2019 FACULTY RESEARCH DAY
DEPARTMENT OF SURGERY

University of Saskatchewan

Saskatchewan Health Authority

"Any institution that relies on its clinical services alone without coincident medical research rarely gains distinction."

- Sir William Osler, 1895

Dr. Ivar Mendez

Fred H. Wigmore
Professor and
Provincial Head

Department of Surgery

University of
Saskatchewan
and
Saskatchewan Health
Authority

Research in the Department of Surgery is thriving. Our productivity has continued to increase year after year. This academic year the Department's research has attracted over 2.7 million dollars in research funding and 73 research papers were published by our faculty. Dr. Francisco Cayabyab has finished his tenure as a Research Director. He was instrumental in increasing research productivity and focused his attention to resident and faculty research. We thank him for all of his efforts. We also want to welcome our new Research Director, Dr. Daryl Fourney, from the Division of Neurosurgery, who will be taking the helm of research in the Department.

We are convinced that research is fundamental to our ability to provide the best surgical care to the Province of Saskatchewan and its' people. Our Department is at a forefront of academic productivity at the College of Medicine and has integrated clinical and basic research as a core mission of surgery at the Saskatchewan Health Authority.

This year during the annual faculty research banquet, we will be featuring the videos of 5 of our faculty members that are doing exciting research both at the laboratory bench and in the clinical setting.

This year's Faculty Research Day promises to be exciting as 18 faculty members from all of the Divisions of the Department will be presenting their scientific papers. I want to take this opportunity to thank all the members of the Department of Surgery for their commitment to research and for supporting our faculty members, residents and students in advancing knowledge in surgery.

The Department of Surgery has thrived as a key innovator and proponent of interdisciplinary research, teaching and collaboration with diverse communities in the Province of Saskatchewan. Our programs have produced not only excellent surgeons and clinicians, but also skilled researchers. As the new Director of Research, I am eager to promote our Department's vision to lead Canada's innovation in surgery-related basic science and clinical-translational research. I want to leverage our strengths within each of the Divisions to enhance our research intensiveness and help facilitate a new level of success at the national and international level.

Our research output continues to grow over the years, as shown by increases in peer-reviewed Faculty publications, abstracts at national and international meetings, and success with highly competitive peer-reviewed grants. Our Faculty actively collaborate with premier local research at the Canadian Light Source and across Colleges and Departments at the University of Saskatchewan and the University of Regina.

Today's program will showcase just a small part of the exciting research activities around our Department, with topics that range across multiple specialties. Please take the opportunity to network with your colleagues to learn more about new technologies and ongoing investigations by Faculty.

I wish to thank all of the presenters today, as well as the judges and session chairs for their valuable contributions. I want to thank Dr. Michelle Clarke for joining us as Visiting Professor. I wish to thank my predecessor, Dr. Francisco Cayabyab for his leadership in Research within this Department. I would also like to thank members of the Surgery Research Committee and the support staff within Department of Surgery Research and Communications for coordinating and promoting such an excellent program. Finally, I wish to thank all of you for attending, listening, and collaborating as we share today's discoveries and look forward to tomorrow's innovations.

Dr. Daryl Fourney

Professor and
Director of Research

Department of Surgery
and
Division of Neurosurgery

University of
Saskatchewan
and
Saskatchewan Health
Authority

FACULTY RESEARCH AWARDS

2018 Award Recipients

Surgery
Faculty Research Day

Platform Presentations:

1st Prize	Hye Ji (Jay) Kim (Dr. Francisco Cayabyab)
2nd Prize	Dr. Mike Moser
3rd Prize	Dr. Daryl Fourney

2017 Award Recipients

Surgery
Faculty Research Day

Clinical Presentations:

1st Prize	Dr. Daryl Fourney
2nd Prize	Dr. Nael Shoman

Basic Science Presentations:

1st Prize	Dr. Jake Pushie (Dr. Michael Kelly)
2nd Prize	Elisabet Jakova (Dr. Francisco Cayabyab)

2019
SURGERY FACULTY RESEARCH DAY

November 14, 2019

Contents

Introduction

Saskatoon City Hospital
Asher Auditorium

08:00 - 08:20

BREAKFAST

08:20 - 08:25

WELCOME AND INTRODUCTIONS

Dr. Ivar Mendez
Fred H. Wigmore Professor & Provincial Head
Department of Surgery

Dr. Daryl Fourney
Professor & Director of Research
Department of Surgery

08:25 - 08:30

Premiere of Surgery Department Video

Session I

Saskatoon City Hospital
Asher Auditorium

CHAIR: Dr. Nathan Ginther

08:30 - 09:30

Session II

Saskatoon City Hospital
Asher Auditorium

CHAIR: Dr. Anthony King

9:30 - 10:20

Break 10:20 - 10:50

KEYNOTE SPEAKER

Saskatoon City Hospital
Asher Auditorium

10:50 - 11:50

THE SCIENCE AND ETHICS OF PRIMARY TUMOR SURGERY

Dr. Michelle J. Clarke

Professor of Neurosurgery & Science Professor of Orthopedics
Mayo Clinic of Medicine, Mayo Clinic
College of Medicine, Rochester, Minnesota

Science Program Director
Mayo School of Graduate Medical Education
College of Medicine, Rochester, Minnesota

Lunch
Foyer outside of Auditorium
Main Floor, Saskatoon City Hospital
11:50 - 13:00

Dr. Clarke studies spinal column and spinal cord tumors from a clinical and translational research perspective, focusing on novel surgical techniques and optimizing patient outcomes. This includes multicenter and multidisciplinary prospective and collaborative projects on rare primary tumors of the spine.

