![McGill University Department of Surgery logo]

# McGILL UNIVERSITY
# DEPARTMENT OF SURGERY

# 32ND ANNUAL
# FRASER N. GURD
## SURGICAL RESEARCH FORUM



## THURSDAY, JUNE 2ND, 2022

# VIRTUAL MEETING
# ABSTRACT BOOKLET

**LINK TO THE VIRTUAL EVENT:**
https://vpsolution.tv/2022-fraserngurd-vvp

www.medicine.mcgill.ca/surgery

# PROGRAM

# VIRTUAL EVENT PROGRAM

## Thursday, June 2nd, 2022

Link to the virtual event:

https://vpsolution.tv/2022-fraserngurd-vvp

| | |
|---|---|
| 7:30 – 7:35 | **DR. LIANE FELDMAN**<br>CONFERENCE INTRODUCTION AND WELCOME |

| | |
|---|---|
| 7:35 – 8:30 | **DR. SUSAN MOFFAT-BRUCE**<br>"Learning Health Systems: Our Roles and Opportunities" |

| | |
|---|---|
| **SESSION A PART I**<br>8:45 –10:04 | **SESSION A: CLINICAL SCIENCES** |
| | **PART I: SURGICAL OUTCOMES 1**<br>CHAIR: **DR. STEPHANIE WONG**   CO-CHAIR: **DR. RICHARD GARFINKLE**<br>KEYNOTE: **DR. STEPHANIE WONG**<br>"Optimizing Surgical Decision Making in Women With Elevated Breast Cancer Risk" |
| | 8:56  SURGICAL OUTCOMES PRESENTATIONS |
| 9:44 –9:49 | 5-MINUTE BREAK |

| | |
|---|---|
| **SESSION A PART II**<br>9:49 –10:44 | **PART II: SURGICAL OUTCOMES 2** |
| | 9:49  SURGICAL OUTCOMES PRESENTATIONS |
| 10:44 –10:49 | 5-MINUTE BREAK |

| | |
|---|---|
| **SESSION A PART III**<br>10:49 –11:49 | **PART III: EDUCATION**<br>CHAIR: **DR. MELINA VASSILIOU**   CO-CHAIR: **DR. JENNY MOON**<br>KEYNOTE: **DR. MELINA VASSILIOU**<br>"FLS 2.0-Coming to a Test Centre Near You" |
| | 11:00  EDUCATION PRESENTATIONS |

| | |
|---|---|
| **SESSION B PART I**<br>8:45 –9:53 | **SESSION B: LABORATORY SCIENCES** |
| | **PART I: BASIC SCIENCE**<br>CHAIR: **DR. LISBET HAGLUND**   CO-CHAIR: **LI LI, MSc.**<br>KEYNOTE: **DR. LISBET HAGLUND**<br>"Senolytic Therapy for IVD Related Chronic Low Back Pain in Mice and Men" |
| | 8:56  BASIC SCIENCE PRESENTATIONS |
| 9:53 –9:54 | 1 MINUTE CHANGEOVER |

| | |
|---|---|
| **SESSION B PART II**<br>9:54 –11:17 | **PART II: CANCER RESEARCH**<br>CHAIR: **DR. DAVID LABBÉ**  CO-CHAIR: **DR. LIVIA GARZIA**<br>KEYNOTE: **DR. DAVID LABBÉ**<br>"Single-Cell Transcriptomics Uncovers Novel Therapeutic Strategies to Intercept Aggressive Prostate Cancer" |
| | 10:05  CANCER RESEARCH PRESENTATIONS |
| 11:17–11:18 | 1-MINUTE CHANGEOVER |

| | |
|---|---|
| **SESSION B<br>PART III**<br>11:18 – 12:05 | **PART III: INTERVENTIONS**<br>CHAIR: **DR. AMIR HOOSHIAR AHMEDI**  CO-CHAIR: **DR. JUNKO TOKUNO**<br>KEYNOTE: **DR. AMIR HOOSHIAR AHMEDI**<br>**"Surgical Robots: Promises, challenges, and innovation"** |
| | 11:39  INTERVENTIONS PRESENTATIONS |
| 12:05 – 12:30 | LUNCH BREAK |

| | |
|---|---|
| | **SYMPOSIUM ON TRANSFORMING SURGICAL QUALITY AND OUTCOMES** |
| 12:30 – 12:35<br>12:35 – 12:45<br>12:45 – 12:55<br>12:55 – 13:05<br>13:05 – 13:15<br>13:15 – 13:25 | **DR. LIANE FELDMAN**  Introduction<br>**DR. SUSAN MOFFATT-BRUCE**  Dispelling Leadership Myths in Surgery<br>**DR. MICHAEL TANZER**  Lessons Learned from Leading through Crisis<br>**DR. SHANNON FRASER**  Quality, Safety and Informatics<br>**DR. JASON HARLEY**  Enhancing Teamwork<br>**PANEL DISCUSSION:** Q&A (Moderator: **DR. FELDMAN**) |
| 13:25 – 13:30 | CLOSING REMARKS |

| | |
|---|---|
| | **FRASER GURD AWARDS CEREMONY** |
| 18:00 | **RITZ CARLTON HOTEL**<br>1228 Sherbrooke St. West<br>Montreal, Quebec, H3G 1H6 |

## DR. FRASER N. GURD

**DR. FRASER GURD** (1914-1995) graduated from the Faculty of Medicine at McGill University in 1939. He succeeded Dr. H. Rocke Robertson as Chairman of the Department of Surgery, McGill University in 1962. Throughout his career, Dr. Gurd demonstrated a remarkable interest in research with several significant investigations into the treatment of shock and trauma. Perhaps his greatest contribution relates to the development of surgical scientists. Dr. Gurd received many honours including the Royal College's Duncan Graham Award for outstanding service in medical education. He was an Emeritus Professor of Surgery at McGill University. The presentations by the residents and fellows are a tribute to the many contributions of Dr. Fraser Gurd.

# ORDER OF PRESENTATIONS

# SESSION A: CLINICAL SCIENCES

## PART I: SURGICAL OUTCOMES 1

8:45    CHAIR: **DR. STEPHANIE WONG**
        CO-CHAIR: **DR. RICHARD GARFINKLE**
        KEYNOTE: **Optimizing Surgical Decision Making in Women with Elevated
        Breast Cancer Risk**

8:56    UROLOGY
        **ALSHAMMARI, Ahmad**   (Supervisor: Dr. A. Zini)
        Microsurgical Testicular Sperm Extraction (Micro-Tese) Sperm Retrieval Rate (Srr) Post
        Testicular Sperm Aspiration (Tesa)

9:04    GENERAL SURGERY
        **POOK, Makena**   (Supervisor: Dr. J. F. Fiore Jr.)
        Patients' Experiences Receiving Cancer Surgery During The Covid-19 Pandemic:
        A Qualitative Study

9:12    COLORECTAL SURGERY
        **ZAMINPEYMA, Roxaneh**   (Supervisor: Dr. J. Tchervenkov, Dr. S. Paraskevas
        & Dr. A. Andalib)
        Outcomes Of Kidney Transplant Recipients Who Underwent Pre-Transplant Bariatric
        Surgery for Severe Obesity: A Long-Term Follow-Up Study

9:20    GENERAL SURGERY
        **MOON, Jeongyoon Jenny**   (Supervisor: Dr. M. Boutros)
        Evaluation Of Current Rectal Cancer Survivorship Care: Unmet Patient Needs and
        Fragmented Care Among Specialists and General Practitioners

9:28    GENERAL SURGERY
        **KIS, Allyson**   (Supervisor: Dr. E. G. Wong)
        Assessing Surgical, Trauma and Telehealth Capacity in Indigenous Communities in
        Northern Quebec: A Cross-Sectional Survey

9:36    VASCULAR SURGERY
        **KIM, Angela**   (Supervisors: Dr. H. Gill)
        Timing of Complications Following Carotid Endarterectomy for Symptomatic and
        Asymptomatic Carotid Artery Stenosis

9:44    5-MINUTE BREAK

## PART II: SURGICAL OUTCOMES 2

9:49    GENERAL SURGERY
        **CAMINSKY, Natasha**   (Supervisor: Dr. M. Boutros)
        Cost Of Stoma-Related Hospital Readmissions for Rectal Cancer Patients Following
        Restorative Proctectomy with a Diverting Loop Ileostomy: A Nationwide Readmissions
        Database Analysis

9:54    PLASTIC SURGERY
        **SAFRAN, Tyler**   (Supervisor: Dr. J. Vorstenbosch & Dr. T. Dionisopoulos)
        Topical Tranexamic Acid in Breast Reconstruction: A Double-Blind, Randomized
        Controlled Trial

▶

9:59   GENERAL SURGERY
**KOUYOUMDJIAN, Araz**   (Supervisor: Dr. P. Chaudhury)
Recipient Outcomes After Kidney and Liver Transplantation From Medical Assistance in Dying (Maid) Organ Donation

10:04   GENERAL SURGERY
**APOSTOLOVA, Carla**   (Supervisor: Dr. S. M. Wong)
Surgical Decision Making in Genetically High-Risk Women: Quantifying Postoperative Complications and Short and Long-Term Risks Of Supplemental Surgery

10:09   GENERAL SURGERY
**FERROUM, Amina**   (Supervisors: Dr. S. M. Wong)
Incidence of Occult Breast Cancer in BRCA1/2 and Other High Penetrance Mutation Carriers Undergoing Prophylactic Mastectomy: When is Sentinel Lymph Node Biopsy Indicated?

10:14   ORTHOPEDIC SURGERY
**GAGNON, Marianne**   (Supervisor: Dr. M. Bernstein)
Derotational Osteotomy for Youth with Patellofemoral Syndrome

10:19   VASCULAR SURGERY
**NAIEM, Ahmed**   (Supervisor: Dr. E. Girsowicz)
Severe Inframalleolar Disease Is an Independent Predictor of Adverse Limb Outcomes After Revascularization in Patients with Chronic Limb-Threatening Ischemia

10:24   GENERAL SURGERY
**GROSZMAN, Lilly**   (Supervisors: Drs. E. Wong, B. Hopkins, N. Alshahwan)
Predicting Acute Cholecystitis on Final Pathology to Prioritise Surgical Urgency: An Evaluation of the Tokyo Criteria and Development of a Novel Predictive Score

10:29   GENERAL SURGERY
**EL-KEFRAOUI, Charbel**   (Supervisor: Dr. J. F. Fiore Jr.)
Opioid Versus Opioid-Free Analgesia After Surgical Discharge: A Systematic Review and Meta-Analysis of Randomized Trials

10:34   VASCULAR SURGERY
**KINIO, Anna**   (Supervisor: Dr. H. Gill)
Spinal Drain Outcomes in Aortic Surgery at McGill

10:39   GENERAL SURGERY
**AL-AZZAWI, Zaid**   (Supervisor: Dr. D. Poenaru)
Use of Machine Learning for Clinical Prediction Tools in Pediatric Surgery: A Systematic Review

10:44   5-MINUTE BREAK


## PART III: EDUCATION

10:49   CHAIR: **MELINA VASSILIOU**
CO-CHAIR: **DR. JENNY MOON**
KEYNOTE: **FLS 2.0-Coming to a Test Centre Near You**

11:00   GENERAL SURGERY
**HANSON, Melissa**   (Supervisor: Dr. L. Feldman)
Implementation Of Entrustable Professional Activities into Fellowship Council Accredited Programs – A Pilot Project

▶

11:08    GENERAL SURGERY
         **BALVARDI, Saba**   (Supervisor: Dr. L. Feldman)
         Effect of Video-Based Guided Self-Reflection on Intraoperative Skills: A Pilot Randomized
         Controlled Trial

11:16    CARDIAC SURGERY
         **ALHARBI, Mohammed A**   (Supervisors: Dr. K. Lachapelle & Dr. J. Harley)
         Mapping Simulation Fidelity in Cardiac Surgery using a Multidimensional Framework:
         A Thematic Literature Review

11:24    PLASTIC & RECONSTRUCTIVE SURGERY
         **LORANGE, Justin-Pierre**   (Supervisor: Dr. M. Gilardino)
         Role of Online Suturing Sessions in the Development of Medical Students' Surgical Skills

11:29    CARDIAC SURGERY
         **SAYADI, Amir**   (Supervisors: Dr. R. Cecere & Dr. A. Hooshiar)
         Assessment of Accuracy and Repeatability of Augmented Reality-Assisted Epidural
         Needle Insertion

11:34    VASCULAR SURGERY
         **SEPULVEDA, Reyna & JAVIER, Francisco**   (Supervisor: Dr. E. Girsowicz)
         Effects of Transcranial Direct Current Stimulation on Surgical Skills Acquisition and
         Retention

11:39    GENERAL SURGERY
         **AZHER, Sayed**   (Supervisor: Dr. J. Harley)
         Comparison of Two Virtual Simulation Technologies in Medical Education: An
         Assessment of Cognitive Load, Usability, and Performance Differences

11:44    PLASTIC & RECONSTRUCTIVE SURGERY
         **ELHAWARY, Hassan**   (Supervisor: Dr. S. Thibaudeau)
         Gender Equality in Plastic Surgery Training: A Canadian Nationwide Cross-Sectional
         Analysis

11:49    END

## SESSION B: LABORATORY SCIENCES

### PART I: BASIC SCIENCE

8:45    CHAIR: **DR. LISBET HAGLUND**
        CO-CHAIR: **LI LI, MSc**
        KEYNOTE: **Senolytic Therapy for IVD Related Chronic Low Back Pain in Mice and Men**

8:56    THORACIC SURGERY
        **PAL, Sanjima**   (Supervisor: Dr. L. Ferri)
        Esophageal Adenocarcinoma on A Chip: Modelling A High-Fidelity Platform For Precision
        Oncology

9:04    ORTHOPEDIC SURGERY
        **ALAD, Muskan**   (Supervisors: Dr. F. Mwale & Dr. J. Antoniou)
        IL-1β-Induced DRG Neuronal Hypersensitivity Is Arogated by Link N.

9:12    CARDIAC SURGERY
        **DERISH, Ida**   (Supervisor: Dr. R. Cecere )
        Characterization of Patient-Specific Differences in Induced Pluripotent Stem Cell-Derived

►

Cardiomyocytes Following Hypoxia-Induced Injury

9:20     PLASTIC SURGERY
**ALSHARQI, Maha**    (Supervisor: Dr. A. Philip)
Regulation of Pulmonary Fibrosis by Cd109 in A Murine Model

9:28     ORTHOPEDIC SURGERY
**ZAKARIA, MATTHEW**    (Supervisors: Dr. E. Harvey & Dr. G. Merle)
Facilitated Fracture Repair via Noninvasive Localized Cold Therapy

9:33     PLASTIC SURGERY
**VELA LASAGABASTER, Arturo**    (Supervisor: Dr. J. Barralet)
Efficacy of Oxygen Delivery Biomaterial for Ischemic Skin Preservation

9:38     ORTHOPEDIC SURGERY
**DSOUZA, Chrisanne**    (Supervisor: Dr. S. Komarova)
Age-Associated Changes in Calcium Signaling and Membrane Injury in Osteoblasts and Osteoclasts

9:43     PLASTIC SURGERY
**NEPON, Hillary**    (Supervisor: Dr. J. Vorstenbosch)
Breast Implant Insertion Plane Is Associated with Distinct Capsular Inflammatory and Fibrotic Signaling Patterns: A Possible Link to Capsular Contracture Susceptibility

9:48     UROLOGY
**COVARRUBIAS, Claudia**    (Supervisor: Dr. L. Campeau)
Increased Urinary Ratio Bdnf/Probdnf in a Female Population with Overactive Bladder Syndrome

9:53     1-MINUTE CHANGEOVER

## PART II: CANCER

9:54     CHAIR: **DR. DAVID LABBÉ**
CO-CHAIR: **DR. LIVIA GARZIA**
KEYNOTE: **Single-Cell Transcriptomics Uncovers Novel Therapeutic Strategies to Intercept  Aggressive Prostate Cancer**

10:05     GENERAL SURGERY
**MIGUEL ROMERO, Joan**    (Supervisor: Dr. G. Zogopoulos)
A 4-Chemokine Signature Predicts T Cell-Inflammation and Response to Immune Checkpoint Inhibition Across Tumor Types

10:13     UROLOGY
**ALAHMADI, Walaa**    (Supervisor: Dr. D. Labbé)
Precision Nutrition Increases Efficacy of DNA-Damaging Therapies in Prostate Cancer

10:21     GENERAL SURGERY
**DI LENA, Élise**    (Supervisor: Dr. S. Meterissian)
Sentinel Lymph Node Biopsy in Women Over 70: Evaluation Of Rates Of Axillary Staging and Impact on Adjuvant Therapy in Elderly Women

10:29     UROLOGY
**DERDERIAN, Seta**    (Supervisor: Dr. S. Chevalier)
Identifying Therapeutic Options for Patients with Advanced Prostate Cancer through Genes in Liquid Biopsies

▶

10:37    GENERAL SURGERY
**BENSLIMANE, Yasmine**   (Supervisor: Dr. P. Brodt)
Estrogen Regulates the Immune Microenvironment of Colorectal Liver Metastases

10:42    UROLOGY
**MICHAUD, Eva**   (Supervisor: Dr. W. Kassouf)
Treatment Combination Strategies to Improve Radiation Efficacy in Immunologically Cold Tumors *In Vivo*

10:47    THORACIC SURGERY
**SU, Xin Daniel**   (Supervisors: Dr. L. Ferri & Dr. J. Cools-Lartigue)
Cancer Extracellular Vesicles Induce Lymph Node Metastasis via Neutrophil Extracellular Traps

10:52    THORACIC SURGERY
**BRASSARD, Ariane**   (Supervisor: Dr. J. Cools-Lartigue)
Nets Downregulate Cd8 T Cell Function in Tumour-Draining Lymph Nodes

10:57    ORTHOPEDIC SURGERY
**CASTILLO OROZCO, Ana Isabel**   (Supervisor: Dr. L. Garzia)
Genetic Drivers of Medulloblastoma Leptomeningeal Metastasis

11:02    PLASTIC SURGERY
**HASSAN, Amani**   (Supervisor: Dr. A. Philip)
Cd109-Il6rα Interaction Drives Squamous Cancer Cell (Scc) Stem Cell Plasticity through Stat3/Nrf2 Pathway

11:07    THORACIC SURGERY
**DE MEO, Meghan**   (Supervisor: Dr. J. Spicer)
Cxcr2 Inhibition as a Candidate for Immunomodulation in the Treatment of K-Ras-Driven Lung Adenocarcinoma

11:12    UROLOGY
**NORMAN, Claire**   (Supervisor: Dr. Y. Riazalhosseini)
Characterizing Tertiary Lymphoid Structures and their Functions in Renal Cell Carcinoma

11:17    1-MINUTE CHANGEOVER


## PART III: INTERVENTIONS

11:18    CHAIR: **DR. AMIR HOOSHIAR**
CO-CHAIR: **DR. JUNKO TOKUNO**
KEYNOTE: **Surgical Robots: Promises, Challenges, and Innovation**

11:29    UROLOGY
**SIRMAKESYAN, Stephanie**   (Supervisor: Dr. L. Campeau)
Ngf Secretion Is Regulated by Nitric Oxide Levels in Bladder Cells

11:37    ORTHOPEDIC SURGERY
**ARANETA, Karla Teresa**   (Supervisor: Dr. A. Aoude)
Joint-Sparing Reconstruction for Extensive Periacetabular Metastases: Literature Review and a Novel Minimally Invasive Surgical Technique

11:45    PLASTIC SURGERY
**WATT, Ayden**   (Supervisor: Dr. M. Gilardino)
Artificial Intelligence Assisted Automatic Diagnosis of Positional Plagiocephaly: A Validation Study

▶

11:50   ORTHOPEDIC SURGERY
**LORINCZ, Amy**   (Supervisor: Dr. G. K. Berry)
Telemedicine Scheduling Optimization in Surgical Outpatient Clinics

11:55   UROLOGY
**HAMOUDA, Aalya**   (Supervisor: Dr. L. Campeau)
Antagonism of the P75 Neurotrophin Receptor Increases Secretion of Nerve
Growth Factor by Decreasing Extracellular Matrix Metalloproteinase-9 Activity and
A2-Macroglobulin Levels in Mouse Urothelial Cell Culture

12:00   ORTHOPEDIC SURGERY
**AITA, Rachad**   (Supervisor: Dr. C. Gao)
Novel Murine Model For The Study Of Spinal Cord Injury-Induced Neurogenic Heterotopic
Ossification

12:05   END

# ABSTRACTS

# SESSION A, PART I & II: SURGICAL OUTCOMES

## KEYNOTE: *OPTIMIZING SURGICAL DECISION MAKING IN WOMEN WITH ELEVATED BREAST CANCER RISK*

### STEPHANIE WONG
**MD, MPH**

**Assistant Professor of Surgery at McGill Medical School**
**Surgical Oncologist, JGH Segal Cancer Centre**

**OBJECTIVES:**

› Describe the clinical characteristics of breast cancers that develop in women with a history of chest wall radiation for Hodgkin Lymphoma

› Discuss the risk of contralateral breast cancer in affected Hodgkin lymphoma survivors with a newly diagnosed breast cancer

**Stephanie Wong** is an assistant professor of surgery at McGill Medical School and a breast surgical oncologist at the JGH Segal Cancer Centre in Montreal, Canada. She received her medical degree and completed general surgery residency at McGill University, her MPH at the Harvard School of Public Health, and in 2019, completed a breast surgical oncology fellowship at Dana-Farber/Brigham and Women's Cancer Centre and Massachusetts General Hospital. Her clinical and research interests focus on surgical outcomes following neoadjuvant treatment and high-risk patient populations. She directs the High Risk Breast Clinic at the JGH Stroll Cancer Prevention Centre and holds an FRQS Clinical Research Scholars award for research on Optimizing Surgical Decision Making and Prevention Strategies for Women at High Risk of developing Breast Cancer.

# MICROSURGICAL TESTICULAR SPERM EXTRACTION (MICRO-TESE) SPERM RETREIVAL RATE (SRR) POST TESTICULAR SPERM ASPIRATION (TESA)

Ahmad AlShammari, MD[1] Adel Arezki, MD[1] Rabea Akram, MD[1]
Iman Sadri[1] Ahmad H. Al-Malki, MD[1] Armand Zini, MD[1,2]

[1]Division of Urology, Department of Surgery, McGill University
[2]OVO Fertility Clinic, Montreal, Quebec, Canada.

**OBJECTIVE** Studies have shown that micro-TESE (Microsurgical Testicular Sperm Extraction) outcome may be adversely influenced by a prior surgical sperm retrieval (performed in the preceding 6 months). We sought to evaluate the micro-TESE sperm retrieval rate (SRR) post-TESA (Testicular Sperm Aspiration) in a cohort of infertile men with non-obstructive azoospermia.

**METHODS** We conducted a retrospective review of infertile men who underwent micro-TESE for non-obstructive azoospermia (NOA) between 2007 and 2020 and recorded Micro-TESE sperm retrieval rates (SRR) in these men. We included men with and without a history of TESA prior to micro-TESE. We further categorized the men with a prior TESA according to the time interval between TESA and micro-TESE. In all cases, the prior TESA was unsuccessful (no sperm recovered). We compared SRR in patients with and without TESA prior to micro-TESE. We also compared SRR in men who underwent TESA less than or more than 6 months before micro-TESE. Chi-Squared analysis was performed to compare SRR in each subgroup.

**RESULTS** We identified twenty-five men that underwent a TESA prior to micro-TESE and 146 men with no intervention prior to micro-TESE. The micro-TESE SRR was 64% (16/25) in the men with a history of TESA prior to micro-TESE and 46% (71/146) in men with no prior intervention (P=0.22). However, men with a prior TESA had more favorable parameters (lower FSH and greater testicular volume). The micro-TESE SRR were 60% (6/10) and 66% (10/15), when performed ≤6 months and >6 months post TESA, respectively (P=0.973) and we did not identify any significant differences between these groups in terms of age, testicular volumes, or hormonal parameters.

