15th Annual Lorne D. Sullivan Lectureship & Research Day

Program & Abstracts Booklet

Date: Tuesday, June 15, 2021
Time: 8:30 AM – 12:00 PM (PDT)
Location: Zoom
Dr. Christopher E. Barbieri, MD, PhD

Associate Professor of Urology
Associate Professor of Cell and Developmental Biology
Weill Cornell Medicine and New York-Presbyterian Hospital
Walter B. Wriston Research Scholar

Dr. Christopher Barbieri, MD, PhD is Associate Professor of Urology and Associate Professor of Cell and Developmental Biology at Weill Cornell Medicine and New York-Presbyterian Hospital. He is a urologic surgeon who takes care of patients with prostate cancer, and whose long-term goal is using molecular information to improve the care of prostate cancer patients. Dr. Barbieri received his undergraduate degree from Dartmouth College and then attended Vanderbilt University School of Medicine, where he obtained both his MD and PhD degrees. He then completed both his Urology Residency and Urologic Oncology Fellowship at Weill Cornell Medical College. Dr. Barbieri's research focuses on improving molecular classification of prostate cancer and identifying novel drivers, defining the signaling pathways and biology underlying distinct subtypes of the disease, and exposing new therapeutic avenues. His work has led to recognition and awards from the Prostate Cancer Foundation, AACR, Urology Care Foundation, and Damon Runyon Cancer Research Foundation, and his laboratory is funded by the National Cancer Institute.
Dr. Lorne D. Sullivan

Dr. Sullivan was raised in Moss Bank, Saskatchewan, and graduated from the University of Saskatchewan, Faculty of Medicine in 1962. After an Internship at Vanderbilt University, he completed his urological training at UBC under the mentorship of Dr. John Balfour. He pursued postgraduate training in Urological Oncology as a Royal College Traveling Fellow at several US Cancer Centres before establishing his practice in British Columbia in 1971. During his years of clinical practice, he developed a highly recognized centre for the surgical management of urological cancer at UBC and was a visionary in the establishment of the Prostate Research Centre. He was a respected teacher and clinician responsible for training an entire generation of British Columbia urologists.

At the national and international level, he served as President of the Canadian Urological Association, the Northwest Urological Society, the Western Section of the AUA, and Chaired the Specialty Committee in Urology and was Chief Examiner for the Royal College of Physicians and Surgeons of Canada. He was Head of the Division of Urology at UBC from 1991-1999. He retired in 1999 to spend time with his family and grandchildren, but continues to grace the Department with his presence at academic and social functions.

Previous Sullivan Lectureship & Research Day Lecturers

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Previous Division of Urology Graduation Dinner Guest Speakers

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Program

Welcome
8:30 AM – 8:45 AM  Dr. Martin Gleave, CM, MD, FRCSC, FACS
Distinguished Professor and Head
Department of Urologic Sciences, UBC
Executive Director, Vancouver Prostate Centre
British Columbia Leadership Chair in Prostate Cancer Research

Dr. David Granville, PhD, FAHA
Executive Director, Vancouver Coastal Health Research Institute
Professor and Associate Dean, Research
Faculty of Medicine, University of British Columbia

Lorne D. Sullivan Lectureship
8:45 AM – 9:35 AM  Modeling Drivers of Prostate Cancer Progression and Therapeutic Sensitivity

Dr. Christopher E. Barbieri, MD, PhD
Associate Professor of Urology
Associate Professor of Cell and Developmental Biology
Weill Cornell Medicine and New York-Presbyterian Hospital
Walter B. Wriston Research Scholar

Session I: Basic Science Abstracts
(7-minute talk and 3-minute Q&A)

Moderator: Dr. Nathan Lack

9:35 AM – 9:45 AM  THE ROLE OF RECEPTOR TYROSINE KINASE ROR2 IN STEMNESS AND IMMUNE EVASION
Nakisa Tabrizian, Paul Ann, Daksh Taper, Amina Zoubeidi

9:45 AM – 9:55 AM  DEEP LEARNING-BASED AUTOMATED SPERM IDENTIFICATION FOR NON-OBSTRUCTIVE AZOOSPERMIA PATIENTS
Ryan Lee, Luke Witherspoon, Ryan Flannigan, Hongshen Ma

