Syllabus

JK Wyatt Urology Residents Research Day

Friday, June 2, 2017
London Convention Centre
London, Ontario

Schulich MEDICINE & DENTISTRY

Western

Remembering...

Dr. John (Jack) Kenneth Wyatt

Jack Wyatt completed his undergraduate and medical school training at Western. During his university days he excelled in sports and was captain of the Western football team. His medical school classmates described him as the class prankster.

After completion of residency training Dr. Wyatt began his urological career in 1960 at Victoria Hospital, practicing general urology with a special interest in cancer and reconstructive surgery. He later went on to serve as Residency Program Director and Division Chair, and aided the building of the Western Urology division into a strong clinical and academic program.

Dr. Wyatt is fondly remembered by alumni for his care in their well being as residents, and his sharp clinical acumen. He was also a great storyteller with a razor-sharp wit and dry sense of humor. He is remembered by former patients for his common sense approach, easy -going nature and empathy.

During his career Dr. Wyatt was actively involved in both the Northeastern Section of the American Urological Association and Canadian Urological Association. He served as CUA President in 1984.

Dr. Jack Wyatt passed away in 2004 after a long and distinguished urological career. We are indebted to his many contributions to Urology in London and beyond. His legacy is celebrated through our annual Research Day.

Western University
Jack Wyatt Urology Residents' Research Day
2017

RESIDENTS:

PGY5

Jeffrey Campbell
Victor McPherson
Siobhan Telfer

PGY4

Garson Chan
Melissa Huynh
David Mikhail

PGY3

Justin Kwong
Nahid Punjani
Wen Yan Xie

PGY2

Harmenjit Brar
Roderick Clark

PGY1

Jeffrey Law
Samir Sami
Heena Singh

FELLOWS

Katherine Henriquez — Andrology

Abdulaziz Al-Athel — EndoUrology

Bijad Alharbi— Transplant
Shahid Aquil — Transplant

Malcolm Dewar—UroOncology

RESEARCH STUDENTS PRESENTATING

Aymon Ali

Ryan Chanyi

Noah Stern

Samantha Whiteside

GUEST PROFESSOR 2017

Arthur L. Burnett

M.D., M.B.A., F.A.C.S.

Dr. Arthur (Bud) Burnett received his A.B. degree in Biology from Princeton University and M.D. and M.B.A. degrees from Johns Hopkins University. His post-graduate training in general surgery, urology, and reconstructive urology and urodynamics was performed at the Johns Hopkins Hospital. He subsequently joined the faculty at the Johns Hopkins University School of Medicine, receiving an American Foundation for Urologic Disease scholarship, and thereafter he ascended to his current rank as the Patrick C. Walsh Distinguished Professor of Urology. Dr. Burnett also holds a faculty appointment in the Cellular and Molecular Medicine Training Program, Honorary Professor, Department of Surgery, Radiology, Anesthesia & Critical Care, Faculty of Medical Sciences, University of the West Indies, Mona, Jamaica, and Professor, Oncology Center, Johns Hopkins University School of Medicine. Additional appointments are that of Director of the Basic Science Laboratory in Neuro-urology of the James Buchanan Brady Urological Institute and Director of the Male Consultation Clinic. He is an alumni member of the Alpha Omega Alpha Honor Medical Society and Fellow of the American College of Surgeons. He received the 2016 Urology Care Foundation Distinguished Mentor Award, for exceptional leadership, skill and ability in serving as a high-quality mentor. Dr. Burnett specializes in sexual medicine, major pelvic reconstruction, voiding dysfunction, female urology, and prostate cancer. Dr. Burnett has served in multiple professional capacities with medical organizations and advisory committees to include chairperson of the Urology Study Section, National Institutes of Health (2004-2007); the Research Council, Prostate Cancer Guidelines Update Panel, and Prostate Cancer Outcomes Working Group of the American Urological Association; member of the American Board of Urology Examination Committee (2001-2005); member of the FDA Advisory Committee for Reproductive Health Drugs (2003-2007); and member of the Board of Directors, Treasurer and President of the Sexual Medicine Society of North America (2005-Present). Dr. Burnett has written more than 300 original peer-review articles and 50 book chapters, along with numerous additional editorials and publications relating to his biomedical research and clinical activities. His work has appeared in many prominent journals such as *Science, Nature Medicine, Proceedings of the National Academy of Sciences, Journal of Urology, Urology* and *Journal of Andrology*. Dr. Burnett also has held journal editor appointments such as Co-Editor-in-Chief of the *Journal of Andrology*, Assistant Editor of the *Journal of Urology*, and Reviews Editor of the *Journal of Sexual Medicine*.

Western University

Jack Wyatt Urology Residents' Research Day

2017

This program was supported in part by educational grants from the following:

JK Wyatt Urology Residents' Research Day

Friday, June 2, 2017
London Convention Centre, London, Ontario

AGENDA

7:00- 8:00 Registration and Continental Breakfast

8:00- 8:15 Welcome and Introductions: Dr. H. Razvi and Dr. A. Sener

SESSION I Transplantation Moderator Dr. Sener

8:15-8:30 B. Al-Harbi: Impact of Pancreas Transplant Failure: A Quality of Life Assessment in Simultaneous Kidney and Pancreas Transplant Patients

8:30-8:45 J. Law: Significance of Atypical Cytology in the Evaluation of Patients with End Stage Renal Disease for Transplantation

8:45-9:00 H. Singh: Longer Functional Warm Ischemic Times Do Not Impact Donation After Cardiac Death Renal Allograft Outcomes

9:00-9:15 D. Mikhail: The Impact of Elevated Doppler Resistive Indices in Renal Transplant Recipients with Delayed Graft Function

9:15-9:45 **Western Faculty Presentation Dr. J. Denstedt:** ***"Surgical Training in the 21st Century"***

9:45-10:15 Refreshment/Health Break

SESSION II Oncology I Moderator Dr. Power

10-15-10:30 H. Brar: Triple Positive Microparticles as a "Liquid Biopsy" for Risk Stratification of Prostate Cancer

10:30-10:45 V. McPherson: A Window Of Opportunity Study to Evaluate the Role of the Combination of Metformin and Simvastatin as a Neoadjuvant Therapy In Invasive Bladder Cancer

10:45-11:00 N. Punjani: Trends in Stage I Non-Seminomatous Germ Cell Tumors in the United States

11:00-11:15 W. Xie: Assessment of the Paris System for Reporting Urine Cytology: A Quality Assurance Review

11:15-12:00 **Guest Professor Dr. A. Burnett:** ***"Priapism - Management and Emerging Therapies"***

12:00-13:00 LUNCH

SESSION III Functional Urology Moderator Dr. Welk

13:00- 13:15 R. Clark: The Ability of Prior Urine Cultures to Predict Future Urinary Culture Organisms and Resistance Patterns Among Individuals with Neurogenic Bladder Dysfunction

13:15 -13:30 S. Whiteside: Bacterial Production of Neurotransmitters: What does This Mean for the Bladder?

