/Methods: Subjects were Stage I/II female breast cancer pts age 20-79 years (yrs) diagnosed from 1989-2005 and treated with adjuvant RT at our institution. Pts were included if they survived >3 yrs after diagnosis and did not have a SM within 3 yrs of diagnosis. Standardized incidence ratios (SIR) with 95% confidence intervals (CI) were calculated to compare SM incidence to the cancer incidence in the general age-matched population. SM risks in pts treated with local RT (LRT) to the breast/chest wall were compared to pts treated with locoregional RT (LRRT) to the breast/chest wall and regional nodes using multivariable regression analysis (MVA) to adjust for age, stage, laterality, grade, estrogen receptor (ER) status, type of surgery, chemotherapy, hormone therapy, yr of diagnosis and relapse.

Results: The cohort includes 12,836 pts with a median follow-up of 8.4 yrs and 4789 pts at risk beyond 10 yrs. LRRT was used in 18% of pts. Pts receiving LRRT were younger (median age 52 vs 57 yrs) and had higher risk cancer with more Stage II (98% vs 31%), Grade 3 (43% vs 28%) and ER negative (24% vs 18%) disease (all p<0.0001). Pts treated with LRRT had higher rates of mastectomy (46% vs 3%), chemotherapy (78% vs 26%), hormone therapy (68% vs 50%) and relapse (17% vs 13%, all p <0.0001). Overall, 1119 pts (8.7 %) developed a SM. The SIR comparing pts treated with LRT to the general population was 1.29 (CI 1.21-1.38). Excluding second breast cancers, the SIR was 1.10 (CI 1.01-1.19). SIRs were elevated for breast (SIR 1.84, CI 1.66-2.04), uterine (SIR 1.63, CI 1.27-2.07) and ovarian cancer (SIR 1.87, CI 1.36-2.51). No statistically significant increased incidence of in-field malignancies (SIR 1.04, CI 0.87-1.23) and lung cancers (SIR 1.06, CI 0.88-1.26) was detected. The SIR comparing pts treated with LRRT to the general population was 1.39 (CI 1.17-1.64).

Excluding second breast cancers, the SIR was 1.36 (CI 1.11-1.66). SIRs were elevated for breast (SIR 1.46, CI 1.05-1.98) and uterine cancer (SIR 2.13, CI 1.13-3.64). No statistically significant increased incidence of in-field malignancies (SIR 1.26, CI 0.77-1.94) and lung cancers (SIR 1.27, CI 0.76-1.98) was detected.
On MVA comparing the LRRT group to the LRT group, the adjusted hazard ratio was 1.20 for in-field malignancies (CI 0.68-2.16) and 1.26 for lung cancer (CI 0.67-2.36).
Conclusions: No statistically significant increased in-field SM risk was observed with the addition of regional RT to local RT in this cohort of Stage I/II breast cancer pts. The analysis is limited by a modest number of pts with long-term follow up.

P03 ***Omamah Hamad Almousa*****,** Thoracic Surgery

Title: Image-Guided VATS Excision of Small Peripheral Lung Nodules (SPPN) in Patients with Previous Extra-Pulmonary Malignancies

Omamah Almousa, Joyce Leo, John Mayo, Joanne Clifton, Annette McWilliams, Stephen Lam, Kyle Grant, John C. English, Richard Finley

INTRODUCTION: Poor diagnostic accuracy of bronchoscopy, needle biopsy or PET scan of growing SPPN in patients with previous malignancies who are at high risk for metastatic lung cancer leads to requests for VATS wedge resection for pathological diagnosis and accurate management. Failure to visualize or palpate subpleural SPPN at VATS results in thoracotomy.
OBJECTIVES: The purpose of this study is to determine the utility of preoperative CT guided microcoil localization (CTML) of SPPN followed by fluoroscopically guided VATS resection in the management of these nodules.
METHODS: Patients with previous extra-thoracic cancers underwent preoperative localization of undiagnosed SPPN using percutaneously placed CT guided platinum microcoils (CTML). Coils were placed with the distal end deep to the nodule and the superficial end coiled on the visceral pleural surface. Nodules were removed by VATS wedge excision using endostaplers with visualization by intraoperative fluoroscopy and VATS.
RESULTS: Between August 2003 and September, 2013, 50 patients (57% female, mean age 62 yrs) had 58 nodules (median size = 11 mm, depth from visceral pleura = 27 mm) excised using CTML and fluoroscopic guided VATS wedge excision. The previously treated extra-thoracic tumor sites were colorectal (16), breast (10), sarcoma (5), genitourinary (11), melanoma (5), lymphoma (3) other (8). Nodule histology showed metastasis (25/50 patients), benign (11/50) and 14 new Stage 1 primary lung cancer. The CTML procedure allowed diagnostic VATS wedge resection in all cases (median OR and fluoroscopy time = 31 and 1.16 mins). There were no clinically significant complications related to the coil placement, or wedge resection.
CONCLUSIONS: Pre-operative localization of small peripheral pulmonary nodules using percutaneous CT guided microcoil localization followed by fluoroscopic guided VATS resection changed management and influenced the prognosis in 50% of patients with presumed metastasis with minimal morbidity. The 22% of patients with benign disease required no further therapy while the 28% 0f patients with Stage 1 primary lung cancer underwent curative surgical resection.

P04 **Alan Nichol,** Radiation Oncology

Title: A phase II study of whole brain radiotherapy with simultaneous integrated boost using volumetric modulated arc therapy for one to ten brain metastases

Alan Nichol, Michael McKenzie, Roy Ma, Fred Hsu, Arthur Cheung, Lovedeep Gondara, Michael Peacock, Hannah Carolan, Robert Olson, Francois Germain, Devin Schellenberg, Rosie Vellani; Division of Radiation Oncology and Developmental Radiotherapeutics

Background: Local control of brain metastases reduces risk of death from intracranial progression and improves survival in selected patients. Volumetric modulated arc therapy can deliver a fraction of whole brain radiotherapy (WBRT) and a simultaneous integrated boost (SIB) to multiple brain metastases in five 5-10 minute fractions. This is the first registered clinical trial (NCT01046123) to report the results of WBRT & SIB for up to 10 brain metastases.
Objective: The phase II primary endpoint was a comparison of local control, using Response Evaluation Criteria in Solid Tumors, with that of the WBRT (37.5 Gy/15) and stereotactic radiosurgery (SRS: 15-24 Gy/1) arm of the RTOG 95-08 study (94% at 3 months and 80% at 2 years).
Methods: Sixty subjects with 1-10 brain metastases consented to a phase II study of 20 Gy WBRT and 50 Gy SIB in 5 fractions. Treatments were delivered at four of the BC Cancer Agency centres. Eligible subjects had Karnofsky Performance Status (KPS) ≥ 70, maximum diameter of the largest metastasis ≤ 3 cm, and ≥ 6-month median life expectancy. All subject enrolments were approved by a tumour board. Subjects were immobilized in a head shell with a mouth-piece. The SIB covered 98% of the volume of each metastasis with 95-120% of the prescription dose. The treatment was delivered using two axial 360-degree arcs on five consecutive working days with daily online translational setup correction using kV imaging. Overall survival for subgroups with 1-3 and 4-10 metastases were compared. Subjects were followed with clinical assessments and MRI every 3 months.
Results: The median number of brain metastases was 2 in the 1-3 metastases subgroup of 33 subjects and 5 in the 4-10 metastases subgroup of 27 subjects. The median follow-up was 9 months. Actuarial local control was 100% at 3 months and 90% at 2 years. The median survival was 11 months in the 1-3 metastases subgroup and 11 months in the 4-10 metastases subgroup ($p = 0.8$). Seven subjects developed radionecrosis: 2 had grade 4 (required craniotomy but had no permanent neurological deficit); 3 had grade 3 (permanent neurological deficit); and 2 had grade 2 (reversible neurological deficit), for a crude clinical radionecrosis rate of 12% (7/60). The 3-year cumulative incidence of both imaging-only and clinical radionecrosis was 30%. Multivariable analysis of overall survival showed that lower KPS of 70-80 vs. 90-100 (HR = 3.2, $p < 0.004$), presence of extracranial disease (HR = 2.9, $p = 0.04$) and no use of biologically targeted systemic therapy (HR = 7.5, $p = 0.0003$) were associated with worse survival, but age (HR = 0.98, $p = 0.1$) and number of metastases 1-3 vs. 4-10 (HR = 1.1, $p = 0.8$) were not.
Conclusions: With a boost prescription of 50 Gy in 5 fractions, WBRT & SIB demonstrated similar 3-month local control to the WBRT & SRS arm of the RTOG 95-08 trial, but the actuarial rate of late radionecrosis was not acceptable for use in eloquent brain.

P05 **Christopher Dickman,** Otolaryngology

Title: Serum miRNAs and Their Role as Biomarkers for Oral Squamous Cell Carcinoma

Serum miRNAs and Their Role as Biomarkers for Oral Squamous Cell Carcinoma, Christopher Dickman[1], James Lawson[1], Sara MacLellan[1], Yi Huang[2], Jiahua Chen[2], Catherine Poh[3], Cathie Garnis[1,4].
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Background: Individuals with oral cancer have a poor survival rate and a high level recurrence due mainly to the late stage of diagnosis. New methods new methods to address this issue are required in order to increase the survival rate. miRNAs, are a group of small nucleotide molecules, involved in gene regulation that have been linked to tumour suppressing and oncogenic roles in cancer. Circulating miRNA expression profiles have been shown to be useful in delineating healthy individuals from those with various types of cancer.
Objective: We aim to determine the ability of serum miRNAs to act as a biomarker for oral squamous cell carcinoma.
Methods: Serum was collected from patients with oral squamous cell carcinoma (OSCC) and oral carcinoma *in situ* (CIS) as well as demographically matched non-cancer controls. RNA extracted from the serum samples was profiled using miRCURY LNA Universal RT miRNA PCR panels to test the expression of 742 miRNAs. miRNAs known to be affected by haemolysis in blood samples were excluded from analysis. A model to distinguish between OSCC/CIS and non cancer individuals was created using logistic regression on miRNAs included in the model by LASSO analysis, a method that preferentially creates statistical models with fewer miRNAs.
Results: By performing statistical analysis on our samples after they had been randomly split into training and test sets we were able to determine that our model was able to achieve a higher than 80% accuracy in differentiating between cancer and control samples by including 18 miRNAs in our model/biomarker. By including all of our samples in our analysis we discovered a set of miRNAs that are promising for validation on a future independent sample set.

Conclusions: These results show that there is the potential for serum miRNAs to act as a biomarker for oral cancer and provide a set of miRNAs suitable for further analysis. These results could in the future assist with the diagnosis of oral cancer.

P06 **Perry Gdalevitch,** Plastic Surgery

Title: **Effects of Nitroglycerin Ointment on Mastectomy Flap Necrosis in Immediate Breast Reconstruction: A Randomized Controlled-Trial**

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Background: Mastectomy flap necrosis is a common complication of immediate breast reconstruction that impacts recovery time and reconstructive success. Nitroglycerin ointment is a topical vasodilator that has shown to improve skin flap survival in an animal model.

Objective: To evaluate if the application of nitroglycerin ointment to the breast skin after mastectomy and immediate reconstruction causes a decrease in the rate of mastectomy flap necrosis compared to placebo.

Methods: This study was conducted as a randomized controlled trial and included patients aged 21 to 69 years undergoing mastectomy and immediate breast reconstruction at the University of British Columbia affiliated hospitals (Vancouver, Canada). Patients with a medical history that precluded the administration of nitroglycerin were excluded from the study. The target sample size was 400 patients. Nitroglycerin ointment (45mg) or a placebo was applied to the mastectomy skin at the time of surgical dressing.

Results: The trial was stopped at the first interim analysis after 165 patients had been randomized (85 treatment vs. 80 placebo). Mastectomy flap necrosis developed in 27 patients (33.8%) receiving placebo and in 13 patients (15.3%) receiving nitroglycerin ointment; between-group difference = 18.5% (p=0.006, 95% CI: 5.3% to 31.0%). Post-operative complications were similar in both groups (nitroglycerin: 22.4% (19/85) vs. placebo: 28.8%, (23/80)).

Conclusion: In patients undergoing mastectomy and immediate reconstruction, there was a marked reduction in mastectomy flap necrosis in patients who received nitroglycerin ointment. Nitroglycerin ointment application is a simple, safe and effective way to help prevent mastectomy flap necrosis.

P07 **Karen Slater,** Plastic Surgery

Title: **Autologous Breast Reconstruction In Women Over vs. Under 65 Years of Age: A Multi-Centre Analysis**

Diana Song, Karen Slater, Peter Lennox, Nancy Van Laeken, Toni Zhong, Alexes Hazen, Andrea Pusic, Dale Vidal, Michael Papsdorf, Sheina Macadam

Introduction: More than 250, 000 new cases of breast cancer are diagnosed annually in North America, with more than 40% occurring in women age 65 and over. Breast reconstruction post-mastectomy is integral to comprehensive breast cancer management. The overall rate of reconstruction is increasing, however, elderly patients significantly underrepresented. Despite autologous reconstruction demonstrating lower complication and failure rates, a trend towards lower costs, and higher patient satisfaction, the majority of reconstructions in elderly patients are implant-based. This may be attributed to perceived operative risk, complications, and misconception that reconstruction is not important for elderly.

Objectives: To compare outcomes and satisfaction for abdominally-based autologous reconstruction in post-mastectomy patients under 65 versus over 65 years of age.

Methods: A mixed retrospective and cross-sectional study was performed with data from five North American centres (University of British Columbia, New York University, University of Toronto, Memorial Sloan-Kettering Cancer Center, Dartmouth Medical Center) from 2002 -2012. Patients were identified retrospectively and chart reviews were performed for demographic information. Patients were sent the BREAST-Q© questionnaire and a self-addressed, postage-paid return envelope by post. A $5 Starbucks card was included as an incentive to respond. Non-responders were contacted 2 months after the first mail-out. One additional copy of the questionnaire was distributed to non-responders three months after the first mail-out. Additional patient-reported data collected from the questionnaire included: marital status, level of education, employment status, income, ethnicity, and medical history.

Results: A total of 1829 patients were included. 1770 patients were under age 65 and 59 patients were over age 65.Statistically significant differences in age, BRCA status, marital status, and employment status, with women from the older group more likely to be widowed, retired, and BRCA negative. There were no significant differences in complication rates between groups. Older women were more likely to develop infections (p=0.044) or seromas (p=0.033), though these differences were not significant. There were no significant differences in mean BREAST-Q© scores for patient satisfaction and well-being.

Conclusions: Abdominally-based breast reconstruction is a viable option for the elderly post-mastectomy population. Complication rates for abdominally-based autologous reconstruction in women 65 and over are comparable to those for their younger counterparts. In addition, it achieves high patient satisfaction and garners similar psychosocial benefits to those previously demonstrated for younger patients.

P08 **Ameen Amanian,** Otolaryngology

Title: **Identification of potential risk factors associated with development of synechiae following functional endoscopic sinus surgery: A retrospective review.**

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Background: Synechiae formation in the middle meatus is one of the most common complications of functional endoscopic sinus surgery (FESS). Synechiae describes the adhesion of two opposing mucosal surfaces in the nasal cavity that can cause scarring and obstruction of the nasal passage.

Objectives: 1) To determine the incidence of synechiae occurring in a cohort of patients who had undergone FESS; 2) To determine characteristics associated with development of synechiae postoperatively.

Methods: This retrospective study examined CRS patients with or without nasal polyposis that had undergone bilateral FESS at a tertiary rhinology centre. All patients received middle meatal merocel spacers intraoperatively left *in situ* for six days and followed up in clinic at least once per month for the first three months following FESS.

Results: Two-hundred CRS cases with a history of bilateral FESS were retrospectively reviewed. Thirty-eight (19.0%) patients developed synechiae within an average of 60.9 ± 57.8 days post-FESS. Individuals receiving primary sinus surgery and nasal septal reconstruction were strongly associated with the development of post-operative synechiae (OR: 4.5, 95%CI: 1.6,13.0; OR: 4.4, 95%CI: 1.4,13.8). Subject demographics and preoperative factors such as gender, age, nasal polyposis, Lund-Mackay CT score and endoscopic evidence of concha bullosa were not associated with the development of post-operative synechiae.

Conclusion: Patients undergoing primary FESS and nasal septal reconstruction are at greater odds of developing synechiae than those having revision surgery and thus, warrant careful postoperative evaluation. Possible methods of preventing synechiae formation in this population should be evaluated in future studies.

P09 **Daniel Mendelsohn,** Neurosurgery

Title: **Patient and Surgeon Exposure to Radiation during Intraoperative CT-Based Spine Navigation**

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BACKGROUND: Intraoperative imaging is critical in spine surgery for determining the spinal level, visualizing alignment, and guiding implant placement. Imaging modalities include plain x-rays, fluoroscopy with C-arm and intraoperative CT scanning (O-arm). These imaging modalities emit ionizing radiation to the surgical team and the patient.

PURPOSE: The amount of radiation emitted to the patient and the surgeon with intraoperative CT-based spine navigation were compared. The impact of intraoperative CT on the use of intraoperative x-rays and postoperative x-rays and CTs was investigated.

METHODS: An ambispective review of surgical cases using intraoperative CT at Vancouver General Hospital over one year was performed. The number of intraoperative x-rays, fluoro and CT dosages were recorded and standardized to effective doses. The number of peri-operative imaging investigations was compared with a cohort of surgical cases involving only intraoperative x-rays and fluoroscopy. A literature review was performed to enable a comparison of radiation exposure to historical values for fluoroscopic-guided spine instrumentation.
RESULTS: Seventy-three surgical cases involving an average of 5.44 levels of instrumentation were reviewed. Thoracic and lumbar spine instrumentations were associated with the highest radiation emission from all modalities compared to cervical and cases (TL: 5.65 mSv vs. C: 2.19 mSv). Major deformity and degenerative cases involved more radiation exposure than trauma and oncology cases (5.81 mSv vs. 3.54 mSv). On average, the patient was exposed to 5.9 times more radiation compared to the surgical team. Patient exposure was 3 times the values reported in the literature for open thoracolumbar fusions. In comparison, radiation exposure to the surgeon was reduced by 35% compared to conventional fluoroscopically-guided open thoracolumbar fusions and 70% less than minimally invasive thoracolumbar fusions. The average radiation total radiation exposure to the patient was 6.05 mSv, a value less than a single lumbar CT scan (7.5 mSv to 10 mSv). The use of intraoperative CT did not reduce the number of postoperative x-rays or CT scans obtained.
CONCLUSIONS: Intraoperative CT increases the radiation exposure to the patient and reduces the radiation exposure to the surgeon when compared to the fluoroscopic-guidance radiation exposure reported in the literature. Thoracolumbar instrumentations for major deformity and degenerative diagnoses are associated with the highest radiation exposure. Although intraoperative CT can improve the accuracy of spine instrumentation, surgeons should be aware of the increased radiation exposure to the patient compared to conventional fluoroscopy-guidance.

P10 **Victoria Cheung,** General Surgery

Title: Resident Attrition from Surgical Specialties in Canada

Victoria Cheung, MD and Tracy Scott MD FRCSC, University of British Columbia, Division of General Surgery

Background: In the United States, resident attrition from general surgery has received attention due to concerns about a shortage of general surgeons. Attrition from surgical specialties is higher than from non-surgical specialties, with the resident attrition rate from general surgery reported around 20%, mostly to non-surgical specialties and often early in training. These rates have been consistent over the past decade despite longtime recognition of this issue. Common factors cited are lifestyle, work hours and personal reasons. However, surgical resident attrition in Canada has not been clearly reported in the literature. It would be important to assess if resident attrition is as significant an issue in Canada.
Objectives: The objective of this study is to determine the rate and pattern of attrition from surgical residencies in Canada in the past five years, with a focus on general surgery.
Methods: A cross-sectional retrospective study was performed. Resident data by surgical specialty, including number of resident transfers and total residents by PGY year, for the 2008-2012 academic years was obtained from the Canadian Post-MD Education Registry (CAPER). The overall rate of attrition for each academic year was calculated as the total number of resident transfers divided by the total number of residents. The cumulative risk of attrition during residency training was estimated by taking the sum of the attrition rates across the post-graduate years required to complete surgical training (i.e. attrition rate in PGY-1+attrition rate in PGY-2+attrition rate in PGY-3+attrition rate in PGY-4+attrition rate in PGY-5 = cumulative risk of attrition for five-year training program).
Results: During the 2008-2012 academic years, the overall rate of attrition in general surgery ranged from 1.93-3.04%, with the estimated cumulative risk of attrition during residency between 9.65-15.03%. Among the surgical specialties, the highest rates of attrition were seen in neurosurgery, general surgery and cardiac surgery. All resident transfers from a surgical specialty were to a non-surgical specialty.
Conclusions: The overall attrition rate and risk of attrition from general surgery residency programs in Canada are high, though less than those reported in the US. Further analysis will be performed to determine if age, gender or postgraduate year is associated with attrition, and if the overall attrition rate and risk of attrition have changed over the past 15 years.

