

## Unmoderated Posters

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### UP-01

#### The impact of pelvic and extremity immobilization after bladder exstrophy closure: experience from a third world country

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**Introduction and Objective:** Failure of initial bladder exstrophy closure and the need for subsequent reclosure severely impacts the functional bladder outcome of these patients. One of the most important factors that greatly enhance the chances of successful repair is the use of pelvic osteotomy and effective immobilization of the lower extremities after closure. We reviewed our experience with bladder exstrophy repair to determine the impact of osteotomy and the various methods of pelvic and extremity immobilization on the surgical outcome.

**Materials and Methods:** Retrospective chart review of all classic bladder exstrophy cases done at our hospital, from March 2000 to October 2007. A total of 19 patients were found. The records were reviewed with respect to age at bladder closure, primary (initial) or redo closure, presence and type of osteotomy, method of pelvic immobilization, complications related to the immobilization technique & the use of osteotomy.

**Results:** Total of 19 patients identified with classic bladder exstrophy, all underwent CPER repair. Seven females and 12 males. Eight patients (43%) had failed initial bladder closures. Two of these patients were done outside without osteotomies or immobilization and referred for redo closure. Of the 17 initially closed at our institution all underwent bilateral pelvic osteotomy expect 1, and 6 (36%) failed initial closure. The method of immobilization used in all failed closures was a cervical collar with a sling or no immobilization. The success rates for initial and second closures were best when the patients were immobilized with traction with or without Fixceters (69% v. 0% and 75% v. 25%, respectively). Of 19 patients who underwent primary bladder closure, 17 (89%) had minor to major surgical complications ranging from vesicocutaneous fistula to wound dehiscences and loss of hemiglans (Table 1).

**Table 1. UP-01. Complications after bladder exstrophy closure without proper pelvic and extremity immobilizations**

Complication	After primary closure, n = 19	After secondary closure, n = 8	After third closure, n = 4
Wound dehiscence	26.31% (5)	25% (2)	0
Bladder prolapse	31.57% (6)	37.5% (3)	25% (1)
Vesico-cutaneous fistula	31.57% (6)	12.5% (1)	25% (1)
Hemiglans/corporal atrophy	5.2% (1)	0	0
Epispadias failure	10.5% (2)	0	0

**Conclusion:** Proper and effective postoperative immobilization of the pelvis and extremity is important to achieve a successful closure. An agreement should be achieved in each centre on the proper immobilization technique for each age group. Having a dedicated and interested pediatric orthopedic surgeon for these cases is important for successful closures.

### UP-02

#### Study of hydrophilic-coated catheter appreciation in a pediatric population

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**Introduction and Objective:** To compare the satisfaction of hydrophilic-coated catheters (SpeediCath) versus uncoated catheters in a paediatric population presenting with myelomeningocele or spinal cord injury, in order to identify a target group for this hydrophilic-coated catheter. The main hypothesis was that patients who will benefit the most would be females using the SpeediCath compact catheter.

**Materials and Methods:** A comparative prospective study was initiated, with an objective of recruiting 30 pediatric patients with neurogenic bladders. These patients agreed to try for 1 week the SpeediCath catheter and to answer a satisfaction questionnaire. The catheters and the questionnaire were supplied to the patients for free. Thirty-one patients agreed to participate and their medical records were reviewed for age, neurologic disease, intellectual deficit, impaired dexterity and method of catheterization (Mitrofanoff/urethra).

**Results:** The mean age for the 31 patients was 14 years old. Of these patients, 19 were females (61%), 26 were self-sufficient (84%), 4 had a significant intellectual deficit (16%), 9 had impaired dexterity (29%), 8 had spinal cord injury (26%) and 6 had Mitrofanoff (19%). Twenty-three of the 31 patients completed and returned the satisfaction questionnaire. Seven answered by phone and 1 didn't answer. Fifteen (50%) of the 30 patients reported difficulty at insertion secondary to excess of lubricant. Eleven children (37%) would be ready to proceed with SpeediCath. Of these 11 children, 9 were females (82%), 10 performed catheterization by urethra (91%), 1 had impaired dexterity (9%), 8 used SpeediCath compact (73%) and all were self-sufficient. One hundred percent of females on SpeediCath compact who answered the questionnaire would be ready to continue with this catheter. Male patients catheterizing per-urethra and patients using a continent stoma requiring long catheters had problems with the excess of lubricant and preferred to continue to use their usual catheter with some added lubricant.

**Conclusion:** The majority of the children prefer their uncoated catheter and would not change for SpeediCath hydrophilic-coated catheter. A female patient catheterizing per-urethra with a SpeediCath compact catheter seems to benefit the most from hydrophilic-coated catheter.

### UP-03

#### A wide array of procedures necessary for pediatric urinary reconstruction

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**Introduction and Objective:** We propose the hypothesis that a wide variety of surgical procedures is necessary for the surgical rehabilitation of children who present in childhood bladder dysfunction that has failed medical therapy.

**Materials and Methods:** We have conducted a retrospective review of a comprehensive contemporary series of patients who presented for treatment in a recently established tertiary pediatric centre. Over a 2-year period, 38 patients who had failed maximal medical therapy underwent surgical treatment for intractable urinary incontinence, progressive hydronephrosis, or persistent UTI. All had failed to respond to maximal medical therapy. Underlying diseases included spina bifida (n = 15), bladder exstrophy

( $n = 4$ ), VATER anomaly ( $n = 5$ ), prune belly syndrome ( $n = 3$ ), PUV ( $n = 2$ ) and rhabdomyosarcoma posttreatment ( $n = 1$ ). Postoperative outcomes were evaluated and compared to preoperative status with respect to clinical, radiological and, in some instances, urodynamic features.

**Results:** An operative plan was based on preoperative assessment, classified in terms of defects in bladder storage, bladder outlet competence, and ability to undertake catheterization. In the first instance, bladder storage was achieved by bladder augmentation in 34 patients, by total neobladder in 2 patients, and 1 patient received an autologous regenerated neobladder augment. Bowel segments included detubularized ileum ( $n = 29$ ), composite neobladder ( $n = 2$ ), detubularized large bowel ( $n = 2$ ), native bladder ( $n = 4$ ) and the single regenerated neobladder. Catheterizing conduits included appendicovesicostomy, Monti, and Double Monti channels, with a small number of females utilizing native urethra. Bladder outlet procedures included bladder neck closure ( $n = 8$ ), sling ( $n = 5$ ). Adjunctive procedures included ureteral reimplantation and Malone Cecostomy in select cases. Continence was achieved in 34 patients. Repeat operations have included 1 stone removal and 4 stomal revisions.

**Conclusion:** Although fundamental principles regarding bladder storage and emptying can lead to a therapeutic design that is similar in most instances, there is a large variety of procedures which are sometimes necessary to achieve these aims. Pre-existing conditions, either of congenital nature, or as a result of previous treatments, often pose limitations on the intended course of therapy. A flexible armamentarium may be necessary to achieve the desired outcomes. We also observed that temporary urinary diversion may result in considerable deterioration of renal function.

#### UP-04

##### Men with mild erectile dysfunction should be taken seriously

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**Introduction and Objective:** Very few studies have prospectively looked at a population of men with mild erectile dysfunction (ED). We wanted to determine if these men presented with the same demographics as the typical clinical trial ED population and if their sexual satisfaction could be improved with sildenafil.

**Materials and Methods:** Men with mild ED (IIEF-EF 22-25) were enrolled in an 8-week, Canadian prospective, double-blind, randomized, placebo-controlled study. Satisfaction with treatment was evaluated using the EDITS questionnaire and treatment efficacy was assessed using the IIEF, GAQ as well as event log worksheets (erection hardness scale, second erection within 24 h of dosing). The full analysis set had 164 men, with a mean age of 50 years. Approximately 40% of men had never smoked and 3.5 years had elapsed between ED onset and their entry in the study. One-third of the men had psychogenic ED. Approximately 30% had metabolic problems and 26% had hypertension.

**Results:** Subjects randomized to sildenafil were more satisfied with their treatment compared to those randomized to placebo (mean EDITS score 80 v. 62, respectively,  $p < 0.0001$ ). All IIEF domains, except orgasmic function, were statistically significantly improved with sildenafil treatment when compared to placebo. Twice as many subjects reported that sildenafil, as opposed to placebo, improved their erections, had grade 4 erections and were able to obtain a second erection within 24 hrs of taking their dose of medication (82% v. 44%,  $p < 0.0001$ ; 47% v. 25%,  $p < 0.0001$ ; 38% v. 19%,  $p = 0.0002$ , respectively). Sildenafil was efficacious and well tolerated in these men. Surprisingly, this population had the same risk factors as the typical ED clinical trial population.

**Conclusion:** Men with mild ED should thus be identified rapidly after ED onset in order to benefit from adequate early intervention.

#### UP-05

##### Prospective analysis of intracavernosal injection use in postprostatectomy patients

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**Introduction and Objective:** Intracavernosal injection (ICI) of vasoactive agents is a common strategy to treat postprostatectomy erectile dysfunction (ED). The objectives of this study are to prospectively evaluate ICI use patterns, reasons for discontinued use, incidence of prolonged erections/priapism and efficacy of treatment in a contemporary group of men with postprostatectomy ED.

**Materials and Methods:** Postprostatectomy patients prescribed ICI by a single urologist from January 2006 to January 2008 were included. Demographics, prostate cancer and treatment parameters and comorbidities were retrospective reviewed. Data on current ICI use patterns, incidence of prolonged erections/priapism and efficacy were collected via questionnaire (telephone or mailed).

**Results:** Questionnaire was completed by 117 patients (70% telephone, 30% mailed). Mean patient age was 65 (standard deviation [SD] 6.2) years. Eighty percent of patients had open surgery with the remaining 20% having a robotic-assisted approach. Nerve-sparing (unilateral or bilateral) was accomplished in 58%. Eighty-three percent of patients had organ-confined prostate cancer with 91% having less than Gleason 8 disease. Comorbidities included hypertension (38%), dyslipidemia (26%), coronary artery disease (8%) and diabetes (6%). Patients were 4.1 (SD 2.7) years postprostatectomy. When questioned, 51% of patients actively used ICI with a median of 3 uses per month. Intracavernosal injection was discontinued for the following reasons: ineffective (48%), pain (21%), prolonged erections (11%), low libido (7%), poor personal/partner health (7%), inconvenience (4%) and development of fibrotic plaques (2%). Twenty-eight percent of patients had erections lasting longer than they had wished at some point in their treatment with 10% having at least 1 priapism episode. Sixty-eight percent of all patients were sexually active (98% of ICI users v. 36% of ICI nonusers,  $p < 0.001$ ). In sexually active patients, ICI was associated with significantly higher IIEF scores (20.8, SD 4.1, v. 16.0, SD 6.9;  $p = 0.008$ ).

**Conclusion:** Intracavernosal injection use in postprostatectomy patients can be highly effective; however this study demonstrates a significant attrition rate (49%). This study emphasizes the need for the health care provider to support the patient early following adoption of ICI with information concerning optimal dosing and expected complications. The identification of reasons for discontinued use may aid health care providers to direct their counselling more effectively.

#### UP-06

##### A ketorolac-eluting ureteral stent to improve patient comfort: testing its safety profile in a porcine model

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**Introduction and Objective:** Ureteral stents often cause significant patient morbidity including dysuria, flank pain and hematuria. Treatment of symptoms typically involves oral analgesics, anticholinergics or early stent removal. New drug-eluting stent technology allows the steady local delivery of a drug. Our previous work demonstrated that ketorolac instilled intravesically at the time of ureteral stent insertion significantly decreased flank pain compared to controls. Ketorolac has now been incorporated directly into a ureteral stent (Boston Scientific Corp.). We sought to determine the safety of ketorolac-eluting ureteral stents in a porcine model.

**Materials and Methods:** A total of 92 farm pigs were randomized to 1 of 5 groups. The oral control group ( $n = 12$ ) were stented with ureteral stents (6 Fr, 20 cm Percuflex Plus, Boston Scientific) and 5 days of oral ketorolac 40 mg QID. Animals were terminated at days 2, 5 and 15. Twenty animals in each of the remaining groups received a Percuflex Plus stent (control), or 15%, 13% or 7% ketorolac-loaded stents. Ketorolac levels were measured in plasma, urine and tissue sampled from ureters, bladder, kidneys and liver.

**Results:** Ketorolac was released in a dose-dependent fashion. Ureteral tissue levels of ketorolac (determined by HPLC) were significantly higher in the 13% (183 ng/g) and 15% (1385 ng/g) groups compared to the oral

control (87 ng/g). Measurable levels of ketorolac in plasma and liver occurred in the oral control group while the stent groups had insignificant or nondetectable levels. No adverse events occurred in any of the ketorolac stent groups. Tissue inflammation was similar across all groups. No abnormalities were identified in any internal organs in any group.

**Conclusion:** The use of ketorolac-eluting ureteral stents is safe in a porcine model. Ureteral tissues displayed the highest levels of ketorolac demonstrating that the drug is at the highest concentration where it can be the most potentially effective against stent pain. A clinical trial is being undertaken to test the effectiveness of ketorolac-eluting stents on patient symptoms.

## UP-07

### Mechanisms of oxalobacter formigenes — triggered reverse oxalate transport in the gastrointestinal tract

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**Introduction and Objective:** Calcium oxalate stones are the most common type of stones. Dietary oxalate is eventually filtered by the kidney where it can combine with calcium to form insoluble calcium oxalate crystals/stones. Dietary oxalate can combine with calcium in the GI tract to form an insoluble salt or be degraded by oxalate-degrading organisms such as *Oxalobacter formigenes*. Oxalate can also be secreted from the body into the GI tract for excretion via the feces. We hypothesized that *O. formigenes* triggers cellular responses in the GI tract that leads to secretion of oxalate from the body and subsequent excretion in feces. Furthermore, we tested the hypothesis that it is a secreted product from *O. formigenes* that elicits these responses.

**Materials and Methods:** We utilized Caco-2 cells, an intestinal epithelial cell culture line, to measure oxalate secretion in response to exposure to whole cells of *O. formigenes*, its cell lysates or supernatants. *O. formigenes* was added to the mucosal side of Caco-2 cell monolayers and oxalate transport/flux was measured at 20, 40, 60, 90 and 120 minutes using 6  $\mu\text{M}$   $^{14}\text{C}$  labeled oxalate.

**Results:** Bacterial lysates significantly increased oxalate flux from the serosal to mucosal compartment of Caco-2 cell monolayers (i.e. secretion from the body). An increase was observed as early as 20 minutes (28.7, standard deviation [SD] 0.3, pmol/cm<sup>2</sup>/h lysates v. 18.5, SD 0.3, pmol/cm<sup>2</sup>/h control) following exposure and the flux peaked at 60 minutes (39.6, SD 4.3, pmol/cm<sup>2</sup>/h lysates v. 16.6, SD 0.6, pmol/cm<sup>2</sup>/h control). Bacterial supernatants elicited similar effects, although not as pronounced (20.4, SD 0.3, pmol/cm<sup>2</sup>/h lysates v. 18.9, SD 0.3, pmol/cm<sup>2</sup>/h control at 20 min and 30.3, SD 3.5, pmol/cm<sup>2</sup>/h lysates v. 13.3, SD 0.9, pmol/cm<sup>2</sup>/h control at 60 min). Whole bacteria did not affect oxalate secretion.

**Conclusion:** These data support our theory that *O. formigenes* produces a compound that stimulates oxalate secretion. The fact that bacterial lysates affect oxalate flux to a greater extent suggests that the compound is synthesized in excess, stored in the cell and released in a controlled manner. Further research to fully characterize this compound is currently underway as it may potentially be used therapeutically to decrease urinary oxalate by triggering oxalate excretion via feces to treat patients with hyperoxaluria and hyperoxalemia.

## UP-08

### The continued design and integration of a novel online problem-based learning resource to enhance undergraduate medical education

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**Introduction and Objective:** To bridge the gap between preclinical knowledge and the diagnostic approach to common genitourinary conditions, the University of British Columbia (UBC) Department of Urologic Sciences created an online library of problem-based learning (PBL) modules. The cases were published on Diagnosis X server as a collaborative project between UBC, the Molson Medical Informatics Institute and McGill

University. Diagnosis X was launched to provide learners from all UBC distributed medical sites with a variety of easily accessible cases.

**Materials and Methods:** A total of 65 cases were written by medical students, reviewed by urology residents and edited by faculty members. Using the comprehensive template of Diagnosis X, the students authored cases that simulate a real-life patient encounter. Cases were developed in a pedagogical manner to provide a systematic review of clinical presentations, patient assessment, radiographic imaging and treatment plans. Cases also had supplemental questions and comprehensive explanations to facilitate critical thinking. Therefore students could access these materials to enhance their learning experience.

**Results:** In April 2008, FERGU block (Fluids, Electrolytes, Renal, Genitourinary block) of first-year medical curriculum (FMED 404) was augmented with 4 PBL online cases as supplemental material. Approximately 35% of the class accessed the cases and 40% reported that the online cases enhanced their understanding of the clinical approaches to common urological problems.

**Conclusion:** Therefore our objective is to further integrate Diagnosis X as a supplemental resource in FERGU while we continue to improve and enhance the diversity of the online cases for medical students at all levels. Even though the Department of Urologic Sciences was one of the pioneers in expanding Diagnosis X, other departments including pediatrics, family practice and psychiatry have already started similar projects. Therefore, integrating and enhancing such study tools can provide an extensive learning resource to medical professionals from all levels.

