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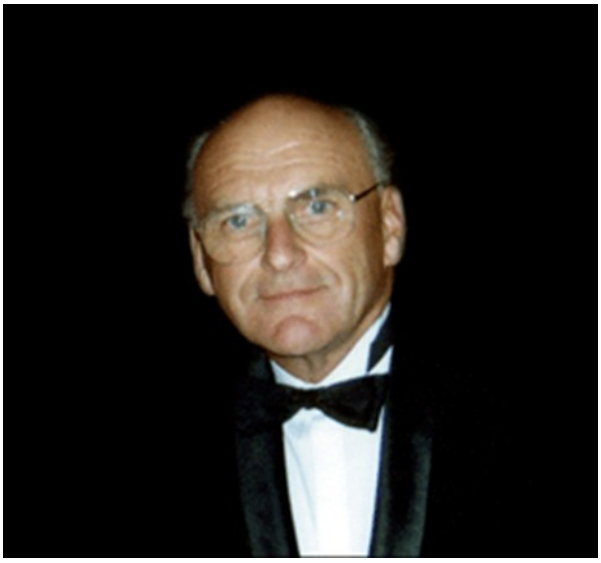
JACK WYATT UROLOGY RESIDENTS' RESEARCH DAY

April 19, 2013

Syllabus

Western

Dr. John Kenneth Wyatt



John Kenneth Wyatt was born in Detroit, Michigan and grew up in London, Ontario where he attended the University of Western Ontario, graduating in Medicine in 1954. While an undergraduate at Western, Jack excelled in many sports and was captain of the Western Mustangs football team.

Dr. Wyatt completed his General Surgery and Urology training in London and joined the small Urology faculty here in 1960. He published one of the first papers on the beneficial effects of chemotherapy for testis cancer. Dr. Wyatt steadily built the UWO Urology Program, serving as the Program Director and Division Chair for 15 years. He was best known for his clinical acumen and his caring attitude towards his patients as well as his residents. An excellent clinical teacher, Dr. Wyatt was well-known for his common touch and sense of humor, whether he was lecturing to medical students, doing bedside or operating room teaching, or chatting with the janitor. Dr. Wyatt was an active contributor to the Royal College and the Canadian Urological Association, serving as CUA President in 1984.

Dr. Wyatt passed away December 6, 2004. We continue to honor his memory through our Annual Residents' Research Day.

Western University
Jack Wyatt Urology Residents' Research Day 2013

RESIDENTS:

PGY5
Shawna Boyle
Francisco Garcia
Paul Martin
Daniel Yanko

PGY4
Varunkumar Bathini
R. Michael Lang
Linda Lee

PGY3
Marie Dion
Kim-Chi Tran
Peter Wang

PGY2
Adiel Mamut
Stephanie Tatzel
Siobhan Telfer

PGY1
Jeffrey Campbell
Victor McPherson
Golnaz Naderkhani

FELLOWS

Michele Billia
Nader Fahmy
Joe King Lee
Neal Rowe
Philippe Violette
Vladimir Yutkin

GUEST PROFESSOR 2013

Stephen Y. Nakada

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

The Uehling Professor and Chairman,
Department of Urology,
University of Wisconsin
School of Medicine and Public Health,
Madison, Wisconsin

Dr. Nakada received his undergraduate degree from Dartmouth College in 1984 and medical degree from the University of Rochester School of Medicine and Dentistry in 1988. He completed residency training at Strong Memorial Hospital in Rochester, New York in 1994. Dr. Nakada completed his Endourology Fellowship at Barnes Hospital in St. Louis, Missouri and subsequently joined the faculty at the University of Wisconsin as an Assistant Professor in 1995. In 2001, Dr. Nakada was named Chairman of the Division of Urology and the first David T. Uehling Professor of Urology at the University of Wisconsin. Dr. Nakada has published over 200 peer-reviewed articles, edited 5 textbooks, and authored over 50 book chapters, all primarily focusing on endourology and laparoscopy. In 2004, he received the AUA Gold Cystoscope Award. Dr. Nakada is an Associate Editor for *Urology*, and serves on the editorial boards of the *Journal of Endourology* and *Urology Times*. Dr. Nakada is a member of the AUA Board of Directors and is Secretary-General of the Endourological Society. He is also a member of the American College of Surgeons, the American Association of Genitourinary Surgeons, and the Clinical Society of the Genitourinary Surgeons.

We thank Cook Canada for the educational grant in support of Dr. Nakada's visit.

Western University
Jack Wyatt Urology Residents' Research Day 2013

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

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Schulich MEDICINE & DENTISTRY

Western

JK Wyatt Urology Residents' Day

Western University

Friday, April 19, 2013

Best Western Lamplighter Inn, 591 Wellington Rd.S., London

AGENDA

7:00 – 7:45 **Registration and Continental Breakfast**

7:45 – 8:00 **Welcome and Introductions: Dr. H. Razvi**

SESSION I **ONCOLOGY** **Moderator: Dr. S. Pautler**

8:00-8:15 V.Bathini: Evaluating the Clinical Significance of CD151 Expression in Patients that Underwent a Radical Cystectomy for Urothelial Carcinoma of the Bladder

8:15-8:30 S.Leith: Complete Genome-Wide SHRNA Screen for Modulators of Prostate Cancer Disease Progression

8:30-8:45 P.Wang: The Prognostic Role of Fractal Geometry in Renal Cell Carcinoma Photomicrograph Analysis

8:45-9:00 H.Leong: Prostate Cancer Microparticles as a Next Generation Screening Tool for Prostate Cancer

9:00-9:30 **State-of-the-Art Lecture I: Dr. Nicholas Power**
An Update on Testes Cancer

9:30-10:00 **Health Break**

SESSION II **ANDROLOGY AND BASIC SCIENCE** **Moderator: Dr. B. Welk**

10:00-10:15 F.Garcia: Predictive Factors for Return of Erectile Function in Robotic Radical Prostatectomy: Case Series From a Single Centre

10:15-10:30 J.Lee: A Novel Rat Model to Study Penile Corporal Healing After a Shunt Procedure

10:30-10:45 L.DeYoung: Peyronie's Disease: A Novel Rat Model

10:45-11:00 N.Fahmy: Investigating Ochratoxin A and Biotin Levels in Patients with Renal and Testicular Tumors

11:00-12:00 **Guest Professor: Dr. Stephen Nakada**
Renal Ablation in 2013: For Whom and When?