13:30- 13:45 J. Campbell: Intracavernosal Injection of Botulinum Toxin to Improve Erectile Function in Older Rats

13:45- 14:00 K. Henriquez: Platelet Rich Plasma for Erectile Dysfunction and Other Evolving Therapies

14:00-14:45 Guest Professor
Dr. A. Burnett: *"Penile Transplantation - An Option for Major Genital Loss"*

14:45- 15:15 Refreshment/Health Break

SESSION IV Basic Science Moderator Dr. Reid

15:15- 15:30 A. Ali: The Drosophila Melanogaster Model of Human Uric Acid Nephrolithiasis as a Novel in vivo High Throughput Drug Screening Platform

15:30- 15:45 R. Chanyi: The Importance of Xenobiotic Metabolism by the Microbiome in Prostate Cancer

15:45- 16:00 A. Al-Athel: The Effects of Shockwave Lithotripsy on the Urinary Microbiome and on Bacterial Dispersion Using a Phantom Kidney Stone Model

16:00- 16:15 M. Huynh: Clinical Correlation of Patient-derived Xenograft Model Using the Ex-ovo Avian Embryo to Predict Targeted Therapy Tumor Resistance in Renal Cell Carcinoma

SESSION V Surgical Outcomes Moderator Dr. Pautler

16:15- 16:30 G. Chan: Partial Nephrectomy does not Greatly Alter Long Term Cardiovascular and Renal Outcomes and Non-Cancer Related Mortality vs Radical Nephrectomy

16:30- 16:45 S. Telfer: Factors Contributing to Delay in Time to Orchidopexy in Ontario, Canada

16:45-17:00 J. Kwong: Return to Continence Following Radical Prostatectomy: A Single Surgeon Comparison of Robot-Assisted with Multi-Layer Closure, Robot-Assisted Alone, Laparoscopic and Open Approaches

17:00- 17:15 N. Stern: A Prospective Study on the Operative Timing and Learning Curve of Robotic Pediatric Urology Procedures in the Canadian Health Care System

17:15 Wrap Up and Evaluations

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*Note: Guidelines = 15 minute presentations = 10 minute presentation, 5 minute Q & A
30 minute presentations = 20 minute presentation, 10 minute Q & A
45 minute presentations = 30 minute presentation, 15 minute Q & A

"This event is an accredited group learning activity (section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, approved by the Canadian Urological Association (CUA). The specific opinions and content of this event are not necessarily those of the CUA, and are the responsibility of the organizer(s) alone."

This year's program is intended to provide participants with:

1. Incorporating evidence-based medicine into resident education and research
2. To update new paradigms in surgical training in the 21st century
3. To review current clinical practice guidelines in the management of priapism
4. To review state-of-the-art care in the management of major external genital trauma
5. To review the results of clinical and basic science research projects of the training staff from Western University in the following subspecialty areas:
   a. Oncology
   b. Endourology
   c. Transplantation
   e. Transplantation
   d. Andrology
   e. Urinary voiding dysfunction

IMPACT OF PANCREAS TRANSPLANT FAILURE IN QUALITY OF LIFE IN SIMULTANEOUS KIDNEY PANCREAS TRANSPLANTATION

Alharbi B, Aquil S, Ali A, Sener A, Luke P

Background:
Both kidney and pancreas transplantation have been shown to be associated with improved quality of life (QoL). In fact, one of the most important outcomes with pancreas transplantation is the improvement of recipient QoL.

Objective:
As it is unclear whether QoL remains good the pancreas allograft is lost, we measured the quality of life (QoL) in simultaneous kidney pancreas transplant (SPK) patients in order to determine whether QoL remains high despite loss of the pancreas allografts.

Methods:
Short Form Health Quality of life Survey 36-Item (SF-36) questionnaires were prospectively administered to 59 SPK recipients 3 months, 1 and 5 years post-transplantation between 2004-2016. Of the recipients, 9 patients developed pancreas transplant failure. Statistical analysis was done by descriptive and analytical statistics (ANOVA, independent sample T-test and regression model) using SPSS version 23.

Results:
There was no difference in median age, or gender in either group. There was no statistically difference in both groups regarding energy and emotions with 60% of both groups reported calm, peace and lot of energy. As well, <10% patients from both groups reported physical health and emotional problems interfering social activities (p = NS). The failed transplant cohort of patient reported significant reduction in activity compared to functioning transplant cohort (p=0.04, log Likelihood ratio 3.5). The failed transplant cohort of patient had more physical health problems (p=0.01, log Likelihood ratio 18.95). The likelihood ratio of emotional health problems in failed transplant cohort was 12.6 (p=0.002). This resulted in impaired social activities and interference with work vs control (both p=0.001). Overall, the failed transplant cohort reported poor general health vs control (p=0.004), log likelihood ratio 8.7.

Conclusion:
SPK recipients with pancreas graft loss had significantly worse QoL vs those with maintained graft function. Whether QoL was impaired as a consequence of the persistence of diabetes mellitus or the process that led to graft failure is yet to be determined.

SIGNIFICANCE OF ATYPICAL CYTOLOGY IN THE EVALUATION OF PATIENTS WITH ESRD FOR TRANSPLANTATION

Law J, Ali O, Brar H, Luke P, Sener A

Introduction And Objectives:
Our goal was to determine the incidence of urothelial carcinoma and the significance of urinary atypia in ESRD patients being investigated for transplantation and to establish if it was necessary to perform cystoscopy on all ESRD patients with atypical cytology.

Methods:
We reviewed all patients with ESRD for renal transplantation at our institution from January 2000 to December 2015. A total of 1289 patient charts were retrospectively reviewed.

Results:
8 patients of 1289 (0.62%) patients were found to have urothelial carcinoma (6 males: 2 females), 6 of which were found on pre-transplant surveillance and 2 of which developed subsequent urothelial carcinoma several years after transplant. Mean age of patients who had urothelial carcinoma (65.6±10.1years) was significantly greater than those who did not (50±14.2years; p=0.0018). Of these patients, 67% had a history of smoking but all had microscopic hematuria at presentation. Of the 1289 patients, 494 ESRD patients had available screening urinary cytology, 180 (36%) had urinary atypia; subsequent cystoscopy revealed cancer in 6 patients (3%). All tumors were treated with TURBT/ fulguration ± mitomycin instillation. Pathology showed papillary non-invasive urothelial carcinoma. No patient required subsequent cystectomy or radiation therapy. All patients who had urothelial carcinoma discovered pre-operatively eventually underwent renal transplant and only one of these patients has had recurrent disease requiring further treatment.

Conclusion:
The urinary atypia rate is higher in ESRD patients but the incidence of urothelial carcinoma is lower compared to the general population.

LONGER FUNCTIONAL WARM ISCHEMIC TIMES DO NOT IMPACT DONATION AFTER CARDIAC DEATH RENAL ALLOGRAFT OUTCOMES

Singh HK, Huynh MJ, Weernick C, Sener A, Luke PP

Introduction & Objectives:
Donation after circulatory death (DCD) renal transplants are associated with long-term outcomes comparable to that of donation after neurological donor death (NDD) transplants, but the effect of longer functional warm ischemia time during withdrawal is unknown. Nevertheless, a hard cutoff of 2 hours warm ischemic time has been used to exclude the use of DCD donors.

Methods:
We retrospectively analyzed the impact of mean arterial pressure (mAp) <55 during donation for different time points (30, 45, 60, and 90mins) on delayed graft function time (DGF), creatinine clearance (CrCl) at 1 year and overall graft survival. A total of 190 single donations after DCD renal transplants were performed at our institution between July 2006 and June 2016. Outcome variables such as CrCl, hospital stay, readmission rate, DGF and overall graft loss and rejection were compared between groups using the Student t-test and the Pearson chi-square test. A linear regression model was also used for independent prognostication.

Results:
Mean age of recipients and donors were 54.7 and 44 years old respectively and 13% of the population were expanded criteria donors. Patients were followed for a median of 39 months (range 1 - 122 months). The functional warm ischemia time >80 min was not associated with DGF (X^2=1.51, p=0.22), patient death (X^2=0.08, p=0.77), cell mediated (X^2=0.24, p=0.63) or antibody-mediated rejection (X^2=0.03, p=0.87) of the graft, antibody and cellular rejection (X^2=0.07, p=0.79), or graft failure (X^2=3.35, p=0.07) if mAP >80 min. Similarly, actual warm ischemia time >80 min was not associated with DGF (X^2=0.01, p=0.92), patient death (X^2=0.39, p=0.53), cell mediated (X^2=1.12, p=0.29) or antibody-mediated rejection (X^2=0.13, p=0.72) of the graft, antibody and cellular rejection (X^2=0.33, p=0.57), or graft failure (X^2=0.003, p=0.95) if mAP >80 min. Actual WIT <45 min was associated with CrCl at 7 days (t=2.50, p=0.01) but not 1, 3,12 month or 3 and 12 month ratios Independent multivariate regression model looking at actual WIT as an independent predictor of Cr Cl at 7 days (p=0.39), 1 month (p=0.69), 3 month (p=0.92) or 1 year (p=0.76) and patient survival (p=0.68), graft survival (p=0.17), readmission length of stay (p=0.43), did not show any significance. However higher warm ischemia time (R^2=-0.81, F(3,105)=6.99, p <0.05) was an independent predictor of poor graft survival. . The graft survival, patient survival, readmission length of stay, CrCl at 1 week, 1, 3, and 12 months were not an independent prognosticator of functional warm ischemic time.