## UP-09

### The relevance of donor renal arterial resistance index in predicting short-term outcomes after living donor kidney transplantation

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**Introduction and Objective:** Renal arterial resistive index (RI) is a parameter obtained by Doppler ultrasonography, and measures the peak renal systolic blood velocity relative to the minimal diastolic velocity. Most physicians consider an elevated RI above 0.7 to be a nonspecific marker of transplant dysfunction. However, the effects of baseline donor RI values and the transplant operation on postoperative RI values are not well established, which is important since baseline RIs in the donor may reflect either unrecognized pathology or may bias the follow-up Doppler studies in the recipient. We sought to investigate the relevance of these factors to postoperative RI values and to see whether baseline RIs are predictive of graft function within the first month after surgery.

**Materials and Methods:** This study retrospectively compared the preoperative RIs of donor kidneys to the immediate and follow-up postoperative RIs in the recipients of 33 donor-recipient pairs. The Student *t* test and correlation coefficient was utilized to compare preoperative and postoperative RIs for significance. A *p* value of less than 0.05 was used to indicate statistical significance.

**Results:** The mean preoperative and 1 day postoperative RI value was 0.6 (standard deviation [SD] 0.07) and 0.6 (SD 0.09), respectively, and no statistical difference was found (*p* = 0.19). As well, correlation coefficient of preoperative and 1 day postoperative RIs did not reach statistical significance for the sample size (*p* = 0.22). Furthermore, the 1-tailed *t* test revealed that baseline donor RIs were not significantly higher between corresponding recipients who received graft-related complications versus recipients without any complications during the first month after surgery (*p* = 0.27), suggesting that preoperative donor RIs are not predictive of short-term posttransplant outcomes.

**Conclusion:** Renal arterial resistive index is a measurement that is affected by a complex interaction of systemic and graft-related factors. Many researchers have documented the lack of sensitivity and specificity of an elevated posttransplant RI in diagnosing graft-related complications. Our study suggests that this lack of sensitivity and specificity is not due to variability in baseline donor RIs nor is it due to the effects of the transplant operation on the kidney graft. Further research is needed to establish the relevance of pretransplantation RIs to posttransplant outcomes.

**UP-10****Laparoscopy, dorsal lumbotomy and flank incision in live donor nephrectomy: comparison of donor outcomes**

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**Introduction and Objective:** Compared with standard open flank incision, donors undergoing laparoscopic nephrectomy have been shown to require less analgesia postoperatively and have shorter hospital stays. Furthermore, graft function and the incidence of recipient complications are similar for both techniques. However, as dorsal lumbotomy is also common, no study has compared donor nephrectomy via this approach versus laparoscopic techniques. In this study, donor outcomes are compared amongst laparoscopic (LDN), flank incision (FL) and dorsal lumbotomy (DL) donor nephrectomy.

**Methods:** A retrospective chart review was conducted of all donors undergoing open (DL or FL) and LDN between 2002 and 2007. Preoperative donor characteristics, operative time, blood loss, postoperative analgesia use, length of hospital stay, and intraoperative and postoperative complications were evaluated. Additionally, corresponding recipients were evaluated for postoperative allograft function and early complications.

**Results:** Donors required an average of 96.3 (standard deviation [SD] 14) mg, 63.4 (SD 10) mg and 120.4 (SD 25) mg of morphine for LDN, DL and FL, respectively ( $p < 0.001$  DL v. LDN or FL and  $p = 0.09$  LDN v. FL). Mean intraoperative blood loss was 75.5 (SD 8.9) mL, 280.9 (SD 42.4) mL, and 177.8 (SD 20.7) mL for LDN, DL and FL procedures, respectively ( $p < 0.001$  LDN v. DL or FL). Length of hospital stay was 3.9 (SD 0.2), 4.1 (SD 0.3) and 4.6 (SD 0.2) days for LDN, DL and FL patients, respectively ( $p = 0.08$  LDN v. DL and  $p < 0.01$  LDN v. FL). An increased incidence of major and minor intraoperative and postoperative complications was found in both FL and DL groups when compared to LDN ( $p < 0.01$ ). No significant difference in mean serum creatinine of recipients at 2 weeks, 6, 12 and 24 months postoperatively was found among the 3 groups ( $p > 0.45$ ).

**Conclusion:** In this study, donors undergoing LDN had significantly less blood loss, experienced a lower rate of intraoperative and postoperative complications and were discharged sooner than those undergoing either open approach (FL or DL). Patients undergoing LDN also used less analgesia than patients undergoing a flank incision, but more than those undergoing DL, who were not offered patient controlled analgesia. Thus, this study supports that LDN has a superior safety profile compared with either open approach, offers significant benefits to the donor in the postoperative period, and provides equivalent long-term graft function.

**UP-11****Vaginal entrapment of bathwater may mimic urinary incontinence**

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**Introduction and Objectives:** To present 2 cases of females, 1 prepubertal and 1 premenopausal, with dribbling incontinence occurring only after bathing. To present the paucity of literature on the subject of vaginal entrapment of fluid as an etiology of incontinence.

**Materials and Methods:** With REB approval, the child's mother was phone-interviewed and the adult performed and permitted further prospective assessment of her symptoms. Computer-based literature search was performed.

**Results:** Case 1: 8-year-old female referred to urologist with 9-month history of bothersome wetness of her underwear noted only at bedtime or upon waking. History revealed she bathed almost nightly. She was instructed to shower or bath exclusively, each for 1 week. The wetting occurred only after bathing. She now showers exclusively. Case 2: 39-year-old female, G2P2 with normal genitalia who noted periodic significant dribbling into her underwear only after baths. She concluded this to be secondary to bathwater accumulating within her vagina, which she routinely evacuates by digital penetration of the vaginal opening. Further investigation revealed the following: 1) vaginal entrapment occurs unpredictably and follows less than 50% of her baths; 2) without evacuation,

fluid can soak through to her outerwear; 3) dribbling can occur 25 minutes or more postbath; 4) volumes are 28 mL or less; 5) fluid is consistent with bathwater based on pH and colour (including dyed bathwater) and inconsistent with postbath voided urine. Literature review: only 1 article discusses the issue of bathwater entering the vagina and concludes that it does not occur. The literature acknowledges that urine may reflux into the vagina during voiding in both children and adults; however, in review articles and texts this is mentioned only in the differential diagnosis of childhood female incontinence. Failure to diagnose this in an adult has resulted in inappropriate surgery for stress incontinence.

**Conclusion:** Postbath dribbling, secondary to entrapment of bathwater in the vagina, should be considered within the differential diagnosis of incontinence in females of any age. It is simple to rule out on history. Upon diagnosis, the dribbling can be managed by avoiding baths, or digital evacuation. History should also seek to rule out vaginal reflux of voided urine.

**UP-12****Quality of life assessment and patient satisfaction in men after insertion of artificial urinary sphincter for urinary incontinence**

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**Introduction and Objective:** We assessed satisfaction and quality of life (QOL) in men who had undergone artificial urinary sphincter (AUS) placement.

**Materials and Methods:** We identified 39 men who had AUS placement between December 2003 and June 2008. A retrospective chart review was conducted and patients completed questionnaires including the ICIQ-SF, PGI-I, Incontinence Impact Questionnaire – Short Form (IIQ-SF) and Urogenital Distress Index (UDI-SF). Patients were also assessed for global satisfaction.

**Results:** At the time of chart review, 28 of 39 questionnaires (71.8%) were available for assessment of QOL, satisfaction and surgical outcome. Follow-up ranged from 7 to 60 months with a mean of 26.9 and median of 23.5 months. Of these, 18 (64.3%) underwent AUS placement after radical prostatectomy alone, 6 (21.4%) for radical prostatectomy plus radiation, 1 (3.6%) for radiation, 2 (7.1%) for salvage cryotherapy plus radiation and 1 (3.6%) following a pelvic fracture. Surgical revisions were required in 5 patients (12.8%) due to infection (1), erosion (1), combined infection and erosion (1), device failure (1) and placement of a second cuff (1). All evaluable patients presently have functioning devices. Quality of life was assessed using the IIQ-SF and UDI-SF, with mean scores of 11.9 and 22.2 respectively, indicating low impact on quality of life (scores out of 100 with lower scores indicating lesser impact on QOL). The mean score for the ICIQ-SF was 8.4, well below the maximum (worst) possible score of 20. Of the men who used pads for protection, the number using more than 1 pad per day dropped from 21 preoperatively to 6 postoperatively. The majority of patients described their urinary condition as "very much better" (19/28) or "much better" (7/28); 2 responded it was "a little better." Most patients (26/28) responded that they would be willing to undergo the procedure again; 1 was undecided and 1 was unwilling. Similarly, 25 patients responded they would recommend the procedure to a friend, 2 replied they would do so but with reservation and 1 would not recommend the procedure.

**Conclusion:** Treatment of urinary incontinence with AUS has a positive effect on QOL with high patient satisfaction and reasonably low complication rates.

**UP-13****Validating bladder cancer xenograft bioluminescence with magnetic resonance imaging**

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**Introduction and Objective:** Bioluminescent imaging allows longitudinal assessment of tumour burden in orthotopic tumour models. We have encountered poor correlation between tumour size and luminescence in several cell lines growing as bladder cancer xenografts. We hypothesized that the lack of correlation was due to hypoxia and necrosis in the tumours.

**Materials and Methods:** Orthotopic bladder tumours were established in 5-week-old nude mice with KU7 or 253J-BV cells (10 mice each) that had been previously transduced with a lentiviral luciferase construct. Bioluminescence and MRI imaging were performed weekly. Tumour volume was calculated from T1 and T2 weighted images at each time point. The mice were sacrificed at 4 weeks 45 minutes after intraperitoneal injection of 60 mg/kg piminidazole. The tumours were excised, weighed and frozen whole. Step sections were obtained at 1-mm intervals. Hematoxylin and eosin staining and immunohistochemical analysis of piminidazole adduct formation were performed to assess necrosis and hypoxia. CD31 staining was used to quantitate vascularity. Relative areas of each section containing total tumour, hypoxic tumour and necrotic tumour were quantitated with ImagePro software (Media Cybernetics).

**Results:** KU7 xenograft bioluminescence showed minimal correlation to tumour volume on MRI during the first 2 weeks of imaging but none thereafter ( $R^2 < 0.1$ ) and also none to tumour weight. KU7 xenografts showed extensive hypoxic and necrotic areas lacking blood vessels, so that bioluminescence was found to correlate to the volume of perfused, nonhypoxic, nonnecrotic tumour. The correlation between MRI volume and luminescence was stronger ( $R^2 = 0.93$  at 4 wk) in 253J-BV xenografts, where hypoxia and necrosis were less prominent. MRI tumour volume tripled in size between the first and second week in KU7 but remained constant in 253J-BV.

**Conclusion:** The correlation between tumour bioluminescence and tumour size depends on the growth kinetics of the individual cell line used in xenograft studies. These parameters do not correlate in xenografts that rapidly outgrow their vascular supply and develop broad areas of hypoxia and necrosis. In these cases, however, the bioluminescence does yield information about the amount of viable tumour, and should therefore still be considered a useful parameter.

## UP-14

### Inhibition of ErbB4/HER4 cleavage potentiates gefitinib sensitivity in urothelial carcinoma

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**Introduction and Objective:** Inhibition of epidermal growth factor (EGFR) has proven to be an efficacious therapy for various cancers including lung cancer, but only a subset of patients respond. As EGFR inhibitors are brought into clinical trial also for bladder cancer, we are studying mechanisms of resistance to these novel agents. Here we show that human EGF receptor 4 (HER4/ErbB4) modulates response to EGFR inhibition in urothelial carcinoma.

**Materials and Methods:** A panel of urothelial carcinoma cells was analyzed by 3H-thymidine uptake assay to determine their antiproliferative response to the EGFR-inhibitor gefitinib. ErbB4 activation, which requires sequential cleavage by 2 specific proteases (gamma-secretase (GS) and (TNF- $\alpha$  converting enzyme (TACE)), was enhanced by treatment of the cells with neuregulin (NRG) and inhibited by treatment with a GS-inhibitor. The subsequent change in antiproliferative response to gefitinib was measured. mRNA expression profiles for TACE and the GS-complex proteins were analyzed by RT-PCR. The effect of ErbB4 silencing with siRNA on antiproliferative response was also measured. Cleavage of the intact 185 kDa ErbB4 into 80 kDa ErbB4 was analyzed by FACS and western blot.

**Results:** All cells tested demonstrated TACE and GS expression, suggesting the presence of the ErbB4 cleavage machinery in urothelial carcinoma. The gefitinib-sensitive cell lines expressed E-cadherin, the hallmark of the epithelial phenotype, along with 185 kDa ErbB4, but not 80 kDa ErbB4. Depletion of 185 kDa ErbB4 by siRNA and NRG treatment significantly attenuated gefitinib sensitivity. Conversely, treatment of otherwise resistant cells lines with a GS-inhibitor led to accumulation of 185 kDa ErbB4 and significant enhancement of gefitinib-induced growth suppression. Moreover, anchorage-independent culture of these resistant cells induced E-cadherin and intact ErbB4 expression, subsequently rendering the cells highly sensitive to gefitinib.

**Conclusion:** Our data demonstrate that dynamic changes of ErbB4 determine the antiproliferative efficacy of EGFR inhibition. Modulation of ErbB4 signaling with a GS-inhibitor or by other means may improve response to EGFR-inhibition.

## UP-15

### Receptor heterodimerization: a new mechanism for platelet-derived growth factor-induced resistance to anti-epidermal growth factor receptor therapy in bladder cancer

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**Introduction and Objective:** We recently discovered that human bladder cancer cells resistant to anti-epidermal growth factor receptor (EGFR) therapy often coexpress platelet-derived growth factor receptor (PDGFR)- $\beta$ . The objective of this study was to determine whether there is a functional crosstalk between EGFR and PDGFR- $\beta$  and how this regulates biological functions in bladder cancer.

**Materials and Methods:** We characterized EGFR and PDGFR- $\beta$  expression in a panel of human bladder cancer cells by western blot. Heterodimerization and colocalization of both were demonstrated by immunoprecipitation and confocal microscopy, respectively. The antiproliferative effects of specific inhibitory monoclonal antibodies to each receptor (provided by ImClone Systems, Inc) were tested by 3H-thymidine uptake assay. We transfected a non-PDGFR- $\beta$  expressing bladder cancer cell line (UMUC5) with the PDGFR- $\beta$  gene. These cells were analyzed in vitro by 3H-thymidine uptake and a Matrigel invasion assay, and in vivo for tumorigenicity, metastatic potential and orthotopic growth. In a treatment study, nude mice were inoculated with orthotopic tumours and treated with the inhibitory antibodies alone and in combination over 4 weeks.

**Results:** Immunoprecipitation demonstrated the existence of EGFR/PDGFR- $\beta$  heterodimers in all PDGFR- $\beta$ -expressing cell lines. Forced expression of PDGFR- $\beta$  in EGFR-sensitive UMUC5 cells (IC50 < 10 nM) significantly reduced responsiveness to the EGFR inhibitor (IC50 > 100 nM) and increased three-fold their invasive potential in vitro, as well as their in vivo tumorigenicity. Confocal microscopy analysis of PDGFR- $\beta$ -expressing UMUC5 cells costained for EGFR and PDGFR- $\beta$  proteins demonstrated their cytoplasmic internalization and colocalization. Increased invasiveness was associated with EGF-triggered PDGFR- $\beta$  transactivation, increased MAPKinase and GSK-3 $\beta$  phosphorylation, and decreased E-cadherin expression. In vitro dual inhibition of the EGFR and PDGFR- $\beta$  receptors blocked cell invasion, reduced cell proliferation, and rescued the E-cadherin expression to levels comparable to those found in parental UMUC5 cells. A significant reduction of tumour growth was associated with increased E-cadherin expression in UMUC5/PDGFR xenografts after administration of the EGFR and PDGFR- $\beta$  specific inhibitory antibodies.

**Conclusion:** In EGFR-expressing bladder cancers, coexpression of PDGFR- $\beta$  appears to have implications for tumour biology and therefore should be further evaluated for a therapeutic strategy involving dual receptor targeting.

## UP-16

### Effects of lactobacillus by-products on the growth and virulence of uropathogenic escherichia coli

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**Introduction and Objective:** Pathogens residing within the vagina have the potential to colonize stents and catheters and cause infection. Thus, it is especially important for woman being treated with urinary devices to maintain a healthy urogenital tract. Lactobacilli are the most common microorganisms isolated from the vaginas of healthy women, and studies have shown their ability to inhibit uropathogen growth and attachment, including uropathogenic *E. coli* (UPEC). However, little is known regarding their precise role in UPEC growth and virulence inhibition. The objective of the study was to determine the effects of *Lactobacillus*

by-products on the growth, survival and virulence factor expression in a clinical isolate of UPEC.

**Materials and Methods:** Gradients of lactic acid, hydrogen peroxide and culture supernatants from *Lactobacillus rhamnosus* GR-1 and *L. reuteri* RC-14 were applied to clinical isolate UPEC C1212 to assess effects on growth. Luciferase reporter constructs were generated containing the promoters for several critical adhesive and stress-related UPEC virulence factors and transformed into C1212. The *Lactobacillus* by-products were applied to these reporter transformants and luminescence observed over 24 hours to investigate the effects on virulence factor expression.

**Results:** In a dose- and pH- dependent manner, lactic acid, hydrogen peroxide and the culture supernatants all strongly inhibited C1212 growth and increased the promoter activity of outer membrane proteins A and X, 2 porins normally up-regulated in response to UPEC stress. Lactic acid and the culture supernatants also down-regulated the promoter activity of type 1 and P fimbriae, pili important for UPEC adherence within the urogenital tract.