**CONCLUSION** The data suggest that micro-TESE sperm retrieval rate is not influenced by a prior TESA, whether recent (≤ 6 months) or remote (>6 months). The data also indicate that the salvage micro-TESE SRR in patients with a prior negative TESA is comparable to the SRR in men undergoing primary micro-TESE for NOA.

# PATIENTS' EXPERIENCES RECEIVING CANCER SURGERY DURING THE COVID-19 PANDEMIC: A QUALITATIVE STUDY

Makena Pook,[1]; Tahereh Najafi Ghezeljeh,[2]; Maxime Lapointe-Gagner,[1]; Philip Nguyen-Powanda,[1]; Hiba Elhaj,[3]; Fateme Rajabiyazdi,[4]; Lawrence Lee,[3,5,6]; Liane S. Feldman,[3,5,6]; Julio Fiore Jr.[3,5,6]

[1]Division of Experimental Surgery, McGill University, Montreal, QC, Canada. [2]School of Nursing and Midwifery, Iran University of Medical Sciences, Tehran, Iran. [3]Steinberg-Bernstein Centre for Minimally Invasive Surgery and Innovation, McGill University Health Centre, Montreal, QC, Canada. [4]Department of Systems and Computer Engineering, Carleton University, Ottawa, ON, Canada. [5]Department of Surgery, McGill University, Montreal, QC, Canada. [6]Centre for Outcomes Research and Evaluation, Research Institute of the McGill University Health Centre, Montreal, QC, Canada.

**INTRODUCTION**  In response to COVID-19, Quebec repurposed surgical care infrastructure and delayed many elective cancer surgeries. However, postponing cancer surgery is known to cause anxiety and distress. Currently, cancer patients' perspectives towards undergoing surgery during the pandemic are unknown. As healthcare systems face the proliferation of novel strains of coronavirus, it is imperative that patient perspectives are taken into consideration.

**OBJECTIVE**  To understand patients' perspectives towards receiving surgical cancer treatment during the COVID-19 pandemic.

**METHODS**  Patients who underwent general surgery for cancer at the McGill University Health Centre between March 2020 and January 2021 were invited to one-to-one interviews. Patients were purposefully selected for maximum variation using quota sampling (i.e., targeting delay status, pandemic phase, cancer site, and clinical/demographic characteristics) until interviews produced no new information (i.e., thematic saturation). Interviews were conducted using a semi-structured guide, audio-recorded, transcribed verbatim, and analyzed independently by two researchers. Data were managed using MAXQDA2020 and analyzed according to inductive thematic analysis.

**RESULTS**  Interviews were conducted with 20 patients [mean age 64; male (n=10); cancer sites: breast (n=8), skin (n=4), hepato-pancreato-biliary (n=4), colorectal (n=2), and gastro-esophageal (n=2)]. Surgery was delayed for 14 patients: 8 by the hospital, 4 by the patient, and 2 due to a positive COVID-19 test. Thematic analysis revealed that patients considered their susceptibility to infection, hospital safety measures, and burden on healthcare resources when determining willingness to undergo surgery. Patients weighed these risks against the urgency of their health condition and recommendations of their provider. Changes to the hospital environment (e.g., COVID-19 preventative measures) and deviations from expected treatment (e.g., alternative treatments, remote consultations, rescheduled care) caused diverse psychological responses, ranging from increased satisfaction to severe distress. Patients employed coping strategies (e.g., reframing care interruptions, communicating with clinicians, information seeking) to mitigate distress.

**CONCLUSIONS**  Changes in care during the pandemic elicited diverse psychological responses from patients undergoing cancer surgery. Patient coping was facilitated by open, consistent communication with clinicians, emphasizing the importance of patient-centered discussions regarding surgical delays within and beyond the pandemic.

# OUTCOMES OF KIDNEY TRANSPLANT RECIPIENTS WHO UNDERWENT PRE-TRANSPLANT BARIATRIC SURGERY FOR SEVERE OBESITY: A LONG-TERM FOLLOW-UP STUDY

Roxaneh Zaminpeyma[1]; Matias Claus[2]; Steven Paraskevas MD, PhD[1]; Olivier Court MD[2]; Jean Tchervenkov MD[1]; Amin Andalib MD, MSc[2]

[1]Multi-organ Transplant Program, Department of Surgery, McGill University, Montreal, QC, Canada.
[2]Center for Bariatric Surgery, Department of Surgery, McGill University, Montreal, QC, Canada.

**INTRODUCTION**   Kidney transplantation (KT) is the preferred therapy for end-stage renal disease (ESRD). While a major cause for ESRD, severe obesity is also a key obstacle to candidacy for KT. Bariatric surgery, particularly sleeve gastrectomy (SG) is increasingly used as a bridge to KT in these patients but the literature especially on outcomes after transplant remains lacking. We aimed to provide a long-term follow-up analysis of efficacy and outcomes of a previously described cohort of patients with obesity, who underwent SG as a bridge to KT.

**METHODS**   This is a single-center retrospective follow-up study of 32 patients with advanced chronic kidney disease or ESRD, who were referred and underwent SG between 2013-2018 as a bridge strategy to KT. The primary outcome was successful KT. Ninety-day outcomes and graft function at 1-year along with changes in weight and obesity-related comorbidities after KT were also evaluated. Descriptive statistics are presented as count(percentage) or median (interquartile range).

**RESULTS**   At baseline, 18(56%) were male with a median age and BMI of 51(11) years and 42.3(5.2) kg/m2, respectively. Median follow-up time post-SG was 53(54) months. At last follow-up, 23(72%) patients received KT, and another 3 patients were successfully listed for transplant. The median time to KT was 16(20) months and median BMI was 34.0(5.1) kg/m2 at time of transplant. At time of KT, 13(57%) and 20(87%) had diabetes and hypertension, respectively. Median follow-up post-KT was 16(47) months. There was one graft loss requiring return to dialysis. At 1-year post-KT, median eGFR was 57(21) ml/min/1.73m2. After KT and at last follow-up, median BMI remained at 34.0(12.0) kg/m$^2$.  Of those transplanted, 7/13 (54%) and 5/20 (25%) of patients with diabetes or hypertension had either an improvement or remission of their comorbidities, respectively.

**CONCLUSIONS**   SG is a strategy to increase accessibility to transplant in patients with severe obesity. Transplant recipients also continue to benefit from sustained weight loss and improved related comorbidities that may positively impact their graft function after KT.

# EVALUATION OF CURRENT RECTAL CANCER SURVIVORSHIP CARE: UNMET PATIENT NEEDS AND FRAGMENTED CARE AMONG SPECIALISTS AND GENERAL PRACTITIONERS

Jenny Moon, Ebram Salama, Anna Wang, Mylène Arsenault, Nathalie Leon, Carmen Loiselle, Fatemeh Rajabiyazdi, Marylise Boutros

*McGill University, Montreal, Quebec*

**INTRODUCTION**  With advances in rectal cancer management and improved prognosis, there is a growing number of rectal cancer survivors with unique needs. We hypothesize that the current rectal cancer survivorship care is limited in terms of communication among healthcare professionals, access to general practitioners (GPs), and targeted, dedicated care, leading to preventable emergency department (ED) visits.

**METHODS**  A mixed-methods study of rectal cancer patients and healthcare professionals was conducted. Part 1: A retrospective cohort study was performed on rectal cancer survivors who underwent proctectomy and completed all adjuvant treatment from 2005-2021 in a tertiary-care practice in Canada. The main outcome of interest was survivorship-related ED visits, defined as those related to bowel, sexual, and urinary dysfunction, chemotherapy-related complications, and stoma/wound-related complications not requiring an admission. Part 2: A qualitative study was performed with 5 colorectal surgeons, 2 medical oncologists, 1 radiation oncologist, and 4 GPs with rectal cancer patients in their practice. Semi-structured interviews were conducted to explore rectal cancer survivors' needs and their existing survivorship care. Grounded theory was used to thematically analyze the transcribed interviews.

**RESULTS**  Part 1: In total, 441 rectal cancer survivors completed treatment. Median age was 72 (IQR 63-82) years, 189 (42.9%) were female. There were 156 (35.4%) patients who did not have a GP. There were 673 ED visits for all patients, of which 60 visits were related to survivorship-related unmet needs. The most common reason for ED visit was bowel dysfunction (n=36), followed by chemotherapy-related neuropathy (n=14) and ostomy/wound-related complications (n=9). On Cox proportional hazards analysis, lack of access to a



Figure 1: Survival probability over time

GP was associated with a higher probability of having survivorship-related ED visits (p=0.003, Figure 1). Part 2: Interviews of specialists (n=8) and GPs (n=4) revealed 6 overarching themes: (1) Several unmet needs specific to rectal cancer survivors exist; (2) Specialists experience lack of resources and support in providing ancillary care to rectal cancer survivors; (3) GPs feel limited in providing survivorship-related care due to lack of information and knowledge; (4) There is no formal process to transition care from specialists to GPs during the survivorship phase; (5) Existing communication among specialists and GPs is lacking and fragmented; (6) A survivorship care document and dedicated nursing support have the potential to improve communication among specialists, GPs, and patients.
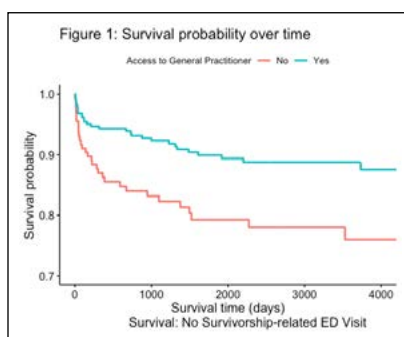
**CONCLUSIONS**  Existing rectal cancer survivorship care is fragmented. Lack of access to GPs or lack of their involvement in. survivorship care likely contribute to unmet needs. Rectal cancer survivors could benefit from improved, individualized follow-up coordinated among specialists and GPs.

# ASSESSING SURGICAL, TRAUMA AND TELEHEALTH CAPACITY IN INDIGENOUS COMMUNITIES IN NORTHERN QUEBEC: A CROSS-SECTIONAL SURVEY

Allyson Kis[1], Sébastien Dubé[2], Tarek Razek[1], Jeremy Grushka[1], Nathalie Boulanger[2], Larry Watt[3], Dan Deckelbaum[1], Kosar Khwaja[1], Paola Fata[1], Evan G. Wong[1]

[1]McGill University, Montreal, QC; [2]Régie Régionale de la Santé et des Services Sociaux du Nunavik, Kuujjuaq, QC; [3]Tulattavik Health Center, Kuujjuaq, QC.

**INTRODUCTION**   Novel hormonal agents (NHAs) such abiraterone acetate (ABI) and enzalutamide (ENZ) are two oral drugs that are frequently used in metastatic castration-resistant prostate cancer (mCRPC). Despite their overall tolerable risk profiles, certain signals of cardiovascular toxicity were reported for these agents in clinical trials but little is known about their incidence in clinical practice. The objective was to assess the comparative cardiovascular safety of ABI and ENZ in patients with mCRPC in the real-world.

**METHODS**   A retrospective population-based cohort was extracted from Quebec public healthcare administrative databases. Patients were selected on the basis of having initiated a novel hormonal agent (ABI or ENZ) between 2012 and 2016. The primary outcome of interest was cardiovascular-related hospitalization (composite outcome that included acute coronary syndrome, cerebrovascular stroke, heart failure, arrhythmia and others). Inverse probability of treatment weighting (IPTW) with the propensity score was used to adjust for measured baseline characteristics including pre-existing cardiovascular disease.

**RESULTS**   The cohort comprises 2,183 patients, with 1,773 (81.2%) in the ABI group and 410 (18.8%) in the ENZ group. Crude incidence rates of cardiovascular-related hospitalization were of 9.8 events per 100 person-years (PYs) and of 7.1 events per 100 PYs for the ABI and ENZ groups, respectively. After applying IPTW, the ABI group was at greater risk of cardiovascular-related hospitalization compared to the ENZ group (hazard ratio (HR) 1.82; 95% confidence interval (95%CI) 1.09-3.05). The risk of hospitalization for heart failure was greater in ABI (HR 2.88; 95%CI 1.09-7.63).

**CONCLUSIONS**   Our findings suggest that ABI users may be at greater risk of cardiovascular-related hospitalization compared to ENZ users, in particular for hospitalization for heart failure. These results provide clinicians with additional insight on the cardiovascular risks of mCRPC patients treated with NHAs in the real-world and further large studies are required to corroborate these findings.

# TIMING OF COMPLICATIONS FOLLOWING CAROTID ENDARTERECTOMY FOR SYMPTOMATIC AND ASYMPTOMATIC CAROTID ARTERY STENOSIS

Angela Y. Kim, Robert J. Doonan, Navid Zuberi, Oren Steinmetz, Kent Mackenzie, Daniel Obrand, Jason Bayne, Elie Girsowicz, Heather L. Gill

*Division of Vascular Surgery, McGill University, Montreal, QC, Canada*

**INTRODUCTION**  Current decision-making for safe discharge following carotid endarterectomy is based on clinical judgment after routine overnight observation. The aim of this study is to examine the time to early postoperative complications and identify risk factors of early complications to assess the safety of implementing same-day discharge following carotid endarterectomy.

**METHODS**  A retrospective cohort study of patients undergoing carotid endarterectomy from 2009 to 2020 at two university hospital centres was performed (n = 732). Detailed information regarding patient demographics, clinical characteristics, primary complications including 30-day and 1-year death, stroke or transient ischemic attack (TIA), and secondary complications including 30-day myocardial infarction (MI), other cardiac complications, and return to the operating room were extracted from inpatient and outpatient records. Clinical variables that have exhibited a univariate association with early complications at P < 0.05 level were included as a variable in multivariate analysis. Multivariate logistic regression analysis was used to identify independent clinical characteristics associated with early complications.

**RESULTS**  Of 732 patients, 597 (81.6%) patients presented with symptomatic carotid artery stenosis. There was no mortality within 30-days postoperatively and death within 1-year occurred in 4 (0.5%) patients. The overall incidence of 30-day and 1-year stroke or TIA was 9 (1.2%) and 11 (1.5%). Within 30 days postoperatively, MI occurred in 3 (0.4%), other cardiac complications in 2 (0.3%), and return to the operating room in 16 (2.2%) patients. Stroke or TIA within 24 hours involved 5 patients, of which 1 (20.0%), 3 (60.0%), and 1 (20.0%) occurred within the first 6 hours, 7-12 hour, and 13-24 hour intervals respectively. Of the 9 patients who experienced 30-day stroke or TIA, 8 (88.9%) patients initially presented with symptomatic carotid artery stenosis. MI occurred once within 6 hours and another within 13-24 hours. All other cardiac complications (n = 2) and return to the operating room (n = 10) within the 24-hour window occurred in the first 6 hours. Multivariate analysis demonstrated degree of stenosis to be associated with 30-day stroke or TIA and return to the operating room.

**CONCLUSIONS**  The timing of complications following carotid endarterectomy suggests that the majority of primary and secondary complications occur within the first 12 hours postoperatively and it may be unsafe to discharge patients before that window. Patients with high-degree carotid artery stenosis may be at risk of 30-day postoperative stroke or TIA and return to the operating room.

# COST OF STOMA-RELATED HOSPITAL READMISSIONS FOR RECTAL CANCER PATIENTS FOLLOWING RESTORATIVE PROCTECTOMY WITH A DIVERTING LOOP ILEOSTOMY: A NATIONWIDE READMISSIONS DATABASE ANALYSIS

Caminsky N, Marinescu D, Ghitulescu G, Vasilevsky C-A, Pang A, Alqahtani M, Boutros M

*Division of Colon and Rectal Surgery, Sir Mortimer B. Davis Jewish General Hospital, Montreal, Quebec, Canada*

**INTRODUCTION** Rectal cancer patients often undergo creation of a diverting loop ileostomy (DLI) to prevent the clinical consequences of an anastomotic leak. Stomas are not without their own complications; however few studies have investigated the associated costs. This study aimed to characterize long-term risks for readmission with stoma-related complications and their concomitant costs.

**METHODS** Through a retrospective cohort study using the Nationwide Readmissions Database, adult patients admitted with a rectal neoplasm (ICD-9/10 codes) who underwent restorative proctectomy (RP) with DLI (2010-2018) were identified. The date of RP and DLI defined cohort entry. Six-months post-RP and DLI or the time of DLI closure (whichever came first) defined cohort exit. Main outcome measures were emergency readmission for stoma-related complications (ICD-9/10 codes) and total cost of care (index admission for RP and DLI + readmission). Multivariate logistic and linear regression were used to identify risk factors and cost of readmission.

**RESULTS** Of 12,027 patients with RP and DLI, 9.5% (n=1,148) were emergently re-admitted for stoma-related complications which included: dehydration and acute renal failure (83.0%), hernia with obstruction (6.6%), and stoma malfunction (6.1%). Patients readmitted with stoma-related complications were significantly older [62.5±11.2 vs 59.1±12.0 (no readmission) vs 57.8±11.9 (readmission for non-stoma related complications) years, p<0.0001]. On multiple logistic regression, factors independently associated with stoma-related complications included female gender [OR=1.21 (95%CI=1.07–1.38)], chronic blood loss [OR=1.57 (95%CI=1.01–2.45)], depression [OR=1.39 (95%CI=1.12–1.74)], and diabetes [OR=1.94 (95%CI=1.48–2.53)]. Stoma-related complications requiring readmission independently increased total cost of care by $55,443.37 (95%CI=55,443.31–55,443.43) versus $47,101.30 (95%CI=47,101.23–47,101.37) for non-stoma related complication readmissions (Figure 1).
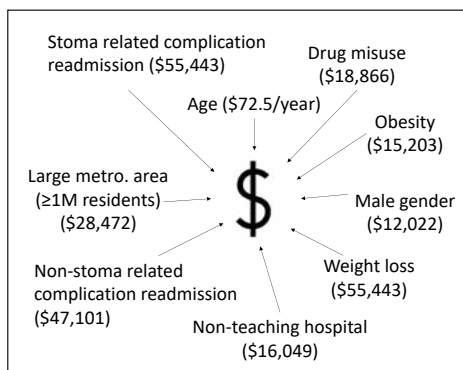


**FIGURE 1.** FACTORS PREDICTING TOTAL COST OF CARE (INDEX ADMISSION + READMISSION). NUMBER IN BRACKETS IS ESTIMATED CHANGE IN TOTAL COST OF CARE GIVEN PRESENCE OF FACTOR.

**CONCLUSION** Readmissions for stoma-related complications following RP and DLI are common and represent a substantial proportion of the rectal cancer patients' total cost of care. Increased support and consideration of selective early ileostomy closure could help reduce the financial burden on patients and the health care system.

# TOPICAL TRANEXAMIC ACID IN BREAST RECONSTRUCTION: A DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL

Tyler Safran, MD MSc[1], Joshua Vorstenbosch, MD PhD FRCSC[1], Alex Viezel-Mathieu MD Msc FRCSC[2], Peter Davison, MD S.M.Epi FRCSC[1], & Tassos Dionisopoulos, MD FRCSC[2]

[1]Division of Plastic and Reconstructive Surgery, McGill University Health Center, Montreal, Quebec, Canada,
[2]Division of Plastic and Reconstructive Surgery, Jewish General Hospital, Montreal, Quebec, Canada

**INTRODUCTION**   Excess fluid accumulation (seroma/hematoma) around the breast implant post reconstruction can lead to significant complications. Topical administration of tranexamic acid (TXA) may reduce fluid accumulation and reduce post-operative complications. This trial aims to investigate if TXA treated mastectomy pockets will exhibit less postoperative fluid production and complications.

**METHOD**   This paired, double-blinded, randomized-controlled trial enrolled patients undergoing bilateral mastectomies with immediate direct to implant reconstruction.  In each patient, one breast was randomized to receive 3g TXA (100cc), and the other received 100cc of NS. The blinded solutions were soaked in the mastectomy pocket for five minutes before implant placement. Postoperatively, daily drain outputs, complications, and baseline demographics were recorded.

**RESULTS**   53 eligible patients, representing 106 breasts, were enrolled. All patients underwent bilateral nipple-sparing mastectomies. After randomization, TXA was placed in the right breast in 56.6% (n=30) of patients. The use of topical TXA resulted in a mean drain output reduction of 30.5% (RANGE: -83.6% - 26.6%). Drains on the TXA treated breast were eligible for removal 1.4(RANGE: 0-4) days sooner than the control side. TXA treated group had three complications (5.67%) versus 15 (28.3%) in the control group (Odds Ratio: 0.1920, p= 0.0129). Specifically, for operative hematomas, the TXA group had none(0%) versus three in the control group (5.7%)(Odds Ratio: 0.1348, P=0.18).

**CONCLUSIONS**   Soaking the mastectomy bed with 3% topical TXA before implant insertion leads to a decrease in drain output and a decrease in complications. Topical administration of TXA represents an option to decrease complications in alloplastic breast reconstruction.

# RECIPIENT OUTCOMES AFTER KIDNEY AND LIVER TRANSPLANTATION FROM MEDICAL ASSISTANCE IN DYING (MAID) ORGAN DONATION

Kouyoumdjian A.[1], Saberi N.[1], Metrakos P.[1], Tchervenkov J.[1], Barkun J.[1], Zogopoulos G.[1], Paraskevas S.[1], Sandal S.[2], Cantarovich M.[2], Baran D.[2], Sapir-Pinchhadze R.[2], Wong P.[3], Deschenes M.[3], Benmassaoud A.[3], Chen T.[3], Chaudhury P.[1]

[1]Division of General Surgery, Department of Surgery, McGill University Health Centre (MUHC), Montreal, QC, Canada; [2]Division of Nephrology, Department of Medicine, MUHC, Montreal, QC, Canada; [3]Division of Gastroenterology & Hepatology, Department of Medicine, MUHC, Montreal, QC, Canada.

**INTRODUCTION** After the adoption of ''Death with Dignity'' Legislation in June 2014, organ donation following medical assistance in dying (MAiD) began in Quebec. While MAiD donations continue to increase, there remains paucity of outcome data. This study aims to compare recipient outcomes between MAiD donation and donation after circulatory death (DCD) for kidney and liver transplants.

**METHODS** A retrospective study of patients receiving kidney or liver transplant recovered from MAiD or DCD donation was performed. Kidney transplant recipients were matched 1:2 (MAiD to DCD ratio) from 2016-2021. Liver transplant recipients were matched 1:1 (MAiD to DCD ratio) from 2017-2021. Multivariable logistic regression analysis (MVA) was performed for delayed graft function (DGF).

**RESULTS** 26 liver transplantations (13 MAiD, 13 DCD) were included. Kaplan-Meier survival analysis of overall survival and graft survival showed no statistically significant difference. There was no statistically significant difference regarding stricture rates ($X2=0.72$, $p=0.39$).

92 kidney transplantations (24 MAiD, 68 DCD) were included. Kaplan-Meier survival analysis of overall survival and graft survival showed no statistically significant difference. MVA demonstrated that both MAiD donation and lower cold ischemia times was associated with decreased DGF incidence (OR 28.81, 95% CI 4.9-168.7, $p=0.00$ and OR 1.07, 95% CI 1.01-1.14, $p=0.03$ respectively).

**CONCLUSIONS** Kidney transplantation after MAiD is associated with decreased incidence of DGF. Liver transplant outcomes did not differ statistically between MAiD and DCD donation. This supports continued use of MAiD donors in kidney and liver transplantation with prospective outcome assessment.

# SURGICAL DECISION MAKING IN GENETICALLY HIGH–RISK WOMEN: QUANTIFYING POSTOPERATIVE COMPLICATIONS AND SHORT AND LONG–TERM RISKS OF SUPPLEMENTAL SURGERY

Carla Apostolova[1,2], Amina Ferroum[1,2], Basmah Alhassan MD MSc[1,3], Ipshita Prakash MD MSc[1,2,3], Mark Basik MD[1,3], Jean Francois Boileau MD MSc[1], Sarkis Meterissian MD Msc[1,3], Alex Viezel-Mathieu MD MSc[4], Nora Wong MS CGGC[2,5], William D. Foulkes MBBS PhD[2,3,5], Stephanie M Wong[1,2,3]

[1]Department of Surgery, McGill University Medical School, Montreal, QC, Canada. [2]Jewish General Hospital Stroll Cancer Prevention Centre, Montreal, QC, Canada. [3]Department of Oncology, McGill University Medical School, Montreal, QC, Canada. [4]Department of Plastic and Reconstructive Surgery, McGill University Medical School, Montreal, QC, Canada. [5]Department of Human Genetics, McGill University Medical School, Montreal, QC, Canada

**INTRODUCTION**   Prophylactic mastectomy provides the greatest risk reduction for breast cancer in high-risk women, yet also carries a risk of postoperative complications and supplemental surgeries. Considering the significance revisional surgeries hold in patient-centered decision-making, we sought to determine the short and long-term risk of supplemental surgeries following prophylactic mastectomy with or without reconstruction.