Conclusions:
The duration of actual and functional warm ischemic time was not associated with patient death, graft failure or rejection (cell, antibody or both or delayed graft function), CrCl at 1 month, 3 month, 12 month, hospital stay, graft survival or patient survival if time was less than 30, 45 or 60 min or greater than 90 min. The duration of actual warm ischemia time was associated with CrCl 7 days. No association was found for functional warm ischemia time. The graft survival, patient survival, readmission length of stay, CrCl at 1 week, 1, 3, and 12 months were not an independent prognosticator of functional warm ischemic time however higher warm ischemia was an independent predictor of poor graft survival, but not patient survival, or CrCl at 7 days, 1, 3, and 12 months. Utilization of selected DCD donors with warm ischemic times > 2 hr should be considered.

THE IMPACT OF RESISTIVE INDICES IN DECEASED DONOR RENAL TRANSPLANT RECIPIENTS OF WITH DELAYED GRAFT FUNCTION

Mikhail DM, Chan D, Cruise S, Aboalsamh G, Aquil S, Mohamed M, Sener A, Luke PP

Introduction:
Doppler Ultrasonography is often carried out to determine renal allograft perfusion in the early post-operative period. An elevated resistive index (RI) is associated with Acute Kidney Injury (AKI). We hypothesize that patients with delayed graft function (DGF) and elevated RIs and therefore AKI have a different functional outcome vs. patients with normal RIs.

Methods:
We retrospectively reviewed early post-op (<24hr) renal allograft doppler ultrasounds for 250 renal allograft transplants. We analyzed deceased donor recipients only patients with DGF and separated those with intra-renal RIs >0.8 vs. ≤0.8. Outcomes were GFR at 3 months and 1 year (MDRD) as well as graft survival (GS). Patients with insufficient or incomplete follow-up data were excluded. Statistical analysis was performed using T-test and Chi-squared where appropriate. Graft survival analysis was performed with Kaplan-Meier curves.

Results:
In total, 69 deceased donor recipients had DGF. Of DGF patients, 48 (70%) had intrarenal RIs ≤ 0.8 while 21 (30%) had RIs >0.8. Both groups had similar proportions of DCD vs NDD donors (45% vs 57%, p = 0.43). Patient and donor characteristics were not statistically different between the two groups. GFR at 3 months for the high RI group was 57 ml/min/1.72m2 vs 45 ml/min/1.72m2 for the lower RI group (p=0.02). Similarly, at 1 year the GFRs were 58 and 48 ml/min/1.72m2 respectively (p=0.03). Death censored GS and Overall GS were not significantly different between these groups at a median follow-up of 6.75 years (90% vs. 96%).

Conclusion:
Deceased donor renal transplant recipients with DGF and early post-operative RIs greater than 0.8 had superior GFR vs. patients with normal RIs. Although counterintuitive, we believe that the presence of DGF in recipients without severe ischemic reperfusion injury (normal RIs) may represent those individuals that have received kidneys with inferior intrinsic renal functional capacity.

TRIPLE POSITIVE MICROPARTICLES AS A "LIQUID BIOPSY" FOR RISK STRATIFICATION OF PROSTATE CANCER

Brar H, Lucien F, Pautler S, Power N, Leong H

Background:
The combination of Prostate Specific Antigen (PSA), digital rectal exam and tissue biopsy is the only current method for risk stratification of prostate cancer. Unfortunately, 4% of patients undergoing biopsy require hospitalization for life-threatening urosepsis in addition to other complications. Prostate cancer releases fragments known as prostate cancer microparticles (PCMPs). Using nanoscale flow cytometry, we can identify specific tumor markers on the surface of these micro-particles in plasma. Previous studies in Dr. Leong's lab have shown that prostate specific membrane antigen (PSMA) can accurately identify patients with Gleason Score (GS) ≥ 8 from controls.

Hypothesis:
The enumeration of triple positive PCMPs that co-express prostate specific biomarkers (PSMA and STEAP1) and one putative cancer biomarker (CD151, GHSR1, or GRPR) can differentiate patients who have GS 3+3, GS 3+4, GS 4+3 and GS 4+4 prostate cancer.

Material and Methods:
Plasma samples of various GS's from patients post-radical prostatectomy have been obtained from the Genitourinary Biobank at Princess Margaret Hospital in Toronto and the Ontario Tumor Bank (OICR). Biomarkers of interest were identified through the use of specific fluorophore-conjugated monoclonal antibodies. An Apogee Nanoscale flow cytometer (Apogee FlowSystems Inc., UK) was used to detect triple positive microparticles within patient plasma. All plasma samples have been de-identified to maintain experimental blinding.

Results:
Results are pending and will be available at time of conference meeting.

Conclusion:
A blood test that can enumerate triple positive PCMPs in patient plasma will provide clinicians with an accurate and non-invasive method to risk stratify their patients. This will ultimately limit the the need of repeat tissue biopsies and decrease associated risks

A WINDOW OF OPPORTUNITY STUDY TO EVALUATE THE ROLE OF THE COMBINATION OF METFORMIN AND SIMVASTATIN AS A NEOADJUVANT THERAPY IN INVASIVE BLADDER CANCER

McPherson VA, Winquist E, Power N, Chin J, Howlett C, Wehrli B, Leong H, Izawa J

The current gold standard therapy for muscle invasive UC is radical cystectomy, with a 5 year recurrence rate of 32-34%. Neoadjuvant chemotherapy provides improvement, however gains in disease-free survival are 5-15% and morbidity is high. Additionally, patients with advanced or systemic disease have a 5 year survival of 13-15% with cisplatin based chemotherapy regimens, while patients who fail chemotherapy have a survival of only 6.9 months. Therefore, improvements in concurrent medical therapy for invasive UC are necessary.

Metformin and simvastatin synergistically reduce Akt signaling in castrate resistant metastatic prostate cancer, and have greater preclinical anti-cancer activity than the standard of care, docetaxel chemotherapy. PI3K/Akt/mTOR is frequently mutated in invasive urothelial carcinoma (UC) and promotes growth and proliferation, migration and invasion, and inhibits apoptosis.

Metformin therapy was evaluated in window of opportunity trials in both breast and prostate cancer, and showed a reduced tumor proliferation rate via Ki67. In UC cystectomy patients, increased Ki67 is associated with advanced pathologic stage, grade, lymphovascular invasion, nodal metastasis, disease recurrence and cancer specific survival. Anti-cancer activity by metformin is primarily through suppression of PI3K/Akt/mTOR, and the combination of metformin and simvastatin synergistically inhibit this pathway.

Here we present the 12 months interim analysis of a phase II window of opportunity clinical trial evaluating the neoadjuvant use of the combination of metformin and simvastatin as anti-cancer therapy for muscle invasive bladder cancer prior to cystectomy.