**Conclusion:** *Lactobacillus* culture supernatants and derived factors protect the urogenital tract from UPEC infection by inhibiting growth, inducing stress and down-regulating proteins critical for attachment. This data supports the use of lactobacilli in maintaining a healthy urogenital tract and in the prevention of urinary tract infections, including those associated with urinary devices.

## UP-17

### Targeting insulin-like growth factor-1 receptor with antisense oligonucleotides in prostate cancer

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**Introduction and Objective:** Initiating as an androgen-dependent adenocarcinoma, prostate cancer (PCa) gradually progresses to a castrate-resistant disease (CRPC) following androgen deprivation therapy (ADT) with a propensity to metastasize. Altered expression of insulin-like growth factor (IGF) axis components have been consistently found in PCa. The action of IGFs is mediated through IGF-I receptor (IGF-IR) and modulated by IGF binding proteins (IGFBPs). We hypothesize that increased expression and/or responsiveness of IGF-IR may promote CRPC progression in patients undergoing ADT. In this study, we assessed ATL1101, a 2'-MOE-modified antisense oligonucleotide (ASO) targeting human IGF-IR, with regard to potency and anticancer activity of IGF-1R ASO treatment on androgen-responsive (LNCaP) and independent (PC3) PCa cells in vitro and in vivo.

**Materials and Methods:** IGF-IR mRNA and protein expression in ATL1101- and control oligonucleotides (ODN)-treated LNCaP and PC3 cells were observed by QT-PCR and western blotting. The effect of IGF-1R ASO on LNCaP and PC3 cell growth and apoptosis in vitro was examined by MTT assay and flow cytometry. Effects of the IGF-1R ASO on various putative targets were evaluated using western blotting. For in vivo xenograft studies, LNCaP or PC-3 cells were inoculated s.c. in the flank region of athymic nude mice. Mice were castrated and randomly treated with ATL1101 or control ODN injected i.p. Tumour volume and serum prostate-specific antigen (PSA) were evaluated.

**Results:** We observed dose- and sequence-specific suppression of IGF-IR mRNA and protein expression in ATL1101-treated LNCaP and PC3 CaP cells in vitro. Suppressed IGF-IR expression correlated with decreased proliferation and increased apoptosis of PC3 cells under standard culture conditions and increased apoptosis of LNCaP cells under androgen-deprived culture conditions. Compared to control ODN, ATL1101 significantly suppressed PC3 tumour growth as a monotherapy in murine xenografts. Similarly ATL1101 significantly delayed CR progression of LNCaP xenografts as measured by tumour growth and serum PSA levels.

**Conclusion:** This study reports the first preclinical proof-of-principle data that this novel IGF-IR ASO selectively suppresses IGF-1R expression, suppresses growth of CRPC tumours and delays CRPC progression in vitro and in vivo.

## UP-18

### Interrogating the mTOR signalling pathway for bladder cancer therapy

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**Introduction and Objective:** Radiation therapy for invasive bladder cancer allows for organ preservation but systemic toxicity and local control remains problematic. As such, there is a need to increase radiosensitization of tumour cells to improve efficacy. The aim of this study was to investigate if mTOR (mammalian target of rapamycin), a downstream kinase of the phosphatidylinositol 3-kinase/Akt survival pathway, may be a target for bladder cancer therapy.

**Materials and Methods:** A panel of 9 representative human urothelial carcinoma cell lines reflecting different stages of bladder cancer (from superficial to invasive and metastatic) was screened for their sensitivity to the mTOR inhibitor, RAD001. Growth inhibition was monitored by MTT assays. Effects on cell cycle and apoptosis were ascertained by FACS analysis. Clonogenic assays were used to analyse the response of RAD001-resistant and RAD001-sensitive cell lines alone and in combination with radiations. The expression of Akt and mTOR as well as the mTOR substrate, S6, was assessed by Western blots, including phosphorylated state. In the in vivo study, transgenic nude mice were injected with KU7 and 253J-BV bladder cancer cells. Mice were either treated with RAD001 (1.5 mg/kg, daily), fractionated ionizing radiation (9 Gy), or combined RAD001 and radiation (14 tumours/treatment arm). After 4 weeks of therapy, the mice were sacrificed and the tumours were harvested.

**Results:** RAD001 was a very potent growth inhibitor for the 9 screened bladder cancer cell lines, causing a G0/G1 phase arrest but not significantly affecting cell death. From the established dose-response curves, IC50 values ranging from 0.1 nM to 100 nM were found. Western blots revealed baseline aberrant activation of various members of the Akt/mTOR signalling pathway in all 9 cell lines. RAD001 effectively inhibited the mTOR downstream signal (pS6) in tested cell lines. A significant decrease in colony formation was observed in all the bladder cancer cell lines in the combined treatment when compared to RAD001 or radiation alone. In vivo, a significant decrease in tumour weight was observed in the combined treatment arm when compared to either treatments alone ( $p < 0.05$ ), consistent with our in vitro studies.

**Conclusion:** This is the first study to demonstrate that mTOR inhibition appears promising as therapeutic modality for bladder cancer and effective in sensitizing bladder cancer cells to radiation therapy.

## UP-20

### Expression of the Hsp90 cochaperone FKBP52 correlates with prostate cancer: an immunohistochemical study

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**Introduction and Objective:** FKBP52 is a cochaperone of the Hsp90 chaperone system, which is a central player in androgen receptor (AR) signalling. It has been shown, using a mouse knock out model, that absence of FKBP52 results in an atrophic prostate and seminal vesicles as well as ambiguous genitalia. Interaction with FKBP52 and Hsp90 is also necessary for transcriptional activity of AR. In this study, we sought to establish a correlation between FKBP52 expression and prostate cancer.

**Materials and Methods:** A tissue microarray template using cores obtained from radical prostatectomy specimens ( $n = 64$ ) was stained for FKBP52 and scored by a single pathologist on a 0–3 scale. The same procedure was carried out for tissue obtained on TURP specimen for benign disease ( $n = 42$ ). Patients' age ranged from 49 to 70 years. Preoperative PSA in patients with cancer ranged from 0.6 to 36.3 ng/mL (average 15.2 ng/mL). Gleason scores ranged from 5 to 9 (median 6). The relationship between staining score and prostate cancer was tested using univariate and multivariate analysis.

**Results:** There was a highly statistically significant difference for FKBP52 staining between cancer cores obtained from prostatectomy specimens versus normal cores obtained from the same specimens ( $p < 0.001$ ). There also was a statistically significant difference in FKBP52 expression between normal cores obtained from prostatectomy specimens versus normal cores obtained from TURP specimens. A ROC curve with an AUC of 0.81 yielded an optimal cut-off point of 2.1 for defining cancer. Sensitivity was 77% and specificity was 80%. Staining was shown to be independent of PSA value, Gleason score, or margin status.

**Conclusion:** These data establish a novel correlation between the expression of the Hsp90 cochaperone FKBP52 and prostate cancer. We have also shown that normal tissue in prostate cancer contains more FKBP52 than does normal tissue in non-prostate cancer specimens, suggesting a "cancer field defect," whereby transformed cells extend beyond histologically obvious tumour. This precedent sets the stage for further molecular investigations on the role of FKBP52 in prostate cancer biology including its possible validation as a novel molecular target for drug development.

## UP-21

### Combined inhibitory effect of adiponectin and rapamycin on mTOR in renal cell carcinoma

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**Introduction and Objective:** Constitutive activation of the mammalian target of rapamycin (mTOR) is one of the molecular events in renal cell carcinoma (RCC) initiation and progression. Accordingly, temsirolimus a specific inhibitor of mTOR have been shown to improve overall survival among patients with metastatic RCC and poor prognosis. We have previously shown that adiponectin, a hormone that is exclusively secreted from fat tissue of which levels are reduced in obesity, portrays an inhibitory effect on RCC progression. In this work we examined the effects of adiponectin on mTOR activation.

**Materials and Methods:** As a model we used the human clear cell RCC cell line-CRL1932. The effect of recombinant human adiponectin on AMPK and mTOR activation was examined using specific antibodies (immunoblotting) to p-AMPK $\alpha$ , p-mTOR, p-p70 S6 kinase and ribosomal protein S6. The combined effect of adiponectin and rapamycin on VEGF secretion from the cells was tested using human VEGF specific ELISA assay.

**Results:** Concentrations of 15 ng/mL and 30 ng/mL of recombinant human adiponectin were shown to increase phosphorylation of AMPK $\alpha$  (Thr172), and inhibit phosphorylation of mTOR (Ser2448) and its downstream targets p70 S6 kinase (Thr389) and ribosomal protein S6. Combinatory treatment of adiponectin (30 ng/mL) and rapamycin (50 mM or 200 mM) demonstrated increased inhibition of VEGF secretion from CRL-1932 cells, when compared to treatment with adiponectin or rapamycin alone.

**Conclusion:** Adiponectin inhibits mTOR activation in a dose-dependent manner through activation of mTOR upstream inhibitor-AMPK. When combined with rapamycin, adiponectin significantly augments the pharmacological inhibition that is achieved by rapamycin. These findings raise important questions: Does pharmacological inhibition of mTOR work better in nonobese RCC patients in whom adiponectin levels are higher? Can plasma adiponectin levels serve as a biomarker to predict response to temsirolimus in RCC patients?

## UP-22

### WST11-mediated vascular targeted photodynamic therapy in the dog prostate model

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**Introduction and Objective:** Vascular targeted photodynamic therapy (VTP) with the bacteriochlorophyll derivative WST09 as the photosensitizer was proven efficient for the treatment of localized prostate cancer. However the low solubility of WST09 in aqueous solutions limits the scope of clinical applications. The aim of this study was to assess the safety and efficacy of a new water soluble bacteriochlorophyll, WST11, for VTP in the dog prostate model.

**Materials and Methods:** WST11-VTP was performed on 25 mongrel dogs. One or two 1-cm optic fibers, connected to a 753-nm diode laser, were placed in the prostate lobes by laparotomy. WST11 (1–15mg/kg) was intravenously infused over 10 minutes. The laser was turned on at 5–10 minutes. Power was fixed from 150 to 250 mW/cm. The energy doses varied from 100 to 400 J/cm/fiber. Blood pressure was monitored prior, during, and after VTP. Blood was assayed for total proteins, albumin, bilirubin, creatinine, liver enzymes, BUN/urea, electrolytes, white cells, platelets and WST11. Clinical follow-up was performed daily. Necropsy was on day 8. Prostate, lung, and liver were submitted for histopathology.

**Results:** The procedure was well tolerated with no VTP-associated change in blood pressure and biochemical or hematological parameters. The level of WST11 in blood varied in parallel with the infusion and declined rapidly over time to reach undetectable levels by 60 minutes. Subjects did very well. Lower urinary tract symptoms were mild and resolved within 1–2 days. There was neither macro- nor microscopic changes in the liver and lung. Macroscopic hemorrhages were present in all prostates. A threshold level of WST11 and light energy was required to induce necrosis. It was consistently associated with a loss of the endothelial layer in blood vessels. Necrosis was optimal at 5.0 mg/kg WST11 and 400 J/cm. Under these conditions, 50%–80% of treated lobes underwent necrosis. The average necrotic area represented 2.24 cm<sup>2</sup>/section and was independent of prostate size.

**Conclusion:** WST11 appears a safe and efficient photo-sensitizer to mediate light-induced necrosis in the dog prostate. These preclinical findings support the assessment of WST11 for VTP in patients with localized prostate cancer.

## UP-23

### Regulation of major histocompatibility complex class I chain-related (MIC) molecule expression in bladder cancer: a possible therapeutic target to improve BCG immunotherapy

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**Introduction and Objective:** The major histocompatibility complex class I chain-related (MIC) molecules, MICA and MICB, play important roles in tumour surveillance by NK cells, lymphokine-activated killer (LAK) cells, and cytotoxic T cells. The interaction of cell surface MIC molecules with the NKG2D receptor on NK, LAK and effector T cells leads to the activation of innate and adaptive immune responses. The loss of MIC expression, associated with cellular hypoxia, has been demonstrated to be a negative prognostic factor for several neoplastic diseases, including prostate cancer, but its role in bladder cancer has not been explored.

**Methods:** Flow cytometry was used to determine MIC A/B expression on a panel of bladder cancer cell lines including 253 J, MB49 and 647 V. Expression of MIC A/B on fresh-frozen human bladder cancer samples after TURBT was determined using immunohistochemistry. The hypoxic regulation of MIC on the bladder cancer cell lines was determined by incubating cells for 24 hours in different oxygen culture conditions (0.5%–20% O<sub>2</sub>) with MIC A/B expression determined by flow cytometry.

**Results:** Flow cytometry demonstrated significant expression of MIC A/B on all cell lines tested although there was significant variability observed. Immunohistochemical analysis did demonstrate expression of MIC A/B on the cell surface of non-muscle invasive specimens obtained after resection. Cell surface MIC expression determined by flow cytometry demonstrated a significant decrease after exposure to hypoxia.

**Conclusion:** These preliminary results demonstrate for the first time that MIC, a stress-related protein, is expressed in human bladder cancer lines and tumours. The hypoxia-mediated regulation of MIC expression is similar to that previously demonstrated for prostate and breast cancer. Given MICs important role in both adaptive and innate immune responses, further study into the regulation of MIC expression in bladder cancer may lead to improved outcomes for BCG immunotherapy.

## UP-24

### Capsaicin in combination with micronutrients decreases proliferation of prostate cancer cells in vitro

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**Introduction and Objective:** Prostate cancer (PCa) is the most common internal malignancy and the second most frequent cause of cancer death in men. It is estimated that over 450 Canadian men will be diagnosed with PCa weekly, and 85 will die from it. The relationship between diet and risk for PCa is well known in literature. Capsaicin, a compound found in chili peppers, is a well known pain reliever. Based on our limited clinical data on Capsaicin, our present study aims to investigate the chemopreventive effect of capsaicin in combination with other micronutrients specifically, lycopene, selenium and vitamin E. We hypothesize that capsaicin in combination with micronutrients (lycopene, selenium, vitamin E) decreases the proliferation of prostate cancer cells in vitro.

**Materials and Methods:** Two human PCa cell lines were analyzed: LNCaP (AR+) and PC3 (AR-). Cells were treated with Capsaicin (0–200 µM) alone, or in combination with any of the 3 micronutrients. Cells were incubated for up to 72 hours and proliferation assessed using MTS assay. Alterations in PSA, cell-regulatory molecules, and apoptotic markers were assessed by Western blot analysis. In parallel studies, DNA was extracted for fragmentation.

**Results:** There was a significant ( $p < 0.05$ ) decrease in the proliferation of LNCaP and PC3 cells at 72h, when treated with 200 mM of capsaicin. Combination studies revealed a significant ( $p < 0.05$ ) decrease in proliferation when capsaicin was combined with lycopene, Western blot revealed a significant decrease (2-fold change) in PSA expression in LNCaP cells when treated with capsaicin alone. There was a significant up-regulation of p27<sup>Kip1</sup> indicating cell-cycle arrest. It was interesting that the treatment resulted in the expression of cleaved PARP, demonstrating that the cells are undergoing apoptosis.

**Conclusion:** These studies may eventually help identify patients likely to benefit from the use of capsaicin in combination with specific micronutrients. Ultimately these strategies may have a more meaningful impact on PCa morbidity and mortality than other therapeutic strategies currently in use.

## UP-25

### Notch-1 staining intensity and survival in patients with renal cell carcinoma

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**Introduction and Objective:** The Notch signaling pathway is a key pathway essential for vascular development and recent studies have elucidated the role of its ligand, Dll4, in angiogenesis. Notch signaling is dysregulated in many cancers. The role of Notch-1 in renal cell carcinoma is unclear. The recent success of tyrosine kinase inhibitors in treating renal cell carcinoma has prompted investigation into exploring alternate avenues of angiogenesis that may potentially be therapeutic targets. The purpose of this study was to analyze the expression of Notch-1 in renal cell carcinoma and to assess its prognostic significance.

**Materials and Methods:** The expression of Notch-1 was analyzed by immunohistochemistry in a cohort of 77 patients undergoing nephrectomy for renal cell carcinoma using tissue microarray analysis. Pearson correlation was used to explore the relationship between staining intensity (none, mild, moderate, strong) and staining percentage (0%, < 33%, 34%–66%, > 67%) with established clinical parameters such as nuclear grade, pathological stage, lymph node invasion, extracapsular extension, vascular invasion, distant metastasis, and patients' survival.

**Results:** There were 45 men and 32 women in the study. The mean age at diagnosis was 62 (standard deviation 13). In normal kidney tissue, intense nuclear and cytoplasmic staining for Notch-1 was uniformly observed within the distal and proximal tubules; however, the glomerulus and the rest of the normal tissue did not exhibit any staining. In tumour tissue, there

were varying degrees of membranous, cytoplasmic and nuclear staining. Notch-1 staining was found to be present in 73 of 77 (95%) of renal cell tumours. Increased Notch-1 staining intensity was significantly associated with a decrease in the number of years and months lived (Pearson correlation  $r = -0.272$ ,  $p < 0.05$  and  $-0.281$ ,  $p < 0.05$ , respectively). When we divided Notch-1 staining intensity into a high (3+) and low (0–2+) staining score, there was a trend towards a difference in survival in univariate Kaplan–Meier analysis ( $p = 0.08$ ); however, this was not statistically significant.

