Tom Williams
Surgical Research Day

Host Division: Plastic Surgery
Department of Surgery
University of Alberta

Friday, May 13, 2016

Edmonton Clinic Health Academy L1-490

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification program of The Royal College of Physicians and Surgeons of Canada, and approved by the University of Calgary Office of Continuing Medical Education and Professional Development.
TOM WILLIAMS SURGICAL RESEARCH DAY

The first Department of Surgery Resident Research Day occurred on a rainy November 4, 1989. Throughout the years the event has grown and undergone a name change. From 1989 to 1996 and from 2004 to 2006 the event was called the Department of Surgery Resident Research Day. In 1993 (and until 2003) the event was dedicated as the Tom Williams Surgical Research Day to honor Dr Williams and to recognize his contributions to the Department of Surgery. In 2007, after Dr Williams’ passing, the Department of Surgery Resident Research Day was officially rededicated as the Tom Williams Surgical Research Day.

The Tom Williams Surgical Research Day (TWSRD) is an accredited event which occurs annually on the second Friday of May. The Research Committee invites the Divisional Host who then secures a Distinguished Visiting Scholar and Judge. The Distinguished Visiting Scholar and Judge is the May Grand Rounds speaker and will also preside as a podium judge for the research day. Both oral and poster presentations are given at this event.

In 1989 the Department of Surgery Resident Research Day showcased 22 oral presentations. In 2010, the Tom Williams Surgical Research Day received 44 abstracts for consideration and 37 abstracts were selected for presentations - 25 oral and 12 poster presentations. In 2016, 36 abstracts (24 oral and 12 posters) were chosen from 54 submissions.
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PROGRAM AT A GLANCE

7:30 am  **Department of Surgery Grand Rounds**  
Dr Steven Morris  
“Shifting Dogma: Flaps, Innovation and Patient Care”

8:45 am  **Research Day, Oral Presentations**

10:00 am  Coffee Break

10:15 am  **Research Day, Oral Presentations**

11:30 am  Surgical Exploration and Discovery (SEAD) Program Graduation

11:35 am  Lunch

11:58 am  **Research Day, Poster Presentations** *

1:00 pm  **Research Day, Oral Presentations**

2:15 pm  Coffee Break

2:30 pm  **Research Day, Oral Presentations**

3:45 pm  Closing Remarks

6:30 pm  **Cocktail Reception – by RSVP only**  
Fairmont Hotel Macdonald Empire Ballroom

6:45 pm  **Photo Sessions for Graduates – by RSVP only**  
Fairmont Hotel Macdonald Empire Ballroom

7:30 pm  **Surgical Awards Dinner – by RSVP only**  
Fairmont Hotel Macdonald Empire Ballroom

**Department of Surgery Grand Rounds and oral presentations are located in Edmonton Clinic Health Academy (ECHA) L1-490**

Poster presentations will be held in the **Foyers outside of L1-490**

*Posters will be on display throughout the day outside ECHA L1-490*
Steven F. Morris, MD, MSc, FRCSC
Professor of Surgery, Division of Plastic Surgery, Dalhousie University

Dr. Steven Morris is a Professor of Surgery and Medical Neurosciences at Dalhousie University in Halifax, Nova Scotia. Originally from Vancouver, Dr. Morris trained in Ottawa, Toronto, Newfoundland, Melbourne and Louisville before settling in Halifax with his wife Kay, a family physician and 2 children.

He is a practicing plastic surgeon specializing in microsurgery including free microvascular tissue transfers. His research work has concentrated on the pathophysiology and anatomical basis of tissue transfers. Earlier work concentrated on the effects of ischemia and reperfusion injury and surgical delay on flap survival. Later work has continued to examine the anatomical basis of tissue transfer.

Dr. Morris has been involved in the development of perforator flaps which have advanced the field of plastic and reconstructive surgery.

Selected Papers


GRAND ROUNDS (ECHA L1-490)

Guest Speaker: Steven F. Morris, MD, MSc, FRCSC

Talk Title: Shifting Dogma: Flaps, Innovation and Patient Care

Learning Objectives:
1. Provide a coherent history of flap surgery with emphasis on the development of perforator flaps
2. Describe the climate of innovation in plastic surgery and illustrate the challenges facing physicians

ORAL PRESENTATIONS, MORNING SESSION (ECHA L1-490)

CHAIR: Dr Colin Anderson

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<tr>
<td>8:45</td>
<td>Improved Lung Function Using A Cellular Based Perfusate On Ex Vivo Lung Perfusion</td>
<td>Nader Aboelnazar</td>
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<tr>
<td>8:57</td>
<td>Outcomes of establishing the Acute Stone Clinic: A single centre review</td>
<td>Mark Assmus</td>
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<td>9:09</td>
<td>Intraoperative brief electrical stimulation for prevention of shoulder dysfunction after oncologic neck dissection: a double-blinded, randomized controlled trial</td>
<td>Brittany Barber</td>
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<tr>
<td>9:21</td>
<td>Optimal Seeding Densities for In Vitro Chondrogenesis of Two and Three Dimensional-Isolated and Expanded Bone Marrow Mesenchymal Stem Cells within a Collagen Scaffold</td>
<td>Troy Bornes</td>
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<tr>
<td>9:33</td>
<td>Benefits of Open Anterior Release of the Superior Transverse Scapular Ligament for Decompression of the Suprascapular Nerve during Brachial Plexus Surgery</td>
<td>Kate Elzinga</td>
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<tr>
<td>9:45</td>
<td>miRNA profiling: A comparison of early stage NSCLC and healthy controls</td>
<td>Jennifer Gyoba</td>
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9:57 COFFEE

CHAIR: Dr Tom Churchill

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<tr>
<td>10:15</td>
<td>Alloderm tissue matrix as a graft for nasal septal perforation reconstruction</td>
<td>Dustin Conrad</td>
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<td>10:27</td>
<td>Treating type 2 diabetes with bariatric surgery – a predictive tool</td>
<td>Jerry Dang</td>
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<tr>
<td>10:39</td>
<td>The von Hippel Lindau (VHL) Tumor Suppressor inhibits p21 to promote proliferation and inhibit apoptosis in Cancer</td>
<td>Adam Kinnaird</td>
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<tr>
<td>10:51</td>
<td>Augmentation of Clinical Grade Neonatal Porcine Islets using Novel Maturation Media</td>
<td>Tarek Hassouna</td>
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<td>11:03</td>
<td>Gastroesophageal Motility and Reflux Following Laparoscopic Sleeve Gastrectomy for the Treatment of Severe Obesity: Preliminary Results</td>
<td>Andrew Jack</td>
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<tr>
<td>11:15</td>
<td>The effect of Low Intensity Pulsed UltraSound (LIPUS) on Tissue Engineered Human Meniscal Tissue</td>
<td>Christopher DeSutter</td>
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<td>11:27</td>
<td>Surgical Exploration and Discovery (SEAD) Program Graduation LUNCH</td>
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**BASIC SCIENCE POSTER PRESENTATIONS (ECHA L1-490 FOYER)**

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<tr>
<td>11:58</td>
<td>Combining Traditional Lap Box Practice with Video Gaming: A Randomized Control Trial</td>
<td>Simon Byrns</td>
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<td>12:06</td>
<td>Investigation of EZH2 Pathways for Novel Epigenetic Treatment Strategies in Oropharyngeal Cancer</td>
<td>Sherif Idris</td>
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<tr>
<td>12:14</td>
<td>Characterization of Human Immune Cell-Mediated Rejection of Neonatal Porcine Islet Xenograft</td>
<td>Wenlong Huang</td>
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<td>12:22</td>
<td>Kinesthetic guidance expedites proficiency in a navigational laparoscopic task</td>
<td>David Pinzon</td>
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<tr>
<td>12:30</td>
<td>Use of Droplet Digital PCR for Ultrasensitive Gene Expression Profiling and Mutational Analysis of Salivary Gland Lesion FNA Biopsies</td>
<td>Graeme Mulholland</td>
<td>30</td>
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<tr>
<td>12:38</td>
<td>Isolated hypoxia induced inflammation and fibrotic pathways in Human Bladder Smooth Muscle Cells</td>
<td>Bridget Wiafe</td>
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**CLINICAL SCIENCE POSTER PRESENTATIONS (ECHA L1-150)**

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<tr>
<td>11:58</td>
<td>Association between mortality and renal replacement therapy after cardiac surgery among octogenarians: A retrospective population-based cohort study</td>
<td>Wei Wang</td>
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<tr>
<td>12:06</td>
<td>Patterns of neck metastases in human papillomavirus positive and negative oropharyngeal squamous cell carcinomas</td>
<td>Jessica Clark</td>
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<tr>
<td>12:14</td>
<td>Evaluation of surgical skills in plastic surgery: validity and reliability of assessment using the O-SCORE</td>
<td>Curtis Budden</td>
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<td>12:22</td>
<td>A comparison between selective and non-selective PICU admission post-supraglottoplasty</td>
<td>Timothy Cooper</td>
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<tr>
<td>12:30</td>
<td>Outcomes of split-thickness skin graft reconstruction for major genital skin loss: the adverse impact of systemic disease processes</td>
<td>Ryan McLarty</td>
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<td>12:38</td>
<td>Modification of the Submandibular Gland Transfer Procedure</td>
<td>Scott Murray</td>
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**ORAL PRESENTATIONS, AFTERNOON SESSION (ECHA L1-490)**

**CHAIR: Dr Jaret Olson**

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<tr>
<td>1:00</td>
<td>Ulnar Nerve Versus Hematoma Block for Closed Reduction of Boxer’s Fractures</td>
<td>Terence Kwan-Wong</td>
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<td>1:12</td>
<td>The prebiotic fructooligosaccharide worsens systemic inflammation in a murine model of post-operative Crohn's disease</td>
<td>Michael Laffin</td>
<td>41</td>
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<td>1:24</td>
<td>A minimum conditioning protocol towards transplantation tolerance in nod mice by mixed chimerism.</td>
<td>Jiaxin Lin</td>
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<td>1:36</td>
<td>Epigenetic Targeting of Human Papillomavirus Positive and Negative Oropharyngeal Squamous Cell Carcinomas</td>
<td>Cameron Lindsay</td>
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<td>1:48</td>
<td>Combination Trophic Peptide Therapy for Neonatal Short Bowel Syndrome</td>
<td>David Lim</td>
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<td>2:00</td>
<td>Electrical stimulation enhances muscle reinnervation and functional recovery following cubital tunnel surgery – a randomized controlled trial</td>
<td>Hollie Power</td>
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**CHAIR: Dr Douglas Hedden**

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<tr>
<td>2:30</td>
<td>Patient Centered Outcomes in Head and Neck Oncology Patients</td>
<td>Adrian Mendez</td>
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<td>2:42</td>
<td>Cancer control outcomes of robot-assisted radical prostatectomy for high risk clinically localized prostate cancer: prospective analysis of 124 consecutive men from the University of Alberta</td>
<td>Jan Rudzinski</td>
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<td>2:54</td>
<td>Ex vivo perfusion in a loaded state improves the preservation of donor heart function</td>
<td>Christopher White</td>
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<td>3:06</td>
<td>The effect of electrical stimulation on cold sensitivity after digital nerve injury: a randomized controlled trial.</td>
<td>Joshua Wong</td>
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<td>3:18</td>
<td>Urine I-FABP Predicts Acute Mesenteric Ischemia in Patients</td>
<td>Pang Young</td>
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<td>Formal Mentorship in a Surgical Residency Training Program: a Prospective Interventional Study</td>
<td>Han Zhang</td>
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**SURGICAL AWARDS DINNER**