12:00-1:00 **LUNCH**

Con't...

SESSION III TRANSPLANTATION, ONCOLOGY & RENAL PHYSIOLOGY Moderator: Dr. A. Sener

1:00-1:15 P.Violette: Predictors of Prolonged OR Procedural Time During Robotic Assisted Radical Prostatectomy

1:15- 1:30 M.Lang: Novel Urinary Marker Expression Associated with Shock Wave Lithotripsy

1:30- 1:45 S.Boyle: Renal Function Assessment Post Laparoscopic Partial Nephrectomy: Is 6 Weeks Enough?

1:45-2:00 M.Dion: First Canadian Experience in Pediatric En-Bloc Renal Allograft Donation After Cardiac Death

2:00- 2:15 N.Rowe: Contrast-Enhanced Ultrasound of Solid Renal Masses: Non-Invasive Discrimination Between Renal Cell Carcinoma and Benign Renal Tumors

2:15-2:30 D.Yanko: Effects of Post-operative Intravenous Heparin Infusion on Simultaneous Kidney-Pancreas Transplant Outcomes

2:30-3:00 **Health Break**

3:00-4:00 **Guest Professor: Dr. Stephen Nakada**
Urinary Stone Disease: Find It, Treat it, Beat It

SESSION IV PEDIATRICS/UTI Moderator: Dr. P. Luke

4:00-4:15 S.Whiteside: Sub-Acute Levels of Antibiotics Used to Treat Recurrent Urinary Tract Infections May Promote Pathogen Growth and Internalization: Implications for Clinical Practice

4:15-4:30 L.Lee: Outcomes After Pyeloplasty with Externalized Ureteropyelostomy Stents in Pediatric Patients

4:30-4:45 P.Martin: Idiopathic Hydrocele Repair With Gubernaculum Preservation Can Be Easily and Safely Performed Through a Subinguinal Incision; Comparing a Novel Technique to Traditional Repairs.

4:45-5:30 **Imaging Contest:** K-C. Tran

5:30 Wrap up

6:30 **Faculty Dinner** (by invitation)

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

This year's program is intended to provide participants with:
A state-of-the-art review of the management of urinary tract stone disease.
A state-of-the-art review of the surgical management of testis cancer.
An update on the role of renal tumor ablation in patients with kidney cancer.
Results of clinical and basic science research projects of the resident staff from Western University in the following subspecialty areas:

Oncology
Endourology
Transplantation
d. Andrology
e. Urinary voiding dysfunction

This program was supported in part by an educational grant from the following: (list organization name(s): Abbvie, Eli Lilly, Watson Pharma, Coloplast, Janssen, Cook Medical, Abbott, Allergan, AstraZeneca Canada, Paladin, AMS Canada, Astellas Pharma Canada, Boston Scientific, Clarion Medical Technologies, ConMed Canada, Merck, Olympus, Pfizer Canada Inc., Pendopharm (a division of PharmaScience), Red Leaf and Sanofi Oncology.

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification program of The Royal College of Physicians and Surgeons of Canada and approved by Continuing Professional Development, Schulich School of Medicine & Dentistry, Western University (8.0 hours). Each participant should claim only those hours of credit that he/she actually spent participating in the educational program.

EVALUATING THE CLINICAL SIGNIFICANCE OF CD151 EXPRESSION IN PATIENTS THAT UNDERWENT A RADICAL CYSTECTOMY FOR UROTHELIAL CARCINOMA OF THE BLADDER

V Bathini, V McPherson, AK Williams, SM Chan, KS Rizkalla, M Ong, JD Lewis, JI Izawa

Background and Purpose:
CD151 is a member of the transmemebrane 4 superfamily, also known as the tetraspanins. Normally CD151 is involved with cell development, activation, growth and motility. Recent evidence suggests that this protein is also involved with motility, invasion, and metastasis of cancer cells. Although an association between high levels of CD151 and poor prognosis has been reported in different tumours, including prostate cancer, non-small cell lung cancer, and certain types of breast cancer, the relationship with bladder urothelial carcinoma is still under investigation. The aim of this pilot study was to evaluate if CD151 expression could be used as a prognostic indicator for patients with advanced urothelial carcinoma of the bladder.

Materials and Methods:
In total 46 patients who underwent a radical cystectomy for urothelial cancer with negative margins from 2002 – 2006 were evaluated. Tissue samples were analyzed for CD151 using immunhistochemistry. Retrospective data was collected for up to 10 years. The outcomes we investigated included recurrence rate, time to recurrence, overall survival and disease specific mortality.

Results:
Of the 46 pts 27 stained positively for CD151 and while 19 stained negatively. 20 out of the 46 patients received either neoadjuvant or adjuvant chemotherapy. 44% (12/27) of CD151 positive patients had a recurrence after cystectomy, while 47% (9/19) of CD151 negative patients recurred. Mean time to recurrence in the CD151 positive group was 6.86 months while in the CD151 negative group it was 10.9 months. Neither the recurrence rate nor time to recurrence was statistically different between the two groups ($p>0.05$). The overall mean survival time was 50.1 months in the CD151 positive group and 54.2 months in the CD151 negative group ($p>0.05$). The overall number of deaths was 14 in the CD151 positive and 8 in the CD151 negative group. Bladder cancer was the attributable cause in 79% (11/14) of the CD151 positive group and 88% (7/8) of the deaths in the CD151 negative group.

Conclusions:
In our study CD151 expression did not provide any additional prognostic information. It is a novel pilot study limited by the small sample size and heterogeneous population.

