UNIVERSITY OF SASKATCHEWAN
College of Medicine
DEPARTMENT OF PATHOLOGY AND LABORATORY MEDICINE
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The 5th Department Research Day

Department of Pathology & Laboratory Medicine

University of Saskatchewan College of Medicine

November 4, 2024

Event Location: Louis' Loft UofS Campus

Date & Time: 0900-1600. Nov 4 2024

This event showcases innovative research in medical science, including advanced topics in Pathology & Lab Medicine.

Welcome Message from the Provincial Head

It is my distinct pleasure to welcome you to the 2024 Department Research Day, an event dedicated to celebrating the remarkable research, scholarly accomplishments and collaborative spirit of our faculty, residents, and trainees. Today, we come together to recognize the hard work and dedication of our colleagues and to explore a diverse range of topics that showcase the innovative and impactful research being conducted within the Department of Pathology and Laboratory Medicine.

Our Research Day has become a cornerstone of the department's commitment to academic excellence, fostering a culture of inquiry, and advancing patient care through clinical and translational research. This year's program highlights contributions from our talented faculty and trainees, spanning various fields of study and emphasizing the interdisciplinary nature of our work. Each presentation embodies our shared vision of pushing the boundaries of knowledge in pathology and laboratory medicine, ultimately leading to enhanced diagnostics, improved clinical outcomes, and a deeper understanding of human health and disease. We are honored to welcome Dr. Vijayanda Kundapur, Medical Director of the Saskatoon Cancer Agency, as our plenary speaker. His insights and ground breaking research will inspire us all and set the stage for a day of stimulating discussions and knowledge sharing.

This event would not have been possible without the dedication and hard work of our 2024 Research Day Planning Committee members: Dr. Fang Wu, Dr. Jay Kalra, Dr. Ahmed Mostafa, Dr. Camille Hamula & Dr. Pramath Kakodkar and Dr. Mark Milne. I would also like to express my sincere gratitude to our event moderators: Dr. Roland Auer, Dr. Camille Hamula & our esteemed judges, who have graciously volunteered their time and expertise to evaluate the UGME Graduate Students and PGME trainee presentations: Dr. Areej Khatib, Dr. Donna Ledingham, Dr. Viktor Zherebitskiy, Dr. Rani Kanthan, Dr. Oksana Prokopchuk-Gauk, Dr. Roland Auer, Dr. Yanwei Xi and Dr. Alysa Poulin.

Research Day is not only a celebration of academic achievements but also a platform for sparking new ideas, fostering collaborations, and building connections across our department and beyond. Together, we can advance the science of pathology and laboratory medicine, translating discoveries into clinical practice to improve the lives of our patients.

Warm regards

Dr. J. Fergall Magee
Provincial Department Head, Pathology and Laboratory Medicine
University of Saskatchewan & Saskatchewan Health Authority

Research Day Schedule

Session 1: Research Day Opening Remarks 9:00-9:10

9:00 - 9:05: Dean, College of Medicine, Opening Remarks **–Dr. Sarah Forgie**

9:05 - 9:10: Provincial Department Head Opening Remarks- **Dr. Fergall Magee**

Session 2: Plenary Presentation 9:10-9:35

9:10 – 9:35: Dr. Vijay Kundapur - Saskatoon Cancer Centre
Presentation Title: What is mini beam radiation and what is the impact on cancer management?

Session 3: Faculty Presentations 9:35-11:30
Moderator: Dr. Roland Auer

9:35 - 09:50: Dr. Oksana Prokopchuk-Gauk
Presentation Title: Albumin Utilization and Appropriateness: A Provincial Healthcare Quality Improvement Project

9:50 - 10:05: Dr. Oksana Prokopchuk-Gauk
Presentation Title: Albumin Utilization and Appropriateness: A Prescriber's Perspective

10:05 -10:20: Dr. Heather Panchuk
Presentation Title: Physician Blood Transfusion Orders and Compliance with the Standards: Results of a Single-Centre Audit

10:20 - 10:35:Dr. Kris Barreto
Presentation Title: Near Infrared Imaging Human EGFR Positive Lung Cancers Using IRDye800CW-nimotuzumab

10:35 - 11:00: Coffee Break

11:00 - 11:15: Dr. Yanwei Xi
Presentation Title: Implementation of Pharmacogenomic DPYD-guided Fluoropyrimidine Dosing for Cancer Patients in Saskatchewan

11:15 - 11:30: Dr. Claire Carson
Presentation Title: Retrospective Analysis and Clinical Performance of BD MAX Enteric Pathogen Testing at a Canadian Tertiary Care Center

11:30 - 11:45: Dr. Nick Baniak
Presentation Title: Utilization of TRIM63 in the Distinction of Gynecologic PEComas from Leiomyomas and Leiomyosarcomas

Session 4: PGME Presentations 11:50-14:20
Moderator: Camille Hamula

11:50 - 12:00 Dr. Bryan Johnston
Presentation Title: The Pacinioma Puzzle: Rare Lesion, High Stakes—Unlocking the Enigma of Cutaneous Stigmata, Spinal Dysraphism, and Tethered Cord Syndrome

12:00 - 12:10 Dr. Joel Scott
Presentation Title: Reducing Unnecessary Thyroid Function Testing Through Optimizing Test Ordering Protocols

12:10 - 12:20 Dr. Javera Tariq
Presentation Title: Homologous Recombinant Deficiency Does Not Share the Morphologic Surrogates of BRCA-mutated Ovarian Cancer Patients

12:20 - 12:30 Dr. Dan Zhang
Presentation Title: Comparative Analysis of eGFR Estimation: Performance of the CKD-EPI_2021 vs. Race-independent 2009 CKD-EPI Equations in a Local Population

12:30 - 13:00: Lunch Break

13:00 - 13:10: Dr. Richard Zhu
Presentation Title: A Rare Presentation in a Patient Previously Treated for Hodgkin's Lymphoma

13:10 - 13:20: Dr. Pramath Kakodkar
Presentation Title: Pilot Study: Innovative Application of Optical Genome Mapping for Alpha-Thalassemia Diagnosis.

13:20 - 13:30:Dr. Henry Pan
Presentation Title: Utility of Cytomegalovirus (CMV) and Mycobacterium Tuberculosis (MTB) Molecular Detection on Formalin-Fixed Paraffin-Embedded (FFPE) Tissue; From Pathology to Patient

13:30 - 13:40:Dr. Yayuan Zhao
Presentation Title: Human Leukocyte Antigen antibody profile and COVID-19 Vaccination in Waitlisted Renal Transplantation

13:40 - 13:50:Dr. Ingrid Tam
Presentation Title: Upgrade Rate of Radial Scars/Complex Sclerosing Lesions on Core Needle Biopsies of the Breast: a single-institution study

14:00 - 14:10:Dr. Daniel Markewich
Presentation Title: Melanoma Sentinel Lymph Node Practice in a Multi-Institutional Canadian Study: Toward Establishing National Quality Indicators in the Pathologic Assessment of Sentinel Lymph Node Specimens for Melanoma Patients

14:10 - 14:20:Dr. Peter (JingYang) Xu
Presentation Title: An Intriguing Case of the Green Plasma

Session 4: Graduate Students& UGME Presentations 14:20 – 15:20
Moderator: Dr. Ahmed Mostafa

14:20 - 14:30: N. Daneshvar Baghbadorani (Graduate Student)
Presentation Title: A Novel Tumoroid model of Breast cancer to Profile Cancer stem cells

14:30 - 14:40: Dr. Bryan Johnston
Presentation Title: Leading with Quality: Enhancing Pathology Residency Training through Continuous Quality Improvement and Case-Based Learning

14:40 - 14:50: Jing Liu
Presentation Title: Personalized Medicine: The effect of tacrolimus level on kidney allograft rejection outcomes

14:50 - 15:00: Eric Wang
Presentation Title: Utilization of in Silico Analysis for Prediction of Graft Failure in Kidney Transplant

14:50 - 15:00: Brooke Heinbigner
Presentation Title: Defining the Grey Zone in Homologous Recombinant Testing in Ovarian Cancer – Using Bioinformatics to Determine Response to Precision Medicine

15:00 - 15:10: Hasan Jamil (virtual presentation)
Presentation Title: When Less is More: Analyzing Out-of-Control Vitamin Testing in Saskatchewan