*By RSVP only*

Fairmont Hotel Macdonald Empire Ballroom

6:30 pm – 7:30 pm    Cocktail Reception
7:00 pm               Photo Session for Graduating Residents and Graduate Students
7:30 pm               Surgical Awards Dinner*

*Research Day award winners will be announced at the Surgical Awards Dinner*
Panel of Judges

Oral Presentations

Dr Steven Morris  Professor of Surgery
Division of Plastic Surgery
Dalhousie University

Dr Fred Berry  Associate Professor
Division of Surgical Research
University of Alberta

Dr Tejas Sankar  Assistant Professor
Division of Neurosurgery
University of Alberta

Poster Presentations

Basic Science Posters
Dr Nadr Jomha  Professor
Division of Orthopaedic Surgery
University of Alberta

Dr Christine Webber  Associate Professor
Division of Anatomy
University of Alberta

Clinical Science Posters
Dr Adil Ladak  Assistant Professor
Division of Plastic Surgery
University of Alberta

Dr Scott Johnson  Assistant Clinical Professor
Division of Thoracic Surgery
University of Alberta

Presentation Awards

Oral Presentations

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Poster Presentations

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# SCORING CRITERIA

## Oral Presentations

*Score each field 0, 1 or 2*

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<th>Abstract</th>
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<tr>
<td><strong>Writ</strong></td>
<td>accuracy, brevity and clarity of writing: background, objectives, methods, results, conclusions</td>
<td><strong>Q/H</strong></td>
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<td><strong>Clarity</strong></td>
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## Poster Presentations

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ABSTRACTS

ORAL PRESENTATIONS, MORNING SESSION
**Improved Lung Function Using a Cellular Based Perfusate on Ex Vivo Lung Perfusion**

**Background:** The number of donor lungs for transplantation continues to be in shortage, due to the fact that <25% of lungs being donated are accepted for transplantation. Ex-vivo lung perfusion (EVLP) is used to “resuscitate” donor lungs improving their suitability for transplantation. Nonetheless, EVLP is clinically limited to 4-6 hours. Furthermore, there is a discrepancy in literature towards the “optimal” perfusate composition that should be utilized, which will extend the perfusion window safely and allow for further resuscitative targeted therapies (including cell and gene therapies).

**Objectives:** Investigating which perfusate composition will further extend perfusion safely to 12 hours, without diminishing lung function. Moreover, any differences with perfusate specific composition in leukocyte and/or edema formation throughout the perfusion.

**Methods:** Using a custom-made, fully automated and portable EVLP platform, 18 porcine lungs (37-47kg) were individually perfused for 12 hours. Three treatment/perfusate groups: 1. STEEN solution™ (n=6), 2. packed Red Blood Cells (pRBCs) + STEEN solution™ (n=6) and 3. Whole Blood + STEEN solution™ (n=6). Every two hours, physiological parameters were recorded, a perfusate sample taken (for ELISA analysis of TNFa, IL-6, IL-8, and IL-10), and a hypoxic pulmonary vasoconstriction (HPV) challenge conducted: for assessment of vascular function and integrity.

**Results:** Lung oxygenation (P/F ratios) remained acceptable (>400 mmHg), along with stable physiological parameters for 12 hours on our EVLP platform. At 7 hours the lungs demonstrate maximal HPV across all three perfusates, with pRBCs+STEEN showing the greatest increase in PVR of 597±127 dyn*s/cm5. However, beyond the 7th hour of perfusion, HPV was blunted. Interestingly, there is an ongoing accumulation of pro-inflammatory cytokines, in parallel with the decrease in HPV in all three groups. Finally, the acellular perfusate showed an 80±18% in weight gain, whole blood (22.4±7.7%), and pRBCs (25.6±7%), p<0.01, after 12 hours.

**Conclusions:** Established a reproducible EVLP technique up to 12 hours, with stable physiological parameters - extending the limited perfusion window. HPV challenge is a more sensitive index of lung health than the current standard (P/F ratio). Lastly, cellular perfusates demonstrate superior vascular function and integrity (50% less edema) over acellular perfusates. Targeted anti-inflammatory strategies may allow significant extension of the EVLP with direct clinical implications.
OUTCOMES OF ESTABLISHING THE ACUTE STONE CLINIC: A SINGLE CENTRE REVIEW

Importance: Patients with symptomatic urolithiasis often present to emergency departments (ED) or family physicians preceding referral to urologists. Given significant pain, time of lost work, and potential renal function decline, prompt transition to definitive management is crucial. In 2014, the University of Alberta, Division of Urology established an Acute Stone Clinic (ASC), with the goal of improving access to specialist care for adults with symptomatic upper tract stones.

Objective: Our hypothesis is that average time to urologic consultation and definitive management is shorter following ASC implementation.

Design & Setting: We retrospectively reviewed 337 adult patients referred to urology for stone management at our institution.

Participants: Three distinct cohorts were studied. Group 1 includes patients seen during 2 consecutive months (Feb-March 2009) prior to inception of a general urology Emergency Clinic (pre-EC). Group 2 were seen Feb-March 2012 after creating the Emergency Clinic (EC), and group 3 was seen after establishing the ASC (Feb-March 2015).

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Not applicable

Main Outcome Measure(s): We examined time to consultation, management and outcomes.

Results: 337 patients (75-pre-EC, 91-EC, 171-ASC) with mean age of 50 years (range: 18-93) were reviewed. Referrals came from the ED in 67% (227/337), primary care physicians in 26% (88/337), from urologists in 6% (20/337) and other in 1% (2/337) of cases. The median time to urology consultation for pre-EC, EC and ASC cohorts was 20, 7 and 6 days respectively (p<0.05 between pre-EC and EC or ASC). On average, the number of patients seen per week in the pre-EC, EC and ASC groups was 8, 10 and 19 respectively. The median time to resolution of the referred calculi from date of referral for the pre-EC, EC and ASC cohorts was 42, 32 and 18 days respectively (p<0.05 between all cohorts).

Conclusions and Relevance: These outcomes reveal our improved institutional triaging system, with more patients seen in conjunction with shorter time to consultation and treatment.
**Intraoperative Brief Electrical Stimulation for Prevention of Shoulder Dysfunction After Oncologic Neck Dissection: A Double-Blinded, Randomized Controlled Trial**

**Importance:** Shoulder pain and dysfunction are common after neck dissection for head and neck cancer (HNC) due to traction injuries of the spinal accessory nerve (SAN). Intraoperative brief electrical stimulation (iBES) is a novel technique that has been shown to enhance and accelerate neuronal regeneration after peripheral nerve injury in both humans and animals.

**Objective:** To assess the efficacy of iBES in preventing shoulder dysfunction after oncologic neck dissection in HNC patients. Follow-up was completed over 12 months.

**Design:** Double-blinded, randomized controlled trial.

**Setting:** Tertiary HNC referral center.

**Participants:** Adult patients with a new diagnosis of HNC undergoing neck dissection including Level IIb/V were randomized to “iBES” or “No stimulation (NS)” in a 1:1 allocation scheme. Participants underwent iBES after neck dissection for 60 min continuously (20 Hz, 3-5 V, 100-msec) in the neck with the most extensive nodal burden. Pre- and postoperatively, blinded participants underwent assessment with the Neck Dissection Impairment Index (NDII), Constant-Murley Shoulder score (CMS), electromyographic (EMG), and nerve conduction studies (NCS) by a blinded neurophysiologist and physiotherapist. The change from the preoperative score each patient was calculated for both tools (ΔNDII, ΔCMS) and compared between iBES and NS groups.

**Intervention(s) for Clinical Trials:** iBES.

**Main Outcome Measure(s):** Primary (ΔNDII) and secondary outcomes (ΔCMS, NCS, and EMG) were assessed at 12 months. The minimally important clinical difference (MICD) was applied to ΔCMS (10.4 points) and ΔNDII (18.1 points) scores. Mann-Whitney and Chi-squared analyses were applied to continuous and dichotomous values.

**Results:** Fifty-four patients were recruited for the trial. 82.6% of patients were advanced-stage (>T2, >N0) at the time of surgery. 46.3% of patients underwent an additional Level V neck dissection. At 12 months, patients in the BES cohort undergoing both Level IIb and IIb+V neck dissections demonstrated significantly smaller absolute ΔCMS values (p=0.041) than controls, and this value remained significant when dichotomized using the MICD (p=0.029).

**Conclusions and Relevance:** iBES applied to the SAN after Level IIb and V neck dissection may help prevent clinically significant shoulder dysfunction at 12 months. iBES may provide an effective adjunct to post-neck dissection functional shoulder rehabilitation.
OPTIMAL SEEDING DENSITIES FOR IN VITRO CHONDROGENESIS OF TWO AND THREE DIMENSIONAL-ISOLATED AND EXPANDED BONE MARROW MESENCHYMAL STEM CELLS WITHIN A COLLAGEN SCAFFOLD

Background:
Bone marrow mesenchymal stem cells (BMSCs) are a promising option for treating articular cartilage defects given their high proliferative capacity and ability to differentiate into cartilage cells without the requirement of a major surgical procedure for harvesting the tissue. Quality of cartilaginous neo-tissue derived from BMSC transplantation has been correlated with clinical outcome. Therefore, culture conditions capable of modulating neo-tissue phenotype are under investigation.

Objectives:
The objective was to assess the impact of BMSC seeding density within a collagen I scaffold on in vitro chondrogenesis following BMSC isolation and expansion in two-dimensional (2D) and three-dimensional (3D) environments. It was hypothesized that both expansion protocols would produce BMSCs capable of chondrogenesis with an optimal seeding density of $10 \times 10^6$ cells/cm$^3$.

Methods:
Ovine BMSCs were isolated and expanded in a conventional 2D environment within flasks containing expansion medium, and seeded within collagen I scaffolds at densities of 50, 10, 5, 1, and $0.5 \times 10^6$ BMSCs/cm$^3$. For 3D isolation and expansion, aspirates containing known quantities of mononucleated cells (BMNCs) were seeded on scaffolds at 50, 10, 5, 1, and $0.5 \times 10^6$ BMNCs/cm$^3$ and cultured in expansion medium for an equivalent duration to 2D expansion. Constructs were differentiated in chondrogenic medium for 21 days and assessed with RT-qPCR, proteoglycan staining with safranin O, histological scoring (Bern Score), collagen immunofluorescence, and glycosaminoglycan quantification.

Results:
Two dimensional-expanded BMSCs seeded at all densities were capable of proteoglycan production. Collagen II deposition was apparent with seeding at $0.5-10 \times 10^6$ BMSCs/cm$^3$. Chondrogenesis following 2D expansion was most pronounced in scaffolds seeded at $5-10 \times 10^6$ BMSCs/cm$^3$ based on aggrecan and collagen II mRNA, safranin O staining, Bern Score, and glycosaminoglycan quantity. For 3D-expanded BMSCs, proteoglycan deposition was present in scaffolds seeded at $0.5-50 \times 10^6$ BMNCs/cm$^3$, while collagen II deposition occurred with seeding at $10-50 \times 10^6$ BMNCs/cm$^3$. The highest levels of aggrecan and collagen II mRNA, Bern Score and glycosaminoglycan quantity occurred at $50 \times 10^6$ BMNCs/cm$^3$.