COMPLETE GENOME-WIDE SHRNA SCREEN FOR MODULATORS OF PROSTATE CANCER DISEASE PROGRESSION

SJ Leith, SE Kuruvilla, J Moffat, JL Chin, HS Leong, EA Turley

Introduction and Objectives:
Metastasis in prostate cancer is caused by genetic reprogramming leading to increased cell motility and the formation of invasive structures which allow cells to migrate out of the primary tumour in a process known as intravasation. In order to search for novel genes driving or inhibiting invasive phenotypes responsible for intravasation, a genome-wide high throughput short hairpin RNA screen was used to identify genes which mediate aggressive phenotypes in various prostate cell lines such as PC3 (malignant prostate cancer) and BPH (Benign Prostatic Hyperplasia) when grown in 3D matrigel culture conditions.

Methods:
Using the TRC lentivirus shRNA library that covers the entire human transcriptome (80,000 unique constructs), PC3 and BPH cells were infected such that each cell would integrate a single shRNA construct that will target mRNA expression of a known human gene. Cells were plated at 1500 per well in 96 well plates until a 5X genome-wide coverage was achieved. In 3D matrigel culture conditions, PC3 colonies exhibit a highly fibroblastic invasive morphology, indicating a metastatic phenotype whereas BPH colonies exhibit a large round morphology in 3D. Hence, we screened for clonogenic PC3 colonies that appeared round in shape and BPH colonies that appeared fibroblastic and spindle-shaped. Collection of these "hits" will yield gene identities that drive metastasis and suppress tumorigenesis respectively.

Results:
In this ongoing study, we have achieved 5x coverage of the genome-wide TRC shRNA library in BPH cells. After 11 days of growth, 15 "hits" from the BPH screen that exhibit an invasive phenotype were isolated, and are currently being validated again in 3D matrigel culture. Once validated, the DNA will be extracted and sequenced to identify what genes were inhibited in the cells.

Conclusions:
Overall, we provide a high-throughput and high-content screen for discovering novel genes that drive or inhibit prostate cancer progression. These functional genomics screens which focus on altered prostate cell colony phenotypes may open new doors for potential drug treatments and a greater understanding of prostate cancer and BPH.

THE PROGNOSTIC ROLE OF FRACTAL GEOMETRY IN RENAL CELL CARCINOMA PHOTOMICROGRAPH ANALYSIS

P Wang, HS Leong, N Power

Introduction:
A fractal dimension is a mathematical index for characterizing complexity. It was initially described by Benoit Mandelbrot in 1967 to characterize the coastline of Britain. Fractal geometry has since been used in many other real-world phenomena and has been applied to fields such as physics, acoustics, physiology and neuroscience. In medicine, fractal dimensions have been calculated using computer based fractal analysis techniques to describe the histopathology of breast, colon, prostate and pancreatic malignancies. This pilot study aims to explore the role of fractal dimension in renal cell carcinoma.

Methods:
A total of 22 cases of patients who underwent nephrectomies were obtained from the Ontario Tumor Bank. These cases comprised the major subtypes of renal cell carcinoma. Each case included information on patient demographics, clinical outcomes, operative parameters and pathology. Digital photomicrographs of hematoxylin and eosin (H&E) stained slides of the tumor and normal adjacent were obtained for each case. ImageJ, an open source java-based software was used to determine the fractal dimension of each H&E slide using the box-counting algorithm. The fractal dimensions of the tumors were compared to the normal adjacent tissues. Sensitivity and specificity was calculated.

Outcomes:
The primary outcome of this pilot study is to assess the ability of fractal analysis to differentiate between normal and tumor as a proof of concept. Secondary outcomes include assessing the ability of fractal dimensions to predict cancer-specific death and metastases. The results of this study are pending.

Impact:
Fractal analysis may provide an automated and possibly more accurate method to identify patients with renal cell carcinoma at risk for disease recurrence and progression. In turn, this may help in defining patients who would benefit from adjuvant therapies and closer surveillance.

PROSTATE CANCER MICROPARTICLES AS A NEXT GENERATION SCREENING TOOL FOR PROSTATE CANCER

H.Leong

Prostate cancer (PCa) microparticles, which are tumor cell fragments released by prostate cancer cells into the blood circulation, offer a non-invasive means of sampling the primary tumor, an ideal platform for a prostate cancer-specific fluid biopsy. My laboratory has recently developed a blood test that enumerates prostate cancer microparticles in minute volumes of patient blood in a high-throughput and multi-parametric manner. This blood test has shown promise in successfully distinguishing BPH patient plasmas from localized PCa patient plasmas in a small prospective pilot study. This proposal aims to validate the clinical utility of this microparticle-based blood test in a large scale, prospective clinical trial which will compare the accuracy of this microparticle test against the PSA test in identifying patients with localized PCa out of the rest of the screened population that is typically biopsy negative. Hence, the objective is to perform these blood tests prior to histopathological TRUS biopsy assessment by a GU pathologist. The blood test relies on the use of nanoscale flow cytometry to enumerate and analyze cell-derived microparticles present in patient blood plasma. Plasmas will be labeled with prostate-specific (PSMA-RPE mAb) and cancer-specific (biomarker X) agents to identify and enumerate prostate cancer microparticles (PSMA+ biomarker X+). It is anticipated that biopsy negative patients will have low PSMA+ biomarker X+ microparticle counts whereas patients with histologically confirmed prostate cancer will exhibit significantly higher counts of PMSA+ biomarker X+ microparticles. Implementing this test in a large prospective clinical study will allow us to develop cutoffs for PSMA+ biomarker X+ microparticle counts that will enable clinicians to distinguish PCa patients from non-PCa patients ahead of TRUS biopsy. This microparticle-based test when used in conjunction with the PSA test, will minimize the false positive rate in PCa screening tests such that unnecessary biopsies will be minimized, thus lowering the economic and health costs to the entire prostate cancer population and address the emerging problem of overtreatment in prostate cancer.