15:00 - 15:20: Zoher Rafid-Hamed (virtual presentation)
Presentation Title: Quality Care and Patient Safety in Focus: Best Practice Guidelines for Medical Error Disclosure Across Canada

15:20 - 15:40: Coffee Break

Session 5: Award Announcement & Closing Remarks 15:40 – 16:00
Dr. Fergall Magee

2024 Research Day Planning Committee

Dr. Fang Wu (Co-Chair)
Dr. Jay Kalra (Co-Chair)
Dr. Ahmed Mostafa
Dr. Camille Hamula
Dr. Pramath Kakodkar
Dr. Mark Milne (Department Research Facilitator)

PGME Presentation Judges

Dr. Rani Kanthan
Dr. Areej Khatib
Dr. Donna Ledingham
Dr. Oksana Prokopchuk-Gauk
Dr. Viktor Zherebitskiy

Graduate Student & UGME Presentation Judges

Dr. Roland Auer
Dr. Alysa Poulin
Dr. Yanwei Xi

Awards

PGME Presentation Awards

Dr. Harry E. Emson Award – Best Senior Pathology Resident research presentation ($300)

Jack Adolph Award – Best Junior Pathology Resident research presentation ($200)

Dr. Lorne Massey Award – Best interdisciplinary research presentation ($200)

Graduate Student & UGME Presentation Awards

The Best Presentation Award ($100)

The Second Place Presentation Award ($100)

The Third Place Presentation Award ($100)

Plenary Speaker Bio

Dr. Vijayananda Kundapur

Dr. Kundapur is a Clinical Professor and currently working as a Staff Radiation Oncologist in Saskatoon Cancer Centre since 2006. He is the Medical Director for Quality Safety and Disease site groups for Saskatoon Cancer Centre. Dr. Kundapur, an Associate Member of the Department of Pathology & Laboratory Medicine, U of S College of Medicine since 2022, is a visiting Professor at the University of Manipal, India.

Besides being a clinician, he is also an avid researcher. Dr. Kundapur has authorships in three major practice changing intergroup studies. He created a small bowel displacement device to reduce treatment related long-term side effects on small bowel loops that has been accepted in many parts of the world. He holds a patent for a new form of a radiation delivery system called mini beam radiation which has shown huge promise in brain tumor treatment with over 70% tumor control while causing almost no side effects on the normal part of brain. Based on his work he is a member of Working Group created by the National Institutes of Health (NIH) called GLMF (GRID, Lattice Microbeam and Flash). He is hoping to bring this as a phase 1 human study.

Plenary Presentation Abstract

What is mini beam radiation and what is the impact on cancer management?

[1]Vijayananda Kundapur, [+2]Emina Torlakovic, [2]Roland Auer, [3]Gilbert Bigras.

[1]Saskachtachewan Cancer Agency, [2] Department of Pathology & Lab Medicine, University of Saskatchewan; [3]Department of Pathology & Lab Medicine, University of Alberta

Objectives: The main challenge in treating malignant brain neoplasms lies in eradicating the tumor while minimizing treatment related damage. Long-term treatment-related morbidity always accompanies tumor control which has significant impact on quality of life of the patient who has survived the cancer. Spatially fractionated radiation has the potential to achieve both cure and to avoid dreaded long-term sequelae. We have created a new clinical device which produces mini-beams on a linear accelerator, to provide a new type of treatment called mini-beam radiation therapy (MBRT). The objective of this study was to compare the treatment outcomes of MBRT versus standard radiation treatment (SRT), to evaluate the tumor response and the treatment-related changes in the normal brain.

Methods: Pet dogs with de-novo brain tumors were accrued for treatment. Dogs were randomized between standard fractionated stereotactic (9 Gy/3 fractions) radiation treatment vs. a single fraction of MBRT (26 Gy mean dose). Dogs were monitored after treatment for clinical assessment and imaging. When the dogs were euthanized, a veterinary pathologist assessed the radiation changes and tumor response.

Results: We accrued 16 dogs, 8 dogs in each arm. In the MBRT arm, 71% dogs achieved complete pathological remission. The radiation-related changes were all confined to the target region. Structural damage was not observed in the beam path outside of the target region. In contrast, none of the dogs in control group achieved remission and the treatment related damage was more extensive. Therapeutic superiority was observed with MBRT, including both tumor control and the normal structural preservation. The MBRT findings are suggestive of an immune related mechanism which is absent in standard treatment.

Conclusion: The first ever randomized study of MBRT of canine brain tumor has clearly shown the ability to achieve this goal. The results augur potential for conducting human studies with MBRT.

FACULTY ABSTRACTS

Abstract# 2024-DPR-1

Albumin Utilization and Appropriateness: A Provincial Healthcare Quality Improvement Project

Madeline Owens[1], Lindsey Zimmermann[1], Ryan Lett[1,2,3], **Oksana Prokopchuk-Gauk[1,2,4]**

[1] College of Medicine, University of Saskatchewan, [2] Saskatchewan Health Authority, [3]Deparment of Anesthesiology, Regina, [4]Department of Pathology and Lab Medicine, Division of Transfusion Medicine, Saskatoon.

Background: There are few evidence-based indications for albumin use in clinical care. Recently published audits of intravenous albumin utilization have identified that most albumin administered is for inappropriate indications. In the 2021/2022 fiscal year, Saskatchewan was found to have the highest rate of albumin use per capita in Canada. The aim of this study was to determine the distribution of albumin use and its appropriateness our tertiary care hospitals.

Methods: A multi-center retrospective chart audit was conducted on all patients who received albumin 5% and/or 25% transfusions in five hospital sites from two large urban centers (Centre 1 and Centre 2) between January 1-February 28, 2023. Data collected included patient demographics, the documented albumin dose and indication for use, prescriber specialty, and adverse reactions. Use was classified as appropriate if it was given for an evidence-based indication as listed in Transfusion Ontario's Bloody Easy 5. Data was merged for comparative statistical analysis.

Results: A total of 1235 albumin orders for 411 patients were reviewed; 661 orders were from hospitals in Centre 1 and 574 were from Centre 2. Overall, 91.0% of albumin 25% orders and 63.2% of albumin 5% orders were prescribed for inappropriate indications. Only 6.6% of albumin 25% orders at Centre 1 and 11.8% at Centre 2 were appropriate; however, 21.3% of albumin 5% orders at Centre 1 and 70.3% at Centre 2 were appropriate. At least 25% of all albumin orders were by General Internal Medicine physicians. Only one adverse transfusion event was reported during the study period.

Conclusions: Our study confirms that the majority of albumin transfused in Saskatchewan is for inappropriate indications, with Center 1 identified to have a greater rate of inappropriate albumin use. This audit identifies that development and implementation of strategies are required to improve albumin use appropriateness and reduce patient exposure to an unnecessary treatment.

Abstract# 2024-DPR-2

Albumin Utilization and Appropriateness: A Prescriber's Perspective

Stephanie Bigsby[1], **Oksana Prokopchuk-Gauk[1,2,3]**

[1] College of Medicine, University of Saskatchewan, [2] Saskatchewan Health Authority, [3]Department of Pathology and Lab Medicine, Division of Transfusion Medicine

Background: Albumin is a human plasma derived protein which may be used as a therapeutic intervention. Appropriate albumin utilization is essential to ensure patient safety and appropriate product stewardship. Recently, Saskatchewan has been identified as having the highest use of albumin per capita in Canada. This study aims to objectively assess the practices and perspectives of physicians as they relate to albumin use.

Methods: Survey questions were developed to explore key themes related to albumin 5% and 25% prescription. Questions were administered using the REDCap online survey platform. The survey link was disseminated by email via provincial Department Heads and published within the monthly Saskatchewan Medical Association newsletter. Submissions were collected over a 4-week period. Anonymized individual responses were analysed and reported in a descriptive manner.

Results: A total of 43 complete submissions were analyzed. Most respondents were from Saskatoon and Regina, and from Anesthesia and Internal Medicine specialties. The most common indications for prescribing albumin 5% included post-operative hypotension (50.0%) and sepsis (25.0%), neither of which are appropriate according to current clinical practice guidelines. The most common indications for albumin 25% included hepatorenal syndrome (66.7%), paracentesis >5L (52.4%), and spontaneous bacterial peritonitis (42.9%), which are supported by evidence. All respondents reported routinely obtaining transfusion consent; however 42.9% reported omitting discussion about adverse reactions to albumin prior to its administration. Prescribing practices learned during residency were reported as having the greatest influence on current clinician practice. Finally, grand rounds presentations or use of pre-printed order sets were reported as preferred resources for knowledge enhancement.