Conclusions: Within a collagen I scaffold, 2D- and 3D-expanded BMSCs are capable of hyaline-like chondrogenesis with optimal seeding densities of $5-10 \times 10^6$ BMSCs/cm$^3$ and $50 \times 10^6$ BMNCs/cm$^3$, respectively. These densities could be considered in transplantation protocols related to articular cartilage regeneration.
**Benefits of Open Anterior Release of the Superior Transverse Scapular Ligament for Decompression of the Suprascapular Nerve during Brachial Plexus Surgery**

**Importance:** The suprascapular nerve (SSN) originates from the upper trunk of the brachial plexus. It is formed by the roots of C5 and C6 at Erb’s point. It passes through the suprascapular notch under the superior transverse scapular ligament (STSL) to provide motor innervation to the supraspinatus and infraspinatus muscles. Entrapment of the SSN can result in loss of abduction and external rotation of the humerus, neurogenic pain, and significant impairment of shoulder function.

Most commonly, SSN decompression is performed via an open posterior approach or arthroscopically. We describe the benefits of release of the STSL at the suprascapular notch through an open anterior supraclavicular approach during brachial plexus reconstruction.

**Objective:** Reconstruction of the SSN often involves nerve grafting or nerve transfers. To allow optimal reinnervation of the SSN, any potential compression points should be released. For that reason, the authors divide the STSL in all patients undergoing upper trunk reconstruction.

**Design:** Description of a novel surgical technique

**Setting:** University of Alberta and Royal Alexandra Hospitals

**Participants:** Pediatric and adult brachial plexus reconstruction patients

**Intervention(s) for Clinical Trials or Exposure(s) for observational studies:** Division of the STSL for decompression of the SSN

**Main Outcome Measure(s):**
1. Recovery of supraspinatus and infraspinatus muscle function, as well as overall shoulder and upper limb function
2. Improvement of neurogenic pain
3. Improvement of patient quality of life

**Results:** The anterior open release eliminates the need for an additional posterior incision or an additional arthroscopic procedure. It is well visualized and has minimal morbidity. It facilitates a tension free nerve transfer and prevents a potential double crush syndrome. Following SSN reconstruction, supraspinatus and infraspinatus muscle function and patient quality of life have shown significant improvements.

**Conclusions and Relevance:** SSN decompression via the open anterior release of the STSL at the suprascapular notch is an important element of upper trunk reconstruction at the time of initial brachial plexus surgery.
Background: Lung cancer has the highest mortality rates of all the cancers in Canada with a 5 year survival rate of less than 15%. Asymptomatic in its early stages, methods to screen high risk individuals are in dire need to allow earlier diagnosis and curative intent treatment. MicroRNAs (miRNAs) are small, non-coding strands of RNA that are shown to lead to carcinogenesis when dysregulated. They are promising candidates for biomarkers as they are stable, detectable in small quantities and are expressed in a tissue specific manner. Through the use of a previous miRNA panel developed by our group that demonstrated good sensitivity and specificity, the aim was to validate this panel and establish miRNA profiles for Non-Small Cell Lung Cancers (NSCLC) using miRNA 21, 210 and 223 in blood serum.

Objectives: The main objective of the project is to validate and establish the use of miRNAs in the evaluation of subjects with early stage NSCLC using blood serum.

Methods: A prospective cohort study of 32 patients with stage I/II NSCLC, matched with 16 healthy controls with similar smoking history, age, and gender, was performed. Blood serum is obtained from patients at the Royal Alexandra Hospital pre-operatively and miRNA is isolated using the Qiagen miRNeasy serum/plasma kit. miR-21, 210 and 223 were quantified via RT-PCR using *C. elegans* miR-39 as an endogenous control. Data is analyzed using binary logistic regression (SPSS20).

Results: The statistical analysis shows that miR-21, 210 and 223 are all significantly different in lung cancer patients compared to healthy controls (odds ratio = 1.07, 6.22, -0.423 respectively with p-values 0.029, 0.034, 0.038, respectively). The cluster analysis shows that the group of three miRNA provided a sensitivity of 84.4% (95% CI: 67.2; 94.7) and a specificity of 87.5% (95% CI: 61.7; 98.5).

Conclusions: Through the use of miRNA profiling, screening the high risk population for lung cancer appears to be possible which could allow early detection and curative intent treatment. Further investigation and validation with larger external tissue bank samples is currently being performed.
Importance: Patients with nasal septal perforations can have a decreased quality of life from symptoms including congestion, impaired airflow, crusting, discharge, sleep disturbances and discomfort. At present conventional repair techniques are imperfect with nasal button prosthesis as a primary modality having only an estimated 60% tolerance rate and low patient satisfaction.

Objective: To determine if the use of Alloderm tissue graft results in improvement in patient symptoms following nasal septal perforation reconstruction.

Design: Prospective interventional cohort study with nasal septal perforation reconstruction using alloderm tissue graft. Patient symptoms were measured using the SNOT-22 scale and a total follow-up of 3 months duration.

Setting: Tertiary referral center for head and neck surgery.

Participants: Patients aged 16-60 years with symptomatic nasal septal perforations measuring 10-20 mm in diameter. Exclusion criteria included: granulomatous disease, cocaine use in previous year, and patient ASA IV or greater.

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Patients underwent baseline testing using the SNOT-22 scale, nasal endoscopy and acoustic rhinometry. The senior author conducted all septal perforation reconstruction surgeries using an open procedure for exposure and insertion the Alloderm graft in conjunction with raised mucopericondrial flaps. The patients underwent repeat measurements at 2, 4 and 12 weeks post operatively.

Main Outcome Measure(s): Patient symptom improvement postoperatively using SNOT-22 scale after nasal septal perforation repair using Alloderm tissue matrix. Secondary outcomes include repair confirmation with nasal endoscopy and acoustic rhinometry to assess nasal cross sectional area.

Results: Overall, all nasal septal perforation reconstruction surgeries have been successful and closure confirmed with nasal endoscopy. Patients report significant improvement of symptoms reflected in the SNOT-22 scores by 4 weeks (P<0.05). Acoustic rhinometry scores demonstrated significant changes to the cross sectional area of the nasal cavity (P<0.5). No complications or adverse reactions were reported by the patients.

Conclusions and Relevance: The use of allderm tissue matrix shows to be a viable material for nasal septal perforation repair with excellent patient toleraance and significant symptom improvement postoperativly.
TREATING TYPE 2 DIABETES WITH BARIATRIC SURGERY – A PREDICTIVE TOOL

Importance: Bariatric surgery induces remission of type 2 diabetes (T2DM) in the majority of patients. In order to accurately inform bariatric teams and patients, a predictive tool is needed to estimate likelihood of long-term remission.

Objective: To determine preoperative predictive factors of diabetes remission and to develop a tool that predicts diabetes remission after bariatric surgery.

Design, Setting, Participants: A retrospective review was performed for all T2DM patients that underwent bariatric surgery from January 2008 to July 2014 at a single center. A total of 241 diabetic patients had bariatric surgery during this period and data were collected up to two years postoperatively. Univariate and multivariate analyses were performed to identify factors independently associated with diabetic remission. Predictive tools were then created with LASSO (Least Absolute Shrinkage and Selection Operator) and decision-tree modeling.

Interventions: Bariatric procedures were laparoscopic adjustable gastric band (LAGB), laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (LRYGB).

Main Outcome Measure(s): Preoperative and postoperative clinical and biochemical data were collected. Diabetic remission was defined as: absence of hypoglycemic medications, fasting blood glucose < 7 mmol/L and HbA1c < 6.5%.

Results: 235 patients were included in the analysis. Diabetes remission occurred in 45.1% (n = 106) of patients at one year. Multivariate logistic analysis showed that LRYGB had the highest odds of remission (OR 28.7, 95% CI 6.6-125.9) while LSG had second highest (OR 4.6, 95% CI 1.1-19.3). Remission rates were 57.7%, 38.1% and 10.7% for LRYGB, LSG and LAGB, respectively. Additionally, shorter T2DM duration (OR 0.91, 95% CI 0.84-0.98), less number of oral hypoglycemic medications (OR 0.53, 95% CI 0.32-0.87) and the absence of long-acting insulin (OR 0.0022, 95% CI 0.000014-0.34) predicted remission in multivariate logistic analysis. Decision-tree and LASSO models were created, with a predictive accuracy of 76.5% and 74.2%, respectively.

Conclusions and Relevance: Type of bariatric procedure (LRYGB and LSG), shorter duration of T2DM, less preoperative oral hypoglycemic medications, and the absence of long-acting insulin were independent predictors of remission. Our decision-tree tool can be helpful to clinicians in predicting which patients will achieve diabetes remission following bariatric surgery and, potentially, in resource allocation.
THE VON HIPPEL LINDAU (VHL) TUMOR SUPPRESSOR INHIBITS p21 TO PROMOTE PROLIFERATION AND INHIBIT APOPTOSIS IN CANCER

Background: VHL is characterized as a tumour suppressor, being suppressed in up to 90% of clear cell Renal Cell Carcinomas (ccRCC). Canonically, VHL binds to and mediates degradation of hypoxia inducible factors (HIF). However, VHL has been discovered to bind other proteins, like p53, thereby altering the cell in more ways than just HIF degradation. Furthermore, there are conflicting reports on the impact of VHL on cancer proliferation and apoptosis, both of which can be regulated by p53 target, p21.

Objectives: We hypothesize that VHL binds to and degrades p21 leading to increased proliferation and reduced apoptosis.

Methods: VHL-deficient (786-O) ccRCC cells were acutely (adenoviral) or chronically (lentiviral) transduced with VHL protein. Co-immunoprecipitations, immunoblots, confocal immunofluorescence and siRNA transfections were performed using standard techniques.

Results: Acute and chronic VHL expression significantly decrease p21 protein levels. Loss of p21 was independent of VHL-mediated HIF degradation as neither HIF knockdown, nor hypoxic induction of HIF, nor overexpression of a HIF mutant that cannot be degraded by VHL altered p21 levels. VHL expression increased cell number as well as PCNA and reduced cleaved caspase 3. Induction of both p21 and apoptosis by Doxorubicin was significantly blunted in cancer cells expressing VHL. Treatment of VHL-expressing cells with the proteasome inhibitor MG-132 restored p21 to the same level as VHL-deficient cells and VHL co-immunoprecipitated with p21 in MG-132 treated VHL-expressing cells. However, expression of mutant VHL that lacks the protein binding domain did not result in a reduction in p21 level.

Conclusions: These results suggest an inhibitory physical interaction between VHL and p21, in which VHL mediates p21 degradation. Furthermore, the attenuation of doxorubicin treatment in VHL-expressing cancer cells suggests that this chemotherapy may be more effective against VHL-deficient tumours or in combination with a VHL inhibitor. This work suggests that through a previously undescribed mechanism, a known tumour suppressor may paradoxically be capable of potentiating cancer growth and apoptosis resistance.
Background: Current clinical islet cell transplantation relies solely on human cadavers as a source of graft tissue. Much research has been focused on neonatal porcine islets as an alternative due to their ability to be mass-produced, showing strikingly similar physiology and biological activity to human insulin, and extensive research in various type I diabetic animal models. Our lab has demonstrated the feasibility of transplanting neonatal porcine islets in diabetic mice with successful reversal of diabetes. However, islet composition and time-to-normalization have remained suboptimal due to a low number of β-cells within each immature islet transplanted.

Objective: We formulated a maturation protocol for islets in long-term culture in hopes of maintaining a purely β-cell phenotype that will exclusively produce insulin and reverse diabetes sooner than islets grown in standard media.

Methods: Pancreata from 1 to 3-day old neonatal pigs were procured and cultured in standard HAMS-F10 media for 4 days. Subsequently, each pancreas was split and further cultured in DMEM-F12 maturation media containing a variety of growth added in a stepwise fashion, or cultured in control HAMS-F10 media. After 20 days, a portion of islets was transplanted into immunodeficient diabetic mice under the kidney capsule. Remaining islets underwent in vitro experimentation to assess insulin secretory capacity, β-cell composition, gene expression, total cellular insulin content per pancreas, and immunohistology.