Focus Areas:

- **Primary spinal column tumors.** Dr. Clarke contributes to a multi-institutional study of rare primary spinal column tumors, their treatment, outcome and effect on patient quality of life. Specifically, this work focuses on optimizing multimodality treatment delivered in a collaborative environment.
- **Degenerative spine disease.** An additional area of focus is the delivery of high-quality, timely and cost-effective care for degenerative spine disease through the use of quality-of-life metrics.
- **Tumor treatment.** Dr. Clarke also studies intradural and spinal cord tumor treatment, with multi-institutional collaboration.

Significance to Patient Care:

Dr. Clarke's hope is that through her research, better tools will be developed to counsel and treat patients suffering from spinal cord or spinal column tumors. She aims to understand the causes, study improvements to treatment, and determine the best method of treatment delivery for these rare and unusual tumors.

Dr. Michelle Clarke

Professor of Neurosurgery & Science
Professor of Orthopedics, Mayo Clinic of Medicine

Science Program Director, Mayo School of Graduate Medical Education

Mayo Clinic, College of Medicine, Rochester, Minnesota

Session III

Saskatoon City Hospital
Asher Auditorium

CHAIR: Dr. Silvana Papagerakis

13:00 - 14:00

Break 14:00 - 14:20

Session IV

Saskatoon City Hospital
Asher Auditorium

CHAIR: Dr. Brian Ulmer

14:20 - 14:50

Closing Remarks 14:50 - 15:00

2019
SURGERY FACULTY RESEARCH DAY
BANQUET

Sheraton Cavalier
Top of the Inn

Sheraton®

Reception
18:00

Dinner
19:00

Presentation of prizes:
Drs. Ivar Mendez & Daryl Fourney

Acknowledgments

The Departments of Surgery would like to thank the following individuals for serving as judges and sessions chairs for the 2019 Faculty Research Day.

Judges

Dr. Roland Auer
Professor
Department of Pathology & Laboratory Medicine
College of Medicine, University of Saskatchewan

Dr. Francisco Cayabyab
Professor, Department of Surgery
Neuroscience Cluster
College of Medicine, University of Saskatchewan

Dr. Michelle J. Clarke
Professor, Neurosurgery/Professor, Orthopedics
Program Director, Graduate Medical Education
College of Medicine, Mayo Clinic of Medicine & Science

Dr. Lissa Peeling
Associate Professor, Department of Surgery
Division of Neurosurgery
College of Medicine, University of Saskatchewan

Dr. Marek Radomski
Vice Dean, Research
College of Medicine, University of Saskatchewan

Session Chairs

Dr. Nathan Ginther
Assistant Professor, Department of Surgery
Division of General Surgery
College of Medicine, University of Saskatchewan

Dr. Anthony King
Associate Professor, Department of Surgery
Division of Orthopedic Surgery
College of Medicine, University of Saskatchewan

Dr. Silvana Papagerakis
Associate Professor, Department of Surgery
Division of Otolaryngology
College of Medicine, University of Saskatchewan

Dr. Brian Ulmer
Clinical Professor, Department of Surgery
College of Medicine, University of Saskatchewan
Saskatoon Area Lead, Saskatchewan Health Authority

2019

FACULTY RESEARCH DAY ABSTRACTS

Surgery

The Unsalvagable Radial Head in Patients 30 Years and Younger

Platform Presenter: Laura Sims

Division of Orthopedic Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
William Aibinder, University of New York Downstate Medical Center; Graham King, Western University; Kenneth Faber, Western University.

Rationale:
Concern exists regarding the use of radial head arthroplasty (RHA) in younger patients. This study sought to assess clinical, functional, and radiographic outcomes of RHA in patients 30 years of age and younger.

Methods:
A retrospective review identified 26 elbows that underwent a smooth stem modular RHA in patients 30 years and younger at a mean follow-up of 4.6 years. Mean age was 24.0 +/- 5.2 years. Indications were acute trauma in 13 and chronic pathologies in 13. Patients underwent clinical, functional, and radiographic evaluation.

Results:
Average Arc of motion was from 8˚ ± 14˚ to 136˚ ± 11˚. Sixteen patients had functional outcome scores available with a mean patient reported elbow evaluation (PREE) score of 27 ± 19, a mean QuickDASH of 20 ± 17, and a mean MEPI score of 85 +/- 13. Severe capitellar erosion was present in one (4%). Radiographic stem lucency was seen in all cases with 10 (38%) graded as severe. Four (15%) developed moderate to severe ulnohumeral arthritis, three of which were in the chronic reconstruction group. Two (8%) required reoperation, one for persistent instability and one for stiffness. For all measures, there were no clinically significant differences between acute and chronic patients.

Conclusion:
For acute trauma and challenging chronic conditions involving the radial head, a smooth stem modular RHA demonstrates reasonable early clinical and radiographic outcomes with a low reoperation rate in patients 30 years of age or younger. Osteoarthritis is common when used for post-traumatic conditions. Close follow-up and long-term outcomes are needed.

Funding Sources:
None

Facilitators and Barriers to Clinical Pathway Uptake and Utilization among Primary Care Providers in Saskatchewan – A Qualitative Study

Platform Presenter: Gary Groot

Division of General Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Terry Blackmore, Saskatchewan Ministry of Health; Donna Goodridge, University of Saskatchewan; Mahasti Khakpour, University of Saskatchewan; Leigh Kinsman, University of Tasmania/University of Newcastle; Joshua Lloyd, University of Saskatchewan; Shaliny Ollegasagrem, University of Saskatchewan; Adel Panahi, University of Saskatchewan; Thomas Rotter, Queen's University; Zane Tymchak, University of Saskatchewan.

Rationale:
Clinical Pathways (CPWs) are multidisciplinary, evidence-based, complex interventions designed to standardize care. In Saskatchewan (SK), development, implementation, and evaluation of these provincial CPWs (Hip & Knee, Spine, Pelvic Floor, Prostate Assessment, Fertility Care, Lower Extremity Wound Care, Bariatric Surgery, and Acute Stroke) present significant challenges, leading to lower uptake and utilization by Family Physicians (FPs).