P11 **Grace Chan,** *Pediatric General Surgery*

Title: Audit of Emergent and Urgent Surgery for Acutely Ill Pediatric Patients: is Access Timely?

Grace Chan and Sonia A. Butterworth, MD, Department of Medicine and Division Pediatric Surgery, UBC

Background: Elective surgery wait times are frequently measured (and reported) however, there is a paucity of literature (and no reporting) about wait times for emergent and urgent surgeries in Canada. Delays to operation as well as performance of less urgent operations late at night are well established factors which have been shown to increase patient morbidity and mortality. At our institution emergent/urgent operations achieve access to the operating room through one of three ways: bumping of elective cases, access to "open" operating room time (bookings close 21 hours prior, are available to all specialties, are prioritized based on medical urgency and only available 3 days a week) or surgery out-of–hours (OOH). Emergent/urgent surgeries are classified into Class 1, 2A, 2B, and 3 designations, with target operating in-room times of 1, 6, 24, and 72 hours respectively.
Aims: To determine: 1) The relative proportions of the four levels of emergent/urgent surgery and the percentage of surgeries performed OOH vs. within regular working hours (IH=7:45 AM-3:30 PM, M-F). 2) Wait times as well as the proportion of surgeries performed within target times. 3) Frequency and wait times for emergent/urgent surgeries performed throughout the day. 4) The impact of emergent/urgent surgeries on elective surgery.
Methods: With REB approval**,** a retrospective analysis (June 2011-December 2013) of all emergent/urgent surgeries performed at BC Children's Hospital was conducted using the ORSOS database (prospective patient and operative data). A p-value<0.05 was considered significant.
Results: There were 4668 operations during the study period: Class 1 (5.8%), 2A (29.1%), 2B (42.1%), and 3(23%). The proportion of Class 1, 2A, 2B, and 3 operations performed OOH was 74.7%, 72.1%, 56%, and 28.1% respectively. There were 63 Class 2B and 3 surgeries with in-room times at or after 2300 [10 (2011), 16 (2012) and 37 (2013)]. There was a statistically significant increase in the overall percentage of surgeries started IH, from 41.8% in 2011 to 49.6% in 2013. For Class 1, 2A, 2B, and 3 surgeries performed from 2011 to 2013, the mean in-room time was 120 minutes, 4.7 h, 15.4 h, and 54 h respectively. Overall, the proportion of Class 1, 2A, 2B, and 3 cases performed within target was 59.2%, 81.9%, 81.2% and 74.4% respectively. Mean Class 1 time to incision was 170 min (2011), 190 minutes (2012) and 94 minutes (2013). General Surgery patients accounted for the majority of operations (34%) and the most frequent bumped elective procedure was inguinal hernia repair.
Conclusion: During the audit period, though there has been an increase in the proportion urgent/emergent operations performed IH, the majority still occur OOH. In addition, there has been an increase in Class 2B and 3 surgeries starting at or after 2300. While the majority of the less emergent operations occur within target, the most unstable of patients requiring emergent surgery are least likely to have their operation within 1 hour. Further research and expanded audits are required to better understand the potential for unintended harm, which children may be subject to during OOH surgery, as well as identifying sustainable approaches to transform the way children with emergent/urgent surgical conditions are cared for.

P12 **Michael Bleszynski,** General Surgery

Title: Surgical Abdominal Sepsis: Insight Into Inflammatory Cytokines in Peritoneal Fluid and Serum During Initial Source Control Surgery

Michael Bleszynski, Tiffany Chan, Alice Mui, David Ansley, Morad Hameed, Juan Ronco, Andrzej Buczkowski; Departments of Anesthesiology, Internal Medicine and Surgery, UBC

Introduction: Retrospective surgical abdominal sepsis (SABS) data (unpublished) has shown in severe sepsis/septic shock a significant difference in mortality between primary abdominal closure (PAC) (38.7%) and vacuum assisted closure (VAC) (22.8%), even though VAC is reserved for increased clinical severity of

sepsis. There is no definitive inflammatory cytokine distinguishing between severity of sepsis or mortality in order to guide the decision for PAC or VAC at initial source control laparotomy (SC1). Hepatocyte growth factor (HGF) is released in response to systemic inflammation.

Objective: The goal of this study was to determine if concentrations of serum or peritoneal fluid (PF) cytokines are able to differentiate between PAC and VAC.

Methods: Prospective case series of patients screened pre-operatively to full-fill criteria of severe sepsis/septic shock according to 2012 ACCP/SCCM criteria requiring emergent SC1. Surgeon at time of SC1 determined the decision for PAC or VAC. In OR blood samples obtained via an arterial line pre- and post-operatively of SC1. PF samples were obtained via 10cc syringe after abdomen opened prior to any other intra-abdominal manipulation. Samples kept on ice, centrifuged within 1 hour at 1500g for 5 minutes, supernatant collected and frozen at -70 degrees Celsius. Serum/PF fluid analyzed with a Human Cytokine 30-Plex Panel. Observed concentrations reported as pg/ml. Mann-Whitney U test used to compare PAC and VAC.

Results: Twelve patients, 4 PAC and 8 VAC cases from SC1. PAC mortality 25%, septic shock prior to SC1 75% and mean age was 68.5. VAC mortality 37.5%, septic shock prior to SC1 100%, and mean age was 56.5. PAC PF concentrations of IL-6, IL-17, (pro-inflammatory cytokines), IL-5 and HGF; 9746, 1.45, 3.68 and 613 respectively compared to 17176, 6.2,12.8 and 4350 in VAC $p < 0.05$.

Conclusions: Peritoneal fluid concentrations of IL-6, IL-17, IL-5, and HGF significantly differentiated between VAC and PAC cases and also indicated that VAC cases had a more severe sepsis at the time of SC1.

P13 **Romy Hoeppli,** General Surgery

Title: Evaluation of Thymus as a Novel Source of T Regulatory Cells for Therapy after Transplantation

Romy Hoeppli[1], Esme Dijke[2,3], Jessica Qing Huang[1], Alicia McMurchy[1], Lori West[2,3,4], Megan Levings[1; 1]Department of Surgery, University of British Columbia, Vancouver, BC; [2]Department of Pediatrics, University of Alberta, Edmonton, AB; [3]Alberta Transplant Institute, Edmonton, AB; [4]Department of Surgery, University of Alberta, Edmonton, AB.

Introduction: Transplantation is often subject to the risk of graft rejection or graft-versus-host disease (GVHD). Cell-based therapy with $FOXP3^+$ T regulatory cells (Tregs) to induce tolerance to alloantigens could eliminate these complications. However, expanding enough human Tregs from blood to use in patients is challenging due to limited growth and potential for contamination with effector T cells (Teff). Discarded pediatric thymuses from cardiac surgery could provide an alternative source of Tregs which are less likely to be contaminated with effector T cells. However, whether thymic Tregs are as effective as peripheral Tregs at suppressing responses to transplanted antigens is unknown.

Hypothesis: Tregs isolated from pediatric thymic tissue are more pure and have higher expansion potential and are at least equally potent at suppressing Teff *in vitro* and development of xenoGVHD *in vivo* than Tregs from peripheral blood.

Methods: Human Tregs were isolated from peripheral blood or pediatric thymus and stimulated with high doses of human IL-2 and artificial antigen presenting cells that express human CD58, CD86 and the human CD32 Fc receptor to immobilize soluble anti-CD3 mAbs. The suppressive function was measured with a standard suppression assay *in vitro* and with a humanized-mouse model of GVHD *in vivo*. In brief, immunodeficient NSG mice were injected with $10x10^6$ peripheral blood mononuclear cells (PBMCs) with or without equal numbers of expanded Tregs from thymus or peripheral blood.

Results: Culture for ~14 days resulted in over 500-fold expansion of peripheral and about 40-fold expansion of thymic Tregs. Due to considerably higher starting cell numbers of thymic Tregs similar final counts were achieved and thymic Tregs retained a significantly higher proportion of $FOXP3^+$ cells compared to peripheral Tregs. Tregs from both sources were equally effective at suppressing proliferation of Teff *in vitro*. In our *in vivo* xenoGVHD model, mice receiving Tregs from either source showed significantly delayed onset of GVHD compared to mice receiving no Tregs. The proportions of the human $CD45^+$, $CD4^+$ and $CD8^+$ cell populations in the blood supported the clinical GVHD scores.

Conclusion: We have optimized the expansion conditions for peripheral and thymic Tregs and demonstrated that thymic Tregs are at least equally suppressive *in vitro* and *in vivo* compared to Tregs from peripheral blood. Further comparison of the method of suppression used by Tregs from either source will reveal whether thymuses are a suitable source for continued development of Treg cell-based therapy.

P14 **Ryan Hartwell,** Plastic Surgery

Title: An in-situ forming, bio-hybrid skin substitute system as biological coverage for the fibrotic wound

Ryan Hartwell, Malihe Pourmasjedi-Meibod, Claudia Chavez-Munoz and Aziz Ghahary; BCPFF Burn and Wound Healing Lab, Div. Plastic Surgery

BACKGROUND: Wound repair requires a sequential series of biological events that begins with the deposition of a temporary scaffold within which cells can repair the skin. Without a scaffold, repair is essentially impossible. Aberrant wound healing, such as hypertrophic scarring or non-healing has a tremendous burden on healthcare and quality of life. Timely wound closure dramatically reduces the risk of infection and scarring. Cellular skin substitutes are opportune to meet this need. Our goal was to create an *in-situ* forming scaffold that can be easily combined with cells to rapidly form a dermal substitute within the wound bed. In this study we evaluated the application of a reconstitutable, biohybrid-Collagen-GAG based biohybrid scaffold system in full thickness wounds on a rabbit fibrotic ear model.

METHODS: Punch wounds (6mm) were either untreated, filled with an acellular scaffold, a scaffold containing xenofibroblasts or a scaffold containing xenofibroblasts expressing Indoleamine 2,3-dioxygenase (IDO). The wounds were evaluated for healing outcome, fibrosis, cellularity, neovessel formation, innervation and the ability of the scaffolds to withstand contraction by fibrotic fibroblasts.

RESULTS: Rabbit wounds treated with either an acellular scaffold or a scaffold containing IDO expressing cells, were found to exhibit significantly reduced scar elevation index (SEI) (1.24±0.05 and 1.25±0.03; $p<0.05$) compared to xenofibroblast scaffolds and untreated wounds. Further, significant increases in vasculature (6 vs. 2 vessels/hpf; $p<0.05$) and nerve fibers (36 vs. 12 immunoreactive fibers/hpf; $p<0.05$) were also noticeable in both IDO and gel treated wounds.

CONCLUSION: The results demonstrated that the use of the in situ forming scaffold, and even more so when delivering IDO-expressing cells, improved healing outcome in full thickness rabbit ear wounds. Translating our results to clinic, we are in the works of constructing a kit that can be easily manufactured into a medical device for clinical application.

P15 **Alison Wallace,** General Surgery

Title: Assessment of Electronic-cigarettes in the Reduction of Postoperative Pulmonary Complications in Smokers Undergoing Thoracic Procedures

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2) Department of Medicine, Division of Pulmonary, Sleep and Critical Care Medicine, Mount Sinai, New York, NY

Background: Electronic cigarettes, or e-cigarettes, are claimed to be safer than cigarettes, however, the public health effects of e-cigarettes are poorly understood and clinical studies will take years to complete. Smoking cessation prior to elective surgery improves a number of outcomes such as wound healing and postoperative pulmonary recovery.

Hypothesis: An important clinical question is whether a switch from cigarettes to e-cigarette prior to surgery will reduce the postoperative pulmonary complications.

Methods: Using in vitro and in vivo models to examine the lung health effects of exposure to these products, we assessed key parameters in the development of COPD. Furthermore, smokers undergoing elective thoracic surgery procedures will be randomly assigned to the cigarette or e-cigarette group one month prior to surgery. Biologic parameters such as MMPs and inflammatory cytokines will be examined in lavage fluid on postoperative day 0 and in plasma on postoperative days 0, 1, and 7. The clinical parameters will be time to extubation, ventilator free days in the first 30 postoperative days, and incidence of pneumonia requiring antibiotics in the first 30 days.

Results: Our preliminary results indicate that acute e-cigarette smoke exposure alters ion current and ciliary function in lung epithelial cells and induces lung inflammation in exposed mice. Chronic e-cigarette smoke exposure in mice causes emphysematous changes, induces airway hyper-reactivity, as well as induces airway remodeling, mucin production and apoptosis.
Conclusions: These findings demonstrate the adverse health affects associated with e-cigarette use and show that exposure to these products produces similar results to cigarette smoke exposure. The results also implicate nicotine as a causative factor in the pathogenesis of COPD.

P16 **Ronak Rahmanian,** Pediatric General Surgery

Title: Placing the port: location matters

Eric M. Webber [1], Cynthia Verchere [2], Marija Bucevska [2], Ronak Rahmanian [3], Jasna Levi [4], Sheila L. Pritchard [5]
Division of Pediatric Surgery [1], Division of Plastic Surgery [2], Division of Otolaryngology – Head and Neck Surgery [3], Department of Family Practice [4], Division of Oncology, Hematology and Blood and Marrow Transplantation [5], Faculty of Medicine, University of British Columbia, and BC Children's Hospital

Introduction: The traditional infraclavicular placement for the port of a port-a-cath often results in prominent scar formation. For more than ten years we have inserted some ports in an inframammary position. This study compares the two sites in terms of both function and appearance.
Methods: Two groups of patients were studied: 60 children with indwelling ports, and 60 children whose port had been removed at least 24 months previously. Children currently with ports and the oncology nurses were asked to evaluate its function, while children whose ports had been removed were asked to evaluate the scar. Three plastic surgeons, blinded to the port location, evaluated the appearances of the surgical scars.
Results: The location of the port did not affect its function. Children with inframammary ports reported significantly less pain with accessing their ports. Following removal of the port children with inframammary scars reported being happier with both the location and the appearance of the scar. The plastic surgeons rated the inframammary scars as significantly better in appearance than the infraclavicular scars.
Conclusions: The appearance of the infraclavicular scar was a significant concern to many children, and it was rated objectively as appearing significantly less satisfactory than the scar in the inframammary location. These findings should be considered when planning port placement for a child.

P17 **Nazgol Seyednejad,** General Surgery

Title: Unplanned Admissions Following Daycare Laparoscopic Cholecystectomy

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Background: Laparoscopic cholecystectomy is the standard of care for symptomatic cholelithiasis. Many institutions have developed the practice of day care laparoscopic cholecystectomies. However, there is a low rate of adverse complications, which result in unplanned admissions following this procedure.
Objectives: The objective of this study was to recognize the factors that are associated with an increase in unplanned admissions in order to better identify the cohort of patients suitable for daycare laparoscopic cholecystectomies. In addition, we identified the time interval over which most unplanned admission occur.
Methods: A multicentred, case-controlled study design was performed using retrospective charts. Data was collected from January 1, 2009 to December 31, 2011 on consecutive patients undergoing planned laparoscopic cholecystectomy in three hospitals. Patient demographics, surgical details, and postoperative details were obtained and analyzed.
Results: Over this time period, 1256 daycare laparoscopic cholecystectomies were performed. One-hundred and twenty-one (9.6%) required unplanned admission the day of surgery. Forty (3.2%) were admitted within one month of surgery. The median time from surgical procedure to unplanned admission was 218 minutes +/- 143. Compared to case-controls, the unplanned admitted patients were older (54.6 years vs 45.1 years, $p<0.005$), and had ASA scores 3 or higher (24% vs 3%, $p<0.005$). The comorbid conditions that resulted in unplanned admissions included patients with hypertension (41% vs 26%, OR 1.97), cardiac conditions (45% vs. 30%, OR 1.88), and chronic pain (76% vs 49%, OR 3.36).
Conclusions: Daycare cholecystectomy for symptomatic cholelithiasis has been adopted by many centers and has been beneficial for both patients and health care institutions. While many patients can be successfully managed with daycare surgery, a standard observation time following surgery needs to be established to assess the need for unplanned admissions and allow for early intervention when adverse complications occur. We found that patients with increased age, higher ASA scores, hypertension, cardiac comorbidities and chronic pain were at an increased risk of unplanned admissions following laparoscopic cholecystectomies. These factors should be taken into account when assessing a patients' appropriateness for daycare surgery.

P18 **Paul Mick,** Otolaryngology

Title: Hearing Loss is Associated with Poorer Ratings of Patient-Physician Communication and Healthcare Quality

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Background: Hearing loss (HL) affects over 50% of older Canadians and is associated with dementia, poor health outcomes and early mortality. HL may interfere with patient-physician communication, and thus quality of healthcare.
Objective: We assessed, in a representative sample of American adults, the associations between HL and 1) patient perceptions of quality of communication with their physicians, and 2) patient perceptions of quality of healthcare.
Methods: Pooled data were derived from years 2001-2011 of the Medical Expenditure Panel Survey Household Component, a nationally representative survey of the US civilian non-institutionalized population. Participants were included if they were 18 years or older and visited a physician at least once in the previous year. HL was based on self-report. Perceptions of communication and healthcare quality were assessed with validated measures developed for the Agency for Healthcare Research and Quality. The probability of higher ratings was analyzed using multivariate logistic regression.
Results: Our analytic cohort was comprised of 122,556 participants (9,747 with HL;112,809 with normal hearing). Individuals with HL were more likely to be older, male, of lower socio-economic status, and in poorer health. In fully adjusted models, individuals with HL versus those with normal hearing had significantly lower odds of having ratings of patient-physician communication (Odds ratio [OR] 0.906, 95% confidence interval [CI]: 0.858, 0.957; $p<0.001$) and overall healthcare (OR 0.939, 95% CI: 0.890, 0.990; $p=0.021$) that were greater than the median.
Conclusions: Effective communication is necessary for patient-centered care that is respectful and responsive to individual preferences, needs, and values, and facilitates knowledge transfer, shared decision-making, and patient autonomy. It is an important predictor of how patients perceive quality of care. Physicians should ensure that their patients with HL fully understand healthcare discussions.

P19 **Diana Song,** Plastic Surgery

Title: What is the Best Way to Track Surgical Complications? Comparing ACS NSQIP versus Traditional M&M Rounds

Jacques Zhang, Diana Song, Julie Bedford, Douglas Courtemanche, Marija Bucevska, Jugpal Arneja

Background: Morbidity and Mortality (M&M) rounds have traditionally played a role in fulfilling quality assurance/improvement. The American College of Surgeons (ACS) National Surgical Quality Improvement Project (NSQIP) is a rigorous, risk-adjusted means to track complications. Herein, we report a comparison of the two methods.
Purpose: To determine the best way to track pediatric plastic surgery complications comparing ACS-NSQIP and M&M rounds.

Methods: With research ethics board approval, ACS-NSQIP and M&M data were extracted for 2012 and 2013. Raw complication rates and an equivalent comparison by removing ACS-NSQIP-ineligible cases from the M&M data were analyzed. Concordance and discordance rates were determined. Complications were classified by severity and type. Statistical analysis was performed.
Results: 1261 procedures were performed in the study period. Only 51.4% of cases were ACS-NSQIP-eligible. The overall complication rates of ACS-NSQIP (6.62%) and M&M (6.11%) were similar (p = 0.662). Comparing the two systems for ACS-NSQIP-ineligible cases also yielded a similar rate (6.62%, 5.71%, p = 0.503). The concordance rate for M&M and ACS-NSQIP was 35.1% and 32.5% respectively and consisted mostly of major complications.
Conclusion: ACS-NSQIP is able to track complications at a similar rate to M&M, although only sampling half of all plastic surgical procedures. Differences in definitions for each system led to low concordance rates. Although both systems offer value, both also have limitations. To improve the tracking and management of complications, we recommend expansion of ACS-NSQIP to include currently excluded cases and potentially extending the post-operative evaluation interval to 90 days.