Results: Higher levels of insulin expression, insulin positive cells, and β-cells were observed in matured islets compared to control islets. Increased insulin, β-cell progenitors, and PCNA positive cells were observed in mature islets compared to control islets. Less TUNEL staining and amylose were observed among mature islets compared to control. Mice transplanted with matured islets had significantly lower blood glucose values at weeks 18 and 20 compared to control islets.

Conclusions and Relevance: It is clear that long-term culture of islets in a maturation media have proven to be successful in vitro. The increase insulin production did translate into faster achievement of normalization after transplantation. However, more transplantation experiments are needed in other animal models to suggest that a purely β-cell phenotype is beneficial for a type I diabetic recipient.
Motor Cortex Electrical Stimulation to Promote Spinal Cord Injury Recovery in an Animal Model

Background:
Many treatment regimens for spinal cord injury (SCI) have been trialed with limited success. Electrical stimulation (ES) to promote corticospinal tract repair has been more recently examined, though remains under investigated.

Objective
We examine the role of motor cortex ES on axonal collateralization (outgrowth rostral to SCI), dieback (death rostral to SCI), and functional recovery in a SCI rat model.

Methods
A dorsal lateral quadrant transection at C4 in 48 rats was performed after Montoya grasping stairwell training. Animal groups included: 1) ES333 (n=14; 333Hz, biphasic pulse, 0.2ms duration every 500ms); 2) ES20 (n=14; 20Hz, biphasic pulse, 0.2ms duration every 1ms); 3) SCI only (n=10); 4) sham (n=10; electrode insertion without ES). ES of the injured forelimb’s motor cortex for 30 minutes at the time of SCI surgery was performed. Post-injury grasping scores were recorded weekly for 4 weeks. Axonal collateralization and dieback at multiple points were quantified using microscopy. Behavioral and histological outcomes were found to be no different between SCI control and sham rats, and as such the two groups were combined. Significance level for between-group comparisons was set at p<0.05.

Results
Post-SCI grasping success and farthest well reached scores were significantly lower than baseline values (p<0.01) for all groups. ES20 animals had significantly lower grasping scores and lower farthest well reached scores post-SCI than controls (p=0.03 for both).

Significantly more axonal collateralization was found in the ES333 animals compared to control animals (p<0.01, M-W). No difference was found with respect to collateralization between the ES groups (p=0.10, M-W), nor between the ES20 and control groups (p-value 0.16, M-W).

Beginning at 100μm rostral to the injury, ES20 rats had significantly more axonal dieback than the ES333 cohort (p=0.03, tukey). At both 50μm rostral to injury and at the injury site, ES20 animals had more axonal dieback than controls and ES333 animals (50μm mark: p=0.02 and 0.02, respectively, tukey; lesion site: p=0.01 and 0.02, respectively, tukey).

Conclusion
Cortical ES of the injured CST results in greater axonal outgrowth, and influences functional outcomes depending on ES parameters. ES is a potentially promising SCI therapy, but further investigation is required.
THE EFFECT OF LOW INTENSITY PULSED ULTRASOUND (LIPUS) ON TISSUE ENGINEERED HUMAN MENISCAL TISSUE

Background: Preliminary work with meniscal fibrochondrocytes (MFCs) in three-dimensional (3D) porous scaffolds shows evidence of retaining extracellular matrix (ECM)-forming phenotype. Research investigating low intensity pulsed ultrasound (LIPUS) shows that it modulates the expression of genes responsible for ECM formation in cartilage. Since, the ECM of cartilage and meniscus have similar properties, we hypothesize that LIPUS will similarly modulate ECM formation in meniscal tissue thus providing a potential avenue for meniscal repair.

Objectives: To assess the effect LIPUS stimulation +/- fibroblast growth factor (FGF-2) has on the production of DNA, glycosaminoglycan (GAG), aggrecan, type 1 collagen and type 2 collagen in human meniscal tissue.

Methods: Healthy human meniscal tissue was harvested from five young female knees at the time of partial menisectomy for meniscal tears. Human MFCs were isolated and seeded on 3D collagen scaffolds. The proliferation group was cultured in a modified DMEM basic media +/- FGF-2 for 14 days. The chondrogenic group was cultured in a modified DMEM basic media +/- FGF-2 for 14 days followed by 14 days cultured in a serum and FGF-2 free modified DMEM media supplemented with TGF-β3, dexamethasone and ascorbic acid. The groups were further divided into exposed and not exposed to LIPUS, giving a total of four groups each in the proliferation and chondrogenic groupings. The cell-collagen constructs underwent processing for DNA and GAG content as well as gene expression via qRT-PCR for the predominant ECM genes of the meniscus; aggrecan, type 1 collagen and type 2 collagen. Results were analyzed and statistical differences between groups were determined using parametric and non-parametric tests depending on Levene analysis for homogeneity of data.

Results: In the proliferation groups, the cell-scaffolds cultured in the presence of FGF-2 demonstrated a significant increase in DNA content (p<0.05). The presence of LIPUS +/- FGF-2 in the proliferation or chondrogenic groups showed no significant increases in DNA, GAG, aggrecan, type 1 collagen and type 2 collagen (p>0.05).

Conclusions: Based on the parameters used in this study, LIPUS was not shown to increase levels of DNA, GAG, aggrecan, type 1 collagen and type 2 collagen in human meniscal tissue.
ABSTRACTS

Basic Science Poster Presentations
COMBINING TRADITIONAL LAP BOX PRACTICE WITH VIDEO GAMING: A RANDOMIZED CONTROL TRIAL

Background: While there is consensus regarding a positive effect of video gaming on surgical dexterity, little is known regarding how much traditional practice can or should be substituted with video gaming.

This randomized control trial was designed to assess the effect of varying the amount of traditional practice in a lap box trainer and video gaming on performance in two Fundamentals of Laparoscopic Surgery (FLS) tasks. A structured training program was designed to test the hypothesis that video gaming can be substituted for lap box practice with a negligible effect on FLS task performance.

Methods: 67 undergraduate and medical students were recruited and randomized into one of four groups including a control, exclusive laparoscopic, exclusive gaming and a combination training group with 50% of time allotted to each modality. FLS task performance was assessed both prior to and post-training.

Analysis: A mixed Repeated Measures Analysis of Variance (RMANOVA) was carried out to compare pre and post-training FLS performance between each of the 4 cohorts. A second RMANOVA was used to compare the learning curves between the laparoscopic exclusive and combination training groups.

Results: Comparison of FLS peg transfer performance following training showed a statistically significant improvement in task time in the lap box (-135 s, SE = 15.0, p < 0.001) and combined training group (-76 s, SE = 14.9, p < 0.001) compared to the control group. There was a marginal improvement in the peg transfer performance in the video gaming exclusive group (-15 s, SE 14.8, p = 0.75). For the precision cutting task there was a significant interaction effect between time and training cohort.

Examination of the learning curves demonstrated that participants in the combination group required 35.7% more time compared to individuals in the laparoscopic exclusive group by the 6th training session. The lack of divergence in these curves suggests that video gaming contributed to laparoscopic skill acquisition or aided with skill retention.

Conclusion: While traditional lap box training remains the most effective method for improving simulated laparoscopic surgery performance, video gaming can be encouraged to enhance skills retention and supplement simulated practice.
INVESTIGATION OF EZH2 PATHWAYS FOR NOVEL EPIGENETIC TREATMENT STRATEGIES IN OROPHARYNGEAL CANCER

Background: Epigenetic deregulation of cellular programs is a key hallmark of human cancers. Epigenetic modifications are defined as heritable changes in gene expression not encoded in a DNA sequence. These modifications include DNA methylation, noncoding RNAs and a variety of histone post-translational modifications. EZH2 is an epigenetic regulatory protein associated with tumor aggressiveness and negative survival outcomes in several human cancers.

Objectives: We aimed to determine the role of EZH2 as a potential therapeutic epigenetic target in HPV+ and – oropharyngeal squamous cell carcinoma (OPSCC).

Methods: The expression of EZH2 was measured by immunohistochemistry (IHC) and droplet digital PCR (ddPCR) in 2HPV positive and 2 HPV negative cell lines. The cell lines were then cultured and treated with one of 3 EZH2 epigenetic inhibitors (3-deazaneplanocin A, GSK-343 and EPZ005687) or DMSO (control). Following 2, 4 and 7 days of treatment, cells were analyzed and compared by gene expression, cell survival and proliferation assays.

Results: EZH2 targeting resulted in greater inhibition of growth and survival in HPV + vs - cells lines. The expression profile of genes important in OPSCC also differed according to HPV positivity for Ki67, CCND1, MET and PTEN/PIK3CA, but remained unchanged for EGFR, CDKN2A and p53.

Conclusions: Inhibition of EZH2 has anti-tumorigenic effects on OPSCC cells in culture that is more pronounced in HPV positive cell lines. EZH2 is potentially an excellent epigenetic target in the treatment of OPSCC.
CHARACTERIZATION OF HUMAN IMMUNE CELL-MEDIATED REJECTION OF NEONATAL PORCINE ISLET XENOGRAFT

Background: Islet transplantation is being considered as an alternative treatment for Type 1 Diabetes Mellitus (T1DM); however, the shortage of human donors limits its wide application in the clinic. Hence, scientists in the field are studying porcine islets as potential alternative source. In preparation for transplantation of porcine islet into patients with T1DM, rejection mediated by human immune cells must be studied.

Objectives: To investigate the rejection of porcine islets by human immune cells in vivo.

Methods: Neonatal porcine islets were isolated and cultured for 7 days, then 2,000 IEQ were transplanted under the kidney capsule of immune-deficient diabetic NOD.SCID gamma mice (n=10). Blood glucose levels (BGL) of mice were monitored once a week for >100 days post-transplantation. Four weeks after mice have achieved normoglycemia, they were injected with 15 million human PBMCs from donors with or without T1DM. Kidneys bearing the islet xenograft were harvested 1-4 weeks post-cell reconstitution. The islet grafts were analyzed for the presence of porcine endocrine cells and immune cells by immunohistochemistry and transmission electron microscopy (TEM).

Results: Eight of the 10 mice became normoglycemic (BGL < 8.4 mmol/L) at 71-135 days post-transplantation. All islet grafts showed some insulin and glucagon positive stained cells; however only the islet grafts from reconstituted mice had positive human CD45 stained cells. TEM analysis of islet grafts from non-reconstituted mice showed porcine endocrine cells and mouse innate immune cells within the blood vessels and some have lodged where the porcine islets were located. In the reconstituted mice, human immune cell infiltration, damage of hormone secreting cells and formation of collagen were observed, which revealed the rejection of the islet graft. In addition, selective autophagy was observed in some immune cells present in the graft.

Conclusions: Both innate and adaptive human immune cells are involved in the rejection of neonatal porcine islet xenograft. Further characterization of the identity of these cells warrants further investigation.
Kinesthetic Guidance Expedites Proficiency in a Navigational Laparoscopic Task

Background: Touching is one of the most important sensations for a surgeon to perform optimal surgery. However, our knowledge on kinesthetic and tactile feedback (often called haptic) remain rudimentary. This is partially due to the fact that haptic is difficult to record and playback during human performance. At the Surgical Simulation Research Lab, we implemented an advanced system (SensAble™ PHANTOM® Omni) that enables us to record an expert surgeons’ haptic features from both hands and deliver them to a surgeon-in-training while learning a complex surgical procedure. In this study, we examine the impact of using this newly developed training paradigm for learning laparoscopic skills in simulation. It is our hypothesis that this haptic guidance received from the expert will facilitate skill learning.