9:55 AM – 10:05 AM  PROFILING NUCLEOSOME POSITIONING PATTERNS IN METASTATIC PROSTATE CANCER USING DEEP WHOLE GENOME SEQUENCING OF CIRCULATING TUMOUR DNA
Xinyi E. Chen, Sarah W.S. Ng, Cameron Herberts, Matti Annala, Joonatan Sipola, Olga Korhonen, Kevin Beja, Elena Schönlaub, Elie Ritch, Cecily Bernales, Daniel J. Khalaf, Matti Nykter, David A. Quigley, Felix Y. Feng, Kim N. Chi, Alexander W. Wyatt

10:05 AM – 10:15 AM  ASCL1 FACILITATES THE NEUROENDOCRINE LINEAGE REPROGRAMING THROUGH REMODELING OF CHROMATIN LANDSCAPE
Shaghayegh Nouruzi, Dwaipayan Gangul, Daksh Thaper, Nakisa Tabrizian, Max Kobalev, Alastair Davies, Amina Zoubeidi

10:15 AM – 10:25 AM  HOXB13-SWI/SNF COMPLEX ALTERS THE EPIGENETIC LANDSCAPE OF PROSTATE CANCER
Shreyas Lingadahalli, Umut Berkay Altintas, Betul Ersoy, Bengul Gokbayrak, Ivan Yu, Ugur Meric Dikbas, Tunc Morova, Nathan A. Lack
State of Art Lecture I

10:25 AM – 10:40 AM RNA splicing in Prostate Cancer

Dr. Xuesen Dong, PhD
Senior Research Scientist, Vancouver Prostate Centre
Associate Professor, Department of Urologic Sciences
University of British Columbia

Break

10:40 AM – 10:50 AM

Session II: Clinical Abstracts
(7-minute talk and 3-minute Q&A)

Moderator: Dr. David Harriman

10:50 AM – 11:00 AM PROSPECTIVE RANDOMIZED TRIAL OF 2 WEEKS VS 3 MONTHS OF POSTOPERATIVE ANTIBIOTICS AFTER PERCUTANEOUS NEPHROLITHOTOMY IN COMPLEX PATIENTS WITH INFECTION-RELATED KIDNEY STONES.
Alina Reicherz, Ben H. Chew, Amy E. Krambeck, Nicole L. Miller, Ryan His, Kymora B. Scotland, David Miller, Ryan F. Paterson, Victor K.F. Wong, Michelle J. Semins, Dirk Lange

11:00 AM – 11:10 AM SECOND-OPINION READS IN PROSTATE MRI: ADDED VALUE OF SUBSPECIALTY INTERPRETATION AND REVIEW AT MULTIDISCIPLINARY ROUNDS
Drew Phillips, Jessica Li, Sohrab Towfighi, Amanda Wong, Alison Harris, Silvia Chang, Peter Black

11:10 AM – 11:20 AM LONG TERM SURVIVAL OUTCOMES OF LOW RISK NMIBC – HOW LONG IS CYSTOSCOPIC SURVEILLANCE NECESSARY?
Joshua Ma, Mathieu Roumigué, Yuki Kohada, Stéphan Lévy, Tetsutaro Hayashi, Peter Black

11:20 AM – 11:30 AM CAN URODYNAMIC STUDIES PREDICT THE NATURAL HISTORY OF LIPOENGOMYEOCLE (LMM)?
Elaine L. Redmond, Thomas De Los Reyes, Matthew Ho, Andrew Amenyo, Kourosh Afshar

11:30 AM – 11:40 AM BASELINE FRAILTY AND PHYSICAL FUNCTIONING STATUS OF KIDNEY TRANSPLANT RECIPIENTS: A NEED FOR PREHABILITATION
Colin Davey, Annie Tsung, Katie Lyman, David Harriman, Christopher Nguan

State of Art Lecture II

11:40 AM – 11:55 AM A New Reality for Surgeons

Dr. Christopher Nguan, MD, FRCSC
Associate Professor, Department of Urologic Sciences
Director, Postgraduate Medical Education, UBC Urology
University of British Columbia

ADJOURN
Basic Science Abstracts
THE ROLE OF RECEPTOR TYROSINE KINASE ROR2 IN STEMNESS AND IMMUNE EVASION

Nakisa Tabrizian1,2, Paul Ahn1,2, Daksh Taper1,2, Amina Zoubeidi1,3

1 The Vancouver Prostate Centre
2 Experimental Medicine program, University of British Columbia
3 Department of Urologic Sciences, University of British Columbia

Prostate cancer is characterized as an immunologically “cold” tumor with loss of effector CD8+ T-cells and expansion of M2 macrophages and Tregs. These features explain, at least in part, the poor efficacy of immunotherapy in prostate cancer. An increasing number of genomic, epigenomic, transcriptomic profiles, and experimental analysis have suggested negative associations between the cancer stem cell (CSC) phenotype and cytotoxic T-cell responses and anticancer immunity in different cancers. However, the molecular mechanisms responsible for immunomodulating features of CSCs remain poorly understood.