PREDICTIVE FACTORS FOR RETURN OF ERECTILE FUNCTION IN ROBOTIC RADICAL PROSTATECTOMY:

CASE SERIES FROM A SINGLE CENTRE

F. Garcia, P. Violette, L. Nott, S. Pautler

Schulich School of Medicine & Dentistry, Western University, London, ON, Canada, McMaster University Hamilton, ON, Canada, St. Joseph's Health Care, London, ON Canada

Prostate cancer represents the most common solid malignancy in men. Approximately 80% of these men present with localized disease, and thus are suitable candidates for local therapy including radical prostatectomy. Despite many advances in diagnosis resulting in early case finding and improvements in surgical technique, significant morbidity associated with radical prostate surgery remains. Postprostatectomy erectile dysfunction is a frequent complication and a source of distress for many men despite modifications in surgical technique, most notably the nerve sparing prostatectomy described by Walsh. While nerve-sparing grading scales have been developed for specific institutions, they have not been shown to have great inter-observer reproducibility outside of the institutions that developed them. We wished to look retrospectively to attempt to identify objective predictors of good and poor erectile recovery in a population of potent men undergoing robotic radical prostatectomy. Data was collected prospectively and includes the learning curve of a single surgeon at a single centre with a single technique. Men were required to have 2 years of complete follow-up, pre-operative IIEF scores of $\geq$ 22 without erectogenic aids/devices, and no adjuvant or hormonal therapy. 2 groups were compared looking at post-operative IIEF of $\geq$ 17 vs <16 at 2 years, with 41 and 45 patients in each group respectively. Of the pre-operative variables examined, pre-op PSA was statistically higher in those with worse post-op IIEFs ($P = 0.05$), however clinical T stage and number of positive cores were not statistically significant, but trending towards significance in the poor recovery group (p value of 0.11 and 0.06 respectively). Intraoperative variables examined demonstrated statistically significant longer apical dissection time in those with poor erectile recovery, as does the subjective assessment of the surgeon on quality of nerve spare ($P < 0.05$). None of the post-operative variables reached significance. Interestingly patients BMI, age, grade, pre-op prostate volume estimation or pathologic weight were not significantly different between groups. Given the small numbers being examined here some of the variables might achieve significance if more patients were studied such as number of cores or clinical T stage. We present some objective parameters that can help inform a patient of their likelihood of post-operative erectile recovery.

A NOVEL RAT MODEL TO STUDY PENILE CORPORAL HEALING AFTER A SHUNT PROCEDURE

KCJ Lee, L De Young, G Brock

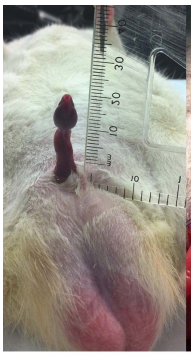
Introduction and Objective:
Distal penile corporo-glanular shunt procedures are commonly done for patients with major ischemic priapism. Many of these patients develop irreversible penile fibrosis and erectile dysfunction which require penile implants subsequently. Early insertions of penile prostheses are associated with fears of corporal perforation requiring surgical revisions. Delayed insertions are technically more difficult due to dense fibrosis that has formed. To date, there is no animal model that allows us to study distal corporal healing and the tensile strength of corporal scar tissue with respect to time.

The objective of our work was to develop a new rat model to study distal corporal healing and the tensile strength of corporal scar tissue with relations to time.

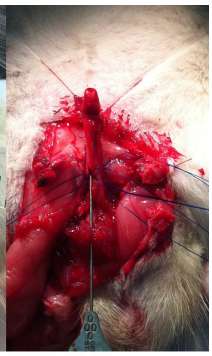
Method:
Corporo-glanular shunt procedures were performed on 20 anesthetized male Sprague-Dawley rats after erection had been created using a vacuum device and constrictive band. Sham surgery was performed for 8 rats. At every 3-days, 1-week, 2-weeks and 4-weeks intervals, the intra-cavernosal pressure of 5 rats in the shunt group and 2 rats in the sham group were measured. The rats were sacrificed thereafter. Strength-testing of corporal tissue at the ex-shunt site was done by inserting a customized intra-cavernosal probe on a force gauge through a proximal penile corporotomy in the rat. The maximal tensile strength was measured by the peak force required for the probe to perforate the corporo-glanular junction.

Results:
The intra-cavernosal probe on a force gauge allowed corporal tissue strength to be measured in a reliable way. The temporal relationship between corporal healing and tensile strength of corporal scar tissue can be evaluated using this new model.

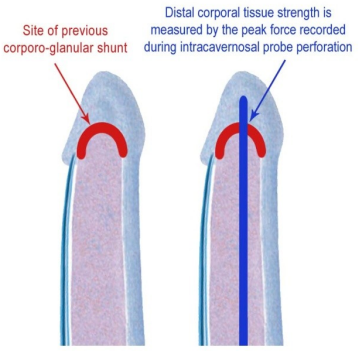
Conclusion:
Penile corporal healing and tensile strength can be evaluated using this rat model.



Picture 1. Erection of rat penis induced by vacuum device and constrictive band.



Picture 2. Strength of distal corporal issue measured using an intracavernosal probe.



Picture 3. Distal corporal tissue strength is measured by the peak force recorded when the blunt intracavernosal probe is advanced to the point of corporal perforation.

PEYRONIE'S DISEASE: A NOVEL RAT MODEL

L De Young, E Chung, F Garcia, P Wang, L Lee, J Lee and Brock G

Introduction:
Peyronie's disease (PD) was first described more than 250 years ago, the exact mechanism of PD remains an enigma. At the present time, research into PD is hampered by the lack of a universally accepted animal model. Limited insight into the precise PD mechanism and difficulties faced by current animal models to truly represent the complexity and complete spectrum of human disease represents a major deficiency in this field of investigation.