Objectives: The objective of this study is twofold: first, can kinesthetic guidance decrease the total time of error in a laparoscopic task? And second, can kinesthetic guidance chance the amount of force from the non-dominant hand?

Methods: Eight novice students performed a navigational laparoscopic task. Half of them were exposed to a kinesthetic-guided training while the other half applied self-directed learning. The task was to move a ring through a twisted wire from one side to the other. In the self-directed group, subjects practice 30 trial without receive any feedback from expert surgeon. In the kinesthetic-guided group, subjects obtained 2 guided trials after every 10 self-directed trials. Total task time, drops of the ring, and error duration made during each trial were recorded and evaluated between the two training groups. A one-way repeated measures ANOVA was conducted to determine whether there was a statistically significant difference in the total of time of error over the three trial.

Results: Task time (p =.007), error duration (p<.001) and drop counts (p<.001) were reduced with significant differences between two training groups. However, the effect was only noticeable during the first block, and it was similar for the remaining of the blocks for the two groups.

Conclusions: The kinesthetic guided group completed the task with less error time than the self-directed group. Future studies will look into changes in forces and motion of the non-dominant hand.
USE OF DROPLET DIGITAL PCR FOR ULTRASENSITIVE GENE EXPRESSION PROFILING AND MUTATIONAL ANALYSIS OF SALIVARY GLAND LESION FNA BIOPSIES

Background: Salivary gland tumors (SGT) represent a commonly occurring neoplasm within the head and neck. To date, preoperative diagnostic tools yield limited information to differentiate between benign and malignant lesions. Additional diagnostic tools are needed to more effectively treat these lesions.

Objectives: Fine needle aspirate biopsies (FNABs) of salivary gland tumors (SGT) have high diagnostic specificity but relatively low sensitivity. The recent discovery of biomarkers associated with distinct SGT provides the opportunity to enhance the pre-operative diagnostics. We aimed to utilize novel, highly sensitive technology termed droplet digital PCR (ddPCR) to identify diagnostic gene expression signatures from SGT FNAB samples.

Methods: Basic science description of epigenetic characteristics in SGT. FNABs were pre-operatively collected from patients with SGTs and processed for ddPCR analysis. Gene expression levels were measured relative to internal control for EGFR, p53, Ki67, c-KIT, PTEN, PI3K, p16, MEK and fusion genes CRTC1–MAML2, MYB–NFIB, EWSR1-POU5F1, PLAG1-fusions and HMGA2-fusions. Expression profiles were correlated to post-surgical pathologic diagnosis.

Results: FNAB samples from 48 patients with SGTs were collected for ddPCR analysis. Compared to other methods of biomarker analysis gene expression data was reliably obtained with small amounts of nucleic acid. Fusion gene products and distinct gene expression profiles were predictive of final surgical pathology.

Conclusions: The detection of biomarkers of SGTs by ddPCR is a powerful diagnostic tool. The detection of altered gene expression and signature fusion-gene products associated with SGTs may be useful for pre-surgical planning.
Background: Partial bladder outlet obstruction (pBOO) can result in extensive structural and functional damage with significant morbidity. pBOO results in an inflammatory response, then smooth muscle hypertrophy, and eventually progresses to fibrosis. Several studies have implicated hypoxia in the etiology of pBOO; however, it has been difficult to separate this from the stress of increased hydrostatic pressure and tissue stretch. Therefore, the isolated effects of hypoxia on the smooth muscle cells of the bladder are not yet known.

Objectives: Therefore, in order to characterize the effects of isolated hypoxia on bladder cells, we cultured subconfluent normal human detrusor smooth muscle cells in hypoxic conditions. We hypothesized that the resultant hypoxic response will result in a pro-inflammatory and pro-fibrotic phenotype.

Methods: Commercially acquired human bladder smooth muscle cells (hbSMC) were cultured in 3% O₂ for 2, 24, 48 or 72 hours. We subcategorized our analysis to a) hypoxic cascade; b) anti-inflammatory response; c) epithelial-mesenchymal transformation (EMT), and d) pro-fibrotic cascade. RT PCR and ELISA were performed to assess mRNA and protein production, while the culture media was isolated to assess extra-cellular cytokine and collagen production.

Results: Our hypoxic analysis demonstrated that HIF 1 and 2 were transiently induced after 2 hours of hypoxia (p<0.05) whereas HIF 3 was upregulated after 72 hours (p<0.005). VEGF increased significantly after 24, 48 and 72 hours (p<0.005). The inflammatory cytokines demonstrated a time-dependent increase in production (TGFB, IL 1β, 1L6 and TNFα). Furthermore, the anti-inflammatory IL-10 was down regulated after 72 hours (p<0.05). Evidence of EMT was seen with myofibroblast activation (αSMA, vimentin and desmin). We believe that the increases in CTGF, SMAD 2 and 3 as well as collagens 1, 2, 3, 4, fibronectin, aggrecan and TIMP 1, (p<0.05) provide evidence of pro-fibrotic changes.

Conclusions: Together, these results show that culture in a reduced oxygen environment results in hypoxic cascade, including inflammation, EMT, and pro-fibrotic changes. We are the first to describe HIF-3 in the bladder. This work will allow for an improved understanding of bladder deterioration after pBOO, result in tailored in-vivo experiments, and ultimately translate into improved clinical outcomes.
ABSTRACTS

CLINICAL SCIENCE POSTER PRESENTATIONS
ASSOCIATION BETWEEN MORTALITY AND RENAL REPLACEMENT THERAPY AFTER CARDIAC SURGERY AMONG OCTOGENARIANS: A RETROSPECTIVE POPULATION-BASED COHORT STUDY

Background: Acute kidney injury (AKI) is a devastating complication following cardiac surgery. Renal replacement therapy (RRT) is often utilized to support kidney function in the post-operative period. The resource implications and outcomes associated with RRT among octogenarians undergoing elective cardiac surgery have been poorly explored.

Methods: In this retrospective population-based cohort study, data from patients aged ≥80 years undergoing elective cardiac surgery between 2004 and 2009 at Mazankowski Alberta Heart Institute were collected. Primary exposure was severe AKI treated with RRT compared to those with AKI not treated with RRT. Primary outcome was 30-day mortality. Secondary outcomes evaluated post-operative complications and mortality at 1 and 5 years. We used multi-variable analysis to identify independent risk factors for 30-day mortality.

Results: Ninety two out of 546 patients (16.8%) aged ≥80 years undergoing elective cardiac surgery developed AKI. Of these, 27 patients (4.9%) received RRT, whereas 65 (11.9%) received conservative non-RRT treatment. Compared to patients treated conservatively, RRT treated patients had significantly higher 30-day mortality (29.6% vs. 7.7%, P<0.017), 1-year mortality (70.4% vs. 16.9%, P<0.001) and 5-year mortality (77.8% vs. 41.5%, P=0.003). RRT treated patients were also more likely to have undergone re-operation (14.8% vs. 1.5%, P=0.025) and had longer cardiopulmonary bypass exposure (175.3±85.6 vs. 145.4±54.7, P=0.048). RRT treated patients had higher rates of post-operative infection, neurologic events, prolonged ventilation, cardiac arrest and ICU readmission. The ICU and hospital length of stay were also significantly longer in patients who received RRT. Multivariate regression analysis, after adjusting for pre-operative characteristics and peri-operative events, found only pre-op left ventricular ejection fraction (LVEF) (OR 4.29, 95% CI 0.497-0.981, P=0.038), re-do surgery (OR 6.88, 95% CI 0.000-0.675, P=0.045), and post-op cardiac arrest (OR 5.73, 95% CI 0.000-0.201, P=0.017) were independently associated with 30-day mortality. Peri-operative treatment with RRT for AKI, was not independently associated with 30-day mortality (OR 0.733, P=0.392).

Conclusion: The incidence of AKI after elective cardiac surgery in octogenarian patients is high and RRT treatment is associated with higher risk for post-operative complications and death; however, mortality in multivariate analysis would appear to be driven by LVEF, re-do surgery and post-op cardiac arrest.
Patterns of Neck Metastases in Human Papillomavirus Positive and Negative Oropharyngeal Squamous Cell Carcinomas

Importance: Oropharyngeal squamous cell carcinoma (OPSCC) is composed of two distinct disease entities. Those cancers related to the oncogenic human papillomavirus (HPV) have been shown to be very different from traditional OPSCC associated with tobacco and alcohol consumption. These diseases not only differ in epidemiological profiles and treatment responses, but also in aggressiveness of local-regional tissue invasion. Despite this, little is known of the patterns and extent of neck metastases for HPV-related OPSCC.

Objective: To compare patterns of neck metastasis and extensiveness of neurovascular invasion in HPV-positive and negative OPSCC.

Design: Systematic, retrospective chart review.

Setting: Tertiary referral center for head and neck surgery.

Participants: We identified consecutive patients undergoing surgical resection and neck dissection for OPSCC from a prospectively collected database. Univariate analysis was used to identify factors predictive of neurovascular injuries associated with neck dissections and patterns of neck metastasis in the cervical lymph nodes.

Main Outcome Measures: Patterns of neck metastasis and rates of nerve and vascular injury following neck dissections in HPV-positive and negative OPSCC.

Results: One hundred patients were included and 56 patients were found to have HPV-positive disease. 82 patients had unilateral and 18 patients received bilateral neck dissections. HPV positivity was associated with higher rates of level two neck metastasis, as well as increased pathologic stage (OR=1.8, p=0.03). Advanced tumor and nodal stage, and ipsilateral nodal disease were associated with contralateral neck metastasis (p<0.05). HPV status was not a significant predictor of contralateral disease. HPV-negative OPSCC was associated with statistically significantly higher rates of ipsilateral spinal accessory (p=0.02) and ipsilateral marginal mandibular (p=0.03) nerve erosion. There was no statistically significant difference in ipsilateral hypoglossal nerve and ipsilateral internal jugular vein invasion between the two groups (p>0.05)

Conclusions and Relevance: This is the first study to date to contrast the patterns and aggressiveness of HPV-positive and negative OPSCC. While not predictive of contralateral neck metastasis, HPV-negative tumors have significantly more extensive local-regional neurovascular invasion within the neck.
EVALUATION OF SURGICAL SKILLS IN PLASTIC SURGERY: VALIDITY AND RELIABILITY OF ASSESSMENT USING THE O-SCORE

Importance: Competency based training requires valid and reliable assessment. The evidence for assessment of surgical skills in plastic surgery is lacking. The O-SCORE tool was developed for use in orthopaedic and general surgery. It is not known how global assessment tools perform when used in plastic surgery.

Objective: The purpose of this study was to examine the validity and reliability of the O-SCORE when used in a Canadian plastic surgery residency program.

Design: Plastic surgery residents at the University of Alberta were evaluated on breast reduction mammoplasty, mandibular fracture ORIF and hand fracture fixation over an 8 month period. In total 41 evaluations were completed. Generalizability theory was used to determine overall reliability based on two facets. A MANOVA analysis was conducted to compare ratings on individual items and overall score based on year of training. Internal consistency of the items was determined based on 7 raters evaluating a surgical video under controlled conditions.

Setting: University of Alberta

Participants: Plastic surgery residents, Plastic surgeons

Main Outcome Measure(s): absolute error variance, index of dependability of O-SCORE measurements

Results: There were significant differences between PGY1-3 and PGY 4-5 on all items and overall score. The reliability coefficient using G-theory was 0.909 based on two facets: item and occasion. D study results show that 7 occasions would be required to achieve a reliability coefficient of 0.95. The internal consistency of the technical items was also quite high. The Cronbach alpha on the technical items was 0.904.