TRENDS IN STAGE I NON-SEMINOMATOUS GERM CELL TUMORS IN THE UNITED STATES

Punjani N, Seisen T, Beard C, Sweeney C, Trinh Q-C, Rider J, Preston M

Introduction and Objective:
Testicular malignancies are the most common solid tumor in men 15-34 years and affect approximately 8400 men in the United States each year. Almost half can be classified as non-seminomatous germ cell tumors (NSGCT). Treatment options for stage I include surveillance, chemotherapy, or retroperitoneal lymph node dissection (RPLND). Our study aimed to examine demographic and socioeconomic trends around treatment patterns.

Methods:
Using the National Cancer Database, we retrospectively examined 55,756 patients between January 1, 2004 and December 31, 2013. Data was extracted on 6,426 individuals with ICD histology diagnosis for stage I NSGCT after exclusions were applied. We obtained data on various demographic and socioeconomic variables including race, education, income, location and health insurance. We used multivariable logistic regression models to estimate odds ratios with 95% confidence intervals.

Results:
Throughout 2004-2013 fewer patients received RPLND ($p<0.01$). No trends were seen for overall treatment versus surveillance. Patients were more likely to receive adjuvant treatment based on Medicaid status (OR 1.45, $p<0.01$), if they lived in a rural county (OR 1.70, $p=0.03$), low income (OR 1.22, $p<0.01$) and distance from hospital (OR 1.53, $p<0.01$). Age favored surveillance (OR 0.94, $p=0.03$). Among those patients treated, RPLND was favored for patients living at a greater distance (OR 1.85, $p<0.01$) and volume (OR 5.62, $p<0.01$). Contrarily chemotherapy is favored for those with Medicaid (OR 0.61, $p<0.01$). Advanced clinical and pathologic stage favored treatment ($p<0.01$ *respectively*) and also chemotherapy ($p<0.01$ *respectively*).

Conclusion:
Our study illustrates that fewer patients are undergoing RPLND, which may be due to increased surveillance. Race, education or academic centers did not predict any form of treatment. Insurance status, center volume, and distance all predicted treatment type.

ASSESSMENT OF THE PARIS SYSTEM FOR REPORTING URINE CYTOLOGY: A QUALITY ASSURANCE REVIEW

Xie WY, Kubica K, Joseph M, Power N, McLachlin CM,. Pautler SE

Background:
Urine cytology is a critical investigation in the assessment and surveillance of urothelial carcinoma. Unlike low-grade urothelial carcinoma, the natural history of high-grade urothelial carcinoma (HGUC) is more aggressive and can result in muscle-invasive disease. Subsequent treatment for muscle-invasive disease can be highly morbid and as such, having the ability to accurately diagnose HGUC is of important clinical interest. Until recently, there were no standardized criteria for reporting urine cytology. In addition, the term "atypical urothelial cells" varied in its use across institutions and groups, and lacked clarity in its clinical correlation. The Paris System for Reporting Urinary Cytology (TPS) was developed as a means of standardizing urine cytology reporting by setting morphological criteria and diagnostic categories. TPS was implemented by the cytopathology division at London Health Sciences Centre (LHSC) in September of 2016.

Objective:
Primary objective of this review is to assess the change in rate of reporting of the diagnostic categories before and after the introduction of TPS. Secondary objectives include identifying changes in the rate of subsequent investigation triggered by urine cytology results, and assessing the sensitivity and specificity of urine cytology results for subsequent histologic diagnosis of urothelial carcinoma.

Methods:
Urine cytology results from two time periods: before (September-December 2015) and after (September-December 2016) the implementation of TPS at our centralized pathology laboratory were compared. Any non-negative results were followed with examination of the patient's electronic medical record to assess if subsequent imaging, endoscopy, invasive urine sampling, biopsy or resection was performed. Histologic results of biopsy and resection were correlated with urine cytology results. Statistical comparisons in rates of diagnostic categories and the rate of using adjunct investigations were performed using chi-square analyses. Sensitivity, specificity, and positive predictive value were calculated for each cytological category.

Results:
2576 urine cytology in total were collected during the study period. 1317 specimen were submitted before the introduction of TPS and 1259 specimen were submitted after. The rate of reporting for atypical urothelial cells was significantly lower after implementation of TPS (22% vs 9%, $p<0.001$) as was the rate of reports suspicious for HGUC (2.2% vs 0.3%, $p<0.001$). Negative cytology results were reported at a significantly higher rate (89% vs 74%, $p=0.002$). The rate of positive urine cytology remains unchanged (1.7% vs 1.4%). Results of rate of use of adjunct investigation is still pending.

Discussion:
Implementation of TPS at our institution has resulted in an increase in the proportion of negative cases reported, with a corresponding significant reduction in atypical and suspicious cases reported. The proportion of positive cases did not differ between time periods. This would suggest that TPS has provided more clarity in the reporting of urine cytology and some of the specimen that would have previously been reported as atypical/suspicious is now reported as negative. This provides a clearer diagnostic direction for

THE ABILITY OF PRIOR URINE CULTURES TO PREDICT FUTURE URINARY CULTURE ORGANISMS AND RESISTANCE PATTERNS AMONG INDIVIDUALS WITH NEUROGENIC BLADDER DYSFUNCTION

Clark R, Welk B

Introduction:
The predictive ability of prior urine cultures has been evaluated in non-NB patients, but their value in the NB population has not been evaluated. Our objective was to determine if previous urinary cultures can predict the identity and susceptibility of subsequent urinary cultures in NB patients.

Methods:
Patients with NB who were seen in an outpatient tertiary care urology clinic between July 2015-July 2016 were identified (n=152). Their electronic provincial laboratory record was reviewed to identify all urine cultures in the prior 2-year period.

Results:
We identified 82 men and 70 women with NB (median age 48, IQR 30-59) due to spinal cord injury (n=61), multiple sclerosis (n=26), spina bifida (n=25), and other causes (n=40). These individuals used spontaneous voiding (n=83), clean intermittent catheterization (n=76), indwelling catheter (n=14), or condom catheter (n= 14). 50 patients (33%) had at least 2 positive urine cultures and the most common organism was E. coli (125/280, 45%). Consecutive cultures were compared and the organism concordance rate between the 242 paired cultures that were at least 7 days apart was 55% (n=135/242). Organism species showed higher concordance among cultures ≤90 days apart (61%) compared to those >90 days apart (36%). Prior resistance profiles showed high concordance with future resistance profiles; ciprofloxacin resistance status was the same in 79% of consecutive cultures done with 90 days, and 71% of cultures done >90 days apart. Similarly, nitrofurantoin (81% at ≤90 days and 70% at >90 days) and trimethoprim/ sulfamethoxazole (75% at ≤90 days and 74% at >90 days) showed a high concordance between consecutive cultures.

Conclusions:
Previous urine culture can provide valuable information when treating infections in NB patients, even when they are relatively remote. This reinforces the importance of utilising electronic health records to look at prior resistance patterns before initiating empirical antibiotic therapy.

BACTERIAL PRODUCTION OF NEUROTRANSMITTERS: WHAT DOES THIS MEAN FOR THE BLADDER?