Interrogating different sequencing datasets from metastatic prostate cancer patients revealed an inverse correlation between CSC score and AR activity. Patients were then segregated based on AR expression/activity and were screened for receptor tyrosine kinases (RTK). We identified ROR2 as the most common upregulated RTK in AR low/indifferent patients with increased CSCs markers. Combined transcriptional profiling and functional studies revealed that ROR2/JNK signaling is a powerful inducer of CSC phenotype via up-regulation of the reprogramming transcription factors Oct4 and Sox2. Moreover, depletion of ROR2 decreases immunosuppressive checkpoints (i.e., PD-L1, CD70, Vista, TDO) and dysregulation of cytokines and chemokines that are associated with an immunosuppressive tumor microenvironment. Notably, we found that ROR2 loss of function significantly induces CD8+ T-cell-mediated tumor cell-killing along with a decrease of expression of CCL2 and BMP6 known to recruit M2 macrophages on tumor site.

Our findings identify targetable mechanisms by which ROR2/JNK signaling regulate the reprogramming transcription factors Oct4 and Sox2 expression that may drive the immunomodulatory gene expression and may contribute to the immunosuppressive microenvironment in AR-indifferent prostate cancers.
DEEP LEARNING-BASED AUTOMATED SPERM IDENTIFICATION FOR NON-OBSTRICTIVE AZOOSPERMIA PATIENTS

Ryan Lee¹,²,₅, Luke Witherspoon⁴,⁵, Ryan Flannigan⁵,⁶, Hongshen Ma¹,²,³,₅

¹ Department of Mechanical Engineering, University of British Columbia
² Centre for Blood Research, University of British Columbia
³ School of Biomedical Engineering, University of British Columbia
⁴ Division of Urology, The Ottawa Hospital
⁵ Department of Urologic Sciences, University of British Columbia
⁶ Department of Urology, Weill Cornell Medicine

Introduction:
Over 30 million men worldwide are infertile, and the most severe form of male infertility is non-obstructive azoospermia (NOA). NOA patients require andrologists to find viable sperm to proceed with vitro fertilization (IVF) intracytoplasmic sperm injection (ICSI), which often requires hours seeking rare sperm under a microscope. We evaluate the feasibility of using machine learning methods for the identification of rare sperm in microscopy images taken from a semen sample to improve IVF success rates.

Methods:
We prepared samples using density gradient centrifugation to isolate healthy sperm with no debris or non-sperm cells. Sperm are stained using SYBR-14 and propidium iodide nucleic acid to be identified and then imaged using a fluorescent microscope. Images are then combined, binarized, and used as the ground truth to train a U-Net architecture using binary cross-entropy loss to segment sperm pixels. Individual sperm are identified using the watershed algorithm and evaluated through precision-recall metrics and receiver operating characteristic curves.

Results:
Unlike previous work, the model is trained on brightfield (BF) images with unwashed and unstained samples to mimic clinical practice. Pilot detection tests showed F1-scores of 0.96, 0.93, and 0.74 for 20x, 10x, and 4x magnification, respectively. 10x magnification was chosen over 20x to optimize for both model performance and imaging speed as 10x imaging by area is 4 times as quick as 20x. Heavily unbalanced datasets were counteracted using weighted losses. At 10x magnification, our model achieves 91% precision and 96% recall in finding sperm in BF semen images.