Methods:
A qualitative study consisting of: one-on-one interviews with 8 key informants (KI) associated with design and implementation of CPW and a purposive sample of 5 focus groups (FGs) with 30 FPs practicing in Saskatoon, Regina, Prince Albert and Swift Current. Inductive, thematic analysis was used to identify facilitators and barriers to CPW uptake by FPs, which were structured based on Theoretical Domains Framework (TDF) for behavioral change.

Results:
KI interviews informed the FG interview guide. From 5 FG discussions, 51 themes emerged and were mapped under 14 TDF domains. Major barriers were: conceptual (unclear objectives); systems-level (lack of communication about existence/usage of CPWs); technical and resource related (administrative, access to local specialists); and socio-cultural (lack of FP engagement). Facilitators were recognized to mitigate barriers, and ranged from need for better IT services (i.e. Electronic Medical Record (EMR)), to optimism towards patient outcomes.

Conclusion:
Although there is ample evidence suggesting CPWs are effective in optimizing patient care, based on perceived facilitators and barriers, recommendations will be introduced to enhance uptake among FPs in SK. Furthermore, an innovative theory-based survey instrument will be developed based on these findings to further evaluate CPW throughout Saskatchewan.

Funding Sources:
Saskatchewan Health Research Foundation (SHRF), Saskatchewan Medical Association (SMA).

The HERG Potassium Channel Interaction with Transcription Factor STAT1 in Cancer: A Non-Torsadogenic Anti-Cancer Target

Platform Presenter: Francisco Cayabyab

Neuroscience Research Cluster, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Siyi He, Department of Surgery, University of Saskatchewan; Min Yong Jung, Department of Physiology, University of Saskatchewan; Le Gui, Department of Surgery, University of Saskatchewan; Veronica Campanucci, Anatomy Physiology and Pharmacology Department, University of Saskatchewan; Shareen Amin, Biochemistry Department, University of Regina; Mohamed Taha Moutaoufik, Biochemistry Department, University of Regina; Khaled A. Aly, Biochemistry Department, University of Regina; Mohan Babu, Biochemistry Department, University of Regina.

Rationale:
Most investigational new drugs fail to get FDA approval due to their cardiotoxicity side effects. The potassium channel HERG (human ether-a-go-go-related gene), a pharmacological target causing long QT syndrome, is aberrantly over-expressed in all types of cancers. We recently found that HERG functionally interacts with transcription factor STAT1 (signal transducer and activator of transcription 1). Here, we further investigated the functional consequences of HERG-STAT1 interaction in human breast, prostate and glioblastoma cancer cell lines.

Methods:
To determine whether HERG and STAT1 contribute to human cancer cell growth, we employed CRISPR/Cas9 genetic knockdown of HERG and/or STAT1 genes. Using molecular docking studies to determine potential overlapping amino acids and biochemical and confocal imaging microscopy to demonstrate a physical interaction between HERG and STAT1, we also studied the functional consequences of HERG-STAT1 protein -protein interaction with cell biological assays, including cell proliferation and electrophysiological assays.

Results:
Knockdown of HERG or STAT1 gene decreased HERG currents and cell proliferation of hormone-sensitive breast cancer cell lines. Using molecular docking simulation, we found that HERG and STAT1 were situated in close proximity at two sites (HERG(D609)-STAT1(H406); HERG(D509)-STAT1(H19)). Moreover, the Src-homology 2 (SH2) domain of STAT1 mediates coupling with HERG, as the STAT1 SH2 domain-derived peptide decreased HERG-STAT1 co-immunoprecipitation and colocalization. This peptide inhibitor decreased HERG current contribution to proliferation of only hormone-sensitive breast and prostate cancer cells. HERG-STAT1 interaction was notably undetectable in cardiac myocytes.

Conclusion:
Together these results suggest that HERG-STAT1 binding could serve as a novel HERG-directed anti-cancer therapy that does not promote torsadogenesis.

Funding Sources:
This research was funded by the NSERC, SHRF, CBCF and CFI to FSC.

Stem Cell Transplantation in Parkinson's Disease: Clinical Translation

Platform Presenter: Ivar Mendez

Division of Neurosurgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Damaso Sadi, Department of Surgery, College of Medicine, University of Saskatchewan; Aniket Kumar, Department of Surgery, College of Medicine, University of Saskatchewan; Jan-Eric Ahlfors, Fortuna Fix, Montreal, Quebec.

Rationale:
Parkinson's disease is characterized by the progressive degeneration of dopaminergic cells in the substantia nigra. As medical (L-Dopa) and surgical (Deep Brain Stimulation) approaches for the treatment of Parkinson's disease have limitations and do not address the loss of dopamine neurons, a cell replacement therapy to repair the brain makes sense. We have studied the potential of autologous reprogrammed stem cells to repair the brain in a rat model of Parkinson's disease.

Methods:
We tested 4 different batches of human stem cells derived from bone marrow and reprogrammed to become dopaminergic cells. This was done to refine a clinical grade cell to be used for a Phase I trial. Cells were implanted into the rat model of Parkinson's Disease. Animals were immunosuppressed with cyclosporin. All groups were tested for functional recovery with rotational behaviour. Histological analysis for surviving transplants was also conducted.

Results:
Significant functional recovery was observed in batch # 3 eight weeks after transplantation. This was correlated with surviving dopaminergic transplants that were positive for Tyrosine Hydroxylase in the host substantia nigra.

Conclusion:
This study has identified an ideal batch of human reprogrammed bone-marrow derived stem cells to be use on a Phase I clinical trial. This trial will be aimed at bringing an autologous stem cell strategy to brain repair in Parkinson's Disease.