Conclusions and Relevance: This is the first study to report validity and reliability evidence on a global rating scale in plastic surgery. Assessment decisions made with the O-SCORE yields valid and reliable results. The assessments also differentiated junior from senior residents. Using this tool as part of an assessment tool armamentarium will keep plastic surgery programs on track with competency based training as mandated by the Royal College of Canada.
A Comparison Between Selective and Non-Selective PICU Admission Post-Supraglottoplasty

Importance: Laryngomalacia is a congenital laryngeal condition which is the most common cause of stridor in infancy. Although the majority of patients are managed conservatively, those with persistent work of breathing, swallowing dysfunction, or sleep disordered breathing may require supraglottoplasty (SGP), and recent evidence suggests a rise in its utility. Post-supraglottoplasty care is currently based on tradition and surgeon preference rather than on evidence. Post-operative care settings range from intubation and admission to pediatric intensive care (PICU) to close observation on the ward with cardiorespiratory monitoring. Decreased utilization of PICU without compromising safety is desirable.

Objective: To compare PICU admission rates, post-operative respiratory complications and duration of admission before and after adopting a selective PICU admission care plan following SGP.

Design: Retrospective case series.

Setting: Tertiary pediatric otolaryngology referral center.

Participants: All pediatric patients with an endoscopically confirmed diagnosis of laryngomalacia undergoing SGP with cold steel technique.

Methods: Eligible patients were identified through a prospectively kept surgical database. Historical cohorts with routine admission to PICU and selective admission to PICU were identified based on a shift in surgeon practice. The cohorts were compared with respect to demographics, presenting features, endoscopic findings, baseline sleep study results, respiratory complications, repeat or unplanned PICU admission and length of post-operative hospital admission.

Main Outcome Measure(s): Rate of PICU admission, respiratory complications, and length of hospitalization in the routine and selective PICU admission cohorts.

Results: Between 2003 and 2015, 150 eligible patients were identified (mean age 1.49±2.25 years) with 39 in the routine PICU admission cohort and 111 in the selective admission cohort. Patient demographics and comorbid conditions were comparable between the two groups. Rate of PICU admission was reduced from 79% to 30% with a selective PICU admission strategy (P<0.01, χ²). Mean duration of post-operative hospital stay was reduced from 5.29±3.43 days to 1.99±2.33 days (p<0.01, Student’s t-test). Respiratory complications were rare in both the routine and selective PICU admission groups.

Conclusions and Relevance: Selective PICU post-operative admission following SGP significantly reduces PICU admission and reduces length of hospital stay without compromising safety and care.
OUTCOMES OF SPLIT-THICKNESS SKIN GRAFT RECONSTRUCTION FOR MAJOR GENITAL SKIN LOSS: THE ADVERSE IMPACT OF SYSTEMIC DISEASE PROCESSES

Importance: Major genital skin is a devastating event. Regarding outcomes, there currently exists only small series in the literature with no Canadian data.

Objective: To report clinical outcomes of genital reconstruction using split-thickness skin grafts (STSG) for various local and systemic disease processes.

Design: Retrospective review of 31 males undergoing genital STSG reconstruction at the University of Alberta between 2006 and 2015.

Main Outcome Measure(s): The primary outcome was success defined as patient satisfaction with acceptable cosmesis, preserved standing micturition, and erectile function. Etiology, age, graft-take, 90-day complications, delayed complications and semi-quantitative assessment of patient satisfaction, cosmesis, erectile and voiding function were also evaluated. Outcomes were analyzed using Pearson Chi-square.

Results: Average patient age was 48 years (19-80) and the most common etiology of genital skin loss was infection (41.9%) followed by buried penis (25.8%), neoplasia (16.1%) and lymphedema (16.1%). Reconstruction of the penis, scrotum or both was performed in 71.0% (22/31), 19.4% (6) and 9.6% (3) of patients respectively. Overall success was 87.1%, with a mean follow-up of 18 months. 93.5% of patients experienced good (>90%) graft-take with early maturation but 64.5% (20) experienced a 90-day complication. The majority (95%) of these complications were Clavien 1 or 2, including focal epidermolysis requiring local wound care (32.2%), cellulitis (12.9%) requiring antibiotics, UTI (3.2%) or hematoma requiring observation (3.2%). One patient (3.2%) required surgery for abscess debridement and repeat grafting. 90.3% of patients reported satisfaction and acceptable cosmesis. Patients reported preserved erectile function (96.1%; 25/26) and standing micturition (96.3%; 26/27). 9.7% (3) of patients had late complications requiring either local excision of granulation tissue or dilation of meatal stenosis. Specific etiologies did not impact outcome, however patients with systemic disease processes were more likely to experience a 90-day complication (100% 6/6 vs. 56% 14/25; p=0.04) or impaired graft take (33% 4/6 vs. 0% 0/25; p=0.003).

Conclusions and Relevance: We present the first Canadian series of genital STSG reconstruction. It is an effective method for functional reconstruction of major genital skin loss with acceptable morbidity. Patients with systemic disease processes are more likely to experience 90-day complications and delayed graft-take.
MODIFICATION OF THE SUBMANDIBULAR GLAND TRANSFER PROCEDURE

Importance: Adjuvant radiotherapy (RT) is an important part of treatment for advanced head and neck mucosal cancers. However, xerostomia remains a prevalent morbidity of that significantly impairs patients’ quality of life. The submandibular gland transfer has been shown to be superior in preventing radiation-induced xerostomia compared to pilocarpine in a phase III randomized control trial. However, its original description of transferring the gland into the submental area precludes its use in the oral cavity. Therefore, we developed the modified submandibular gland transfer (M-SGT) for use in oral cavity cancers where the submandibular gland contralateral to the disease process is transferred to the the peri-parotid space.

Objective: To study the radiation sparing potential of the modified submandibular gland transfer.

Design: Retrospective chart review

Setting: Tertiary academic head & neck cancer center

Participants: Head & neck cancer patients who have had surgery followed by radiation as their treatment and who have had a modified submandibular gland transfer

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Modified submandibular gland transfer

Main Outcome Measure(s): Radiation dose received by the transferred submandibular gland

Results: We collected data on 16 patients who have had a modified submandibular gland transfer procedure performed by a single surgeon (HS). The mean radiation dose received by the transferred submandibular gland was 21 Gy (SD 14 Gy) which was significantly lower than the mean dose it would otherwise have received in the submandibular triangle, which was 54 Gy (SD 9 Gy, p = 0.0001). The received dose was well below the TD50 and maximum tolerable dose of the submandibular gland, which are 33 and 39 Gy respectively.

Conclusions and Relevance: The modified submandibular gland transfer technique is successful at reducing the radiation dose sustained by the gland during adjuvant treatment. It can be used to reduce the morbidity of xerostomia in oral cavity cancer patients.
ABSTRACTS

ORAL PRESENTATIONS,
AFTERNOON SESSIONS
**Ulnar Nerve Versus Hematoma Block for Closed Reduction of Boxer’s Fractures**

**Importance:** Transverse fifth metacarpal neck (Boxer’s) fractures account for up to 60% of all hand fractures. Closed reduction of these fractures can restore normal hand function without the need for surgery. To date, there is no published literature comparing methods for providing analgesia during closed reduction of Boxer’s fractures.

**Objective:** To determine whether ulnar nerve or hematoma blocks provide better analgesia when performing closed reduction of Boxer’s fractures. Volume of local anesthetic required and pain of injection were also assessed.

**Design:** An HREB-approved prospective randomized controlled clinical trial was conducted between July 2014 to July 2015.

**Setting:** The study was conducted at the University of Alberta Hospital Resident Hand Clinic.

**Participants:** 24 adult patients with isolated displaced fifth metacarpal fractures were recruited. Using sealed and coded envelopes, patients were randomly allocated to receive either ulnar nerve (n=12) or hematoma (n=12) blocks. Patients with clinically healed, open, or multiple hand fractures were excluded.

**Intervention(s) for Clinical Trials or Exposure(s) for observational studies:** 5cc’s of local anesthetic (9:1 mixture of 1% plain lidocaine and 8.4% sodium bicarbonate) was administered as an ulnar nerve or hematoma block. After 10 minutes, cutaneous anaesthesia over the fracture site was checked, injecting additional local anesthetic if needed. Closed reduction was then performed.

**Main Outcome Measure(s):** Pain of injection and closed reduction rated on an eleven point (NRS-11) pain scale.

**Results:** Patient demographics and injury characteristics were similar between experimental groups. The amount of local anesthetic needed to achieve anesthesia was not statistically different between ulnar nerve and hematoma block groups (6.7cc vs. 6.7cc, p=1). Pain of injection was similar between ulnar nerve and hematoma blocks (1.37 vs. 1.73, p=0.25). Patients experienced less pain during closed reduction following ulnar nerve blocks compared to hematoma blocks (4.33 vs. 6.83, p=0.03). There was no statistically significant difference in total complication rates between ulnar nerve and hematoma block groups (8% vs. 0%, p=1).

**Conclusions and Relevance:** Ulnar nerve blocks provide better analgesia than hematoma blocks for closed reduction of Boxer’s fractures. The two blocks are comparable in terms of patient discomfort during injection, total volume of local anesthetic required, and complication rates.
The Prebiotic Fructooligosaccaride Worsens Systemic Inflammation in a Murine Model of Post-Operative Crohn's Disease

Background: Fructooligosaccaride (FOS) is a fermentable prebiotic fiber that stimulates the growth of bifidobacteria, which has been shown to have beneficial anti-inflammatory effects. Patients with Crohn’s disease frequently undergo ileocolic resection (ICR), but disease commonly recurs in the neo-terminal ileum (TI). We have previously shown using a mouse model of ICR that surgery induces an acute gut dysbiosis with a depletion of anaerobic microbes, including bifidobacteria.

Objectives: We hypothesized that the addition of FOS to a post-operative diet in a mouse model of ICR would stimulate the growth of bifidobacteria and reduce systemic and local inflammation.

Methods: ICR was performed in adult IL10-/- mice with established colitis. Following ICR, mice were placed on a chow diet ± 10% FOS or cellulose (n=12) for 28 days. Non-operative controls received FOS or cellulose as a control. Tissues were analyzed for cytokine expression by MesoScale discovery-platform. DNA was extracted from stool using a FastDNA spin-kit and analyzed using quantitative-PCR.

Results: Following ICR, all mice had significant weight loss over the first 7 days followed by a recovery to ~85-90% of their pre-operative weight. At 28 days post-surgery, ICR mice had increased systemic inflammation as evidenced by increased levels of serum inflammatory cytokines (IL-2, IL-12, IL-4) (p<0.05). Also, total fecal bacteria remained decreased as did a depletion of bifidobacteria (p<0.05). FOS administration post-ICR resulted in greater proportions of lactobacilli and bifidobacteria compared to post-ICR controls (p<0.05). Contrary to our hypothesis, mice on the FOS-supplemented diet had a significantly reduced extent of recovery along with enhanced levels of systemic IL-6. Reduced recovery was associated with increased ileitis and colitis, with elevated IL-1β in the TI and IFNγ and TNFα in the colon. In all ICR mice, serum IL-6 levels demonstrated a significant correlation with numbers of bifidobacteria (R=0.72;p=0.013). Non-operative mice which received FOS had increased levels of bifidobacteria as well as increased levels of colonic IFNγ and KC (p≤0.05)

Conclusions: Supplementation with fructooligosaccharide during the post-operative period in the IL-10-/- mouse model of colitis increased levels of bidifobacteria but promoted systemic inflammation and delayed recovery suggesting that FOS supplementation during this period may worsen recovery.
Background: Stable mixed hematopoietic chimerism is a robust method for generating donor specific tolerance with the potential to allow islet transplant tolerance in diabetic recipients. However its clinical application is prevented by the toxicity of current recipient conditioning regimens (e.g. use of irradiation). We previously showed that an irradiation-free mixed chimerism protocol in diabetes prone NOD mice is achievable with antibodies to T cells and CD40L together with busulfan and high dose rapamycin.