Conclusions:
Our results indicate it is feasible to use convolutional neural networks to semantically segment sperm to support andrologists for IVF-ICSI. Our custom lab protocol creates training data containing stained sperm and unstained miscellaneous cells, allowing for the first example of a real-world application of AI for assisted sperm identification.
PROFILING NUCLEOSOME POSITIONING PATTERNS IN METASTATIC PROSTATE CANCER USING DEEP WHOLE GENOME SEQUENCING OF CIRCULATING TUMOUR DNA

Xinyi E. Chen1,2, Sarah W.S. Ng1,2, Cameron Herberts1,2, Matti Annala4, Joonatan Sipola4, Olga Korhonen4, Kevin Beja1,2, Elena Schönlau1,2, Elie Ritch1,2, Cecily Bernales1,2, Daniel J. Khalaf3, Matti Nykter4, David A. Quigley5, Felix Y. Feng5, Kim N. Chi3, Alexander W. Wyatt1,2

1 Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada
2 Vancouver Prostate Centre, Vancouver, BC, Canada
3 BC Cancer Agency, Vancouver Centre, Vancouver, BC, Canada
4 Institute of Biosciences and Medical Technology, Tampere, Finland
5 Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco (UCSF), San Francisco, CA, USA

Introduction and Objectives:
Circulating tumour DNA (ctDNA) profiling is an emerging non-invasive alternative to metastatic tissue biopsy for tumour genotyping. Fragmentation patterns of ctDNA recovered via whole genome cell-free DNA sequencing footprint the positions of nucleosomes and transcription factors in cells of origin. Preliminary evidence suggests that gene expression can be inferred from ctDNA fragmentation patterns. Our objective was to assess whether ctDNA-fragmentation profiling can recapitulate patient-matched tumour tissue transcriptomes, and to investigate its potential to clarify patterns of tumour evolution during systemic therapy for metastatic disease.

Methods:
We analyzed deep whole genome sequencing data from 81 serial cfDNA samples from 33 patients with metastatic castration resistant prostate cancer (mCRPC), 13 of whom had RNA-seq data from time-matched metastatic tissue biopsy. We examined ctDNA fragmentation patterns at gene transcription start sites (TSS) and at 4200 highly curated androgen receptor (AR) binding sites.

Results:
Nucleosome positioning at TSS inferred by ctDNA fragmentation is strongly correlated with gene expression from tissue biopsy (|R| > 0.98, p < 0.001, Spearman correlation). We observed the strongest nucleosome positioning amongst the most highly expressed genes (n = 1000) with high nucleosome occupation at ~60bp downstream of TSS and a depletion of nucleosomes at the TSS. In one patient whose tumour progressed to an androgen receptor-independent genotype, we found a corresponding decrease in the strength of nucleosome positioning at AR binding sites over serial cfDNA samples.

Conclusions:
CtDNA-fragmentation analysis is a possible method to analyze tumour gene expression and androgen receptor activity, which may add to the practicality of cfDNA assays in clinical settings. Continuing work will include the development of a bespoke targeted sequencing panel that can capture ctDNA-fragmentation patterns. This may yield a cost-effective clinical tool for monitoring changes in tumour transcriptional activity to provide clinicians with additional information with which to guide treatment selection.
ASCL1 FACILITATES THE NEUROENDOCRINE LINEAGE REPROGRAMMING THROUGH REMODELING OF CHROMATIN LANDSCAPE

Shaghayegh Nouruzi1,2, Dwaipayan Ganguli1, Daksh Thaper1, Nakisa Tabrizian1,2, Max Kobalev1,2, Alastair Davies1, Amina Zoubeidi1

1 Vancouver Prostate Centre, Vancouver, BC, Canada, 2 Department of Urologic Sciences, Faculty of Medicine, University of British Columbia, Vancouver, Canada