Methods:
Phase one: We evaluated PD plaque formation among15 adult male rats aged 9-11 months old. They were injected with 0.1 ml of a plaque inducing agent (prepared with 0. 5ug TGF-1and 0.1 ml Tromboject® 3% sodium tetradecyl sulfate) into the cavernosal body. Expression of wound healing and fibrosis-associated proteins markers, and immune-histochemistry were carried out at 2, 4, 6, 8 and 10 weeks. Phase two: A total of 12 adult male rats had plaque induction, and were maintained for 4 weeks. The rats received intralesional injections of 0.1mg/0.1cc of verapamil (Group 1/5 rats) into the subtunical space, q2days for 2 weeks. Group 2 (5 rats) received 0.1cc of intralesional normal saline injection. Group 3 (2 rats) underwent microscopic surgery where 2 plicating horizontal mattress sutures were placed on each side of the stable plaque to exert longitudinal stress. At week 6 an additional plicating suture was placed on each side. Group 4(2 rats) untreated rats which were kept as controls. After penile pressures measurement at weeks 8 all rats were sacrificed and serial penile tissue sections were prepared for histochemical analysis.

Results:
Sub-tunical injection of TGF β-1/Trombojet® solution induced a Peyronie's-like plaque formation as early as week 2 with excessive collagen deposition, alteration in elastic fibres and evident penile deformity, which persisted to week 10. An over-expression of TGF β-1, smooth muscle a-actin and β-catenin was measured. Intralesional injection of verapamil and normal saline resulted in macro- and microscopic changes to penile curvature and Peyronie's plaque size. There were decreased collagen and elastin fibers and smooth muscle α-actin on histochemical stains. The changes observed were greater in Group 1 than Group 2. Intralesional verapamil injection was associated with greater recovery of penile pressure (a surrogate for erection) than Group 2, but did not achieve return to normal erect penile pressure. The traction group achieved higher penile pressures than the untreated control group with cavernous nerve electrostimulation. Smaller plaque with less non-polarized collagen in the traction group compared to the untreated control group.

Conclusions:
TGF β-1/ Trombojet® injection develops into a robust animal model for the study of Peyronie's disease. This novel study described for the first time, histological evidence of cellular changes within an induced Peyronie's-like plaque following intralesional injections and penile traction. Volume expansion by hydrodistension appears to play an important role in the observed plaque remodeling.

INVESTIGATING OCHRATOXIN A AND BIOTIN LEVELS IN PATIENTS WITH RENAL AND TESTICULAR TUMORS

N Fahmy, M Woo, M Alameldin, K MacDonald, L Goneau, P Cadieux, S Pautler
Departments of Surgery (Division of Urology), Anatomic Pathology and Microbiology and Immunology, Western University

Background:
Ochratoxin-A (OTA) is one of the most abundant food contaminating mycotoxins. It is a fungal metabolite known for its nephrotoxicity, neurotoxicity, gonadotoxicity, teratogenicity, immunsuppression and carcinogenesis. It can be acquired through inhalation or ingestion and has been found in a variety of animal and human tissues. OTA has been linked to several genitourinary (GU) pathologies, including Balkan nephropathy and GU malignancies. Its mechanism of action is still unclear. The aim of this study was to examine OTA levels in serum samples and tumor specimens collected from patients with renal tumors.

Methods:
Frozen samples were obtained from the Ontario Tumor Bank, a program established by the Ontario Institute for Cancer Research. It is a province-wide biorepository and data bank focused on collection of tumour-related human biospecimens. Specimens included serum and renal tumor biopsies. Normal tissue from the negative safety margin of each tumor served as a control. OTA levels in the serum were measured using ELISA, while OTA staining in tissue specimens was determined using Immunohistochemistry (IHC).

Results:
Specimens collected from 56 patients (36 men and 20 women) were included in this study. Histopathology of the 52 renal tumors included 31 (60%) conventional type RCC, 5 (10%) chromophobe, 5 (10%) papillary, 1 (2%) oncocytoma and 10 (19%) upper tract TCC. The 4 testicular tumors included 1 seminomatous (25%) germ cell tumor and 3 (75%) non seminomatous germ cell tumors. OTA was detected in the serum of renal tumor patients with a range from 0.004 to 0.25 ng/mL (mean: 0.07 and median 0.06ng/mL). Interestingly, preliminary IHC staining showed significantly high levels of positive signal only in the control tissue and not in the tumors. This was subsequently determined to be due to the streptavidin-conjugated secondary antibody used, which was detecting high levels of endogenous biotin within the healthy tissue, but not in tumors. No OTA was detected in human tissues.

Conclusions:
OTA levels detected in the serum of patients were found to be highly variable and relatively low. While there was no OTA detected within the tissue samples, endogenous biotin expression in the non neoplastic surgical margin of the renal tumors was identified and suggest a potential use for biotin as a cheap marker for renal tumors.

PREDICTORS OF PROLONGED OR TIME DURING ROBOTIC ASSISTED RADICAL PROSTATECTOMY

P.Violette, S.Pautler

Introduction and Objectives:
Time efficiency during robotic radical prostatectomy is of critical importance to improving resource utilization in the operating room. However, little is known about the determinants of robotic OR time after the initial learning curve period. Therefore our objective is to determine predictors of prolonged OR time during robotic radical prostatectomy.

Methods:
We prospectively collected data from 440 consecutive patients who underwent robotic radical prostatectomy performed by a single surgeon at an academic institution from 2006 to 2012. The first 40 cases from the early learning curve were excluded, as previously defined[1]. Our primary outcome, prolonged OR, was defined as greater than one standard deviation above the mean OR time. The Student-t test was used to compare continuous data, and Chi-square for categorical data. A multivariate logistic regression was conducted to identify predictors of prolonged OR time, and a multivariate linear regression was used to further characterize their impact.

Results:
Our cohort was made up of men aged 60 ± 7 years, with low or intermediate risk prostate cancer (PSA 7±3, 60% Gleason 6, 40% Gleason 7, and 71 % stage 1 disease). These men had a mean BMI and IIEF scores of 28±3 and 17±8, the majority of which underwent bilateral (62%) or unilateral (21%) nerve sparring prostatectomy with pelvic lymph node dissection (49%). The mean OR time was 185±33 min. Logistic regression revealed 5 independent predictors of prolonged OR time (Table 1). According to the multivariate linear model, OR time was most clearly affected by the presence of a robotic malfunction 30 min, blood loss 6 minutes/100cc, PSA 1 min/unit and gland volume 3 min/10cc, when controlling for all other variables.