P20 **Aaron Knox,** Plastic Surgery

Title: ***If a picture is worth a thousand words, is a video worth a thousand pictures? Comparing Dynamic vs. Static Instructional Multimedia for Learning Complex Surgical Skills***

Aaron Knox[1], Kinga Eliasz[2], Dimitri Anastakis[3], Matthew Lineberry[4], Ara Tekian[4], Ryan Brydges[2]; University of British Columbia, Division of Plastic and Reconstructive Surgery
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Purpose: Educational multimedia helps trainees develop a mental representation of complex procedures (e.g., Z-plasty) prior to hands-on performance. One design feature that Mayer's theory of multimedia learning has yet to clarify is whether to present information as static vs. dynamic — an important distinction given the materials trainees typically use to study (e.g., textbook pictures vs. surgical videos). A recent meta-analysis in the general education literature demonstrated an advantage of dynamic multimedia for procedural skills, though the few included studies reported inconsistent results.
Objective: We compared the effect of dynamic vs. static multimedia for preparing novice medical trainees to perform a complex surgical procedural skill. (Z-plasty)
Methods: Using a prospective two-arm design, novice medical trainees (n=44) were randomly assigned to one of two conditions. The dynamic video showed a complete performance of the Z-plasty procedure, whereas the static video showed a number of key still frames from the dynamic video. Auditory information was identical in both conditions. Following the intervention (multimedia viewing, a Z-plasty pretest, and physical practice for 30 minutes), participants completed post-, retention, and transfer tests. We measured performance using a global rating scale (GRS), and analyzed those data using an analysis of covariance (ANCOVA).
Results: The ANCOVA [group (dynamic, static) by test (post-test, retention); covariate: pre-test] revealed a significant interaction between group and test ($F(1, 41) = 4.33$, $p = .044$). Post-hoc tests showed the interaction arose from the dynamic group improving from post- to retention test ($p<0.05$), whereas the static group's performance deteriorated over that time ($p=0.18$). There were no significant differences for transfer testing ($p=0.45$).
Conclusion: Our study suggests that dynamic multimedia is advantageous for novice medical trainees learning to perform a Z-plasty. However this benefit is small 0.25 points on a 5 point GRS) and may not be meaningful in clinical practice. Additional studies are needed to clarify if the cost associated with dynamic multimedia justifies this small educational benefit.

P21 **Yasmin Halwani,** General Surgery

Title: **Transanal Minimally Invasive Surgery (TAMIS): Review of Initial Experience**

Yasmin Halwani, Elena Vikis; Division of General Surgery, University of British Columbia, Vancouver, BC

Background: Transanal minimally invasive surgery (TAMIS) was developed as an alternative to transanal excision and transanal endoscopic microsurgery for local excision of benign and malignant rectal neoplasms. This novel technique makes use of a disposable flexible port and conventional laparoscopic instruments. Since its development, TAMIS application has expanded beyond local excision, ranging from repair of rectourethral fistula to total mesorectal excision. Despite increasing adoption, only a few series have been published evaluating the versatility and outcomes of TAMIS.
Objectives: The aim of this study is to review the variety of applications, as well as the clinicopathologic, technical, and perioperative outcomes of TAMIS for the treatment of rectal pathology.
Methods: This is a retrospective cohort study of consecutive patients who underwent TAMIS by a single colorectal surgeon at a tertiary care academic centre over a 15-month period. TAMIS procedures reviewed included local excision, total mesorectal excision (TAMIS-TME), repair of rectourethral fistula, stricturoplasty, completion proctectomy and control of bleeding. Patients with benign neoplasms, T1 lesions without high-risk pathologic features, or T2-T3 lesions who were too unfit for formal resection, were selected for TAMIS local excision. Primary endpoints evaluated included feasibility of TAMIS, resection quality, and perioperative outcomes.
Results: Forty-one patients have undergone TAMIS, including 33 local excisions for rectal neoplasms, 3 TAMIS-TME, 1 completion proctectomy, 1 repair of rectourethral fistula, 1 stricturoplasty, and 2 cases for control of bleeding. The average patient age was 67.9, with 22 male and 21 female patients. Twenty-two benign neoplasms and 11 malignant lesions were excised. Average tumour size was 2.85cm (range 0.5-7.5cm). Mean distance from the anal verge was 5.9 cm (range 2-15cm). All specimens had grossly negative margins, with 3 specimens (6.9%) with microscopically positive adenoma at the margins. The mean operative time was 67 min for local excision, and 292min for TAMIS-TME. The mean length of stay for local excision was 0.56 days. One patient who was planned to undergo TAMIS local excision required conversion to Parks local excision. There were no recurrences. One patient who underwent local excision required salvage low anterior resection for a T1sm3 lesion. Complications were recorded for seven patients.
Conclusions: Transanal minimally invasive surgery is an innovative, safe and effective platform for the local excision of benign rectal neoplasms and select rectal malignancies. Furthermore, the versatility of this technique allows for several applications beyond local excision, including total mesorectal excision, repair of rectourethral fistulas and strictures, completion proctectomy, and control of bleeding.

Lunch and Learn

Simultaneous Session A

A01 **Paul D'Alessandro,** General Surgery

Title: **Operating theatre: medical humanities increase empathy and inter-professionalism in first-year surgical residents**

Paul D'Alessandro[1] MD MSc, Sonia Butterworth[1] MD FRCSC, Gerri Frager[2] MD FRCPC; 1. Division of General Surgery, Department of Surgery, University of British Columbia, 2. Division of Palliative Care, Department of Paediatrics, Dalhousie University

Background/Objectives: Medical humanities, including theatrical presentations of clinical cases, have been used to create engaging forums in which trainees can encounter difficult issues; develop non-technical competencies; and engage in reflection. The use of medical humanities to generate empathy and inter-professional learning in postgraduate surgical residency is novel. Ed's Story: the Dragon Chronicles is a verbatim play based on the journal of a 16 year-old with advanced cancer and transcripts from 25 interviews conducted after his death with his family, friends and healthcare team. Viewings of the play (both

live performance and recorded on DVD) and facilitated post-performance discussions have been met with positive responses from medical students in extra-curricular settings and as part of mandatory undergraduate medical curriculum across Canada, and our aims were to assess the play's potential as a teaching tool for surgical residents.

Hypothesis: We hypothesized that resident perceptions would be positive, and that empathy and interprofessionalism would increase post-viewing.

Methods: Forty-seven eligible first year residents from nine surgical subspecialties viewed Ed's Story on DVD with facilitated discussion in mandatory curriculum. Twenty-seven residents completed feedback surveys (55.6% male, age 27.5±1.9, response rate 57.4%). In the project's second year, empathy and inter-professionalism were measured pre- and post-viewing (Jefferson Scale of Physician Empathy, JPSE, Readiness for Interprofessional Learning Scale, RIPLS.) Response rates: 83.3% (both pre-tests), 59.2% (JSPE post-test), 51.8% (RIPLS post-test.)

Results: A majority of residents agreed viewing the play was a good learning experience; increased their capacity for empathy and compassion; increased understanding of components of care that affect quality of life; and would facilitate honest communication with future patients and families, and respectful interactions with other health professionals. Post-performance JSPE and RIPLS scores increased in 56.3% and 57.1% of trainees, respectively. Paired t-test subset analysis demonstrated higher mean post-viewing JPSE scores for participants whose pre-viewing scores were above the median ($p<0.05$.) Trainees highlighted the play's multiple perspectives and insights into patient experiences, however some felt the play better suited for medical students.

Conclusions: Surgical residents responded positively to verbatim theatre in postgraduate training. Post-viewing empathy scores increased in trainees whose pre-viewing scores were higher than their peers ($p<0.05$.)

A02 **Aaron Knox,** Plastic Surgery

Title: Challenges When Measuring Cognitive Load in Novice Medical Trainees Using Dynamic or Static Multimedia to Learn Surgical Skills

Aaron Knox[1], Kinga Eliasz[2], Dimitri Anastakis[4], Matthew Lineberry[3], Ryan Brydges[2], Ara Tekian[3]; 1.University of British Columbia, Division of Plastic and Reconstructive Surgery, 2.University of Toronto, The Wilson Centre, 3.University of Illinois at Chicago, Department of Medical Education, 4.University of Toronto, Division of Plastic and Reconstructive Surgery

Background: Mixed effects of multimedia learning are thought to reflect a misalignment between instructional design and cognitive processing. Three types of cognitive load contribute to demands on working memory during multimedia learning. Intrinsic load is due to volume and complexity of information, whereas extraneous load is due to irrelevant or excessive information, and germane load is due to learning or building cognitive schemas. Measurement of load experienced while watching multimedia may provide insight towards the effectiveness of dynamic or static forms presentation formats and inform design of effective learning environments. Cognitive load may be subjectively measured using rating scales or objectively measured using dual task reaction time.

Objectives: Determine the relative proportions of cognitive load types experienced by users while watching dynamic or static multimedia. Determine if subjective and objective cognitive load measures correlate with performance.

Methods: Following visual spatial assessment, novice medical students (n=20) were randomized into one of two multimedia conditions. The dynamic group video contained a complete procedure (Z-plasty) whereas the static group video contained a small number of still frames from the complete video. Auditory information was identical. During the intervention, all participants were simultaneously required to manually respond to a second visual stimulus at random intervals. Cognitive load measures included reaction times, and a modified self-reported questionnaire. Performance outcomes included a knowledge test and drawing exercise.

Results: Groups were equal for sex, handedness, age, and mental rotation. Following the intervention, there were no group differences for learning outcomes, dual-task reaction times, and across all levels of cognitive load type. There was no significant correlation between overall load, type of load or participant reaction times which is unexpected and creates challenges when selecting the best instrument to measure cognitive load in the context of surgical simulation.

Conclusion: Current measures of cognitive load that were not originally intended for use in the setting of motor learning present challenges when attempting to use them in this context. If we are going to continue to use cognitive load theory to explain differences in effectiveness of instructional multimedia in the context of learning procedural skills additional work will be necessary to clarify the best way to measure cognitive load.

A03 **Benjamin Chan,** Plastic Surgery

Title: Pre-clinical/manufacture validation of a novel biohybrid skin substitute

Ben Chan, Ryan Hartwell and Aziz Ghahary; Faculty of Medicine and Department of Surgery, Division of Plastic Surgery

Background: Time is of the essence in wound care. The generation of a non-rejectable and patient-ready skin substitute could prevent scarring, preserve neighbouring tissue, and promote recovery in patients burdened by complicated wounds. Previous works have demonstrated the utility of a liquid-based skin substitute system as a rapid modality to create biological wound coverage at the bedside. Medical device regulations require the creation and validation of pre-clinical and manufacture steps so that a device, such as the skin substitute system, may be fabricated with quality and consistency. Moving toward the evolution of our system into new clinical modality our the objectives of this study were to 1) optimize key production steps and 2) analyze various nuances in raw material grades, chemical properties and reaction conditions.

Methods: All biohybrid scaffolds were optimized and compared with both non-crosslinked and crosslinked collagen-glycosaminoglycan scaffolds, similar to those that are commercially available. Scaffold consistency was assessed spectrophotometrically. Stability was assessed using ASTM standards of accelerated aging. Cellular viability was measured using live/dead cell staining and assessing cell migration rates. Commercialization strategy development involved research into medical device regulatory requirements for application filing.

Results: Nuances in raw material grade and selection were found to have a large impact on scaffold fabrication consistency. It was found that gelation rates and activation energy could be altered by concentration and polymer chemical composition. Cells remained viable in all compositions however, the rate of cellular migration was markedly improved in the biohybrid scaffolds compared to controls. Progress was made in commercializing the product – the application to Health Canada was developed further and a surgical protocol was drafted - however this objective is still ongoing.

Conclusion: The potential that this biohybrid scaffold holds is incredibly vast. As a liquid biological skin substitute, it overcomes many of the barriers seen by the solid scaffolds that are currently commercially available, such as immediate integration with the host wound bed.

A04 **Nick Zhygan,** General Pediatric Surgery

Title: Predictors of low APGAR score following emergency cesarean section and surgical care at a regional referral hospital in rural Uganda Nick Zhygan[1], John Ekunait[2], Nathan O'Hara[1], Damian Duffy[1], Mary Margaret Ajiko[3], Geoffrey Blair[4]; *1) Office for Pediatric Surgical Evaluation and Innovation, BC Children's Hospital, Vancouver, Canada; 2) Division of Obstetrics, Soroti Regional Referral Hospital, Soroti, Uganda 3) Division of Surgery, Soroti Regional Referral Hospital, Soroti, Uganda; 4) Department of Surgery, BC Children's Hospital, Vancouver, Canada*

Background: Uganda has a fertility rate of 6.2 and a mainly rural (80%) population. Around 164 facilities are equipped to provide emergency obstetric care within the country. Soroti Hospital is a tertiary referral center that performs on average 80 cesarean deliveries per month. This study analyzed demographic, socioeconomic and surgical data to identify predictors of low APGAR scores and poor surgical outcomes in patients requiring emergency surgical care.

Objectives: To determine predictors of low APGAR scores following emergency cesarean surgical care in a Ugandan regional referral hospital.

Methods: Prospective data collected between June 23–July 15, 2014. All obstetric emergencies requiring cesarean surgical care at Soroti Hospital were included. Multiparous women were excluded. Chi-squared test used for categorical predictors of low APGAR scores. T-tests used for continuous predictors, comparing mean value of risk factor between case and controls. Logistic regression analysis used to assess interactions and joint effects of predictors.

Results: 64 Patients were recruited to the study with a mean age of 25.8yrs (SD 6.53). Patients were separated based on low APGAR (<7) (n=9) and normal APGAR (7-10) (n=55) scores following emergency cesarean surgical care. Low APGAR scores (<7) were found to be associated with mechanism of transport (p-value=0.029), distance travelled (p-value<0.01) and patient residence (p-value=0.019). No relationship was found between low APGAR scores and surgical procedure length, indication, delay or use of general anesthesia.

Conclusions: Women who live in rural Uganda face an increased risk for poor neonatal outcomes following surgical care. Regardless of implications, ministry initiatives, reflection and availability of surgical resources, our study demonstrates that rural residence has a higher probability for lower APGAR scores following surgical care beyond time and distance factors involved.

A05 **Mohammadreza Pakyari,** Plastic Surgery

Title: Development of non-rejectable skin graft by induction of local immune tolerance

Mohammadreza Pakyari, Mohsen Khosravi Maharlooei, Reza Baradar Jalili, Aziz Ghahary and Erin Brown; Division of Plastic Surgery, Department of Surgery, University of British Columbia

Background and Rationale: Autotransplantation of skin (skin grafts) is a common method of managing soft-tissue injuries, such as extensive traumas (i.e. burns), infections (e.g. necrotizing fasciitis) or oncologic defects. Despite the effectiveness of skin autotransplantation, the high degree of immunogenicity of skin precludes the use of allogenic transplantation of skin. Systemic immunosuppression can provide adequate management of the immune response to skin in composite tissue transplantation (hand transplants), but is generally felt to be inappropriate for isolated skin grafts. At present, multiple engineered permanent skin substitutes have proven to be unsuccessful. This study examines the potential to create an allogeneic skin transplant that avoids rejection by inducing localized immonosupression. Specifically, IDO-expressing fibroblasts are introduced into the dermis of donor subjects to provide a tryptophan depleted local environment in the recipient. IDO is effectively an immuno-supressive enzyme due to its catabolism of the essential amino acid Tryptophan. In nature, it protects semi allogeneic fetus against the maternal immune system during the course of pregnancy.

Hypothesis: In this study we investigate the efficacy of IDO expressing fibroblasts in preventing rejection of allogeneic full thickness skin graft. Robust expression of IDO within the graft might lead to development of an immune privileged area and therefore local immune tolerance toward the graft.

Method: We examined a cell therapy approach for inducing consistent overexpression of IDO in full thickness skin grafts. Regular (control) and IDO-fibroblast were injected intra dermally in syngeneic and allogeneic recipients (n=5/group). Viability and functionality (IDO expression) of the cells post injection will be compared to control at different time points (7days, 2, 4, 8 weeks (ongoing)). This is done by Live/Dead assay, PCR, western blot and Kynurenine level from tissue extraction. In the next step, 4 days post injection of the cells; grafts with regular and IDO fibroblast were transplanted to allogeneic recipients and monitored until graft rejection, or for a maximum of 6 weeks postoperative. To investigate any possible cumulative effect of multiple injections on the survival rate of grafts, cells will be injected at different time point (days 0, 5, 10) to the same area and a 6mm graft will be harvested from that region and transplanted to the allogeneic subjects.

Preliminary results: Five days after intra-dermal injection, injected fibroblasts remain viable and functional (93% of IDO-expressing fibroblasts were alive after injection). Kynurenine levels, an indicator of IDO activity, were significantly higher in IDO group compared to regular fibroblast group ($p=0.006$) and un-injected skin ($p<0.001$). We also observed migration of IDO expressing fibroblasts and dendritic cells to regional lymph nodes in allogeneic subjects. Preliminary results from skin transplantation studies demonstrates that IDO expressing grafts remain viable for significantly longer than control allogeneic grafts ($p=0.01$).

Conclusion and Significance: These data suggest that local immunosuppression can be provided by the delivery of IDO expressing fibroblasts in allogeneic skin transplantation. This "cell-based" approach to localized immunosupression provides numerous potential opportunities to alter the need for systemic immuosupression in transplantation. the potential of this research goes far beyond the promising role for skin transplantation. If local immune tolerance can be induced by the use of IDO expression in skin transplantation, with some modifications, an immune privileged graft could also be utilized as a scaffold for cell transplantation such as islet, thyroid or adrenal cortical cells. This approach provides the potential to reduce or eliminate the need for systemic immunosupression for various transplants, and thereby reduce the systemic toxicity associated with life long administration of immune-suppressive medications.

A06 **Mohsen Khosravi-Maharlooei,** Plastic surgery

Title: Intra peritoneal injection of IDO-expressing fibroblasts increases the survival of skin allografts through induction of tolerogenic dendritic cells and regulatory T cells

Mohsen Khosravi-Maharlooei, MohammadReza Pakyari, Sanam Salimi-Elizei,Reza Jalili, Ruhangiz T. Kilani, Aziz Ghahary; Department of Surgery, University of British Columbia

Introduction: Local over-expression of indoleamine 2,3 dioxygenase (IDO), an immunomodulatory enzyme which is involved in tryptophan metabolism, creates an environment within which transplanted cells can survive but attacking immune cells are selectively destroyed. Despite that, long-lasting immune tolerance could be achieved through more generalized stable expression of IDO in the body. Recently, we developed a strategy for induction of systemic tolerance via intraperitoneal (IP) injection of IDO-expressing primary dermal fibroblasts at the time of transplantation.

Hypothesis: IP injection of IDO-fibroblasts prevents skin allograft rejection through different mechanisms including: 1) generation of donor-specific regulatory T cells (Tregs) and 2) induction of a tolerogenic phenotype in dendritic cells.

Methods: In different groups, intra peritoneal injection of C57BL/6 (B6) fibroblasts, B6 IDO-fibroblasts (10^7 cells/mouse) and control medium was done 4 days prior to B6 to C3H skin transplantation. Graft sites were checked for signs of rejection. To test the mechanisms, allogeneic (B6) regular and IDO-expressing fibroblasts as well as syngeneic fibroblasts were injected into the peritoneal cavity of C3H recipient mice. After 10 days, the peritoneal lavage (PL) dendritic cells were checked regarding their tolerogenic effects. Tregs were evaluated within the lymphatic tissues of recipient mice.

Results: IP injection of IDO-fibroblasts increased skin graft survival. There was a significantly higher number of DCs that expressed co-inhibitory molecules within the peritoneal cavity of fibroblast treated groups. These DCs were able to migrate to lymphatic tissues including spleen and MLN. The percentage of Tregs increased in mesenteric lymph nodes of IDO-fibroblast-treated group mice.

Conclusion: IP-injection of IDO-expressing fibroblasts increases the survival of skin allografts through induction of tolerogenic dendritic cells and regulatory T cells.