Whiteside S, Lendor S, Mousavi F, Reid G, Pawliszyn J, Burton J

Bacterial interactions with the nervous system and its constituent molecules have been documented for over 80 years. To date, most studies have focused on aggressive nervous system pathogens and neurotoxins, such as *Mycobacterium leprae* and botulinum toxin. However, the study of microbial endocrinology and subsequent work on the microbiota-gut-brain axis has opened new research avenues, including interactions between bacteria and the bladder's sensory and motor systems. Bacterial production of neurotransmitters and neuroactive substances is well studied; however, researchers have not linked this production to uropathogens or alterations in bladder function. *Enterococcus faecalis* is one of the most common etiologic agents of asymptomatic bacteriuria (ABU), yet these strains carry the same virulence traits as those isolated from acute symptomatic urinary tract infection (UTI). We hypothesised *E. faecalis* produces neurotransmitters, and that these interact with the urothelium to modulate the host response to the pathogen. To test this hypothesis, we created a list of 40 metabolites found in the urine or bladder and using targeted solid-phase microextraction coupled with liquid chromatography-mass spectrometry (SPME-LC-MS) assayed for these metabolites in the supernatant from enterococcal culture. Our preliminary analysis identified bacterial production of tyramine, dopamine, norepinephrine, epinephrine, methoxytyramine, tryptamine, GABA, acetylcholine, agmatine, and serotonin. Interestingly, production of these metabolites occurred under multiple growth conditions and by isolates from different sources. Additionally, identification of these metabolites was also noted in bacterial-uroepithelial cell culture. This is particularly interesting given the role of the urothelium in bladder sensation. Host gene expression studies of specific receptors and catabolic enzymes are ongoing, yet preliminary data suggests the host is adapting to these neuroactive substances. Multiple theories have been postulated as explanations for the development of ABU; however, to the best of our knowledge, we are the first group investigating direct bacterial interactions with the nervous system of the bladder. Understanding these interactions will not only further our understanding of UTI and ABU, but will assist in unravelling the relationship between the urinary microbiota and diseases such as overactive bladder, urge urinary incontinence, and interstitial cystitis.

INTRACAVERNOSAL INJECTION OF BOTULINUM TOXIN TO IMPROVE ERECTILE FUNCTION IN OLDER RATS

Campbell J, De Young L, Radomski S, Alzubaidi R, Brock G

Introduction:
Erectile dysfunction (ED) in the aging male is exceptionally-common and unfortunately difficult to treat. ED in this population is multi-factorial secondary to structural changes in the penis, alterations in contractile properties through nNOS and RhoA pathways and systemic effects of comorbid conditions. Botulinum toxin (BTX) has many demonstrated therapeutic uses in medicine due to its robust effects on skeletal and smooth muscle relaxation. In this novel study, we investigated BTX utility as a treatment for erectile dysfunction in an aged population.

Methods:
Ten Sprague Dawley rats with an average age of 8.5 months were randomized into two study groups: BTX or control. Under isoflurane anaesthesia, the rat penis was retracted and a 30-gauge needle was used to penetrate the corpora, near the crus. Rats were injected with either 10 units of BTX in 80ul saline or 80ul of normal saline (NS). The injection solutions were deposited in three areas near the crus bilaterally. Rats were observed for 8 days for any complications. On day 8, erectile function was assessed via cavernous nerve electro-stimulation induced intracavernosal pressure change (ICP). Penile tissues were harvested and analyzed with immunohistologic staining for Masson's Trichrome stain and smooth muscle a-actin.

Results:
There were no significant complications from the injections in either group. The BTX group had a significantly higher ICP on day 8 following injection when compared to the control group (ICP peak: 54.26 ± 4.5 cmH_2O (NS), 79.06 ± 5.4 cmH_2O (BTX) p=0.001. A larger sinusoidal volume was measured in the BTX group compared to the saline group, however the findings did not reach statistical significance.

Discussion:
Intracavernosal injection of BTX appears to be safe in rats. BTX increases sinusoidal volume by inducing enhanced cavernous smooth muscle relaxation, resulting in increased blood flow to the penis during stimulation. This leads to an increase in ICP with BTX injection, demonstrating a potential benefit to erectile function. This is a novel study investigating BTX as a potential treatment for ED in the aging male. Short-term data is promising, but studies with longer follow-up are required to determine duration of efficacy. This animal model can be used as a trigger to investigate BTX as an off-labelled use for ED, particularly as salvage therapy among PDE5i non-responders or partial responders.

PLATELET RICH PLASMA FOR ERECTILE DYSFUNCTION AND OTHER EVOLVING THERAPIES

K Henriquez, G Brock

Introduction:
ED is a prevalent health problem that seriously impacts the quality of life of men and their partners. Approximately 50% of men between the ages of 40 and 70 years have some degree of ED. A stepwise management approach has been developed and starts with oral medications using phosphodiesterase type 5 inhibitors (PDE5i), with intracavernous injections (ICI) as second-line therapy and finally surgical options. Our objective is to review contemporary basic research and clinical trials concerning other evolving therapies for ED.

Methods
A search of English language journal articles for the following terms was performed using PubMed: 'erectile dysfunction treatment', 'platelet rich plasma' (PRP), 'low-intensity extracorporeal shock-wave therapy' (LI-ESWT) and 'stem cell therapy' (SCT).

Results
There are 3 studies published after bilateral nerve injury in rat models that demonstrated the neurotrophic effect of PRP on cavernous nerves (CNs) regeneration. The PRP treated group had increased intracavernosal pressure, increased numbers of myelinated axons of CNs and reduced fibrosis in the corpus cavernosum compared to the vehicle-only group ($P < 0.05$). The meta-analysis of 14 studies including 833 patients revealed that LI-ESWT could significantly improve IIEF (2.00; 95% CI, 0.99–3.00; $p < 0.0001$) and EHS (0.16; 95% CI, 0.04–0.29; $p = 0.01$) for 3 months. Energy flux density, number of shock waves per treatment, and duration of LI-ESWT treatment were closely related to clinical outcome. Bone marrow-derived mesenchymal and adipose-derived stem cells have demonstrated a paracrine effect on penile tissue, and can differentiate into smooth muscle, endothelium, and neurons. To date, stem cells have proven safe and effective in both animal and human models of ED.

Conclusions
The lack of an optimized PRP preparation protocol limits evaluation of the various reports and their therapeutic effects. Well-designed and randomized controlled trials are required to provide evidence of the efficacy of techniques for preparing PRP. The standardization of the LI-ESWL technique is not well established, the current protocol is empirical with the total number of treated patients, low. Long-term, multicenter studies are needed. The next step for SCT is to define a maximally effective therapy that determines the mode of action, safety over the long term, most efficacious delivery, ideal timing, type and dosage of SCs, ease of isolation and culture and cost. Phase II and Phase III trials are needed, before offering these novel therapies to the patients.

THE DROSOPHILA MELANOGASTER MODEL OF HUMAN URIC ACID NEPHROLITHIASIS AS A NOVEL IN VIVO HIGH THROUGHPUT DRUG SCREENING PLATFORM

Ali AN, Dayarathna T, Kim J, Singh Padda R, Spagnuolo P, Razvi H, Leong HS

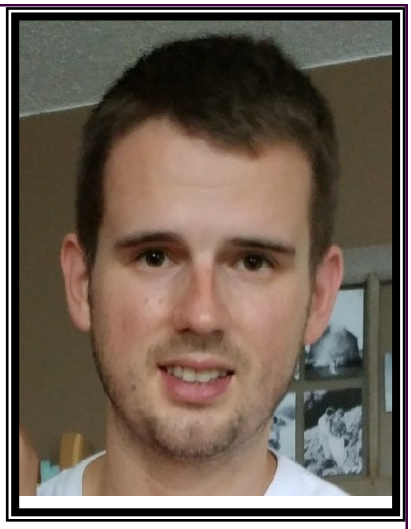
Introduction and objective:
Uric acid calculi account for approximately 10% of all kidney stones and are being observed with an increasing prevalence worldwide. The development of novel therapeutic agents for this multifactorial disorder has been hampered by the lack of a practical pre-clinical model, particularly in metabolic milieus where established treatments are poorly tolerated. Here, *Drosophila melanogaster (DM)*, an emerging model for calcium oxalate nephrolithiasis, was investigated as a disease model and high throughput functional drug discovery platform for human uric acid nephrolithiasis.