**Conclusion:** Notch-1 is expressed on renal cell carcinomas and high Notch-1 staining intensity negatively correlates with survival. This suggests that Notch-1 is involved in renal cell carcinogenesis and may be a promising target for antiangiogenesis therapy, but is not a robust biomarker to predict survival.

## UP-26

### The use of triclosan-eluting ureteral stents in short-term stented patients

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**Introduction and Objective:** The use of ureteral stents is complicated by biofilm-related infection and encrustation, promoting the frequent use of prophylactic antibiotics, even in patients requiring short-term indwell times. In an attempt to reduce these infections and the associated antibiotic use, the broad spectrum antimicrobial Triclosan (TCN) was incorporated into a ureteral stent (Triumph, Boston Scientific). This device provides local antibiosis directly within the urinary tract through the constant elution of TCN. In this study, we sought to determine the clinical effects of the TCN-eluting stent in patients requiring short-term (~1–2 wk) ureteric stenting.

**Materials and Methods:** Patients were randomized to receive either the TCN-eluting stent alone or a control stent (Perccuflex Plus, Boston Scientific) in combination with antibiotic therapy (20 patient endpoint). Urine samples were obtained for culture both at the time of stent placement and removal, and all stents were cultured upon removal. All isolated microorganisms were identified to at least the genus level and profiles of their susceptibility to several clinically-relevant antibiotics were generated where possible.

**Results:** In the TCN-eluting stent group 4/10 and 1/10 had positive urine and stent cultures while controls were 2/10 and 1/10, respectively. Organisms cultivated were *Corynebacterium* sp., *Enterococcus* sp., *Lactobacillus* sp., *Streptococcus viridans* and *Staphylococcus auricularis*. No significant encrustation was found on any of the stents upon removal.

**Conclusion:** TCN-eluting stents did not show a clinical benefit compared to controls in terms of urine and stent cultures. However, since only 1 of 4 TCN-group patients with positive urine cultures also showed a positive stent culture, the Triumph stent appears to inhibit (at least temporarily) the formation of viable biofilms on its surface when exposed to infected urine. Thus, although the use of the triclosan-eluting stent can reduce antibiotic usage, it remains to be determined whether the combination of an antimicrobial stent and oral antibiotics may be of clinical value in patients with difficult and/or recurrent infections.

## UP-27

### The relationship between histologically diagnosed prostatitis and urinary retention in men with underlying benign prostatic hyperplasia or carcinoma of the prostate

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**Introduction and Objective:** The aim of this study was to determine whether prostatitis (diagnosed on histology) is a precipitating or contributing factor in men with urinary retention and underlying benign prostatic hyperplasia (BPH) or carcinoma of the prostate (CaP).

**Materials and Methods:** We reviewed the clinical records of patients with

urinary retention admitted to our hospital from September 1998 to June 2007, a total of 558 male admissions. Statistical analysis was performed with Student *t*, Mann–Whitney and Fisher exact tests, as appropriate.

**Results:** Acute urinary retention (AUR) was present in 506 (91%) and chronic urinary retention (CUR) in 52 men (9%). The most common causes of retention were BPH (37%), CaP (36%) and urethral stricture (14%). Prostatitis was present histologically in 62% of men with histological BPH and in 25% with CaP on histology. Comparing men with histological BPH only (*n* = 69) to those with BPH plus histological prostatitis (*n* = 114), the mean age was 71.4 versus 67.7 years, mean serum prostate-specific antigen (PSA) was 13.3 versus 24.3 ng/mL, and PSA above 4 ng/mL was present in 61% versus 87% (all differences *p* < 0.01). Comparing men with histological CaP only (*n* = 150) to those with CaP plus prostatitis (*n* = 51), showed the following differences: digital rectal examination (DRE) stage cT1c in 8% versus 35%, cT2 in 7% versus 15%, cT3-4 in 85% versus 50%, mean prostate volume 67 versus 53 mL, anemia (haemoglobin < 10 gm/dL) in 28% versus 19%, renal failure (serum creatinine elevated > 2 above normal) in 15% versus 10%, mean (median) serum PSA 1123.4 (146) and 232.4 (20) ng/mL, and serum PSA greater than 50 ng/mL in 69% versus 30% (all differences *p* < 0.001).

**Conclusion:** In men with underlying BPH, concomitant prostatitis leads to presentation in AUR at a younger age and higher serum PSA. Men with CaP and prostatitis presenting with AUR have earlier T-stage disease, smaller prostate volume, a lower prevalence of anemia and renal failure, and lower mean serum PSA, indicating that prostatic inflammation in men with CaP predisposes to AUR at an earlier stage of the disease.

## UP-28

### Meta-analysis of robotic-assisted versus traditional laparoscopic pyeloplasty for patients with ureteropelvic junction obstruction: effect on operative time, length of hospital stay and postoperative complications

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**Introduction and Objective:** Although there is growing evidence that robotic-assisted procedures may be more advantageous over "simple" laparoscopic ones, few studies have shown clear superiority of robotic-assisted laparoscopic pyeloplasty (RAP) over traditional laparoscopic pyeloplasty (TLP) for UPJO. The objective was to undertake a systematic review and meta-analysis to evaluate the effect of RAP versus TLP for patients with UPJO focusing on operative time, length of hospital stay and postoperative complications.

**Materials and Methods:** We searched 4 electronic bibliographical databases including "related articles" PubMed feature, reference lists from articles and program abstracts from scientific meetings. As a result, 58 citations were identified. Two individuals independently screened the titles and abstracts of each citation to select the articles (90% agreement). Intervention: Studies that compared RAP versus TLP for treatment of UPJO were included. Case-series on RAP or TLP were excluded because of large heterogeneity. Measurements: We utilized weighted mean difference (WMD) to measure operative time and length of hospital stay and odds ratio (OR) and risk difference (RD) to measure complication and success rates. These ORs were pooled using a random effects model and tested for heterogeneity.

**Results:** We identified 8 publications that strictly met our eligibility criteria. Meta-analysis of extractable data showed that RAP was associated with a 10-minute operative time reduction (WMD = -10.4 min; 95% CI -24.6 to 3; *p* = 0.15) and significantly shorter hospital stay compared to TLP (WMD = -0.5 d; 95% CI -0.6 to -0.4; *p* < 0.01). There was no difference between the approaches in regard to complication (OR 0.7; 95% CI 0.3–1.6; *p* = 0.40) and success (OR 1.3; 95% CI 0.5–3.5, *p* = 0.62) rates.

**Conclusion:** Robotic-assisted laparoscopic pyeloplasty and TLP appear to be equivalent in regard to postoperative urinary leaks, hospital readmissions, success rates and operative time. When previous experience with TLP is considered, RAP operative time appears shorter by almost 1 hour

versus TLP in centres with modest TLP experience. Furthermore, although duration of hospital stay with RAP was half a day shorter than TLP, this reduction in hospitalization may reflect a trend towards early patient discharge over a real effect of RAP on reducing hospital stay.

## UP-29

### Body mass index has minimal impact on perioperative outcomes during the learning curve for robotic-assisted laparoscopic radical prostatectomy

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**Introduction and Objective:** Obesity, defined as body mass index (BMI) greater than 30, has in previous studies of robotic-assisted laparoscopic radical prostatectomy (RALRP) been a risk factor for worse perioperative outcomes. We evaluated whether BMI adversely affected perioperative outcomes, specifically overall operative times, blood loss and pathological outcomes.

**Materials and Methods:** A prospective collected database of 150 RALRP performed by a single surgeon was analyzed. Obesity was defined as BMI 30 or greater, normal BMI less than 25 and overweight as 25–30. Two separate analyses were performed: firstly, the first 50 cases (the initial learning curve) and secondly the entire cohort of 150 RALRP.

**Results:** In the initial cohort of 50 cases there were 14 obese patients (BMI ≥ 30). They were statistically comparable for PSA and Gleason score. There was no statistically significant difference between obese and nonobese patients with regard to operative times (253 v. 243 min), port placement times (23 v. 26 mins) and EBL (457 v. 451 mL). Length of stay was longer in the obese group (4.3 v. 2.9 d); BMI remained an independent predictor of increased length of stay on multivariate linear regression analysis (*p* = 0.002). There was no statistically significant difference in the postoperative outcomes of leak rates, positive margin rates, and incisional hernia rates. In the entire cohort of 150 patients, when comparing obese patients (BMI ≥ 30) to those with a normal BMI (BMI < 25), there was no statistically significant difference in operative times (215 v. 198 min); EBL (350 v. 193 mL; *p* = 0.06); LOS (3.8 v. 3.2 d); positive margin rates; or the complications of leak and incisional hernia. However, on multivariate linear regression analysis, after adjusting for age and prostatic volume, BMI was an independent predictor of increased operative time (*p* = 0.007).

**Conclusion:** Obese patients do not have an increased risk of blood loss, positive margins or the postoperative complications of incisional hernia and leak during the learning curve. They do however have mildly increased operative times, and we noted an increased length of stay in our first 50 cases for those patients who were obese.

## UP-30

### Early postoperative renal scintigraphy as a predictor of long-term outcomes after laparoscopic pyeloplasties

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**Introduction and Objective:** Laparoscopic pyeloplasty (LP) is a well established minimally invasive technique with high clinical and scintigraphic success rates reported. However, success rates are not always as good as expected when strict scintigraphic criteria are used. Controversy exists about long-term failure rates and strategies to predict which patients are likely to face unfavourable outcomes are yet to be put forward. We intend to correlate early postoperative scintigraphic results with late clinical and scintigraphic data in order to identify patients requiring closer follow-up after laparoscopic pyeloplasty.

**Materials and Methods:** We reviewed retrospectively 111 adult cases of laparoscopic pyeloplasties performed between 2003 and 2007. We recently updated our clinical and scintigraphic follow-up for these patients, trying to have, after prior early scan done 3 months postoperatively, another MAG-III-Lasix scan, 18 months later. The majority of patients also had preoperative renal scans. They were all contacted at a median of 19 months postoperation and asked about adverse outcomes or pain, using visual analog scale.

**Results:** This series has a 91% nonobstructive scintigraphic success rate (defined by T fi 20 min on Mag-III-Lasix) at 21 months of follow-up. No patients with T fi less than 10 minutes at early postoperative renal scan developed signs of obstruction at longest scintigraphic follow-up. Amongst our patients having a T fi greater than 20 minutes at early postoperative scan, 94% have a long scintigraphic and clinical follow-up ( $n = 15$ ). Approximately 87% of them have little or no pain, but 47% of them still show a T fi greater than 20 minutes. Patients that have improved results with long term T1/2 no longer greater than 20, now have an increase of differential function of 2.8% while patients still showing a long-term obstructed renal scan (T fi > 20 min) have an ipsilateral differential function decreased by 1.6% on average. This early difference suggests a trend for long term evolution (+2.8% v. -1.6%,  $p = 0.06$ ).

**Conclusion:** Early postoperative renal scan helps urologists to determine which patients are at risks of long-term failure after laparoscopic pyeloplasties. Changes in differential renal function as well as scintigraphic signs of obstruction represent objective measures of prognostic value.

### UP-31

#### Are long-term complications after robot-assisted laparoscopic radical prostatectomy related to postoperative urinary leak? An analysis of the learning curve

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**Introduction and Objective:** Anastomotic leak occurs in 10–15% of patients undergoing robot-assisted laparoscopic radical prostatectomy (RALRP); however it is unclear whether there are any long term effects from this complication. We investigated whether postoperative anastomotic leak was associated with urethral strictures, bladder neck contractures, incontinence or other adverse reactions, in the initial series of RALRP.

**Methods:** A prospective institutional database with ethic research board approval was the data source. All consecutive cases of RALRP performed before April 2008 were included in the analysis. This cohort of patients includes the initial series of patients (i.e., the learning curve). No patients were lost to follow-up. Patients were divided into 2 groups — those who had a leak (Group 1), and those who did not have a postoperative leak (Group 2). Urinary function outcomes and long-term complications were evaluated in the 2 groups. All patients completed a self-administered standardized urinary continence evaluation.

**Results:** There were 154 patients in the group for analysis. Of this group of 154 patients, 7.1% of patients had a postoperative leak, which was diagnosed clinically and confirmed with a cystogram. There was no statistically significant difference between the 2 groups with regards to age, intraoperative times (median 192 v. 206 min), anastomosis time (median 48.5 v. 42.0 min), estimated blood loss (median 150 v. 200 mL), BMI (28.2 v. 27.7 kg/m<sup>2</sup>), gland size (43.9 v. 43.06 mL) for Group 1 versus Group 2, respectively. Length of stay was longer in the group which had a leak (8 v. 3 d;  $p < 0.0001$ ). There was no statistically significant difference in continence between the 2 groups of patients at 3 months ( $p = 0.46$ ), 6 months ( $p = 0.66$ ) or 12 months ( $p = 0.38$ ). No correlations with urethral strictures, bladder neck contractures or other adverse reactions were noted for the group of patients who had a postoperative leak.

**Conclusion:** Patients who have a postoperative urinary leak have a longer length of stay, but do not have evidence of increased risk of urinary retention, urinary incontinence, urethral stricture, bladder neck contractures or any long-term complication.

### UP-32

#### Laparoscopic entry technique preferences of Canadian urologists

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**Introduction and Objective:** Numerous laparoscopic entry techniques and technologies have been described to minimize entry related injuries. At present, no evidence exists to support an advantage using any single technique in terms of preventing major complications. Preferences for different methods vary between surgeons, and depend on differences in training, speciality and personal experience. Several studies have surveyed

general surgeons and gynecologists determining that they prefer the open technique and the closed/Veress technique respectively. A recent survey shows 36.5% of Canadian urologists perform laparoscopic surgery, however, to our knowledge no literature exists examining their preferred technique of entry. Our aim was to identify the practice patterns for laparoscopic entry of Canadian urologists.

**Materials and Methods:** An online survey was designed to determine the different laparoscopic entry methods and locations, injuries encountered, and demographics of practicing urologists in Canada. The survey was translated into French for Francophone respondents. The Web-based survey was sent by the Canadian Urological Association to 407 urologists across Canada.

**Results:** One hundred ten urologists responded (27% response rate) from 8 of 10 provinces across Canada. Eighty percent of respondents perform laparoscopy. The majority of respondents (76%) had participated in advanced laparoscopic training outside of residency. The most common primary methods of entry in a virginal abdomen were the disposable visual trocar/visual cannula (44.7%) and open Hasson technique (28.2%), followed by the closed/Veress technique (18.8%). Comparatively, in patients with previous open abdominal surgery, the most common primary method of entry was the open Hasson technique (50%), followed by disposable visual trocar/visual cannula (41.3%) and the closed/Veress technique (8.8%). A primary port entry complication was experienced or witnessed by 27.6% of urologists and was most commonly bowel injury. A secondary port site entry complication was reported by only 10.7% of urologists and was primarily small vessel injury (e.g. inferior epigastric).

**Conclusion:** The results of our survey of Canadian urologists, demonstrate that no single entry technique is used predominantly, unlike the established practice patterns of general surgeons and gynecologists. Rather, Canadian urologists prefer the visual trocar entry and open Hasson technique in both the virginal and nonvirginal abdomen.

### UP-33

#### Office-based UroTeleHealth: bringing urology health care nearer home: a work in progress

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**Introduction and Objective:** To assess the role of Telemedicine in the management of urology patients who live great distances from the urologist.

**Materials and Methods:** Application to the Ontario Telemedicine Network (OTN) to install office-based urotelehealth equipment was approved. Ontario Telemedicine Network Studio #0285 was certified as live for clinical video services on Nov. 3, 2006. Policy and procedural manuals were developed for the program. Regional Health Authorities and health care providers in Northern Ontario were informed. The clinic was planned to operate 4 hours/month. Referrals received by fax were to be booked every 15 minutes by the OTN Referral Management and Scheduling Service (RMSS) staff. A schedule was faxed to the urologist 24–48 hours before the clinic. Patients were seen in hospital-based studios run by specially trained nurses. Primary health care providers were welcome. The urologist's and RMSS's records were reviewed to determine the number of clinics, patient encounters and the type of clinical encounters. Patient demographics, diagnosis and time utilized were studied.

**Results:** There were 22 clinics held between 2006 and 2008. A total of 389 patients — 276 males and 113 females aged between 3 and 96 (mean 64) years — were evaluated through OTN. Patient encounter included: counselling (35) consultation (85), and follow-up to discuss results of tests and surgical outcomes (269). Clinical diagnoses include prostate cancer (46), bladder cancer (26), kidney cancer (13), BPH (120), urinary incontinence (28), overactive bladder (13), erectile dysfunction (10), scrotal mass (12), UTI (54), abnormal PSA (40) and others (49). Total time logged was 71 hours, average of 3.2 hours/month (expected 4.0 hr/mo). The average time per encounter was 11 minutes. Cancellation due to technical problems occurred once, resulting in 8 patients being rescheduled.

**Conclusion:** Telemedicine resulted in rapid follow-up and review of test

results and surgical outcomes, reducing patient anxiety. Counselling patients in complex cases occurred, usually with the presence of the primary care physician, nurse practitioner and/or relatives. Time management for the urologist has been efficient exceeding the goal of 352 encounters by 37. Travel time for both the urologist and the patients was reduced from several hours to minutes. Decreased "wait time" may be a benefit but was not measured in this study.