Objectives: We sought to generate a more clinically feasible chimerism protocol and tested the hypothesis that more efficient recipient T cell depletion would eliminate the need for anti-CD40L (known to cause thromboembolism in humans) and rapamycin.

Methods: We preconditioned NOD mice with donor specific transfusion (DST) from fully mismatched C3H or FVB mice (day -10), cyclophosphamide (day -8), anti-T-cell antibodies against CD90 and/or CD4+CD8 (day -6, -1, 4, 9, 14), and busulfan (day -1). Donor bone marrow transplantation (BMTx) was done at day 0. Body weight and blood glucose levels of recipient mice were assessed weekly. Flow cytometry was used to detect chimerism and different lineages of cells from recipient and donor mice.

Results: By using this protocol, we successfully induced mixed chimerism in 28/38 NOD mice with the level of donor cells up to 90%. Stable chimerism with multi-lineage donor cells, including T, B, NK and Dendritic cells was maintained in 16/27 recipients. Loss of chimerism could be predicted by a lower early level of chimerism at 4, 9 or 14 days post BMTx as well as a lower level of donor T cells by 8 weeks post BMTx. We determined that inclusion of anti-CD90 mAb in the conditioning regimen could significantly accelerate the depletion of recipient T cells and facilitate stable chimerism. The loss of anti-donor V beta 11+ T cells in stable chimeric mice indicated the establishment of chimerism involves clonal deletion.

Conclusions: A rapid and robust recipient T cell depletion protocol generated chimerism without the need for anti-CD40L or rapamycin. This protocol is the most clinically feasible to have achieved fully allogeneic mixed chimerism in NOD mice.
Background: Head and neck squamous cell carcinoma is the sixth leading cancer worldwide, with incidence rates of oropharyngeal cancers rapidly increasing due to human papillomavirus (HPV)-related infections. Epigenetic therapies have shown great promise in a clinical setting and are quickly moving to the forefront of chemotherapeutic research. Specific targeting of EZH2 pathways has been of particular interest in solid tumors but their role in oropharyngeal carcinomas remains largely unexplored.

Objective: To determine and compare the efficacy of three epigenetic inhibitors on HPV positive and negative squamous cell carcinoma cell lines.

Methods: Two EZH2 inhibitors; EPZ-5687, GSK-343, and the S-adenosylmethionine-dependent methyltransferase inhibitor, DZNeP, were compared for efficacy using two squamous cell carcinoma cell lines, SCC-104 and SCC-9 (HPV positive and negative, respectively). Cells were cultured and treated at logarithmic growth with an inhibitor for 7 days at varying concentrations. Cells were then processed for immunofluorescence microscopy to detect H3K27me3 and EZH2. Droplet digital PCR (ddPCR) analysis was used to detect changes in RNA expression levels of EGFR, TP53, MKI67, CDKN2A, CCND1, MET, EZH2, PTEN and PIK3CA. Western blot analysis was used to detect changes in H3K27me3 and EZH2 in response to epigenetic inhibitors.

Results: ddPCR gene expression analysis: SCC-104 cells showed a decrease in EGFR expression and PTEN:PIK3CA at all concentrations of DZNeP. MKI67 expression increased with increasing DZNeP concentrations. EPZ-5687-treated SCC-104 cells displayed decreased PTEN:PIK3CA at 0.5uM and 5.0uM and increased EZH2 expression at 1.0uM. GSK-343-treated SCC-104 cells displayed dramatic decreases in EGFR, TP53, and MKI67, and small decreases in CCND1 expression at 5uM. Decreases in CDKN2A and MET were seen at all concentrations of GSK-343 (0.5uM, 1.0uM, and 5.0uM).

Western Blot: GSK-343 treatment resulted in a decrease in H3K27me3 only in SCC-104 cells, whereas EPZ-5687 treatment decreased H3K27me3 only in SCC-9 cells.

Conclusions: Epigenetic inhibitors targeting the EZH2 pathway may be effective in treating oropharyngeal carcinoma. HPV positive and negative cells lines respond differently to EZH2 inhibitors. Further investigation with additional cell lines, primary cultures and tumor explant models would be suggested prior to clinical assessment of these inhibitors.
COMBINATION TROPHIC PEPTIDE THERAPY FOR NEONATAL SHORT BOWEL SYNDROME

Background: Short bowel syndrome (SBS) is a significant cause of morbidity and mortality in neonates. Growth factors are being investigated as a potential therapy. The glucagon-like peptide-2 (GLP-2) and epidermal growth factor (EGF) pathways may potentially be synergistic in intestinotrophic action.

Objective: To determine if combined GLP-2 and EGF administration translates to improved intestinal adaptation in neonatal SBS.

Methods: Neonatal piglets (n=38) were block randomized to saline control, GLP-2 (11 nmol/kg/day) alone, EGF (80 μg/kg/day) alone, or combined GLP-2 and EGF therapy for seven days following a 75% distal intestinal resection (removing all ileum) or no resection (sham control). Piglets were maintained on 100% parenteral nutrition and 20% paired enteral feeding. Structural adaptation was assessed by gross intestinal morphology and histology. Functional adaptation was assessed by intestinal permeability via Üssing chamber analysis. Remnant intestinal qRT-PCR was performed to determine the relative expression of genes involved in intestinal repair (trefoil factor 3, TFF3), barrier function (claudin-15) and secondary messaging (insulin-like growth factor-1, IGF-1). Data was analyzed by 2-way ANOVA, with a level of significance set at p < 0.05.

Results: Combination therapy increased remnant intestinal length compared to saline control (p=0.01) while mono-therapy did not. GLP-2 alone increased intestinal weight (p<0.01) and mucosal weight (p=0.04) over EGF alone. Both GLP-2 and combination therapy increased jejunal villus height over saline (p<0.01). EGF alone reduced crypt depth compared to saline control (p<0.01). Combination therapy reduced intestinal permeability to mannitol (p=0.04) and polyethylene glycol compared to saline (p<0.01). Combination therapy increased the expression of TFF3 (p=0.03) and claudin-15 (p=0.06) over saline. In the resection group, IGF-1 expression decreased with GLP-2 and increased with EGF treatment (p=0.01).

Conclusions: In this preclinical neonatal SBS model lacking ileum, which reflects the remnant anatomy most commonly encountered clinically in human infants, combined GLP-2 and EGF administration demonstrated the most beneficial impact on remnant intestinal morphology, histology and function. Combination therapy further increased the expression of genes involved in tissue repair and permeability. The morphologic and histologic changes suggest an increase in absorptive surface area while reductions in permeability potentially signify a decreased risk for bacterial translocation and sepsis.
Electrical Stimulation Enhances Muscle Reinnervation and Functional Recovery Following Cubital Tunnel Surgery – A Randomized Controlled Trial

Importance: Patients with severe cubital tunnel syndrome often have poor functional recovery with conventional surgical treatment. Post-surgical electrical stimulation (ES) enhances motor and sensory axonal regeneration in humans following carpal tunnel release and repair of digital nerve transection.

Objective: In this study, we investigated the hypothesis that ES following cubital tunnel surgery in patients with severe ulnar neuropathy would result in better muscle reinnervation and functional recovery compared to surgery alone.

Design: Double blind randomized controlled trial with yearly follow up for 3 years

Setting: Academic hospital

Participants: Patients with severe axonal loss from ulnar nerve compression at the elbow (McGowan grade III) were randomly assigned to the treatment or control group in a 2:1 ratio.

Intervention: Those in the control group received cubital tunnel surgery alone, while patients in the treatment group received 1 hour of 20Hz ES following surgery. Stimulation was delivered via two stainless electrodes placed adjacent to the ulnar nerve intraoperatively.

Main Outcome Measure(s): At each post-operative visit, axonal regeneration was quantified using motor unit number estimation (MUNE) and functional recovery was evaluated using grip strength and key pinch strength. Statistical analysis was performed using non-parametric tests, with statistical significance set at p<0.05.

Results: Twenty-four patients were enrolled with 8 receiving surgery alone and 16 receiving surgery and ES. Patient characteristics were similar between groups. Three years following surgery, MUNE was significantly higher in the ES group (176±23, mean±SE) compared to controls (88±11, p<0.05). Grip strength was significantly improved in the treatment group (43±3kg) at 3 years post-operatively compared to controls (39±3kg, p<0.05). Key pinch strength was also significantly better in the treatment group (5.2±0.5 kg) compared to controls (4.4±0.8kg, p<0.05).

Conclusions and Relevance: Our results suggest that post-surgical ES enhances axonal regeneration, muscle reinnervation and functional recovery following cubital tunnel surgery in humans. We propose that ES may be a clinically useful adjunct to surgical decompression for severe ulnar neuropathy, where functional recovery with conventional treatment is poor.
Importance: Cancers in the head and neck often lead to disability in basic function. Restoration of these functional impairments is the main treatment goals in managing patients affected by head and neck cancer. Increasingly, it is now believed that conventional outcome measures do not provide all the information needed to fully capture treatment effects. Incorporation of patient perspectives, or patient-reported outcomes (PRO), into functional outcomes measures has been gaining increasing prominence in the reconstructive literature.

Objective: The objective of this study is to create and validate the first instrument to measure the main functional areas of concern of the head and neck oncology patient.

Design: This is a four phase qualitative study. In phase I and II, function domains of importance were identified through patient interviews. The itemized PRO was created (Edmonton-33) in phase III with expert and patient input. In the final phase, patients completed the Edmonton-33 as well as performed video fluoroscopic swallowing study (VFSS), speech intelligibility (SI) testing, and the EORTC quality of life head and neck questionnaire in order to perform convergent and divergent validity testing.

Setting: University of Alberta Hospital, Edmonton, Alberta and Mount Sinai Hospital, New York City

Participants: Head and neck cancer patients 1 year or greater post-treatment

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Administration of the Edmonton-33, VFSS, and speech intelligibility testing

Main Outcome Measure(s): Correlation between the Edmonton-33 and subjective and objective testing of swallowing, speech, and dry mouth.

Results: 70 head and neck oncology patients participated in the study. The final version of the Edmonton-33 was a 33-item, Likert-type scale containing the domains of swallowing, speech, chewing, and xerostomia. Validity of the Edmonton-33 was demonstrated by excellent correlation between the Edmonton-33 and 1) VFSS, with a correlation coefficient of 0.79, 2) EORTC-35, with a correlation of 0.69, and 3) speech intelligibility, with a correlation coefficient of 0.59. All correlations were statistically significant.

Conclusions and Relevance: The Edmonton-33 is the first validated patient-reported outcome instrument designed to assess functional outcomes in head and neck oncology patients and could serve as a single comprehensive measure for functional outcomes.
CANCER CONTROL OUTCOMES OF ROBOT-ASSISTED RADICAL PROSTATECTOMY FOR HIGH RISK CLINICALLY LOCALIZED PROSTATE CANCER: PROSPECTIVE ANALYSIS OF 124 CONSECUTIVE MEN FROM THE UNIVERSITY OF ALBERTA

Importance: Approximately 20-30% are diagnosed with high risk clinically localized prostate cancer (HR-CLPC) at initial presentation. Radical prostatectomy and external beam radiation therapy with androgen deprivation are standard therapies for HR-CLPC. However, limited data are available examining the efficacy of Robot-Assisted Radical Prostatectomy (RARP) for HR-CLPC.