Conclusions: The results of this survey indicate that most respondents use albumin 5% inappropriately, while albumin 25% is used more appropriately. Current albumin prescribing practices are significantly influenced by residency training. These results can be used to inform educational resource development to optimize albumin utilization and improve patient safety.

Abstract# 2024-DPR-3

Physician Blood Transfusion Orders and Compliance with the Standards: Results of a Single-Centre Audit

Heather Panchuk[1], Oksana Prokopchuk-Gauk[1,2,3], Sarah Tehseen[1,2,3], Sheila Rutledge Harding[1,2,3]

[1]Saskatchewan Health Authority, [2]College of Medicine, University of Saskatchewan, [3]Department of Pathology and Lab Medicine, Division of Transfusion Medicine

Background: Blood transfusion is the most common medical procedure in hospitalized patients. Documentation of a comprehensive transfusion order is an essential means of communication between the most responsible practitioner, nursing staff and the transfusion medicine (TM) laboratory; it is also a fundamental requirement of TM lab accreditation standards. In preparation for an upcoming lab accreditation visit, we completed an audit of physician transfusion orders at our centre to assess compliance with accreditation requirements.

Methods: Nursing and clerical staff from inpatient and outpatient areas of 5 transfusing facilities within our centre were notified of this planned audit prior to its initiation. Copies of physician transfusion orders submitted to the TM Lab between February 1-28, 2023 were included in this retrospective audit. Our Transfusion Safety Officer reviewed the orders for completeness, in accordance with the *Canadian Society of TM Standards for Hospital Transfusion Services, 5.9.1.4*.

Results: A total of 213 physician orders were received and reviewed during our study period; the majority were hand-written (pre-printed order set not used). All orders reviewed included required patient demographics. The indication for transfusion was absent in 142 (67%) orders. The date of transfusion was not specified in 188 (88%). All orders included the blood component or product to be given; however, the dose was not specified in 12 (6%). The rate of blood administration was not specified in 167 (78%) orders. Overall, none of the orders audited included all information required to be considered complete.

Conclusion: All physician orders were missing at least one requirement for completeness. These results highlight the need to develop and implement strategies to optimize compliance with lab standards to enhance patient safety, and may include physician education, revision of existing paper-based pre-printed order sets, expansion of pre-printed order set use to all patient care areas, and implementation of an electronic order entry system.

Abstract# 2024-DPR-4

Near infrared imaging human EGFR positive lung cancers using IRDye800CW-nimotuzumab

Wendy Bernhard[1], **Kris Barreto[1]**, Steven Bharadwaj[2], Emina Torlakovic[1], Darryl Yu[1], C. Ronald Geyer[1]

[1]Department of Pathology and Laboratory Medicine, College of Medicine, University of Saskatchewan. [2]Department of Surgery, College of Medicine, University of Saskatchewan.

Background: Epidermal growth factor receptor (EGFR) is overexpressed in many cancers. Nimotuzumab is a humanized therapeutic antibody that targets EGFR. Surgical resection is used to treat non-disseminated non-small cell lung cancer (NSCLC). 40-80% of NSCLC overexpress EGFR. Detection of lung cancer during surgery can be difficult when there are deeply located lesions that can be impossible to see by white light alone. Image-guided surgery using a fluorescent probe provides a way to increase detection of tumors during surgery and during back-bench analysis to improve negative resection margins.

Methods: We are recruiting for a phase I/II clinical trial in Canada to evaluate this probe in lung cancer surgery. Participants receive an infusion of IRDye800CW-nimotuzumab. Blood, vitals, and lab parameters are collected for safety and pharmacokinetics (PK), and surgical resection is performed following probe injection. The resected tissue is analyzed for fluorescence (from the probe), H&E staining, and for EGFR expression by immunohistochemistry.

Results: IRDye800CW-nimotuzumab had high uptake in the tumor and a high tumor to background ratio (TBR) compared with normal tissue (Figure 1A). The fluorescent signal from the probe in the resected tissue correlated with EGFR staining (Figure 1B). Pharmacokinetics showed that IRDye800CW-nimotuzumab had a half-life of ~1.6 days. Immunohistochemistry of the tumor tissue with an EGFR antibody showed a strong correlation with fluorescence from IRDye800CW-nimotuzumab in tissues. We did not observe related adverse events from the probe.

Conclusions: In this study, we have shown that IRDye800CW-nimotuzumab had high accumulation in NSCLC tumors in humans, which shows the potential for this probe to be used during surgical resection of NSCLC. We also observed uptake in nearby lymph nodes, highlighting another potential benefit of using this probe during surgery to detect disseminated cancer cells in lymph nodes.

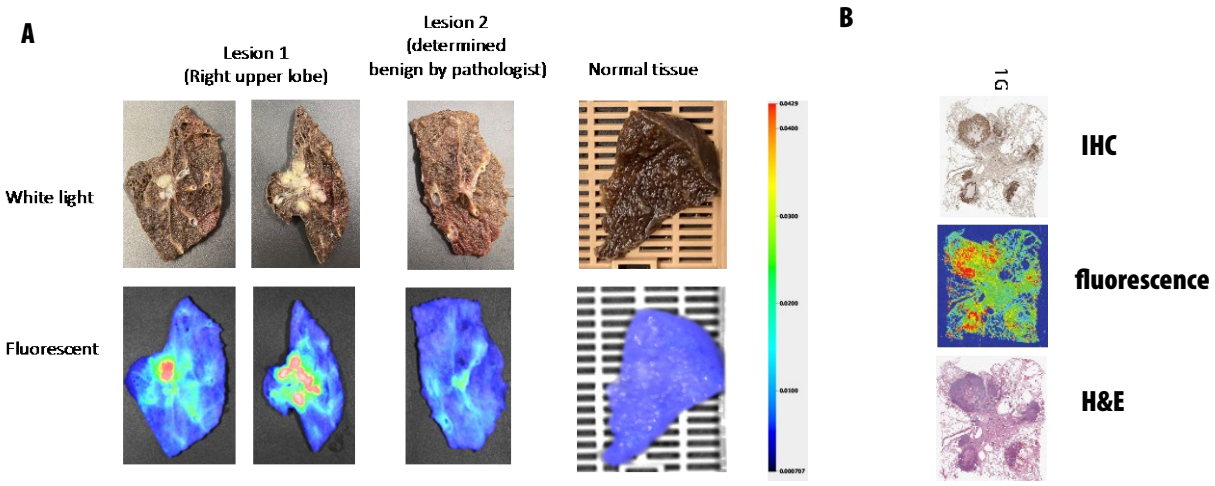

Figure 1. Resected lung tissue. (A) Fluorescent and white light images showing lesions and normal lung tissues resected during surgery. (B) Lung tissue processed to slides stained with EGFR antibody, fluorescence from the injected probe and H&E.

Abstract# 2024-DPR-5

Implementation of pharmacogenomic *DPYD*-guided fluoropyrimidine dosing for cancer patients in Saskatchewan

Yanwei Xi[1,2], Rena Clark[2], Nelly Abdelfatah[2], Zafar Nawaz[1,2], Fang Wu[1,3], Vijayananda Kundapur[4]

[1]Department of Pathology and Lab Medicine, [2]Genomics Laboratory, Royal University Hospital, [3]Biochemistry Laboratory, St. Paul's Hospital, [4]Department of Oncology, Saskatchewan Cancer Agency.

Background: Dihydropyrimidine dyhdrogenase (DPD) is the key enzyme responsible for the metabolism and inactivation of fluoropyrimidine drugs, like 5-fluorouracil (5-FU) and capecitabine, used in chemotherapy treatment. Patients with reduced DPD enzyme activity are at high risk of severe side effects from standard doses of these drugs when receiving chemotherapy treatment. Genetic variants in *DPYD,* the gene encoding DPD enzyme, have been associated with reduced enzyme activity. A joint consensus from Oncologists across Canada recommend *DPYD* testing before chemotherapy. Previously, testing were referred to a laboratory outside of Saskatchewan after patients reported experiencing symptoms, with results taking approximately two to three weeks. Therefore, there is an urgent need to implement a local such testing to prevent drug toxicity and improve patient safety.