Table 1- Multivariate logistic regression

Variable	Multivariate Logistic analysis	
	Odds ratio (95% CI)	p-value
Blood loss (per 100ml)	1.50 (1.26, 1.80)	<.001
Pre-op PSA	1.09 (1.02, 3.79)	.037
Robot Malfunction	8.35 (2.60, 26.8)	<.001
Gland Volume (per 10cc)	1.19 (1.02, 1.39)	.025
Pelvic Node dissection	1.01 (0.89, 3.26)	.10

Conclusions:
Robotic malfunction was the strongest predictor of prolonged OR time. Blood loss, PSA, node dissection and gland volume were also associated with prolonged OR time. Knowledge of these predictors may assist in improving resource utilization.

References:
Martinez CH, Chalasani V, Lim D, Nott L, Al-Bareeq RJ, Wignall GR, Sitt L, Pautler SE Effect of prostate gland size on the learning curve for robot-assisted laparoscopic radical prostatectomy: Does size really matter initially? J Endourol 2010;24:261-266.

NOVEL URINARY MARKER EXPRESSION ASSOCIATED WITH SHOCK WAVE LITHOTRIPSY

RM Lang, N Fahmy, A Sener, B Welk, L Nott, S VanEerdewijk, VS Sabbisetti, JV Bonventre, H Razvi

Introduction and Objective:
Shockwave lithotripsy (SWL) is a minimally invasive treatment alternative for kidney stones. Although less invasive, SWL subjects the renal parenchyma to a high level of energy potentially causing renal injury. To date, not all kidney injuries caused by SWL can be reliably detected by conventional imaging techniques. Kidney Injury Molecule-1 (KIM-1) and N-acetyl-glucosaminidase (NAG) are 2 proteins secreted by the kidney into urine and found to be sensitive markers of acute kidney injury in transplant patients. The aim of this work was to evaluate the urinary levels of KIM-1 and NAG in kidney stone patients treated by SWL.

Methods:
Voided urine samples were collected before, 2 hours, 2 days and 2 weeks post SWL treatment. Patients having ureteric or radiolucent stones, ureteric stents, elevated creatinine or UTI were excluded. KIM-1 was measured by microbead based assay on Luminex. NAG was measured by spectrophotometry based enzymatic assay. KIM-1 and NAG values are reported as a normalized ratio to urinary creatinine.

Results:
23 patients with a mean age of 55 (range 36 to 74) years were included. Stone size ranged from 5 to 16 mm (mean 7.9 mm). Mean KIM-1 and NAG levels pre SWL were 6.8 pg/ml and 2.9 mU/ml. At 2 hours post SWL these levels increased significantly to 11.7 pg/ml and 4.8 mU/ml. Mean NAG levels returned to baseline at 2 days post SWL and KIM-1 at 2 weeks.

Conclusions:
KIM-1 and NAG levels significantly increased post treatment suggesting these novel markers may have a potential role in identifying tissue injury post SWL.

RENAL FUNCTION ASSESSMENT POST LAPAROSCOPIC PARTIAL NEPHRECTOMY: IS 6 WEEKS ENOUGH?

S.Boyle, F.Cui, L.Lee, N.Rowe, PPW.Luke

Introduction and Objective:
The negative effects on renal function after laparoscopic partial nephrectomy are commonly assessed using a surrogate marker of serum creatinine to represent kidney function. Recent literature suggests that nuclear renography may be a better way to look at the recovery after partial nephrectomy. The optimal timing and follow-up for this type of assessment has not been established, and we hypothesis that by 6 weeks optimal recovery is seen.

Methods:
Between 2002 through 2012 111 patients underwent laparoscopic nephrectomy. 97 had with pre-operative renograms and serum creatinine as well as post operative renograms and serum creatinine at 3days, 6 to 12 weeks and 12 months. Included in this data set are clamp times, tumor size, pathologic piece size and tumor location from radiologic imaging.

Results:
The functional GRF contribution for the affected side was calculated using the Cockoft-Gualt and multiplying by the percent function as provided by the nuclear renogram. The pre-operative values 47.6 ml/min/m^2 (+/- 19.3) and post op day 3 showed a decrease to 34.2 ml/min/m^2 (+/-18) but recovered at 6-12 weeks to 36.8 ml/min/m^2 (+/-21.0) and at one year showed little change from that at 37.4 ml/min/m^2 (+/-20.0) We analyzed clamp time, endophytic tumor, all non T1a tumors and pathologic specimen volume for affects on post operative, early post operative and late post operative functional unit GFR. No significant differences were found between 6 weeks and one year of follow-up.

Conclusions:
Analysis of renal function post partial nephrectomy with nuclear renography shows optimal recovery is reached by 6-12 weeks. In further studies regarding functional renal recovery post laparoscopic partial nephrectomy this time point should be used for analysis when assessing risk factors that affect renal recovery.

FIRST CANADIAN EXPERIENCE IN PEDIATRIC EN-BLOC RENAL ALLOGRAFT DONATION AFTER CARDIAC DEATH

M Dion, N Rowe, J Shum, C Weernink, S Langford, A Sener, P Luke

Introduction:
The use of small pediatric kidneys obtained from very young donors after cardiac death (DCD) has been very limited. This is based on concerns regarding allograft function and growth, as well as limited experience in issues of consent for organ donation and withdrawal of life support in infants. A limited number of such transplants have been reported. Despite the success of small en-bloc grafts from neurological determination of death (NDD) infant donors and good outcomes with larger DCD grafts, DCD en-bloc allografts from very young donors remains an underutilized organ source. In this study we report our outcomes and first experience with transplantation of DCD en-bloc kidneys obtained from donors less than 4 years of age.

Methods:
We reviewed all renal transplants at our institution from 2000 to 2012 to identify recipients who received an en-bloc pair of kidneys from pediatric donors less than 4 years of age. We examined recipient characteristics, perioperative characteristics, surgical complications, and allograft outcomes. The outcomes of DCD en-bloc allografts were compared with NDD en-bloc allografts.