**METHODS**   We performed a retrospective cohort study of all female patients with a confirmed pathogenic variant in a breast cancer susceptibility gene (*BRCA1/2, PALB2, TP53, CHEK2, ATM, PTEN,* or *CDH1*) who underwent bilateral or contralateral prophylactic mastectomy at our institution between 2006-2021. Supplemental surgeries were defined as any operation requiring local or general anesthesia within the operating room performed outside of the initially planned procedure. The Kaplan-Meier method was used to calculate 2 and 5-year cumulative incidence of supplemental surgery, and multivariable logistic regression was performed to evaluate factors predictive of reoperation.

**RESULTS**   Of 523 carriers, prophylactic mastectomies were performed in 248 women. The median age of the cohort was 44 years (IQR, 37-52 years). Following prophylactic mastectomy, 33 patients (10.3%) developed early (<30 day) post-operative complications. At a median follow up of 42 months, 93 (37.5%) patients underwent at least one reoperation. The 2-year risk of supplemental surgery was 28.3% (95% CI, 22.7-34.9), increasing to 42.5% (95% CI, 38.5-50.6) at 5 years. Following adjustment for year of surgery, early post-operative complications remained the strongest risk factor associated with reoperation (OR 16.9, 95% CI 6.03-47.2). Participants who experienced an early post-operative complication had a higher likelihood of requiring two or more additional surgical interventions (42.4% vs 9.3%, p<0.001). The 5-year rate of supplemental surgery in patients without early post-operative complications was 34.8% (95% CI, 27.3-43.7).

**CONCLUSIONS**   Unanticipated postoperative complications and supplemental surgeries in high-risk women are common following prophylactic mastectomy. The immediate postoperative period highly influences the likelihood of experiencing multiple reoperations and is an important quality metric in breast surgical care.

# INCIDENCE OF OCCULT BREAST CANCER IN *BRCA1/2* AND OTHER HIGH PENETRANCE MUTATION CARRIERS UNDERGOING PROPHYLACTIC MASTECTOMY: WHEN IS SENTINEL LYMPH NODE BIOPSY INDICATED?

Amina M. Ferroum MD(c)[1,2], Carla Apostolova MD(c)[1,2], Basmah Al Hassan MD[1,2], Ipshita Prakash MD MSc[1,2,4], Mark Basik MD[1,3], Jean Francois Boileau MD MSc[1], Sarkis Meterissian MD Msc[1,3], Nora Wong MS CGGC[2,4], William D. Foulkes MD PhD[2,4], Stephanie M Wong MD MPH[1,2,3]

[1]*Department of Surgery, McGill University Medical School, Montreal, QC, Canada*
[2]*Jewish General Hospital Stroll Cancer Prevention Centre, Montreal, QC, Canada*
[3]*Department of Oncology, McGill University Medical School, Montreal, QC, Canada*
[4]*Department of Cancer Genetics, McGill University Medical School, Montreal, QC, Canada*

**INTRODUCTION**   We sought to determine the likelihood of occult malignancy at the time of prophylactic mastectomy in high-penetrance pathogenic variant carriers to refine axillary staging recommendations.

**METHODS**   We performed a retrospective cohort study of all female carriers of pathogenic variants in *BRCA1/2, PALB2*, or high-penetrance genes who underwent prophylactic surgery at our institution between 2006-2021. Occult breast cancer was defined as the unanticipated presence of in situ or invasive malignancy on pathologic evaluation of prophylactic mastectomy specimens.

**RESULTS**   Of 523 women, 243 female carriers met inclusion criteria for the study; 124 (51.0%) *BRCA1*, 108 (44.4%) *BRCA2*, and 11 (4.6%) *PALB2, TP53, CDH1* or *PTEN* pathogenic variant carriers. The median age was 44 years (IQR 37 – 52 years). Overall, 128 (52.7%) women underwent bilateral prophylactic mastectomies and 115 (47.3%) underwent contralateral prophylactic mastectomy. In 371 mastectomies performed, 16 (4.3%) occult malignancies were diagnosed. The majority of occult malignancies were ductal carcinoma in situ (13 mastectomies, 3.5%), whereas 3 (0.8%) mastectomies contained invasive breast cancer. If BIRADS I-II or BIRADS III findings were reported on preoperative MRI performed within 6 months of surgery, the rate of occult malignancy decreased to 3.0% and 2.8% per prophylactic mastectomy, respectively. Patient-level factors associated with a greater than 10% likelihood of occult breast cancer included a history of prior breast cancer (14%), age over 60 years (11%), and BIRADS IV findings on preoperative imaging (20%).

**CONCLUSIONS**   Occult invasive malignancy was detected in less than 1% of prophylactic mastectomies performed in *BRCA1/2* or *PALB2* carriers. Sentinel lymph node biopsy can be safely avoided in the majority of carriers when BIRADS I-III findings are reported on preoperative MRI.

# DEROTATIONAL OSTEOTOMY FOR YOUTH WITH PATELLOFEMORAL SYNDROME

Marianne Gagnon[1,2]; Louis-Nicolas Veilleux[1,2]; and Mitchell Bernstein[1,2]

[1]Department of Surgery, McGill University. [2]Shriners Hospitals for Children-Canada

**INTRODUCTION**   About 29% of adolescents have knee pain. One of the underlying causes of this pain is a combination of femoral and tibial torsion, which is often leading to functional limitations and to the cessation of sports activities. In patients that do not respond to conservative interventions, derotational osteotomy of the femurs and/or tibia is indicated. These procedures require careful planning, as errors in the correction may lead to poor functional outcomes. Yet, there are no clear guidelines regarding the amount of correction to perform, which segments result in the most symptomatic relief, and the optimal osteotomy location. In order to provide optimal treatment, the effect of these torsional deformities on mobility, function, pain and gait pattern, as well as the effect of surgery on these aspects must be studied.

**METHODS**   Participants aged 14 to 21 years with a combination of femoral and tibial torsion and candidates for surgery are recruited at the Shriners Hospitals for Children-Canada. Bone rotational profile is obtained by a computed tomography scan (CT scan) before surgery. Before and one year after surgery, participants have a quantitative gait analysis (QGA), a clinical examination (range of motion [ROM] and muscle strength) and they complete the "Pediatric Outcomes Data Collection Instrument (PODCI)", a patient reported outcomes questionnaire measuring the level of mobility, function, pain and happiness. The Wilcoxon Signed Rank test was used to assess whether pre-post-surgery changes are statistically significant. The results are reported as: median (95% confidence interval [CI]).

**RESULTS**   To date, eight female participants aged 16.6 years (95% CI: 14.9 years, 20.9 years) have completed the study. Baseline CT scan results demonstrate increased femoral anteversion (31° [95% CI: 15°, 46°]; norms: 14°±7.6 °) and increased external tibial torsion (47° [95% CI: 35°, 72°]; norms: 31.9° ±6.7 °). Derotational osteotomy was performed in 14 femurs (25° external [95% CI: 18 °, 30°]) and in 11 tibias (20° internal [95% CI: 13°, 25°]).

At 13.4 months (95% CI: 12.2 months, 15.8 months) post-surgery, statistically significant improvements were observed in the following domains of the PODCI: sports and physical function with 16 points (95% CI:12.7, 39.3; p=0.01), pain and comfort with 29 points (95% CI:17, 67; p=0.01) and for the global function with 15 points (5.75, 31.2; p=0.008) on a scale of 100. For the clinical assessment, significant changes were observed for the hip internal rotation ROM with a decrease of 20° (95% CI: -30°, -6°; p=0.001), the hip external rotation ROM with an increase of 23.5° (95% CI: 13°, 30°; p=0.001) and for the bimalleolar axis with a decrease of 15° (95% CI: -17°, -4°; p=0.004). For the QGA, a significant decrease of 14° for the mean hip rotation during stance (95% CI: -13°, -15°; p <0.001) and an increase of 12.3° (95% CI: 11.9°, 12.6°; p <0.001) for the mean knee rotation during stance were observed. No statistically significant changes were observed for muscle strength.

**CONCLUSIONS**   Preliminary results suggest that appropriately selected patients, who are evaluated with clinical, radiological and gait analysis parameters, benefit from derotational osteotomies. Clinical and gait analysis parameters improved post operatively. We anticipate two-year outcomes will continue to improve; however, it needs to be examined as well.

# SEVERE INFRAMALLEOLAR DISEASE IS AN INDEPENDENT PREDICTOR OF ADVERSE LIMB OUTCOMES AFTER REVASCULARIZATION IN PATIENTS WITH CHRONIC LIMB-THREATENING ISCHEMIA

Ahmed A. Naiem[1], Ariane Bergeron[2], Kent S. MacKenzie[3], Daniel I. Obrand[4], Oren K. Steinmetz[3], Jason P. Bayne[4], Heather L. Gill[3], Elie Girsowicz[4]

[1]Division of vascular surgery, McGill University; [2]Faculty of Medicine and Health Sciences, McGill University; [3]Division of vascular surgery, McGill University Health Centre; [4]Division of vascular surgery, Jewish General Hospital

**INTRODUCTION**   Inframalleolar disease (IM) is a form of distal arterial occlusive disease involving arteries below the ankle level. This study aims to evaluate the impact of inframalleolar disease (IM) on major adverse limb events (MALE) in patients undergoing endovascular revascularization (ER) for CLTI.

**METHODS**   Patients undergoing ER for CLTI with severe IM (pedal score of 2) were retrospectively compared to mild/moderate IM (score of 0 or 1) based on the Global Vascular Guidelines (GVG) between 2015 and 2019. The primary outcome was MALE (open revascularization), major amputation or minor amputation. Secondary outcomes were mortality, reintervention and limb-based patency (LBP). Kaplan-Meier estimates were used to compare the primary outcome and Cox proportion hazard model to assess impact of IM.

**RESULTS**   The study included 167 limbs in 149 patients (36% females). Severe IM was identified in 43% (n=71) of the limbs studied. There was no difference in baseline characteristics except for a higher prevalence of dyslipidemia in patients with severe IM (66% vs 43%, p=.003). Most patients in both groups had WIFI 3/4 (86% in both groups, p=.462) and GLASS II/III (78% in severe IM and 79% in mild/moderate IM, p=.752). During follow
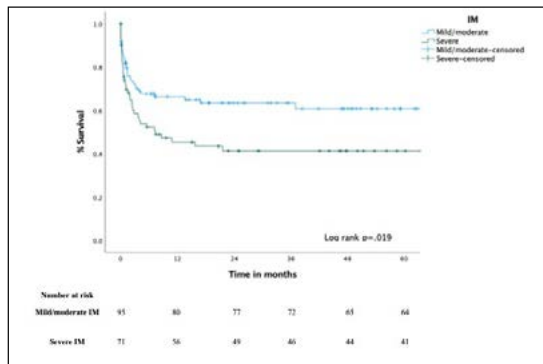


up, severe IM patients had similar mortality (27% vs 31%, p=.567), reintervention (42% vs 38%, p=.608) and LBP (78% vs 85%, p=.391) to mild/moderate IM. Kaplan-Meier estimates (figure 1) showed that severe IM was associated with lower freedom from MALE or amputations (47% vs 65%, p=.019). Cox proportion hazard regression model showed that severe IM was an independent predictor of increased MALE and amputations risk (HR 1.716 [95% CI 1.019 – 2.889], p=.042) after adjusting for covariates.

**CONCLUSIONS**   Severe IM was prevalent in 43% of limbs undergoing endovascular revascularization for CLTI. It was associated with lower freedom from major adverse limb events and amputations. Severe IM also independently increased the hazard of adverse limb outcomes in patients with CLTI by 72%.

# PREDICTING ACUTE CHOLECYSTITIS ON FINAL PATHOLOGY TO PRIORITISE SURGICAL URGENCY: AN EVALUATION OF THE TOKYO CRITERIA AND DEVELOPMENT OF A NOVEL PREDICTIVE SCORE

**Lilly Groszman, Brent Hopkins, Nawaf AlShahwan, Evan Wong**

*Department of General Surgery, McGill University Health Centre, Montreal, Quebec, Canada*

**INTRODUCTION**    INTRODUCTION: The Covid pandemic has compounded limitations in access to the operating room, highlighting the need for improved surgical prioritization rules for common pathologies, including acute cholecystitis.

The objective of this study was to compare the performance of our institution's surgical prioritization rules to the Tokyo diagnostic criteria and to develop a novel decision rule to predict acute cholecystitis on surgical pathology.

**METHODS**    All consecutive adult patients undergoing emergency cholecystectomy at a single academic institution between April 2017 to April 2021 were reviewed. The primary outcome was diagnosis of acute inflammation on final pathologic analysis. Multiple logistic regression was performed with a training subset using relevant clinical variables that were selected a priori. A simple weighted decision rule was created and compared to the Tokyo diagnostic criteria and the institution's existing prioritization rules via an analysis of receiver operating curves on a second subset of the population.

**RESULTS**    Among 756 patients undergoing emergency cholecystectomy, 97.6% of patients met criteria for acute cholecystitis as per Tokyo diagnostic criteria. Tokyo criteria (AUC = 0.51, sensitivity 99%, specificity 3%) poorly discriminated for acute inflammation on final pathology. Discrimination of the hospital's case prioritization rules was moderate (AUC = 0.63, sensitivity 48%, specificity 78%), and a new simple decision rule incorporating fever, Murphy's sign, leukocytosis and inflammation on imaging was significantly higher (AUC =0.69, sensitivity 72%, specificity 64%, p<0.003). In this large cohort of emergency cholecystectomies, the Tokyo diagnostic criteria were highly sensitive but non-specific for acute cholecystitis on final pathology.

**Regression model for acute inflammation**

| Characteristic | OR | 95% CI | p-value |
|---|---|---|---|
| Documented Fever | 2.12 | 0.94, 5.01 | 0.076 |
| Murphy's Sign on Exam | 3.20 | 1.95, 5.32 | <0.001 |
| Leukocytosis > 12 x 10 9 cells/L | 3.01 | 1.69, 5.50 | <0.001 |
| Inflammation on Imaging | 5.64 | 0.96, 107 | 0.11 |
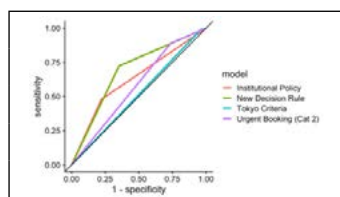


**CONCLUSIONS**    An existing institutional case prioritization rule demonstrated moderate discrimination for these outcomes but was outperformed by a novel parsimonious score incorporating readily available pre-operative variables. These findings may be useful in the prioritization of emergency cholecystectomies at busy centers but remains to be validated in outside cohorts.

# OPIOID VERSUS OPIOID-FREE ANALGESIA AFTER SURGICAL DISCHARGE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED TRIALS.

El-Kefraoui C[1], Olleik G[1], Chay MA[2], Powanda PN[1], Do U[1], Rajabiyazdi F[3], Kouyoumdjian A[3], Derksen A[4], Landry T[5], Amar-Zifkin A[5], Agnihotram R[6], Martel M[7], Lee L[1,3], Baldini G[1,7], Feldman LS[1,3], Fiore JF Jr.[1,3]

[1]McGill Dept. of Experimental Surgery, [2]McGill School of Medicine, [3]McGill Dept. of Surgery, [4]Patient rep., [5]MUHC Medical libraries, [6]RI-MUHC Biostats unit, [7]McGill Dept. of Anesthesia.

**INTRODUCTION** Excessive opioid prescribing after surgery has contributed to the current opioid crisis; however, the value of prescribing opioids at surgical discharge remains uncertain. We aimed to estimate the extent to which post-discharge opioid prescribing impacts self-reported pain intensity and adverse events in comparison with an opioid-free analgesic regimen.

**METHODS** In this systematic review and meta-analysis, we searched MEDLINE, EMBASE, the Cochrane Library, Scopus, Amed, Biosis, and CINAHL from January 1990 until July 2021. We included multi-dose randomized trials comparing opioid versus opioid-free analgesia in patients ≥15yo discharged after undergoing a surgical procedure (minor, moderate, major, or major-complex). We screened articles, extracted data, and assessed risk of bias (Cochrane's RoB-2) in duplicate. The primary outcomes of interest were pain intensity on post-discharge day one (standardized to 0-10cm visual analogue scale) and vomiting up to 30 days. Pain intensity at further timepoints, pain interference, other adverse events, risk of dissatisfaction, and healthcare reutilization were also assessed. We conducted random-effects meta-analyses and appraised evidence certainty using GRADE. The review was registered with PROSPERO (CRD42020153050).

**RESULTS** Forty-seven trials (n=6607) were included; 30 involved elective minor procedures (63% dental) and 17 procedures of moderate extent (47% orthopedic, 29% general surgery). Compared with opioid-free analgesia, opioid prescribing did not reduce pain at the first-day post-discharge [WMD 0.01cm (95% CI -0.26 to 0.27); moderate certainty] or at other postoperative timepoints (moderate-to-very low certainty). Opioid prescribing was associated with increased risk of vomiting [RR 4.50 (95% CI 1.93 to 10.51); high certainty] and other adverse events, including nausea, constipation, dizziness, and drowsiness (high-to-moderate certainty). Opioids did not impact other outcomes.

**CONCLUSIONS** Findings from this meta-analysis support that opioid prescribing at surgical discharge does not reduce pain intensity but did increase adverse events. Evidence relied on trials focused on elective surgeries of minor and moderate extent, suggesting that clinicians can consider prescribing opioid-free analgesia in these surgical settings. Data were largely derived from low quality trials, and none involved patients undergoing major or major-complex procedures. Given these limitations, there is a great need to advance the quality and scope of research in this field.

# SPINAL DRAIN OUTCOMES IN AORTIC SURGERY AT McGILL

**Anna E. Kinio, MD, MSc[1]; Xheni Khonci[2]; Heather L. Gill, MDCM, FRCSC[1]; Rober James Doonan, MD, PhD, FRCSC[1]**

[1]*Division of Vascular Surgery, McGill University, Montréal, Québec.*
[2]*McGill Faculty of Medicine and Health Sciences, Montréal, Québec*

**INTRODUCTION**   Spinal drains (SD) are an important component of spinal cord protection for patients undergoing complex aortic surgery. However, SDs are not benign and can lead to important complications such as intracranial hemorrhage and spinal hematomas. We sought to evaluate the outcomes of SD placement, including drain-related complications and spinal cord ischemia at two McGill University-affiliated hospitals.

**METHODS**   Patients who underwent aortic repair between 2014 and 2020 at the Royal Victoria Hospital and Jewish General Hospital were identified using procedure codes and were divided into two groups based on SD placement at the time of aortic surgery. A retrospective chart re   view was then performed to identify patient demographics, comorbidities, characteristics of the index surgery, post-operative outcomes, and SD-related complications.

**RESULTS**   One hundred and forty-five patients were included in the analyses. Ninety-one patients (62.8%) underwent SD placement and 54 patients (37.2%) underwent aortic repair without SD placement. Patients who did not undergo SD placement were more likely to present with ruptured aneurysms (p < 0.001) or traumatic aortic injuries (p < 0.001) and to undergo stand-alone thoracic endovascular aortic repair (TEVAR) (p = 0.01). Ten patients (11.0%) experienced intra-operative SD events including transient paresthesias during insertion and bloody spinal taps. Post-operatively, 10 patients (11.0%) developed drain-related complications, including two patients (2.2%) who developed intra-cerebral hemorrhages without long-term sequelae. Overall, there was no difference in post-operative rates of spinal cord ischemia between the groups (p = 0.412), however a total of eight patients (8.8%) in the SD group experienced either transient (N = 4, 4.4%) or permanent (N = 4, 4.4%) paraplegia (p = 0.046). These patients all presented with thoracoabdominal aneurysms and underwent open or complex endovascular repair. Transient episodes were associated with hypotension or low CSF drain output and resolved with medical optimization of cerebral perfusion. Permanent paraplegia was attributed to spinal cord ischemia in 3 (3.3%) of patients.

**CONCLUSIONS**   SD-related complications occurred in 11.0% of patients, with only 2.2% experiencing severe complications without long-term sequelqe. SD insertion therefore remains a safe practice despite variation in Anesthesia teams across our institution. Furthermore, all spinal cord complications occurred in thoracoabdominal patients who underwent open or complex endovascular repair. Aortic repair without SD may therefore be safe in select patients with isolated thoracic disease or in those undergoing stand-alone TEVAR.

# USE OF MACHINE LEARNING FOR CLINICAL PREDICTION TOOLS IN PEDIATRIC SURGERY: A SYSTEMATIC REVIEW

**Zaid A.M. Al-Azzawi[1], Amanda Bianco[1], Elena Guadagno[2], Esli Osmanlliu[4], Jocelyn Gravel[3], Dan Poenaru[2]**

[1]*Faculty of Medicine and Health Sciences, McGill University.* [2]*Department of Pediatric Surgery, McGill University and The Montreal Children's Hospital, McGill University Health Centre.* [3]*Department of Pediatrics, Sainte-Justine Hospital.* [4]*Department of Pediatrics, McGill University*

**INTRODUCTION**   Clinical prediction tools (CPTs) are decision-making instruments utilizing various components of patients' clinical history, physical examination, and biomedical profile to predict a specific clinical outcome, risk-stratify patients, or suggest a personalized diagnostic or therapeutic course of action. Historically, CPTs were developed using standard statistical models to create an objective clinical decision-making framework. Recent advancements in artificial intelligence and data science have resulted in a proliferation of CPTs created using machine learning (ML). This systematic review aims to compare the validity and clinical efficacy of ML-based CPTs to statistical pre-existing CPTs currently in use in pediatric surgery.

**METHODS**   A senior medical librarian searched nine databases from 2000 until July 9, 2021. The search strategy used variations in text words found in the title, abstract or keyword fields, and relevant subject headings, to retrieve articles reporting on clinical prediction tools and machine learning in the pediatric surgical setting. Screening was performed in Rayyan and completed by two independent reviewers, with a third arbitrator resolving conflicts. Risk of bias was assessed using the ROBIS tool.

**RESULTS**   Out of a total of 8336 studies, 135 met the inclusion criteria. Preliminary results show that the most represented surgical specialties were general (22, 16.3%), cardiac (22, 16.3%) and orthopedic surgery (15, 11.1%). Diagnostic, risk stratifying, interventional, and prognostic ML-based CPTs showed similar distributions in the literature. Most studies compared their instrument to other ML-based CPTs or pre-existing statistical CPTs but lacked external validation and/or evidence of clinical implementation.

**CONCLUSIONS**   While most studies claim significant potential improvements by incorporating ML-based CPTs in clinical decision-making, both external validation and clinical application remains very limited.  Further studies must focus on validating already existing instruments or developing validated tools and incorporating them in the clinical workflow.

# SESSION A, PART III: EDUCATION

## KEYNOTE: *FLS 2.0-COMING TO A TEST CENTRE NEAR YOU*

**MELINA VASSILIOU**
**MD**
Associate Professor, Department of Surgery, Faculty ofMedicine and Health Sciences, McGill University

Department of Surgery, Division of Adult General Surgery, MUHC

Associate Investigator, RI-MUHC, Montreal General Hospital
Injury Repair Recovery Program

**OBJECTIVES:**

❯ Describe the changes being implemented to the FLS Program and exam as part of FLS 2.0.