Methods: *DPYD* genotyping is performed at RUH Genomics Laboratory for cancer patients prior to receiving chemotherapy treatment, to rapidly detect six of the most common genetic variants that are known to indicate DPD deficiency, with results available in two to seven days. This test was first piloted in Saskatoon in May 2024. In July 2024, testing was expanded and made available to cancer patients across the province. This ensures thorough detection of over 95% of DPD deficiencies within the population. In addition, in house *DPYD* full gene sequencing will be launched in September 2024 to detect rare variants other than the most common ones.

Results: So far, 93 cancer patients have been subjected to *DPYD* genotyping prior to chemotherapy. Six of them were detected to have a reduced function or non-function allele, which accounts for ~ 6.5% in patient population. Their doses of 5-FU/ capecitabine were adjusted accordingly to prevent the risk of severe side effects.

Conclusion: *DPYD* testing allows for the early detection of DPD deficiencies, which improves patient outcomes by adjusting the dosage of fluoropyrimidine drugs used in chemotherapy treatment, overall reducing the risk of severe side effects. Local availability of these tests allows cancer patients to access safe, effective treatment much faster.

Abstract# 2024-DPR-6

Retrospective analysis and clinical performance of BD MAX Enteric Pathogen Testing at a Canadian tertiary care center

Claire Carson[1,2], Ninad Mehta[1,2], Jay Rabari[3], Justin Kosar[4], Joe Blondeau[1,2], Camille Hamula[1,2]

[1]Department of Laboratory Medicine, Royal University Hospital, Saskatoon, Saskatchewan, Canada. [2]Department of Pathology and Laboratory Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. [3]College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada. [4]Department of Pharmacy, Royal University Hospital, Saskatoon, Saskatchewan, Canada.

Infectious diarrhea is a significant health concern, particularly for immunocompromised or pediatric patients. Because traditional stool culture methods are labor-intensive and face challenges in sensitivity, PCR-based gastrointestinal pathogen panels (GIPPs) are increasingly favored in clinical laboratories. This study aims to evaluate the performance of the BD MAX™ GIPP compared to traditional culture methods, with a focus on the accuracy of automatic interpretations provided by the platform. Here, we reviewed results for stool samples processed via traditional stool culture (2016-2020) to the results for stool samples processed via GIPP (2021-2023). Data extracted from each record included BD MAX Ct values, interpretations, amplification curves, and the identity of pathogen(s) recovered. The positivity rate increased after the implementation of the BD MAX system, although the trends in organism relative abundance remained consistent. The BD MAX detected significantly more *Vibrio* spp. and *Yersinia enterocolitica* than was previously seen with traditional stool culture, and the majority of these positives were unable to be recovered in parallel stool culture. Irregular PCR amplification curves were often observed in cases where culture failed to recover viable organisms. Numerous instances of irregular amplification curves generating positive automatic interpretations on the BD MAX were observed, particularly for *Vibrio spp.* and *Yersinia enterocolitica*. These findings suggest a need for cautious interpretation of results, particularly for certain targets, and highlight the importance of incorporating a review of amplification curves into laboratory workflows to mitigate potential false positives.

Abstract# 2024-DPR-7

Utilization of TRIM63 in the Distinction of Gynecologic PEComas from Leiomyomas and Leiomyosarcomas

Dinh A[1,2], Hirsch M[3], Gilks B[4], Kinloch M[1], **Baniak N**[1]

[1]Departmet of Pathology and Lab Medicine, College of Medicine, University of Saskatchewan, Saskatoon, SK, Canada. [2]UCD School of Medicine, University College Dublin, Belfield, Dublin.
[3]Department of Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. [4]Department of Pathology and Laboratory Medicine, University of British Columbia and Vancouver General Hospital, Vancouver, Canada.

Background: Perivascular Epithelioid Cell Tumour (PEComa) are uncommon mesenchymal neoplasms with varied behavior that express both smooth muscle and melanocytic markers. Differentiating uterine PEComas from leiomyosarcomas (LMS) can be challenging due to overlapping histological and immunohistochemical features. *TRIM63* RNA in situ hybridization (ISH) has previously been shown to be expressed in tumors driven by *TFE3* and the *TSC/mTOR* complex and to be positive in a small subset of PEComas (unspecified sites). We sought to assess the utility of *TRIM63* ISH as a marker distinguishing uterine PEComas from leiomyomas (LM) and LMS.

Design: Cases from three institutions resulted in 19 gynecologic PEComas, which were compared to 19 LMS, 40 LM, and seven non-gynecologic PEComas (three kidney, one bladder, two liver, one omental metastasis from an unknown primary). Tissue microarrays were constructed for the LMS and LM, while whole sections were used for the PEComas. Cathepsin K and HMB-45 immunohistochemistry was performed on selected PEComas (those without molecular confirmation). RNA-ISH was performed using the RNAscope 2.5 HD Brown kit and target probe against TRIM63, with positive and negative control probes used to evaluate RNA quality. Stained slides were evaluated under light microscope for RNA-ISH signals, resulting in semi-quantitative scoring (H-score). The expression level was evaluated according to the RNAscope scoring criteria (previously published).

Results: There was a complete absence of staining (H score 0) in all LM and LMS. All five (two pending) non-gynecologic PEComas were *TRIM63* positive (average H-score 197). One of two (remainder pending) gynecologic PEComas was *TRIM63* positive (H-score 270) and was positive for Cathepsin K and HMB-45. However, the second case was Cathepsin K and HMB-45 negative (pending morphology/additional IHC review)

Conclusion: Pending remainder of staining

PGME ABSTRACTS

Abstract# 2024-DPR-8

The Pacinioma Puzzle: Rare Lesion, High Stakes—Unlocking the Enigma of Cutaneous Stigmata, Spinal Dysraphism, and Tethered Cord Syndrome

Bryan Johnston[1], Katelynn Campbell

[1] Department of Pathology and Laboratory Medicine, College of Medicine, University of Saskatchewan, Saskatoon, Canada. [2] Saskatoon City Hospital, Saskatchewan Health Authority, Saskatoon, Saskatchewan, Canada.

Background: Closed spinal dysraphism (CSD) is a congenital anomaly resulting from failed secondary neurulation, often accompanied by cutaneous stigmata. While rare, some cutaneous markers have been associated with complex intraspinal lipomas and pacinian corpuscle hyperplasia. This case explores a unique occurrence of pacinian corpuscles within an acrochordon-like lesion in an infant with CSD and a potential tethered cord syndrome (TCS).

Methods: An 8-month-old female presented with a midline lumbosacral acrochordon-like lesion. MRI revealed a midline lipomatous lesion at S2-S3 with a fibrovascular stalk possibly continuous with the acrochordon. The skin lesion was excised for cosmesis, and histopathology was performed to evaluate its characteristics. Intraoperative exploration was limited to the cutaneous lesion, and no further surgical interventions were performed to assess the deeper spinal structures.

Results: Histopathology revealed a central fibrous stalk surrounded by abundant adipose tissue and embedded with 37 mature pacinian corpuscles, measuring 0.1 to 0.4 mm in diameter, each containing 10 to 26 lamellae. There were no signs of peripheral nerve sheath tumours, such as neurofibromas. This case is consistent with the few reports in the literature that describe paciniomas occurring in association with complex intraspinal lipomatous lesions. However, this case is unique in the fact that the pacinian corpuscle hyperplasia occurred within an acrochordon-like lesion in the setting of CSD. Given the limitations of the surgical approach, it remains unclear whether the observed lesion was continuous with deeper spinal structures or represented an isolated cutaneous anomaly.

Conclusion: This case of pacinioma within a cutaneous stigmata of CSD is rare and underscores the critical link between cutaneous markers and potential serious conditions like TCS. While paciniomas are benign, their association with spinal dysraphism necessitates further investigation, particularly in the context of tethered cord syndrome.

Abstract# 2024-DPR-9

Reducing Unnecessary Thyroid Function Testing Through Optimizing Test Ordering Protocols

Joel Scott[1], Jay Kalra[1,2], Jason Vanstone[1], Shravan Murthy[1], Ahmed Mostafa[1,2], Fang Wu*[1,2]

[1]College of Medicine, University of Saskatchewan; [2]Department of Pathology and Lab Medicine, Saskatchewan Health Authority

Background: Thyroid dysfunctions are among the most common endocrine disorders in clinical practice. Hyperthyroidism and hypothyroidism are typically diagnosed based on the abnormal levels of thyroid-stimulating hormone (TSH), thyroxine (T4) and triiodothyronine (T3). Current Thyroid guidelines recommend TSH alone as the optimal test for screening for thyroid dysfunction in most clinical circumstances. A normal TSH result excludes further testing of T4 and T3 in most clinical circumstances. Unnecessary testing can lead to economic burden to the healthcare system but also patient harm.