A07 **Alykhan Rajwani,** Otolaryngology

Title: Omalizumab therapy for refractory allergic fungal rhinosinusitis patients with moderate or severe asthma

Alykhan Rajwani, Eng Gan, Al-Rahim Habib, Amin Javer, Division of Otolaryngology, Department of Surgery, Faculty of Medicine, University of British Columbia

Background: Allergic fungal rhinosinusitis (AFRS) is a severe phenotype of chronic rhinosinusitis characterized by nasal polyposis, allergic mucin, and often, a raised total serum immunoglobulin E (IgE). The management of AFRS involves functional endoscopic sinus surgery (FESS) followed by a combination of adjunct medical treatments. These can include topical and systemic corticosteroids, and antifungal agents. However, it has been found that the standard medical management of AFRS may fail in alleviating sinonasal symptoms in approximately 15% of patients. Therefore, an alternative post-FESS therapy is needed for such patients.

Objectives: 1. To assess the efficacy of omalizumab therapy to improve sinonasal symptoms, and quality of life as measured by the Sino-Nasal Outcome Test 22 (SNOT-22). 2. To determine if omalizumab therapy reduces the usage of corticosteroids or antifungal therapy in AFRS patients

Methods: Clinical charts were retrospectively reviewed of patients with AFRS with moderate or severe asthma. Patients received at least three subcutaneous injections of omalizumab therapy between January 2012 and February 2013. All patients had undergone bilateral FESS and were unresponsive to both adjunct medical treatments (oral or topical corticosteroids and antifungal therapy).

Results: Seven patients met the inclusion criteria and were included in this case series. The mean age of the patients was 48.1 years. The mean difference between pre- and post-omalizumab treatment SNOT-22 scores was 16.9 points, representing a 32% improvement. The mean difference between endoscopic scores assessing sinonasal mucosal inflammation was 8.3 points, representing a 41% improvement from baseline. The mean difference between pre- and

post-omalizumab IgE levels was 60.9, representing a 26% decrease. After commencement of omalizumab therapy, four of seven patients (43%) decreased frequency of corticosteroid use, one (14%) discontinued corticosteroid use, and one of two patients (50%) taking anti-fungals ceased its use. No patients experienced significant complications from subcutaneous omalizumab therapy.

Conclusion: Our case series shows that omalizumab therapy may be a safe and effective treatment for patients with refractory AFRS with moderate or severe asthma. However, future trials with larger sample sizes are required to confirm its safety and efficacy.

A08 **Al-Rahim R. Habib,** Otolaryngology

Title: Sinonasal Outcome Test-22 as a Tool to Identify Chronic Rhinosinusitis in Adults with Cystic Fibrosis

Al-Rahim R. Habib, Bradley S. Quon, Saad Alsaleh, Jamil Manji, Jane A. Buxton, Amin R. Javer, Division of Otolaryngology, Department of Surgery, Faculty of Medicine, University of British Columbia

Background: In the past four decades, the median age of survival has nearly doubled for individuals living with cystic fibrosis (CF). However, the prevalence of age-related, extra-pulmonary co-morbidities like chronic rhinosinusitis (CRS) has risen. CRS is associated with significantly reduced health-related quality of life and can be often overlooked given competing respiratory conditions. The purpose of this study was to construct a predictive model to assist CF specialists identify individuals with or without CRS.

Objectives: 1. Investigate the ability of the Sinonasal Outcomes Test-22 (SNOT-22) to distinguish clinically significant chronic rhinosinusitis (CRS) among adults with CF. 2. Determine an appropriate cutoff score with sufficient test sensitivity and specificity, to assist caregivers in identifying patients who may warrant specialist referral and treatment.

Methods: Participants were enrolled at an adult-specific CF clinic, in a tertiary academic hospital in Vancouver, Canada. Subjects completed the SNOT-22 followed by endoscopic assessment by otolaryngologists. The Canadian Clinical Practice Guidelines for Chronic Rhinosinusitis were used to confirm diagnosis of CRS.

Results: One hundred thirteen of 121 (93%) individuals with a confirmed diagnosis of CF participated in this study. The prevalence of CRS was 64%. Aggregate SNOT-22 scores were significantly higher among individuals with CRS compared to non-CRS counterparts (39.4±20.0 vs. 22.7±8.7, p=0.007, 95%CI for mean difference: 4.7, 28.7). A SNOT-22 score >26 was found to have a test sensitivity of 74.4% and specificity of 66.7% for diagnosis of CRS (AUC=0.77, p<0.01). Utilizing SNOT-22 scores related to rhinological symptoms increased the likelihood ratio of a positive test when compared to aggregate scores (8.3 vs. 2.2, respectively).

Conclusion: The SNOT-22 significantly discriminates CF adults with or without CRS. Utilizing rhinological symptom scores increases the likelihood of detecting true CRS cases. The use of this questionnaire may assist CF specialists in identifying individuals who have clinically significant CRS, warranting specialist referral and treatment.

A09 **Krista Genoway,** Plastic Surgery

Title: The safety, efficacy and patient outcomes following new major burn clinical practice guideline implementation

Krista Genoway[1], Sol Gregory[1], Misha Zarbafian[1], Mark Vu[2], Donald Griesdale[2] & Anthony Papp[1]; [1]UBC Department of Surgery, Division of Plastic & Reconstructive Surgery, [2]UBC Department of Anesthesia, Pharmacology & Therapeutics.

Background: A major focus in the acute management of burn injuries is resuscitation, particularly in the first 24 hours. Literature supports the need for appropriate fluid resuscitation with the goals of balancing end organ perfusion while minimizing the effects of over resuscitation. This proves particularly challenging in British Columbia where burn care is delivered by single providers in low volume rural settings and by quaternary multidisciplinary teams. In BC clinical practice guidelines were implemented in 2011 to standardize resuscitation and minimize iatrogenic complications.

Objective: To provide an interim review of the BC clinical practice guidelines implemented in 2011 to standardize burn fluid resuscitation.

Methods: A retrospective review of TBSA estimation, resuscitation records and clinical outcomes following implementation of provincial major burn clinical practice guidelines. Two groups were defined as patients initially assessed in a quaternary centre or those referred from peripheral hospitals. Results were compared to previously published BC burn outcome data prior to guideline implementation.

Results: Twenty-eight patients met the study inclusion criteria. Eighteen patients were transferred to and ten patients were directly treated in our centre. Mean transfer time from the periphery to Vancouver was 9.5 hours post burn. The patient demographics were similar between all groups. Twenty-five percent of patients in the periphery had over estimated TBSA by greater than 10% after the guidelines. In the 24h post burn iv-fluids received in the peripheral transfer group was 7.9cc/kg/%TBSA prior to the guideline and 6.75cc/kg/%TBSA after guideline implementation. In these groups 9% percent of patents developed abdominal compartment syndrome before the guidelines and one patient (5%) developed abdominal compartment syndrome afterwards. Five-percent of patients required dialysis prior to the guidelines compared to 11% (2 patients) afterwards. The patients that required dialysis after the guidelines had above average TBSA (41%), fluid given in the first 24hour (8cc/kg/%TBSA) and transfer time to the burn center (11.5 hours). No patients in the study have required long term dialysis.

Conclusion: The implementation of new clinical practice guidelines to aid in fluid resuscitation following major burns has improved peripheral TBSA estimation and decreased IV fluid administration for patients initially assessed in peripheral low volume centers.

A10 **Joshua Gurberg,** Otolaryngology

Title: Pediatric First Branchial Cleft Anomalies: Management of the Facial Mass and the Occasionally Novel Otologic Malformation

Joshua Gurberg, Paul Moxham, Jeffrey Ludemann; BC Children's Hospital, Division of Otolaryngology – Head & Neck Surgery, UBC

Introduction: Branchial anomalies account for approximately 17% of pediatric neck masses and 30% of all congenital neck lesions; of these, less than 1% involve the first branchial cleft.

Objectives: Report several novel otologic malformations encountered in children with first branchial cleft anomalies and the results of our surgical technique.

Methods: We conducted a retrospective chart review of all patients consecutively referred to the senior authors at a tertiary-care Pediatric Otolaryngology clinic for first branchial cleft anomalies over a 14-year period. All patients underwent computerized tomography, micro-otoscopy with surgery when indicated (29%), methylene blue mapping of the cutaneous opening when present (57%), intra-operative facial monitoring, and anterograde or retrograde facial nerve dissection.

Results: Seven patients presented with first branchial cleft anomalies at an average age of 3.9 years. Five patients presented with infection. Four of the anomalies were sinuses, 2 were cysts and 1 was a fistula. Two patients had a classic myringeal web. One patient had a large posterior intratympanic keratoma, partial myringeal duplication, and wax-pocket; while another patient had external auditory canal triplication and a small intratympanic keratoma. In 6 cases (86%) there was distortion of anatomical landmarks and retrograde facial nerve dissection was therefore employed. Reanastomosis of a distal branch of the facial nerve was undertaken in 2 patients. Five patients (71%) experienced transient facial nerve weakness. However, with a mean length of follow-up of 6.25 years, no permanent facial nerve weakness, recurrence, or hearing loss has been identified.

Conclusions: We present several novel otologic first branchial cleft findings and the experience of a two-surgeon team using methylene blue mapping plus monitored and primarily retrograde facial nerve dissection. This approach appears relatively safe and effective in children with these highly variable anomalies.

A11 **Joshua Gurberg,** Otolaryngology

Title: The Canadian Contribution to the Otolaryngology Literature: a Five Year Bibliometric Analysis

Joshua Gurberg, June Lin, Eli Akbari, Paul White, Desmond Nunez, Division of Otolaryngology – Head & Neck Surgery, UBC

Introduction: The future of Otolaryngology – Head & Neck surgery relies on ongoing knowledge creation. Bibliometry, defined as the quantitative evaluation of scientific literature, is an accessible tool to evaluate the progress of the specialty.

Objectives: To assess the 2008-2012 Canadian contribution to the Otolaryngology literature.

Methods: All articles published from January 2008 - December 2012 in 5 Otolaryngology journals were reviewed. Nationality, number of authors, and study type were extracted. The output, number of authors, and study type of Canadian papers were compared to International papers using Mantel-Haenszel Common Odds Ratio Estimate, Pearson's Chi-Squared, or Fishers exact tests.

Results: 4519 papers were analysed. There was a statistically significant decrease in Canadian authored papers from 12.8% in 2008-9 to 10.2% in 2011-12 (Fishers exact, p = .01). Multi-authorship increased in Canadian papers ($\chi 2$, p= .01). There was no change in the types of studies published by Canadian authors over time.

Conclusions: Canadian authored papers in a sample of Otolaryngology journals decreased from 2008 to 2012. The increase in multiauthorship, whilst indicating increasing collaboration, suggests reduced per capita publication productivity. These findings warrant further study.

A12 **Shahrzad Joharifard,** General Surgery

Title: ACCESS: The Design of a Novel Tablet-Based Consultation, Elective Admission, and Patient Rounding List "App" for General Surgical Services at Vancouver General Hospital

Shahrzad Joharifard MD, Gurp Johal MD, Benjamin Matthew MD MHSC, Seyed Morad Hameed MD MPH FRCSC FACS; Division of General Surgery, Department of Surgery, University of British Columbia

Background: General surgical services at Vancouver General Hospital (VGH) are high volume with rapid patient turnover. The Acute Care Surgery (ACS) service, more specifically, provides round-the-clock consultation services to a large number of often acutely ill patients in both the ED and on inpatient wards. Care of ACS patients is frequently handed over to other clinicians to facilitate timely operative intervention, while overnight, two residents are tasked with performing all general surgery consultations as well as providing comprehensive care to up to 100 surgical inpatients, frequently with minimal handover about their clinical course. General surgical services at VGH predominantly use inefficient paper-based systems to document consultations, facilitate handover, and maintain patient rounding lists.

Objectives: We sought to design an efficient and user-friendly tablet-based app in order to streamline consultation and admission documentation, facilitate transfer of patient care, and optimize patient rounding list management, while simultaneously creating an electronic ACS patient registry.

Methods: We partnered with a health technology firm to design a tablet-based app called ACCESS. Design input was solicited from general surgical residents as well as two staff consultants. An iterative design process was utilized to improve the app as it was developed, which led to a number of key changes. For example, the app initially contained many free text fields, but the design team soon found that dropdown and checkbox fields better ensured standardization of data. Validated sources were identified for each field: the chief complaint field was populated from the Canadian Emergency Department Information System (CEDIS) Presenting Complaint List, the medical history field was populated from the 2010 Global Burden of Disease Study's list of 291 diseases, and the surgical history field was populated from the procedures listed in James Hoballah's text, *Operative Dictations in General and Vascular Surgery.*

Results: The app has three parts: (1) a dashboard that hosts the patient rounding list system, (2) a consult intake form, and (3) an elective admission intake form, essentially an abbreviated version of the consult form. The consult intake form is comprised of the following sections: identification, HPI, past history, medications and allergies, physical exam, imaging, labs, assessment, and review. Key data inputted into the consult and elective admission intake forms auto-populates the appropriate patient rounding list, which can then be updated by users on a real-time basis.

Conclusions: Our team successfully created a comprehensive tablet-based consultation, admission, and list management app. The next phase of our project will be usability testing involving medical students, junior and senior residents, and staff consultants. User feedback will be used to make final changes to ACCESS, which will subsequently be rolled out on the ACS and elective general surgical services. The adoption of ACCESS will build an electronic ACS patient registry, which will allow surgeons and researchers to characterize the ACS patient cohort for the first time since the inception of the service at VGH. These linkages should provide unprecedented insights into the determinants of outcomes for emergency general surgical conditions, and will undoubtedly help to improve the quality of operative and peri-operative care for this complex group of surgical patients.

Simultaneous Session B

B01 **Robert Olson,** Radiation Oncology

Title: Impact of a Multi-pronged Intervention to Improve the Use of Single Fraction Radiotherapy for Bone Metastases Across All BC Cancer Agency Centres

Robert Olson[1,2], Ivo Olivotto[1,3], Manpreet Tiwana[4], Mark Barnes[2], Kelsey Roden[5], Emily Yurkowski[4], Quinn Gentles[5], Ross Halperin[1,6], Stacy Miller[1,2], David Hoegler[1,6], John French[7], [1]UBC Department of Surgery, Division of Radiation Oncology, BC Cancer Agency: [2]Prince George, [3]Victoria, [6]Kelowna and [7]Vancouver, [4]University of Northern British Columbia, [5]UBC Medical School

Background: Extensive level 1 evidence demonstrates that single fraction (SF) radiotherapy (RT) for bone metastases is equally efficacious to more inconvenient and costly multiple fraction courses. Previous work had shown that the use of SFRT for bone metastases varied from 26% to 73% (p<0.001) between five cancer centres in BC, which provides 100% of the RT to the population.

Objective: To assess the impact of a multi-pronged intervention to improve the evidence based prescription of single fraction radiotherapy in BC

Methods: Several province-wide interventions were implemented in 2012 to improve use of SFRT, including meeting with Radiation Oncology practice leaders, and province-wide presentations describing the practice variation by centre and physician. The utilization of SFRT for bone metastases from 2007-2011 was compared to utilization of SFRT in 2013, to assess the impact of the intervention.

Results: 16,898 courses of RT for bone metastases were delivered from 2007–2011 and 3,200 courses were delivered in 2013.The rates of SFRT use in 2007, 2008, 2009, 2010, 2011, and 2013 were 50.5%, 50.9%, 48.3%, 48.5%, 48.0%, and 59.7%, respectively (p<0.001). The anticipated cost savings is estimated at over $300,000 annually. The individual centres' increased utilizations were: Centres A 26% to 32%, B 36% to 56%, C 39% to 57%, D 49% to 56%, and E 73% to 85.0%, but the variation in use of SFRT between centres persisted (range 32%-85%). Centre B, with the largest SFRT increase (20%) had additional rounds presentations on SFRT evidence, in addition to the program-wide interventions.

Conclusion: This study demonstrated an increased utilization of SFRT for bone metastases, after a province-wide intervention on to increase the use of SFRT including dissemination of actual practice by centre and physician. The intervention appeared to reverse a trend to decreasing use of SFRT, and saved over $300,000 dollars in BC for 2013. This suggests that programmatic comparison and dissemination of quality indicators can lead to increased uptake of evidence-based practice.

B02 **J. Conway,** Radiation oncology

Title: Comparison of Patient-Reported Outcomes with Single versus Multiple Fraction Palliative Radiotherapy for Bone Metastasis

J. Conway M.D.1,2, I. Olivotto M.D.1, S. Miller M.D.3, R. Halperin M.D.4, D. Hoegler M.D.4, E. Yurkowski5, Q. Gentles B.Sc.6, W. Beckham Ph.D.7, J. Stephen Ph.D.8, H. Daudt Ph.D.7, J. French M.Sc.1, R. Olson, M.D.3; [1] Department of Radiation Therapy, British Columbia Cancer Agency, Vancouver, BC, [2] Department of Surgery, University of British Columbia, Vancouver, BC, [3] Department of Radiation Therapy, British Columbia Cancer Agency, Prince George, BC, [4] Department of Radiation Therapy, British Columbia Cancer Agency, Kelowna, BC, [5] Department of Science, University of British Columbia, Prince George, BC, [6] Department of Medical Undergraduate Education, University of British Columbia, Prince George, BC, [7] Department of Radiation Therapy, British Columbia Cancer Agency, Victoria, BC, [8] Department of Radiation Therapy, British Columbia Cancer Agency, Surrey, BC

Background: Bone metastases are a common cause of cancer-related pain and palliative radiotherapy (RT) is frequently prescribed to relieve such symptoms. Despite multiple randomized control trials (RCTs) showing equivalent efficacy between single fraction (SF) and multiple fraction (MF) RT for BM, considerable variation still exists in fractionation

Objectives: To compare patient reported outcomes (PROs) following SF as compared with MF RT for bone metastases in a population-based cohort.

Methods: Six BC Cancer Agency centres participated in the Prospective Outcomes and Support Initiative (POSI), to record PROs prior to and 3 weeks following RT for bone metastases. Patients treated in BC between May 2013 and July 2014 who provided PROs before and after RT were identified. PROs were standardized and designed to assess patients' perception of pain, function and symptom distress using a non-dichotomous, ordinal, 5-point scale. Comparisons were made between patients who received SF versus MFRT. SFRT vs. MFRT was at the discretion of the treating oncologist. A multivariate logistic regression analysis was performed.

Results: 648 patients completed both pre and post-RT assessments. The median age at diagnosis was 65 years, 55% were male, 16% were retreated cases, 35% were complicated bone metastases and 56% received SFRT. The three most common primary sites were genitourinary (31%), breast (22%) and lung (22%). Spine (44%) was the most common site treated. There were no significant differences in changes in mean PRO scores for pain (1.29 vs. 1.17 point improvement; p=0.24), function (0.80 vs. 0.96 point improvement; p=0.17) or degree of symptom distress (1.26 vs. 1.26 point improvement; p=0.98) between patients who received SFRT versus MFRT. Likewise, for all patients with painful bone metastases the proportion with achieved a partial pain response (PR) (72.9% vs. 73.3%; p=0.93) and a complete pain response (CR) (18.6% vs. 22.0%; p=0.31) were not different. Similarly, an improvement by at least a 1-point in function (71.1% vs. 76.8%; p=0.20), and symptom distress (76.9% vs. 79.6%; p=0.46) were similar between SFRT and MFRT. After controlling for gender, fractionation, site of delivery, disease site, retreatments and complicated bone metastases there was no significant difference in probability of achieving a pain PR (Odds Ratio=1.00; 95% CI 0.68-1.48; p=0.99) or CR (Odds Ratio=0.83; 95% CI 0.53-1.27; p=0.38) between SFRT and MFRT.

Conclusions: In our study, improvements in PRO for pain, function and degree of symptom distress were similar between SFRT and MFRT supporting the generalizability of RCTs to clinical practice. No differences were observed between SFRT and MFRT for pain PR or CR amongst all painful BM cases. Likewise, improvements in function and degree of symptom distress were similar between SFRT and MFRT. Our study suggests that SFRT should be the standard management policy for patients with uncomplicated BM. No evidence was found that SF was inferior to MF in complicated BM with respect to pain, function or symptom distress but a larger sample size is needed to draw further conclusions.