Lineage plasticity and transformation to small cell neuroendocrine prostate cancer (NEPC) is an increasingly recognized mechanism of treatment resistance in advanced prostate cancer which is associated with poor prognosis. With the exception of alteration in TP53 and RB1, few genetic differences are observed between CRPC and NEPC; suggesting epigenetic regulation as a mechanism supporting treatment resistance and conversion to NEPC. Here we investigate how hormone therapy architect a chromatin landscape to regulate gene expression when promoting neuroendocrine differentiation. To identify activated transcription factors that govern cell plasticity after hormone therapy, we utilized ATAC-seq, to interrogate chromatin accessibility, in combination with transcriptomic (RNA-seq) and ChIP-seq. We find that Enzalutamide (ENZ) treatment of CRPC-Ad cell lines, results in an induction of chromatin accessibility as early as 3 days and continue to expand accessibility at 10 days. The new accessible regions in 10 days post-ENZ treatment significantly resembling the chromatin landscape of NE cells, with close to 70% shared peaks. We discovered the DNA binding motif for the neural lineage transcription factor ASCL1 to be disproportionally enriched in hyper-accessible chromatin regions after ENZ treatment and in treatment-induced NEPC compared to CRPC. Our matched RNA-seq data confirmed that ASCL1 expression and transcriptional activity were upregulated in NEPC cell lines and patient tumours relative to CRPC. Ectopic expression of ASCL1 in CRPC-Ad cells was sufficient to induce conversion to a NEPC state. Conversely, silencing ASCL1 in tNEPC abrogated NE marker expression and neuronal-associated transcriptional networks with extensive chromatin reorganization, coincident with reduced cell proliferation in vitro and tumour growth in vivo. Mechanistically, ASCL1 knockdown led to activation of pathways involved in histone methylation with a drastic decrease in global H3K27me3 imparted by the EZH2-containing Polycomb Repressive Complex 2 (PRC2). These epigenetic changes were not the result of altered expression of the core PRC2 subunits EZH2, SUZ12, and EED but rather an effect on the dissociation of the complex disturbing EZH2 binding to the chromatin. The loss of EZH2 binding to the chromatin after loss of ASCL1 pheno-copied EZH2 inhibition and reactivated canonical AR signaling, and re-sensitizing the cells to further AR inhibition. Altogether, data suggest that ASCL1 may drive early transcriptional and epigenetic reprogramming through the PRC2 complex to facilitate the emergence and maintenance of treatment induced NEPC.

This project is supported by CIHR and Mitacs
HOXB13-SWI/SNF complex alters the epigenetic landscape of prostate cancer

Shreyas Lingadahalli¹, Umut Berkay Altintas², Betul Ersoy², Bengul Gokbayrak², Ivan Yu¹, Ugur Meric Dikbas¹, Tunc Morova¹, Nathan A. Lack¹,²

¹ Vancouver Prostate Centre, Vancouver
² Koc University, Istanbul

Androgen deprivation therapy (ADT) is the standard of care to treat locally advanced and metastatic prostate cancer (PCa). However, even with the use of second generation anti-androgen drugs remission is almost always temporary and the majority of patients develop resistance and progress to a highly lethal castrate-resistant PCa (CRPC). There is an urgent need to develop novel therapies to treat CRPC. Homeobox-B13 (HOXB13) is a master transcriptional regulator which is exclusively expressed in the prostate tissue and has been shown to be crucial for its embryonic development. Recent studies have shown that it also plays an important role in PCa and CRPC. We and others have recently shown that HOXB13 is essential for in vitro and in vivo growth in almost all PCa models. Therefore pharmacological targeting of HOXB13 transcriptional machinery offers a potential therapeutic strategy to treat advanced PCa and CRPC. However, targeting HOXB13 is challenging due to the high conservation of the homeobox domain. As transcriptional specificity is driven by the recruitment of specific co-regulatory proteins, we therefore proposed that inhibiting these critical protein-protein interactions is a promising pharmacological approach to inhibit HOXB13. To determine the HOXB13 interactome we purified all endogenous HOXB13 interacting partners from multiple prostate cancer cell lines. From this we identified and validated SMARCD2, a member of SWI/SNF chromatin regulatory complex as a novel HOXB13 co-regulatory factor. Interrogation HOXB13/SMARCD2 in clinical samples showed a significant correlation of their mRNA expression in PCa. Further supporting this observation, results from our customized in vivo dropout screen shows a strong codependency of HOXB13/SMARCD2 for the survival of PCa cells. Next to delineate its functional role, we defined the core HOXB13 regulated genes and mapped the genome-wide HOXB13 binding regions in various PCa cell models. While there was a marked difference in HOXB13-regulated genes and their cis-regulatory elements in AR-dependent (LNCaP) and AR-independent (PC3) PCa models, interestingly, SWI/SNF complex was highly enriched at the HOXB13 binding sites in both the models. Together, our results show HOXB13-SWI/SNF complex modulate the epigenetic landscape at cis-regulatory elements of pro-mitotic genes to promote PCa growth and development.
Clinical Abstracts
PROSPECTIVE RANDOMIZED TRIAL OF 2 WEEKS VS 3 MONTHS OF POSTOPERATIVE ANTIBIOTICS AFTER PERCUTANEOUS NEPHROLITHOTOMY IN COMPLEX PATIENTS WITH INFECTION-RELATED KIDNEY STONES.