Our group analyzed data retrieved from the Saskatoon Laboratory Information System (LIS) including tests ordered from January 1, 2016, to December 31, 2019 (4 years). The goal of this project is to bring our laboratory thyroid testing protocols in alignment with current testing guidelines for better patient care, optimized laboratory utilization and considerable cost savings. This work has been done in phases as follows: Phase 1, aimed to reduce unnecessary T3 and T4 tests. Phase 2 aims to reduce unnecessary TSH testing.

Methods: The methods involved PDSA cycles for quality improvement, including literature review, environmental scan, change implementation and retrospective analysis to compare pre/post-intervention data. The changes implemented consist of reflexive testing protocols within LIS and audit and feedback reviews to be sent to clinicians. The data is analyzed using run charts and basic descriptive statistics.

Results& Conclusion: The implementation of Reflexive testing protocol led to a 59% reduction in free hormone testing (T3 and T4), which corresponds to annual savings of $684,552.

Conclusion: We have demonstrated considerable cost savings in optimizing our thyroid testing protocols in Saskatoon, with specific reductions in free thyroid hormone tests. The efficacy of the various approaches will be monitored to assess the outcomes of this QI project. In summary, this project highlights the importance of quality improvement projects within the lab.

Abstract# 2024-DPR-10

Homologous Recombinant Deficiency Does Not Share the Morphologic Surrogates of *BRCA*-mutated Ovarian Cancer Patients

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Background: Previous studies have shown a relationship in high-grade serous carcinoma (HGSC) of the ovaries between *BRCA* status and solid, pseudoendometrioid, and transitional morphology. Currently, tumour *BRCA* mutation testing is done to determine genomic instability, which only represents a part of the HRR pathway with additional HRR gene mutations and other genomic scars resulting in HRD. Since *BRCA* mutation is one type of HRD, the goal of this study is to determine if this morphology is specific to *BRCA* mutation or extends to other HRR pathway mutations.

Methods: 36 HGSC patient samples from the University of Saskatchewan's gynecological oncology biobank were identified and H&E slides retrieved from the Saskatoon City Hospital's Anatomical Pathology archive and histologically examined for the presence of solid, pseudo-endometrioid, transitional, papillary, micropapillary, and compressed micropapillary (S, E, T, P, M, and C) architectures. Tumour *BRCA* and Genomic instability scores (GIS) were obtained using the Illumina MyChoiceCDx. Statistical analyses, including Kappa analysis, Chi-square test, and Fisher's Exact test, Likelihood ratio test, were performed using SPSS v28.

Results: 25 (61.1%) patients were *BRCA* wild-type and 11 (38.9%) were *BRCA* mutated. 11 of 25 (69.4%) BRCA negative patients had GIS ≥ 42 and 14 (30.6%) had GIS < 42. There is no association between S, T, P, M, C and HRD or *BRCA* status. There was a potentially significant association between histology E and HRD status (p=0.049 – at borderline significance). HRD status is not exclusively linked to *BRCA* mutations.

Conclusion: Histological morphology does not correlate with *BRCA* status or HRD, highlighting the need for comprehensive genomic profiling to identify HRD patients.

Abstract# 2024-DPR-11

Comparative Analysis of eGFR Estimation: Performance of the CKD-EPI_2021 vs. Race-independent 2009 CKD-EPI Equations in a Local Population

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Background: The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations are widely used for estimating glomerular filtration rate (eGFR), a critical marker of kidney function. The new CKD-EPI_2021 equation is a creatinine-based race-free method for calculating eGFR in adults, which has been recommended by the National Kidney Foundation. The current method of eGFR calculation in our institution is the previous CKD-EPI_2009_NB (non-black) equation. Since this equation was designed to include the race factor, a bias may occur if it is universally applied to all patients. This study aims to compare these two equations using the local patient population prior to the implementation of CKD-EPI_2021 equation.

Methods: The plasma creatinine measured at local hospitals in August 2024 were extracted from the laboratory information system. The de-identified data were used to calculate eGFR by CKD-EPI_2009_NB and CKD-EPI_2021 equations, and CKD staging was performed according to the Kidney Disease Improving global Outcomes (KDIGO) guideline. The main group included 651 patients (≥ 18 years old), representing the typical demographic and creatinine level distribution in the local population, was used to assess the overall concordance between the two equations. Another stratified group (299 patients) with a balanced eGFR stages was selected to compare the difference in CKD staging. Statistical analyses included Deming regression, Chi-square tests, and reclassification rates.

Results: The CKD-EPI_2021 equation demonstrated an overall positive bias (3.527, 95% CI: 3.370 – 3.683) compared to the CKD-EPI_2009_NB equation, and such bias became most apparent close to the CKD diagnosis threshold (60 mL/min/1.73 m²). Conversely, it underestimated eGFR at the high end of the spectrum (>100 mL/min/1.73 m²). In the stratified group, differences in CKD staging were observed in that the CKD-EPI_2021 equation resulted in a less advanced stage than the CKD-EPI_2009_NB equation. In particular, re-classification occurred between stages 2 and 3 or within stage 3: stage 3a to 2 (4/10, 40%), stage 3b to 3a (3/13, 23%). Furthermore, the CKD-EPI_2021 equation also resulted in reclassification from stage 5 CKD (7/117, 6%) to stage 4, and from stage 2 to stage 1 (8/50, 16%).

Conclusions: The CKD-EPI_2021 equation generally calculates a higher eGFR value compared to the CKD-EPI_2009_NB equation, resulting a tendency to classify patients into one less advanced CKD stage. Although a high portion of reclassification occurred between stage 2 and 3, the more significant clinical impact is the reclassification of some patients from end-stage renal disease (stage 5) to stage 4 or from an early CKD (stage 2) CKD to health (stage 1).

Abstract# 2024-DPR-12

A rare presentation in a patient previously treated for hodgkins lymphoma

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Background: Ewing Sarcoma (ES) is an aggressive tumor affecting bones and soft tissues. Extra-skeletal renal ES is an extreme lyrare presentation. Unlike other sarcomas, ES seldom presents as therapy related subsequent malignant neoplasm (SMN). We present a case of metastatic renal ES in an 11-year-old female previously treated for Hodgkin lymphoma (HL).

Methods: An 11- year- old female presented with right eye pre-septal cellulitis. Her medical history was notable for Stage IIIAHL at the age of 8. She had treatment following Children's Oncology Group Protocol- AHOD0331 with doxorubicin,bleomycin, vincristine, etoposide, prednisone and cyclophosphamide. No radiation therapy (RT). Investigations were significant for elevated ESR (109 mm/hr) and LDH (909 U/L). Cross sectional imaging, computed tomography(CT) head neck, chest, abdomen/pelvis and positron-emission tomography (PET) revealed a large left renal mass(10cmx7.7cmx12.4cm) with metastasis to lungs, lymph nodes and bones. Bilateral bone marrow aspirates/biopsies confirmed bone marrow involvement. She underwent upfront left radical nephrectomy. Immuno-histopathology confirmed diagnosis of extra-skeletal renal ES. Whole genome sequencing (WGS) and RNA sequencing (SarcomaNanoString) of the tumor and blood (germline) done following enrollment on Precision Oncology For Young People (PROFYLE). Hereditary cancer predisposition testing was also completed.

Results: Sarcoma NanoString and WGS panel confirmed EWSR1 (Exon7)-FLI1 (Exon5) fusion transcript. Patient had interval compressed cycles of chemotherapy with vincristine, doxorubicin, cyclophosphamide alternating with ifosfamideand etoposide. RT was given to the primary and metastatic sites. Genetic testing was negative for Li Fraumenisyndrome and other mutations or variants of uncertain significance (VUS). WGS identified, heterozygous germline deletion of 5bp, NM_002485.5:c.657_661delACAAA, resulting in NBN: p.Lys219fs.

Conclusions: Renal ES is a rare sarcoma specifically as a SMN. Heterozygous germline NBN loss in tumors suggests a dominantnegative mechanism elevating risk of cancers. This may likely explains development of HL and/or renal ES in this patient.