B03 **Jennifer Locke,** Radiation oncology

Title: ***NKX3.1*** **Haploinsufficiency is Prognostic for Prostate Cancer Relapse Following Surgery or Image-Guided Radiotherapy**

Jennifer Locke, Gaetano Zafarana, Adrian Ishkanian, Mike Milosevic, John Thoms, Cherry Have, Chad Malloff, Wan Lam, Jeremy Squire, Melania Pintilie, Jenna Sykes, Varun Ramnarine, Alice Meng, Omar Ahmed, Igor Jurisica, Theo van der Kwast, Robert Bristow. Department of Urologic Sciences, University of British Columbia, Vancouver, British Columbia, Canada; Departments of Radiation Oncology, Medical Biophysics, Laboratory Medicine and Pathology and Dalla Lana School of Public Health, University of Toronto; Ontario Cancer Institute/Princess Margaret Hospital-University Health Network, Toronto; Department of Pathology and Oncology, Queen's University, Kingston, Ontario; Department of Cancer Genetics and Developmental Biology, British Columbia Cancer Research Centre, Vancouver, British Columbia, Canada

Background: Despite the use of prostate specific antigen (PSA), Gleason-score, and T-category as prognostic factors, up to 40% of patients with intermediate-risk prostate cancer will fail radical prostatectomy or precision image-guided radiotherapy (IGRT). Additional genetic prognosticators are needed to triage these patients toward intensified combination therapy with novel targeted therapeutics.

Objective: We tested the role of the *NKX3.1* gene as a determinant of treatment outcome given its reported roles in tumor initiating cell (TIC) renewal, the DNA damage response, and cooperation with *c-MYC* during prostate cancer progression.

Methods: Using high-resolution array comparative genomic hybridization (aCGH), we profiled the copy number alterations in TIC genes using tumor DNA from frozen needle biopsies derived from 126 intermediate-risk patients who underwent IGRT. These data were correlated to biochemical relapse-free rate (bRFR) by the Kaplan-Meier method and Cox proportional hazards models.

Results: A screen of the aCGH-IGRT data for TIC genes showed frequent copy number alterations for *NKX3.1, PSCA,* and *c-MYC*. *NKX3.1* haploinsufficiency was associated with increased genomic instability independent of PSA, T-category, and Gleason-score. After adjusting for clinical factors in a multivariate model, *NKX3.1* haploinsufficiency was associated with bRFR when tested alone (HR = 3.05, 95% CI: 1.46-6.39, P = 0.0030) or when combined with *c-MYC* gain (HR = 3.88, 95% CI: 1.78-8.49, P = 0.00067). A similar association was observed for patients following radical prostatectomy with a public a CGH database. NKX3.1 status was associated with positive biopsies post-IGRT and increased clonogen radio resistance *in vitro*.

Conclusions: Our results support the use of genomic predictors, such as *NKX3.1* status, in needle biopsies for personalized approaches to prostate cancer management.

B04 **Andrea Lo,** Radiation Oncology

Title: A Cross-sectional Cohort study of Cerebrovascular Disease after Radiation Therapy for Craniopharyngioma

Andrea Lo[1,2], Fuchsia Howard[3], Alan Nichol[1,2], Haroon Hasan[1], Monty Martin[2], Manraj Heran[1,2], Karen Goddard, MD, FRCPC[1,2], [1]Department of Radiation Oncology, British Columbia (BC) Cancer Agency Vancouver Centre; [2]Faculty of Medicine, University of British Columbia; [3]School of Population and Public Health, University of British Columbia; [3]Department of Radiology, BC Cancer Agency Vancouver Centre; [4]Department of Radiology, Vancouver General Hospital

Objective: To determine the prevalence and characteristics of cerebrovascular disease in craniopharyngioma patients treated with radiotherapy (RT).

Methods: Between 1971 and 2007, 118 patients were treated for craniopharyngioma in British Columbia; 80 are still alive. Survivors who were ≤21 years old at diagnosis and had received RT ≥5 years ago were eligible for our study. Of the 35 eligible patients, all 27 patients with available contact information were approached about the study, and 20 agreed to participate. Patients underwent a clinical assessment, blood work, and a magnetic resonance angiogram (MRA) if possible. Two patients had computed tomography angiograms (CTAs) because of metal implants that precluded them from MRAs. One patient exceeded the MRA and CTA equipment weight limitations and could not have imaging. Fasting lipid profiles were obtained on 18 patients, and fasting glucose or hemoglobin A1c tests on 20 patients.

Results: Median age at diagnosis was 10.3 years (range: 2-21), median age at time of study was 29.0 years (range: 17-62), and median time since RT was 13.7 years (range: 7-37). Vascular abnormalities were detected in 6 of the 19 (32%) patients' angiograms. Five of 20 patients (25%) had a history of CVA: patients 1-4 had vascular abnormalities on angiogram, while patient 5 was the patient who could not be imaged. Patient #1 experienced an ischemic CVA in the post-operative setting, before RT; MRA showed a small supraclinoid right internal carotid artery (ICA) and M1 segment. Patient #2 developed an ischemic CVA 7 years after RT; she had irregularity and narrowing of the right middle cerebral artery on MRA. Patient #3 experienced an ischemic CVA 25 years after RT; his MRA revealed possible short segment stenosis of the right P1 segment. Patient #4 suffered a subarachnoid hemorrhage 2 years after RT due to a left A2 aneurysm; her CTA showed the stable clipped aneurysm, a mature right anterior frontal lobe infarct, and a mature small lacunar infarct. Patient #5 experienced an ischemic CVA 3.3 years after RT. Two patients with no history of CVA had abnormalities on MRA: one had stenosis of the left ICA and a small left posterior cerebral artery, while the other had either a cavernous malformation or a remote focus of hemorrhage in the periventricular white matter. The remaining 13 patients had normal angiography and no history of CVA. At the time of the study, 12 of 18 (67%) patients had hyperlipidemia, 1 of 20 (5%) had diabetes, and 1 of 20 (5%) had pre-diabetes. Five patients (25%) had a body mass index (BMI) > 30 and 8 patients (27%) had a BMI of 25-30.

Conclusion: Patients treated with RT for craniopharyngioma have a high prevalence of hyperlipidemia, CVA, and cerebrovascular abnormalities on imaging. These patients should undergo careful monitoring and aggressive modification of stroke risk factors.

B05 **Charles Yu,** Otolaryngology

Titles: Prevalence and Ethnic Variation of Pre-auricular Sinuses in Children

Charles Yu, Kushal Khera, Julie Pauwels, Neil K Chadha; Division of Otolaryngology, Head and Neck Surgery, BC Children's Hospital, Vancouver, British Columbia

Background: Pre-auricular sinus (PAS) describes a congenital ear malformation, sometimes requiring medical and/or surgical treatment. Limited prevalence data on PAS exists from adult studies and anecdotal evidence suggests a potential ethnic variation, but this has not been specifically investigated. Additionally there is a lack of robust evidence to support a potential genetic basis for PAS.

Objective: This study is the first to investigate the prevalence and ethnic variation of PAS using pediatric population level data.

Methods: In this prospective cross-sectional study, we enrolled 1106 healthy volunteers aged under 18 years. Recruitment took place between June and September 2014 from high pedestrian traffic areas in the BC Children's Hospital. Subjects attending the hospital for issues related to PAS were excluded. Participants were visually inspected for the presence of PAS followed by a questionnaire (demographics, self-identified ethnicity, family history of PAS, chronic medical conditions).

Results: Of 1106 participants enrolled (mean age=6.8, 592 males), we identified 26 children with PAS (2.4%), of which 7 were bilateral. Using Chi-Square statistics, a statistically significant ethnic variation was identified ($p<0.001$), with Asians having the highest prevalence (6.6%), followed by African Americans (4.5%), Middle Eastern (3.4%), First Nations (2.0%) and Caucasians (1.2%). No PAS were found in South Asians (n=124) or Latin Americans (n=18). Participants with a positive family history had a higher chance of having PAS (Odds Ratio [OR]=16.7, 95% Confidence Interval [CI] 7.3-38.5, $p<0.001$). There was also a stronger association between positive family history and bilateral PAS (OR=26.5, 95% CI: 5.8-121.7, $p<0.001$) compared to unilateral (OR=12.2, 95% CI: 4.6-32.5, $p<0.001$).

Conclusions: The prevalence of PAS was 2.4% in this pediatric population, whose ethnic diversity was found to be representative of the community. A significant ethnic variation existed and the association between family history and PAS suggested a potential genetic basis, particularly with bilateral PAS.

B06 S. Makarenko, Neurosurgery

Title: Suitability of suprasellar meningiomas for endoscopic endonasal surgery: anatomy and surgical outcomes

S. Makarenko, R. Akagami, E. Carreras, A. Brevner

Background: The treatment of perisellar meningioma intracranial tumours has remained a challenge over the past several decades, mainly attributed to the high risk of visual pathway involvement and vascular encasement. Surgical approaches have remained the mainstay of definitive treatment, but extended endoscopic transphenoidal surgery is emerging as an alternative option for treatment of these lesions. Endoscopic transsphenoidal surgery provides wider access to the anterior skull base when compared to the classical microscopic transsphenoidal approach, and technological advances such as angled endoscopes and image guidance have extended the success rates of this approach. Most authors however agree that only certain tumours would be appropriate for this treatment option, which causes an obvious selection bias. There is a limited number of studies investigating perisellar meningiomas due to the low incidence of the lesion. This is a retrospective review of perisellar meningiomas that were operated on by Dr. R. Akagami at Vancouver General Hospital between 2001-2013 with an open craniotomy approach, but may have been appropriate for an endoscopic treatment. Our aim is to have those patients who may have been candidates for endoscopic surgery identified based on radiographic tumour characteristics, and then compared against those patients who had perisellar meningiomas with anatomy not suitable for endoscopic treatment.

We will attempt to characterize the patients' suprasellar and meningioma anatomy, and then investigate their outcomes following transcranial resection of their tumour. Our hope is that the results will further identification of prospective patients that would be good candidates for endoscopic surgery for perisellar meningiomas, and offer that as an additional treatment option alongside open craniotomy.

Methods: This is a retrospective chart review. We will look at patient demographics, clinical presentation, tumour characteristics based on imaging, specific surgical management, post-operative course, and complications. A combination of univariate, multivariate and logistic regression analyses will be done on data collected.

Results: To date we have reviewed the imaging for 119 patients that had open surgical resection of parasellar meningioma lesions between 2001 and 2013. We have identified 54 patients with tumour anatomy that would be appropriate for endoscopic resection, and analysis is pending ethics approval.

Conclusions: Our hypothesis is that those patients that had perisellar meningiomas with anatomy suitable for endoscopic surgery will have more favourable post-operative outcomes from transcranial surgery.

B07 Jonathan Misskey, Vascular Surgery

Title: Fistula Outcomes in Octogenarians: Is a Fistula First Approach Appropriate?

Jonathan Misskey1 MD, Jason Faulds1,3 MD MSc FRCS(C), Shaun MacDonald1,2 MDCM FRCS(C), Keith Baxter1,3 MD MSc FRCS(C), York Hsiang1,3,4† MB ChB MHSc FRCS(C), 1. Department of Vascular Surgery, University of British Columbia, Canada, 2. Division of Vascular Surgery, Saint Paul's Hospital, 3.Division of Vascular Surgery, Vancouver General Hospital, 4. Professor, Department of Surgery, University of British Columbia, Canada, 5. Principle Investigator

Background: The fastest growing segment of the dialysis population in Canada is in patients over the age of 75, with an overall increase from 5% in 1980 to 28.2% in 2010. These patients present multiple significant challenges to caregivers including differences in life expectancy, comorbid health status, goals of care, and supportive care requirements. Currently the National Kidney Foundation KDOQI guidelines do not take age into account in recommendations for hemodialysis access.

Objectives: The goal of our study is to compare failure to mature, overall survival and complication rates for arteriovenous fistulae in octogenarians and non-octogenarians to determine if our standard approach to renal access should be modified to account for advanced age.

Methods: A review of all patients requiring arteriovenous fistulae for hemodialysis access at two teaching hospitals in Vancouver between 2007 and 2012. The study was designed as a retrospective cohort study with patients stratified by age into octogenarians and nonoctogenarians. Data was collected from a large, prospectively maintained database of all dialysis and predialysis patients in British Columbia.

Results: A total of 1019 patients had their access created during the study period and were eligible for inclusion. 156 (15.3%) of patients were 80 or older at the time of fistula creation. With respect to the primary endpoint, there was no difference between octogenarians and nonoctogenarians with respect to failure to mature of the fistula (38.7% vs. 34.0%; p = NS). Octogenarians had decreased overall survival and were significantly more likely to expire during the study period (45.8% vs. 23.2%; $p < 0.001$). There were no significant differences between the two cohorts and the postoperative incidence of steal syndrome (7.3% vs. 6.3% p = NS) or wound complications (5.3% vs. 5.7%; p = NS).

Conclusions: The results of this study demonstrate no overall differences in maturation rates within the octogenarian group and that age alone should not preclude placement of an autogenous arteriovenous fistula in this cohort. These findings demonstrate that an approach that incorporates limited life expectancy should be utilized when planning hemoaccess in this growing demographic.

B08 Rollin Y. Yu, Vascular Surgery

Title: Determining the Toe-Brachial Index in Young Healthy Adults

Rollin Y. Yu, Whitney L. Quong, Adrian Fung, York N. Hsiang, Division of Vascular Surgery, University of British Columbia, Vancouver, Canada

Background: Despite growing interest in utilizing the toe-brachial index (TBI) for clinical assessment of patients for Peripheral Artery Disease, there has not been any published study on the normal TBI in young, healthy individuals to determine a reference range.

Objective: The purpose of this study was to determine the TBI in healthy young adults and compare the measured value with the currently accepted clinical value.

Methods: Medical Students from the undergraduate class were prospectively recruited. Physical measurements (height, weight), health behaviors (physical activity quantity and type, smoking status, alcohol consumption), and medical history (medications, relevant diagnoses, family history) were collected. Bilateral brachial, toe and ankle blood pressures (using both dorsalis pedis and posterior tibial arteries) were measured. TBI was calculated as the mean toe blood pressure divided by the highest systolic brachial blood pressure.

Results: 40 medical students with a mean age of 24.7 ± 2.1 years without any comorbid conditions were studied. There were no current or past smokers. Participants maintained relatively healthy lifestyles (hours of activity per week: 5.1 ± 3.3; BMI: 21.7 ± 2.4). Caffeine and alcohol consumption was modest (10.6 ± 8.5 and 1.8 ± 2.7 drinks per week respectively). The mean systolic brachial blood pressure was 121 ± 9 mmHg (right), and 116 ± 9 mmHg (left). The TBI was 0.95 ± 0.11 (right) and 0.97 ± 0.13 (left) for males, and 0.86 ± 0.13 (right) and 0.86 ± 0.20 (left) for females.

Conclusion: The distribution of TBI in this healthy population differs significantly from the referenced normal range of 0.6-1.0. Our findings suggest that the accepted value of 0.6 for the low-normal limit is too low; this level may promote underdiagnosis of peripheral vascular disease, and represent foregone opportunities for early intervention. We recommend that the TBI reference range be modified to increase the clinical utility of this measurement.

B09 **Phyllis Kisa,** Pediatric general surgery

Title: Major Thrombotic Complications with Lower Limb PICCs in Surgical Neonates

Phyllis Kisa1, Joseph Ting2, Allison Callejas2, Horacio Osiovich2, Sonia Butterworth1 1Division Of Pediatric Surgery, University Of British Columbia, British Columbia Children's Hospital; 2Division Of Neonatology, University Of British Columbia, British Columbia Children's Hospital

Background: PICC lines are now used routinely to provide central access for the neonatal intensive care population (NICU). Neonates are known to be at high risk for venous thromboembolism (VTE) related to central catheters. No literature exists about VTE PICC- related morbidity in the NICU abdominal surgery subgroup.

Methods: With REB approval, a retrospective review of a NICU database of PICC insertions performed at a tertiary children's hospital was conducted (January 2010-June2013). Information about PICCs and complications were recorded. For patients with a major thrombotic complication, charts were reviewed. A major thrombotic complication was defined as a thrombosis which required medical and/or surgical intervention.

Results: 692 PICCs were inserted (486 upper extremity, 142 in the lower extremity and 64in the scalp). Five patients had a major thrombotic complication; all had significant abdominal pathology. All patients with a major thrombotic complication had a lower extremity PICC which was at or below L1 (L1-S1), running parenteral nutrition.

Conclusions: In the current study, only neonates with abdominal pathology and a lower extremity insertion site suffered major thrombotic complications from PICC lines. Given all patients PICC tips were below the recommended location, more rigorous surveillance (with re-positioning if required) may avoid these complications for future patients.

B10 **Morgan Evans,** Plastic Surgery

Title: Treatment of Toxic Epidermal Necrolysis by a Multidisciplinary Team. A Review.

Sheena Sikora, MD; **Morgan Evans, MD**; Diana Song, MSI; Mark Kirchhof, MD; Monica Miliszewski; PhD; Jan Dutz, MD; Anthony Papp, MD. Division of Plastic Surgery, Vancouver General Hospital

Background: Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are mucocutaneous hypersensitivity reactions, usually to drugs or their metabolites. TEN is the most severe involving greater than 30% of the total body surface area (TBSA). Management of these patients usually requires a large multidisciplinary team of physicians for both wound and medical management. Treatment of these patients vary between centers and physicians and there is lack of a standardized treatment protocol in the medical literature.

Objectives: 1. To review the literature and complete a retrospective review of patients treated at Vancouver General Hospital over a 10-year period. 2. Developing a set of treatment guidelines to standardize care of these complex patients.

Methods: Plastic Surgery and Dermatology joined forces to conduct a retrospective chart review of all patients diagnosed with SJS/TEN and treated at Vancouver General Hospital from 2001-2011 was completed. Data collected include patient demographics, time to transfer to a burn center, SCORTEN calculation, suspected cause of TEN, %TBSA involved, length of stay in hospital and ICU, medications, dressings, infections/cultures, fluids, mucosal involvement, teams involved, associated complications, morbidity and mortality. Data is reported quantitatively.

Results: A total of 64 patients were identified (28 SJS, 21 SJS/TEN overlap, 18 TEN). In SJS/TEN overlap and TEN patients, oral mucosa and trunk were the primary sites involved. SCORTEN calculations were highest in the TEN group. Plastic surgery was consulted in 53% of TEN cases, 52% of SJS/TEN cases and 25% of SJS cases. Patients were admitted to a burn unit in 74% of TEN cases, 57% of TEN/SJS cases and 21% of SJS cases. Time from symptoms to diagnosis and transfer to a burn unit was highest for TEN patients. Time from presentation to diagnosis was highest in SJS/TEN overlap. Triggers were identified in 67-82% of cases. Treatment varied widely. Patients were treated conservatively, with steroids, IVIG, and cyclosporine alone or in combination. Observed mortality was higher than predicted by SCORTEN for patients treated with IVIG and lower for those treated with Cyclosporin. Dressings varied greatly and were often changed throughout a patients stay. Fluid resuscitation in the first 24 hours was 3-4L

Conclusions: SJS and TEN are a spectrum of severe mucocutaneous reactions that have unclear treatment recommendations within the literature and within our level 1 hospital. This research is being used to develop treatment guidelines for TEN/SJS management.

B11 ***Adelyn L Ho*****,** Plastic Surgery

Title: A Review of Post-mastectomy Irradiation in Two-stage Tissue Expander/Implant Immediate Breast Reconstruction with Acellular Dermal Matrix

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Introduction: An increasing number of women undergoing immediate two-stage tissue expander/implant (TE/I) breast reconstruction receive post-mastectomy radiation (PMRT) as part of their management. Acellular dermal matrix (ADM) is increasingly being used in these patients because it may decrease complication rates and ultimately lead to a more favourable outcome by mitigating radiation sequelae.

Objective: The objective of this study was to compare the outcomes of irradiated immediate two-stage TE/I reconstruction with ADM to a group without ADM.

Methods: A retrospective review of patient records undergoing immediate two-stage TE/I reconstruction between January 1998 and December 2013 was performed. Patients reconstructed with ADM and no-ADM at the time of TE placement were identified. Demographic, major complications, capsular contracture, and revision surgery of the ADM were compared to a group who did not receive ADM.