Funding Sources:
CIHR-industry Grant

Examining Trends in E-cigarette Use and the Association with COPD among Canadians

Platform Presenter: Razi Mahmood

School of Public Health
University of Saskatchewan

Team Members/Affiliations:
Silvana Papagerakis, Division of Vascular Surgery, Department of Surgery, College of Medicine, University of Saskatchewan.

Rationale:
Tobacco use is the leading cause of premature death worldwide. Encouragingly, in Canada there has been decreasing trends in tobacco use, though with a corresponding increase in e-cigarette use. E-cigarettes may pose detrimental health effects and may result in tobacco initiation, thus, potentially circumventing current tobacco prevention efforts. Chronic obstructive pulmonary disease of which tobacco use is identified as the dominant cause is expected to become the third leading cause of death worldwide by 2030. Studies examining e-cigarette vapor's in-vitro provide evidence that e-cigarette use may impact airway inflammation, potentially leading to the development of COPD.

Methods:
The Canadian Tobacco, Alcohol and Drugs (CTADS) survey conducted by Statistics Canada on behalf of Health Canada was used to examine trends in e-cigarette usage among Canadians. We used past 30-day e-cigarette use and ever e-cigarette use as our outcome variable stratified by age and sex. The Canadian Community Health Survey (2015/2016) was used to examine whether there is an association between e-cigarette use and COPD. Past 30-day e-cigarette use was the outcome measure and the primary predictor variable was COPD status. Analysis was conducted using SAS 9.4 and we developed a logistic regression model.

Results:
Preliminary results indicate that there have been increasing trends in e-cigarette use, especially among youth. Males have increased rates of e-cigarette use; the increasing trend is also seen among women.

Conclusion:
In our unadjusted model, we found that past 30-day e-cigarette users were 3 times more likely to have COPD compared to non e-cigarette users.

Funding Sources:
Respiratory Research Centre at the University of Saskatchewan, Royal Hospital University Foundation Grant (SP)

Development of a Non-Invasive Biosensor for Salivary Diagnostics Linked to Circadian Clock Disorders

Platform Presenter: Silvana Papagerakis

Division of Otolaryngology, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Dr. Petros Papagerakis, College of Dentistry

Rationale:
A new approach in medicine that is predictive, preventive, personalized and participatory, holds great promise to reduce the burden of chronic diseases by harnessing technology and an increasingly better understanding of environment-biology interactions, evidence-based interventions and the underlying mechanisms of chronic diseases. Saliva is a distinctive biological fluid that contains a variety of molecular and microbial biomarkers that can be used to diagnose and monitor oral and systemic health status, disease onset and progression, and treatment outcome. Saliva protein content and their concentration depends on circadian rhythms regulation. Thus, circadian clock physiology must be taken into consideration for validating potential biomarkers for oral and systemic diseases. There is a major need for a real-time diagnostic device to allow for an accurate assessment of individual circadian rhythms in the era of precision health care.

Methods and Results:
We have patented an innovative intra-oral device that passively collects saliva at set time points during 24 hours. This is an important tool for the measurement of the circadian profile of salivary melatonin and any other disease-discriminatory salivary biomarkers in diagnostic applications in a given patient for health and disease surveillance, including for the diagnosis and monitoring of sleep disorders.

Conclusion:
Because saliva can be used for almost any omics application, our device has the potential to become the ideal tool for the non-invasive collection of clinical specimens for the emerging field of circadiomics, which studies the links between circadian clock disruption and acute and chronic disease in the era of precision medicine.

Funding Sources:
None

The Effect of Radiation Dose on Survival of Bacteria on Experimentally Infected Samples of Vascular Graft Material

Platform Presenter: David Kopriva

Division of Vascular Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Kylie Kvinlaug, Division of Vascular Surgery, Department of Surgery, College of Medicine, University of Saskatchewan; Monique Mayer, Small Animal Clinical Sciences, Western College of Veterinary Medicine; Anatoliy Trokhymchuk, Prairie Diagnostic Services; Warren Berry, Research and Performance Support, Saskatchewan Health Authority.

Rationale:
Current treatments for aortic vascular graft infection are associated with high morbidity and mortality. Various materials can be sterilized with radiation. This study aims to determine the dose of radiation that would be required to effect a meaningful decrease in bacterial burden on samples of vascular prosthetic graft.

Methods:
Samples of vascular graft material (Dacron) were inoculated with laboratory strains of Escherichia coli, Staphylococcus aureus, and Stapylococcus epidermidis and grown to stationary phase in tryptic soy broth. The samples were subjected to various radiation doses at the veterinary radiation oncology facility of the Western College of Veterinary Medicine. The post-irradiation samples of vascular graft material were quantitatively cultured to determine the bacterial survival, expressed in colony forming units per gram of vascular graft material. Data was fitted to dose response curves using R software.

Results:
Ninety percent (1 log) bacterial kill required a dose of approximately 75 Gray (Gy) for E. coli and S. epidermidis, 225 Gy for S. aureus. Ninety-nine percent (2 log) bacterial kill required approximately 325 Gy for S. epidermidis, 350 Gy for E. coli, and 425 Gy for S. aureus.

Conclusion:
Clinically relevant reductions in bacterial load on experimentally infected samples of vascular graft can be achieved with doses of 100 - 300 Gy.

Funding Sources:
CoMRAD grant (2018)

Complications of Arthroscopic Versus Open Biceps Tenodesis in the Setting of Arthroscopic Rotator Cuff Repairs: An Analysis of the ABOS Database

Platform Presenter: Jason Shin

Division of Orthopedic Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Dr. Marco Yeung, University of Pittsburgh; Dr. Bryson Lesniak, University of Pittsburgh; Dr. Albert Lin, University of Pittsburgh.

Rationale:
To compare complication rates between arthroscopic versus open biceps tenodesis in the setting of arthroscopic rotator cuff repair, and to determine the effect of relevant fellowship training on complication rates.