❯ Articulate some of the methods used to conduct the validity examination of FLS

**Dr. Melina Vassiliou** is the Associate Chair for Education and the Adair Family Chair in Surgical Education. Dr Vassiliou's passion for surgical education developed in her residency where she obtained a MEd degree. She has expertise in educational research methods, curriculum development, simulation and assessment. She served as program director for the Surgical Foundations program and is the fellowship director of the Minimally Invasive Surgery fellowship. She has been recognized with awards including the 2018 Canadian Association for Medical Education Certificate of Merit and was named to the McGill Faculty of Medicine Honour List for Educational Excellence. She serves in prominent international leadership roles in education, including as Chair of SAGES Fundamentals of Laparoscopic Surgery (FLS) committee.

# IMPLEMENTATION OF ENTRUSTABLE PROFESSIONAL ACTIVITIES INTO FELLOWSHIP COUNCIL ACCREDITED PROGRAMS – A PILOT PROJECT

Melissa N. Hanson[1,2], Aurora D. Pryor[3], D. Rohan Jeyarajah[4], Rebecca M. Minter[5], Samer G. Mattar[6], Daniel J. Scott[7], L. Michael Brunt[8], Maria Cummings[9], Melina Vassiliou[1,2], and Liane S. Feldman[1,2]

[1]Department of Surgery, McGill University, Montreal, Quebec, H3G 1A4, Canada. [2]Steinberg-Bernstein Centre for Minimally Invasive Surgery and Innovation, McGill University Health Centre, Montreal, Quebec, H3A 0G4, Canada. [3]Department of Surgery, Stony Brook Medicine, Stony Brook, NY, 11794, USA. [4]TCU School of Medicine and Methodist Richardson Medical Center Department of Surgery, Richardson, Texas, 75082, USA. [5]Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, 53792, USA. [6]Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, Texas 77030, USA. [7]Department of Surgery, UT Southwestern Medical Center, Dallas, Texas, 75390, USA. [8]Department of Surgery, Section of Minimally Invasive Surgery, Washington University School of Medicine, St. Louis, Missouri, 63110, USA. [9]Executive Director, The Fellowship Council, Los Angeles, California, 90064, USA

**INTRODUCTION** The Fellowship Council (FC) is transitioning to a competency-based medical education model. This includes the introduction of Entrustable Professional Activities (EPAs) for training and assessment of Fellows. This study describes the implementation process employed by the FC during a ten-month pilot project and presents data regarding feasibility and perceived value.

**METHODS** The FC coordinated the development of EPAs in collaboration with the sponsoring societies for Advanced GI/MIS, Bariatrics, Foregut, Endoscopy and Hepatopancreaticobiliary (HPB) fellowships encompassing the preoperative, intraoperative, and postoperative phases of care for key competencies. Fifteen accredited fellowship programs participated in this project. The assessments were collected through a unique platform on the FC website. Programs were asked to convene a Clinical Competency Committee (CCC) on a quarterly basis. The pilot group met monthly to support and improve the process. An exit survey evaluated the perceived value of EPAs.

**RESULTS** The 15 participating programs included 18 fellows and 106 faculty. A total of 655 assessments were initiated with 429(65%) completed. The average (SD) number of EPAs completed for each fellow was 24(18); range 0-72. Intraoperative EPAs were preferentially completed (71%). The average (SD) time for both the fellow and faculty to complete an EPA was 27(78) hours. Engagement increased from 39% of fellows completing at least one EPA in September to 72% in December and declining to 50% in May. Entrustment level increased from 6% of EPAs evaluated as "Practice Ready" in September to 75% in June. The exit survey was returned by 63% of faculty and 72% of fellows. Overall, 46% of fellows and 74% of program directors recommended full-scale implementation of the EPA framework.

**CONCLUSIONS** A competency-based assessment framework was developed by the FC and piloted in several programs. Participation was variable and required ongoing strategies to address barriers. The pilot project has prepared the FC to introduce CBME across all FC training programs.

# EFFECT OF VIDEO-BASED GUIDED SELF-REFLECTION ON INTRAOPERATIVE SKILLS: A PILOT RANDOMIZED CONTROLLED TRIAL

Saba Balvardi, MD[1]; Melina Vassiliou MD[1]; Carmen Mueller MD[1]; Mohammed Al Mahroos, MD1; Kevin Schwartzman, MD[2]; Julio F Fiore Jr., PhD[1]; Liane S Feldman, MD[1]

*[1]Department of Surgery, McGill University, Montreal, Quebec, Canada. [2]Respiratory Division, Department of Medicine, McGill University and McGill International Tuberculosis Centre*

**INTRODUCTION**   Video-review is a common adjunct to improve performance in sports and music. However, the value of video-based self-reflection in enhancing surgical skill acquisition is still uncertain. This study investigates the feasibility and estimates sample size for a full-scale RCT to evaluate the effectiveness of video-based self-reflection to improve surgical performance of laparoscopic cholecystectomy (LC) in trainees.

**METHODS**   This parallel pilot RCT included general surgery trainees performing supervised LC (targeted n=33, expected attrition 10%) randomized 1:1 to an intervention group (video-based self-evaluation in addition to traditional intraoperative teaching) or a control group (traditional intraoperative teaching alone). Operative performance was measured by the attending surgeon blinded to group assignment at the time of surgery using general and procedure-specific assessment tools (GOALS [score range 5-25, minimal important difference (MID)=2] and OPRS [score range 1-5], MID=0.3). Procedures were recorded and uploaded to a secure web-based platform. The intervention group had access to review their cases and perform a self-assessment using the same instruments. Primary outcome for estimation of sample size was change in faculty-assessed operative performance from the first to 3rd case. Feasibility criteria included >85% adherence to case submission and >85% completion of self-assessment. Multivariate linear regression was used to explorer changes in operative skill between the two groups.

**RESULTS**   Of 37 eligible trainees approached, 32 consented and were randomized (86%). There were 16 in the intervention group and 16 in the control group (55% male, 55% junior trainees). Of 200 eligible cases, 117 were submitted (59%). Forgetting to record or technical difficulties justified 43 (52%) of the unsubmitted cases. Twenty-four (75%) of participants successfully submitted at least 3 intraoperative recordings. Adherence to intraoperative assessment by faculty was 82%. In the intervention group, 13 trainees (81%) accessed the platform and completed 31 (54%) case self-assessments. There was greater improvement in the intervention compared to the control group for GOALS (adjusted difference +3.34, 95%CI –0.07 to 6.76) and OPRS (+0.80, 95%CI –0.07 to 1.67). Estimated sample sizes required for a full scale RCT range from 61 participants for GOALS to 144 for OPRS.

**CONCLUSIONS**   This pilot study contributes important data to inform the design of an adequately powered RCT to estimate the effectiveness of video self-review to enhance surgical performance in trainees. While a *priori* trial feasibility criteria (case submission and adherence to self-evaluation) were not achieved, automated video-capture and storage could significantly improve adherence in future trials.

# MAPPING SIMULATION FIDELITY IN CARDIAC SURGERY USING A MULTIDIMENSIONAL FRAMEWORK: A THEMATIC LITERATURE REVIEW

Mohammed A. Alharbi MBBS, Hellmuth R. Muller Moran MD,
Meagane Maurice-Ventouris BSc, Jason M. Harley MA PhD,
Kevin J. Lachapelle MDCM FACS FRCPSC

*Department of Surgery, McGill University, Montreal, Canada*

**INTRODUCTION**   Simulation-based training is being increasingly utilized in cardiac surgery to train future surgeons. Although low and high-fidelity cardiac surgical simulation has been described in the past, fidelity is poorly defined and not well established as a concept. In this review, we analyze the literature for meanings to better define fidelity and its levels.

**METHODS**   A keyword-based literature review was conducted to retrieve published cardiac surgical simulation literature using MEDLINE and EMBASE from January 1, 2000 up to February 1, 2020. The search was limited by date of publication but not type. Included articles were deductively and thematically analyzed to identify fidelity meanings within predefined dimensions.

**RESULTS**   Twenty-six articles were included for the thematic literature review after duplicates removal, screening and eligibility assessment according to inclusion and exclusion criteria. Seven themes were identified within a physical, a surgical field and an interactional dimension. These were environmental, equipment, anatomical, physiological, procedural, perceptual and psychological fidelity. Using an iterative process three levels of realism were generated for each theme.

**CONCLUSIONS**   Seven dimensional themes for cardiac surgical simulation fidelity were generated from published literature. We also identified what constitutes low, intermediate or high realism for each theme. This framework may be useful in designing cost-effective simulation-based training that will complement competency-based surgical education.

# ROLE OF ONLINE SUTURING SESSIONS IN THE DEVELOPMENT OF MEDICAL STUDENTS' SURGICAL SKILLS

Harrison Watt, BSc[1]; Justin-Pierre Lorange[1]; Hassan ElHawary, MD, MSc[2]; Ali Salimi, MD, MSc[3]; Mirko Gilardino, MD, MSc, FRCSC, FACS[2]

[1]Faculty of Medicine, McGill University, Montreal, QC, Canada. [2]Department of Plastic and Reconstructive Surgery, McGill University, Montreal, QC, Canada. [3]Department of Ophthalmology, McGill University, Montreal, QC, Canada

**INTRODUCTION**   In the last several years, medical students' interest in a surgical career has been declining, partly due to the lack of structured surgical skills training in medical curriculums. This can lead to low confidence in the operating room and a general reduction in interest in surgical specialties. However, many students bypass this gap in training by attending extra-curricular surgical skills workshops. The purpose of the current study is to evaluate the effect of a short, virtual, hands-on suturing skills workshop in increasing medical students' interest in surgical specialties, their subjective confidence, and their objective skills while complying with the COVID-19 restrictions.

**METHODS**   This prospective cohort pilot study assessed the effectiveness of a short, online, hands-on suturing session on increasing medical students' interest in surgical specialties, confidence in their surgical skills, and their objectively measured suturing skills. The focus was on simple interrupted suture, but those interested were taught additional techniques. The participants consisted of junior medical students at McGill University. Participants completed a pre-session questionnaire, attended the 60 min online suturing session, and completed a post-session questionnaire. Objective suturing skills were assessed at the beginning and the end of the session.

**RESULTS**   The questionnaires were completed by 31 participants (mean age of $23.87 \pm 3.21$ years-old). The session significantly increased participants' self-reported confidence in their suturing ability from $2.61 \pm 1.99$ out of a possible 10 points to $5.32 \pm 2.01$ ($P<0.01$). By participating in the session, 83.9% of participants expressed a higher level of interest in a surgical specialty, and no participant reported that the session made surgery less appealing. There was an increase in the percentage of participants expressing confidence in performing simple interrupted sutures (61.3% pre-session vs. 100% post-session; $P<0.01$), as well as horizontal mattress sutures (12.9% pre-session vs. 45.2% post-session; $P<0.01$). The percentage of participants lacking confidence in any type of sutures significantly decreased from 35.5% to 0% ($P<0.01$). Objective grading of the participants' suturing skills showed a statistically significant improvement, with a mean increase from $5.93 \pm 3.64$ out of a possible 15 points pre-session to $12.70 \pm 2.15$ post-session ($P<0.01$).

**CONCLUSIONS**   This study was the first to assess the efficacy of a virtual suturing skills workshop and our encouraging results suggests that undergraduate medical education curriculums across North America could benefit from similarly structured training sessions early in the medical curriculum.

# ASSESSMENT OF ACCURACY AND REPEATABILITY OF AUGMENTED REALITY–ASSISTED EPIDURAL NEEDLE INSERTION

**Amir Sayadi, Renzo Cecere, Amir Hooshiar**

*Department of Surgery of McGill University, Surgical Robotics Lab*

**INTRODUCTION**  Epidural injection is a medical intervention to inject therapeutics directly at the vicinity of the spinal cord and the nerves branching from it. For epidural injection, a long thin needle is inserted into the patient's spinal cavities through the skin and underlying soft tissues. Technically, epidural needle insertion is a blind procedure that relies merely on the physician's tactile feedback. Nevertheless, tactile feedback can be polluted with needle-tissue friction and may vary from patient to patient. Accurate insertion of the needle is a precise task that unless performed correctly may result in irreversible damage to the nerves or spinal cord. In this research, to enable physician's see the needle trajectory while inserting the needle, an augmented reality-based navigation assistance technology was proposed.

**METHODS**  In this study, we evaluated the accuracy and repeatability of epidural needle insertion assisted with an augmented reality projection. To generate patient specific 3D hologram that were projected to the physician's display, first a patient specific anatomical model was created based on a patient's lumbar CT scan using Mimics Medical (Materialise, Belgium) software. Afterward, the vertebral bones were extracted from the 3D model and was manufactured using 3D printing technique. To generate multi-layered soft tissue covering the vertebrae, multi-level molding technique was used using silicon elastomers (Ecoflex 00-30 and Ecoflex 00-10). For the experiments, a novice user inserted a 19G epidural needle into the patient-specific model (L3-L4, and L4-L5 spaces). The augmented reality assistance was provided to the user using a Microsoft Hololens 2. The user repeated needle insertion with and without augmented reality assistance for ten times. The accuracy of needle insertion was quantified by measuring the needle position error and with/without assistance. The needle position error was assumed to be zero when it was 1mm into the epidural space. Moreover, the repeatability was quantified by measuring the standard-deviation of the position error.

**RESULTS**  The average needle position error (accuracy) was 4.3 mm without assistance and 1.03 mm with assistance (76% reduction). Also, the repeatability was 1.8mm without assistance and 0.77mm with assistance (57% reduction). In addition, the user had 100% success in entering the epidural space in the first try with assistance and 70% success rate without assistance. Also, the time to completion of one needle insertion was 7 +/- 2 s with assistance while it was 16+/- 4 s without assistance (56% reduction).

**CONCLUSIONS**  The proposed system improved the accuracy, repeatability and success rate of epidural needle insertion on an anatomical model. It also reduced the procedural time. The proposed system will be investigated in a broader user study that will include more comprehensive user experience and accuracy criteria.

# EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON SURGICAL SKILLS ACQUISITION AND RETENTION

Francisco Reyna, MD[1]; Ahmed Naiem MD[1]; Marie-Amelie Lukaszewski PhD[1]; Alexander Thiel, MD[2]; Elie Girsowicz, MD, MSc[1]

[1]Division of Vascular Surgery, [2]Department of Neurology &Neurosurgery, McGill University.

**INTRODUCTION**   Surgical training involves gaining both theoretical knowledge and necessary skills to perform surgeries safely. While operative exposure is fundamental to acquire technical skills, recent duty hour restrictions potentially reduce that exposure and have unclear effects on ability to attain milestone and competencies. Transcranial direct current stimulation (TDCS) is a form of neuromodulation that uses constant, low direct current delivered via electrodes on the head. When TDCS is applied on the motor cortex concurrent with motor training, an enhancement in skills acquisition is often seen. We hypothesize that TDCS can enhance learning of surgical skills.

**METHODS**   A randomized, double-blinded, and controlled trial was performed. Surgical skills acquisition and retention were evaluated by comparing speed, accuracy, and total mistakes of a surgical task between 3 groups: TDCS, sham-TDCS and control. The clock face suturing model was used as the surgical task. Three different time points were defined: baseline (BL), post-training (PT) and retention (RT) assessment (4 weeks after PT). The training period involved the repetition of the surgical task for a total of 4 times, during this time TDCS and Sham-TDCS stimulation occurred. The accuracy was assessed as a percentage of on-point stitches divided by total possible points. Total mistakes score was defined as the addition mistakes done on hand and pickup adjustments, and total needle drops.

**RESULTS**   59 participants were recruited (TDCS n=19, Sham TDCS n=20, control n=20). A one-way ANOVA was done ($p = <0.05$ considered significant), regarding time to execute the task, a post training (in seconds) in TDCS of 201.4±43.6, sham TDCS 203.8±38.4, and control 230.8±45.2. No statistical difference was seen between groups at baseline: ($F_{(2,56)}=[0.302]$, $p = 0.740$), post training: ($F_{(2,56)}=[2.913]$,$p=0.063$), or retention:($F_{(2,56)}= [0.337]$, $p=0.715$). In terms of accuracy, a post training effect in TDCS was of 59.2±23, sham TDCS of 63.5±19.2, and control 57.5±16.4. No statistical difference was seen between groups at baseline: ($F_{(2,56)}=[0.430]$, $p=0.652$), at post training: ($F_{(2,56)}=[0.498]$,$p=0.611$), or retention: ($F_{(2,56)}=[0.720]$, $p=0.491$). In respect of total mistakes in post training, TDCS had 2.8±2.2, sham TDCS 1.8±1.2, and control 3.3±1.6, statistically significance was achieved in post training ($F_{(2,56)}=[3.843]$, $p=0.027$). No statistical difference was seen between groups at at baseline: ($F_{(2,56)}=[0.403]$, $p=0.670$), or retention: ($F_{(2,56)}=[1.999]$, $p=0.145$).
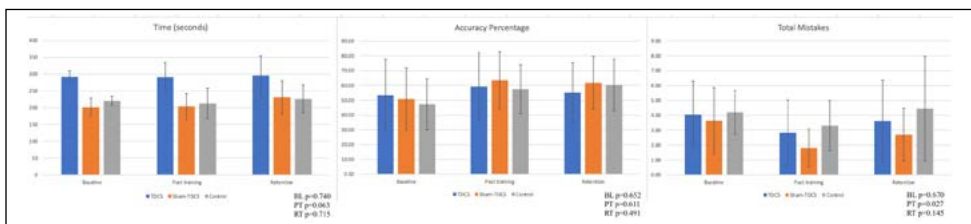


**CONCLUSIONS**   Although a trend in the TDCS and sham-TDCS groups was observed when vs control, our study failed to show an effect on TDCS in acquiring surgical skills. The control group was the worst performer in respect of mistakes with statistical significance, this can be explained by the expectations of outcomes effect and should be considered in TDCS-based experimental studies and clinical trials. Mindsets towards an intervention like TDCS may greatly impact outcomes through placebo-like effects that may influence cognitive performance. Features such as high anticipation have significant implications in TDCS adoption and adherence. Without evaluating the influence of participants expectation of outcome, the therapeutic viability of TDCS and treatment parameters will remain challenging.

# COMPARISON OF TWO VIRTUAL SIMULATION TECHNOLOGIES IN MEDICAL EDUCATION: AN ASSESSMENT OF COGNITIVE LOAD, USABILITY, AND PERFORMANCE DIFFERENCES

Sayed Azher[1], Keerat Grewal[1], Elif Bilgic[2], Jason Harley[1]

[1]McGill University, [2]McMaster University

**INTRODUCTION**   Virtual simulation (VS) is an alternative to in-person simulations and provides medical students with a game-like environment to practice procedures on virtual patients. Screen-based VS creates a virtual 3D world through a monitor, whereas headset VS uses a head-mounted display. Currently, no studies compare the usability or cognitive load requirements of the two modalities (screen-based VS and headset VS) using the same software and educational scenario in a simulated clinical environment. As such, we sought to investigate the usability and cognitive load differences between them, which could have implications on students' learning and the quality of medical education delivered.

**METHODS**   In a currently on-going study, medical students (n=8) were recruited from McGill University. Four participants used a screen-based VS simulation, and four used a headset-based VS simulation. All participants completed a pre-simulation and post-simulation survey. The surveys utilized Leppink's Cognitive Load Scale and the System Usability Scale (SUS) to determine cognitive load and usability differences, respectively. A simulation performance score was calculated for each student by the simulation software.

**RESULTS**   Preliminary results showcase that the modality choice does not contribute to a statistically significant intrinsic, extrinsic, or germane cognitive load difference in students. However, there existed a large mean difference approaching statistical significance ($p = 0.06$) between germane cognitive load ratings for screen-based VS ($M = 7.94$) and headset VS ($M = 4.94$). Additionally, analysis of usability results from the SUS indicated that screen-based VS ($M = 2.90$) and headset VS ($M = 2.93$) did not yield statistically significant differences ($p = 0.90$) with respect to students' usability ratings. Lastly, there was no significant difference in students' simulation performance scores between screen-based VS ($M = 44.24$) and headset VS ($M = 35.18$).

**CONCLUSIONS**   Our preliminary results suggest that screen-based VS and headset-based VS modalities might be similar in terms of the cognitive load required to operate these technologies. Interestingly, our usability findings were also not statistically significantly different between the screen-based VS and headset VS groups. This indicates that, with our current data, one modality does not outperform the other in terms of student ratings of its usability. Additionally, the lack of significant performance score differences between the two modalities suggests that simulation educators may have more flexibility in choosing one technology over the other without significantly impacting student learning. Taken together, the comparable preliminarily cognitive load, usability, and performance scores between modalities indicates that these technologies might offer similar value to students. However, as our current analysis was limited due to our small sample size, these results should be interpreted with caution. It is important to note that the aforementioned findings are preliminary, and future ongoing additions to our dataset will yield more comprehensive results. These findings will help contribute rare insight concerning the use of these VS technologies in healthcare education, allowing us to compare the modalities to determine the effects on students' cognitive demand and usability, potentially leading to enhanced learning.

# GENDER EQUALITY IN PLASTIC SURGERY TRAINING: A CANADIAN NATIONWIDE CROSS-SECTIONAL ANALYSIS

**Hassan ElHawary MD MSc[1], Ali Salimi MD MSc[2], Peter Alam MD[1], Stephanie Thibaudeau, MD, FRCSC[1]**

[1]*Division of Plastic and Reconstructive Surgery, McGill University, Montreal, Quebec, Canada*
[2]*Department of Ophthalmology, McGill University, Montreal Quebec, Canada*

**INTRODUCTION**   One of the important factors in achieving gender equity is ensuring equitable surgical training for all.   Previous studies have shown that females get significantly lower surgical exposure than males in certain surgical specialties.   Gender gap in surgical exposure has never been assessed in plastic surgery.   To that end, the goal of this study was to assess if there are any differences in plastic surgery training between male and female residents.

**METHODS**   A survey was sent to all plastic surgery residency programs in Canada to assess the number of surgeries residents operated on as a co-surgeon or primary assistant during their training.   The survey also assessed career goals, level of interest in the specialty, and subjective perception of gender bias.

**RESULTS**   A total of 89 plastic surgery residents (59.3% participation rate) completed the survey and were included in the study.   The average number of reconstructive cases residents operated on as a co-surgeon or primary assistant was $245 \pm 312$ cases.   There was no difference in either reconstructive or aesthetic surgery case logs between male and female residents ($p>0.05$).   However, a significantly larger proportion of females (39%) compared to males (4%) felt that their gender limited their exposure to surgical cases and led to a worsening of their overall surgical training ($p<0.001$).   Finally, a larger proportion of male residents were interested in academic careers while a larger proportion of female residents were interested in a community practice ($p=0.024$).

**CONCLUSION**   While there is no evidence of differences in the volume of logged cases between genders, female plastic surgery residents still feel that their respective gender limits their overall surgical training.   Gender inequalities in training should be addressed by residency programs.

# SESSION B, PART I: BASIC SCIENCE

### KEYNOTE: *SENOLYTIC THERAPY FOR IVD RELATED CHRONIC LOW BACK PAIN IN MICE AND MEN*

**LISBET HAGLUND**
**PhD**

**Professor, Department of Surgery,**
**Division of Orthopaedic Surgery**
**Co-director, the Orthopaedic Research Laboratory**

**OBJECTIVES:**

❭ **To discuss cell senesence related to discogenic low back pain.**

❭ **To discuss the potential to treat discogenic low back pain with senolytic/senomorphic compounds.**

**Lisbet Haglund** is a basic scientist and a tenured Professor in the Department of Surgery, Division of Orthopaedic Surgery at McGill University, and a Medical Scientist and Principal Investigator at the Shriners Hospital for Children, Montreal, Quebec, Canada. Lisbet received her PhD from the Department of Cell and Molecular Biology, Faculty of Medicine, Lund University, Sweden. She then spent 4 years in a BioTech company with R&D facilities in Lund before returning to academia, and postdoctoral training, at the Shriners Hospital in Montreal. She joined the Department of Surgery at McGill University as an Assistant Professor in 2009.