Results:
20 recipients were identified with heterogeneous causes of end-stage renal disease. The mean age at transplantation was 50.7 ± 16.0 years. Four of the en-bloc kidney pairs were obtained by DCD and the remainder procured from NDD donors. In the DCD cohort the mean donor age was 15.6 ± 12.0 months with weight of 9.9 ± 2.4 kg as compared the NDD group with donor age 21.6 ± 12.0 months and weight 12.9 ± 3.8 kg. Surgical complications were minimal in both groups. All DCD allografts are currently functioning with mean GFR of 79.7 ± 21.5 mL/minute which was the similar to renal function of recipients of NDD allografts (81.5 ± 38.7 mL/minute) at one year follow-up (see figure). Delayed graft function (DGF) was higher in the DCD group affecting two out of four (50%) recipients as compared to 12.5% of the NDD group (RR 4.0, $p = 0.162$).

Conclusions:
We are pleased to report successful transplantation of a small cohort of en-bloc DCD kidneys from donors less than 4 years of age. Outcomes at 1 year are comparable to NDD recipients. Recipients of DCD allografts demonstrated higher rates of DGF although numbers were prohibitively small to make an accurate statistical comparison.

CONTRAST-ENHANCED ULTRASOUND OF SOLID RENAL MASSES: NON-INVASIVE DISCRIMINATION BETWEEN RENAL CELL CARCINOMA AND BENIGN RENAL TUMORS

N Rowe, J Bird, C Romagnoli, P Luke

Introduction and Objective:
Contrast-enhanced ultrasound (CEUS) is an emerging dynamic imaging modality for the diagnostic workup of renal masses. CEUS avoids ionizing radiation for patients and avoids contrast-related toxicity associated with conventional imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI). We evaluated the utility of CEUS in predicting the histopathology of solid renal masses.

Methods:
We assessed the ability of CEUS to predict tumor pathology in 32 solid renal masses in 31 patients (mean age 65 years, 17 males: 14 females) undergoing extirpative therapy at our institution. The presence of four main CEUS characteristic were evaluated in each mass including level of arterial enhancement compared to adjacent renal parenchyma (either hypoenhancment, isoenhancement, or hyperenhancement), enhancement pattern (either homogenous or heterogeneous), washout, and peri-lesional rim enhancement. Two radiologists assessed radiographic findings. The findings for each mass were compared with surgical pathology in order to determine predictive CEUS characteristics.

Results:
Our series consisted of 24 renal carcinomas (19 clear cell, 3 chromophobe, and 2 papillary tumors) and 8 benign tumors (6 oncocytomas, 1 angiomyolipoma and 1 metanephric adenoma). Mean tumor size was 3.1 cm (range 1.2 to 5.7cm). Heterogeneous enhancement alone had a 94% positive predictive value (95% CI 69-99), 44% negative predictive value (95% CI 19-70), 63% sensitivity (95% CI 40-81) and 88% specificity (95% CI 47-99) in predicting malignancy. The combination of isointense or hyperintense enhancement and homogeneous enhancement had a 67% positive predictive value (95% CI 29-92), 91% negative predictive value (95% CI 71-98), 75% sensitivity (95% CI 34-96) and 88% specificity (95% CI 67-97) for a benign tumor.

Conclusions:
Our early experience with CEUS in the evaluation of solid renal masses demonstrates good accuracy in discrimination between malignant and benign tumors. This non-invasive diagnostic modality appears to be better than CT or MRI and may be comparable to percutaneous biopsy. Our initial results have prompted a larger corroborative prospective trial to evaluate the diagnostic accuracy of CEUS in predicting pathology in renal masses. CEUS may have an important role in the management of small renal masses.

EFFECTS OF POST-OPERATIVE INTRAVENOUS HEPARIN INFUSION ON SIMULTANEOUS KIDNEY-PANCREAS TRANSPLANT OUTCOMES

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Departments of Surgery and Microbiology and Immunology, Multi-organ Transplant Program and Matthew Mailing Center for Translational Transplant Studies, Western University, London, Ontario, Canada.

Introduction:
Graft thrombosis is the most common cause of technical failure in pancreas transplantation. It can occur in up to 20% of patients and may be due to both donor and recipient factors. There is no current evidence to suggest that the use of anti-coagulation in the peri-operative period has any potential benefit of reducing the rates of portal vein thrombosis in pancreas transplants.

Objective:
To retrospectively compare the clinical outcomes and complication rates in patients who underwent simultaneous kidney-pancreas (SPK) transplants at our institution to determine the effect of post-operative continuous, low-dose intravenous heparin.

Methods:
There were 55 SPK transplants performed at our institution between 2004 and 2013. All patients since July 2009 (n=23) received a post-operative regimen of continuous heparin (Group 1) at 500U/h for 24h which was tapered to discontinuation by POD#5, whereas patients transplanted prior to that date (n=32) did not (Group 2). All patients were then placed on low-dose ASA on POD#6 which they continued indefinitely. Demographic variables were compared between the two groups. Post operative serum values (Hb, GFR, lipase, amylase, glucose) and complications (pancreatitis, PE, graft loss, hemorrhage, transfusions) were compared between the two groups. Statistical analyses were carried out using the Fisher's exact test and Student's t- test.

Results:
23%(7) of Group 2 recipients lost their grafts to portal vein thromboses versus 0% in Group 1 with an overall graft function of 100% in Group 1 and 77% in Group 2 (p=0.015). One patient in Group 2 died from a pulmonary embolus whereas no fatalities were observed in the heparinized group. Both groups had equal rates of blood transfusions (p=0.42). Serum biochemical parameters for renal and pancreatic function were comparable between the groups at the time of last follow-up.

Conclusion:

This study provides novel information on the use of peri-operative intravenous anti-coagulative therapy in SPK transplantation. There is a statistically significant higher graft survival rate in the heparinized group without an increase in perioperative complications. A larger cohort will be necessary to confirm these findings.