Methods:
The ABOS database was used to identify cases of arthroscopic and open biceps tenodesis in the setting of rotator cuff repair from 2012 to 2016. Surgical, medical and anesthetic complications, location, fellowship training, year of surgery and patient demographic data were recorded. Overall and specific complication rates were calculated and analyzed.

Results:
A total of 1725 cases of arthroscopic and 1637 cases of open biceps tenodesis with arthroscopic rotator cuff repair were analyzed. There was no significant difference between overall complication rates between arthroscopic (11.4%) versus open (13.1%) biceps tenodesis ($p=0.14$). While, open tenodesis had statistically significant higher rates of wound healing issues (0.7% vs 0.2%, $p=0.02$), hematoma/seroma formation (0.5% vs. 0.1%, $p=0.02$), and nerve injury (1.5% vs. 0.4%, $p<0.01$), these rates remain comparably low. With regards to medical and anesthetic complications, open tenodesis had significantly higher rates of deep vein thrombosis (0.49% vs. 0.12%, $p=<0.05$) and general anesthetic complications (0.75% vs. 0.06%, $p=0.03$). Shoulder arthroscopy fellowship-trained surgeons were more likely to perform arthroscopic biceps tenodesis than non-fellowship-trained surgeons ($p<0.01$) but had a significantly higher rate of complication ($p=0.01$).

Conclusion:
No differences were found in overall complication rates between open and arthroscopic biceps tenodesis techniques in the context of concomitant rotator cuff repairs. While open techniques had statistically significant higher rates of nerve injury, wound complications and hematoma/seroma formation, this may not necessarily reflect clinical significance as both techniques demonstrate complication rates of <2%.

Funding Sources:
None

Analysis of Thrombi from Acute Ischemic Stroke Patients

Platform Presenter: Vedashree Meher

Department of Health Sciences
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Roland N. Auer, Department of Pathology and Laboratory Medicine, College of Medicine, University of Saskatchewan; Dr. Michael E. Kelly, Department of Surgery, College of Medicine, University of Saskatchewan; Dr. Lissa Peeling, Department of Surgery, College of Medicine, University of Saskatchewan.

Rationale:
Blood clots are the primary cause of ischemia. Randomized control trials have proven the superiority of endovascular therapy (EVT) over other therapeutic options for patients with ischemic stroke. However, even with EVT, recanalization is only obtained in 70-80% of the patients. Defining clot characteristics may help us better stratify treatment options and achieve good clinical outcomes. The goal of this project was to correlate compositional results with interventional and clinical outcomes. We hypothesized that fibrin-rich clots trapped heavy biological elements, making it difficult to retrieve them, consequently resulting in poor recanalization and clinical outcomes.

Methods:
Freshly retrieved cerebral clots from ischemic stroke patients were analyzed using X-ray fluorescence imaging (XFI) to map the distribution of elements (Cl, K, S, Zn, Fe, I), in combination with conventional histology to characterize platelets, leukocytes, neutrophils, erythrocytes, and fibrin.

Results:
Retrospective XFI analysis revealed that fibrin-rich clots and clots originating from the proximal arteries were more pervious to the contrast agent (I) than erythrocyte-rich clots and clots originating from the heart. Furthermore, XFI results showed that poor outcomes were associated with high Cl and K. Histological results showed that patients with improved recanalization outcomes had clots composed of significantly higher proportions of erythrocytes than fibrin ($p = 0.001$); however, histological composition of clots did not affect the choice of EVT device used for achieving good outcomes.

Conclusion:
Characterizing thrombus composition, identifying appropriate targets, and correlating these findings with clinical information are key steps in improving our understanding of stroke treatment outcomes.

Funding Sources:
The Heart & Stroke Foundation, the Saskatchewan Health Research Foundation, as well as the University Of Saskatchewan, College Of Medicine, for the Clinical Stroke Research Chair awarded to M.E.K; The University Of Saskatchewan College Of Medicine Research Award (CoMRAD) awarded to L.P; Health Sciences Scholarship from the College of Medicine Health Sciences Graduate Program awarded to V.M.

Do Social Factors Mediate the Sensory-Cognitive Associations in Older Adults in the Canadian Longitudinal Study on Aging?

Platform Presenter: Paul Mick

Division of Otolaryngology, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Dr. Anni Hämäläinen, School of Optometry, Université de Montréal; Dr. Natalie Phillips, Department of Psychology, Concordia University; Dr. Walter Wittich, Department of Psychology, University of Toronto; Dr. M. Kathleen Pichora-Fuller, Department of Psychology, University of Toronto.

Rationale:
Sensory and cognitive function both tend to decline with increasing age. Sensory impairments are risk factors for age-related cognitive decline and dementia. One hypothesis about sensory-cognitive associations is that sensory loss results in social isolation which, in turn, is a risk factor for cognitive decline.

Methods:
We tested whether social factors are associated with cognitive and sensory function, and whether sensory-cognitive associations are mediated by social factors. We used cross-sectional data from 30,029 participants in the Canadian Longitudinal Study of Aging, aged 45-85 years, who had no reported cognitive impairment or diagnosis of dementia.

Results:
We found strong independent associations of self-reported social variables with hearing (pure-tone audiometry), vision (pinhole-corrected visual acuity), and executive function and weaker associations with memory. The mediating effects of social variables on sensory-cognitive associations were weak, but social factors could be slightly more important for females and older people. Partial retirement (relative to full retirement or not being retired) may have protective effects on cognition in the presence of hearing loss.

Conclusion:
These findings confirm the association between social factors and sensory and cognitive measures. However, support is weak for the hypothesis that social factors shape sensory-cognitive associations.