Results: 34 patients who received ADM at the time of TE insertion were identified. These ADM patients were compared to 113 patients who did not receive ADM. Demographic and clinical characteristics between these two groups were comparable. There was no significant difference in the rate of major complications in the ADM group (18.2%) and non-ADM group (16.8%). This finding remained after controlling for age, BMI, smoking status, mastectomy weight, and tissue expander type (Odds Ratio 0.78, 95% Confidence Interval 0.23-2.62, p-value=0.69). There was not difference between the ADM and non-ADM group with respect to the proportion of patients that successfully had their TE exchanged for a permanent implant. There was a decrease in clinically significant capsular contracture in the ADM group compared to the non-ADM group, although this did not reach statistical significance.

Conclusions: The outcomes of this study demonstrate that the use of ADM in the setting of immediate TE/implant breast reconstruction patients who undergo post-mastectomy radiation may not confer the benefit that was much anticipated. Despite this, ADM may lend itself to an improvement in clinically significant capsular contracture that warrants further study.

B12 **Layla Nabai,** Plastic Surgery

Title: Controlled delivery of anti-fibrosis agent, FS2, using biocompatible microspheres: A novel approach to prevention of fibrotic scar formation after surgry

Layla Nabai, [1] Malihe-Sadat Poormasjedi-Meibod, [1] Ryan Hartwell, [1] John Jackson,[2] Aziz Ghahary. [1], 1 BC Professional Fire Fighters' Burn & Wound Healing Research Lab. 818 West 10th Ave. ICORD, The Blusson Spinal Cord Centre, Vancouver, 2 Faculty of Pharmaceutical Sciences, The University of British Columbia, 2405 Westbrook Mall, Vancouver

Background: Scar formation, an inevitable consequence of healing after most surgical procedures, may lead to considerable disfigurement and/or discomfort especially in younger age groups. Despite the use, various therapeutic methods that have been practiced for years, there has been only limited success in the prevention or treatment of scars.

Hypothesis: In this study we hypothesised that localized controlled release of anti-fibrosis agents embedded in wound bed before suturing will reduce fibrotic scar formation following surgical procedures.

Methods: Biocampatible controlled release microspheres containing anti-fibrosis agent,FS2, were fabricated using emulsion/solvent evaporation technique. The encapsulation efficiency and in vitro release profile were determined. To evaluate the in vivo efficacy of the microspheres we used an animal model of fibrosis with some modifications. In this model PVA sponges with or without FS2 microspheres were implanted subcutaneously in rats. After four weeks, the PVA sponges and the overlying skin were removed and examined histologically.

Results: The average encapsulation efficiency of the FS2 loaded microspheres was 80.65%±18.49.

The release profile revealed an initial burst release of around 10% of the encapsulated drug in the first 24 hours and 1-1.5% daily in following days. The histological examination of the tissue samples revealed significant reduction in the cellular infiltration and collagen deposition inside and around the PVA sponge implants loaded with FS2 microspheres compared to PVA alone.

Conclusion: The anti-fibrosis agent FS2 can efficiently be encapsulated in a biocompatible polymer with a release profile that prevents fibrosis in vivo. This drug delivery system provides a promising solution for prevention of fibrotic scar formation after surgery.

Simultaneous Session C

C01 **Stephanie Campbell,** General Surgery

Title: The Core Trithorax Group Protein Wdr5 is Essential for Pancreas Progenitor Differentiation

Stephanie Campbell[1,2,3], Bryan Tennant[1,2,3], Cheryl Whiting[1], Brad Hoffman[1,2,3]; [1]Child and Family Research Institute, Vancouver, BC; [2]Department of Cell and Developmental Biology, University of British Columbia, Vancouver, BC; [3]Department of Surgery, Faculty of Medicine, Vancouver, BC

Background: All cells of the pancreas arise from $Pdx1^{+}Sox9^{+}$ pancreas progenitors that begin differentiation into endocrine, exocrine and ductal cells starting at around E12.5. The transcription factor Ngn3 plays a critical role in this process by specifying pancreas endocrine cells that will mature into the various islet cell types, including insulin-producing beta-cells. Exactly how these transcription factors are appropriately regulated is still largely unknown. We have previously compared the chromatin state of mouse pancreatic islets and ES cells using ChIP-seq data and found that islet-specific enhancers need to gain activating marks, such as H3K4me1, during development; however, when and how this occurs is still not clear.

Hypothesis: The Trithorax group (TrxG) complex promotes gene activation by catalyzing H3K4 methylation via MLL/SET1 methyltransferases and we hypothesized that this complex would be critical to the induction of genes such as Ngn3 during pancreas development.

Methods: To begin to test this hypothesis we first examined the expression of select TrxG complex proteins, Wdr5, Dpy30, Mll1 and Mll3, at E12.5 and E14.5 of mouse pancreas development by immunohistochemistry. To study the TrxG complex in an in vitro model of pancreas development, we expanded mouse E13.5 $Pdx1^{+}Sox9^{+}Ngn3^{-}$ pancreas progenitor cells into spheres and induced them to differentiate. After seven days, spheres displayed typical apical-basal polarity of the developing pancreas and differentiated into mature islet cell types, including glucose-responsive insulin-secreting endocrine cells. We next assessed whether the TrxG complex played a role in regulating pancreas sphere differentiation by lentiviral shRNA mediated knockdown of the core TrxG protein Wdr5.

Results: We found that Wdr5, Dpy30, Mll1 and Mll3 proteins were widely expressed in mouse embryonic pancreas and were co-expressed with both $Pdx1^{+}$ and $Ngn3^{+}$ cells. shWdr5 treatment reduced the number of spheres generated per pancreas as well as the diameter of the spheres produced. Interestingly, shWdr5 also almost completely prevented Ngn3 expression and subsequent expression of markers of endocrine cells such as Ins1 and Gcg. This effect was confirmed by experiments in mouse insulin promoter-GFP spheres, which had significantly reduced production of GFP^{+} cells in shWdr5-treated spheres.

Conclusions: Our results suggest that the core TrxG complex protein Wdr5 is essential for Ngn3 induction and subsequent endocrine differentiation of mouse pancreas progenitors.

C02 **Pier-Luc Clermont,** Radiation oncology

Title: Polycomb-Mediated Silencing in Neuroendocrine Prostate Cancer

Pier-Luc Clermont[1,2], Dong Lin[1,3], Francesco Crea[1,4], Rebecca Wu[1], Hui Xue[1], Yuwei Wang[1], Kelsie L. Thu[1,5], Wan L. Lam[1,5], Yuzhuo Wang[1,2,3,6] Cheryl D. Helgason[1,2,4]; 1) Department of Experimental Therapeutics, British Columbia Cancer Research Centre, Vancouver, 2) Interdisciplinary Oncology Program, Faculty of Medicine, University of British Columbia, Vancouver, 3) Vancouver Prostate Centre, Vancouver, 4) Department of Surgery, University of British Columbia, 5) Genetics Unit, Department of Integrative Oncology, British Columbia Cancer Research Centre, Vancouver 6) Department of Urologic Sciences, Faculty of Medicine, University of British Columbia, Vancouver, British Columbia, Canada.

Background: Neuroendocrine prostate cancer (NEPC) represents a highly aggressive malignancy for which the median survival is less than a year, owing to the lack of suitable pre-clinical models to study its molecular basis. Addressing this need, we have previously established a high-fidelity, patient-derived xenograft model of NEPC (331R) arising from the transdifferentiation of a prostate adenocarcinoma (331) following androgen-deprivation therapy *in vivo*. Our initial analysis revealed that 331 and 331R shared a remarkably similar genetic profile, suggesting that epigenetic alterations were likely to drive NEPC pathogenesis.

Objectives: The underlying goals of this research project were to characterize the epigenetic landscape of NEPC and to identify potential epigenetic drug targets for this lethal disease.

Methods: We conducted comparative gene expression analysis between 331R and 331, as well as a clinical cohort, to identify epigenetic regulators that were differentially expressed in NEPC. We also investigated genes that were consistently downregulated in many NEPC models to infer their molecular and biological properties.

Results: By combining expression profiles from multiple NEPC datasets, we provided evidence that multiple PcG family members are overexpressed in NEPC, notably CBX2 and EZH2. Furthermore, CBX2 and EZH2 were specifically upregulated in small cell lung cancer, a neuroendocrine tumor used as a model for NEPC, compared to non-small cell lung cancer. Finally, we derived a neuroendocrine-associated repression signature (NEARS) that was enriched in PcG targets and significantly predicted aggressive clinical progression in clinical prostate cancer cohorts.

Conclusions: Overall, we have explored the epigenetic landscape of NEPC in unique models derived from patient tissues. Our results support a clinically-relevant function for PcG-mediated silencing in NEPC, providing novel avenues for epigenetic therapies in the context of lethal NEPC.

C03 **Nicholas AJ Dawson**, General Surgery

Title: Development of high-dimensional mass cytometry for immune monitoring in hematopoietic stem cell transplant patients

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Introduction: Mass cytometry (CyTOF; DVS Sciences) is a novel approach to flow cytometry, combining traditional flow cytometry fluidics with a mass spectrometer to analyse over 30 targets simultaneously on a single cell basis. Conjugation of target-specific antibodies to metal isotopes instead of fluorophores is preferable because there are minimal concerns for compensation and antibodies remain more stable over time. This results in the ability to observe many more markers on a

single cell to a higher degree of resolution than fluorescence flow cytometry. Since CyTOF is a novel technology, effective reagents and protocols for staining cells have not yet been established in the scientific community. Ultimately, we will utilize mass cytometry to examine reconstitution of the immune system on detailed basis to draw conclusions regarding pathogenesis of chronic graft-versus-host disease (GVHD) in hematopoetic stem cell transplant (HSCT) patients and the effects of anti-thymocyte globulin (ATG) treatment on disease pathology.

Objectives : To establish a working protocol and determine the best reagents and buffers for CyTOF staining, including viability and barcoding indicators, and compare their effectiveness to fluorescence flow cytometry; To develop a novel strategy to stain transcription factors, namely FOXP3, a transcription factor specific to regulatory T cells; To use the technology developed above to show how the immune system reconstitutes post-HSCT and to show how treatment affects reconstitution of the immune system

Methods: To develop mass cytometry technology, healthy, cryopreserved PBMC samples were used to fine-tune methods, establish standard protocols and titrate 24 T cell-specific markers. Different buffer combinations and protocol strategies were used to determine optimal conditions for FOXP3 staining. For GVHD analysis, cryopreserved PBMCs from HSCT patients have been collected at month 0, 3, 6 and 12 post-transplant and will be used for CyTOF analysis.

Results: Mass cytometry staining patterns are highly similar to those found on fluorescence flow cytometry, including viability staining. A novel strategy was developed to reliably stain for FOXP3 (n=3), a previously unreported result. High dimensional clustering analysis (SPADE) reveals expected T cell subsets and will be useful delineating disease patterns.

Conclusion: Mass cytometry is an appropriate substitute for fluorescence flow cytometry, yielding highly accurate, high-dimensional single cell data that can be used for examining disease pathology of chronic GVHD in HSCT patients. We think the resulting GVHD patient data will provide novel insights into the mechanism and pathogenesis of chronic GVHD.

C04 **Nicole A. J. Krentz,** General Surgery

Tittle: Increasing G1 Length During Pancreatic Progenitor Cell Differentiation.

Nicole A. J. Krentz[1,2], Mei Tang[1,2], Akie Watanabe[1,2] and Francis C. Lynn[1,2;1]Child and Family Research Institute, Vancouver, BC, Canada; [2]Deparment of Surgery, Faculty of Medicine, University of British Columbia

Background: Cellular-based therapies for diabetes mellitus, such as the differentiation of human embryonic stem cells (hESCs), require an in-depth understanding of pancreatic development. During early pancreatic development, the Pdx1+Cpa1+ tip multipotent progenitor cells (MPCs) give rise to all three cell types of the pancreas, exocrine, endocrine and ductal cells, while the trunk Pdx1+Cpa1- bipotent progenitor cells (BPCs) give rise to endocrine or ductal cells only. The process that regulates the proliferation and differentiation of these progenitors populations is not fully known. There is evidence during neurogenesis that the length of the G1 phase of the cell cycle can directly influence the differentiation of neural precursors. Thus, we hypothesize that the cell cycle regulates pancreatogenesis and that lengthening the G1 phase of the cell cycle is essential for progenitor cell differentiation.

Methods: Pregnant CD-1 mice (P12.5) were injected with the thymidine analog 5'Ethynyl-2' deoxyuridine (EdU) every 1.5 hours starting at 9 am. Embryos were collected at evenly spaced intervals from 9:30 am to 8 pm. The number of Pdx1+Cpa1+ and Pdx1+Cpa1- cells labeled with EdU was determined using immunofluorescence and confocal microscopy (n>4). The lengths of the G1, S and G2/M phases were determined mathematically from the length of time required to label all dividing cells, the number of cells labeled at time 0, and the proportion of dividing cells.

Results: We determined that the G1 length of cells within the pancreatic epithelium increased from 5 to 8 hours from E11.5 to E13.5 while the lengths of both S and G2/M phases remained similar. This increase in G1 length was also measured in the MPCs and BPCs over the same developmental period. Intriguingly, we measured an increase in the length of S phase in BPCs compared with MPCs at E11.5, E12.5 and E13.5. We also noted a significant difference ($p<0.05$; n=17) in the maximal proportion of EdU labeled cells or the growth fraction of MPCs and BPCs at 90% and 66%, respectively. Preliminary data suggests that these non-dividing Pdx1+ cells are still located within the pancreatic epithelium, express other progenitor cells markers such as Sox9 and Nkx6.1, and are Ki67+. These results suggest that there is a population of progenitor cells that are still in the cell cycle but are not actively dividing.

Conclusions: These findings are consistent with the 'cell cycle length hypothesis' from neural development and suggest that the G1 lengthening is important for pancreatic progenitor cell differentiation. Understanding this process may gave new insight into methods for producing mature beta cells from hESCs for transplantation.

C05 **James Lawson,** Otolaryngology

Title: Mechanisms and Impacts of Exosomal microRNAs on Lung Adenocarcinoma Tumorigenesis

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Background: Lung cancer is the leading cause of cancer death worldwide. With a low five-year survival rate it is important that new methods for treatment are discovered. microRNAs (miRNA) are small non-coding RNA molecules that modulate the activity of specific protein coding genes. miRNAs have been shown to have a number of functions in cancer cells including playing a tumor suppressive and an oncogenic function. miRNAs are packaged into exosomes non-randomly as certain miRNAs are highly enriched in exosomal fractions compared to cellular fractions. Exosomes have been shown to have considerable function in the progression of many cancers including lung cancer.

Objective: To discover the impact of exosomal miRNAs on lung adenocarcinoma tumorigenesis.

Methods: miRNA profiles were generated from exosomal and cellular fractions of lung adenocarcinoma cell lines. Candidate miRNAs that have at least a four–fold change between the two fractions were selected for further analysis. To assess the biological role of the miRNA candidates selectively packaged into exosomes, lentiviral miRNA inhibitors were added into the lung adenocarcinoma cell lines to knockdown candidate miRNAs. After selection for knockdown GW4869, a drug that inhibits exosome formation was added into the cell lines in order to prevent exosomes formation, trapping exosomal miRNAs within the cells thereby increasing their concentration and allowing us to determine miRNA intracellular function.

Results: Seven miRNAs are up regulated in exosomal samples while only one was up regulated in cellular fractions. miRNAs were successfully knocked down by lentiviral inhibitors with ~90% efficiency allowing us to assess function and role in cell growth. miRNAs up-regulated in exosomes appear to regulate key oncogenes, including EGFR and c-Myc.

Conclusion: We have identified a novel mechanism of gene regulation through miRNAs actively being selected for export via exosomes. These miRNAs function to regulate key oncogenes within the tumor and it is predicted that exosomal packaging of miRNAs eliminates tumor suppressive miRNAs from the cell. This is a novel form of gene regulation that could be exploited for the development of novel therapeutics.

C06 **Dominika Nackiewicz,** General Surgery

Title: Resident islet macrophages are M2 skewed in models of islet inflammation and type 2 diabetes in an effort to limit inflammation and beta cell damage

Dominika Nackiewicz, Priya Yoganathan, Amanda Cunningham, Madeleine Speck, Meixia Dan, Jan Ehses; Division of General Surgery, Department of Surgery, Faculty of Medicine, University of British Columbia, and Child & Family Research Institute, Vancouver, BC, Canada

Background: Current estimates indicate that 382 million people are living with diabetes, and 592 million are predicted to be diagnosed with diabetes by 2035 worldwide. Ninety percent of diabetic individuals have type 2 diabetes. Chronic inflammation is a characteristic of type 2 diabetes, and it is becoming increasingly clear that disturbances in the resolution of inflammation are an underlying feature of chronic inflammatory conditions. One of the features of type 2 diabetes is an increased number of macrophages infiltrating pancreatic islets, contributing to IL-1-mediated β cell dysfunction in this disease. While previous work has focused on the detrimental role of pro-inflammatory M1 macrophages (MΦs), little attention has been given to the role of M2 MΦs during islet inflammation. Understanding the role of MΦs during islet inflammation will be critical for targeting these cells to treat diabetes.

Objectives: In the present study, we sought to characterize the role of islet M2 MΦs during islet inflammation, and determine how they affect β cell function and survival.

Methods: Islet M2 MΦs were studied in the Goto-Kakizaki (GK) rat model of type 2 diabetes and multiple low-dose streptozotocin (MLD-STZ) mouse model of β cell death. Clodronate-loaded liposomes (clo-lip) were used to deplete islet M2 MΦs *ex vivo,* flow cytometry was used to sort islet M2 MΦs, and gene expression was assessed by qPCR. To study the role of M2 MΦs *in vitro* we generated bone marrow derived MΦs (BMDMs) and stimulated them with IL-4, IL-10 and TGFβ1 in the absence and presence of lipopolysaccharide (LPS)+/-ATP.

Results: Pancreatic islets isolated from 8-12 wk old GK rats displayed marked up-regulation of genes involved in pro-IL-1β processing (*Casp1*), genes of pro-inflammatory cytokines (*Il1b, Il6, Tnf*), and anti-inflammatory cytokines (*Il1rn, Il*10) compared to age-matched Wistar rats. Depletion of resident islet MΦs from GK islets *ex vivo* resulted in reduced *Il1rn* (IL-1Ra) expression relative to Wistar controls, and a 4-fold increase in tissue *Il1b* expression, with no changes in other cytokine genes. Following STZ-induced β cell death, resident mouse islet F4/80^{+}CD11b^{+}CD11c^{+} MΦs were increased as a proportion of total islet cells, and had up-regulated *Il1rn*, *Il10*, and *Igf1* mRNA on day 1, and increased *Vegfa* mRNA on day 10 post-STZ. No changes in pro-inflammatory cytokine (*Il1b, Tnf*) mRNA expression were detected. Finally, generating M2 MΦs *in vitro* with IL-4, IL-10, and TGFβ1 resulted in increased production of IL-1Ra in response to LPS+ATP, and increased PDGFa and TGFβi secretion in response to LPS only. Skewing MΦs to M2 also partly reversed the effect of M1 MΦs on *Pdx1* expression in mouse islets.

Conclusion: Resident islet MΦs in the GK rat and resident islet MΦs following STZ-induced β cell death are M2 skewed and are likely major contributors of islet IL-1Ra secretion, in an attempt to antagonize IL-1 effects on β cells. Generating M2 MΦs *in vitro* with IL-4, IL-10, and TGFβ1 also resulted in increased IL-1Ra production, and future studies will determine the role of these cells on β cell function and survival. Ongoing studies are also elucidating the role of M2 MΦs following STZ-induced β cell death *in vivo*. Strategies aimed at skewing MΦs to M2 may be used to improve glycemia and treat type 2 diabetes.