Methods:
Knockdown fly lines were generated by RNAi-mediated silencing of the *Uro* gene, encoding for the enzyme urate oxidase. Gene knockdown efficiency was quantified by qRT-PCR. Following a 7-day incubation period in purine rich lithogenic media (1% w/v yeast derived RNA), knockdown flies were dissected to recover intact malpighian tubules against wild-type (Canton S) controls. The presence or absence of birefringent concretions in fly malpighian tubules and fecal matter was determined by confocal microscopy under polarized light (n=40/group). Formed tubule concretions were isolated by broad-spectrum protease dissolution of organic tubule material (n=120) and characterized by SEM/EDX. A fecal birefringence assay was employed to evaluate the *in vivo* efficacy of standardized doses (200 µL [10mM/100mM]) of candidate compounds from a drug library of 300 small molecules via *in silico* birefringent particle area analysis against standard controls.

Results:
Diffuse brilliant birefringence was visualized in *Uro* knockdown fly malpighian tubules and fecal matter, confirming the presence of calculi. A 3.125-fold reduction in *Uro* gene expression following knockdown was observed via qRT-PCR. The elemental composition of isolated concretions was consistent with uric acid. Drug library screening is currently in progress to identify compounds of interest for future study versus currently established treatments.

Conclusions:
The DM model of human uric acid nephrolithiasis is a viable and cost-effective means for rapid drug candidate screening. This innovative translational platform has significant implications for the future of rational drug design for nephrolithiasis. The drug-crystal interactions and mechanism of action of compounds of interest can be further investigated by *in vitro* or *in vivo* methods in a mammalian system.

THE IMPORTANCE OF XENOBIOTIC METABOLISM BY THE MICROBIOME IN PROSTATE CANCER



Chanyi RM, Berish R, Dewar M, Leong HS, Chin J, Burton JP

Introduction:
The collection of microorganisms living inside our body contain a genetic capacity which far surpasses our own. It is unsurprising then that the gut microbiome, plays a vital role in human health and disease. Typically, these bacteria are in direct contact with orally ingested substances before absorption across the intestinal barrier. This is especially important in the context of orally administered pharmaceuticals. The modification of these compounds through microbial metabolism is termed xenobiotic metabolism, can potentially change the efficacy of these agents through inactivation, enhanced activity, immune activation and even through changes in solubility. Understandably, differences in microbiome can have implications on the pharmacokinetic properties of the drugs delivered to patients. One treatment regimen for castrate-resistant prostate cancer patients, includes oral Abiraterone acetate and prednisone. Oral administration of 14C-abiraterone acetate, results in approximately 88% of the radioactive dose recovered in feces, and therefore, is highly insoluble, and the gut microbiome has a significant exposure. The intestinal bacterium, *Clostridium scindens*, has been shown to metabolize hydrocortisone into an androgen that is inactive in humans. However, in the case of prednisone, it is thought to be biologically active and potentially may have huge implications for prostate cancer androgen-deprivation treatments.

Objectives:
We sought to determine xenobiotic factors of the gut microbiome which may affect the treatment of castrate -resistant prostate cancer patients. Firstly, we wished to determine the metabolic capabilities and gene expression of *Clostridium scindens* in the presence of glucocorticosteroids. Secondly, we wished to identify bacteria which had the capability of degrading abiraterone acetate present in feces.

Methods:
Using single culture analysis, we tested the ability of *C. scindens* to metabolize hydrocortisone, prednisone, prednisolone, cholesterol and dexamethasone to produce active androgens. We looked at the gene expression of pathways implicated in the production of other androgens. Using a continuous culture system designed to model the gut microbiome (chemostat), we can mimic the conditions the bacteria in a patient's gut would be exposed to during treatment, we exposed the model to a daily dose of abiraterone acetate for one week. A similar experiment was carried out separately where a sample from the same individual was exposed to prednisone. In addition, we isolated bacteria on selective media containing abiraterone acetate as the sole carbon source.

Results:
Preliminary results have shown the microbiome is drastically altered when exposed to Abiraterone. There is an increase in members of the *Enterobacteriaciae* along with a decrease in *Firmicutes*. We have also demonstrated that, along with hydrocortisone, *C. scindens* can also metabolize prednisone and prednisolone into a potential testosterone analogue.

Conclusion:
C. scindens is able to produce a biologically active androgen which is presumed to be a testosterone analogue. This involves the *desABCD* operon; which is involved in other pathways of androgen production. The addition of this exogenous androgen in patients undergoing androgen deprivation therapy may decrease treatment efficacy and promote tumor growth. The *desABCD* operon is not common in the intestinal tract, further studies are underway to determine if bacterium such as *C. scindens* are more common in men with castrate-resistant prostate cancer. This could change how these patients are treated as we can easily screen for these bacteria; knowing these patients may respond differently to this treatment may allow physicians to add an antibiotic to greatly increase clinical outcome.

THE EFFECTS OF SHOCKWAVE LITHOTRIPSY ON THE URINARY MICROBIOME AND ON BACTERIAL DISPERSION USING A PHANTOM KIDNEY STONE MODEL

AlAthel AH, Chanyi RM, Bao Y, Burton JP, Razvi H

Introduction:
Historically, the bladder has been considered a sterile environment, only containing bacteria during episodes of infection or some other underlying cause. Next-generation sequencing and extended culturing techniques have now shown that the bladder has its own "core" microbiome. The role the urinary microbiome plays in health and disease is an emerging field in urology. Of interest is determining the role these bacteria have in nephrolithiasis. Early published studies have shown the presence of bacteria within kidney stones. Extra corporal shock-wave lithotripsy (ESWL) used to fracture kidney stones may disrupt these communities and promote bacterial dissemination and may partially explain why these patients are at a greater risk of infection and sepsis.

Objectives:
Our aim was to determine if the urinary microbiome changes after ESWL using next-generation sequencing technologies. Then to determine the extent of potential dissemination of bacteria by ESWL process using an ordinance gelatin model which emulated the density of tissue and contained kidney stone phantoms in the presence of bacteria.

Methods:
For studies of the urinary microbiome, we recruited 10 patients scheduled for ESWL (2F, 8M) and 6 healthy controls (3M, 3 F). Urine samples were collected 21 days prior to ESWL, immediately before and after and then at 3 months post procedure. Two samples were collected for the controls 21 days apart. Urine was processed immediately by centrifugation and bacterial pellets were stored separately. DNA was extracted from the bacterial pellets, V4 16S rRNA gene PCR amplified and then Illumina sequenced. Analysis was conducted using QIIME and R statistical packages. The kidney model was prepared using 10% ordinance gelatin. Cylindrical wells (25mm diameter) were created where the kidney stones would be placed such that the "skin to stone" distance was 60 mm. Cylindrical phantom stones were prepared using Begostone plus plaster as per manufacturers recommendations. All stones had a final weight of 2 ± 0.1 g. Stones were soaked in phosphate-buffered saline overnight before *Escherichia coli* was added and ESWL performed. *E. coli* GR-12 containing green fluorescent protein (GFP) was grown over night in LB with tetracycline (10 µg/ml) at 37°C. *E. coli* was resuspended in PBS and chilled to 4°C before 1 x 10^5 CFU were added to each stone in the mold. Each stone was subjected to 3000 shocks at an energy level of 5 and a frequency of 2 Hz on a Modulith SLX-F2 lithotriptor. The precise treatment focus (F2 diameter of 6 mm x 28 mm) was used and targeting was maintained by frequent fluoroscopy.

Results:
Patient urine samples collected after ESWL had a different bacterial profile then prior to ESWL. Post ESWL, the samples had increased diversity suggesting that the stones themselves may harbor their own microbiome. Preliminary experiments have been performed on the *in vitro* ESWL model. Efficient fractionation of the stone phantoms was achieved. Ongoing experimentation will focus on the visualization of bacterial colonies into the surrounding area, away from the region being targeted by ESWL.

Conclusion:
Using culture dependent analyses, we modified a ESWL model developed in this department to determine how ESWL alters bacterial survival and assess whether ESWL will promote bacterial infiltration into surrounding tissue.