Funding Sources:
This research was made possible using the data/biospecimens collected by the Canadian Longitudinal Study on Aging (CLSA). Funding for the Canadian Longitudinal Study on Aging (CLSA) is provided by the Government of Canada through the Canadian Institutes of Health Research (CIHR) under grant reference: LSA 9447 and the Canada Foundation for Innovation. The present research was conducted using the CLSA Baseline Comprehensive dataset version 3.2, under Application Number 160605. This specific study was funded by a Catalyst grant from the Canadian Institutes of Health Research (#373228) and the Réseau Québécois de Recherche sur le Vieillissement (RQRV).

Re-examining Our Understanding of the Brain's Organization: Atypical Findings in fMRI and DTI

Platform Presenter: Layla Gould

Division of Neurosurgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Michael Kelly, Division of Neurosurgery, Department of Surgery, College of Medicine, University of Saskatchewan; Ron Borowsky, Department of Psychology, College of Arts and Science, University of Saskatchewan; Marla Mickleborough, Department of Psychology, College of Arts and Science; Hamid Dabirzadeh, Department of Medical Imaging, College of Medicine, University of Saskatchewan; Tasha Ellchuk, Department of Medical Imaging, College of Medicine, University of Saskatchewan; Josh Neudorf, Department of Psychology, College of Arts and Science; Shaylyn Kress, Department of Psychology, College of Arts and Science.

Rationale:
The presurgical neuroimaging team at RUH uses fMRI to localize functional brain regions near the surgical resection in patients undergoing surgery for various conditions, including epilepsy, tumours, cortical and vascular malformations, and other lesions, in order to avoid disrupting cognitive processes. Our team also uses diffusion tensor imaging (DTI) to visualize white matter tracts in order to see whether tracts are being displaced from a lesion or intimately associated with a mass. The surgeon can use this information to create a surgical plan that will preserve as many of the white matter tracts as possible.

Methods:
We scanned patients in a Siemens 3Tesla MRI. The patients wear goggles while in the MRI in order to view the fMRI paradigms. Our team plans the fMRI tasks based on the location of the surgery and what brain regions underlie cognitive functions.

Results:
This presentation will discuss cases in which the presurgical fMRI and DTI revealed atypical or unexpected findings, which hightlights the importance of using fMRI and DTI for preoperative planning. These unexpected findings can also guide neuronavigation and direct cortical stimulation during craniotomies.

Conclusion:
Performing presurgical fMRI and tractography is valuable for assessing the risk of therapeutic interventions, selection of patients for intraoperative mapping, and guiding brain surgery. In combination with DTI, these techniques reduce postoperative morbidity and therefore hospitalization time. In cases in which brain activation or white matter is in an unexpected region, these techniques become even more valuable.

Funding Sources:
Saskatchewan Health Research Foundation (SHRF); Medtronic, Inc.

Zapping Tumors with the NanoKnife (IRE): Clinical Results and Collaborative Research Underway in Saskatchewan

Platform Presenter: Mike Moser

Division of General Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Shahid Ahmed, Sask Cancer Centre; Gavin Beck, Department of Surgery, College of Medicine, University of Saskatchewan; Yigang Luo, Department of Surgery, College of Medicine, University of Saskatchewan; Maurice Ogaick, Department of Surgery, College of Medicine, University of Saskatchewan; John Shaw, Department of Surgery, College of Medicine, University of Saskatchewan; Chris Wall, Department of Radiology and Diagnostic Imaging.

Rationale:
Irreversible Electroporation (IRE) or NanoKnife ® is a relatively new technology for ablating (destroying) tumors. It is unique in that there is no collateral injury to nearby blood vessels, ducts, and bowel. Saskatchewan has one of only 3 NanoKnife machines in Canada.

Methods:
Retrospective review of patients with liver and pancreas malignancies treated with IRE in our program and report on the research in IRE that is underway, including collaborations with Biomedical Engineering, Immuno-oncology, and Chemistry.

Results:
Between March 2017 and September 2019, our team performed 16 IRE in 15 patients with pancreatic cancers and 6 IRE in 5 patients with unresectable liver tumors. The average age was 65 years, and the mean tumor diameter was 2.7 cm. For patients treated with IRE for pancreatic cancer, the median survival from the time of IRE was 25.2 months, a marked improvement over the historically quoted 9-12 months survival for unresectable pancreatic cancer. For patients treated with IRE for unresectable liver cancers, median survival was 36.2 months from the time of IRE. There were 3 mild (Clavien-Dindo grade 1 or 2) complications and no severe (grade 3,4, or 5) complications.

Conclusion:
IRE appears to provide an oncologic benefit to our patients and can be done safely at our center. Several research collaborations are looking at ways of improving the oncologic effect and increasing the treatment zone to allow for larger tumors to be treated while maintaining the safety of IRE.

Funding Sources:
St. Paul's Hospital Foundation; Saskatchewan Health Research Foundation; Royal University Hospital Foundation

A Novel Neurophysiological Theory of Down Syndrome

Platform Presenter: Jonathan Norton

Division of Neurosurgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Shannon Haugian, College of Medicine, University of Saskatchewan; Salah Almubarak, Pediatric Neurology, Department of Pediatrics, College of Medicine, University of Saskatchewan; Dr. Roland Auer, Department of Pathology, College of Medicine, University of Saskatchewan.

Rationale:
Down syndrome presents with a variety of neurological features along with the more widely recognized facial morphology and cardiac issues.

Methods:
Stimulation amplitude for intraoperative motor evoked potentials and somatosensory evoked potential amplitude were compared between healthy, age-matched controls and individuals with Down Syndrome. Local (Saskatoon and Edmonton) patients were included with a US-based database of intraoperative data, leading to 1572 paired subjects. Coherence measures the similarity between two signals in the frequency domain, it is akin to cross-correlation in the time domain. Coherence analysis using custom written code was performed on both EEG and EMG data from 3 subjects, and compared to healthy controls (EMG) and epileptic patients (EEG).