### UP-34

#### High-resolution analysis of wait times and factors affecting surgical expediency study

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**Introduction and Objective:** Wait times in Canada are a contentious issue increasingly being monitored by hospitals and governments as an indicator of quality healthcare delivery. We created a higher resolution picture of the wait experienced by urological surgery patients beginning with the initial referral. In doing so, we hoped to 1) identify potential bottlenecks & common delays at our centre, and 2) assess the accuracy of our OR booking software for higher resolution calculations of wait times.

**Materials and Methods:** Charts of 322 patients undergoing surgery from November 2007 to March 2008 were reviewed and specific dates (referral received, first visit, diagnosis, decision to operate, and surgery date), patient factors and delays were recorded. The data were used to detail the patient's wait and determine which patient factors were predictive of wait time.

**Results:** The mean time from decision to operate to the day of operation was 75.87 days for all patients (66.31 for repeat and 86.03 for new patients). This accounts for 53% of the wait time while the time from first clinic visit to decision to operate composes 47% of the wait time. Predictors of a decreased wait time include cancer cases, younger age, urgency score, repeat patients and female gender in multivariate analysis. Delays were experienced by 16.8% of patients and were categorized by patient, hospital and physician factors. The most common delays were OR cancellations/time constraints, patients requiring further optimization and delays in referral (4.7%, 3.4%, and 3.1% respectively) while patient factors (travel, preference, etc.), delays in diagnosis and a combination of delays were less common (2.8%, 2.2% and 0.6%, respectively).

**Conclusion:** The waiting process is complex and the actual waiting patient's must endure is much longer than wait times traditionally recorded/reported by hospitals. As strategies are implemented to decrease wait times, it will become increasingly important to monitor the entire wait time from referral to operation, ensuring that changes being made are truly decreasing wait times and not simply shifting where/when the patient waits.

### UP-35

#### Expression and functionality of toll-like receptors in human urothelial cells

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**Introduction and Objective:** Toll-like receptors (TLRs) play a key role in triggering the innate immune response against pathogens. They are also expected to play an important role in nonspecific immunotherapy of bladder cancer using Bacillus Calmette-Guérin (BCG) or other immunomodulating agents. The objective of this study was to characterize the expression of TLRs in normal and tumoral human urothelial cells.

**Materials and Methods:** Expression of TLR1 to 10 mRNA was analyzed by RT-PCR in 4 primary cultures of normal human urothelial cells (NHUC) and 15 bladder cancer cell lines. The functionality of the TLRs was tested in 1 NHUC and 4 cell lines by measuring, in enzyme-linked immunosorbent assay (ELISA), the secretion of inflammatory cytokines in response to 6 specific TLR ligands and to BCG. Expression of TLR2, 3, 4, 5, 7 and 9 was also analyzed on bladder tissue sections of 11 normal urothelia, 11 non-muscle invasive and 2 muscle-invasive bladder cancers using immunohistochemistry (IHC).

**Results:** All TLR mRNAs, except for TLR7, 8, and 10, were detected in the 4 NHUCs. TLR6 and 9 mRNAs were expressed in all cell lines whereas

expression of other TLR mRNAs was more heterogeneous, some cell lines showing no or a reduced expression. Functional TLRs, as measured by secretion of inflammatory cytokines, were observed in the NHUC and the 4 cancer cell lines. Various levels of IL8 induction were obtained with different agonists in each cell line but zymosan and poly (I:C) (TLR2 and 3 agonists, respectively) appeared to be common inducers of IL8 secretion. TLR 2, 3, 4, 5, 7, and 9 proteins were homogeneously expressed in normal urothelia but their expression was reduced and heterogeneous in tumours, except for TLR9.

**Conclusion:** This study provides evidence that TLR 1 to 10 are expressed in urothelial cells. Expression of TLRs is decreased in tumours compared to normal bladder tissues and some are even totally absent in bladder cancer cell lines, suggesting that bladder cancer cells might lose responsiveness to TLR stimulation. The identification of generally expressed and functional TLRs in a majority of bladder tumours could suggest new therapeutic agents for bladder cancer.

### UP-36

#### Achieving pT0N0 at radical cystectomy: outcomes of 135 pT0N0 bladder cancer patients treated with radical cystectomy: the Canadian Bladder Cancer Network experience

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**Introduction and Objective:** Radical cystectomy is the standard treatment for muscle-invasive bladder cancer and is increasingly being offered for treatment of T1G3 disease and in a consolidative approach after treatment with neoadjuvant chemotherapy. This has resulted in a significant number of patients with pT0 pathology after cystectomy. We assessed clinical outcomes in patients found to have no evidence of disease, ie pT0N0, in the cystectomy specimen following radical cystectomy for transitional cell carcinoma.

**Materials and Methods:** We collected and pooled a database of 2287 patients who have underwent radical cystectomy between 1993 and 2008 in 8 different centres across Canada. One hundred thirty-five patients were found to have pT0N0 bladder cancer at time of cystectomy. Variables analyzed included patient age, clinical stage, nodal status, histologic type, previous history of superficial TCC and concomitant CIS, use of neoadjuvant chemotherapy, type of pelvic lymph node dissection (none, standard, extended). Survival data were analyzed using Kaplan-Meier method and Cox proportional regression analysis.

**Results:** Median age of patients was 66 years with a mean follow-up time of 42 months. Clinical stage distribution was Tcis 10%, Ta 2%, T1 24%, T2 52%, T3 6%, T4 5%. Twenty-four percent had a history of concomitant CIS with 35% of patients with a history of previous superficial TCC. Pelvic lymph node dissection was performed in 94% of patients with 65% following standard template and 35% with extended template. Only 8% of patients received neoadjuvant chemotherapy prior to cystectomy. The 5-year recurrence-free survival, disease-specific survival, and overall survival was 83%, 96% and 88%, respectively. The 10-year recurrence-free survival, disease-specific survival, and overall survival was 66%, 92%, and 70% respectively. Eighty-three percent of patients: TCC as primary pathology. On Cox proportional regression analysis, only patient age correlated to overall survival.

**Conclusion:** These results indicate that the finding of pT0N0 is a predictor of superior outcomes from cystectomy with a high 5 and 10 year recurrence-free survival, disease-specific survival and overall survival. It should be noted however that pT0N0 is not a guarantee of recurrence-free survival as there is still a substantial risk of tumour recurrence in this patient population. As clinical stage was not a demonstrable prognostic factor for

positive outcomes, achieving pT0N0 at cystectomy can be used as a surrogate endpoint for survival when evaluating efficacy of neoadjuvant chemotherapy.

### UP-37

#### Associations between age and clinical outcomes after radical cystectomy: results from the Canadian Bladder Cancer Network

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**Introduction and Objective:** Radical cystectomy is the standard treatment for localized or regionally advanced muscle-invasive bladder cancer and high-risk non-muscle invasive disease resistant to intravesical therapy. We constructed a Canadian bladder cancer database consisting of patients treated with radical cystectomy. The objective of the current study was to examine the associations between age and clinical outcomes after radical cystectomy.

**Materials and Methods:** Institutional radical cystectomy databases containing detailed information on bladder cancer patients treated between 1993 and 2008 were obtained from 8 academic centres in Canada. Data were collected on 2287 patients and combined into a relational database formatted with patient characteristics, pathological characteristics, recurrence status, and survival status. Patient age was classified as younger than 60 years, 60–69 years, 70–79 years, or 80 years or older. The clinical outcomes were 90-day mortality, overall survival (OS), disease-specific survival (DSS) and recurrence-free survival (RFS). Cox proportional regression analysis was used to determine the associations between age and clinical outcomes after radical cystectomy.

**Results:** Five hundred fifty-seven (24.6%), 679 (30.0%), 846 (37.4%) and 181 (8.0%) patients were younger than 60 years, 60–69 years, 70–79 years, and 80 years or older, respectively. Mean follow-up duration was 35 months. Compared to patients younger than 60 years, multivariate Cox proportional regression analysis showed that age 80 years or older was independently associated with 90-day mortality (OR 2.98, 95% CI 1.22–7.30), OS (HR 2.03, 95% CI 1.51–2.75), DSS (HR 1.56, 95% CI 1.09–2.24), and RFS (HR 2.06, 95% CI 1.57–2.70).

**Conclusion:** Age 80 years or older was independently associated with an increased risk of 90-day mortality, overall mortality, disease-specific mortality, and recurrence-free events after radical cystectomy. These data suggest that age should be considered in the design and implementation of clinical trials for bladder cancer therapy and in nomograms predicting clinical outcomes.

### UP-38

#### Clinical and pathological stage correlations in patients with bladder carcinoma: Canadian Bladder Cancer Network experience

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**Introduction and Objective:** Discrepancies between pre- and postoperative staging remain a major issue in the management of patients with bladder cancer and the primary reason for lack of widespread use of neoadjuvant chemotherapy. We herein report the correlation between clinical and pathological staging in patients treated with radical cystectomy by urologic oncologists.

**Materials and Methods:** A pooled database of 2287 patients who underwent radical cystectomy has been created. Surgeries were carried out between 1993 and 2008 in 8 different centres across Canada. Collected variables included age, race, gender, clinical stage and nodal status, concomitant carcinoma in situ, histology, pathological stage and nodal status, grade, and surgical margins.

**Results:** Out of 2287 patients, 1440 who did not receive neoadjuvant chemotherapy and had both clinical and pathological stage available and were included in this review. Mean age of patients was 67 years. Clinical stage distribution was 27.3%, 66.7%, 2.8%, and 3.2% for superficial cancer, cT2, cT3 and cT4, respectively. Pathological upstaging occurred in 51.7%, 64.5%, 43.9%, and 34.8% of clinical stages Ta/ClS/T1 (superficial), T2, T3 and T4, respectively. Overall upstaging was 59.4% compared to downstaging in only 16.7% of cases. In patients with cT3 and cT4, only 30% had pathologically organ-confined disease. Across all stages, upstaging was clearly more frequent than downstaging.

**Conclusion:** Our results confirm on a large scale the upstaging phenomenon already reported in the literature. In this series, upstaging occurred mainly in patients with clinical stage T2 disease, which was the stage most cases presented with for radical cystectomy. Given that the majority of patients undergoing radical cystectomy are upstaged, this information may be used in counselling patients with respect to the possibility that neoadjuvant or adjuvant therapies may be useful in patients judged to be high risk. This also highlights the need for better staging modalities in bladder cancer.

### UP-39

#### Impact of adjuvant chemotherapy on outcomes for patients with pT3-4 or pN+ bladder cancer treated with radical cystectomy: Canadian Bladder Cancer Network

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**Introduction and Objective:** The outcomes for unfavourable urothelial carcinoma of the bladder are not well defined and the addition of adjuvant chemotherapy is not substantiated with prospective randomized controlled trials in the literature. Data from a large, multi-institutional, contemporary Canadian series of patients who underwent radical cystectomy for unfavourable bladder cancer are presented.

**Materials and Methods:** All patients undergoing radical cystectomy with the intent to cure, for urothelial carcinoma of the bladder stages  $\geq$  pT3 N0 or pT1–4 N+ between 1993 and 2008 from 8 different centres across Canada were evaluated. These patients did not receive neoadjuvant chemotherapy. The clinical course, adjuvant chemotherapy survival data, pathological characteristics, and long-term outcomes were reported. Data were analyzed using the Kaplan–Meier method and Cox regression analysis.

**Results:** A total of 1180 patients (914 men [77%] and 266 women) with a mean age of 67.3 years were treated with radical cystectomy  $\pm$  standard (55%) or extended (34%) PLND. Adjuvant chemotherapy was received by 321 (27%) patients. Mean follow-up was 2.6 (0.6–12.9) years. Overall survival (OS) at 2, 5 and 10 years for the entire cohort was 42%, 13% and 7%, respectively. Cancer-specific survival (CSS) was 44%, 17% and 11%, respectively. Recurrence-free survival (RFS) was 38%, 13% and 8%, respectively. Those patients who received adjuvant chemotherapy had a 2-, 5- and 10-year CSS of 50%, 24%, 11% versus 42%, 22%, 10% for those who did not ( $p = 0.005$ ). When compared with the no adjuvant therapy group, the patients who received adjuvant chemotherapy were more likely to have any of the following: lymphovascular invasion (LVI), extended PLND, greater number of positive nodes, higher pT and pN stages, younger age

and lower Charlson comorbidity score ( $p < 0.05$  for all). Multivariate analysis showed that younger age, lower pT and pN stages, negative margins, and adjuvant chemotherapy resulted in a favorable outcome.

**Conclusion:** These data from a large group of Canadian patients confirm the poor outcomes of those with surgically managed unfavourable invasive bladder cancer. Significant survival advantages can be achieved in patients who undergo adjuvant chemotherapy.

#### UP-40

##### The incidence of prostate cancer and urothelial cancer in the prostate in cystoprostatectomy specimens

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**Introduction and Objective:** The current gold standard for muscle-invasive bladder cancer is radical cystectomy with removal of the prostate and seminal vesicles. Potential functional consequences of this radical procedure include compromised potency and continence. A growing interest in prostate/sexuality sparing cystectomy in orthotopic neobladder candidates with either partial or total sparing of the prostate and neurovascular bundles has emerged, although recent evidence suggest only a marginal functional benefit. Our objective is to determine the incidence of occult prostate cancer and urothelial cancer of the prostate in cystoprostatectomy specimens conducted for muscle-invasive bladder cancer.

**Methods:** A retrospective review of 83 male patients who underwent radical cystoprostatectomy for muscle-invasive bladder cancer between April 2004 and March 2007 was conducted. The median age of our study group was 71 years. Pathological findings of prostate/urothelial cancer in the prostate were identified. Clinically significant prostate cancer was defined as Gleason score greater than 6, tumour volume less than 0.5 mL, extracapsular extension or perineural invasion.

**Results:** Our review yielded a 30% (standard deviation [SD] 10%, 0.95 CI) rate of prostate cancer, with 19% (SD 8.5%, 0.95 CI) of total specimens being positive for clinically significant prostate cancer. Urothelial cancer in the prostate was identified in 16% (SD 8.5%, 0.95 CI) of patients, with an overlap with prostate cancer in 2 patients. The overall rate of an underlying cancer within the prostate of our cystoprostatectomy specimens was ~46% (SD 10.7%, 0.95 CI).

**Conclusion:** These findings suggest that the oncological risk of leaving behind residual cancer may not justify the practice of prostate-sparing cystectomies.

#### UP-41

##### Patients with renal pelvis upper tract transitional cell carcinoma have significantly worse cancer-specific survival than patients with ureteral primaries

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**Introduction and Objective:** The biological effect of ureteral versus renal pelvis location of upper tract transitional cell carcinoma (TCC) is unknown. We assessed the impact of tumour location (ureteral v. renal pelvis) on the cancer-specific mortality (CSM) in a large, population-based dataset of surgically treated upper tract TCC patients.

**Materials and Methods:** Our study population consisted of 5029 patients with upper tract TCC from the Surveillance, Epidemiology, and End Results (SEER) database. The effect of location of upper tract TCC (ureteral v. renal pelvis) on CSM was tested in univariable and multivariable Cox regression models. Covariates consisted of age, stage (gender, SEER registry of residency, race, year of surgery, grade, and type of surgery (segmental v. radical with bladder cuff v. radical without bladder cuff)).

**Results:** The median follow-up of censored patients was 53 months. In multivariable analysis, patients with upper tract TCC of the ureter had a 19% lower rate of CSM than patients with a primary in the renal pelvis (adjusted hazard ratio [HR] 0.81,  $p = 0.007$ ). In absolute terms, at 5 years after surgery patients with ureteral TCC had a 17.8% CSM rate versus 25.8% CSM rate for patients with upper tract TCC of the renal pelvis.

**Conclusion:** Our report is the first to suggest a difference in the CSM

rates between patients with ureteral and renal pelvis TCC. A number of reasons may explain the more favorable prognosis of a ureteral primary tumour in this patient group. Unfortunately, the current database does not allow identifying these. Nonetheless, our findings suggest that the outcome of patients with renal pelvis upper tract TCC may be undermined by diagnoses and treatment delays.

#### UP-42

##### Laparoscopic partial nephrectomy for renal tumour in solitary kidney in a single institution

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**Introduction and Objective:** We report our experience with laparoscopic partial nephrectomy (LPN) for renal tumours in solitary kidneys in a single institution in Québec City.

**Materials and Methods:** Of 320 patients undergoing partial nephrectomy since August 2003, 21 (6.5%) underwent LPN in a solitary kidney.

**Results:** Mean tumour size was 3.4 cm, total median operative time was 133 minutes, median blood loss was 240 mL, warm ischemic time was 27 minutes and hospital stay was 5 days. One case was converted to open surgery. No postoperative urinary leaks have been reported despite calyceal entry in 15 (71%) patients. Pathological findings confirmed renal carcinoma in 95% with negative margins in all cases. Median pre- and postoperative estimated glomerular filtration rate was (58.4 and 47.5 mL/min per 1.73 m<sup>2</sup>) reflected a change of 19%. One patient (5%) required temporary hemodialysis. At a median follow-up of 24 months, cancer specific and overall survival is, respectively, 95% and 95%. No local recurrence has been reported, and 2 patients are alive with metastatic disease already present at the time of diagnostic.

**Conclusion:** Laparoscopic partial nephrectomy can be performed in this high-risk population with good oncological and renal function results. Advanced laparoscopic skill and a dedicated team are required.

#### UP-43

##### Tyrosine kinase inhibitors for advanced renal cell carcinoma: the Manitoba experience

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**Introduction and Objective:** To assess the efficacy and toxicity of the new TKIs in Manitoban patients with advanced renal cell carcinoma (ARCC).