C07 **Yoo Jin Park,** General Surgery

Title: Blocking IL-1 Receptor Signaling Restores Impaired Processing of Pro-Islet Amyloid Polypeptide and Reduces Amyloid Formation in Human Islets: Implications in Clinical Islet Transplantation

Yoo Jin Park[1], Garth L. Warnock[1], Nooshin Safikhan[1], Ziliang Ao[1], Mark Meloche[1], Timothy J. Kieffer[1,2], Lucy Marzban[1]; Division of General Surgery, Departments of [1]Surgery and [2]Cellular & Physiological Sciences, Faculty of Medicine, University of British Columbia*

Background: In past decade, human islet transplantation has provided a promising approach for treatment of type 1 diabetes (T1D). It is however currently limited by low number of pancreatic donors and islet loss during both pre-transplant culture and post-transplantation that eventually leads to graft failure in most patients. Islet amyloid is a pathologic lesion of pancreas in type 2 diabetes (T2D) that also forms during islet culture and post-transplantation. Islet amyloid is comprised mainly of human islet amyloid polypeptide (hIAPP), a beta-cell peptide produced by cleavage at the C- and N-termini of its precursor prohIAPP. Impaired prohIAPP processing has been implicated in hIAPP aggregation and increased amyloid formation. We previously showed that islet amyloid formation is associated with elevated islet IL-1beta levels.

Objectives: In this study, we examined the effects of IL-1beta on prohIAPP processing and tested if blocking IL-1beta signaling by treatment with Anakinra (Kineret), a clinically approved IL-1 receptor antagonist, can restore impaired prohIAPP processing in islet beta-cells thereby reduce amyloid formation and its toxicity.

Methods: Freshly isolated human islets (n=6 donors) were cultured in CMRL with normal (5.5 mM) or elevated glucose (11.1 mM; to potentiate amyloid formation) in the presence or absence of Anakinra (10 µg/ml) for up to 7 days. (Pro)hIAPP forms were detected in islet lysates by Western blot followed by immunoblot using an antibody that recognizes all (pro)hIAPP forms or antisera specific for N- and C-termini of prohIAPP. Islet IL-1beta levels, amyloid formation, and beta-cell apoptosis were assessed by immunolabeling methods. Beta-cell function was assessed by measuring insulin response to elevated glucose and islet insulin content (ELISA).

Results: Mature hIAPP was the major form detected in freshly isolated human islets with low levels of (pro)hIAPP also detectable, whereas prohIAPP and its intermediates were the main forms detected in cultured islets. IL-1beta treatment during culture reduced beta-cell function (lower insulin response to glucose) and potentiated impaired prohIAPP processing, resulting in increased amyloid formation and beta-cell apoptosis. Blocking IL-1beta signaling improved impaired prohIAPP processing in cultured islets manifested as lower (pro)hIAPP intermediates and higher mature hIAPP than untreated islets, resulting in less amyloid formation and beta-cell death in those islets.

Conclusions: These data provide first evidence that beta-cell dysfunction mediated by IL-1beta leads to impaired prohIAPP processing and potentiates amyloid formation. IL-1 receptor blockers may provide a novel approach to restore impaired prohIAPP processing thereby reducing amyloid formation and its beta-cell toxicity in T2D and islet grafts.

C08 **Alexis Shih,** General Surgery

Title: Bcl-x_L Regulates Pancreatic Beta-cell Function and Dysfunction during Glucotoxic Stress

Alexis Shih and Dan S. Luciani; UBC, Department of Surgery, Division of General Surgery; Child & Family Research Institute, Diabetes Research Program, Vancouver.

Background: Chronic nutrient oversupply increases metabolic load and oxidative stress in the insulin-secreting pancreatic β-cells. This progressively impairs β-cell function and survival, contributing to the development of type 2 diabetes. Bcl-x_L is a pro-survival member of the B-cell lymphoma 2 (Bcl-2) family of apoptosis-regulating proteins. We previously reported that Bcl-2 and Bcl-x_L also suppress β-cell glucose signalling, seemingly via effects on mitochondrial metabolism. Conceivably, this metabolic dampening may help counter β-cell dysfunction during the nutrient excess that precipitate development of type 2 diabetes.

Hypothesis: Bcl-x_L protects β-cell function during metabolic stress via regulation of mitochondrial physiology.

Methods: To determine the roles of Bcl-x_L in β-cell function and dysfunction we overexpressed eYFP-tagged Bcl-x_L in primary mouse β-cells using an adenovirus (Ad.eYFP.Bcl-x_L), and further compared pancreatic islets from mice with β-cell-specific deletion of Bcl-x (BclxβKO) and their wild-type (WT) control littermates. Changes in intracellular Ca^{2+} ($[Ca^{2+}]_i$) and mitochondrial membrane potential ($\Delta\Psi_m$) were imaged using the fluorescent indicators Fura-2 AM and TMRE, respectively. We examined the progressive effects of hyperglycemia on islet function by comparing acute glucose-induced $[Ca^{2+}]_i$ signaling of WT and BclxβKO islets after culturing them in normal (11 mM) or high (25 mM) glucose for 2 days and 6 days. The involvement of reactive oxygen species ROS was examined using the ROS scavenger N-acetyl cysteine (NAC).

Results: Bcl-x_L overexpression suppressed glucose-induced β-cell $[Ca^{2+}]_i$ signals in a NAC-insensitive (ROS-independent) manner. Conversely, BclxβKO islets showed higher steady-state $[Ca^{2+}]_i$ responses to glucose than WT islets. Comparisons of glucose-induced changes in $\Delta\Psi_m$ suggested this was associated with moderately enhanced mitochondrial activity in Bcl-x_L-deficient cells. These results further support an intrinsic role of Bcl-x_L in suppressing β-cell mitochondrial glucose metabolism. When culturing islets under hyperglycemic conditions we observed several striking time-dependent perturbations of normal $[Ca^{2+}]_i$ homeostasis: 1) Elevated baseline $[Ca^{2+}]_i$ levels in low glucose; 2) slight reduction in peak response to a step-wise increase in extracellular glucose; and 3) progressive failure of $[Ca^{2+}]_i$ to return to baseline following withdrawal of the glucose stimulus. Notably, the disruption of baseline $[Ca^{2+}]_i$ and the loss of $[Ca^{2+}]_i$ recovery were significantly worsened in BclxβKO islets.

Conclusions: In addition to controlling apoptosis execution, normal levels of endogenous Bcl-x_L help maintain a metabolic balance that protects β-cells from dysfunction during chronic nutrient stress. Further clarifying these dual roles of Bcl-x_L in β-cell function and death will help clarify the complex pathogenesis of type 2 diabetes.

C09 **Thilo Speckmann,** General Surgery

Title: Regulation Of Npas4 Expression And Stability In Pancreatic Beta Cells

Thilo Speckmann, Paul Sabatini, Cuilan Nian and Francis Lynn; Department of Surgery & Child and Family Research Institute

Background: Elevated blood sugar levels stimulate pancreatic beta cells to release the hormone insulin, which instructs peripheral tissues to take up glucose and restore normoglycemia. In type 2 diabetes, persistent physiological stress can drive beta cell death, leading to chronic hyperglycemia and long term complications such as retinopathy, nephropathy and neuropathy. We previously demonstrated that Npas4, a calcium-dependent transcription factor, is rapidly induced in beta cells in response to physiological beta cell stressors such as high glucose or the fatty acid palmitate. In addition, *in vitro* overexpression of Npas4 protected beta cells from stress-induced apoptosis. We thus hypothesize that during periods of nutrient excess, Npas4 and its gene regulatory network represent an adaptive mechanism to ensure beta cell viability and function. Interestingly, removal of stimulatory conditions or continuous exposure to stressors leads to a decline in Npas4 transcript expression as well as protein levels. Hence, inadequate levels of Npas4 during phases of nutrient excess could be an underlying mechanism leading to beta cell exhaustion. Furthermore, it has been demonstrated in the brain that Npas4 needs specific PAS domain partner factors to regulate transcription, while this has not yet been studied in beta cells. Understanding the regulation of Npas4 expression and stability, as well as identifying Npas4-binding partners, could lead to novel treatment option for type 2 diabetes including stabilizing Npas4 expression to mitigate beta cell stress and death.

Objective: My current research aims to identify signalling pathways involved in the induction of Npas4, post-translational modifications that affect Npas4 protein stability, and Npas4 interaction partners.

Methods: Npas4 expression was induced by depolarization in a culture medium containing high glucose and high potassium, triggering calcium (Ca^{2+}) influx. Using the murine beta cell line MIN6, pharmacological antagonists of major Ca^{2+} signalling pathways were applied *in vitro*, and changes in Npas4 mRNA levels were detected by real-time PCR. Npas4 protein stability was studied using the proteasome inhibitor MG132, while Npas4-binding partners were detected by co-immunoprecipitation.

Results: Under stimulatory conditions, Npas4 mRNA expression was significantly reduced by the calcineurin inhibitor FK-506 or the CaMK inhibitor KN-93. A trend towards decreased Npas4 mRNA induction could be seen using the more specific CaMKII peptide inhibitor AIP. Furthermore, the addition of MG132 prevented Npas4 protein degradation. Lastly, co-immunoprecipation revealed that the PAS domain proteins Arnt and Arnt2 act as Npas4-binding partners.

Conclusions: In beta cells, Npas4 mRNA expression may not be induced by a single signalling cascade but depends on both calcineurin and CaMK signalling. It is noteworthy that FK-506, an immunosuppressant, inhibits Npas4 within therapeutic ranges, since the drug can cause new-onset diabetes after transplantation that may be partially driven through a reduction in Npas4 levels. Future studies aim to identify transcription factors downstream of the implicated signalling cascades that directly control Npas4 expression. Moreover, the prevention of Npas4 degradation after MG132 treatment indicates the involvement of a proteasomal degradation pathway that could be a therapeutic target. Further studies will be aimed at identifying post-translational modifications to understand more about the dynamic regulation of Npas4 protein. Finally, the identification of Npas4-interacting proteins Arnt and Arnt2 will be useful for studying and characterizing the beta cell protective gene regulatory network controlled by Npas4.

C10 **Annika C. Sun,** Thoracic surgery

Title: Novel roles of the negative co-stimulatory molecule B7-H4 in β-cell function and ER stress signaling

Annika C. Sun [1,2,3], Dan S. Luciani [1,2], Garth L. Warnock[1,3; 1]Department of Surgery, University of British Columbia; [2]Child and Family Research Institute, Diabetes Research Program; [3]Vancouver General Hospital, Vancouver, BC

Background: B7-H4 is a negative co-stimulatory molecule that is expressed on the cell membranes of antigen presenting cells, and is known to down-regulate the immune response. B7-H4 mRNA is highly expressed in pancreatic β-cells, but endogenous protein levels are relatively low. We previously reported that overexpression of islet B7-H4 improves graft survival in mouse models of islet transplantation, and that systemic administration of B7-H4.Ig delays diabetes onset in the NOD mouse. Unpublished data further show B7-H4.Ig treatment is accompanied by reduced expression of ER stress-induced genes. Of note, B7-H4 is abundantly expressed in various tumor cells where it can be expressed intracellularly, and may have endogenous metabolic and anti-apoptotic effects. These observations raise the intriguing possibility that B7-H4 may also regulate β-cell function, stress signaling, and survival independently of its established immune-regulatory functions.

Objectives/Hypothesis: We want to examine whether B7-H4 directly affects β-cell function and protects β-cells from ER stress and cell death. We hypothesize that B7-H4 promotes β-cell survival by modulating the Unfolded Protein Response (UPR).

Methods: Islets from transgenic mice with β-cell-specific overexpression of B7-H4 (B7-H4 Tg) and age-matched controls (WT) were compared with respect to function, ER stress signaling, and cell survival. Islet function was compared by loading islets with the fluorescent Ca^{2+} indicator Fura-2AM and recording intracellular Ca^{2+} responses during stimulation with various glucose concentrations. Intraperitoneal glucose tolerance tests (IPGTT) were used to determine the effect of transgenic B7-H4 overexpression on *in vivo* glucose clearance. ER stress was induced *in vitro* using the SERCA inhibitor thapsigargin. The expression of genes related to β-cell function, redox signaling, and the UPR were compared by RT-qPCR. Cell death was measured by propidium iodide staining of dispersed islet-cells.

Results: Kinetic analyses of islet Ca^{2+} responses to stimulation with 15 mM glucose showed indications of altered ER Ca^{2+} homeostasis and/or accelerated glucose metabolism in B7-H4 Tg islets. More detailed dose-response studies revealed significantly augmented glucose responsiveness of B7-H4 Tg islets, specifically at low-to-intermediate glucose levels. Interestingly, B7-H4 Tg islets expressed significantly higher levels of glukokinase (Gck) and the anti-oxidant gene Nrf2, while expression of the SERCA2b ER Ca^{2+} pump did not differ. IPGTTs did not reveal *in vivo* differences in glucose homeostasis between genotypes. Moderate ER stress (12 hours of 100 nM thapsigargin) induced the expression of key UPR genes, Bip, CHOP, and Xbp1s to significantly higher levels in B7-H4 Tg islets compared to WT islets. However, no differences were observed in islet-cell death following more severe and prolonged ER stress (15 uM thapsigargin for up to 72 hours). There was also no difference in cell death in response to a combination of thapsigargin and supraphysiologial glucose levels, or treatment with staurosporine.

Conclusions: Our findings demonstrate that over-expression of B7-H4 amplifies β-cell glucose-stimulated Ca^{2+} responses and amplifies the unfolded protein response during moderate ER stress. The B7-H4-induced increase in glucose sensitivity may result from metabolic effects related to increased glucokinase expression. Further studies of these novel functions of B7-H4 may suggest new approaches for prolonging islet graft survival and promoting the function of endogenous β-cells.

C11 **Bryan R. Tennant,** General Surgery

Title: *Myt3* mediates ECM induced islet migration via regulation of *Tgfbi*

Bryan R. Tennant[1], Jenny Chen[1] and Brad G. Hoffman[1,2; 1]Child and Family Research Institute, British Columbia Children's Hospital and Sunny Hill Health Centre, 950 W28th Avenue, Vancouver, British Columbia, Canada V5Z 4H4; [2]Department of Surgery, University of British Columbia, Vancouver, B.C., Canada V5Z 4E3

Background: Cell migration is a complex cellular process that is critical to a wide array of processes including embryonic development, immune functions, and disease processes. During pancreas development endocrine alpha-, beta-, delta-, epsilon-, and PP-cell precursors migrate away from the SOX9 positive pancreas precursor layer, in which they are initially specified, and join together to form interconnected islet-like structures. Subsequently, islets, composed of the different pancreas endocrine cell types, split off from these structures and migrate apart. Thus, cell migration is critical to both islet formation and the migration of the islets themselves away from the ducts. Despite this, the mechanisms regulating these processes are unclear; although, impairments in Wnt5a, epidermal growth factor-receptor, CDC42, TLE3, and RAC1 signalling all inhibit either normal endocrine cell delamination and migration, or the migration of islets away from ducts.

Aims/hypothesis: We previously demonstrated that the transcription factor Myt3 is a pro-survival factor in adult islet cells, and that the initiation of its expression coincided with the time frame in which islet morphogenesis is occuring. Thus, herein, we sought to confirm that Myt3 is present in migrating endocrine cells, and subsequently to determine whether Myt3 plays a role in this process.

Methods: Myt3 expression was determined in embryonic and neonatal pancreas by immunohistochemistry (IHC). In vitro migration assays, IHC and glucose stimulated insulin secretion assays were used to evaluate islet migration and its relationship to insulin secretion.
Results: We demonstrate that Myt3 is expressed in migrating islets and that suppression of Myt3 significantly inhibits islet spreading in a model of extracellular matrix (ECM) induced islet migration. Further, we show exposure of islets to proinflammatory cytokines, which suppress Myt3 expression, had a similar effect. Our data indicate that the impairment in islet spreading was independent of islet-cell survival or proliferation. In addition, islet-cell adhesion to different ECMs was largely unaltered by Myt3 manipulation; however, Myt3 suppression substantially impaired dispersed islet-cell spreading. To understand how Myt3 affects islet migration we used RNA-seq, and from this determined that Myt3 suppression prevents Tgfbi repression. Exposure of islets to exogenous TGFBI impaired islet-cell migration similarly to Myt3 suppression.
Conclusion/Interpretation: Taken together these data delineate a role for Myt3 in the regulation of islet migration via its regulation of Tgfbi and suggest these data are relevant not only to adult islet-cells but also to the migration of islets during pancreas development. In sum, these data contribute to our understanding of the role of Myt3 in islets and to the mechanisms regulating islet migratory ability.

C12 **Dan Wu,** General Surgery

Title: Investigating the function of tribbles proteins in regulatory T cells

Dan Wu, Megan Levings; Department of Surgery, University of British Columbia, Vancouver, BC and Child and Family Research Institute, Vancouver, BC

Background: Regulatory T cells (Tregs) are potent anti-inflammatory cells important in mediating transplant tolerance. It possesses great potential to be used as a cellular therapy in lieu of the immunosuppressant for higher specificity and less side effects. Our lab is dedicated to understand Treg biology and to develop effective Treg-based therapies. Recently, we identified a protein, Trib1, which was not previously investigated in T cells, is highly expressed in Tregs when compared to the conventional T cells (Tconvs). Trib1 is one of the three members in the tribbles family, a family of pseudokinases that is evolutionarily conserved in mammals. Although lacking the catalytic domain for phosphorylation, the tribbles proteins can modulate various cellular processes by interacting with a number of transcription factors and signalling kinases, including FOXP3 and AKT, which are important regulators of Treg function. Trib1 has been found to elevate significantly in peripheral blood mononuclear cells during acute rejection of kidney transplant; this may be correlated to the increased infiltration of Treg during renal rejection crises, suggesting that Trib1potentially have a role in modulating Treg function in the context of transplant tolerance.
Objective: We aim to establish the expression profiles of tribbles proteins in human and mouse Tregs and to understand their functions in Tregs.
Methods: To establish the tribbles expression profiles, QPCR and western blots were performed on resting and activated human peripheral blood Tregs and mouse Tregs. To investigate the function of tribbles in Tregs, we will knock down tribbles with siRNA and determine whether Treg function is altered.
Results: Among the three tribbles proteins, only Trib1 was differentially expressed between in Tregs and in Tconvs. *In vitro* activation of Tregs transiently increased Trib1 expression.
Conclusion: Our preliminary data confirmed that Trib1 is highly expressed in Tregs. We will continue to investigate whether Trib1 is important for Treg function. This study will enhance our understanding in Treg biology, and will contribute to the future development of Treg-based therapies for clinical use.

C13 **Eric E Xu,** General Surgery

Title: Sox4 cooperates with Neurogenin3 to regulate endocrine pancreas formation

Eric Xu[1,2], Nicole Krentz[1,2], Sam Chow[1], Sara Tan[1], Mei Tang[1], Cuilan Nian[1], Veronique Lefebvre[4], Francis C. Lynn[1,2,3]; [1]Child and Family Research Institute,[2] CELL Grad Program,[3]Dept of Surgery, Faculty of Medicine, UBC, Vancouver, BC, Canada; [4]Lerner Research Institute, Dept of Molecular Medicine Cleveland, OH, USA.

Background: The Sry/HMG box (Sox) family of transcription factors is essential for normal endocrine cell formation and Sox9, the best-studied member of this family, is required for endocrine cell specification. Despite the longstanding knowledge that many other Sox family members are expressed during pancreas development, a role for these factors in establishment of beta-cell fate remains to be determined.
Objectives: To assess how Sox4 regulates beta cell formation during embryogenesis and the mechanism which Sox4 exerts its impact upon endocrine cell development.
Methods: We utilized pancreas (Pdx1-Cre; $Sox4^{flox/flox}$) and endocrine (Ngn3-Cre; $Sox4^{flox/flox}$) specific Sox4 null mice to assess the role of Sox4 at multiple stages of endocrine cell development.
Results: Loss of Sox4 in the pancreatic anlage led to a significant reduction of endocrine cells at embryonic day (E)18.5. Further analyses of this mutant at E15.5 demonstrated that Neurogenin3 (Ngn3)-expressing cells were significantly reduced in number. Using a new cell model, we demonstrated that Sox4 cooperated with Ngn3 to amplify Ngn3 expression in the endocrine progenitor cells. Interestingly, loss of Sox4 in the Ngn3-Cre-expressing endocrine progenitors also resulted in significant reductions in endocrine cells without differences in proliferation, apoptosis or Ngn3 expression. Expression profiling and cell culture models, demonstrated that Sox4 cooperates with Ngn3 to transactivate Pax4 in the nascent endocrine cell progenitors.
Conclusions: Sox4 is essential for normal pancreatic endocrine cell differentiation both concomitant with, and downstream of Ngn3. These studies may allow refinement of stem cell differentiation protocols in order to generate large numbers of beta cells that could be used to treat those with diabetes.