Results:
The results for Downs Syndrome and controls, respectively, are as follows: MEP Stimulation Voltage: 174 ±21V vs. 650±32V; SSEP Amplitude: 52±3μV vs. 4.2±0.8μV; EEG Coherence: 2.14Hz vs. 0.65Hz, and EMG Coherence: 1.466Hz vs. 0.1407Hz.

Conclusion:
There is a wide spectrum of neurological features associated with Down Syndrome. All of these features may represent a common underlying pathophysiological feature and indicate a hyperexcitability, specifically in cortical tissue. In particular coherence relies on very tight coupling between originating cells. We therefore propose that there may be a prevalence of gap junctions in the cortical cells of individuals with Down Syndrome. Gap junctions allow for instantaneous transmission of electrical signals, which would permit high levels of coherence and hyperexcitability of cortical tissue.
The clinical implications of this remain unclear. We are currently seeking post-mortem tissue for electron-microscopic examination.

Funding Sources:
None. Data was from the USA supplied from Specialty Care (Dr. Cohen).

Repurposing the FDA-approved Anti-epileptic agent Perampanel for Stroke Therapy

Platform Presenter: Michael Zaki

Neuroscience Research Cluster, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Dr. Francisco Cayabyab, Neuroscience Research Cluster, Departments of Surgery, College of Medicine, University of Saskatchewan.

Rationale:
Ischemic stroke is followed by rapid increase in extracellular concentrations of glutamate in both ischemic core and penumbra. This elevated glutamate leads to Ca2+ overload and neurotoxicity, which is widely believed to be mediated by excessive activation of NMDA and AMPA receptors (AMPARs). Therefore, we hypothesize that blocking AMPARs with the clinically approved non-competitive AMPAR antagonist Perampanel should ameliorate neuronal damage and behavioral deficits in an animal model of focal cerebral ischemia.

Methods:
Pial vessel disruption (PVD) is a unique model of small vessel stroke in male Sprague-Dawley rats developed in our lab. Perampanel (3mg/kg body weight) was administered intraperitoneally 1 hr after surgery for 3 consecutive days. On day 3, we performed behavioral analyses to assess levels of post-stroke anxiety and memory deficits. On day 4, animals were euthanized and brains were subsequently analyzed for chemically induced long term potentiation (cLTP) using electrophysiology and confocal imaging for propidium iodide (PI)/FluoroJade C (FJC) staining for cell damage/ neurodegeneration. In addition, we assessed the contribution of pro-inflammatory and anti-inflammatory markers in neuronal damage.

Results:
We found that Perampanel significantly attenuated the PVD-induced anxiety-related behavior, cognitive impairment and LTP deficits. Moreover, Perampanel-treated rats showed significantly less hippocampal neuronal cell death and neurodegeneration. Finally, Perampanel prevented both the elevation of pro-inflammatory markers (TNF-α, NO synthase) and suppression of the anti-inflammatory markers (TGF-β1, IL-4) 72 hr following PVD.

Conclusion:
The clinically approved Perampanel showed neuroprotective translational potential in our pre-clinical animal model of cerebral ischemia.

Funding Sources:
SHRF, Heart and Stroke Foundation of Canada, NSERC and UGS (University of Saskatchewan Graduate Scholarship).

Expanding Our Understanding of the Cellular and Tissue Level Changes Following Ischemic Stroke

Platform Presenter: Jake Pushie

Division of Neurosurgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Nicole Sylvain, Department of Surgery, University of Saskatchewan; Huishu Hou, Department of Surgery, University of Saskatchewan; Dr. Michael Kelly, Department of Surgery, University of Saskatchewan.

Rationale:
Our team has developed a multi-modal imaging platform to characterize animal models of ischemic stroke. We have established 3 unique methods of inducing ischemic stroke in mice and characterized each with our imaging methods. Multi-modal imaging is employed to expand our understanding of the changes within the post-stroke brain.

Methods:
We employ synchrotron-based X-ray fluorescence imaging to map the elemental distribution in brain tissue sections. This quantitative technique can simultaneously image P, S, Cl, K, Ca, Mn, Fe, Cu, and Zn throughout an entire brain section. Fourier transform infrared imaging is also used to map multiple biomolecular markers and metabolites in adjacent brain sections. These advanced imaging techniques are combined with conventional histology and immunohistochemistry, providing our team with a true multi-modal platform for stroke neuroimaging.

Results:
Data clustering methods allow us to statistically differentiate unaffected brain tissue from the infarct and the penumbra. This allows us to quantify the volume of potentially rescuable brain tissue, as well as quantitatively assess treatment efficacy based on these volumes. Trends in elemental levels, biomolecules, and metabolic markers reveal that post-stroke changes in the brain are non-local and that the affected tissue rapidly equilibrates with the relatively larger total blood volume.

Conclusion:
Our multi-modal imaging has expanded our understanding of the scale and breadth of changes in the post-stroke brain. Current stroke dogma describes the cellular-level changes as being confined to the affected cells and their immediate extracellular environment. We have recently reported that this picture inadequately depicts post-stroke changes as a 'local' event, however, our results reveal that these changes occur on a much larger scale that is governed by complex diffusion-mediated equilibria between multiple compartments.

Funding Sources:
Heart and Stroke Foundation; University of Saskatchewan College of Medicine

The Novel Rip-Stop Suture Pattern is Superior to the Traditional Suture Bridge for Arthroscopic Rotator Cuff Repair (RCR): A Matched Cohort Study

Platform Presenter: Jeremy Reed

Division of Orthopedic Surgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Zachary Oleynik, College of Medicine, University of Saskatchewan; Mitchell Thatcher, College of Medicine, University of Saskatchewan; Dr. Megan Dash, Department of Family Medicine, College of Medicine, University of Saskatchewan.

Rationale:
Anecdotally the author's novel "rip-stop" (RS) suture technique, initiated in January 2017, for RCR was superior in terms of failure rate. This study set out to quantify, and prove or disprove, that suspicion.