Abstract# 2024-DPR-13

Pilot Study: Innovative Application of Optical Genome Mapping for Alpha-Thalassemia Diagnosis.

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Background: Alpha-thalassemia (AT) is a hemoglobinopathy caused by reduced α-globin protein expression due to deletions in α-globin gene cluster on chromosome 16. While historically rare in Canada, AT has been rising due to immigration from AT prevalent regions. Conventional AT detection involves hemoglobin electrophoresis, and high-performance liquid chromatography (HPLC) followed by confirmatory molecular testing. This confirmatory test is currently a send-out test resulting in a 6-week turnaround time (TAT). We propose a novel Optical Genome Mapping (OGM) assay for the rapid detection of AT.

Methodology: Twelve patients with microcytosis (MCV<81.9fl) or suspected AT by hemoglobin HPLC were selected. Peripheral blood samples were analyzed using OGM (Bionano Genomics Inc.). Ultra-high molecular weight genomic DNA was isolated, labeled, and analyzed on the Bionano Saphyr system. OGM data was compared to the reference human genome (GRCh38/Hg20) to identify deletions in α-globin gene cluster.

Results: The cohort consisted of 12 patients (median age: 21.5y, M:F=7:5) with an average MCV was 68.6±7.2fl and predominant HPLC result of “AT or rare forms of Beta-thalassemia (BT) cannot be ruled out” (n=3), and “repeat after iron-deficiency anemia correction” (n=3). In 2 cases, HPLC results were consistent with BT trait due to elevated HbA2 levels (6.0% and 6.6%). OGM identified five cases of presumptive AT based on homozygous or heterozygous HBA2 deletions (3.2-3.7kb) in 3 patients and cis deletion (16.5-16.7kb) of HbA2 and HBA1 in 2 patients consistent with Southeast Asian (SEA) deletion. No α-gene deletion was detected via OGM in two cases of presumptive BT trait.

Conclusion: OGM identified gene deletions consistent with one and two gene deletional AT in five patients with suspected AT within a 3-day TAT. OGM is superior to conventional testing as it is unaffected by iron deficiency or transfusions. Comprehensive validation using samples from patients with a confirmed diagnosis of AT by conventional molecular analysis will follow.

Abstract# 2024-DPR-14

Utility of Cytomegalovirus (CMV) and Mycobacterium Tuberculosis (MTB) Molecular Detection on Formalin-Fixed Paraffin-Embedded (FFPE) Tissue; From Pathology to Patient

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Objectives: Cytomegalovirus (CMV) and mycobacterium tuberculosis (MTB) are common entities that Saskatoon pathologists encounter in their daily sign-out. Molecular tests such as CMV quantitative real-time polymerase chain reaction (CMV qPCR) and MTB qPCR can be used to aid pathologists and clinicians in the diagnosis and treatment of patients. In our study, we sought to assess the utility and clinical outcomes of CMV qPCR and MTB qPCR testing on FFPE tissue.

Methods: Retrospective case study from January 2021 to June 2023 (2.5 years). A search for CMV qPCR tests and TB qPCR tests ordered was performed on SoftMic® and corresponding signed-out pathology reports in SoftLab® were analyzed. The clinical history of each case was analyzed using eHealth Saskatchewan®. A total of 15 pathologists in Saskatoon ordered either MTB qPCR or CMV qPCR tests. The 15 pathologists were anonymized, and their ordered MTB qPCR tests (n=24) and CMV qPCR tests (n=23) were audited and analyzed. Rare tests such as fungal, entero/parechovirus, and leishmaniasis qPCR were also studied.

Results: A total of 24 MTB and 23 CMV qPCR tests were ordered, and all of these were non-contributory to the patients' clinical course at the time of microbiology test result reporting.

Conclusion: MTB and CMV qPCR testing results were non-contributary to the clinical course in all 47 cases. In cases of MTB qPCR, there was only 1 positive result which was non-concordant with the histology and further characterized as MAC. Conversely, CMV qPCR testing on FFPE tissue was only helpful in cases with CMV IHC positivity. Prior to ordering CMV qPCR on FFPE tissue, the clinical team must order CMV serology upfront in all cases of suspected CMV colitis. Stringent testing algorithms must be enforced to prevent over ordering of MTB and CMV qPCR tests on FFPE tissue in surgical pathology since there is minimal impact to patient care.

Abstract# 2024-DPR-15

Human Leukocyte Antigen antibody profile and COVID-19 Vaccination in Waitlisted Renal Transplantation

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Funding: This research was funded by the College of American Pathologists Foundation John H. Rippey Grant for Expedited Research - The Impact of Laboratory Testing for SARS-CoV-2 on Quality and Patient Safety.

Background: Mass COVID-19 vaccination is required for vulnerable populations within our renal transplant waitlist cohort. However, the impact of COVID-19 vaccination on anti-HLA profiles remains controversial, and the side effects are not yet fully understood. This study aims to evaluate the status of HLA (human leukocyte antigen) antibodies in renal transplant waitlist patients before and three weeks after each vaccination, and to determine whether comorbidities are associated with the HLA antibody profile.

Methods: The study included fifty-nine kidney transplant patients on the waitlist. Anti-HLA antibodies were analyzed before and six months after their final COVID-19 vaccination. The change in Mean Fluorescence Intensity (MFI) of anti-HLA antibody levels was used to categorize patients into three groups: high inducers, low inducers, and non-inducers.

Results: Significant changes in the HLA antibody profile were observed following COVID-19 vaccination, with 21 antibodies generated against HLA class I antigens and 7 against HLA class II antigens compared to baseline levels. Compared to non-inducers, both high and low inducers exhibited a higher prevalence of COVID-19 infection, differences in COVID-19 vaccine type, and a history of background hypertension.

Conclusions: Our data suggest that COVID-19 vaccination induces anti-HLA Class I and II antibodies in renal transplant waitlist patients. The clinical significance of these antibodies requires further investigation. Additionally, comorbidities such as a history of COVID-19 infection and hypertension appear to exacerbate this effect. Monitoring anti-HLA antibodies may be advisable for vaccinated renal transplant waitlist patients with a history of COVID-19 infection or hypertension.

Abstract# 2024-DPR-16

Upgrade rate of radial scars/complex sclerosing lesions on core needle biopsies of the breast: a single-institution study

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Background: Radial scar (RS)/complex sclerosing lesion (CSL) is a benign breast lesion that is histologically characterized by a lobulocentric proliferation of fibrocystic changes, central dense hyalinized collagen and elastosis, and a retained myoepithelial cell layer. With the increasing use of digital breast tomosynthesis, the detection of RS/CSL has risen. These lesions often mimic invasive carcinoma on imaging, usually warranting classification as at least indeterminate or suspicious (BI-RADS categories 3 or 4). While there is consensus that RS/CSL associated with epithelial atypia should be excised, the management of RS/CSL without atypia remains controversial. This is in part due to the highly variable malignant upgrade rates reported upon excision of isolated RS/CSL initially identified on core biopsy. Indeed, reported rates are as high as 45%, suggesting that institution-dependent factors may be at play.

Therefore, the main objective of this study was to determine the upgrade rate to malignancy (ductal carcinoma in situ or invasive carcinoma) of isolated RS/CSL in our institution.

Methods: We performed a retrospective search for core needle biopsies diagnosed as radial scars in our institution from January 1, 2017 to December 31, 2023.

Results: We identified 250 biopsies diagnosed as definite (n=207) or probable (n=43) isolated RS/CSL without atypia. The biopsy modalities included tomosynthesis (n=123), ultrasound (n=120), and MRI (n=7). The biopsies were categorized as BI-RADS 4 (n=200) or BI-RADS 5 (n=18); BI-RADS scores were not provided in the remainder. Out of 125 isolated RS/CSL managed with surgical excision, 8 were upgraded to malignancy (6.4%). Atypical ductal hyperplasia was found in 7 excisions of isolated RS/CSL (5.6%).

Conclusion: In our institution, the overall upgrade rate to malignancy of isolated RS/CSL is low at 6.4%. Further work is needed to identify the factors that can predict upgrade to malignancy on excision, which can better inform the management of these lesions.