Objective: Our aim was to examine cancer control and perioperative outcomes in men who underwent RARP for HR-CLPC.

Design: A prospective analysis of data from the University of Alberta Radical Prostatectomy Database was performed. Between September 2007 and January 2013, 124 consecutive men underwent RARP for D’Amico classification HR-CLPC. Cancer control outcomes were biochemical recurrence (BCR) and salvage therapy (ST) rates. BCR was defined as a PSA ≥ 0.2 ug/l followed by a subsequent confirmatory value or initiation of ST. The Kaplan-Meier method was used to estimate freedom from BCR and ST. Multivariable Cox regression analysis was used to determine predictors of BCR. Statistical tests were two-sided (p<0.05).

Participants: 124 consecutive men underwent RARP for D’Amico classification HR-CLPC.

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Robot-Assisted Radical Prostatectomy (RARP).

Main Outcome Measure(s): Cancer control outcomes were biochemical recurrence (BCR) and salvage therapy (ST) rates.

Results: Mean age and BMI were 61.9 years (range, 47.0 to 78.0 years) and 29.1 kg/m² (range, 18.1 to 45.0 kg/m²), respectively. 83 out of 124 men (67%) had preoperative biopsy composite Gleason score ≥ 8. The median follow-up duration was 37.9 months (range, 0.4 to 82.7 months). Pathologic characteristics demonstrated that 114 (92%) had ≥pT2c and 100 patients (81%) had pN0 disease. 108 patients (87%) underwent pelvic lymph node dissection with 100% of patients requiring no intra-operative blood transfusions. The 5-year freedom from BCR rate was 65.0%. The 5-year freedom from ST rate was 75.1%. Multivariable Cox regression analysis showed that pTstage and pNstage were independently associated with BCR (≤pT2 vs. ≥pT3: HR 0.32, 95% CI 0.15 to 0.69, p=0.004; pN0 vs. pN1; HR 0.23, 95% CI 0.10 to 0.54, p<0.001).

Conclusions and Relevance: RARP conferred intermediate-term cancer control outcomes with minimal post-operative complication rates for men with HR-CLPC. Extended follow-up of this cohort with assessment of clinical end points is warranted.
EX VIVO PERFUSION IN A LOADED STATE IMPROVES THE PRESERVATION OF DONOR HEART FUNCTION

Background: Ex vivo heart perfusion (EVHP) has been proposed as a means improving heart preservation and expanding the donor pool. Current clinical EVHP protocols involve preservation in an unloaded and non-working state; however, the impact of this approach on the preservation of donor heart function is unknown.

Objectives: We sought to determine if myocardial load during EVHP impacts the preservation of donor heart function.

Methods: Donor porcine hearts were perfused ex vivo in a beating state for 12 hours. Loaded hearts (N=4) were perfused in a working mode (left atrial pressure=6 mmHg, heart rate=100 beats/minute) for the entire EVHP interval. Unloaded hearts (N=4) were briefly transitioned into a working mode at hours 1 (T1), 5 (T5), and 11 (T11) for metabolic and functional assessments, but were otherwise perfused in a resting mode (left atrial pressure=0 mmHg).

Results: Myocardial function (T11 cardiac index (mL/minute/gram): loaded=6.9±1.0 vs. unloaded=2.0±1.2, p=0.02) and mechanical efficiency (T11: loaded=11±1 vs. unloaded=2±1 %, p<0.01) were better preserved in loaded hearts. Myocardial injury (T11 troponin I (ng/mL): loaded=11.6±0.4 vs. unloaded=12.1±0.3, p=0.39) and edema formation (% weight gain: loaded=14±8 vs. unloaded=24±3 %, p=0.15) did not account for these differences. Free fatty acids were rapidly depleted in both groups; however, triglycerides were continually consumed by loaded hearts and secreted by unloaded heats.

Conclusions: EVHP in a loaded state improves the preservation of myocardial function. Uncoupling of fatty acid oxidation may contribute to the decline in myocardial function observed in unloaded hearts; however, further research is required to elucidate the mechanism underlying these observations. These results highlight the need for an EVHP device capable of preserving the donor heart in a physiologic working mode.
The Effect of Electrical Stimulation on Cold Sensitivity After Digital Nerve Injury: A Randomized Controlled Trial

Importance: Cold hypersensitivity and intolerance are severely debilitating consequences following digital lacerations involving repair of neurovascular structures. In fact, some long-term studies show that cold sensitivity may be the most common sustained symptom and serious complaint following digital replantation. The etiology to this symptom is multifactorial, ranging from decreased thermoregulatory vascular rewarming to disproportionate re-innervation of cold receptor free nerve endings. Multiple studies have shown that brief post-surgical electrical stimulation (ES) accelerates peripheral sensory and motor nerve regeneration. However, the effect that this treatment has on cold sensitivity after nerve repair has yet to be published.

Objective: The purpose of this study is to test the hypothesis that ES after complete digital nerve transection injury and repair will improve cold sensitivity recovery compared to surgery alone.

Design: Single-center randomized double-blind controlled trial.

Participants/Setting: Patients with complete digital nerve transection underwent epinerial nerve repair. After coaptation of severed nerve ends, fine-wire electrodes were implanted before skin closure.

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Post-operatively, patients were randomized to either receive 1h of 20Hz continuous ES or sham-stimulation in a double-blinded manner.

Main Outcome Measure(s): Patients were followed monthly for 6 months by a blinded evaluator to monitor quantitative cold determination threshold (CDT) testing and a modified cold intolerance symptom severity questionnaire.

Results: A total of 36 patients were recruited with 18 in each group. Those in the ES group showed recovery advantage by 5 to 6 months postoperatively based on CDT (p=0.020). Modified cold intolerance symptom score comparison also showed improved cold intolerance in the ES group compared to controls (p=0.34).

Conclusions and Relevance: Physiologic and subjective results support improved cold stimulation sensitivity after nerve injury and repair when ES treatment is provided. ES may be an effective treatment for improving small-fiber cold sensory function in a broadened range of scenarios including digital and extremity replantation, composite tissue transplantation, as well as mixed motor and sensory nerve injury.
Urine I-FABP Predicts Acute Mesenteric Ischemia in Patients

Importance: Acute mesenteric ischemia (AMI) has a high morbidity and mortality and often presents as a diagnostic challenge. Currently there is no blood, urine or radiological tests that provide a definitive diagnosis of AMI.

Objective: The objective of this study was to evaluate the clinical accuracy of urine intestinal fatty acid binding protein (I-FABP) to diagnosis AMI.

Design: Prospective observational cohort study

Setting: Academic teaching hospital

Participants: Twenty patients referred to the Acute Care Surgery service at University of Alberta Hospital with suspected AMI, taken to the operating room for definitive diagnosis, were recruited.

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Pathological findings from surgical specimens confirmed a gold standard diagnosis of intestinal ischemia. The patients found to be non-ischemic became the internal controls.

Main Outcome Measure(s): Conventional clinical markers were examined in blood, i.e. WBC, lactate, and creatinine. Serum was examined by ELISAs for I-FABP and IL-6. Urine was examined at pre-operatively and post-operatively (at 6 and 24 hr) for I-FABP.

Results: Thirteen patients were pathologically diagnosed with AMI while five patients were non-ischemic. There was no difference in age or gender between ischemic and non-ischemic patients. There was no difference in serum lactate and creatinine between groups. Serum IL-6 levels in patients with AMI were significantly higher than non-ischemic controls (0.4±0.2 ng/mL vs. 0.2±0.0 ng/mL, respectively, p=0.03). There was a non-statistically significant increase in serum I-FABP in AMI patients compared to controls (9±3 ng/mL vs. 2.4±0.9 ng/mL, p=0.2). Urine I-FABP was significantly higher in patients diagnosed with AMI than in controls (7+1 ng/mL vs. 2+1 ng/mL, p=0.007). The receiver operating characteristic (ROC) illustrated that urine I-FABP discriminates between patients with AMI and controls (AUC 0.88, p=0.03).

Conclusions and Relevance: The traditional clinical markers of lactate and WBC were unable to differentiate AMI from non-ischemic bowel. However, we found that urine I-FABP was a non-invasive biomarker with high specificity and sensitivity for accurately diagnosing AMI. A non-invasive accurate tool for AMI would facilitate rapid treatment, while preventing unnecessary surgical interventions in high-risk patient populations.
FORMAL MENTORSHIP IN A SURGICAL RESIDENCY TRAINING PROGRAM: A PROSPECTIVE INTERVENTIONAL STUDY

Importance: Otolaryngology-Head and Neck surgery resident physicians (OHNSR) have a high prevalence of burnout, job dissatisfaction and stress as shown within the literature. Formal mentorship programs (FMP) have a proven track record of enhancing professional development and academic success. More importantly FMP have an overall positive impact on residents and assist in improving job satisfaction.

Objective: To determine the effects of a FMP on the well-being of OHNSR.

Design: Prospective Interventional Study

Setting: Otolaryngology-Head and Neck Surgery Residency Program

Participants: A FMP was established and all OHNSR participation was voluntary. 8 OHNSR participated in the program.

Intervention(s) for Clinical Trials or Exposure(s) for observational studies: Demographics, Perceived Stress Survey (PSS) and the Maslach Burnout Inventory (MBI) were administered at baseline and then at 3, 6, 9, and 12 month intervals. World Health Quality of Life Questionnaire (WHQOL) was administered at baseline and at 12 months.

Main Outcome Measure(s): Effects of FMP on burnout, stress, and quality of life as indicated by the PSS, MBI, and WHQOL.

Results: Baseline statistics found a significant burden of stress and burnout with an average PSS of 18.5 with a high MBI of 47.6, 50.6, and 42.5 for the emotion, depersonalization, and personal achievement domains respectively. Quality of life was also found to be low with a WHQOL score of 71.9. After implementation of the FMP, PSS was reduced to 14.5 at 3 months (p=0.174) and a statistically significant lower value of 7.9 at 12 months (p<0.0001). Participants were also found to have lower emotional scores (14.9, p<0.0001), levels of depersonalization (20.1, p=0.005), and personal achievement (16.5, p=0.005) on MBI testing at 12 months. Overall quality values using the WHQOL was also found to be significantly improved (37.5, P<0.0001) with statistically significant lower scores for the physical health (33.9, p<0.0001), psychological (41.1, p<0.0001), and social relationship (46.9, p<0.0001) domains.

Conclusions and Relevance: This is the first study to show that FMP can not only alleviate high levels of stress and burnout within a surgical residency program but also achieve higher levels of personal satisfaction as well as overall quality of life.
RESEARCH SUPPORT

The Department of Surgery is grateful to our partners in research for their support.

- Alberta Diabetes Institute (ADI)
- Alberta Innovates – Health Solutions (AIHS)
- Alberta Innovate – Technology Futures (AITF)
- Alberta Team Osteoarthritis
- Alberta Urology Institute
- CAMIS
- Canadian Institutes of Health Research (CIHR)
- Canadian National Transplant Research Program (CNTRP)
- Clinician Investigator Program (CIP)
- Covidien Canada
- Diabetes Research Institute Foundation (DRIF) Canada
- Edmonton Civic Employees’ Charitable Assistance Fund
- Edmonton Orthopaedic Research Committee
- Saudi Cultural Bureau
- University Hospital Foundation
- Women and Children Health Research Institute (WCHRI)

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