C14 **YUN ZHANG,** General Surgery

Title: Amyloid Formation Reduces Phospho-PKB Levels in Islet β-Cells via IL-1β Signaling Pathway

YUN ZHANG, GARTH L. WARNOCK, ZILIANG AO, MARK MELOCHE, YOO JIN PARK, NOOSHIN SAFIKHAN, AZIZ GHAHARY, LUCY MARZBAN; Department of Surgery, Faculty of Medicine, University of British Columbia*

Introduction: Islet transplantation provides a feasible approach for treatment of type 1 diabetes (T1D) but is currently limited by insufficient donors and islet loss during pre-transplant culture and in islet grafts. Aggregation of human islet amyloid polypeptide (hIAPP), a hallmark of pancreas in T2D, also occurs during islet culture and transplantation. Amyloid formation contributes to β-cell death in all three conditions. Protein kinase B (PKB) signaling pathway plays a key role in the regulation of β-cell survival, function and proliferation.
Hypothesis: hIAPP aggregates can reduce PKB phosphorylation via inducing islet IL-1β production. Blocking amyloid or IL-1β can restore reduced PKB phosphorylation associated with amyloid formation.
Methods: Transformed INS-1 β-cells treated with hIAPP and cultured islets from cadaveric pancreatic donors and transgenic mice were used to examine the effects of hIAPP aggregates on PKB phosphorylation. Human and mouse islets embedded in collagen matrix or cultured with an amyloid inhibitor (Congo red) were used as two potential approaches to restore hIAPP-induced decrease in PKB phosphorylation. Human islets were also treated with a clinically approved IL-1 receptor antagonist (anakinra) or a GLP-1 agonist (exenatide). hIAPP aggregates and islet IL-1β were detected by immunolabelling. β-cell phospho-PKB levels, apoptosis and proliferation were assessed by Western blot or quantitative immunolabelling.
Results: hIAPP-treated INS-1 β-cells had markedly lower phospho-PKB levels, reduced proliferation and higher apoptosis than non-fibrillogenic rat IAPP-treated or untreated cells, all of which were restored by the amyloid inhibitor Congo red. Human islets and transgenic hIAPP-expressing mouse islets formed amyloid during culture associated with elevated IL-1β and reduced β-cell phospho-PKB levels, both of which were prevented by Congo red. Prevention of amyloid formation during islet culture by collagen matrix reduced islet IL-1β and restored β-cell phospho-PKB levels. Blocking IL-1 receptor (anakinra) or treatment with GLP-1 agonist (exenatide) restored β-cell phospho-PKB levels in amyloid forming islets.
Conclusions: These data suggest that amyloid formation reduces phospho-PKB in islet β-cells likely via IL-1β signaling. Blocking amyloid or amyloid-induced IL-1β production may enhance β-cell survival by restoring phosphorylation of PKB during pre-transplant culture and in islet grafts.

Evening Program at the Vancouver Aquarium

6:30 pm - Cocktails
7:00 pm – Award Presentations in Goldcorp Theatre
7:30 pm – Dinner among the fish

The Vancouver Aquarium is a recognized leader in connecting people to our natural world. As a self-supporting, non-profit association, the Aquarium is dedicated to effecting the conservation of aquatic life through display and interpretation, education, research and direct action. More than 35 million people have visited the Aquarium since their opening in 1956.

Location: 845 Avison Way (Stanley Park), Vancouver BC V6G 3E2

2014 Department of Surgery Faculty Achievement Awards

Hjalmar Johnson New Investigator Award – **Dr. Sheina MacAdam** is a Clinical Assistant Professor with the Division of Plastic Surgery at the University of British Columbia. She is active in both clinical and research-oriented work within the division. Dr Macadam has completed a Masters of Science in Epidemiology and Research Design at the Harvard School of Public Health and is a funded Clinician-Scientist Investigator at UBC. Her interests include breast reconstruction outcomes, patient satisfaction, breast cancer care and epidemiological trends in breast reconstruction. Her current focus is a CBCF grant funded, multi-center study comparing patient outcomes and satisfaction between the five types of autologous breast reconstruction.

Richard J Finley Senior Investigator Award – **Dr. Richard Simons** is a General and Trauma Surgeon at VGH and Professor in the UBC Division of General Surgery. After MSc and medical degrees from Cambridge University, England and residency training in London, and he worked as a trauma surgeon for the Red Cross in Thailand/Cambodia. He then completed a trauma fellowship and further training in Trauma and General Surgery at the University of Washington in Seattle. Dr Simons joined UBC in 1996 and has established one of the primary academic trauma programs in Canada supporting undergraduate, residency, fellowship and Canadian Forces Medical Services trauma training. He and his colleagues have developed a strong research program attracting numerous CIHR, NIH and MSHRF grants and reflected in numerous publications. He serves as editorial board member or reviewer on several journals and is active on many national committees. He is the past president of the Trauma Association of Canada, a recent RCPSC McLaughlin-Gallie visiting professor, and was recently awarded the Meritorious Achievement award by the Committee on Trauma of the American College of Surgeons for his work on establishing trauma systems in BC and Canada.

Kudos & Congratulations 2014

Dr. Richard Simons (General Surgery) has received the Meritorious Achievement Award of the American College of Surgeon- Committee on Trauma (ACS-COT) for his many significant contributions to trauma in general, to trauma systems development in Canada, and for his services as an ACS-COT region chief.

Dr. Yarrow McConnell's (**General Surgery**) successful development of a Hyperthermic Intraperitoneal Chemotherapy (HIPEC) program here in BC was profiled in the Vancouver Sun. The combination of surgery and in situ elevated temperature chemotherapy saves the lives of patients with tumours for which there is no other effective therapy.

Dr. Heather Denroche (supervisor **Dr. Bruce Verchere, General Surgery**) has won fellowships from both the CIHR and JDRF (Juvenile Diabetes Research Foundation) to study the formation of islet amyloid contributes to inflammation, and beta-cell dysfunction in islets transplanted into diabetic recipients.

Dr. Alice Mui (General Surgery) has received a NSERC grant to study Interleukin-10(IL10) regulation of miRNA maturation. IL10 is a surgeon's best friend since it is produced by the body at the site of surgical incisions and reduces harmful inflammation. miRNA are special RNA's that have also been referred to as molecular scalpels. Dr. Mui's lab has found that IL10 inhibits inflammation by stimulating the maturation of miRNA.....ie, sharpening these molecular scalpels.

The international Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) has awarded **Dr. Neely Panton** (**UBC Head of General Surgery**) a SAGES Recognition of Excellence Coin for his "Tireless commitment to improving the quality of patient care in British Columbia through leadership and training of surgeons in minimally invasive surgery."

Dr. Tamara Mijovic, currently finishing her OHNS residency at McGill, has received one of only 2 fellowships awarded each year from the Canadian Society of Otolaryngology-Head and Neck Surgery. She has chosen to do a one-year fellowship in Otology and Neurotology with **Dr. Brian Westerberg, Dr. Jane Lea and Dr. Desmond Nunez** (**Otolaryngology**) prior to returning to McGill as full time Faculty.

Congratulations to **Dr. Garth Warnock** (**General Surgery**) on his election to the Canadian Academy of Health Sciences (CAHS). Fellows of the Academy are chosen based on their demonstrated leadership, creativity and commitment to advance academic health sciences. The academy recognizes the full breadth of academic health science ranging from fundamental science to social science and population health. Membership is one of the highest honours for members of the Canadian health sciences community (www.cahs-acss.ca).

Dr. Eiman Zargaran (PGY4 **General Surgery**) has won the prize for best project at this year's Clinical Investigator Program Research Day, which is the pinnacle event of this prestigious research program at UBC. Eiman studies injury surveillance in low resource settings. His work includes development of the electronic Trauma Health Record (eTHR), an iPAD App for trauma surveillance and care in low resource settings that has already attracted international awards, and which may also be implemented here at home. His supervisors are **Dr. Morad Hameed** (**General Surgery**) **Dr. Robert Taylor** (**Branch for International Surgery**) and Dr Bori Sobolev (UBC School of Population Health).

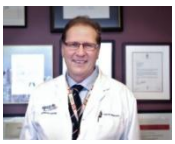
Congratulations to **Dr. Jeffrey Ludemann** (**Otolaryngology**) and his team for his www.dontchoke.ubc.ca website. This site is designed to improve understanding of choking hazards and prevention primarily among high school students but has guiding pages for preteens and parents. The goal is to educate the parents of tomorrow, today (http://dontchoke.ubc.ca/about/).The site fits with the current science and social responsibility curriuculae for grades 5 and 12 in BC. In December 2013, the website was evaluated in 122 students in Grades 11 and 12 in Vancouver. The data showed clear improvement in understanding of choking hazards and prevention (presented at ESPO 2014 in June in Dublin). Spanish and Mandarin translations of the website should be on-line later this week. 8 other translations (including French), by Pediatric Otolaryngology colleagues, are pending.....

Dr. Chadha and the **Pediatric Otolaryngology Research Unit** (PORU) has received a Child and Family Research Institute (CFRI) Clinical Research Capacity Award. The CFRI Clinical Research Capacity Building Award aims to empower clinical research teams by providing salary support to clinical research program coordinators over a 5 year period in order to enhance the research environment, increase productivity, build critical mass and improve integration of clinical research. The PORU is a research group within the Division of Pediatric Otolaryngology at BC Children's Hospital and is comprised of Dr. Neil Chadha, Dr. Frederick Kozak, Dr. Jane Lea, Dr. Brian Westerberg and Dr. Jeffery Ludemann. The PORU's aims are to improve the efficacy and quality of care of children suffering from otolaryngological diseases and conditions through novel and impactful research.

Dr.Aziz Ghahary (**Plastic Surgery**), Dr. K. McElwee (Department of Dermatology) and Dr. R. Jalili have recently received a 5 year grant from the Canadian Institute of Health Research (CIHR). This team of researchers proposed to use dermal fibroblasts expressing IDO, a tryptophan-degrading enzyme, in preventing the progression of autoimmune diseases such as Alopecia Areata in which hair follicles are attacked by the immune system. They provided compelling evidence that IDO expressing dermal fibroblasts serve as immuno-regulatory cells prevent host's antigen presenting cells from being activated against auto-antigens in autoimmune diseases. These investigators hope to use skin cells as a therapeutic modality in preventing any inflammation in general and particularly the progression of autoimmune diseases such as and alopecia areata and type I diabetes.

Dr. Nadine Caron (General Surgery) has been appointed by the Government of Canada to a 2nd three year term to the Canadian Institutes of Health Research **(CIHR) Governing Council**. Dr. Caron has made substantial contributions to the CIHR Governing Council for the last 3 years especially with her leadership in the community (particularly as it pertains to Aboriginal health) and her expertise in Canadian health research and health policy.

Dr. Anne Pesenacker (supervisor, **Dr. Megan Levings, General Surgery**) has been awarded a fellowship from the JDRF for her studies focused on development of methods to induce immune tolerance in pancreas and islet transplantation.

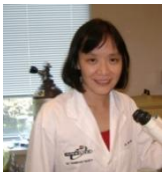


Dr. Garth Warnock (General Surgery) is the recipient of this year's UBC Faculty of Medicine's Distinguished Researcher in Clinical Science. This award recognizes his contributions to the treatment of diabetes mellitus. His lecture next Monday at the Life Sciences Centre at UBC will be video linked to the distributed medical school sites.

Dr. Timothy Kieffer, Dr. Megan Levings and Dr. Garth Warnock (General Surgery) have been funded by JDRF Canada and the Canadian Clinical Trial Network (CCTN) to accelerate translational research into new treatments for diabetes. Dr. Kieffer and his collaborators will explore the potential of using human embryonic stem cells to develop into functional, insulin-producing beta cells in the pancreas. His lab has already demonstrated that stem cell-derived islets can reverse diabetes in mice, and can even respond to fluctuating levels of insulin in the bloodstream, just as normal beta cells do. The CCTN funding will enable him to investigate the use of an encapsulation device – which he likens to a "teabag" – that would enable insulin to flow to and from the beta cells, allowing them to respond to the fluctuating insulin levels while preventing the intrusion of T-cells that would destroy the islets. If it works, it would eliminate the need for chronic immunosuppression.

Dr. Aziz Ghahary (**Plastic Surgery**) recently received two grants from the Canadian Institute of Health Research (CIHR).The first grant is to fund the Proof of Principle (POP1) research that is geared to prepare prospective technology for commercialization. Dr. Ghahary and his Ph.D. student, Ryan Hartwell, proposed to make a novel reconstitutable skin substitute powder that can easily form a liquid or solid scaffold once hydrated. This low cost injectable collagen-hydrogel hybrid can rapidly form a solid gel matrix within a wound or within any void cavity. Both the architecture and mechanical properties of this injectable matrix are unique among currently available scaffolds, as it mimics normal tissue architecture, cellularity and reduces contracture. The second grant awarded Dr. Ghahary and his colleagues, Dr. K. McElwee and Dr. Reza Jalili proposed the use of IDO expressing dermal fibroblasts to prevent the progression of the autoimmune disease Alopecia Areata. IDO is an enzyme that degrades the essential amino acid tryptophan and thus suppresses the growth of activated immune cells. IDO based therapies can also be used to prevent the progression of other immune diseases such as type I diabetes.

Dr. Cathie Garnis (Otolaryngology) has received a CIHR grant to: Evaluate circulating small RNA markers as simple blood test biomarkers for detecting and predicting outcomes in oral cancer. . The objective of her proposal is 1) to identify candidate markers in blood for oral cancer detection, and 2) to evaluate the effectiveness of these markers in predicting disease recurrence after treatment before patients present with recurrent disease symptoms. Success with this project will yield clinically useful and cost-effective blood tests for screening individuals with both new and recurrent oral malignancy, setting the stage for more effective patient management and improved patient outcomes.



Dr. Alice Mui (General Surgery) who has received a CIHR grant to study: Negative Regulation of Immune Cell Function The anti-inflammatory cytokine interleukin-10 prevents over-enthusiastic immune cell activation that can lead to tissue injury and disease. In fact IL10 is released at the site of surgical incisions. The objective of this grant is to study the mechanism by which IL10 calms cells down, and to continue developing strategies to treat diseases such as colitis in which the normal response to IL10 has been lost.

Dr. Azadeh Tabatabaei (supervisor, **Dr. Bruce Verchere, General Surgery**) has won a JDRF fellowship to prevent pancreatic islet autoimmunity by manipulating beta cell metabolism. Insulin-producing beta cells in pancreatic islets have a very specialized metabolism that we propose may make them more susceptible to autoimmune attack in type 1 diabetes. Dr. Tabatabaei aims to help beta cells escape immune attack, by making small changes in the expression of key metabolic enzymes that are normally not expressed in beta cells. She will investigate this approach both in prevention of autoimmune diabetes and rejection of islet transplants.

Dan Wu (supervisor, **Dr. Megan Levings**) has won a CIHR Canadian Graduate Scholarship to support his PhD studies. He will study gene signatures associated with organ transplant tolerance in order to gain insight to processes required for immune tolerance.

Yoo Jin Park a 4th year PhD student with **Dr. Lucy Marzban** (**General Surgery**) has received an award of excellence (Gold category) for her presentation at the national Canadian Institutes of Health Research (CIHR) - Canadian student health research forum held at the University of Manitoba, June 10-12, 2014. The presenters were doctoral students nominated by their graduate programs (top 5% of doctoral students) from universities across Canada (~120 students) to participate in this event. Yoo Jun presented her work showing that the IL-1 receptor antagonist anakinra reduces amyloid formation and enhances beta-cell survival and function in cultured human islets: implications in clinical islet transplantation.

Congratulations to **Dr. Lucy Marzban** (General Surgery) who has won a teaching award from the Faculty of Dentistry. She received her award at the Dentistry reception on Sept 20th.

A History of WB & MH Chung Lectureship

In 1995 Madeline and Wally Chung made a generous donation to the Department of Surgery at the University of British Columbia.

The purpose of the donation was to support an annual UBC Department of Surgery research day and invite the W.B. & M.H. Chung Lecturer to present new academic work as well as judge academic productivity, not only by the Residents but also by the Faculty.

The format was directed toward the new work developed by the Residents, Fellows, Basic Scientists and Faculty. Each paper was 10 minutes in duration and a five minute discussion period followed for each paper.

The visiting professor presented original research as part of the day as well as judged the clinical and basic science presentations.

The first visiting professor was Lloyd D. MacLean, MD, FRCSC, FACS who was head of the Department of Surgery at McGill University as well as President of the American College of Surgeons.

Each of the Research Days has been attended by Dr. Chung who has been actively involved in the Department for almost fifty years.

Dr. Chung was heartened by the active interests of the Residents as well as Basic Scientists and Faculty in exchanging information at the Research Day. The Department is grateful for this wonderful legacy that Madeline and Wally Chung have left for the Department.

1995 Lloyd MacLean, McGill University

1996 John Duff, University of Western Ontario
"Multisystem organ failure: manifestations and mediators"

1997 K. Wayne Johnston, University of Toronto
"Issues in the management of abdominal aortic aneurysms in a rapidly changing health care environment"

1998 Charles H. Tator, Professor and Chair, Division of Neurosurgery, The Toronto Hospital
"The breadth of surgical research in the 1990's"

1999 Garth Warnock, Chief General Surgery, University of Alberta Hospitals
Director, Division of Surgical Research, University of Alberta
"Progress in transplantation of insulin-secreting tissues for diabetes mellitus"

2000 Paul Walker, Vice President, Toronto General Hospital
Professor of Surgery and Laboratory Medicine, Pathobiology, University of Toronto
"The continuing challenge of sepsis"

2001 James C. Thompson, Ashbel Smith Professor of Surgery, University of Texas Medical Branch
"Endocrine tumors of the pancreas"

2002 Richard J. Finley, Professor, Department of Surgery
Head, Division of Thoracic Surgery, University of British Columbia
"Future of image guided minimally invasive thoracic surgery"

2003 Douglas W. Wilmore, Frank Sawyer Professor of Surgery, Department of Surgery
Brigham and Women's Hospital, Boston, Massachusetts
"The pathophysiology and treatment of intestinal failure"

2004 John Wong, Chair of Surgery & Head, Department of Surgery
University of Hong Kong Medical Centre, Queen Mary Hospital, Hong Kong
"Complications of esophagectomy: confess and remember"

2005 Richard K. Reznick, R.S. McLaughlin, Professor and Chair, University of Toronto
Department of Surgery , Banting Institute, Toronto, Ontario
"Surgical training in 35 hours per week: laudable or lunacy?

2006 James T. Rutka, Janes Visiting Professor in Surgery
Dan Family Chair in Neurosurgery, Professor and Chairman,
Division of Neurosurgery, University of Toronto
"Astrocytoma invasiveness: molecular mechanisms form the leading edge"

2007 Markus W. Büchler, Professor of Surgery, Division of General Surgery
Chairman Surgical Unit, University of Heidelberg
"Evidence based pancreatic surgery"

2008 Thomas M. Krummel, Emile Holman Professor and Chair
Stanford University School of Medicine, Department of Surgery
Susan B. Ford Surgeon in Chief, Lucile Packard Children's Hospital, Stanford, CA
"From Blood and Guts to Bits, Bytes and Beyond-- Upgrading the Surgical Apprentice Model"

2009 Andrea L. Pusic, Assistant Attending Surgeon, Plastic and Reconstructive Surgery
Memorial Sloan-Kettering Cancer Center, New York
"Measuring patient reported outcomes in surgery"

2010 Yvan Douville, Chief, Department of Surgery, University of Laval
"Evolution of Stentgraft for Treatment of Abdominal Aortic Aneurysms"

2011 Gerald Fried, Chair, Department of Surgery, McGill University
"Teaching Billy how to operate: can we do better?"

2012 Haile Debas, Executive Director of UCSF Global Health Sciences (GHS); former Dean of the UCSF School of Medicine (1993-2003); former Chair, UCSF Department of Surgery
"Precious Times"

2013 Lorelei Lingard, Professor and Director of the Centre for Education Research & Innovation, Schulich School of Medicine & Dentistry, Western University, London, ON
"Beyond communication skills: A rhetorical approach to communication for advancing the practice and teaching of teamwork"