Lisbet has been actively involved in bone, cartilage, and intervertebral disc research throughout her career. Her research program is aiming to enhance our understanding of the molecular mechanisms leading to pain in spine pathology. More precisely, to develop molecular markers to follow disease state, progression, or effect of treatment, and most importantly to develop novel therapeutic interventions for painful spine conditions. Internationally she is the Chair Elect of the ORS spine section. Nationally, she is a Member of Alan Edwards Centre for Research on Pain, a Member Quebec Pain Research Network, the Past President and Board Member of the Canadian Connective Tissue Society and a member of the McGill Scoliosis and Spine Group, and she is working closely with the clinical team. This has allowed her to generate an extensive cell and tissue bank of symptomatic (surgical) and non-symptomatic (organ donor) cells and tissues. Her research program is currently funded through the Canadian Institute for Health Research (CIHR) and the Arthritis Society.

# ESOPHAGEAL ADENOCARCINOMA ON A CHIP: MODELLING A HIGH-FIDELITY PLATFORM FOR PRECISION ONCOLOGY

**Sanjima Pal[1], Julie Berube[2], Elee Shimshoni[3], Donald E. Ingber[3], Veena Sangwan[1], Lorenzo Ferri[1,2]**

[1]*Department of Surgery, McGill University, Montreal, Canada.*
[2]*Division of Thoracic Surgery, RI-MUHC, Montreal, Canada*
[3]*Wyss Institute for Biologically Inspired Engineering, Harvard University, Boston USA*

**INTRODUCTION**   Esophageal adenocarcinoma (EA) is one of the leading causes of cancer-related morbidity and mortality in the world. Lack of biological markers and cost-effective early screening results in late diagnosis. Systemic cytotoxic, platinum-based neoadjuvant chemotherapy currently represents the best standard of care (SOC) for patients with EA. However, 40% of the patients showed innate resistance to chemotherapy and half of the initial responders develop acquired resistance. Traditional 2D cell culture or rodent-based preclinical models are ill-suited for predicting anti-EA therapy and drug safety assessment. 3D organoids models failed to maintain tumor microenvironment. Ongoing research works emphasized the need for an improved, high-fidelity platform manifesting human-relevant esophageal organ physiology and the mechanisms of carcinogenesis.

**METHODS**   Syngeneic 'dual-cell' human esophageal tissue was developed on commercially available microfluidic chips. Primary tissues were obtained either from the sites of adenocarcinoma or adjacent disease-free regions at time of patients' biopsy or surgical resections. Patient derived organoids (PDOs) and syngeneic fibroblasts were established and expanded for future studies. The optically transparent membrane that separates parallel microchannels was coated with components of extracellular matrix. PDOs derived epithelial cells were grown at the upper mucosal channel while the lower vascular or tumor microenvironment (TME) channel was designated for syngeneic fibroblasts. Once cells adhered to the membrane, they were subjected to physiologically relevant flow of media. In-house developed expansion and differentiation media were used to maintain tissue on chips. Permeability coefficient parameter was measured by Cascade blue assay. Tissue response to DCF (docetaxel, cisplatin, and 5-fluorouracil; 1:1:10) based neoadjuvant therapy was also demonstrated. Fluorescent-NucBlue™-Live Ready probe was used to assess tissue development, cellular fate prior to or post- neoadjuvant therapy in real-time.

**RESULTS**   Real-time microscopic (bright field and fluorescence) observations revealed that the EA chip remains healthy for at least 12-15 days under continuous flow and displays in vivo-like stratified squamous epithelial morphology, and mucin production, Chips were also able to demonstrate the morphological differences arising due to the origin of adenocarcinoma. Cell viabilities were also monitored in real-time for 10-12 days using fluorescent probes. Tissue permeability was also evaluated. Precisely developed EA chips were exposed to either sub-cytotoxic or cytotoxic dose of DCF at the top channel for 72 h-96 h and cell death was assessed.

**CONCLUSIONS**   The Human esophageal adenocarcinoma chip is a novel, high-fidelity, physiological organ biomimetic platform built on a microfluidic chip and can replace inadequate animal models in the future

# IL-1B-INDUCED DRG NEURONAL HYPERSENSITIVITY IS ABROGATED BY LINK N.

**Muskan Alad[1,2], Michael P Grant[1], Laura M Epure[1], Olga L Huk[1,2], David J Zukor[1,2], John Antoniou[1,2], Fackson Mwale[1,2]**

[1]*Lady Davis Institute for Medical Research, Montreal, QC, Canada,*
[2]*McGill University, Montreal, QC, Canada.*

**INTRODUCTION**    Osteoarthritis (OA) is a painful and disabling chronic condition that constitutes a major challenge to health care worldwide. One of the main factors implicated in OA pain is abnormal sensory input (nociception) by dorsal root ganglia neurons that innervate the joint. IL-1β is a key proinflammatory cytokine involved in the progression of degeneration and pain in OA. There is currently no cure for OA, and available analgesics do not offer adequate and sustained pain relief. We have demonstrated that LN, a 16-residue peptide derived from link protein, can suppress the upregulation of catabolic enzymes and inflammatory and pain factors in human chondrocytes. We have also demonstrated that LN can modulate pain behavior in a murine model with advanced OA. It remains unclear as to the mechanism(s) of LN on pain behavior. We hypothesize that LN plays a direct role in regulating IL-1β signaling in joint and DRG neuronal cells to alter sensory pain in OA.

**METHODS**    *Western Blotting:*  Human OA chondrocytes and synovial fibroblasts isolated from donors (ages 45-65 yrs) undergoing knee arthroplasty were treated with LN [1 µg/mL] with or without IL-1β [1ng/mL] for up to 60 min. Cell lysates were collected and processed for Western blotting to identify changes in P-NFκB, the transcription factor activated by the canonical signaling pathway of IL-1β. *Ca$^{2+}$-mobilization:*  DRG neurons were isolated from lumbar regions L2-5 in 15-week-old C57BL/6 mice and cultured in glass chamber slides for 7 days with IL-1β with or without LN [1 µg/mL]. Cells were loaded with Fura-4, AM and imaged for changes in intracellular Ca$^{2+}$ either at resting state or following stimulation with capsaicin [100 nM] using a Zeiss LSM800 confocal microscope.

**RESULTS**    In both chondrocytes and synovial fibroblasts, LN significantly suppressed the activation of P-NFκB to levels comparable to controls for up to 60 min (ANOVA, posthoc Tukey; $p < 0.01$; n = 4). Ca-mobilization is used as a surrogate marker for excitability in DRG neurons. When DRGs were incubated with IL-1β, basal intracellular Ca$^{2+}$ levels were elevated when compared to controls ($p < 0.001$; n = 4) but significantly decreased when LN was present ($p < 0.0001$; n = 4). When DRG neurons were stimulated with capsaicin, IL-1β preconditioned neurons



**FIGURE 1.** EFFECT OF LN ON IL-1β-INDUCED HYPERALGESIA IN ISOLATED MURINE DRG NEURONS. DRG NEURONS WERE STIMULATED WITH CAPSAICIN [100 nM] FOR 240 X FOLLOWED BY KCL (100 nM) FOR 120 S. N=6.

demonstrated a sustained increase in intracellular Ca$^{2+}$. Co-treatment with LN blunted the sustained Ca$^{2+}$ increase induced by IL-1β (Fig 1).

**CONCLUSIONS**    In summary, LN inhibits IL-1β signaling and regulates DRG neuronal-induced hypersensitivity. These results may support the use of LN in the treatment of OA pain.
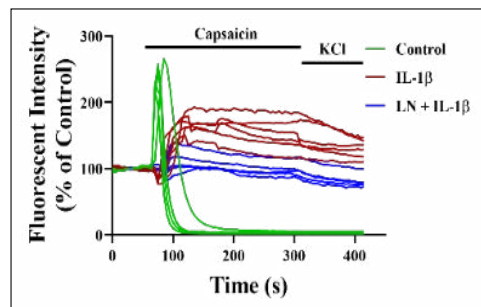
# CHARACTERIZATION OF PATIENT-SPECIFIC DIFFERENCES IN INDUCED PLURIPOTENT STEM CELL-DERIVED CARDIOMYOCYTES FOLLOWING HYPOXIA-INDUCED INJURY

Ida Derish[1], Jeremy Zwaig[1], David Derish[2], Janice To[3], Patrick Young[4], Bin Yu[5], Adel Schwertani[5], Renzo Cecere[1,6]

[1]Experimental Surgery, [2]Medicine, [3]Pharmacology, [4]Kinesiology, [5]Experimental Medicine, [6]Cardiac Surgery
McGill University, Montreal, Quebec, Canada

**INTRODUCTION**    The increasing rate of cardiovascular disease (CVD) in surviving patients contributes to a worsening quality of life as well as a socioeconomic burden on the healthcare system. The implementation of novel therapeutics into the treatment workflow to specifically boost tissue repair and regeneration is of particular interest. However, newly investigated therapies present unforeseen side effects and occasionally entail adverse cardiovascular responses in patients. Indeed, modern treatments do not account for the variability of individual patient reactions, due to a lack of a representative *in vitro* cardiac model. While the use of induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) has gained traction as a viable model when compared to cardiac biopsies and immortalized cell lines, cardiovascular patient-specific differences remain poorly understood and understudied. We hypothesized that 1) cardiomyopathic patient-derived iPSC-CMs have differing baselines of beating rate, contractility, viability, metabolic activity and protein expression, when compared to healthy controls, and that 2) cell lines have patient-specific responses to hypoxic injury. The purpose of this study was to perform a characterization of patient iPSC-CM function, and to study patient-specific cellular responses to hypoxia-induced injury.

**METHODS**    First, we generated iPSCs (n=5 cardiomyopathic patients, n=2 healthy donors). from peripheral blood through transfection of reprogramming factors (Oct4, Sox2, Lin28, Klf4, and L-Myc) and performed an assessment of cell line quality via immunocytochemistry (with pluripotency markers OCT4, Nanog, SSEA-4 and TRA-1-60), RT-PCR (with confirmation of markers SOX2, Lin28, NANOG, TDG1, Oct3/4, DPPB5) as well as trilineage differentiation and immunostaining (with ectoderm marker Otx2, mesoderm marker Brachyury and endoderm marker Sox17). After iPSC-CM differentiation, we confirmed the expression of prominent cardiac markers (CXN43, SERCA2a, GATA4 and cardiac Troponin T), as well as a lack of pluripotency markers (OCT4, Nanog, SSEA-4 and TRA-1-60) in the iPSC-CMs, via immunocytochemistry.

**RESULTS**    Preliminary assessment of iPSC-CMs (days 1-20 post-differentiation) revealed significant baseline differences in beating rate ($p < 0.01$) and contractility amplitude ($p < 0.01$) between iPSC-CMs derived from cardiomyopathic patients and healthy donors. We then subjected iPSC-CM lines to hypoxic conditions (24 hours, 0% oxygen anaerobic chamber), to mimic ischemic injury. Diseased patient-derived lines had significantly decreased viability and metabolic activity when compared to the controls, under normoxic ($p < 0.01$) and hypoxic conditions ($p < 0.001$).

**CONCLUSIONS**    Taken together, these results suggest that the detected differences at the cellular level after hypoxia-induced injury might be translatable to the inter-individual variability currently observed in the CVD patient population. With this preliminary study, we hope to shift the focus towards these patient-specific differences at the cellular level, in the search for tailored regenerative cardiac therapies and a higher standard of care for CVD patients.

# REGULATION OF PULMONARY FIBROSIS BY CD109 IN A MURINE MODEL

**Maha Alsharqi[1], Yumiko Ishii[2], Meryem Blati[1], James Martin[2] and Anie Philip[1,2]**

[1]*Division of Plastics Surgery, Department of Surgery, McGill University,*
[2]*Department of Medicine, McGill University*

**INTRODUCTION** Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease characterized by inflammation, excessive fibroblasts proliferation, and deposition of extracellular matrix (ECM) in the interstitium. It leads to impaired lung function and decreased quality of life. Transforming Growth Factor-ß1 (TGF-ß1) is a multifunctional growth factor, with a wide range of functions in homeostasis and tissue repair. TGF-ß1 signaling is mediated via Smad2/3 intracellular proteins leading to gene transcription and ECM protein expression, and the TGF-ß1/Smad2,3 signaling pathway has been shown to play an important role in the pathogenesis of lung fibrosis and other fibrotic disorders. Our team has previously identified CD109, a glycosylphosphatidylinositol (GPI)-anchored protein as a TGF-β1 co-receptor that negatively regulates TGF-β1 signaling and responses and have shown that CD109 deficient mice display enhanced TGF-ß1 signaling leading and fibrosis in the skin using an animal model of skin fibrosis. In the current study, we aimed to investigate the role of CD109 in lung fibrosis using a CD109 deficient mouse model.

**METHODS** Using CD109 Knockout (KO) and wild-type (WT) littermate mice, we established a mouse model of lung fibrosis by intratracheal instillation of bleomycin, with the control groups receiving PBS. The architecture of the lung alveoli and collagen deposition were analyzed in all groups by hematoxylin and eosin staining, and Masson's trichrome staining, respectively. Im munohistochemistry was performed to evaluate the expression of different ECM markers, and the number of neutrophils and M1 and M2 macrophages. Also, lung compliance was evaluated using FlexiVent. Using isolated lung fibroblasts, we also determined ECM protein expression and cellular migration.

**RESULTS** H&E staining reveals that the KO lungs exhibit increased cellularity and distinct alveolar morphology with obliteration of the alveolar sacs, when compared to WT lungs. Trichrome staining demonstrates a markedly increased collagen content in CD109 KO lungs compared to WT lungs. Furthermore, the KO lung tissue shows increased expression of collagen, fibronectin and alpha-smooth muscle actin, as detected by immunohistochemistry. In addition, the KO lung tissue shows markedly increased numbers of both M1 and M2 macrophages while the neutrophil count remains unchanged. In addition, isolated CD109 KO lung fibroblasts display greater basal and TGF-β induced ECM protein expression and cellular migration than WT lung fibroblasts ($p < 0.05$).

**CONCLUSIONS** Our finding that CD109 deficiency results in markedly increased fibrosis with enhanced TGF-ß signaling, cellularity, and macrophage numbers in the lung implicates an essential role for CD109 in lung homeostasis and reveals its potential as a molecular target for therapeutic intervention in lung fibrosis.

# FACILITATED FRACTURE REPAIR VIA NONINVASIVE LOCALIZED COLD THERAPY

**Matthew Zakaria[1,2], Dr. Yazan Honjol[2], Dr. Lucy Luo[2],**
**Dr. Jose Garcia Ramirez[2], Dr. Edward J. Harvey[2], Dr. Geraldine Merle[3]**

[1]*McGill University,* [2]*McGill University Health Centre,* [3]*Polytechnique University*

**INTRODUCTION**   The ability of fractured bone to regenerate and undergo repair is often compromised. Successful fracture healing involves an inflammatory cascade leading to bone repair. Cold treatment is commonly used to prevent inflammation after musculoskeletal injuries and earlier work on using cold stimuli for critical cortical defect healing has shown to enhance bone growth. However, no study has looked at its effect or mechanism on fractures.

Here, we hypothesized that enhanced bone healing demonstrated using cold therapy in cortical defects will be replicated in a clinically relevant fracture model and cold therapy stimulates angiogenesis leading to improved vascularity.

**METHODS**   Bilateral femoral fractures using retrograde nailing were formed in C3H strain mice. Initially, a guidewire was inserted followed by usage of a home-made 3-point impact device to produce a closed midshaft femur fracture. A 23-gauge stainless steel needle-tip was then implanted over the guide wire to stabilize the fracture and the guide wire removed.

Experimental legs were immersed in a cold-water bath reaching an internal bone temperature of 19 degrees Celsius for 15 minutes daily. Core-body and control leg temperatures were maintained with a heating pad. Femurs were harvested at days 7, 14, 28 and underwent micro-CT analysis. Staining of ALP, TRAP, and VEGF followed.

**RESULTS**   Day 28 timepoint analysis revealed daily exposure of fractured femurs to cold therapy increased bone volume/tissue volume (BV/TV) by 15% when compared to untreated controls (p-value<0.001). Simultaneously, a 1.42% increase in channel volume/tissue volume within cold treated femora illustrates the prevalence of an enhanced vascular network (p-value<0.05). Biomarkers ALP and TRAP demonstrated expressions consistent with physiological bone remodeling within cold-treated femora at day 28, with staining revealing a significant 5.3% reduction in ALP (p-value=0.028) detection without significant alteration of TRAP expression (p-value=0.44).

Bony callus formation is visibly enhanced at the 14-day timepoint from daily exposure of fractured femurs to cold therapy, reflecting a 6.61% increase in BV/TV when compared to untreated controls (p-value<0.001).

**CONCLUSIONS**   Findings confirm that localized cold treatment accelerates bone growth in a clinically relevant closed femoral fracture model. A strong increase in BV/TV coupled with decreased ALP staining of osteoblasts without significantly altered TRAP staining of osteoclasts indicates osteoclastic driven bone remodeling is attained faster within cold-treated femora. Simultaneously, improved vascularity indicates enhanced angiogenesis. Currently, potential fluctuations in genetic expression, vasomotor tone, pH, and hemoglobin oxygen saturation are being investigated to uncover the mechanistic propensity of therapeutic hypothermia.

# EFFICACY OF OXYGEN DELIVERY BIOMATERIAL FOR ISCHEMIC SKIN PRESERVATION

**Arturo Vela Lasagabaster[1], Arghavan Rastinfard[1], Benjamin Dalisson[2], Mirko Gilardino[3], Kevin Watters[4], Yassine Ouhaddi[1], Jake Barralet[1,2]**

[1]Division of Orthopaedics, Department of Surgery, Faculty of Medicine and Health Sciences, Montreal General Hospital Site, McGill University Health Centre, QC, Canada. [2]Faculty of Dentistry, McGill University, 2001 McGill College Avenue, Montreal, QC, Canada. [3]Division of Plastic and Reconstructive Surgery, Montreal General Hospital Site, McGill University Health Centre, QC, Canada. [4]Department of Pathology, Glen Site, McGill University Health Centre, QC, Canada.

**INTRODUCTION**   Insufficient or impaired vascularization is often the cause behind the development of chronic wounds. Diabetes, impaired cardiovascular functions, direct pressure due to immobility and advanced age are some of the etiological factors that drive to these cutaneous injuries. Often, these factors act together to worsen this impairment. During reconstructive surgeries, the raising of skin flaps produces a traumatic wound that can sometimes result in partial necrosis of the distal area of the flap due to impaired vascularization. Furthermore, sufficient vascular remodelling to sufficiently prevent tissue death can be exacerbated by these comorbidities. This work aims to test the effects of oxygen delivery biomaterials for the reduction of necrosis of poorly vascularized skin in normal and diabetic rat random skin flap models.

**METHODS**   We developed an implantable solid peroxide-biomaterial based system to provide sustained delivery of oxygen directly to tissues with reduced hydrogen peroxide release by virtue of incorporation of iron oxide to catalytically decompose it. A preclinical trial was conducted on male Wistar rats of 5-6 months old, divided into 2 groups (N=9 per group). Following standard rat ischemic skin flaps model, full depth skin flaps of 9×2 cm2 in size were created on the back. A silicon sheet was placed over the muscle to prevent revascularization and reperfusion of the dermal side of the flap from the underlying tissue, then the oxygen releasing film was positioned distally, and the skin was re-replaced on top of it and sutured. The control group received no film. In every group, five animals were sacrificed on day 6, four animals on day 10. A second trial with was conducted on Goto Kakizaki male diabetic rats, divided in 2 groups (N=6). The surgical technique is the same as in previous with minor changes tailored to the difference in weight of the strain. Exposed rats received the same biomaterial and the control rats received no biomaterial. All 6 animals were sacrificed after 10 days.

**RESULTS**   When comparising time points, the skin flap in the control group showed a bigger area of necrotic tissue (40% vs 31%; P<0.05). The rate at which animals presented necrosis was very different between subjects even in the same groups. When comparing endpoints, (Did extent of necrosis exceed 40% at any time during healing in a particular subject? (Y/N)), we determined a statistical difference of P<0.05 at a power of 98.4%. Rats showed no difference in intradermal oxygen levels in between animals of the same group, but showed difference between groups, with less oxygen levels in the control group (P<0.001). Other measures of comparison did not show differences or were not comparable (intradermal lactate quantification; thermal images). Immunohistochemistry showed differences in macrophage polarisation though it was not clear whether this was a direct effect of the material or a consequence of better healing.

**CONCLUSION**   We report the fabrication of a polymer film composite oxygen delivering biomaterial that can placed subdermally. This biomaterial can prevent and limit the extent of necrosis but not prevent it and so may have a role as an adjuvant therapy.

# AGE-ASSOCIATED CHANGES IN CALCIUM SIGNALING AND MEMBRANE INJURY IN OSTEOBLASTS AND OSTEOCLASTS

**Chrisanne Dsouza[1,2], Svetlana V Komarova[1,2,3]**

[1]*Shriners Hospital for Children, Montreal Canada,* [2]*Department of Experimental Surgery and* [3]*Faculty of Dental Medicine and Oral Health Sciences, McGill University, Montreal, Canada*

**INTRODUCTION**  Physical activity is important for maintaining skeletal health. However, the skeleton of older individuals is unable to adapt to mechanical loads for yet unknown reasons. Mechanical stimulation results in the release of ATP and ADP which act on purinergic P2X and P2Y receptors, leading to downstream intracellular calcium signals. The objective of this study was to 1) assess membrane injury 2) characterize ATP and ADP-mediated calcium signaling in mechanically stimulated osteoblasts and osteoclasts from young and old mice.

**METHODS**  Primary osteoblast and osteoclast cultures were obtained from young (10–12-week-old) and old (69–73-week-old) mice. Cells were loaded with Fura 2-AM ($Ca^{2+}$ indicator dye) and a single cell was mechanically stimulated with a micropipette. Cytosolic free calcium [$Ca^{2+}$]i changes in primary (mechanically-stimulated) and secondary (neighboring) cells were analyzed. Membrane injury was assessed in mechanically stimulated cells by change in intensity of 340 nm excitation due to Fura-2 AM dye loss.

**RESULTS**  The severity of membrane injury in mechanically stimulated cells was graded as minor (no dye loss), intermediate (limited dye loss) or severe (high dye loss). Osteoblasts from older mice had a higher proportion of cells with minor injury compared to osteoblasts from younger mice. Mechanical stimulation in osteoclasts led to a higher proportion of severely injured cells in younger osteoclasts compared to older osteoclasts. The [$Ca^{2+}$]i response (area under curve) in mechanically stimulated young osteoblasts was significantly higher than in older osteoblasts. Release of ATP and ADP from mechanically stimulated cells stimulate responses in secondary, non-stimulated cells. We observed a trend of reduction in the signaling radius (maximal distance from primary cell) and a higher percentage of oscillators in secondary responses of osteoblasts from older animals. In osteoclasts, mechanically stimulated cells from older animals showed a trend towards higher calcium amplitudes and a faster decay time. Secondary responders in old osteoclasts demonstrated significantly higher [$Ca^{2+}$]i responses and a trend of a higher responding fraction compared to osteoclasts from young mice.

**CONCLUSIONS**  In osteoblasts, increase in age is associated with less injury upon mechanical stimulation, and reduced calcium response in secondary osteoblasts suggesting decrease in ATP and ADP release. In osteoclasts, increase in age is associated with lower injury from mechanical stimulation, but higher calcium responses in secondary cells. Thus, aging has opposing effects on the mechanosensitivity of osteoblasts and osteoclasts, suggesting that both cells contribute to diminished mechanoadaptation of the skeleton of older individuals.

# BREAST IMPLANT INSERTION PLANE IS ASSOCIATED WITH DISTINCT CAPSULAR INFLAMMATORY AND FIBROTIC SIGNALING PATTERNS: A POSSIBLE LINK TO CAPSULAR CONTRACTURE SUSCEPTIBILITY

Nepon H[1], Julien C[1], Safran T[2], Murphy A[2], Dionisopoulos T[2], Davison P[2], Vorstenbosch J[2]

[1]Division of Experimental Surgery, McGill University
[2]Division of Plastic & Reconstructive Surgery, McGill University

**INTRODUCTION**   Soft implants are essential to restore function and form in a variety of surgical procedures including breast reconstruction, hernia repair, or cataract surgery. However, fibrosis in the capsule around the implant leads to patient morbidity and substantial costs to the health care system. From clinical data we know that scarring around breast implants, or capsular contracture, occurs more commonly when the implant is placed in the subglandular plane compared to the subpectoral plane. However, the cellular and molecular mechanisms underscoring these differences in susceptibility to fibrosis remain unexplored. Here, we aim to characterize the inflammatory and fibrotic phenotypes of subpectoral, subglandular, and subcutaneous breast implant capsules to better understand how the tissue abutting the implant contributes to cellular and molecular signaling in the capsule.