Alina Reicherz1, Ben H. Chew1, Amy E. Krambeck2, Nicole L. Miller3, Ryan His3, Kymora B. Scotland6, David Miller4, Ryan F. Paterson1, Victor K.F. Wong1, Michelle J. Semins5, Dirk Lange1

1 Department of Urologic Sciences, Vancouver, British Columbia V5Z1M9, Canada
2 Department of Urology, Mayo Clinic, Rochester, USA
3 Department of Urologic Surgery, Vanderbilt University Medical Center, Nashville, USA
4 Department of Urology, University of Pittsburgh Medical Center, Pittsburgh, USA
5 James Buchanan Brady Urological Institute and The Russell H. Morgan Department of Radiology and Radiological Science, The Johns Hopkins University School of Medicine, Baltimore, USA.
6 Department of Urology, UCLA Medical Center, Los Angeles, USA

Introduction & Objective:
Struvite kidney stones are associated with bacterial urinary tract infections (UTIs) and cause disproportionate mortality (up to 67%). Treatment of struvite stones requires complete surgical stone removal followed by antibiotic therapy to eliminate the UTI to reduce stone recurrence. The optimal duration of antibiotic therapy is unknown. We sought to determine if there is a difference in outcomes between 2 weeks or 3 months of antibiotics post percutaneous nephrolithotomy (PCNL).

Methods:
This multi-center, prospective randomized trial evaluated patients with the clinical diagnosis of struvite stones. Patients were randomized to 2 weeks or 3 months of postoperative oral antibiotics (nitrofurantoin or culture-specific antibiotic) and included PCNL achieved stone-free status (residual fragments ≤4mm) on computed tomography imaging (CT). CT and urine culture was performed at 3-, 6-, and 12-months post-procedure. The study was powered to 80%, with 11 patients in each group.

Results:
Thirty-eight patients were enrolled and randomized to either 2 weeks (n=20) or 3 months (n=18) of antibiotic therapy post-PCNL. Twelve patients were excluded due to residual fragments, and 2 patients were lost to follow-up. Age was similar between groups (49.4±5.0 vs 55.1±5.8y), as was BMI (29.5±2.3 vs 32.5±3.9kg/m²) and maximal stone diameter (22.4±2.3 vs 27.4±5.2 mm, p=0.36), respectively. At 3-, 6-, and 12-month follow-up, positive urine cultures were 50.0 vs 37.5%, 50.0 vs 83.3%, and 37.5% vs 100% between 2 weeks and 3 months groups, respectively (p=ns). At 3-, 6-, and 12-months follow-up, stone-free rates were 75.0% vs 70.0%, 70.0% vs 57.1%, 80.0% vs 57.1% (p=ns), between 2 weeks and 3 months groups, respectively.

Conclusions:
No significant difference in stone recurrence or recurrent UTI comparing 2 weeks versus 3 months of postoperative antibiotics. For patients with stone removal following PCNL, 2 weeks of postoperative oral antibiotics are sufficient to prevent recurrent UTI and stones.
SECOND-OPINION READS IN PROSTATE MRI: ADDED VALUE OF SUBSPECIALTY INTERPRETATION AND REVIEW AT MULTIDISCIPLINARY ROUNDS

Drew Phillips, Jessica Li, Sohrab Towfighi, Amanda Wong, Alison Harris, Silvia Chang, Peter Black

1 Vancouver General Hospital Department of Urologic Sciences, University of British Columbia, Level 6, 2775 Laurel St, Vancouver, BC V5Z1M9, Canada.
2 Vancouver General Hospital Department of Radiology, Jim Pattison Pavilion, 899 W 12th Ave, Vancouver, BC V5Z1M9, Canada.

Introduction and Objectives:
Interobserver variability in multiparametric prostate magnetic resonance imaging (MRI) interpretation for cancer detection has been investigated since the introduction of PI-RADS. This study aims to evaluate how often second-opinion review of prostate MRIs by multidisciplinary review board at a tertiary care centre is discordant with initial community radiologist interpretation.