Source of Funding: None
Conflict of Interest: None

SUB-ACUTE LEVELS OF ANTIBIOTICS USED TO TREAT RECURRENT URINARY TRACT INFECTIONS MAY PROMOTE PATHOGEN GROWTH AND INTERNALIZATION: IMPLICATIONS FOR CLINICAL PRACTICE

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Introduction and Objectives:
Recurrent urinary tract infections (RUTI) remain a common reason for patient visits to Urology clinics. In many cases, antibiotic prophylaxis is prescribed to prevent overgrowth of pathogens within the bladder; however, antibiotic concentrations are not always constant and repeatedly fall to sub-minimal inhibitory concentrations (sub-MIC). The goal of this study was to investigate the role of antibiotics at sub-MICs on enterococcal species, an increasingly important cause of RUTI.

Methods:
Strains of *Enterococcus faecalis* and *E. faecium* were profiled for antibiotic susceptibility using 12 antimicrobial agents commonly used in the treatment of uncomplicated and complicated urinary tract infection (UTI). Profiling was performed by standard CLSI disk-diffusion and microdilution methodologies using media of varying nutrient load to mimic variation in urine concentration. Additionally, internalization and intracellular survival within a bladder cell line (T24) was assayed to determine if antibiotic pre-treatment increased these phenomena.

Results:
Antibiotic susceptibility remained constant for most antibiotics irrespective of the culture media. However, notable exceptions included ciprofloxacin, levofloxacin, and doxycycline, which demonstrated altered susceptibility status for 8/8, 7/8, and 7/8 *Enterococcus* strains, respectively. More importantly, there was increased growth beyond the zone of inhibition, suggesting that enterococci may actually utilize antibiotics to actively grow.

Conclusions:
The issue of antibiotic use with regards to UTI has come under scrutiny in recent years. In fact, 25-42% of UTI cases resolve without antibiotics and only 2% develop pyelonephritis. The goal then is to achieve good symptom control and interestingly German researchers have reported equivalent success with ibuprofen (400 mg 3 times daily) over ciprofloxacin. Our finding that enterococci not only resist antibiotics used in RUTI prophylaxis, but may use them as a substrate could explain breakthrough infections or low-grade symptoms and signs. Additionally, increased internalization and intracellular survival may provide an explanation for enterococcal recurrence, as the bacteria escape the antibiotic challenge. Overall, further re-evaluation of antibiotic prophylaxis is warranted.

OUTCOMES AFTER PYELOPLASTY WITH EXTERNALIZED URETEROPYELOSTOMY STENTS IN PEDIATRIC PATIENTS

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Purpose:
Pyeloplasty with double J stents often require postoperative urethral catheterization, manipulation of the UVJ and a second anesthetic for removal in pediatric patients. In contrast, pyeloplasty with externalized ureteropyelostomy "Salle" stents avoids these issues. We compare outcomes of laparoscopic and open pyeloplasty with Salle stents compared to double J stents in pediatric patients.

Methods:
76 patients underwent surgery for ureteropelvic junction (UPJ) obstruction from January 2011 to July 2012 by five pediatric urologists at the Hospital for Sick Children. Exclusion criteria included ureterocalicostomy, complex concomitant surgery, drainage with ureteral catheter, stentless pyeloplasty or patients who were lost to follow-up. Twenty four patients had a Salle stent and 39 patients had a double J stent post-pyeloplasty.

Results:
Median follow-up was 9.1 months (0.7-24.6). Median age for the Salle stent group was 40 months and the double J group was 78 mos ($p=0.04$). The Salle stent group had a greater number of open pyeloplasty (71%) versus the double J group (41%), which approached but did not reach statistical significance ($p=0.06$). There was no statistically significant difference in operative time, length of stay and overall complication rate between the two groups.

Conclusions:
Laparoscopic or open pyeloplasty using Salle stents does not prolong operative time, length of stay or alter complication rate when compared to double J stents. Salle stents are a safe alternative and have many advantages over conventional double J stents.

IDIOPATHIC HYDROCELE REPAIR WITH UBERNACULUM PRESERVATION CAN BE EASILY AND SAFELY PERFORMED THROUGH A SUBINGUINAL INCISION; COMPARING A NOVEL TECHNIQUE TO TRADITIONAL REPAIRS

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Introduction and Objective:
Adult idiopathic hydrocele is a common benign disorder that merits surgical correction when symptomatic. The two traditional methods of repair are plication (Lord's procedure), or excision & eversion of the tunica vaginalis (Jaboulay procedure). These procedures are performed through a scrotal incision. We describe a novel technique of hydrocele repair with gubernaculum preservation through a subinguinal incision. Results are compared to a contemporary cohort of traditional repairs.

Methods:
The novel technique is described in detail. A retrospective review was performed of those patients treated by a single surgeon with the novel technique. Demographic information, indication for treatment, success rate, and details regarding complications were collected. Results were compared to a contemporary cohort of patients treated surgically with traditional repairs.

Results:
We term the technique the "tug & stitch" repair. Through a small subinguinal incision the tunica is wrapped around the cord and testes without resection of the hydrocele sac or gubernaculum. 10 patients with post-operative follow-up were identified and compared to 66 patients that had a traditional repair. At one month, 9 patients (90%) treated with the novel technique were cured compared to 39 (59%) treated with a traditional repair ($p=0.08$). Lord's technique had resolution in 62% of cases (28/45). Jaboulay repair had resolution in 52% of cases (11/21). There was only one complication recorded after the novel technique: a wound infection. There were 4 hematomas and one orchidectomy from traditional repairs.

Conclusions:
Idiopathic hydrocele repair with gubernaculum preservation can be easily and safely performed through a small subinguinal incision.

PREVIOUS RESIDENTS' DAY GUEST PROFESSORS 1984 – 2012

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
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1988	Dr. Gerald Sufrin
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1986	Dr. J. Edson Pontes
1985	Dr. Alan Perlmutter

IMAGING CONTEST ANSWER PAGE

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4	a	
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