Methods:
A matched cohort study drawing data from a chart review and patient phone interviews. The primary outcome was failure rate of RCR. The secondary outcomes were patient satisfaction with procedure (Sane score) and patient function following the procedure.

Results:
A cohort of 93 rip-stop patients with more than 1yr f/u was identified via EMR. We were able to match to 77 patients from the pre-ripstop group to the RS based on age (10 year strata) and tear size. 77 patients were eligible for study in each group after matching. No difference in groups in terms of age (61+/- 9, p=0.17) or tear size (large 37% vs. 57% in RS group, p=0.156), or sex (65% male in traditional, 72% male in RS, p = 0.271). The RS group demonstrated a significant decrease in failure rate over the traditional technique (RS - 2/77, 2.6%, traditional 10/77, 13%, p=0.017).

Conclusion:
Although it cannot be declared conclusive due to it's retrospective nature, this study demonstrates strong evidence that the rip-stop suture technique is superior to traditional suture bridge techniques in terms of failure rate. In the practice of the author it has proven itself as safe, cost neutral, and relatively easy to perform for an experienced arthroscopist.

Funding Sources:
U of S Dean's Project

Novel Wistar Rat Model of Progressive Parkinson's Disease with Unilateral Lesion of Substantia Nigra with Selective Adenosine A1 Receptor Agonist

Platform Presenter: Elisabet Jakova

Neuroscience Research Cluster, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
Damaso Sadi, Laboratory Technician, Department of Surgery, College of Medicine, University of Saskatchewan; Aniket Kumar, Postdoctoral Fellow, Department of Surgery, College of Medicine, University of Saskatchewan; Dr. Ivar Mendez, Department of Surgery, College of Medicine, University of Saskatchewan; Dr. Francisco Cayabyab, Department of Surgery, College of Medicine, University of Saskatchewan.

Rationale:
The majority of in vivo Parkinson's disease (PD) models focus only on understanding the late-stage processes of dopaminergic neuron depletion and Alpha-Synuclein (α-Syn) aggregation. A new immediate approach is needed to comprehend the early pathogenesis of the disease, specifically the early stages of α-Syn misfolding.

Methods:
Our team has been looking at adenosine signalling for over 10 years, and recently discovered using in vitro techniques that adenosine could lead to the misfolding patterns of α-Syn. In our in vivo animal studies, a 7-day i.p. injection of Sprague-Dawley rats with a vehicle control, N6-Cyclopentyladenosine (CPA, adenosine A1 agonist), or 1,3-dipropyl-8-cyclopentylxanthine (DPCPX, A1 antagonist) + CPA revealed animal behavioural abnormalities consistent with hippocampal-dependent spatial memory deficits, heightened depressive-like behaviour and motor deficits in the CPA-treated groups. Co-administration of DPCPX and CPA attenuated such behavioural abnormalities. Immunohistochemical and confocal imaging analyses revealed neurotoxicity not only in the hippocampus but also more prominently in the substantia nigra (SN) after CPA treatments. We then tested whether unilateral intracerebral infusion of CPA produced similar neurodegeneration in the SN of Wistar rats.

Results:
After 3, 6, and 12 weeks following the initial CPA infusion, behavioral tests were conducted to characterize motor function. CPA caused unilateral lesioning of SN, which was accompanied by motor deficits and reduced tyrosine hydroxylase staining of SN.

Conclusion:
Uilateral lesioning of SN with CPA could be a helpful model to elucidate the early cellular mechanisms of PD, which involves the adenosine A1 receptor signalling pathway.

Funding Sources:
This research was funded by the NSERC, SHRF, HSFC and CFI to FSC.

Traumatic Spinal Cord Injuries among Aboriginal and Non-Aboriginal Populations of Canada: A Prospective Outcomes Study

Platform Presenter: Daryl Fourney

Division of Neurosurgery, Department of Surgery
College of Medicine, University of Saskatchewan

Team Members/Affiliations:
S. Uzair Ahmed, Division of Neurosurgery, Department of Surgery, University of Saskatchewan; Carly Rivers, Rick Hansen Institute; Suzanne Humphreys, Rick Hansen Institute; Lucy Liu, Division of Neurosurgery, Department of Surgery, University of Saskatchewan

Rationale:
People of Aboriginal (Indigenous) ancestry are more likely to suffer traumatic spinal cord injury (TSCI) compared to other Canadians; however, outcome studies are limited. This study aims to compare the Canadian Aboriginal and non-Aboriginal populations with acute TSCI with respect to pre-injury baseline, injury severity, treatment, outcomes, and length-of-stay characteristics.

Methods:
We completed a retrospective analysis of 3478 participants with TSCI enrolled in the prospective Rick Hansen Spinal Cord Injury Registry (RHSCIR) from all sites Canada between 2004 and 2018. Demographic, injury, and management data was assessed to identify any differences between the populations.

Results:
Of the participants, 166 (4.8%) were identified as Aboriginal, and 3312 as non-Aboriginal. Aboriginal participants were younger, had fewer medical comorbidities, and had similar severity of neurological injury and similar clinical outcomes compared to non-Aboriginal participants. Aboriginal participants were more likely to suffer TSCI as a result of assault than non-Aboriginals (12.0% vs 3.5%). Aboriginal participants were more likely to be injured in a rural setting, and to be discharged to a rural location ($p<.0001$). Aboriginal participants had 21.4% longer stays in acute care ($p=0.0377$).

Conclusion:
This study provides a snapshot of the landscape of TSCI in Aboriginal patients in Canada. Given the significant rural disease burden of TSCI for Aboriginal patients, better allocation of resources for transition to the community for Aboriginal peoples with TSCI should be a priority.

Funding Sources:
Rick Hansen Institute, Vancouver, British Columbia

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