Methods:
Cases were collected retrospectively from multidisciplinary prostate MRI rounds from 2017-2020 at a single tertiary care centre. Patients were referred for consideration of transrectal ultrasound (TRUS)/MRI fusion biopsy based on community-read prostate MRIs. All MRIs were re-read by a single subspecialized abdominal radiologists and a PI-RADS score assigned. Targeted fusion and 8-12 core systematic biopsy was performed in patients with PIRADS≥3 lesions. Cohen kappa values were used to quantify interobserver agreement. Positive predictive value (PPV) was used to determine accuracy of PIRADS score for detection of clinically significant prostate cancer (csPCa) (Grade Group ≥2).

Results:
In total, 332 lesions in 303 patients were reviewed and 252 lesions in 198 patients biopsied. The PI-RADS score was concordant in 60.5% of lesions, downgraded in 17.8%, and upgraded in 7.8%. 36 lesions were missed, 10 of which contained csPCa. Agreement between community and tertiary centre interpretation was fair (κ=0.354), with greater agreement for PI-RADS≥4 (κ=0.523) than PI-RADS≥3 (κ=0.456). Prevalence of csPCa in biopsied lesions was 40.9%. In PI-RADS≥4 lesions, the PPV for csPCa was higher in tertiary centre than community interpretations (55.0% vs 44.6%). Re-interpretation altered clinical management in 55 patients.

Conclusion:
There is variability in community and tertiary care centre interpretation of prostate MRI in cancer detection. Concordance rates were improved for higher grade lesions, with tertiary centre reinterpretation demonstrating higher PPVs. Discrepancies in the interpretation of prostate MRI for cancer detection between community and tertiary care centres highlight the need for ongoing education and feedback.
LONG TERM SURVIVAL OUTCOMES OF LOW RISK NMIBC – HOW LONG IS CYSTOSCOPIC SURVEILLANCE NECESSARY?

Joshua Ma1, Mathieu Roumiguie1,2, Yuki Kohada3, Stephan Lévy2, Tetsutaro Hayashi4, Peter Black1

1 Vancouver Prostate Centre, Department of Urologic Sciences, University of British Columbia, Vancouver, Canada.
2 Department of Urology, CHU-Institut Universitaire du Cancer de Toulouse, France
3 Department of Urology, Hiroshima Prefectural Hospital, Hiroshima, Japan
4 Department of Urology, Hiroshima University, Graduate School of Biomedical Sciences, Hiroshima, Japan

Introduction and Objectives

While low-risk non muscle invasive bladder cancer (LR-NMIBC) has a low propensity to progress, the risk of recurrence remains high (50% at 4 years). Guidelines recommend a cystoscopic surveillance after diagnosis, but the duration of follow-up continues to be a subject of discussion, and the longer-term natural history of LR-NMIBC remains poorly defined. In this study, we aim to report the risk of recurrence beyond 5 years after diagnosis, and to identify prognostic factors of late recurrence for LR-NMIBC.

Method

In this international multicentric retrospective observational study, patients who received their first transurethral bladder tumour resection (TURBT) before 2016 for a LR-NMIBC were included. Low-risk was defined as primary, solitary, low grade (G1 WHO1973 or low grade WHO2004), Ta bladder tumour measuring <3cm.

Results

Among 576 patients included, 125(21.7%) were female and median age was 71 years. The median follow-up was 66.1(39.2-92.1) months and a recurrence was observed in 236(41%) patients. Kaplan-Meier curves showed that lack of single postoperative dose of chemotherapy and tumor size > 1cm were independent prognostic factors of recurrence. The risk of recurrence was highest in the first 2 years after diagnosis, (26.2%;151/576) and decreased progressively beyond 2 years (13.4%;57/425) and 5 years (6.8%;27/398;p<0.001). High-risk recurrence occurred in 4.9%(28/576) of patients, and 5(0.87%) of these occurred after 5 years. The likelihood of high-risk recurrence diminished with time: 1.7% in first 12 months and 0.87% beyond 60 months.

Conclusion:

The risk of recurrence decreases progressively after 2 years and remains low beyond 5 years in LR-NMIBC. Since the infrequent tumor that recurs after 5 years is likely to be low grade and papillary, cystoscopic surveillance can be discontinued after 5 years in patients with low risk NMIBC. Tumor size larger than 1cm and lack of postoperative chemotherapy may be relevant variables to identify patients who will benefit from longer cystoscopic follow-up.
CAN URODYNAMIC STUDIES PREDICT THE NATURAL HISTORY OF LIPOMENGOYEOLEOLE (LMM)?