**Materials and Methods:** The Manitoba Cancer Registry was utilized to identify consecutive patients diagnosed with RCC, and seen by a medical oncologist, from early 2006 to June 2008. Detailed review of the electronic health record was undertaken for those found to have ARCC and to have been prescribed a TKI. Survival was evaluated using the method of Kaplan and Meier. Prognostic factors were evaluated using Cox proportional hazards regression. Clinical and treatment parameters were analyzed using standard descriptive statistics.

**Results:** A total of 78 patients were found to have ARCC; all 38 patients treated with TKIs were reviewed for this analysis. Median age at start of TKI therapy was 60 (range 42–80) years. Histology was available in only 21 patients; a clear cell component was seen in 18. Two or more sites of metastases were seen in 32. The majority (23) had not had a nephrectomy. First-line TKI was sunitinib in 27, sorafenib in 11. Median number of cycles was 4 (range 1–31) for sorafenib, and 3 (1–23) for sunitinib. Median follow-up for the 15 still surviving is 25.3 months (range 5.1–31.6). Median overall survival for both sunitinib and sorafenib was 8.5 (95% confidence interval 5.7–11) months; survival curves were superimposable for the 2 agents. Low hemoglobin, elevated LDH, poor performance status and especially MSKCC poor risk status ( $n = 13$ ) were strongly associated with an inferior outcome. Fifty percent of the patients required at least 1 dose reduction or delay at a median number of 3.1 cycles (range 1–10). The only unexpected toxicity was life threatening thrombocytopenia in 2 patients, profound hypothyroidism in 1 and acute liver failure in 1.

**Conclusion:** This preliminary evaluation of the use of TKIs in Manitobans with ARCC suggests toxicities congruent with the literature. Median survival was considerably lower than in the Phase III sunitinib registration

trial due to less stringent selection criteria. Our findings clearly underline the importance of appropriate patient selection and the validity of the MSKCC prognostic index. We are continuing to capture data.

**UP-44**

**Renal tumours and the risk of malignancy based on size**

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**Introduction and Objective:** To determine the incidence of malignancy in resected renal tumours in a subpopulation of Canadian patients and the significance of tumour size, patient's age, gender, and whether the tumour was an incidental finding.

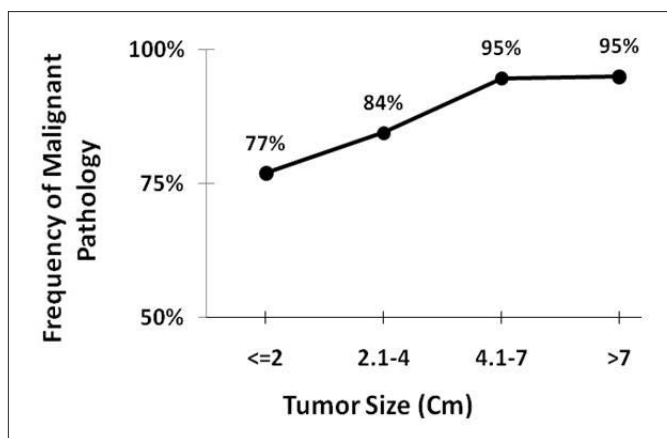
**Materials and Methods:** Medical records of 168 consecutive nephrectomies performed at our institute were reviewed retrospectively.

**Results:** Average age of the patients was 61 (SD 11, range 28–89) years and male to female ratio was 1.3:1. Total of 180 masses were resected in 168 nephrectomies (128 radical, 40 partial) during the study period. Of the 180 masses, 20 (11%) were benign and 160 (89%) were malignant lesions. Pathological subtypes are summarized in Table 1. The incidence

**Table 1. UP-44**

Benign	Total	20	11%
	Oncocytoma	15	
	Angiomyolipoma	2	
	Myelolipoma	1	
	Cystic Nephroma	1	
	Cystic lesion	1	
Malignant	Total	160	89%
	Clear Cell RCC	135	
	Papillary RCC	12	
	Chromophobe RCC	6	
	Sarcomatoid RCC	5	
	Angiosarcoma	1	
	Others	1	

of malignancy was not affected by age and gender. The pathological nature of the incidental and symptomatic masses did not differ. Based on the pathology reports, the average size of the masses was 5.5 (SD 3.9, range 0.3–25.0) cm. The larger masses had higher chance of malignancy ( $\chi^2$  test,  $p = 0.032$ ) as depicted in Figure 1.



**Fig. 1.**

**Conclusion:** Using modern imaging techniques, many renal tumours can be visualized thus providing patients and surgeons with treatment choices. The present study assists us to adequately assess the risk of malignancy of a renal mass based on size. We recommend more aggressive therapies for masses larger than 4 cm and parenchymal sparing procedures for masses smaller than 4 cm as larger proportion of these are benign.

**UP-45**

**Laparoscopic partial nephrectomy in solitary kidney**

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**Introduction and Objective:** We report our experience with laparoscopic partial nephrectomy (LPN) for renal tumour in solitary kidney in a single institution in Québec City.

**Materials and Methods:** Of 320 patients undergoing partial nephrectomy since August 2003, 21 (6.5%) underwent LPN in a solitary kidney.

**Results:** Mean tumour size was 3.4 cm, total median operative time was 133 minutes, median blood loss was 240 mL, warm ischemic time was 27 minutes and hospital stay was 5 days. One case was converted to open surgery. No postoperative urinary leaks have been reported despite caliceal entry in 15 (71%) patients. Pathological findings confirmed renal carcinoma in 95% with negative margins in all cases. Median pre- and postoperative estimated glomerular filtration rate was (58.4 and 47.5 mL/min per 1.73 m<sup>2</sup>) reflected a change of 19%. One patient (5%) required temporary hemodialysis. At a median follow-up of 24 months cancer specific and overall survival are, respectively, 95% and 95%. No local recurrences have been reported and 2 patients are alive with metastatic disease already present at the time of diagnostic.

**Conclusion:** Laparoscopic partial nephrectomy can be performed in this high-risk population with good oncological and renal function results. Advanced laparoscopic skill and a dedicated team are required.

**UP-46**

**Prospective study comparing 2 techniques of renal clamping in laparoscopic partial nephrectomy: impact on perioperative parameters**

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**Introduction and Objective:** Laparoscopic partial nephrectomy (LPN) for renal tumour requires the control of the renal hilum to ensure an adequate excision of the lesion. Any modification of the clamping technique that reduces warm ischemia time is mandatory. During our learning curve, we modified our technique switching from a control of the artery alone (AO) to a complete en-bloc clamping of the renal hilum (AV). We evaluated the implications of these modifications on renal function and perioperative parameters.

**Materials and Methods:** From March 2003 to December 2008, 205 patients underwent a LPN by transperitoneal approach and by one surgeon in a single institution. The first 102 LPN were achieved with artery only clamping (AO) with a Bulldog clamp. The last 103 LPN were realized under control of the renal hilum (AV) with a Satinsky clamp. Data was collected prospectively. Renal function was evaluated by baseline creatinine level and its variation, by estimation of the glomerular filtration rate (GFR) according to the MDRD equation and by assessment of split renal function using renal MAG-3-lasix scintigraphy at 10 days. Sixty-two of 205 patients had renal scintigraphy before and after surgery.

**Results:** There was no significant difference between the 2 groups regarding age, sex, operative time, pathological stage, tumour size or location. The warm ischemia time was lower in the AV group: 30.4 versus 23.3 minutes ( $p < 0.0001$ ). The GFR was significantly higher in the AV group during the postoperative period: 65.1 versus 71.0 mL/min ( $p = 0.0435$ ). Variation in the operative blood loss, the hospital stay and the leakage rate were nonsignificant. Loss of differential function of the operated kidney was 13,6% for the artery alone group and 14,3% for the en bloc group ( $p = 0,8016$ ).

**Conclusion:** En-bloc clamping of the renal hilum is not associated with more renal function impairment in patients undergoing LPN for tumour.

In our study, over, this technique is correlated to a lower warm ischemic time, most important predictor of decrease in renal function.

#### UP-47

##### Conditional survival predictions after nephrectomy for renal cell carcinoma

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**Introduction and Objective:** Conditional survival implies that, on average, long-term cancer survivors have better prognosis than newly diagnosed individuals. We explored the effect of conditional survival in renal cell carcinoma (RCC).

**Materials and Methods:** The analyses relied on 3560 patients with RCC of all stages treated with nephrectomy (NT). We applied the conditional survival methodology to the previously reported posttreatment nomogram predicting survival after NT for patients with stages I-IV RCC. We relied on the same predictor variables that were integrated in the original multivariable Cox regression models. To validate our new conditional survival nomogram, we relied on an independent cohort of 3560 patients from 15 institutions, who were not included in the original development cohort.

**Results:** The 5-year survival of patients immediately after NT was 74.2%. It increased to, respectively, 80.4%, 85.1%, 90.6% and 89.6% for RCC survivors at 1, 2, 5 and 10 years after NT. The predicted probabilities varied by as much as 50%, when for example predictions of RCC-specific mortality at 10 years were made after NT versus 5 years later. Within the external validation cohort, the accuracy of the conditional nomogram was 89.5%, 90.5%, 88.5% and 86.7% at 1, 2, 5 and 10 years after nephrectomy.

**Conclusion:** We developed ( $n = 2530$ ) and externally validated ( $n = 3560$ ) a conditional nomogram for predicting RCC-specific mortality that allows to account for length of survivorship after NT with 89.5%, 90.5%, 88.5% and 86.7% accuracy at 1, 2, 5 and 10 years after NT. To date, no such model exists and our tool provides the most realistic prognosis estimates, with high accuracy.

#### UP-48

##### Nephron-sparing surgery is equally effective to radical nephrectomy for T1bN0M0 RCC: a population-based assessment

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**Introduction and Objective:** To date, only few series from tertiary care centres supported the use of nephronsparing surgery (NSS) for T1bN0M0 (range 4–7 cm) renal cell carcinoma (RCC). We decided to test the effect of NSS versus radical nephrectomy (RN) on cancer specific mortality (CSM) in patients with T1bN0M0 RCC in a population-based cohort.

**Materials and Methods:** The Surveillance, Epidemiology and End Results (SEER) 9 database allowed us to identify 275 NSS (5.3%) and 4866 RN (94.7%) patients treated for T1bN0M0 RCC between 1988 and 2004. Analyses, matched for age, year of surgery, tumour size and Fuhrman grade, addressed the effect of nephrectomy type (NSS v. RN) on CSM.

**Results:** At 5 years after surgery, the surviving proportion in the age, gender, tumour size, and year of surgery matched cohort of NSS and RN cases was respectively 91.4% and 95.3% and 90.1% and 93.8% in the cohort of NSS and RN cases where additional matching for Fuhrman grade was performed. Neither of the matched analyses resulted in statistically significant CSM difference ( $p = 0.1$  and  $0.4$ ) between NSS and RN. Similarly, competing-risk regression analyses based on both matching schemes also failed to reveal statistically significant CSM differences ( $p = 0.3$  and  $0.3$ ).

**Conclusion:** Our study represents the largest and the only population-based analysis of cancer control efficacy of NSS versus RN in T1bN0M0 RCC. It indicates that NSS does provide equivalent cancer control relative to RN. In consequence, based on cancer control equivalence, NSS should be given equal consideration for surgical treatment decisions of T1bN0M0 lesions.

#### UP-49

##### A comparative population-based analysis of the rate of partial versus radical nephrectomy for clinical localized renal cell carcinoma

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**Introduction and Objective:** Among other considerations, a survival benefit due to avoidance of surgically induced renal insufficiency distinguishes partial nephrectomy (PN) from radical nephrectomy (RN). We examined contemporary (1989 to 2004) PN trends within the Surveillance, Epidemiology and End Results (SEER) database.

**Materials and Methods:** Diagnostic, stage and surgical codes focused on patients with T1-2 N0 M0 renal cell carcinoma (RCC) treated with either PN or RN. Proportions, trends and multivariable logistic regression models tested the predictors of PN use.

**Results:** Of 19 733 assessable patients, 2614 (13.2%) and 17 119 (86.8%) respectively underwent PN or RN. PN use decreased with increasing tumour size ( $p < 0.001$ ), was more frequent in younger patients ( $p < 0.001$ ) and increased with more contemporary years of surgery ( $p < 0.001$ ). Intriguingly, important geographic variability was recorded ( $p < 0.001$ ). For example, in the San Francisco–Oakland region absolute PN rate was 16.4% versus 7.6% in New Mexico ( $p < 0.001$ ). In multivariable analyses, tumour size, age, year of surgery, gender and SEER region represented independent predictors of PN use.

**Conclusion:** Although expectedly, the rate of partial nephrectomy use increased over time, unexplained variability remained. For example, gender and SEER regions affect the likelihood of partial nephrectomy. These variables warrant further analyses to reduce unnecessary variability and to maximize partial nephrectomy use and its benefit.

#### UP-50

##### Age is an independent predictor of cancer-specific mortality in patients with transitional cell carcinoma of the upper urinary tract

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**Introduction and Objective:** Advanced age predisposes to a delay of therapy in several pathologies. For example, older patients have higher cancer-specific mortality (CSM) rates after cystectomy. We tested the effect of age on CSM in a large, population-based cohort of patients diagnosed with upper tract transitional cell carcinoma (TCC), who were treated with segmental ureterectomy or nephroureterectomy.

**Methods:** Our analyses relied on 5029 patients with upper tract TCC from the Surveillance, Epidemiology, and End Results (SEER) database. The effect of age, coded both as a continuous and a categorized variable ( $< 60$  v.  $60-69$  v.  $70-79$  v.  $\geq 80$  yr), on CSM was tested in separate univariable and multivariable Cox regression models. Covariates consisted of location of the primary tumour (ureter v. renal pelvis), gender, SEER registry of residency, stage (localized v. regional v. nonregional lymph-node metastases), race, year of surgery, grade and type of surgery (segmental v. radical with bladder cuff v. radical without bladder cuff).

**Results:** The median follow-up of censored patients was 53 months. Age coded as a continuous variable (hazard ratio [HR] 1.02;  $p < 0.001$ ), as well as coded as a categorical variable ( $p < 0.001$ ) achieved independent predictor status in multivariable analyses addressing CSM. For example, 80-year-old or older patients had a 90% higher risk of CSM than 60-year-old or younger patients.

**Conclusion:** Our data indicate that diagnosis and treatment delay may undermine the survival of older patients with UT-TCC. This observation should be considered with the intent of improving cancer control outcomes in this patient group.

#### UP-51

##### The effect of partial nephrectomy on postoperative blood pressure with a follow-up of at least 1 year

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**Introduction and Objective:** The risk of chronic hypertension from radical nephrectomy has been described, however, this risk from partial nephrectomy (PN) has not been determined. PN could theoretically cause upregulation of the renin-angiotensin cascade by compressive effects of bolstering sutures and scarring or by possible renal arterial injury during clamping. Our study compares the change of patients' blood pressure (BP) values before and after PN.

**Methods:** This institutional ethics review board approved study included 112 patients who underwent PN for cancer suspicion at our institution from June 2001 to October 2007. Of these patients, 75 provided informed consent for retrieval of BP and medication data from their family physicians. Physicians were contacted and the patients who had adequate perioperative BP data within 2 years prior and at least 1 year following surgery were included in our analysis ( $n = 48$ ). To assess early and long-term BP changes, the average preoperative systolic and diastolic values were compared to those from 1 to 12 months after surgery and those from beyond 1 year of follow-up. Comparisons were performed with Student *t* test. The number of BP medications prescribed preoperatively and postoperatively were recorded. Differences between groups were analyzed with the Wilcoxon signed rank test.

**Results:** Thirty-three (68.7%) patients had a diagnosis of hypertension preoperatively. At a mean follow-up time of 24 months, the overall average preoperative systolic and diastolic BPs (132.4 mm Hg and 78 mm Hg, respectively) were not different from the postoperative measurements (132.2 mm Hg and 76.7 mm Hg, respectively;  $p = 0.87$  systolic and  $p = 0.16$  diastolic). The average preoperative systolic and diastolic BPs (133.2 mm Hg and 78 mm Hg, respectively) were not different compared to the early (1–12 mo follow-up) postoperative values (132.3 mm Hg and 77 mm Hg, respectively;  $p = 0.59$  systolic and  $p = 0.30$  diastolic). For the long-term analysis (average 29.2 mo follow-up), the average preoperative systolic BP was not different from values obtained beyond 1 year after surgery (132.7 mm Hg v. 131.2 mm Hg respectively;  $p = 0.34$ ). However, the corresponding average diastolic BP values were lower in the long term (79.1 mm Hg v. 76.3 mm Hg, respectively;  $p = 0.0138$ ). There was no significant difference between the average number of BP medications prescribed preoperatively (1.2) compared to early (1.4) or long-term (1.3) follow-up periods ( $p = 0.17$  and  $p = 0.36$ , respectively).

**Conclusion:** Partial nephrectomy for the management of renal masses does not result in early or long-term postoperative increases in BP. We did not observe a significant difference in the number of BP medications used before and after PN.

### UP-52

#### Retrospective analyse of patients with supradiaphragmatic inferior vena cava involvement in renal cell carcinoma

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**Introduction and Objective:** Renal cell carcinoma (RCC) is the third most common cancer of the urinary tract with incidence between 6 and 12 cases per 100 000 of population. Up to 10% of patients with renal cancer have involvement of the inferior vena cava (IVC). In 2008, Wagner B. reviewed an experience of 13 European centres where from 1982 to 2003, 1192 patients underwent open radical nephrectomy for RCC with venous involvement. Among these patients 5.4% (63 patients) have supradiaphragmatic thrombus of IVC, so we reviewed our experience for this surgery and compared our results with literature data.