**METHODS**   Capsule against each tissue type (subglandular (N=16); subpectoral (N=18); subcutaneous (N=20)) was collected from consenting patients undergoing revision breast surgery. Capsular thickness and collagen organization were assessed histologically with hematoxylin and eosin, and masson trichrome staining. Capsular cell populations per high powered-field were measured by immunohistochemsistry (fibroblasts, myofibroblasts, CD26+ pro-fibrotic fibroblasts, total macrophages, M1 macrophages, M2 macrophages, CD3+ total T-cells, and CD4+ helper T-cells). RT-PCR was used to measure extracellular matrix (Col1, Col3) and cytokine (transforming growth factor-β, interleukin-1β, interleukin-6) expression. Statistical analysis included one-way ANOVAs.

**RESULTS**   Demographics were matched and similar across all groups. All groups displayed statistically similar capsule thickness and collagen organization. No differences were observed in the number of fibroblasts and myofibroblasts. Subcutaneous capsule contained fewer pro-fibrotic CD26+fibroblasts (p<0.01). No differences were observed in number of macrophages or total CD3+T-cells. Subglandular capsule contained increased CD4+helper T-cells (p<0.05). Extracellular matrix expression (collagen 1) was elevated in subglandular capsule (p<.05). Cytokine analysis revealed increased expression of pro-fibrotic TGF-β (p<.05) and pro-inflammatory IL-1β in subglandular capsule (p<.05).

**CONCLUSIONS**   Our data suggests that increased susceptibility to capsular contracture in subglandular breast implants could be mediated by T-helper cells and associated expression of Collagen 1, TGF-β, and IL-1β. Further investigations into the molecular mechanisms underlying these differences could yield molecular therapeutic targets to reduce the incidence of capsular contracture.

# INCREASED URINARY RATIO BDNF/PROBDNF IN A FEMALE POPULATION WITH OVERACTIVE BLADDER SYNDROME

**Claudia Covarrubias[1], Philippe Cammisotto[1], Samer Shamout[1], Lysanne Campeau[2]**

[1]*Lady Davis Institute for Medical Research, Montreal, Canada. [2]Lady Davis Institute for Medical Research, Urology Department, Jewish General Hospital, Montreal, Canada*

**INTRODUCTION**   Urine storage and voiding by the bladder are controlled by the peripheral and central nervous systems. Neurotrophins are essential for the maintenance and activity of nerve endings. Among them, brain-derived neurotrophic factor (BDNF) controls neuroregeneration while its precursor proBDNF triggers inflammation and apoptosis. A dysregulation in the ratio of BDNF and proBDNF could contribute to pathologies of the urinary tract and have been proposed to be markers for overactive bladder syndrome (OAB). We herein examine the levels of proBDNF, BDNF and associated proteins and microRNAs in the urine of a female aging population.

**METHODS**   Urine and blood samples from 20 controls and 20 OAB patients (50-80 years) were obtained with validated questionnaires. ProBDNF, BDNF, $p75^{ECD}$, sortilin and cortisol were measured using specific ELISA kits (Biosensis). MicroRNAs involved in the control of proBDNF translation were measured by RT-qPCR. Activity of MMP-3 and -9 were measured using enzymatic kits. Results were adjusted with creatinine levels. Data were further adjusted for age, renal function and insulin resistance.

**RESULTS**   BDNF/creatinine levels were not statistically different between the urine of controls versus OAB patients. ProBDNF/creatinine measures were statistically lower in the OAB population. The ratio BDNF/proBDNF was therefore higher (0.051 ± 0.0078 vs 0.135 ± 0.027) in the OAB population (P<0.005), with an AUC of 0.732 after ROC analysis. MicroRNAs known to control the translation of proBDNF mRNA by binding its 3'UTR sequence, namely MiR-26b-5p, Mir-26-1a-5p, MiR-10a-5p and MiR-103a-3p were expressed at similar levels between groups. Other miRNAs, MiR-15b-5p, MiR-142-3p and MiR-103a-3p that control proBDNF expression through downstream or upstream pathways were not affected as well. On the other hand, enzymatic activity of MMP-9, one of the main enzyme converting proBDNF to BDNF was higher in the OAB group (P<0.05) while MMP-3 activity was similar. We confirmed in vitro the specificity of MMP-9 for proBDNF digestion using CripsrCas9. MicroRNA MiR-491-5p, that binds the 3'UTR sequence of MMP-9 expression was in accordance potently decreased in the OAB group (P<0.005). On the other hand, $p75^{ECD}$, an index of p75NTR cleavage, was increased by OAB. There was no statistical significance between the urinary levels of sortilin (co-receptor of $p75^{NTR}$) or cortisol (hormone modulating MMP-9) of controls when compared to OAB patients (P>0.005).

**CONCLUSIONS**   These results suggest that the ratio BDNF/proBDNF might be a better indicator of OAB than BDNF or proBDNF alone. The decrease in proBDNF levels together with increased $p75^{ECD}$ could constitute a protective response to OAB.

# SESSION B, PART II: CANCER RESEARCH

## *KEYNOTE: SINGLE-CELL TRANSCRIPTOMICS UNCOVERS NOVEL THERAPEUTIC STRATEGIES TO INTERCEPT AGGRESSIVE PROSTATE CANCER*



### DAVID P. LABBÉ
**PhD, Agr, Chm**

**Assistant Professor, Department of Surgery, Division of Urology**
**William Dawson Scholar**

**OBJECTIVES:**

> Introduce the use of single-cell transcriptomics in solid tumours

> Provide examples of murine and human data integration

> Discuss a novel mechanism of therapy resistance in prostate cancer

**Dr. Labbé** is an Assistant Professor in the Department of Surgery, Division of Urology at McGill University and a 2016 Prostate Cancer Foundation Young Investigator. He is also an Associate Member of the Rosalind and Morris Goodman Cancer Research Centre and a Junior Scientist at the Research Institute of the MUHC (Cancer Research Program). Initially trained as a Food Scientist (Université Laval), Dr. Labbé was initiated to cancer research during his M.Sc. under Dr. Richard Béliveau (Université du Québec à Montréal). Dr. Labbé completed his doctoral education in the Department of Experimental Medicine at McGill University under Dr. Michel L. Tremblay, where he studied the role of protein tyrosine phosphatase 1B in prostate cancer using genetically engineered mouse models. Dr. Labbé completed his postdoctoral training at the Dana-Farber Cancer Institute / Harvard Medical School with Dr. Myles Brown where he worked on diet-induced epigenetic reprogramming and aggressive prostate cancer.

Dr. Labbé's laboratory relies on high-throughput experiments, bioinformatics analyses, animal models and patient-derived tissues to uncover the basis to aggressive prostate cancer and molecular underpinnings to diet-dependent prostate cancer progression. His overreaching goal is to use precision nutrition to expose vulnerabilities that could be exploited through precision oncology strategies to improve outcomes for men with lethal prostate cancer.

Dr. Labbé is the recipient of a Scholarship for the Next Generation of Scientists from the Cancer Research Society, a Research Scholar-Junior 1 award from The Fonds de Recherche du Québec – Santé, an Early Career Award in Cancer from the Canadian Institutes of Health Research and is a William Dawson Scholar of McGill University.

# A 4-CHEMOKINE SIGNATURE PREDICTS T CELL–INFLAMMATION AND RESPONSE TO IMMUNE CHECKPOINT INHIBITION ACROSS TUMOR TYPES

**Joan Miguel Romero[1], Emma Titmuss[2], Yifan Wang[1,3], James Vafiadis[1], Alain Pacis[4], Gun Ho Jang[5], Amy Zhang[5], Bryn Golesworthy[1], Tatiana Lenko[1], Laura M. Williamson[2], Barbara Grünwald[6], Grainne M. O'Kane[5], Julie M. Wilson[5], Steven Gallinger[5], Janessa Laskin[2], George Zogopoulos[1,3]**

[1]Research Institute of the McGill University Health Centre, Montreal, Quebec; [2]Canada's Michael Smith Genome Sciences Centre, BC Cancer, Vancouver, British Columbia; [3]Department of Surgery, McGill University, Montreal, Quebec; [4]Canadian Centre for Computational Genomics, McGill University and Genome Quebec Innovation Centre, Montreal, Quebec; [5]PanCuRx Translational Research Initiative, Ontario Institute for Cancer Research, Toronto, Ontario; [6]Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, Ontario

**INTRODUCTION**  Immune checkpoint inhibitors (ICI) are highly effective in select cancers. Novel predictors of T cell-inflammation may identify a broader subset of tumors with ICI responsiveness. Our group has identified four chemokines (*CCL4, CCL5, CXCL9, CXLC10*) able to predict a T cell-inflamed phenotype in primary and metastatic pancreatic tumors. Here, we test whether this signature can predict T cell-inflammation across additional tumor types and response to ICI.

**METHODS**  Using matched genomic and transcriptomic data from 6,455 patients spanning 25 tumor types from The Cancer Genome Atlas, we searched for associations between the 4-chemokine signature and metrics of antitumor immunity. Further, we tested the association of this signature with markers of DNA damage repair deficiency. We also investigated the ability of this signature to predict response to immunotherapy using real-world data from a pan-cancer cohort of 82 patients in the Personalized OncoGenomics Program who had received ICI.

**RESULTS**  The majority of tumor types displayed sub-populations with high expression of the 4-chemokines (4-chemokinehi) and transcriptional hallmarks of the cancer-immunity cycle. Testicular germ cell tumors, cervical squamous cell carcinomas, and head and neck squamous cell carcinomas were the strongest expressors of the signature. Immunomodulatory genes, including *PD-L1, PD-1, TIM3, LAG3, TIGIT, CTLA-4,* and *FASLG*, were significantly overexpressed (P<0.05) in the 4-chemokinehi cohorts. Genesets of processes involved in the cancer-immunity cycle, including MHC I expression and cytolytic activity, were upregulated in the 4-chemokinehi cohorts (P<0.05). While a global relationship between tumor mutation burden (TMB) and 4-chemokine expression across tumor histological type was seen (rho=0.42, P=0.02), high TMB was associated with only a subset of 4-chemokinehi tumors. Among patients treated with ICIs, those with 4-chemokinehi tumors had a longer median time to progression (103 versus 72 days, P=0.012) and overall survival (382 versus 196 days, P=0.038). The 4-chemokine signature outperformed TMB for overall survival prediction.

**CONCLUSIONS**  Sub-populations of T cell-inflamed patients exist across tumor types and may therefore respond favourably to ICI. The 4-chemokine signature has the potential to select a wider spectrum of patients that may benefit from ICIs.

# PRECISION NUTRITION INCREASES EFFICACY OF DNA-DAMAGING THERAPIES IN PROSTATE CANCER

**Walaa Alahmadi[1,2], Anna de Polo[2], Nadia Boufaied[2], David P. Labbé[1,2,3]**

[1]Division of Experimental Medicine, Department of Medicine, McGill University;
[2]Cancer Research Program, Research Institute of the McGill University Health Centre;
[3]Division of Urology, Department of Surgery, McGill University

**INTRODUCTION**   Despite the advances in our knowledge of prostate cancer (PCa) biology and treatment, PCa is the third leading cause of death from cancer in Canada. Therapies geared toward overwhelming the tumor cell DNA repair by creating an amount of DNA damage that exceeds the repair capacity and leads to cellular catastrophe are a cornerstone of cancer treatments. Obesity and high fat diet (HFD) feeding in mice has been shown to induce DNA damage in multiple organs such as brain and colon. We hypothesize that a short-term saturated fat diet, defined as precision nutrition, can be used as a tool to enhance PCa sensitivity to DNA damaging therapies.

**METHODS**   We used a murine prostate cancer cell line overexpressing the human c-MYC (MyC-CaP) derived from genetically engineered mouse models (GEMM; Hi-MYC model representative of the human PCa) allografted in immune-competent FVB mice. Mice were fed a control diet (CTD, 10% fat) and tumor growth was monitored. Once tumors reached a palpable size, mice were randomized to continue on CTD or switched to a high fat diet (HFD, 60% fat) rich in saturated fat for a short duration (4-6 days). When the tumor reached a size between 79-113 mm3, mice were randomized to receive a single dose of 12 Gy ionizing radiation (IR). Mice were sacrificed when they reached the endpoint (1000 mm3). For the hybrid *in vivo / in vitro* experiment, we collected plasma from tumor-free mice that were fed a CTD for 3 weeks, followed by 10 days of short-term HFD along with mice maintained on a CTD. We used plasma collected from each diet group to treat MYC-CaP cells *in vitro*.

**RESULTS**   We have shown that a short-HFD feeding didn't affect the weight of tumor-bearing mice. Interestingly, a short-term HFD resulted in increased DNA damage (gH2A.X, a marker of DNA damage) in MyC-CaP allografts compared to CTD fed mice. Based on the results demonstrating increased DNA damage by HFD, we set out to evaluate the ability of HFD to sensitize PCa to radiotherapy. Importantly, mice treated with IR while on HFD responded better to therapy than mice fed a CTD by extending the tumor doubling time from an average of 7.7 days to 9.6 days. Using the hybrid *in vivo / in vitro* system, we tested whether circulating factors in the plasma are sufficient to induce DSBs in MyC-CaP cells *in vitro*. We performed immunofluorescence staining of gH2AX and comet assay on cells treated with CTD- and HFD-derived plasma and we observed a significant increase in the gH2AX signal and comet tail in HFD treated cells compared to CTD.

**CONCLUSIONS**   This study has shown that a short-term dietary intervention with HFD is sufficient to sensitizes tumors to IR. We have also shown that circulating factors in the plasma (lipids) are responsible for the improved response. Therefore, our study supports the use of precision nutrition to enhance the efficacy of radiotherapy and improve the survival of men affected by PCa.

# SENTINEL LYMPH NODE BIOPSY IN WOMEN OVER 70: EVALUATION OF RATES OF AXILLARY STAGING AND IMPACT ON ADJUVANT THERAPY IN ELDERLY WOMEN

Élise Di Lena[1,2], MDCM; Alen Antoun[1], MDCM; Natasha Barone[3], MSc; Uyen Do[2], BSc; Sarkis Meterissian[1,4], MDCM, MSc

[1]Division of General Surgery, Department of Surgery, McGill University, Montreal, Canada. [2]Division of Experimental Surgery, Department of Surgery, McGill University, Montreal, Canada. [3]Faculty of Medicine and Health Sciences, McGill University, Montreal, Canada. [4]Breast Center, McGill University Health Center, Montreal, Canada

**INTRODUCTION**  The 2016 Society of Surgical Oncology Choosing Wisely guidelines recommended against routine sentinel lymph node biopsy (SLNB) in women ≥ 70 years old with favorable histology and clinical staging, given that SLNB does not decrease locoregional recurrence or cancer mortality in this patient population. The objective of this study was therefore to evaluate the use of SLNB and its effect on management in elderly patients at an academic breast cancer center.

**METHODS**  A retrospective analysis of a prospectively maintained database of breast cancer patients was performed evaluating female patients ≥70 years old with stage I or II, clinically node-negative, hormone-receptor positive and HER2 negative disease undergoing upfront breast cancer surgery between 2017- 2019. Primary outcome was rate of SLNB. Secondary outcome was effect of SLNB on adjuvant therapy.

**RESULTS**  148 patients met inclusion criteria. Median age was 76 (IQR 73-81) in the overall cohort and 73% of patients underwent lumpectomy. On final pathology, 58.8% had invasive ductal carcinoma and median tumor size was 15mm (IQR 10-24). 120 (81.1%) patients underwent SLNB; of these, 32 (26.7%) were positive for isolated tumor cells (3 patients), N1mi (7 patients) or N1a disease (22 patients) (SLNB+). On multivariate regression analysis, patients undergoing SLNB were more likely to be younger (OR 0.88, 95% CI 0.80-0.95). Tumor grade on biopsy, clinical T-stage, and breast surgery performed had no effect on odds of undergoing SLNB. The major risk factor for SLNB+ was lymphovascular invasion (OR 8.60, 95% CI 3.25-24.8). Patients with SLNB+ were more likely to receive adjuvant radiation therapy (OR 2.75, 95% CI 1.00-8.28) adjuvant axillary radiation (OR 31.74, 95% CI 4.67-358.89), and adjuvant chemotherapy although the latter was not statistically significant (OR 2.65, 95% CI 0.25-31.47).

**CONCLUSIONS**  Despite the 2016 Choosing Wisely guidelines, over 80% of patients ≥70 years old underwent SLNB at our institution. If SLNB+, this is associated with over 2-fold higher rates of adjuvant radiotherapy and over 30-fold higher rates of adjuvant radiation to the axilla.

# IDENTIFYING THERAPEUTIC OPTIONS FOR PATIENTS WITH ADVANCED PROSTATE CANCER THROUGH GENES IN LIQUID BIOPSIES

Seta Derderian[1], Edouard Jarry[2], Arynne Santos[1], Mohan Amaravadi[1], Quentin Vesval[3], Lucie Hamel[1], Nathalie Côté[1], Raghu Rajan[4], Marie Duclos[5], Armen Aprikian[1,4,6], Simone Chevalier[1,4,6,7]

[1]Urologic Oncology Research Group, Cancer Research Program, RI-MUHC, Montreal, Canada; [2]Department of Urology, Centre Hospitalier Régional et Universitaire de Lille, France; [3]Department of Urology, Centre Hospitalier Régional et Universitaire de Rennes, France; Departments of [4]Oncology, [5]Radiology (Radiation Oncology),[6]Surgery (Urology), [7]Medicine, McGill University, Montreal, Canada

**INTRODUCTION**   Prostate cancer (PCa) is curable in most men but is lethal upon recurrence on androgen deprivation therapy, at which point it is considered castration resistant (CRPC). Current treatments for metastatic (m)CRPC are mostly limited to androgen receptor inhibitors and taxanes. Drugs targeting other pathways have shown mostly low response rates in clinical trials, although some show a significant benefit in subsets of unselected patients (e.g. *VEGFA, EGFR, AURKA*, etc.). This clinical heterogeneity underscores the cellular and functional heterogeneity of tumour cells, stressing the need for biomarkers of therapeutic response. In line with the growing interest in non-invasive liquid biopsies to monitor disease progression, we hypothesized that genes of prostate epithelial cell-subtypes (luminal, neuroendocrine, stem) and/or encoding proteins targetable by drugs may be detectable in blood as predictive biomarkers. Our objective was to identify such representative genes and test them in the blood of patients to determine whether they can stratify patients for optimal disease management.

**METHODS**   60 genes pertaining to cell subtypes and/or drug targets were chosen based on a thorough literature review. The panel was validated in PCa transcriptomic datasets. TaqMan assays were designed and optimized in serial dilutions of RNA from 5 PCa cell lines. The panel was tested in the blood of 9 healthy controls and patients prior to (n=8) and post-curative therapies (n=7) and at the advanced mCRPC stage (n=19).

**RESULTS**   Bioinformatic analyses confirmed the predominant overexpression of our gene panel in mCRPC metastases compared to primary tumours and benign prostate in diverse cohorts. Testing these genes in the blood of donors with no prostatic disease in their lifetime showed low or no expression of most genes, with no correlation with age (29-71 years old). No association was seen between the proportions of different white blood cells and gene expression in the blood of patients. A threshold for overexpression in patients was defined as 2.58 standard deviation above the mean expression from controls (99.5% confidence interval). Varying expression levels were observed along with phenotypic and functional diversity in all categories of patients. Genes patterns were significant in mCRPC cases based on choice of initial curative therapy and treatments received at enrolment in this study. For example, neuroendocrine genes are predominantly overexpressed in patients who underwent radiation therapy, whereas stem cell genes arose in cases under androgen receptor inhibitors at blood draw.

**CONCLUSIONS**   We identified circulating genes of cell subtypes and encoding drug targets that may be clinically meaningful to stratify and follow patients and predict response to therapies. They may allow patient-tailored clinical trials in view of personalized treatments to impact on this unpredictable lethal disease.

# ESTROGEN REGULATES THE IMMUNE MICROENVIRONMENT OF COLORECTAL LIVER METASTASES

Yasmine Benslimane[1,2], Sarah Lapin[1], Julien Chambon[2],
Matthew Leibovitch[2], Stéphanie Perrino[2], Pnina Brodt[1,2]

[1]McGill University, Faculty of Medicine, Division of Experimental Medicine, Montreal, Canada
[2]Research Institute of the McGill University Health Centre, Montreal, Canada

**INTRODUCTION**   Liver metastases (LM) remain a major cause of cancer-related death and many cancers preferably metastasize to the liver due to its unique anatomical location, rich blood supply and immune-tolerant microenvironment. Up to 50% of colorectal carcinoma patients develop liver metastases and this is associated with a poor prognosis. Our laboratory previously identified a sexual dimorphism in the regulation of the immune microenvironment (IME) of LM and showed that estrogen could promote the accumulation of myeloid-derived suppressor cells (MDSCs) and Tregs in the liver in response to invading cancer cells. The objective of this study was to elucidate the role of estrogen in the recruitment and polarization of monocytes/macrophages and in the accumulation and phenotype of natural killer (NK) cells in the IME of colorectal carcinoma LM (CRCLM). Moreover, we sought to determine the therapeutic potential of Selective Estrogen Receptor Degrader (SERD) therapy in tumor bearing female mice.

**METHODS**   Female C57BL6 mice underwent surgical ovariectomy (OVX), Sham-ovariectomy (SHAM), or ovariectomy followed by estrogen replacement (OVX + E2). Following 3-4 weeks post-surgery, MC38 (mouse colorectal carcinoma) cells were injected intrasplenic. Following 7-10 days post-injection, hepatic immune cells were isolated from livers and stained for flow cytometry analysis. Whole livers were frozen and processed for tissue sectioning using Cryostat and analyzed through immunohistochemistry staining.

**RESULTS**   Immunohistochemistry on human liver FFPE sections revealed increased recruitment of CD56+ NK cells towards CK19+ colorectal cancer in representative sections from women over 40 years old with CRCLM. In estrogen-competent female (SHAM) mice bearing CRCLM, we found increased gene and protein expression of the immunosuppressive TGF-b and a decrease in the pro-inflammatory TNF-a. Furthermore, we identified a significant decrease of the immunosuppressive CD68+ F4/80+ CD163+ M2 macrophages, in ovariectomized (OVX) mice as compared to SHAM. The recruitment of pro-inflammatory CD68+ F4/80+ TNF-a + M1 macrophages, and the accumulation of the highly cytotoxic NK1.1+ CD49a+ liver NK cells were increased in OVX mice, and these trends were reversed upon estrogen supplementation (OVX + E2). Moreover, treatment of female mice with Fulvestrant markedly reduced the number and size of CRCLM and the levels of M2 macrophages as compared to vehicle-treated mice, while the levels of NK cells and cytotoxic CD8 T-cells were significantly increased. Interestingly, PD-1 levels were also increased in Fulvestrant treated mice, opening the possibility to combine Fulvestrant with anti-PD-1 immunotherapy to boost anti-tumor immunity.

**CONCLUSIONS**   Our data identify estrogen as a key regulator of the liver IME of CRCLM. Anti-estrogen therapy significantly decreased CRCLM and the accumulation of immune suppressive M2 macrophages. It also increased the NK cells pool in the liver, and PD-1 expression, opening the possibility to combine anti-estrogen therapy with anti-PD-1 immunotherapy to further potentiate cytotoxic T-cell response in the IME.