CLINICAL CORRELATION OF PATIENT-DERIVED XENOGRAFT MODEL USING THE EX-OVO AVIAN EMBRYO TO PREDICT TARGETED THERAPY TUMOR RESISTANCE IN RENAL CELL CARCINOMA.

Huynh M, Lowerison M, McPherson V, Leong H, Power N

Introduction and objectives:
Tyrosine kinase inhibitors (TKIs) are the mainstay of treatment for metastatic renal cell carcinoma (mRCC), with up to 20% of tumours exhibiting *de novo* resistance to TKIs. At present, there is no method of predicting response to systemic targeted therapy. We present a descriptive study of a prospective cohort of mRCC patients & the correlation of clinical outcomes to the responses predicted by patient-derived xenograft (PDX) models using the *ex-ovo* avian embryo.

Methods: We prospectively collected demographic, pathologic, & clinical data on 26 patients with mRCC undergoing cytoreductive nephrectomy. PDX models were tested in 5 patients. Six core biopsies were taken from each primary tumor. Cores were sectioned & engrafted directly onto embryonic day 9 chorioallantoic membranes (CAMs) of avian embryos & treated with topical sunitinib or a DMSO control. On day 6 post-engraftment, Doppler & contrast-enhanced ultrasound were performed to assess vascularity & perfusion of tumours grown on the CAM models. A composite vascularity & perfusion score was obtained and used to determine the presence or absence of a response to TKIs compared to the control. Tumours were considered TKI-sensitive if there was a response in ≥4 cores. Tumours with responses in ≤3cores were considered TKI-resistant. Clinical progression on CT scan was based on RECIST criteria.

Results: Results are summarized in Table 1. All tumours demonstrated heterogeneous responses to TKIs in the PDX model. Using the criteria of ≥4 cores responding to TKI therapy, we would expect a good response in patient 3, who does not have evidence of clinical progression after 5 months of maintenance on sunitinib. Moreover, patient 3 had 3 cores engrafted from a metastatic deposit, which all responded well to sunitinib in the PDX model. Patients 1 & 2 continued to show signs of progression despite switching to alternative agents, and both have discontinued systemic therapy due to intolerable side effects or enrolment in another clinical trial respectively. Patients 4 & 5 have not started on systemic targeted therapy.

Conclusions: Further studies in a larger population are warranted to explore the potential of the PDX model to serve as a novel phenotypic biomarker in the prediction of targeted therapy tumor resistance in RCC.

PARTIAL NEPHRECTOMY DOES NOT GREATLY ALTER LONG TERM CARDIOVASCULAR AND RENAL OUTCOMES AND NON-CANCER RELATED MORTALITY VS. RADICAL NEPHRECTOMY

Breau R, Kapoor A, **Chan G**, Rowe N, Cristea O, Nash D, Dixon S, Izawa J, Arthur E, Tajzler C, Kumar R, Vinden C, Garg A, Luke O

Introduction and objective:
Nephron sparing surgery (NSS) is performed to minimize renal functional loss in order to prevent long term nephrologic and cardiovascular complications in patients with renal cell carcinoma (RCC). We compare both nephrologic and cardiovascular outcomes in patients undergoing radical (RN) and partial nephrectomy (PN) for localized RCC. We aim to examine the effect of RN and NSS in small renal masses (SRM) and the substantial morbidity and mortality as it would apply in the real world setting. We examine the practical results in patients with partial and radical nephrectomy in a Canadian population.

Methods:
We conducted a study of 1457 patients with a minimum follow-up of 5 years undergoing RN (882) and PN (575) for localized RCC in three academic centres in Ontario, Canada. We utilized local data bases as well as the Institute for Clinical Evaluative Sciences (ICES) to conduct a population based retrospective cohort study. Patients were excluded if tumor size was larger than 7 cm, or patients had dialysis in the previous year or had metastatic disease. A prior sub group analyses for primary outcome was planned for pre-operative GFR (<45 and ≥45 ml/min/1.73 m2) and tumor size (≤4 cm vs >4 cm). A multivariable logistic regression model including 11 baseline characteristics was used to calculate propensity scores. The main end points were cardiovascular disease, nephrologic disease, and death.

Results:
The one year eGFR values were 71 and 52 ml/min/1.73 m2 for PN and RN groups ($p<0.0001$) respectively. Also 9.4% vs. 18.8% were evaluated by a nephrologist at that time point ($p<0.0001$). In PN and RN groups, 2.4% vs. 5.0% were classified into CKD stage 4/5 by 1 year ($p<0.0001$). After a median follow up of 7 (6-10) years, all cause mortality was lower in the PN group in the first 4 years, but no different after 5 years. Importantly, all cause mortality from 5 years onward and non-cancer related mortality was not different between groups. Even in patients with eGFR < 45, non-cancer related mortality was similar between groups.

Discussion:
Accordingly, hospitalization with major cardiovascular event, and need for dialysis was not different between PN and RN groups. Despite propensity weighting, cancer-related deaths was higher in RN in the first 4 years of follow-up (HR6.12, $p =0.017$) but not after 4 years (HR 0.83, $p=0.80$). This indicates that the difference in mortality in between groups may be due to oncologic selection bias and not non-cancer related events. Additionally, end stage kidney disease was nearly identical and the beneficial impact of NSS did not result in improved survival. It would seem that NSS in the real world dose not impact cardiovascular or renal out-comes as significantly as initially thought. Contrary to previous studies, surgical renal loss may not be the same as medical renal loss. Limitations included non-standard PN protocol across centres, and the inherent bias from retrospective data.

Conclusions:
Despite reduced renal function in the RN group, non-cancer related mortality, long-term cardiovascular events and need for dialysis was not different between RN and PN groups over the long term in our real world population. This indicates that preservation of nephrons by PN in this patient population does not majorly impact cardiovascular and renal outcomes.

FACTORS CONTRIBUTING TO DELAY IN TIME TO ORCHIDOPEXY IN ONTARIO, CANADA

Telfer S, Liu K, Shariff S, Garg AX, Dave S

Introduction:
The 2015 AUA Guideline on Cryptorchidism recommends early referral to a surgeon, to ensure orchidopexy by 18 months of age. In a prior study, we noted that median time to orchidopexy in Ontario between 1997-2007 was 23 months (IQR 16-34). The objective of this study was to evaluate time to orchidopexy in a more recent cohort (2006-2011) and identify factors contributing to delay in orchidopexy in Ontario.

Methods:
We conducted a population based, retrospective cohort study using several linked administrative databases held at the Institute for Clinical Evaluative Sciences in Ontario. We identified 4399 patients who underwent orchidopexy between 2006-2011 and assessed several patient (socioeconomic status, health care visits and surrogate markers of concern or severity such as hypospadias, use of preoperative ultrasound, bilateral or impalpable undescended testes (UDT)) treating and referring physician (age and specialty) and hospital factors (volume and academic/ community), which could impact timing of surgery. Multivariable logistic regression analyses were performed to compare boys who had orchidopexy before 18 months of age or after.

Results:
The median age at orchidopexy in Ontario between 2006-2011 was 24 months (IQR 12-60). Patients who had an orchidectomy during exploration (OR1.61, CI 1.22-2.13), underwent laparoscopic orchidopexy (OR 1.57, CI 1.13-2.17), were operated by pediatric general surgeons versus urologists (OR1.69, CI 1.40-2.03) and at high volume hospitals (OR 1.79, CI 1.38-2.33) had a greater likelihood of surgery beyond 18 months. Patients with more health care encounters (OR 0.94, CI 0.92-0.95), with prior ICU hospitalizations (OR 0.29, CI 0.15-0.58), hypospadias (OR 0.81, CI 0.58-1-12), or bilateral undescended (UDT) (OR 0.72, CI 0.58-0.89) were more likely to undergo timely surgery. In 3969 patients, where first surgical clinic visit was documented, median age at consult was 20 months (IQR 10-60). Counter intuitively; when there was a delay to the first consult, the eventual surgical procedure was likely to be done earlier (OR 0.84, CI 0.83-0.85).