Redmond EJ, De Los Reyes T, Ho M, Amenyooge A, Afshar KA
BC Children’s Hospital, Vancouver, Canada

Introduction:
The dogma of early surgical detethering in the management of LMM has been questioned. Most centres advocate a conservative approach in the management of asymptomatic patients. However, identifying which patients will develop sequelae of cord tethering and might benefit from early intervention is challenging. The aim of our study was to assess the association between urodynamic (UDS) parameters and clinical outcomes of children with LMM.

Methods:
A retrospective review was performed on pediatric patients (0-18 years) attending the spinal cord clinic with LMM. Baseline demographics, surgical intervention, bowel and bladder function were recorded. UDS parameters were evaluated using a previously validated composite score.1

Results:
Thirty-two patients were identified for inclusion (16 male, 16 female). Baseline UDS were performed at a median age of 6.5 months (1-144). The mean length of follow up was 11 years (2-19). Seven patients perform intermittent catheterisation. The remainder have normal bladder function. Four patients use regular laxatives. The remainder have normal bowel function (missing=10). Seventeen patients required neurosurgical release of the tethered cord (median age 27 months (4-144)). There was no difference in baseline UDS composite score between those who required intervention and those who did not (median 8 vs 10 p=0.09). There was a significant deterioration in UDS scores from baseline in patients who required intervention (median 8 vs 5.7, p=0.05). UDS scores significantly improved in patients following surgical detethering (median 5.7 vs 10, p=0.026).

Conclusion
Baseline UDS parameters were unable to predict which patients developed symptoms of cord tethering requiring intervention. However, patients who required detethering procedures had a significant deterioration in preoperative UDS parameters from baseline. These appeared to improve following surgery. Routine UDS in this cohort might detect changes which precede other neurologic findings and could therefore serve as a tool for risk stratification and outcome monitoring of these patients.

1 MacNeily AL et al. Development of an Objective Score to Quantify the Pediatric Cystometrogram. J Urol 2007;178:1752

.1 MacNeily AL et al. Development of an Objective Score to Quantify the Pediatric Cystometrogram. J Urol 2007;178:1752
BASELINE FRAILITY AND PHYSICAL FUNCTIONING STATUS OF KIDNEY TRANSPLANT RECIPIENTS: A NEED FOR PREHABILITATION

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Background:
Frailty is associated with poor health outcomes after kidney transplantation. However, no current guidelines objectively assess the frailty and physical functioning status of kidney transplant candidates. We sought to quantify frailty status and its relationship to physical functioning.

Methods:
We analyzed the baseline frailty and physical functioning status for (n=86) kidney transplant recipients enrolled in a prospective cohort study at Vancouver General Hospital. Frailty was determined using the Fried Frailty Phenotype (FFP). Physical functioning was assessed using the 6-minute walk, 30-second sit-to-stand and timed-up and go (TUG) tests. Comparisons between frailty status and physical functioning were made using one-way Anova and post hoc Tukey HSD.

Results:
A total of 80 participants performed the baseline frailty and physical functioning assessment with a mean age of 56.1 ± 14.1. Patients were predominately male sex (57.0%), and on hemodialysis (51.2%). Using the FFP the prevalence of frailty was 21.3%, this increased to 27.3% for those receiving hemodialysis. The mean distance (443.5 ± 196.5 m) covered during the 6-minute walk test in the frail group was significantly less than the mean distance (518.4 ± 177.2 m) covered by the non-frail group (p=0.0045). There was also a significant difference between the non-frail and frail group for the 30-second sit-to-stand (p=0.014), timed-up and go (p=0.0025) and fatigue questionnaire (p=0042).

Conclusions:
Frailty is highly prevalent in BC patients who are being considered for kidney transplantation. Furthermore, there is a significant decrease in physical functioning associated with increasing levels of frailty. These preliminary results highlight the potential utility of prehabilitation as a means to improve physical functioning and slow the progression of frailty pre-operatively. Further study is required to determine the impact that prehabilitation and frailty status may have on post-operative recovery.
Organizing Committee

- Dr. Amina Zoubeidi
- Dr. Ben H. Chew
- Dr. Kouros Afshar
- Dr. Peter C. Black

Learning Objectives

- To inform members of the types of clinical and basic science research being conducted in the Department of Urologic Sciences.
- To familiarize members with new innovative research techniques.
- To foster an atmosphere of collaborative research within the Department of Urologic Sciences.

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