**Materials and Methods:** Between March 1999 and May 2008, 18 patients underwent open radical nephrectomy with thrombus excision under cardiopulmonary bypass and deep hypothermic circulatory arrest for RCC with IVC thrombus involvement. All patients had supradiaphragmatic thrombus, 9 patients (50%) with right atrium extension. Our cohort included 11 men and 7 women. Age of the patients varied from 28 years to 79 years, with mean age of 58.5 years.

**Results:** Mean duration of surgery was 255 minutes and mean blood loss was 3142 mL. All patients received blood transfusion. Mean

hospital stay was 12 days. One patient died in the immediate postoperative period from cardiac tamponade. Fifteen patients were available for follow-up of 17.8 months. 10 patients (66.6%) are currently alive with no evidence of disease. Five patients (33.3%) died with mean follow-up of 30.2 months. Four patients died from their cancer, 1 patient died from other disease. The mortality rate was higher in the group of patients with thrombus extension into the atrium (60% v. 40%).

**Conclusion:** Radical nephrectomy with supradiaphragmatic IVC thrombus excision under cardiopulmonary bypass is a rare surgery. The extension of the thrombus into right atrium is associated with increased long-term mortality. Increased number of patients in our group may be needed to confirm this hypothesis. Our survival results seem to be compared favourably with the literature data. This may be related to better surgical techniques and improvement of peri-operative care. The advent of TKI may further decrease the need for such invasive surgery.

### UP-53

#### Role of ethnicity and gender on papillary renal cell carcinoma presentation and survival

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**Introduction and Objective:** Numerous studies have demonstrated that African Americans have a higher incidence and mortality rates from renal cell carcinoma (RCC) as compared to other ethnic groups. However, it is unclear which RCC histological subtypes are contributing to this disparity. In this study, we evaluated the patterns of disease presentation and outcomes among both African Americans and Caucasians with a papillary RCC diagnosis.

**Materials and Methods:** We retrospectively reviewed the charts of 1862 patients who were diagnosed with RCC between 1980 and 2007. We analyzed race, age, gender, stage at diagnosis differences on the incidence and survival among 103 patients (35 Caucasians, 68 African Americans) with papillary RCC. Incidence trends were analyzed by linear regression models and Cox proportional hazard models was used to determine overall survival of patients by race, gender and stage.

**Results:** African Americans presented with higher incidence of localized disease (85% v. 45.7%) and better overall survival (55.9% v. 42.8%) as compared to Caucasians ( $p < 0.05$ ). Among patients with regional and distant disease, overall survival was poor for both ethnicities. The incidence of papillary RCC was higher among males in both ethnic groups as compared to females ( $p < 0.01$ ). Localized disease was the predominant stage at presentation for both African American males and females as compared to their Caucasian counterparts ( $p < 0.01$ ). This was associated with an improved survival for African American males and females over Caucasian males and females with localized disease ( $p < 0.05$ ).

**Conclusion:** Higher localized papillary RCC incidence rates and better overall survival rates were observed for African Americans compared to Caucasians. While African American males accounted for the higher proportion of localized disease at presentation and better overall survival, female African American patients also had better overall survival as compared to Caucasians. This data suggest that the poorer mortality rate seen among African Americans with RCC is not due to the papillary RCC histology.

### UP-54

#### Effect of micronutrients on GSTP1 promotor methylation in prostate cancer

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**Introduction and Objective:** Hypermethylation of CpG islands in the promoter region of tumour suppressor gene is an early event in cancer and correlates with gene silencing. Aberrant methylation of promoter sequences of important genes such as GSTP1, RARB2 and RASSF1 has been shown to be associated with transformation of cells from normal to preneoplasia or malignancy. Methylation profiles of promoter gene CpG islands

serves as an important diagnostic tool to discriminate normal from malignant cells. By using quantitative real-time PCR we are studying the methylation profiles of GSTP1 promoter region during the progressive growth of prostate of Lady transgenic animals placed on varied micronutrient diets. We propose that an effective micronutrient combination causing a significant reduction in the incidence of PCa can reactivate methylation-silenced GSTP1. This study demonstrates the strong correlation between reversal of hypermethylation of CpG islands with reference to GSTP1 and disease-free survival state of transgenic mice.

**Materials and Methods:** At weaning, transgenic males were randomized to the different diets (control; vitamin E, selenium and lycopene [E+S+L]; vitamin E and selenium [E+S]). Animals were also administered E+S+L in a staggered manner to determine the optimal time of micronutrient commencement. Mice were sacrificed, prostate tissue removed, DNA isolated, quantified and used for bisulfite conversion. Methylation of GSTP1 promoter CpG islands was quantitated by methylation specific real-time PCR using TaqMan probe. 5-FAM-AAA CCT CGC GAC CTC CGA ACC TTA TAA AA- TAMRA3/ and forward primer 5/ - GTC GGC GTC GTG ATT TAG TAT TG- 3/ and reverse primer 5/ - AAA CTA CGA CGA CGA AAC TCC AA-3. PMR was calculated based on supermethylated DNA as reference control.

**Results:** The results demonstrate for the first time the inhibition of DNA methylation by commonly consumed dietary constituents, and suggest the potential use of lycopene in combination with vitamin E and selenium for the prevention or reversal of related gene-silencing in prostate carcinogenesis.

**Conclusion:** Studies are in progress to delineate the molecular mechanism of micronutrient induced reactivation of tumour suppressor gene, retinoic acid receptor b2 (RARb2) in Lady transgenic mouse prostate.

## UP-55

### Is active surveillance a safe option for low- and intermediate-risk prostate cancer?

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**Introduction and Objective:** Recent National Institute of Clinical Excellence UK guidelines recommend offering active surveillance (AS) as the preferred management for D'Amico low-risk (Gleason  $\leq 6$ , PSA  $\leq 10$ , clinically T1c/T2a) prostate cancer and discussing AS as an option for intermediate-risk disease (Gleason 7, PSA 11–20, clinically T2b). We studied histopathological reports of 314 radical prostatectomies performed in a UK cancer centre to assess the safety of these recommendations.

**Materials and Methods:** One hundred fifty low-risk and 164 intermediate-risk cases were included. Pathological features studied included Gleason scores and upgrading to  $\geq 7$ , pT3 upstaging, the presence of tumour multifocality/bilaterality and for the presence of clinically significant tumours (CSTs) (by Epstein criteria, including tumour volume  $> 0.5$  mL).

**Results:** Low-risk group ( $n = 150$ ): mean age 63 (48–69) years. One hundred fifteen (75%) and 123 (82%) exhibited multifocal and bilateral disease, respectively. Fifty-seven (38%) were upgraded while 29 (19%) had pT3 cancer on final histopathological analysis. Ninety-three (62%) cases harboured at least 1 CST. Intermediate-risk group ( $n = 164$ ): mean age 62 (51–70) years. One hundred twenty-six (77%) and 143 (87%) exhibited multifocal and bilateral disease, respectively. Twenty-five (15%) were upgraded while 68 (42%) had pT3 cancer. One hundred thirty-one (80%) cases harboured at least 1 CST.

**Conclusion:** One-fifth of low-risk cases and two-fifths of intermediate risk cases had locally-advanced cancer, and many more exhibited aggressive features. Caution should be taken when recommending active surveillance to the patients suitable for radical treatment. In the absence of large randomized trials, these guidelines appear unsafe.

## UP-57

### Predictors of upgrading prostate biopsy Gleason sum 6

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**Introduction and Objective:** Active surveillance (AS) is among the

standard treatment options in the management of good-risk prostate cancer. Prostate biopsy may underestimate the actual Gleason sum of the radical prostatectomy (RP) specimen and this possibility has created reluctance on the part of many urologists in recommending AS. In this study we examine the rate of biopsy Gleason sum 6 underestimating the RP Gleason sum in a contemporary population of surgical patients and determine factors that are predictive of more accurate biopsy grading.

**Materials and Methods:** Between March 1995 and October 2008, 635 patients underwent RP at our institution. One hundred sixty-five of these had a Gleason sum of 6, determined from a minimum 8 core biopsy, which represents the study population. Univariate and multivariate logistic regression was performed on the following variables in order to determine any statistically significant contribution to upgrading: age, clinical stage, pretreatment PSA, number of positive cores, percentage of positive cores, prostate volume and PSA density.

**Results:** Upgrading of the biopsy Gleason sum occurred in 67 (40.6%) of the 165 patients. Of these, 62 (92.5%) were upgraded to Gleason 7, 6 (9.0%) to Gleason 8, and only 1 (1.5%) was downgraded. Pretreatment PSA ( $p = 0.03$ ), the number of positive cores ( $p = 0.03$ ), the percent of positive cores ( $p = 0.01$ ), prostate volume ( $p = 0.03$ ) and PSA density ( $p = 0.008$ ) were statistically significant predictors of upgrading in univariate and multivariate analysis, where age or clinical stage did not contribute to upgrading. Patients with less than or equal to 25% positive biopsy cores and a PSA density of less than 0.15 still had a 26.2% chance of being upgraded.

**Conclusion:** Even with contemporary biopsy technique, underestimation of true Gleason sum remains common. We have identified several features predictive of upgrading low risk biopsies, but even using these variables, there remains a certain risk of upgrading. Inability to predict the true aggressiveness of cancer on biopsy will continue to complicate treatment decisions regarding active surveillance.

## UP-58

### Effect of a high-carbohydrate, high-fat diet on prostate cancer: role of Metformin as a potential growth inhibitor

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**Introduction and Objective:** Epidemiological and laboratory studies point to the fact that obesity is related to insulin resistance, hyperinsulinemia, an elevation in IGF1. These changes are directly related to the development of solid neoplasia, including prostate cancer (PCa). We have reported an association of a high carbohydrate-high fat (HC-HF) diet-induced hyperinsulinemia with accelerated PCa growth. Metformin, an antidiabetic drug, causes a reduction in insulin with AMPK activation. We are characterizing the differential effects of high carbohydrate and high fat diet on the pathological changes in xenograft tumours and prostate. In the same model, we are also investigating the effect of Metformin on the growth of human prostate cancer cells provided a HC-HF diet.

**Materials and Methods:** In Vitro study: Human PCa cells were treated with metformin for 72 hours. Cell proliferation was measured using the MTS assay. In vivo study: Athymic mice with LNCaP xenografts, were randomly assigned to HC-HF diet with/without Metformin. Body weight and tumour volume were measured weekly. Serum insulin and IGF-1 were measured by enzyme immunoassay. AKT and insulin receptor were determined by immunoblotting

**Results:** Metformin caused a significant reduction in the growth of LNCaP cell proliferation, however at high concentrations. The administration of Metformin to animals caused a dose-dependent reduction in body weight relative to the control that was 10% at 50 mg/kg compared to 38% at 250 mg/kg. The administration of Metformin also caused a reduction of food consumption in a dose dependent manner. Similarly, Metformin caused a reduction in body weight and fasting blood glucose level in the xenografts' mice. Prostate enlargement was significant with a HC-HF (surface area: 89.1, standard deviation [SD] 30.5, v. 60.3, SD 23.9, mm<sup>2</sup>,

$p < 0.01$ ). Analysis on levels of insulin and IGF and protein immunoassays are currently underway.

**Conclusion:** Metformin has been shown to cause a reduction in body weight gain partially by reducing food consumption. A reduction in insulin level by Metformin may have a direct implication in prostate cancer growth particularly in a metabolic context. These results will eventually contribute to the rationale for evaluation of the antineoplastic activity of Metformin in hyperinsulinemic prostate cancer patients.

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## UP-59

### Outcome of radical prostatectomy in Ottawa

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**Introduction and Objective:** Surgery and radiation are both standard treatment options in the management of localized or locally extensive prostate cancer. Few direct comparisons of these 2 modalities have been performed. Coinciding with the opening of the Ottawa Prostate Cancer Assessment Centre the aim of this study is to analyze the surgical outcomes of patients treated at the Ottawa Hospital. A parallel analysis will be performed by radiation oncology in patients treated with radiotherapy.

**Materials and Methods:** Between April 1995 and October 2007, 570 patients underwent open radical prostatectomy (RP) at the Ottawa Hospital, Civic Campus. Of these, 434 did not receive preoperative androgen ablation, had complete clinical data, and thus were included in analysis. Two definitions of biochemical recurrence (BCR) were considered, PSA greater than 0.2 ng/mL and PSA greater than 0.4 ng/mL. Additionally, patients receiving postoperative radiotherapy or hormones were considered primary treatment failures.

**Results:** Five- and 10-year recurrence-free survival was 79% (95% CI 73%–84%) and 72% (95% CI 62%–80%) with BCR greater than 0.2 ng/mL compared to 82% (95% CI 77–87%) and 80% (95% CI 73–86%) with BCR greater than 0.4. Clinical stage, pretreatment PSA and biopsy Gleason sum were significant predictors of disease recurrence.

**Conclusion:** These results provide local validation of the effectiveness of RP in the management of men with localized prostate cancer. We await the results of men treated with radiotherapy during this time period. This information can be used to counsel patients being evaluated in the Prostate Cancer Assessment Centre.

## UP-60

### Androgen deprivation therapy is associated with higher rates of osteoporosis and fractures in French-Canadian prostate cancer patients

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**Introduction and Objective:** In men from the United States (US), androgen deprivation therapy (ADT) was shown to predispose to skeletal related events (SREs), namely osteoporosis, hip and spinal fractures. We tested whether this effect is also detectable within a large Canadian population-based cohort.

**Materials and Methods:** We used the Quebec Health Plan database to identify 15 842 assessable men diagnosed with prostate cancer, who were treated between 1992 and 2000 with either luteinizing hormone-releasing hormone agonists [LHRHa] ( $n = 3914$ , 24.7%) or orchiectomy ( $n = 1856$ , 11.7%), or definitive therapy (radical prostatectomy [RP] or radiation therapy [XRT]) without orchiectomy or any other form of ADT ( $n = 10 072$ , 63.6%). Separate univariable and multivariable models tested the effect of orchiectomy versus LHRHa versus no ADT on the incident rate of 3 skeletal-related events (SRE). The effect of LHRHa was analyzed according to the median exposure duration ( $\leq 1.8$  yr:  $n = 2037$ ,  $> 1.8$  yr:  $n = 1877$ ). Covariates consisted of age, administrative region of residence, postal code, definitive therapy (RP v. XRT v. none), other nonskeletal morbidities and year of treatment. The diagnoses of nonskeletal morbidities were used as time-dependent covariates. Finally, we used competing-risks regression analyses to test the effect of ADT exposure

for each SRE after accounting for other cause mortality.

**Results:** Orchiectomy, LHRHa 1.8 years or less and LHRHa greater than 1.8 years were statistically significant univariable predictors of all SREs (all  $p < 0.001$ ). In multivariable analyses, LHRHa 1.8 years or less did not reach statistical significance for any SREs. Conversely, LHRHa greater than 1.8 years increased the risk of osteoporosis (HR 2.1,  $p = 0.001$ ) and spinal fracture (HR 1.8,  $p = 0.03$ ). Similarly, orchiectomy independently increased the risk of all skeletal morbidities: osteoporosis (HR 2.2,  $p < 0.001$ ), hip fracture (HR 2.0,  $p < 0.001$ ) and spinal fracture (HR 1.9,  $p < 0.001$ ). In competing risks analyses, LHRHa greater than 1.8 years and orchiectomy remained independent predictors of all 3 SREs, after accounting for the independent effect of other causes mortality (all,  $p \leq 0.02$ ).

**Conclusion:** The adverse effect of bilateral orchiectomy and LHRHa is not specific to patients from the US. It also applies to French-Canadian prostate cancer patients, where genetic, environmental and dietary risk factors are significantly different from these of men from the US.

## UP-61

### Critical illness insurance in North America: issues regarding patients with cT1 prostate cancer

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**Introduction and Objective:** Critical illness insurance (CII) is a relatively new supplemental health insurance in North America, providing a lump sum benefit to those diagnosed with one of approximately 20 disabling conditions. Prostate cancer, covered by all CII policies, is the most commonly diagnosed cancer in males aside from dermatological lesions. The most commonly diagnosed stage of prostate cancer is T1 disease. This study attempts to define the specific terms of prostate cancer coverage by CII policies, and the implications these will have on the practice of urologists in North America.

**Materials and Methods:** Policies of the major CII providers in the United Kingdom (UK), United States (US), and Canada were reviewed. The definition and coverage of prostate cancer were assessed for each company.

**Results:** Critical illness insurance is well-established the UK, with most Canadian providers adopting such policies in the last decade. American CII availability currently remains limited. The vast majority of companies that offer CII provide payment to those diagnosed with stage T2 prostate cancer, while those with stage T1 disease do not qualify for full compensation. Two Canadian providers have defined stage A (organ confined) disease as early prostate cancer, and therefore not qualified for full compensation. The majority of North American and British providers did not cover T1N0M0 disease, while others provided a reduced payment.

**Conclusion:** Patients with cT1 prostate cancer with CII who may be better candidates for active surveillance, radiation therapy, or brachytherapy may be biased as prostatectomy would ensure payment upon upstaging to pT2 disease. Nonspecific irregularities on digital rectal examination create special considerations for physicians with patients who carry CII, as a diagnosis of cT2 disease would be fully compensated. As critical care insurance increases in the North American marketplace it will be important for urologists to appreciate the influence these policies will have on their practice.