# TREATMENT COMBINATION STRATEGIES TO IMPROVE RADIA-TION EFFICACY IN IMMUNOLOGICALLY COLD TUMORS *IN VIVO*

Eva Michaud[1], Gautier Marcq[1], Sabina Fehric[1], JiaMin Huang[1], José Joao Mansure[1], Ciriaco Piccirillo[2], Wassim Kassouf[1,3]

[1]Urologic Oncology Research Program, Research Institute of the McGill University Health Center, Montreal, Quebec, Canada. [2]Department of Microbiology and Immunology, McGill University, Montréal, QC, Canada. [3]Division of Urology, Department of Surgery, McGill University Health Centre, Montreal, QC, Canada

**INTRODUCTION**   Radiation therapy (RT) is a promising bladder-sparing therapy in muscle-invasive bladder cancer (MIBC). However, 30% of patients exhibit radioresistant tumors requiring salvage surgery. Combining RT with immune checkpoint inhibitor was reported to have synergic effects on anti-tumor immunity. Yet, it is also met with treatment resistance. In addition, activation of the STING pathway was shown to induce cell death, cancer cell antigens release and presentation, and promote the priming, activation and trafficking of T cells into tumors. Previous in vivo results from our team using the MB49 murine bladder cancer cell line – and immunologically 'hot' tumor model – demonstrated significant improvement of survival and immune cell infiltration upon STING agonist treatment, when combined with RT and anti-PDL1 treatment. Oppositely, treating the 'cold' tumor model UPPL with a combination of RT and anti-PDL1 treatment did not improve survival compared to RT alone. Consistently, UPPL tumors present low T cell and high neutrophil infiltration *in vivo*. Thus, the main objective of the present study is to evaluate whether combining RT, anti-PDL-1 and STING agonist treatments can improve the immunogenicity of UPPL tumors.

**METHODS**   Seven-week-old male C57BL/6 mice were subcutaneously injected with $5.10^6$ UPPL tumor cells. Once tumors reached 0.1-0.15 cm3, mice were randomized into the following treatment groups : 1) Untreated; 2) PDL-1; 3) STING; 4) PDL-1 + STING; 5) RT; 6) RT + PDL-1; 7) RT + STING; 8) RT + STING + PDL-1. Midpoint (~0.6-0.8 cm$^3$, n=5) and endpoint (2 cm3, n=8) tumors, spleens and draining lymph nodes (dLN) were harvested and dissociated for flow cytometry analysis of TME composition and cytokine production.

**RESULTS**   We report that RT and RT-combined treatments delayed tumor growth and prolonged survival *in vivo* compared to untreated. Additionally, our combination approaches shifted immune infiltration: compared to untreated, tSNE analyses revealed a specific subset of GrzB$^+$ CD8$^+$ T cells elicited in the triple combination and RT+PDL-1 groups, as well as shifts in the Treg/CD4$^+$ T cell balance in both those groups.

**CONCLUSIONS**   Our results suggest RT and RT combination treatments in cold tumor affect the fine-tuning of CD4$^+$ and CD8$^+$ T cells plasticity, and their respective functionalities, that could predict response to treatments. This preliminary study shows immunologically cold tumors can be modulated through treatment combination, which has relevance in human treatment-resistant tumors. It adds to the very small body of literature taking a deep dive into the immune modulation of a conventionally used 'cold' tumor cell line.

# CANCER EXTRACELLULAR VESICLES INDUCE LYMPH NODE METASTASIS VIA NEUTROPHIL EXTRACELLULAR TRAPS

Xin SU[1], Ariane Brassard[1], Ramin Rohanizadeh[1],
Iqraa Dhoparee-Doomah[1], Betty Giannias[1], France Bourdeau[1],
Veena Sangwan[1], Roni F. Rayes, Jonathan D. Spicer[1,2], Lorenzo E. Ferri[1,2],
Jonathan J. Cools-Lartigue[1,2]

[1]Thoracic and Upper GI Cancer Research Laboratories, Research Institute of McGill University Health Center, Montreal, QC, Canada. [2]Department of Thoracic Surgery, Montreal General Hospital, McGill University, Montreal, QC, Canada

**INTRODUCTION**   In most human cancers, regional lymph nodes (LNs) are the first sites of metastasis and lymph node metastasis has become a crucial clinical intervention point before distant metastasis, the leading cause of cancer-associated deaths. To initiate metastasis, the conditions of LNs need to be optimised for tumour cell deposition and growth. This process is believed to be mediated by the activation of immune cells including polymorphonuclear neutrophils (PMNs), and tumor derived factors, such as tumor derived extracellular vesicles (tEVs), however, the cellular mechanism is not well defined. Early observations suggest that PMNs and neutrophil extracellular traps (NETs) are associated with adverse oncologic outcomes. Moreover, tEVs can polarize PMN toward a pro-tumor (N2) phenotype and induce NET formation. Thus, one potential mechanism of increased LN metastasis is that tEVs recruit PMNs and propend NETs formation.

## METHODS

1. Cell tracker Dil labelled EVs were footpad injected into C57/BL mice to locate the uptake recipient cells, draining LNs were harvested, sectioned and immunofluorescence stained.

2. Human lymphatic endothelial cells (LECs) were culture and treated with CFSE stained A549 (lung cancer) or BEAS-2B (normal bronchial endothelium) EV, fixed and immunofluorescence stained.

3. LECs were treated with EVs and PMN migration assay was performed by Boyden Chambers.

4. Conditioned media from tEVs treated LECs were collected to perform ELISA assays.

**RESULTS**   Last year we demonstrated the deposition of NETs both in human and mouse LNs. Multiple approaches of inhibiting NETs led to decreased LN tumour burden, this year we focused more on the mechanism study and we found:

1. LEC can uptake EVs both in vivo and in vitro; In vitro, LEC uptake significantly more cancer EV than benign EV.

2. tEVs treated LECs can recruit neutrophils.

3. tEVs educated LEC increased secretion of the PMN chemoattractants CXCL8.

**CONCLUSIONS**   Together, these findings highlight tEVs both as PMN recruiters to LNs and inducer of CXCL8. By further investigating the detailed mechanism and the efficiency of NETs targeting agents, this project will lead to major advances in the management of cancer patients.

# NETS DOWNREGULATE CD8 T CELL FUNCTION IN TUMOUR-DRAINING LYMPH NODES

**Ariane Brassard, Xin Su, Iqraa Dhoparee-Doomah, Lixuan Feng, Sabrina Leo, Betty Giannias, France Bourdeau, Qian Qiu, Lorenzo Ferri, Jonathan Cools-Lartigue**

*RI-MUHC, McGill University, Montreal General Hospital, Thoracic Surgery and Upper Gastrointestinal Cancer Research Laboratories*

**INTRODUCTION**    Metastasis is responsible for 90% of all cancer-related deaths, making it the greatest challenge in cancer treatment for clinicians world-wide. Metastasis is thought to occur in a stepwise process, in which local lymph nodes are first colonized by tumour cells before proceeding to distal organs. In order to facilitate lymph node metastasis, tumours are known to recruit immune cells to local lymph nodes to induce an immunosuppressive environment within these organs. This immunosuppressive environment is critical for the establishment of lymph node metastases, as cytotoxic CD8 T cells will otherwise neutralize incoming circulating tumour cells. Neutrophils are among the first cells recruited to tumour-draining lymph nodes to mediate this immunosuppressive environment, and yet their method of action remains unclear. Here, we report that neutrophils induce CD8 T cell shut down within tumour-draining lymph nodes via the release of Neutrophil Extracellular Traps (NETs), an important effector of neutrophil function.

**METHODS**    Wild-type (WT) or PAD4-/- mice, the latter of which cannot generate NETs, were injected with H59-GFP cancer cells in their left flank. After 14 days the mice were sacrificed and their tumour-draining lymph node was extracted and either sliced and stained for various NETs markers and imaged with a confocal microscope, or mashed into a single cell suspension for CD8 T cell antibody staining and flow cytometry analysis.

**RESULTS**    Through the images taken with a confocal microscope, we saw that neutrophils are recruited to tumour-draining lymph nodes prior to the arrival of tumour cells, and that they release NETs. It was also found through flow cytometry analysis that CD8 T cells were downregulated more in WT tumour-draining lymph nodes than in PAD4 tumour-draining lymph nodes, the latter of which were confirmed to be free of NETs. Furthermore, CD8 T cells from the WT tumour-draining lymph nodes had lower expression of both Ki-67 and granzyme B, which are markers of cell proliferation and CD8 T cell cytotoxicity respectively, than in PAD4 lymph nodes.

**CONCLUSIONS**    Based on these results, neutrophil-released NETs are not only present within tumour-draining lymph nodes but also downregulate CD8 T cell function, therefore participating in the establishment of a local immunosuppressed environment to facilitates metastasis. Taken together, these findings describe a novel neutrophil-driven mediator of immunosuppression within tumour-draining lymph node. This also identifies NETs as a potential drug target to prevent lymph node metastasis, and to reduce distal metastasis as well.

# GENETIC DRIVERS OF MEDULLOBLASTOMA LEPTOMENINGEAL METASTASIS

## Castillo-Orozco Ana Isabel, Khazaei Niusha, Danieau Geoffroy, Aghababazadeh Masoumeh, Garzia Livia

*Research Institute of the McGill University Health Center (all authors)*

**INTRODUCTION**   Medulloblastoma (MB) is a highly aggressive and the most common pediatric brain tumor that arises mainly in the cerebellum. MB can metastasize to the leptomeningeal space, which is known as Leptomeningeal Disease (LMD). The presence of metastatic dissemination is a universal predictor of poor outcome among MB patients. MB presents a high intertumoral heterogeneity and at least four molecular subgroups (SHH, WNT, Group 3, and Group 4) have been identified, which can be split into further 12 subtypes. These molecular identities are clinically relevant as subgroup and subtype may determine disease outcome. For example, metastatic MB is mostly found in MB Group 3 type. Although LMD represents a main clinical challenge, it is a vastly understudied field, and its molecular mechanisms are poorly characterized. Recent research has shown that primary and metastases diverge dramatically. Thus, therapies based on targets identified in primary tumors might be ineffective in metastatic patients. Accordingly, there is an urgent need to develop strategies to study metastatic Medulloblastoma.

**EXPERIMENTAL METHODS & RESULTS**   We hypothesize than an in-depth knowledge of the molecular events driving subclones of the primary tumor to metastasize will offer therapeutic targets for effective therapies to treat or prevent LMD. To test this hypothesis, we have established metastatic Patient-Derived Xenografts (PDXs) that faithfully recapitulate LMD features. These models have been achieved by a serial selection of tumors from flank to brain. Overall, we have successfully developed five models comprising three molecular subgroups (Group 3, Group 4 and SHH). We have addressed our efforts in performing bulk RNA seq of PDXes models for MB Group 3 (MMB, Med114FH, and Med411FH) to profile the intertumoral LMD heterogeneity and to identify genetic drivers/pathways that sustain this compartment. Using ssGSEA and deconvolution approaches, we have identified PDXes models retain neoplastic subpopulations previously identified in MB single-cell sequencing studies. Similarly, we have identified slight differences in cell subpopulations proportions between primary and leptomeningeal compartments. Furthermore, we observe profound differences in gene expression between primary and LMD. Gene Set Enrichment Analyses (GSEA) shows significant overrepresented pathways in MB Group 3 models, such as fatty acid metabolism, oxidative phosphorylation, and heme metabolism. We also have identified differentially expressed genes (DEG) across MB Group 3 PDXes, where FcFragment of IgG Binding Protein (FCGBP) was found to be significantly differentially expressed in all Group 3 LMD models. This finding was concordant with DEA results and single cell atlas from GEO expression omnibus datasets for breast and lung cancer metastatic to the leptomeninges.

**CONCLUSION**   Our results support the notion that primary and LMD seem to retain subpopulation clusters present in MB Group 3 tumors with slight changes. We show that primary and LMD are transcriptionally different, with various signally pathways enriched in more than one LMD PDx model. Finally, we have identified FCGB as a significantly DEG across all LMD Group 3 Models. Further work will be required to determine the role of this gene in the development of LMD.

# CD109-IL6Rα INTERACTION DRIVES SQUAMOUS CANCER CELL (SCC) STEM CELL PLASTICITY THROUGH STAT3/NRF2 PATHWAY

Amani Hassan, Tenzin Kungyal, Shufeng Zhou, Kenneth Finnson, Meryem Blati and Anie Philip

*Division of Plastic Surgery, Department of Surgery, Faculty of Medicine, McGill University, Montreal, Quebec, Canada*

**INTRODUCTION** Squamous cell carcinoma (SCC), is one of the most prevalent types of malignancy and its incidence is increasing globally. Despite intensive research, there has been limited success in blocking recurrence and metastasis that occurs in a sizable proportion of head and neck SCC patients. The GPI-anchored membrane protein CD109 is frequently overexpressed in SCC and this overexpression is associated with malignant transformation. The molecular mechanisms by which CD109 may regulate SCC progression are still unknown. CD109 was found to strongly enhance interleukin-6 (IL-6)/Jak/STAT3 signaling in lung adenocarcinoma. The levels of Interleukin-6 (IL-6), a pleiotropic cytokine that regulates cellular proliferation, survival, and invasion, are also elevated in SCC tumors. The elevated expression of IL-6 is associated with increased recurrence and lower survival in SCC patients, and therapies targeting IL-6 and IL-6 receptor have been proposed for the treatment of SCC. In the current study, we aimed to determine whether CD109 regulates IL-6 signaling pathway and tumorigenic potential of SCC cells and to delineate the molecular mechanisms involved.

**METHODS** CD109 association with IL6Rα in CD109 KO versus control cells was studied using A431 and SCC-9 cells by co-immunoprecipitation analysis and co-localization using immunofluorescence. Stabilization of IL6Rα on the cell surface by CD109 was assessed in CD109 overexpressing versus empty vector cells by FACS and western blot. CD109 and IL6Rα expression and IL6-induced phosphorylation of STAT3 and IL6 induced activation of Nrf2/SOD1/HO1 and expression of stem cell markers (Nanog, Oct4, Bmi, Sox2) were measured by western blot and/or immunohistochemistry in CD109 KO and control SCC cells. Also, in-vitro tumorigenicity was assessed by spheroid formation assay.

**RESULTS** Our results show that CD109 associates with IL6Rα and is a pivotal regulator of IL6Rα expression and function in SSC cells. Furthermore, we show that CD109 potentiates IL6R/STAT3 signaling pathways. Specifically, CD109 interacts and stabilizes IL6Rα to promote activation of the IL-6/STAT3/Nrf2 pathway in SCC cells. The loss of membrane CD109 attenuates IL-6/STAT3/Nrf2 signaling pathway and stemness of SCC cells.

**CONCLUSIONS** Our findings show that the loss of membrane CD109 attenuates IL6Rα signaling pathways and stemness in SCC cells and reveal a fundamental role for CD109 in SCC progression. Our result showing that the loss of stemness is accompanied with a loss of the antioxidant protein Nrf2 suggests that targeting the CD109/STAT3/Nrf2 axis has the potential to overcome therapy resistance in SCC. Together, these findings highlight a possible clinical utility for CD109 as a therapeutic target in SCC.

# CXCR2 INHIBITION AS A CANDIDATE FOR IMMUNOMODULATION IN THE TREATMENT OF K-RAS-DRIVEN LUNG ADENOCARCINOMA

**Meghan De Meo[1], Roni Rayes[1,2], Simon Milette[1], Mara Vagai[1], Mariana Usatii[3], Arvind Chandrasekaran[4], Betty Giannias[1], France Bourdeau[1], Veena Sangwan[1], Nicholas Bertos[1], Chistopher Moraes[4], Sidong Huang[2], Daniela Quail[2], Logan Walsh[2], Sophie Camilleri-Broet[3], Pierre-Olivier Fiset[3], Jonathan Cools-Lartigue[1], Lorenzo Ferri[1], Jonathan Spicer[1,2]**

[1]Department of Surgery, McGill University Health Center, Montreal, QC/Canada; [2]Goodman Cancer Research Center, McGill University, Montreal, QC/Canada; [3]Department of Pathology, McGill University, Montreal, QC/Canada; 4Department of Chemical Engineering, McGill University, Montreal, QC/Canada

**INTRODUCTION**   Lung adenocarcinoma (LUAD) is the predominant histological subtype of primary lung cancer accounting for ~40% of all lung cancers. Although driver mutations in the Kirsten Rat Sarcoma (KRAS) oncogene occur in approximately 25% of LUADs, this alteration portends a poor prognosis and lacks dedicated therapeutics. Polymorphonuclear neutrophils (PMNs) are the predominant inflammatory cell to infiltrate the tumor immune microenvironment (TIME) in LUAD. We found that high PMN infiltration in the TIME is associated with the poorest survival compared to other immune infiltrates in lung cancer (PRECOG). PMN recruitment to the TIME is mediated by the C-X-C motif chemokine receptor 2 (CXCR2) and CXCR2 ligand expression, especially IL-8, is shown to be higher in KRAS-driven LUAD compared to the other frequently mutated oncogenes. We also show that overexpression of 8 out of the 9 known CXCR2 ligands in LUAD correlate with poorer survival outcomes (PRECOG). Moreover, we show that CXCR2 expression is at least 18-fold greater in PMNs than other immune cells in LUAD (PRECOG). Since KRAS is a commonly tested oncogene during the diagnostic workup of LUAD we hypothesize that it may serve as a surrogate marker for the utility of CXCR2 inhibition either alone or in combination with other active systemic therapies.

**METHODS & RESULTS**   Our data proves that PMN migration to KRAS, EGFR, ALK and ROS1-driven LUAD cell lines in novel microfluidic devices created to model the CXCR2 axis ex vivo was highest in KRAS-driven LUAD. Moreover, CXCR2 inhibition reduced PMN migration only in KRAS-driven LUAD. Using the same microfluidic experimental set up, we found that murine tumour-associated PMNs promoted the recruitment of regulatory T cells and reduced the recruitment of cytotoxic T cells. Interestingly, we also found that PMN and cytotoxic T cell infiltration in the tumour core of 114 LUAD patients had an inversely proportional relationship only in patients bearing a KRAS mutation. We wish to determine whether CXCR2 inhibition works in synergy with anti-PD-1/PD-L1 therapy by quantifying T cell-mediated cancer killing in real time. The novel well-established TIME-on-Chip 3D microfluidic technology that models the recruitment process of immune components by the tumour from circulation will be used to study these immune cell kinetics (Zhao et al. Biofabrication 2019).

**CONCLUSIONS**   These findings indicate that PMN are heavily recruited into KRAS-driven LUADs via CXCR2 and that recruitment in KRAS-driven LUAD promotes an immunosuppressive TIME. KRAS-driven LUAD is a promising candidate for effective inhibition of PMN migration and we are hopeful that the combination will work in synergy to potentiate existing anti-PD-1/PD-L1 therapies.

# CHARACTERIZING TERTIARY LYMPHOID STRUCTURES AND THEIR FUNCTIONS IN RENAL CELL CARCINOMA

Claire Norman[1,2], Francois Santinon[3], Christophe Goncalves[3], Tamiko Nishimura[1,4], Fadi Brimo[5], Sonia V Del Rincon[3], Simon Tanguay[6], Ciriaco A Piccirillo[2,7], Yasser Riazalhosseini[1,4]

[1]McGill University Genome Centre, [2]Department of Microbiology and Immunology, McGill University, [3]Lady Davis Institute, Jewish General Hospital, [4]Department of Human Genetics, McGill University, [5]Department of Pathology, McGill University, [6]Division of Urology, McGill University, [7]Research Institute of the McGill University Health Centre, McGill University

**INTRODUCTION & METHODS**   The formation of tertiary lymphoid structures (TLSs) has been observed in many solid tumor types where they have frequently been correlated with improved patient survival and response to immune checkpoint inhibitors. Similar results have been described in renal cell carcinoma (RCC), a tumor that shows a high degree of immune infiltration yet maintains a consistently immunosuppressed tumor microenvironment (TME). In RCC, TLSs are thought to enhance immune cell functionality and orchestrate local lymphocyte responses given their similarity to lymphoid follicles. However, our understanding of TLSs in RCC and the mechanisms underlying their beneficial effects is limited. Our study aims to investigate how TLSs may modulate anti-tumor immune responses and shape the TME in RCC.

H&E-stained tumor specimens from 72 RCC patients were manually analyzed, guided by CAP protocol for renal cancer, and classified as TLS+, lymphoid aggregate (LA)+, tumor infiltrating lymphocyte (TIL)-high, or TIL-. Samples were also scored on degree of lymphocyte infiltration and infiltration of select distinguishable myelocytes. Lymphocyte and myelocyte infiltration were compared between TLS+ and combined LA+ and TIL-high RCC samples using Fisher's exact test. Similarly, tumor clinical features were compared between TLS+ and TLS- samples. To investigate the cellular composition of TLS and spatial relationships between TLS-associated (TA) cell types, CODEX immunofluorescence (IF) was performed on one RCC specimen, using markers for T cells (CD3, CD4, and CD8), B cells (CD20), and follicular dendritic cells (FDCs) (CD21). IF data were analyzed using CODEX Multiplex Analysis Viewer.

**RESULTS**   We observed that a large proportion (35/72) of RCC tumors generate TLSs, most of which develop at least one follicle-like TLS as indicated by the presence of FDCs. Using CODEX, we found that TLSs within one RCC tumor demonstrate an organized architecture of a B cell and FDC core surrounded by CD4+ T cells and CD8+ T cells. Compartmentalization of cell types appears to facilitate specific immune cell interactions. TLS-associated (TA) B cells were shown to preferentially interact with TA CD4+ T cells and FDCs, suggestive of the latter cell types facilitating B cell differentiation. TA CD8+ T cells were found to preferentially interact with CD4+ T cells, possibly pointing to TLSs promoting synergistic anti-tumor effects between these cell types. TLSs were significantly associated with increased lymphocyte infiltration—particularly in tumor areas directly adjacent to TLSs—and low myelocyte infiltration. Finally, TLSs may impact cancer cell biology and differentiation since we report a significantly higher frequency of high-grade tumors in TLS- RCC patients in comparison to TLS+ patients.

**CONCLUSIONS**   Our observations are consistent with TLSs acting as an immune cell niche from which beneficial anti-tumor immune responses may be potentiated. By characterizing TA immune cell interactions, and the spatial organization of TLSs and their surrounding TME, our work supports an important role for TLSs in modulating the immune response in RCC tumors.

# SESSION B, PART III: INTERVENTIONS

## KEYNOTE: *SURGICAL ROBOTS: PROMISES, CHALLENGES, AND INNOVATION*

### AMIR HOOSHIAR AHMEDI
**PhD**

**Postdoctoral Fellow**
**Director, Surgical Robotics Center (SRC)**
**Research Institute of the McGill University Health Center (RI-MUHC)**

**OBJECTIVES:**

❯ Review the promises of robotic surgery and the challenges impeded their delivery.

❯ Discuss the fundamental flaws of the current surgical robots and the features next-generation surgical robots shall exhibit.

❯ Discuss how representative robotic innovations have overcome the fundamental flaws of the current surgical robots.

**Dr. Amir Hooshiar** joined the Department of Surgery as Director of the Surgical Robotics Centre (SRC) with a research focus on developing next-generation robot-assisted surgical systems for endoscopic, endoluminal, and percutaneous procedures. His expertise is in the design, modeling, and control of surgical robots. As a graduate student, he received an NSERC Vanier Doctoral Scholarship (2017) and won the NSERC Gilles-Brassard Doctoral Prize for Interdisciplinary Research in 2018. His contributions have been published and presented in the top journals and conferences of the field such as Soft Robotics and IEEE IROS.

Dr. Hooshiar has two active startups in Montreal and served as a Medical Device Expert at the Medical Device Bureau of Iran for five years. He has secured funding for the SRC from NSERC, FRQ, and industry and aims to position the SRC as a center of excellence for surgical robotics in North America.

This talk will be focused on the evolution of surgical robots, the promises of this technology, challenges facing the state-of-the-art, and the recent innovative solutions developed recently to overcome some of the challenges. In this context, Dr. Hooshiar will discuss some recent contributions toward the realization of next-generation haptics-enabled surgical robots such as a wearable input device, sensor-free haptic estimation, and force control of flexible surgical instruments for cardiac teleintervention.