Abstract# 2024-DPR-17

Melanoma sentinel lymph node practice in a multi-institutional Canadian study: Toward establishing national quality indicators in the pathologic assessment of sentinel lymph node specimens for melanoma patients

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Background: Sentinel lymph node biopsy (SNLB) is a routine surgical procedure for managing melanomas greater than 0.8 mm in thickness or with ulceration and other solid tumour malignancies. Currently, the College of American Pathologists (CAP) guidelines have a recommended maximum number of lymph nodes that are considered "sentinel" for invasive breast carcinoma, but this does not exist for melanoma.

Methods: In this multi-institutional Canadian study, we retrospectively quantified total lymph node yields for melanoma SLNB procedures from August 1, 2021, to July 31, 2022, with some interval variation. Positivity rate, immunohistochemical protocols, cost analysis, and local practice variability were also evaluated. Cases were grouped in G1 if the total sentinel lymph node count was one and G>1 if there were more and analyzed.

Results: There were 708 cases evaluated in the 2-year period across all institutions. The average number of sentinel lymph nodes collected by surgeons per SLNB was 2.41 (standard deviation: 1.90). The rate of sentinel lymph node positivity was not significantly different between the two analyzed groups (p=0.09), with a range of positivity across institutions. Surgical techniques for SLNB were similar between institutions. Additionally, costs varied but universally, additional sampled lymph nodes incurred additional costs from reflex immunohistochemistry and pathologist/technologist time.

Conclusion: The lack of standardized sentinel lymph node practice for melanoma leads to 1.) variability in surgical and pathology practices 2.) differential laboratory resource utilization and associated costs, and 3.) non-standardized, center-dependent protocols. Our study supports a need to establish national guidelines for SNLB specimens.

Abstract# 2024-DPR-18

An intriguing case of the green plasma

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Background: A green-colored plasma sample from a breast cancer patient was sent to the lab for chemistry testing. Concerns were raised about potential interferences. After discussion with the clinical care team, the source of the green coloration was identified as methylene blue. Methylene blue is commonly used to treat methemoglobinemia but could also be used as a surgical dye. The patient was administered methylene blue for sentinel node mapping. Methylene blue has peak light absorption at 292 nm, 613 nm, and 664 nm. Additionally, methemoglobin reductase facilitates the oxidization of NADPH to $NADP^+$ through the reduction of methylene blue, potentially causing chemical interference. This study aims to investigate the impact of methylene blue on the laboratory spectrophotometric assays.

Methods: The information on the package inserts were examined, and literature was surveyed to determine if methylene blue interferes with the ordered tests: creatine kinase (NADPH, 340 nM) and high-sensitivity cardiac Troponin T (electrochemiluminescence). The tests ordered were analyzed using Roche Cobas chemistry analyzer. Additionally, chemical interference were studied by examining reaction traces of the glucose assay, which also utilizes NADPH chromogen. Furthermore, spectral interference for assays using different chromogens such as: calcium (Ca^{2+}:NM-BAPTA complex, 340 nM), magnesium (Mg^{2+}:xylidyl blue complex, 600nM), and iron (Fe^{2+}:FerroZine complex: 570 nM), as well as immune-turbidimetry assay such as albumin (340nM), were also studied.

Results & Conclusion: Methylene blue was not listed as a potential interference in the package insert for the tests ordered. Preliminary data shows no abnormally in the baseline values and the shape of the assay tracings, suggesting the internal mechanisms of the Cobas analyzer, such as polychromatic measurements, could mitigate the potential spectral interferences. However, the possibility of chemical interference cannot be ruled out for assays utilizing NADPH as chromogen, and methylene blue spiking studies should be conducted to rule-out chemical interference.

Graduate Student Abstracts

Abstract# 2024-DPR-19

A Novel Tumoroid model of Breast cancer to Profile Cancer stem cells

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The tumor microenvironment (TME) and its features, such as hypoxia, extracellular matrix, and immune cell surveillance are more effective drivers of cancer stem cells (CSCs) than intrinsic oncogenic mutations. However, one of the major challenges for characterization of CSC populations and their properties is development of in vitro models capable of maintaining these external drivers. Modular tissue engineering is one of the methods that allows us to develop cancer microtissues composed of cancer cells embedded in collagen hydrogel as the ECM, which can be enriched with various types of stromal cells to better resemble additional features of a functional TME. We hypothesize to observe expansion of CSC populations in our 3D model compared to 2D-cultured cancer cells.

The preliminary analyses were based on the triple negative breast cancer cell line HCC1806 cultured in microtissues. This included assessment of morphology by H&E, proliferation by immunohistochemical staining of Ki-67, viability by live/dead staining, and CellTiter-Glo® 3D assays, and hypoxia by hypoxiTRAK staining. Additionally, the CSC markers were analysed by flow cytometry.

Our preliminary data showed that microtissue-cultured HCC1806 cells remain viable and proliferative with minimal cell death. Moreover, the establishment of a hypoxic core has also been shown to start developing by day 10. The potency of both paclitaxel and doxorubicin was reduced in killing cells grown in microtissues, while paclitaxel efficacy was also notably diminished. The flow cytometric analysis of CSC populations showed upregulation of CSC markers in microtissues-cultured HCC1806 cells compared to 2D-cultured ones.

Overall, our results proved the capacity of this model to maintain a proper environment for growth and proliferation of cancer cells, and are also in accordance with our hypothesis regarding expansion of CSC population, showing the potential of this model to mimic the drivers of CSCs present in an actual TME.

UGME Abstracts

Abstract# 2024-DPR-20

Leading with Quality: Enhancing Pathology Residency Training through Continuous Quality Improvement and Case-Based Learning

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Background: The landscape of clinical and laboratory medicine residency training in Canada is undergoing significant transformation. The Royal College of Physicians and Surgeons recently rebranded the General Pathology program to Diagnostic and Clinical Pathology, reflecting the evolving role of pathologists in patient care. This study aimed to identify opportunities for enhancing teaching sessions through resident feedback and to establish a foundation for future quality improvement initiatives. We assessed resident satisfaction, achievement of learning objectives, and clinical applicability across three teaching methods: traditional didactic lectures, interactive case-based learning, and asynchronous modules.

Methods: Nine residents from the University of Saskatchewan Diagnostic and Clinical Pathology program participated in a survey evaluating Kirkpatrick level 1 "Reaction" criteria, which included satisfaction, engagement, perceived relevance, and clinical applicability. We measured both course satisfaction and achievement of learning objectives using graded scales across 10 and 7 criteria, respectively. Quantitative responses were analyzed using descriptive statistics, and key themes were extracted from open-ended feedback for qualitative analysis.

Results: The interactive case-based sessions received the highest scores, with 91% of residents expressing satisfaction and 86% reporting that the sessions met learning objectives. Across all teaching methods, 90% of residents felt comfortable applying the knowledge gained to clinical practice, with interactive sessions consistently bridging the gap between theoretical knowledge and clinical application. Open-ended responses highlighted a demand for more case-based teaching across all teaching sessions.

Conclusion: Residents demonstrated a clear preference for interactive case-based learning due to its effectiveness in connecting theoretical knowledge to real-world clinical practice. These findings suggest that future quality improvement initiatives should prioritize expanding case-based teaching within residency programs to better align with clinical demands and enhance the educational experience of pathology residents.

Abstract# 2024-DPR-21

Personalized Medicine: The effect of tacrolimus level on kidney allograft rejection outcomes

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Background: Kidney transplants require immunosuppressants to prevent rejection [e.g. antibody-mediated rejection (AMR) and T-cell mediated rejection (CMR)]. Tacrolimus, which inhibits calcineurin phosphatases, thereby prevents T-cell activation. A recent study in Manitoba showed that patients who develop donor-specific antibodies (DSA), commonly associated with AMR, exhibit lower trough levels compared to patients without DSA. This retroactive study investigates whether lower tacrolimus levels are correlated with AMR or CMR.

Methods: A total of 25,383 tacrolimus results from 329 patients were pulled from the laboratory information system [(LIS), SoftLab] between January 2012 and April 2024. Tacrolimus data were analyzed separately for Saskatoon and Regina due to lack of analytical standardization between sites. Patients were grouped as AMR, CMR, and no evidence of AMR or CMR based on information from patient biopsy reports. Median levels of tacrolimus were calculated at different treatment intervals: 0-3 months, 4-6 months, and 10-12 months post-transplant, as well as 6 months leading up to the first documented AMR or CMR.