Conclusions:
In Ontario, time to orchidopexy does not meet current recommendations, as 75% of patients fail to undergo an orchidopexy by18 months. We identified several patient, physician and hospital factors contributing to this delay. Late first surgeon assessment still seems to be a significant barrier to timely surgical intervention.

RETURN TO CONTINENCE FOLLOWING RADICAL PROSTATECTOMY: A SINGLE SURGEON COMPARISON OF ROBOT-ASSISTED WITH MULTI-LAYER CLOSURE, ROBOT-ASSISTED ALONE, LAPAROSCOPIC AND OPEN APPROACHES

Kwong J, Luke P

Introduction And Objective:
Radical prostatectomy is a common treatment for patients with clinically localized prostate cancer and life-expectancy of ≥ 10 years. Urinary incontinence following radical prostatectomy remains a great concern for most patients with implications on quality of life. Variables that portend early recovery of continence are yet to be defined. Surgical technique has been described to affect continence rates. Total anatomic reconstruction with a multi-layer closure around the urethra-vesical anastomosis during robot-assisted prostatectomy is thought to restore the natural support to the urinary sphincter. Our objective was to compare time to continence following radical prostatectomy between robot-assisted prostatectomy with multi-layer closure, robot-assisted prostatectomy alone, traditional laparoscopic prostatectomy and open prostatectomy. We also determine variables that predict a shorter time to continence.

Methods:
We performed a retrospective review of all radical prostatectomies performed by a single surgeon from January 2009 to March 2017. Our primary endpoint was evaluation of time to continence, defined as 0 to 1 pad per day. Our secondary endpoint was evaluation of variables that predicted a shorter time to continence, including pre-operative, intra-operative, post-operative and histo-pathologic variables. Pre-operative variables included patient age, BMI, PSA and lower urinary tract symptoms. Intra-operative variables included multi-layer closure, estimated blood loss, operative time, nerve sparing and bladder neck reconstruction. Post-operative variables included immediate and delayed post-operative complications. Prostate histopathological data included pathologic stage, prostate volume and margins. We were particularly interested in the effect of multi-layer closure on return to continence.

Results:
In total, 147 patients were analyzed. 50 robot-assisted, 49 laparoscopic and 48 open radical prostatectomies were performed between January 2009 and March 2017. Of the 50 robot-assisted prostatectomies, 44 were performed using the multi-layer closure (post July 2013). Time to continence immediately after catheter removal was determined. Multivariate analysis was conducted to determine variables involved in early recovery of urinary continence.

Conclusion:
We report a single surgeon experience of time to continence following radical prostatectomy comparing the robot-assisted with multi-layer closure, robot-assisted alone, traditional laparoscopic and open approaches. We determine variables that influence time to continence.

A PROSPECTIVE STUDY ON THE OPERATIVE TIMING AND LEARNING CURVE OF ROBOTIC PEDIATRIC UROLOGY PROCEDURES IN THE CANADIAN HEALTH CARE SYSTEM

Stern N, Clark R, Dave S.

Introduction & Objective:
The transition from laparoscopic and open surgery to robotic assisted procedures in paediatric urology leads to an increase in operative times, which adds to health care costs. Attempts to study the learning curve of robotic surgery in adults has focused on structured training to improve operative times at each step, but this has not been translated to paediatric urology. We hypothesize that robotic assisted paediatric urologic procedures will show a decrease in operative times early in the learning curve and most of this reduction will be due to a reduction in intra-corporeal suturing time. The objectives of this study are to investigate the learning curve and operative times of a single surgeon transitioning to robotic assisted pyeloplasty (RAP) and robotic assisted extra-vesical ureteral reimplantation (RUR).

Methods:
This prospective cohort study includes all RAP and RUR procedures performed using a 3-port technique between July 2013-April 2017. Both operations were sectioned into discrete operative steps: ports insertion and closure, dissection of the uretero-pelvic junction (RAP) or ureter (RUR), dismemberment of the renal pelvis and spatulation (RAP) or creation of the submucosal tunnel (RUR), uretero-pelvic anastomosis (RAP) or closure of the submucosal detrusor tunnel (RUR) recorded prospectively by a trained unbiased coder. The primary outcome was the trends of total and step-specific operative times for both procedures. Success was defined for patients who had at least 6 months follow up. For RAP, success was defined as resolution or significant decrease in the grade of hydronephrosis or a MAG-3 renogram showing decreased T-half times (where decrease in grade of hydronephrosis was not adequate). In the RUR group success was defined as resolution of UTI's off antibiotic prophylaxis or negative VCUG (in those who had UTI's after surgery). Operative times were compared using student's t-test by the first and last quartiles.

Results:

	RAP			RUR		
Number of patients	28			20		
Gender (male:female)	20:8			2:18		
Median age (months)	157 (6-1404)			62 (6-129)		
Success rate (>6 month follow up) (%)	100			100		
Complications	Urinoma requiring nephrostomy and prolonged stenting-1, UTI-1			Delayed ureter injury requiring stenting-1, intraoperative acute kidney injury-1		
Mean time (min)	**First quartile**	**Last quartile**	**% change**	**First quartile**	**Last quartile**	**% change**
Total operative time	211.4	156*	-26.2	218.2	160.2	-26.6
Port placement and closure	46.9	33.4*	-28.8	41	33.4*	-18.5
Dissection	36	17*	-52.8	56.8	31.6*	-44.4
Dismember pelvis and ureter spatulation	18.6	13.4	-28.0			
Submucosal tunnel creation				39.8	35.2	-11.6
Suturing	110	45.2*	-58.9	80.6	39.6*	-50.9
Resident console time	5.3	20.4*	284.9	0	20.4*	

Table 1. Patient demographics, outcomes, and operative times for robotic assisted pyeloplasty (RAP) and robotic assisted extra-vesical ureteral reimplantation (RUR).
* $p < 0.05$

Conclusions:
A reduction in intra-corporeal suturing and dissection time is responsible for the greatest efficiency gain when initiating paediatric RAP and RUR. At our centre, despite a low volume of robotic cases (14/year) and a lack of a dedicated robotic OR team, this efficiency was achieved within the first 20 procedures for both procedures. This study will aid Canadian paediatric urologists initiating a robotic program to allow resource planning and supports the argument that robotic assisted procedures can be adapted early and efficiently in the Canadian health care system.

PAST RESIDENTS' DAY GUEST PROFESSORS: 1984 – 2016

2016	Dr. Philipp Dahm
2015	Dr. E. Ann Gormley
2014	Dr. Joel B. Nelson
2013	Dr. Stephen Nakada
2012	Dr. Lawrence Klotz
2011	Dr. Gerald Andriole
2010	Dr. John Michael Fitzpatrick
2009	Dr. Antoine Khoury
2008	Dr. Margaret Pearle
2007	Dr. Martin Gleave
2006	Dr. Leonard Zinman
2005	Dr. Joseph A. Smith Jr.
2004	Dr. Anthony Atala
2003	Dr. Peter T. Scardino
2002	Dr. Inderbir Gill
2001	Dr. Shlomo Raz
2000	Dr. Donald Lamm
1999	CUA in London, no Residents' Day
1998	Dr. Patrick Walsh
1997	Dr. Joseph Oesterling
1996	Dr. Michael Marberger
1995	Dr. E. Darracott Vaughan
1994	Dr. Martin Resnick
1993	Dr. Andrew Novick
1992	Dr. Howard Winfield
1991	Dr. Moneer Hanna
1990	Dr. Drogo Montague
1989	Dr. Ralph Clayman
1988	Dr. Gerald Sufrin
1987	Dr. Alvaro Morales
1986	Dr. J. Edson Pontes
1985	Dr. Alan Perlmutter
1984	Dr. Alan Bennett

NOTES