# NGF SECRETION IS REGULATED BY NITRIC OXIDE LEVELS IN BLADDER CELLS

**Stephanie Sirmakesyan[1], Aya Hajj[1], Aalya Hamouda[1], Philippe Cammisotto[1], Lysanne Campeau[1,2]**

[1]*Lady Davis Institute, McGill University, Montreal, Quebec, Canada.*
[2]*Urology Department, Jewish General Hospital, Montreal, Quebec, Canada*

**INTRODUCTION**   A cohort of female patients with Overactive Bladder Syndrome (OAB) displayed low levels of the neurotrophin nerve growth factor NGF and stable levels of its precursor proNGF in their urine samples. Elevated levels of nitric oxide (NO) were also discovered in the same samples, and has been associated with insulin resistance, a potential causative factor of OAB. Our objective is to determine how hyperglycemia regulates NO levels and in turn, how this controls the synthesis and secretion of NGF and proNGF in bladder cells in culture.

**METHODS**   Urothelial (URO) and smooth muscle cell (SMC) primary cultures were cultivated from rat bladders after collagenase digestion. Using RT-qPCR, mRNA expression was measured for NGF, proNGF and MMP-9. ELISA kits assessed protein content levels of NGF, proNGF and cyclic GMP (cGMP). Semi-quantification of intracellular MMP-9 content was done by immunoblotting. Enzymatic kits were used to assess activity of proteases involved in NGF metabolism (i.e. MMP-9, MMP-7, plasmin). Crispr-cas9 was used for the genomic knockdown of MMP-9.

**RESULTS**   Increased secretion of NO and decreased NGF levels were observed in the media of cells incubated in a hyperglycemic medium. Incubation with the iNOS inhibitor, L-NAME (1 mM), prevented increase of NO in hyperglycemic conditions and partially reversed the decrease in NGF secretion. Treatment of cells with sodium nitroprusside (SNP, 300 μM, 24 hours), a NO generator, decreased NGF secretions and did not affect proNGF, mimicking our observations in hyperglycemic conditions. SNP treatment led to increased levels of cGMP in SMCs but decreased in UROs. Stable permeable analogs of cGMP, 8-(4-Chlorophenylthio)-cGMP (3 mM) and N2,2'-O-Dibutyryl-cGMP (1 mM), and ODQ (100 μM), a cyclic GMP synthetase inhibitor mimicked the changes observed in cGMP and NGF by SNP respectively in SMCs and UROs. NGF and MMP-9 mRNA expressions were stable in SMCs but increased in UROs when treated with SNP. In MMP-9 Crispr-cas9 transfected SMCs, NGF decrease by SNP was unaffected, implying that SNP acts independently of MMP-9. However, in UROs, transfection with MMP-9 Crispr-cas9 only partially inhibited the effect of SNP on NGF secretion, pointing out the essential role of MMP-9 in these cells. Finally, activity of MMP-7 decreased in SNP-treated SMCs, while plasmin levels remained unchanged, linking decrease in NGF by SNP in these cells.

**CONCLUSIONS**   Hyperglycemic conditions are directly linked to an increase in NO secretion by bladder cells, and this subsequently affects the secretion of NGF. Though regulation patterns differ between bladder cell types (UROs vs SMCs), the control involves cGMP, MMP-9 and MMP-7. Our results are consistent with our clinical observations. This suggests that an increased glycemia, leading to an increase in NO levels, could be part of the pathological process of OAB.

# JOINT–SPARING RECONSTRUCTION FOR EXTENSIVE PERIACETABULAR METASTASES: LITERATURE REVIEW AND A NOVEL MINIMALLY INVASIVE SURGICAL TECHNIQUE

Karla Teresa S. Araneta[1], MD; Maroun Rizkallah[1], MD, MSc;
Louis-Martin Boucher[2], MD, PhD, FRCPC; Robert E. Turcotte[1], MD, FRCSC;
Ahmed Aoude[1], MEng, MD, FRCSC

[1]Department of Orthopedic Surgery, McGill University Health Centre, Montreal, Canada
[2]Department of Diagnostic Radiology, McGill University Health Centre, Montreal, Canada

**INTRODUCTION**   Classically, patients with advanced lytic disease of the acetabulum secondary to metastatic bone disease are treated with complex arthroplasty reconstruction techniques. Advancements in percutaneous techniques have extended the indications for safer, minimally invasive procedures for patients with periacetabular metastasis without the need for complex hip replacement and the complications that follow it. The purpose of this report is to revisit the management of this group of patients and provide indications for an alternative minimally invasive joint-sparing technique that uses a combination of percutaneous cryoablation, cementoplasty and two-screw fixation.

**METHODS**   This article is an in-depth description of a novel minimally invasive surgical procedure accompanied by two case reports and a review of the literature.

**RESULTS**   Two patients with advanced metastatic disease of the peri-acetabular region are described. One year after the surgery, both patients continue to be functionally independent and pain-free with stable disease. Comparative radiographs show a stable construct with no signs of failure or progression of local disease. Our indications for a joint-sparing technique that combines percutaneous cryoablation, cementoplasty and screw osteosynthesis include the following: (1) Painful lytic metastatic disease involving the acetabulum (Harrington Type I-III) that may be sensitive to radiation therapy or systemic treatment and (2) with or without minimally displaced (<5mm) pathologic fracture or cortical dehiscence so long that the hip joint remains congruent with subchondral bone or cartilage alone.

**CONCLUSIONS**   With careful consideration of indications, even patients with extensive periacetabular destruction can be successfully treated with a hip-sparing minimally invasive reconstruction of the acetabulum using a combination of cryoablation, percutaneous cementoplasty and two-screw fixation. Excellent functional outcomes one year after surgery is possible without the need for additional procedures. In addition, this technique is considered to be revisable to more invasive hip reconstructions at later stages if they fail. Like other combined percutaneous techniques, it can also help treat patients with less morbidity associated with surgery, initiate systemic treatment and/or radiation earlier which may lead to overall better outcomes. We suggest that this technique be used as a primary modality for treatment while conventional arthroplasty techniques be used as a secondary option in select patients with advanced periacetabular metastasis.

# ARTIFICIAL INTELLIGENCE ASSISTED AUTOMATIC DIAGNOSIS OF POSITIONAL PLAGIOCEPHALY: A VALIDATION STUDY

Ayden Watt[1], James Lee[2], Mirko Gilardino[2]

[1]Department of Experimental Surgery, McGill University
[2]Division of Plastic and Reconstructive Surgery, McGill University Health Center

**INTRODUCTION**   Positional plagiocephaly is a form of infantile cranial deformity with important aesthetic implications. Pronounced occipital flattening, ipsilateral ear shift and frontal bossing are the primary clinical findings, with more severe cases leading to facial asymmetry. The incidence of positional plagiocephaly has increased steadily since the 1990's, spurring an increase in research surrounding long-term sequelae and treatment options. Although positional plagiocephaly is known to not affect a child's neurocognitive development, there is substantial evidence suggesting that earlier diagnosis leads to substantially improved treatment outcomes, reducing or eliminating facial/cranial asymmetry and social stigmatization later in life. Consequently, the authors have conducted a prospective pilot study evaluating a diagnostic artificial intelligence algorithm ported in a mobile phone, with the ultimate goal of supporting early diagnosis of positional plagiocephaly in the community setting.

**METHODS**   This study was approved by the appropriate institutional review board (McGill University Health Center IRB 2021-6964). A total of 21 infants between the ages of 0-12 months were prospectively recruited from the outpatient craniofacial surgery clinic at the Montreal Children's Hospital between November 2021 and February 2022. Patients were excluded if they presented with hydrocephalus, intracranial tumors, intracranial hemorrhage, hardware (e.g., shunts), or prior craniofacial surgery. At the time of recruitment, a single 3 second video of the infants' head taken from a top-down perspective was recorded for all subjects, along with their age, sex, and a clinical diagnosis from the physician of record. This information was transmitted to a cloud-based server hosting the AI algorithm, where the images were processed, and a diagnosis was given following manual frame selection by a member of the research team. The algorithm in question was provided by Little Angel Medical Inc. The research team was blinded to the AI-derived diagnosis until the conclusion of the encounter to prevent bias. The AI results were later compared to a gold standard clinical diagnosis, performed by a pediatric craniofacial surgeon, to evaluate the algorithms' ability to appropriately identify positional plagiocephaly.

**RESULTS**   21 patients were prospectively recruited at the craniofacial surgery clinic between November 2021 and February 2022. The patients were split between the following diagnoses: positional plagiocephaly ($n = 13$), craniosynostosis ($n = 5$), and normal head shapes ($n = 3$). The AI algorithm returned an OFF-1 result of 93.75% (a measure of deviation of more than one class), a precision of 91.67%, a recall of 84.62%, and a F-1 score of 88.00%. Sidedness (left, right, or bilateral flattening) was correctly identified in 100% of cases. One important source of error was difficulty visualizing mild asymmetries from the top-down perspective.

**CONCLUSIONS**   The AI algorithm returned promising results in the validation study. Future integration of automatic frame selection and automated head orientation correction should improve clinical results and support the case for integration of similar diagnostic technologies in the community.

# TELEMEDICINE SCHEDULING OPTIMIZATION IN SURGICAL OUTPATIENT CLINICS

**Amy Lorincz, Dr. Suzanne Morin, Dr. Gregory K Berry**

*McGill University*

**INTRODUCTION**   The COVID-19 pandemic has imposed restrictions on in-person interactions creating a need for exploring alternative methods of healthcare delivery while maintaining high-quality treatment. In an initial study with Orthopaedic (Ortho) and Ear, Nose, and Throat (ENT) surgeons, it was found that 66% of consultations could be completed virtually. This presents the opportunity to reduce unnecessary hospital visits for patients. The objectives of this study were to develop a predictive model that will classify the suitability of patients for in-person versus telemedicine (TM) consultations and to develop an optimal scheduling template for TM consultations. Associated outcomes to be measured were the patient perception of the quality of TM consultations.

**METHODS**   Data was collected from patients requiring surgical outpatient consultations in Ortho, ENT, and plastic surgery in Quebec. A machine learning model was developed where four machine learning classifiers were implemented to compare the accuracy of the classification. A discrete-event simulation model was developed and used to test the various template scenarios that were generated using lean engineering analysis to find the optimal template that minimizes wait time.

**RESULTS**   A logistic regression model was found to predict a patient's suitability for TM with 91% accuracy. It was found that 41% of all patients and 57% of follow up patients were suitable for TM consultations. Lean engineering techniques were used to estimate the optimal number of patients that should be seen in TM clinics for each surgeon where patients would wait a maximum of 10 minutes for their appointment. Patient perception of TM being the same or better quality as an in-person appointment increased by 23% after completing a TM consultation.

**CONCLUSIONS**   Statistical modelling techniques and lean engineering have high potential to eliminate non-value-added activities in the healthcare system. Using this model, patients can prevent unnecessary visits to hospitals and surgeons can increase the amount of suitable TM visits offering an alternative to in person appointments.

# ANTAGONISM OF THE P75 NEUROTROPHIN RECEPTOR INCREASES SECRETION OF NERVE GROWTH FACTOR BY DECREASING EXTRACELLULAR MATRIX METALLOPROTEINASE-9 ACTIVITY AND α2-MACROGLOBULIN LEVELS IN MOUSE UROTHELIAL CELL CULTURE

**Aalya Hamouda[1], Aya Hajj[1], Stephanie Sirmakesyan[1], Philippe Cammisotto[1], Uri Saragovi[1], Lysanne Campeau[1,2]**

[1]*Lady Davis Institute, McGill University, Montreal, Quebec, Canada.*
[2]*Urology Department, Jewish General Hospital, Montreal, Quebec, Canada*

**INTRODUCTION**    Overactive Bladder Syndrome (OAB) was reported to be characterized by low levels of the Nerve Growth Factor (NGF) in the urine of aging female patients, with stable levels of proNGF and a decrease in the NGF/proNGF ratio. This was linked to a high activity of matrix metalloproteinase-9 (MMP-9) that digests NGF. P75 neurotrophin receptor (p75$^{NTR}$) antagonism with THX-B restored normal NGF levels in bladders of type 1 diabetic mice with voiding dysfunction. Separate studies in non-bladder cells have identified that p75$^{NTR}$ antagonism reduced the expression of α2-macroglobulin (α2m), a protein that prevents MMP-9 degradation. Here, we characterize expression patterns of bladder cells and determine the in vitro effect of THX-B on MMP-9 activity and α2m levels as well as the consequences on secreted NGF.

**METHODS**    Primary culture of urothelial cells (UCs) and smooth muscle cells (SMCs) were grown from rat bladders. RT-qPCR assessed NGF and MMP-9 gene expression. Immunohistochemistry and immunoblotting assessed protein expression. NGF and proNGF secretion was measured by ELISA and MMP-9 activity by enzymatic assays.

**RESULTS**    NGF and MMP-9 mRNAs were expressed in UCs and SMCs at similar levels. At the intracellular protein level, NGF and proNGF were abundant in UCs, while SMCs produced a limited amount. Intracellular MMP-9 was 7 times higher in SMCs than in UCs. The opposite patterns were observed extracellularly; secretion of active MMP-9 was 40 times higher in UC medium and was paralleled with lower extracellular NGF and proNGF compared to SMCs. THX-B treatment decreased the synthesis and secretion of active MMP-9 and doubled the NGF concentration in UC medium. ProNGF secretion was unaffected. Reduced MMP-9 was paralleled with decreased intracellular and extracellular α2m. THX-B had little effects on SMCs both at the level of NGF and MMP-9.

**CONCLUSIONS**    UCs secrete most of the active MMP-9 and appear to be the primary target of p75NTR antagonism. The reduction MMP-9 expression and secretion by THX-B may be explained by reduced α2m in the same cells. Our results suggest that THX-B could be a therapeutic tool to improve OAB by targeting the urothelium to increase NGF.

# NOVEL MURINE MODEL FOR THE STUDY OF SPINAL CORD INJURY–INDUCED NEUROGENIC HETEROTOPIC OSSIFICATION

**Rachad Aita[1], Joseph Petruccelli[2], Rahul Gawri MD PhD[3], Chan Gao MD PhD[3,4]**

[1]Division of Experimental Surgery, Department of Surgery, McGill University, [2]Faculty of Medicine, University of Sherbrooke, [3]Division of Orthopedic Surgery, Department of Surgery, McGill University. [4]Division of Physical Medicine & Rehabilitation, Department of Medicine, McGill University

**INTRODUCTION**   Heterotopic ossification (HO) is the painful formation of ectopic bone in muscles and tendons reported in up to 50% of patients with spinal cord injury (SCI). Resulting in discomfort, decreased mobility and nerve and blood vessel entrapment, HO is increasingly being recognized as a common complication of trauma and surgery. While HO is conceptualized as an aberrant healing in response to soft tissue damage, detailed HO pathophysiology remains largely unknown. In the absence of pertinent animal models of spinal cord injury-related HO, we created a novel clinically relevant murine model for the study of neurogenic HO by combining SCI with quadriceps musculotendinous injury (MTI).

**METHODS**   After induction of general anesthesia, 8-week-old wild type C57BL/6J mice were first subjected to a spinal cord transection between T10 and T11 through a posterior approach. A dorsal skin incision above the T10-T11 level was made along the midline of the mice placed in prone position. Dorsal muscles were dissected while avoiding the thoracodorsal artery to expose the vertebrae. A laminectomy followed by a complete transection of the spinal cord was then performed using a surgical blade and spring scissors. In the same mouse, we induced a concurrent MTI by compressing the quadriceps musculotendinous tissue in the LEFT hindlimb. The RIGHT hindlimb of each mouse remained undisturbed as an internal procedural control. Mice were euthanized on postoperative Day 21, and both hindlegs were disarticulated and fixed in 4% paraformaldehyde overnight at 4°C. High-resolution micro-CT scans were then obtained at a spatial resolution of 7 μm to visualize and quantify the volume of ectopic bone in the hindlimbs. Undecalcified samples were then embedded in methyl methacrylate blocks (MMA) and consecutive 5μm sections were obtained and stained with Von Kossa for mineralized tissue, Safranin O for cartilage, Alkaline Phosphatase (ALP) for osteoblast activity, and Tartrate-Resistant Acid Phosphatase (TRAP) for osteoclast activity. Mann-Whitney U test was used for statistical analysis of HO volumes. p values < 0.05 were considered statistically significant.

**RESULTS**   Micro-CT analysis of ten mice revealed ectopic cartilage and bone deposits in the peri-articular region of all LEFT knees but none in the RIGHT knees. The quantified HO volume (in mm3) of the LEFT hindlimb was consistently higher than that of RIGHT hindlimb in each mouse (Q1 – Q3: LEFT 0.00004 – 0.00111 vs RIGHT 0.00000 – 0.00001, **p=0.0040**). Histological evaluations showed ectopic cartilage and bone deposition at the site of MTI in the peri-articular soft tissues of LEFT knees while the peri-articular soft tissues of RIGHT legs were devoid of HO. Safranin O and VonKossa staining in SCI+MTI mice suggests ectopic bone formation with a zonal alignment of proliferative chondrocytes, followed by hypertrophic chondrocytes and zones of ossification.

**CONCLUSIONS**   We have developed a novel and relevant mouse model for neurogenic HO by combining spinal cord injury with musculotendinous injury. This model is featured by ectopic cartilage and bone formation in the peri-articular region of hindlimbs and suggests neurogenic HO forms via an endochondral process. Our preliminary results show that our HO model mimics the clinical progression of HO in SCI patients and will thus provide HO researchers with a relevant tool for further investigations.

# SYMPOSIUM ON TRANSFORMING SURGICAL QUALITY AND OUTCOMES

# DISPELLING LEADERSHIP MYTHS IN SURGERY

### SUSAN MOFFATT-BRUCE
**MD, FRCSC, PhD, MBOE, FACS**

**Dr. Moffat-Bruce** joined the Royal College of Physicians and Surgeons of Canada as Chief Executive Officer in January 2020. She is also the interim Chief Executive Officer of Royal College International.

Dr. Moffatt-Bruce is an academic leader and surgeon, with sharp business acumen and a passion for value-driven care. Dr. Moffatt-Bruce completed her undergraduate degree at McGill University, and medical school and residency in General Surgery at Dalhousie University. She undertook a PhD in Transplant Immunology at the University of Cambridge, England, and completed her Cardiothoracic Surgery fellowship at Stanford University, California. She earned her Masters of Business Operational Excellence and her Executive Masters of Business Administration at the Fisher College of Business at the Ohio State University.

Prior to the Royal College, Dr. Moffatt-Bruce served as executive director at The Ohio State University (OSU) Wexner Medical Center University Hospital. As the OSU Wexner Medical Center's inaugural chief quality and patient safety officer, she lead data analysis, transparent reporting of outcomes and process improvement for a seven-hospital academic medical center. Dr. Moffatt-Bruce and her team were celebrated for their success in developing and implementing a learning healthcare system across the patient care continuum.

A funded health outcomes research scientist and surgeon, Dr. Moffatt-Bruce is a lifelong learner and has used her skills to help develop curriculum for residents and faculty around quality and outcomes research as the educational enablement of learning healthcare systems. She has been the Principal Investigator of an AHRQ P30 program entitled Institute for the Design of Environments Aligned for patient safety (IDEA4PS) that could elevate a learning healthcare system so to improve clinical alarms surveillance, digitally hot spot clinical infections and improve patient communications using EMR portals. She is now a faculty member of the Department of Surgery and Professor at the University of Ottawa, where she is committed to enabling learning cycles, resulting in value-based care.

# LESSONS LEARNED FROM LEADING THROUGH CRISIS

**MICHAEL TANZER**
**MD, FRCSC, FAAOS**

**Professor, Jo Miller Chair of Orthopaedic Research**
**Associate Surgeon-in-Chief, MUHC**
**Vice Chair Surgery (Clinical), McGill**

**Dr Michael Tanzer** is an Orthopaedic Surgeon specializing in adult hip and knee arthroplasty. He obtained his medical degree and did his residency training at McGill University. He did an Adult Reconstruction Hip fellowship at Harvard University with Dr William Harris at the Massachusetts General Hospital. He then returned to the McGill University Hospital Centre (MUHC) in Montreal, Canada. He is the Associate Surgeon-in-Chief of Surgery and Director of Perioperative Services at the MUHC and a Professor; and the Vice Chair (Clinical) of Surgery at McGill University. He holds the Jo Miller Chair of Orthopaedic Research and is the past president of the Canadian Arthroplasty Society. He has published 170 papers and book chapters; and has 11 patents. His research has been recognized with 6 Hip Society Awards, 2 American Academy of Orthopaedic Surgeons Awards of Excellence and 2 Founders Medals. He is a member of the prestigious Hip Society and International Hip Society.

# QUALITY, SAFETY AND INFORMATICS

**SHANNON FRASER**
**MSc, FRCSC, FACS, CCPE (she/her/elle)**

**Chief General Surgery**
**Medical Director Command Centre**
**Jewish General Hospital, CIUSSS CODI**

**Dr. Shannon Fraser** is the Chief of General Surgery at the Jewish General Hospital, as well as the Medical Director of the C4: Command Center at the CIUSSS CODI. Her experience lies in triad leadership and governance structure development, currently being applied for Digital Health Initiatives such as the C4: Command Center and patient flow. Her passion is optimization of patient care: championing the introduction of NSQIP at the LGH, while she was concomitantly chief of surgery (2013-17), as the first community hospital in Quebec to participate. Currently she is developing digital quality performance dashboards for patient flow, director report cards, digital tool development for peri-operative assessments, as well as multidisciplinary/multi-site patient order set development and deployment.

# ENHANCING TEAMWORK

**JASON HARLEY**
**PhD (They/them)**

**Assistant Professor, Department of Surgery**

**Director, Simulation, Affect, Innovation, Learning, and Surgery (SAILS) Lab**

**Director of Research, Steinberg Centre for Simulation and Interactive Learning**

**McGill University | Faculty of Medicine and Health Sciences**

**Scientist, Research Institute of the McGill University Health Centre (RI-MUHC)**

**Professor Harley** completed their FRQSC and SSHRC CGS-funded Ph.D. in Educational Psychology at McGill University in 2014. They held a postdoctoral fellow position in the Department of Computer Science at the University of Montreal (FRQSC postdoc award) from 2014-2015. Before returning to McGill, Prof. Harley was a tenure-track assistant professor in the Department of Educational Psychology at the University of Alberta and Director of the Computer-Human Interaction: Technology, Education, and Affect (CHI-TEA) Laboratory (2016-2019). In 2018, they won the Outstanding Early Career Researcher Award sponsored by the Technology, Instruction, Cognition, and Learning (TICL) SIG of the American Educational Research Association (AERA). As a faculty member and principle investigator, their research has been supported by multiple grants from the Social Sciences and Humanities Research Council of Canada (SSHRC), the Killam Research Foundation, and MITACS. Prof. Harley serves on the editorial boards of the journals, Learning & Instruction (IF = 5.15) Educational Technology Research and Development (IF = 3.57), as well as on program committees for Artificial Intelligence in Education and Intelligent Tutoring Systems. Their research and teaching have led to appearances in The Guardian, CBC News, The Globe & Mail, Global News, CTV News, Radio-Canada: Le Téléjournal, The Montreal Gazette, The Toronto and Edmonton Star, The Edmonton Journal, and other broadcast and print media.

Prof. Harley's research aims to enhance surgical and health professions education and support health care workers by reducing adverse events and inefficiencies, especially those associated with the incidence of undesirable and unregulated emotions, burnout, and harassment. We apply psychological and educational theories using interdisciplinary research methods and leverage a wide range of technologies, including virtual reality (VR) and artificial intelligence (AI), to support the development of health professions competencies with novel technology-enhanced educational interventions and simulations. Our interdisciplinary research draws on mixed methods (quantitative and qualitative) that include both objective (e.g., skin conductance, facial recognition software, eyetracking) and subjective (self-report instruments, semi-structured interviews) measures of emotion and cognition that help us assess a variety of surgical and medical competencies.

This program is co-sponsored by:

**DEPARTMENT OF SURGERY**

The McGill department of surgery
The Montreal General Hospital Foundation
the MUHC foundation

Sponsors of the McGill Department of Surgery:

**CAE** Healthcare

**STORZ**
KARL STORZ ENDOSCOPY

**Medtronic**
Engineering the extraordinary

**Alcon**
SEE BRILLIANTLY

www.medicine.mcgill.ca/surgery