Results: No significant differences were found in the median tacrolimus levels during the first year of treatment. However, in the 6 months leading up to the development of AMR, patients had lower tacrolimus levels compared to those who did not develop AMR ($P < 0.05$, Šídák's multiple comparisons test). No differences in tacrolimus levels were observed in patients with or without CMR.

Conclusion: Patients who develop AMR have lower tacrolimus trough levels 6 months before documented rejection compared to patients without AMR, which is consistent with the Manitoba study, suggesting that lower tacrolimus trough levels may be a predictor for AMR development. Tacrolimus levels in the first year post-transplant did not significantly impact rejection; further investigations are warranted to explore the correlation between tacrolimus and rejection. Overall, tacrolimus trough levels could serve as a useful adjunct for monitoring allograft outcomes post-transplant alongside renal function.

Abstract# 2024-DPR-22

Utilization of in silico analysis for prediction of graft failure in kidney transplant

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Background: In kidney transplantation, HLA epitope mismatch based on high resolution HLA sequencing provides an advantage over conventional antigen match for risk stratification. There are multiple mechanisms by which immune recognition and response can occur, including the direct, semi-direct and indirect pathways. Previously, we had analysed HLA surface epitopes to evaluate immunological compatibility between donors and recipients. Now, we explore how T-cell epitopes, and the indirect pathway are involved in graft rejection.

Methods: We obtained HLA and pathology data from 613 patients who were followed post renal transplant in Saskatchewan. High resolution HLA sequences were either obtained directly or through prediction via the NMDP Haplostats database. Analysis for mismatch scores were calculated through HLA Matchmaker and PIRCHE. Banff criteria were extracted from renal biopsy reports.

Results: Overall and locus specific HLA Matchmaker and PIRCHE scores are not significantly correlated with CMR or AMR ($p>0.05$) but are well correlated with DSA formation ($p=0.003$). CMR is more common than AMR ($p=0.0151$) and tends to occur earlier following transplant. Significant risk cutoff for Matchmaker scores were found at the following loci: A=14.5, B=11.5, C=8.5, DR345=7.5, DQ=10.5 and total 54.5 ($p<0.05$). PIRCHE values were significant for the following: A=15.5, DR345=24.5, DQ=25.5, and total 118.5 ($p<0.05$). Death censored DSA free survival showed significant difference between stratified groups ($p<0.0010$).

Conclusion: HLA epitope analysis is more predictive of DSA formation than for CMR or AMR. However, it is notable that despite not reaching always reaching statistical significance, patients who developed CMR, AMR, and DSA consistently had higher scores for both HLA Matchmaker and PIRCHE. ROC cutoff values can be used individually or in combination with one another for the purposes of risk stratification. Overall, there are valuable clinical applications for epitope-based analysis post-transplant with multiple immune recognition pathways playing a role.

Abstract# 2024-DPR-23

Defining the Grey Zone in Homologous Recombinant Testing in Ovarian Cancer – Using Bioinformatics to Determine Response to Precision Medicine

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Background: High-grade serous carcinoma (HGSC) patients that test positive for homologous recombinant deficiency (HRD) are eligible for PARP-inhibitor therapy (PARPi). HRD is defined as patients with a Genomic Instability Score (GIS) of ≥ 42. Little information is known about those patients who have a GIS score in the "grey zone", defined as within 1-2 integers of the arbitrary 42 cut-off.

Objectives: Determine the reproducibility of a clinically validated HRD test for HRD at various tumour contents to allow better test characteristic prediction and how patients with "grey zone" results will respond to PARPi.

Methods: Patients with HGSC were identified by the USASK Gyn Onc Biobank with a GIS between 40-44. Histologic slides were reviewed for tumour content (t.c.), and clinical pathologic features were collected. DNA was extracted from formalin-fixed paraffin embedded tissue from the same block and core for each patient. Each patient had 3 library preparations with 3 next-generation sequencing (NGS) runs for a total of 9 patient runs for comparison. GIS scores were established using Illumina's TSO500 HRD.

Results: Three patients (67, 71, and 80 years old) were identified with Grey Zone Scores. The highest reproducibility was patient 3 (t.c. 15%) with all 10 runs showing an HRD >42. Similarly patient 2 had a GIS score of 44 (tumour content 90%) and reproducibility HRD > 42 result for 9/10 runs (range 41-49). Patient 2 had a GIS score of 44 (tumour content 60%) and more variability with only 6/10 runs having an HRD > 42 (range 38-45).

Patient Sample	Age	GIS	Tumour Content	Repeated GIS								
				Library Prep 1			Library Prep 2			Library Prep 3		
1	80	44	90%	45	47	48	46	49	49	44	41	44
2	71	44	60%	44	40	44	45	38	40	41	42	43
3	67	42	15%	53	54	47	56	54	52	56	55	55

Table 1. Summary of patient with a Grey Zone HRD and repeated run results

Discussion: Variability within HRD testing is identified. It is important to consider patient range for retesting. The data suggests a patient with a HRD score as low as 38 to as high as 45 could be considered for reassessment.

Abstract# 2024-DPR-24

When Less is More: Analyzing Out-of-Control Vitamin Testing in Saskatchewan

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Background: Testing for vitamins D and B12 is commonly ordered by physicians globally despite their limited testing indications. Over-testing is a catalyst for further unnecessary investigations, increased cost, patient anxiety, overtreatment, and burdening of already at-capacity laboratories. This project described and analyzed testing patterns in the former Saskatoon Health Region.

Methods: Deidentified data from the Saskatoon Hospital Laboratory Information System from Jan. 1st, 2018, to Dec. 31st, 2022, was analyzed and visualized with Microsoft Excel. Collected metrics included total number of tests ordered along with breakdown by city, physician type, and test result, as well as analysis of repeat tests.

Results: From 2018 to 2022, 110078 vitamin D and 192776 vitamin B12 tests were ordered in the former Saskatoon Health Region. Testing was greatest in rural areas, with the highest rate of vitamin B12 testing occurring in Nokomis (population 414, 3395 tests over 5 years) and the highest rate of vitamin D testing occurring in Davidson (population 1044, 900 tests over 5 years). The ten most frequently ordering physicians for each test were all family physicians except for one. 98% of all tests ordered had normal results. Repeat testing analysis within a calendar year showed 8177 people being tested at least twice for vitamin D and 19745 people for vitamin B12.

Conclusion: There is severe and worsening inappropriate testing in the region for vitamins D and B12. Statistical analysis revealed increasing volumes, inappropriate repeat testing, high proportions of normal results, and a small number of family physicians accounting for a high percentage of ordering. The estimated cost of vitamin D and B12 testing in the past 5 years is over $4.8 million, with $1.3 million in 2022 alone. Systemic changes to laboratory ordering practices are needed. Potential future interventions may include laboratory requisition form changes, physician education materials, and physician-specific laboratory audit reports.

Abstract# 2024-DPR-25

Quality Care and Patient Safety in Focus: Best Practice Guidelines for Medical Error Disclosure across Canada

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Background: The prevalence of medical errors in healthcare systems has greatly affected the quality of healthcare delivery. Disclosure of an adverse event is crucial in managing medical error. We have previously reported that the College of Physicians and Surgeons of Canada encourages the open disclosure of adverse events and have suggested a 'no-fault' model. This study explores the complexities of medical error disclosure policies across Canadian provincial and territorial health regions/authorities, aiming to identify best practices that align with a patient-centered care model.

Methods: We evaluated the medical error disclosure policies of each health region/authority from various Canadian provinces and territories based on five critical criteria: an apology or expression of regret, support for the patient, avoidance of blame, provider support, and avoidance of speculation.

Results: In most provincial and territorial health regions (7 of 11), disclosure policies cover all evaluated criteria. In Eastern Canada, more than 90% of the policies included an apology, patient support, and avoidance of blame, while more than 80% included avoiding speculation and support for providers. Similarly, in Western Canada, over 80% of policies contained an apology, patient support, and avoidance of speculation, while at least 60% of policies contained provider support. In Nunavut and the Northwest Territories, all policies included an apology, patient support, avoidance of speculation, and provider support. On average, health region disclosure policies included an apology (98%), patient support (98%), avoidance of speculation (95%), provider support (92%), and avoidance of blame (90%)

Conclusion: We believe that these disclosure policies can provide a framework and guidelines for appropriate disclosure, which can lead to more transparent practices. We suggest implementing a uniform policy centered on addressing errors in a non-punitive manner and respecting the patient's right to honest disclosure as the standard of care.