## UP-62

### The relationship between prostate tumour density and pathological and clinical outcomes

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**Introduction and Objective:** Cancer volume and more recently prostate volume have been suggested to be significant factors predictive of outcome following radical prostatectomy (RP). In this study, we evaluate the interaction of these 2 variables as tumour density in its ability to predict for pathological and clinical outcomes.

**Materials and Methods:** Between 1995 and 2007, 447 consecutive patients were treated with RP alone at the Ottawa Hospital Civic Campus. Of these, 272 had tumour and prostate volume measurements. At Memorial Sloan-Kettering Cancer Center, tumour volume was only recorded between 2001 and 2004. Of 2216 patients who underwent radical prostatectomy during this time period, 451 had tumour and prostate volume measurements. We pooled these 2 data sets resulting in a study population of 723 patients. Univariate and 2 separate multivariate Cox proportional hazards analyses incorporating patient age, pretreatment PSA, RP Gleason sum, and individual components of RP stage were conducted to assess the ability of tumour density (model 1) or cancer volume (model 2) to predict surgical margins (SM), extracapsular extension (ECE), high grade Gleason sum (7–10), and recurrence-free survival. Recurrence was defined as a PSA greater than 0.2 ng/mL and rising or postoperative use of adjuvant radiation or hormonal therapy.

**Results:** Median follow-up was 40.8 months. Tumour density predicted for all pathological and recurrence endpoints in univariate analysis ( $p < 0.0001$ ). In multivariate analysis, tumour density also predicted for all pathological endpoints; SM ( $p = 0.0002$ ), ECE ( $p < 0.015$ ), and RP Gleason sum 7–10 ( $p = 0.001$ ) as well as recurrence-free survival ( $p = 0.01$ ). Cancer volume predicted for all pathological and recurrence endpoints in univariate analysis ( $p < 0.0001$ ); however, it was only predictive of SM ( $p = 0.01$ ) and RP Gleason sum 7–10 ( $p = 0.02$ ) in multivariate analysis. **Conclusion:** Both tumour density and cancer volume are important predictors of pathological outcomes following radical prostatectomy. Tumour density is a more important variable as it predicted for all pathological endpoints and had higher statistical significance. Furthermore, tumour density was also predictive of recurrence-free survival. The significance of tumour density in predicting pathological and recurrence endpoints has implications on the surgical management and role of adjuvant therapy in prostate cancer and thus warrants further study.

## UP-63

### Prostate cancer detection in Canada: a survey of patterns of practice of urologists

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**Introduction and Objective:** Recent data provided in part by the prostate cancer prevention trial have indicated that historical cutoff levels for prostate cancer screening (PC) using a prostate specific antigen (PSA) level of 4 ng/mL may no longer be appropriate with cancer detected at much lower levels, particularly in younger men. Our aim was to conduct a contemporary survey of patterns of practice of urologists towards PC detection in Canada.

**Materials and Methods:** Five hundred ten Canadian urologists were contacted via e-mail through the Canadian Urological Association and were requested to participate in an online questionnaire on PC detection with reminder emails sent weekly for 3 weeks. The questionnaire focused on various scenarios of men whom may present of varying age and with varying PSA levels; urologists were asked to indicate their preferred plan of management.

**Results:** One hundred twenty-five out of 510 (25%) urologists completed the questionnaire. Sixty-seven percent indicated that men should be screened for PC aged 50–60 with 27% preferring 40–50 years. Seventy-five percent indicated annual PC screening should continue into the seventh decade with 20% doing so beyond age 75. Considering a 65-year-old man with no risk factors and a normal digital rectal exam (DRE), 56% would offer a biopsy if the PSA was 4.5; 35% at 3.5 and 10% at 2.5 ng/mL. Considering a 45-year-old man with no risk factors and a normal DRE, 94% would offer a biopsy if the PSA was 4.5; 77% at 3.5 and 33% at 2.5 ng/mL. The recommendations for a 55-year-old man fell in-between. Offering of biopsy increased significantly in all age groups if family history or being of African descent were present as risk factors.

**Conclusion:** A significant proportion of urologists in Canada would still not offer a prostate biopsy at the traditional PSA cutoff of 4 ng/mL for men with no risk factors. Of note, in younger men, despite recent evidence that the traditional PSA cutoff levels for PC are probably too high, only 77%

would offer a biopsy at a PSA of 3.5 ng/mL. Further studies are required to ascertain if this relates to a lack of dissemination of studies into practice or a paucity of guidelines reflecting the recent developments.

## UP-64

### Prostatic evasive anterior tumour syndrome

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**Introduction and Objective:** At our institution, we believe the number of patients presenting with a raised prostate-specific antigen (PSA) and clinical findings suggestive of anterior predominant tumours to be significant, particularly in patients with prior negative biopsy or those with low volume disease undergoing active surveillance. We review our experience with such patients and delineate the role of magnetic resonance imaging (MRI) in identifying tumours by comparing to pathology.

**Materials and Methods:** A retrospective review of our institutional database and records was undertaken to identify patients with anteriorly predominant prostate tumours on MRI whom had also undergone prostate biopsy.

**Results:** We identified 31 patients with anterior predominant tumours on MRI whom also had a biopsy positive for prostate cancer. Fourteen patients were undergoing active surveillance and the remaining 17 had prior negative prostate biopsies. Thirteen patients had radical prostatectomies. MRI was usually triggered by presenting PSA or PSA velocity. Magnetic resonance imaging had a positive predictive value for anteriorly predominant cancers of 87% (27/31) patients (including 1 repeat biopsy refusal counted as negative).

**Conclusion:** There is a subset of patients either having negative TRUS biopsy or low-volume disease undergoing active surveillance who should be considered for MRI and further biopsy as their pathology may be aggressive. A new entity may be emerging with anterior predominant tumours that are nonpalpable and we believe the term prostate evasive anterior tumour syndrome (PEATS) to be appropriate. This requires further analysis in a large prospective database with consideration for triggers as to when to conduct an MRI and targeted biopsies.

## UP-65

### Unilateral prostate cancer cannot be reliably and accurately diagnosed with systematic 10 or more core biopsy

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**Introduction and Objective:** Focal or even unilateral therapy strategies are gaining popularity in patients with low-risk prostate cancer (PCa). The assumption of these therapy modalities is that PCa can be accurately localized by clinical staging. We tested the accuracy of unilateral negative biopsy findings in low-risk PCa patients who were treated with open radical prostatectomy (RP).

**Materials and Methods:** The population consisted of 243 men with clinical stage T1c/T2a, PSA less than 10 ng/mL, a biopsy Gleason sum of 6 or less, and a maximum of 2 positive biopsy cores within 1 of 2 prostate lobes on a 10-core or higher prostate biopsy. None received any form of androgen deprivation therapy or previous prostate surgery. All patients underwent open RP in our institution. Univariable and multivariable logistic regression models were performed to identify significant predictors of unilateral PCa. Variables consisted of PSA, %fPSA, clinical stage (T2a v. T1c), gland volume, and number of positive biopsy cores (2 v. 1).

**Results:** Most of the patients were clinical stage T1c (89.7%). The median PSA was 5.4 ng/mL and a proportion of 28% had a PSA of 4 ng/mL or less. Presence of bilateral or non-organ confined PCa was reported in 64% of all patients. In men with only 1 positive biopsy core, the proportion of

bilateral or non-organ confined PCa was 60%. None of the examined variables was a statistically significant predictor of unilateral PCa in either univariable or multivariable analysis (all *p* values and adjusted *p* values > 0.05). **Conclusion:** Almost two-thirds of patients with low-risk PCa and a maximum of 2 positive unilateral biopsy cores have bilateral or non-organ confined PCa at RP. Our findings indicate that the prediction of unilateral (single lobe) PCa cannot be made with even the slightest degree of confidence. This observation should be taken into consideration when treatment decisions are made.

### UP-66

#### Health-related quality of life outcome after brachytherapy treatment of the prostate: comparison with outcome after radical prostatectomy

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**Introduction and Objective:** Measurements of health-related quality of life (HRQOL) have become a pivotal concern for patients and health care providers in selection of treatment for localized prostate cancer (PCa) given that conventional treatments such as radical prostatectomy (RP), external beam radiation (EBRT) and brachytherapy (BT) all offer similar and excellent recurrence-free survival. In this retrospective cross-sectional study, we sought to compare the HRQOL outcome in patients with PCa treated with RP or BT using a validated questionnaire [Expanded Prostate Cancer Index Composite (EPIC) and Short Form 12 (SF-12)].

**Materials and Methods:** Outcomes reported by patients treated with RP or BT as primary therapy with or without neoadjuvant hormone therapy in our institution between 1998 and 2004 were evaluated. The response rate for RP was 72% (633/883) and 70% (111/159) for BT. Minimal follow-up time was 1 year. HRQOL was compared between therapy groups comparable in prognostic variables such as disease stage, Gleason score, and pretreatment prostate-specific antigen (PSA) levels (RP: *n* = 103; BT: *n* = 111). Factors that influence HRQOL outcomes were also assessed.

**Results:** We found that the BT treatment group showed a significantly higher proportion of patients reporting a more favourable satisfaction outcome than the RP treatment group (*p* = 0.019). Patients in the RP group reported significantly less bother with urinary irritative symptoms (*p* = 0.0029) but showed significantly poorer HRQOL mean scores in the urinary incontinence domain than BT patients (*p* < 0.0001). The BT therapy group showed a significantly more favourable outcome in the obstructive voiding domain than the RP therapy group (*p* = 0.0042). There was no significant difference in mean bowel HRQOL scores between the RP and BT treatment groups (*p* = 0.2952). Both groups showed poor mean scores in the sexual domain, although no significant difference between the groups in sexual HRQOL was reported (*p* = 0.7904). Similar mean scores in both mental and physical components of SF-12 domain (*p* = 0.7644 and *p* = 0.1179, respectively) were reported, and we found equal hormonal HRQOL between the therapy groups (*p* = 0.6392).

**Conclusion:** Despite the retrospective cross-sectional nature of this analysis, our study shows more favourable overall satisfaction with patients undergoing BT treatment for PCa than RP patients. Patients in the RP group reported better urinary irritative HRQOL scores and patients in the BT group reported better urinary incontinence and obstructive voiding HRQOL scores. A larger prospective matched pair analysis comparing the 2 modalities is necessary to validate our results.

### UP-68

#### Prognostic value of insulin-like growth factor I and binding proteins 2 and 3 in patients treated with radical prostatectomy

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**Introduction and Objective:** Several studies have examined the relationship between IGF-I, and its binding proteins IGFBP-2 and IGFBP-3 with prostate cancer risk. Data about IGF family members and cancer recurrence is more controversial. Shariat showed that IGFBP-2 and

IGFBP-3 are both associated with disease progression. However, Yu suggested that IGF-I, IGFBP-2 and IGFBP-3 had no predictive value in the prognosis of prostate cancer. Based on these conflicting results, we propose to study the levels of different members of the IGF family as predictors of clinical outcome in prostate cancer.

**Materials and Methods:** Preoperative plasma levels of IGF-I, IGFBP-2 and IGFBP-3 were measured in 131 patients who were diagnosed with clinically localized prostate cancer and underwent radical prostatectomy between 1999 and 2002. Of these, 11 had received neoadjuvant hormone therapy and were excluded from our analysis because of the reported role of IGFBP-2 as an androgen-dependent predictor of prostate cancer. Clinical data was collected retrospectively and a Student *t* test was done for comparison of categorical variables while a Cox regression model was performed for multivariate analysis.

**Results:** Average age at surgery was 63.6 years, mean preoperative PSA was 11.75 (standard deviation [SD] 14.52) ng/mL and median follow-up was 7.8 years. Thirty-seven patients experienced PSA failure. Average levels of IGF-I, IGFBP-2 and IGFBP-3 were 140.5 (SD 36.2) ng/mL, 307.8 (SD 185) ng/mL and 2.023 (SD 0.554) mg/mL, respectively. Plasma IGF-I levels did not predict risk of biochemical recurrence (*p* = 0.57) nor did IGFBP-2 (*p* = 0.35) or IGFBP-3 (*p* = 0.53). They also did not correlate with clinical stage, PSA level or Gleason grade. We did notice a significant correlation between all 3 markers with the surgical margins status, but when controlling for other known prognostic factors, the correlation was no more significant. Furthermore, there was no correlation with extracapsular extension, seminal vesicle involvement or lymph node status, which suggested that the markers were not useful predictors of organ-confined disease.

**Conclusion:** Despite much interest in IGF family members association to prostate cancer, our study suggests that IGF-I, IGFBP-2 and IGFBP-3 might not be helpful independent predictors of recurrence or progression for patients with clinically localized prostate cancer.

### UP-69

#### Clinical profile of prostate cancer in the Bahamas: real men die from prostate cancer

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**Introduction and Objective:** An annual prostate cancer (PCa) week with community awareness programs and free prostate examinations were introduced in the Bahamas in 1994. This retrospective study sought to evaluate the impact of public health education initiatives on the early disease stage detection rates and cancer mortality rates.

**Materials and Methods:** Prostate cancer detection and staging were retrieved from medical records in hospitals, pathology logs, private practices and the National Department of Statistics for years 1990, 2000 and 2005. Patients were classified using D'Amico low-, medium-, and high-risk clinical profiles for PCa outcomes based on the 3 pretreatment prognostic indicators of PSA, cancer stage and Gleason score. A self-administered questionnaire was given to participants during the annual PCa awareness week to assess the impact of the media campaign to attend the prostate cancer clinic.

**Results:** There were 139 biopsy proven PCa cases identified: 31, 49 and 59 cases in 1990, 2000 and 2005, respectively. In 1990 and 2000, less than 10% had a low-risk favorable profile of a PSA less than 10, a Gleason score less than 6 and a nonclinical palpable disease; there were 16% in 2005 with 42 (70%) patients in the high-risk, poorly favorable group. The national cancer specific death rates for prostate cancer were 13.6, 23.0 and 23.4 /100,000 in 1990, 2000 and 2005.

**Conclusion:** The stage migration phenomenon and decreasing mortalities documented in developed countries, has failed to occur in our developing country. We suggest the failure of our health education initiatives may be due in part to our macho male culture and proposes a community-based participatory intervention program as a behavioral change model in male reproductive health to decrease PCa mortality in Bahamian men.

**UP-70**

**Utility of a novel in vivo prostate magnetic resonance spectroscopic imaging technique**

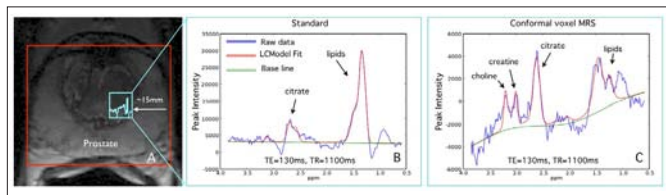
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**Introduction and Objective:** We seek to retrospectively evaluate the application of using a robust in vivo spectroscopic imaging technique in aiding diagnosis of prostate cancer in comparison to current imaging techniques.

**Materials and Methods:** Research was conducted in accordance with the research ethics board. Subjects were scanned on a General Electric 1.5T Signa MR scanner. A standard endorectal coil, in combination with a torso phased-array coil, was used for all imaging. To decrease lipid contamination artifacts, and facilitate optimal coverage of the prostate, our lab has developed a suppression technique called conformal voxel MR spectroscopy (CV-MRS) [1]. This technique automatically optimizes the placement of spatial saturation planes, thereby adapting the excitation to the shape of the prostate and reducing spectral contamination [1].

**Results:** Seventeen subjects were scanned using both the standard PRESS and the modified CV-MRS technique. Each 3D MRSI acquisition used a 16 × 8 × 8 phase encode matrix, with a voxel size of 0.42 cm<sup>3</sup>. All spectra were analyzed using the LCModel fitting package. Figure 1B and



**Fig. 1.** In (A), when the region of interest (ROI), solid line, includes the prostate and some peripheral tissue, the spectrum will be contaminated by lipid, as in (B). In (C), we present spectra from the same voxel location using the CV-MRS technique. In this voxel metabolites are clearly visualized and fitted indicating that suppression of peripheral lipids (~15 mm away) using the conformal voxel technique has an immediate effect.

Figure 1C illustrate spectra and LCModel fits obtained from the same voxel from both acquisitions. We observed a 60% (standard deviation [SD] 18%) reduction in contaminating lipids, which has resulted in a 36% (SD 18%) increase in the number of analyzable spectra when using the conformal voxel MRS technique.

**Conclusion:** Current diagnostic techniques rely on prostate biopsy, which can be subject to sampling error. MR spectroscopic imaging (MRSI) provides 3D information, which can serve as an adjunct to biopsy in delineating tumour involvement. Standard MRSI techniques often suffer from signal bleeding from peripheral voxels containing high amounts of periprostatic lipids, as in Figure 1B. This has limited the clinical application of MRSI, especially in peripheral prostatic regions. In summary, using the CV-MRS technique, which has enhanced the diagnostic quality of spectra, has improved the clinical role of spectroscopic imaging data.

**UP-71**

**Comparison of prognostic factors and outcomes of surgery for prostate cancer between East/Southeast Asians to general population**

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**Introduction and Objective:** Although considered to have a lower risk of prostate cancer in their native countries, Eastern/Southeast Asians (ESA) appear to have rising cancer rates after immigration to Western countries. However, limited data exists to define differences between patients of ESA descent and the general population. Our study assessed differences between ESA and non-ESA patients using both preoperative and postoperative variables in patients undergoing radical prostatectomy at the Prostate Centre.

**Materials and Methods:** Student *t* test and Mann-Whitney Wilcoxon rank sum test were used to assess for differences between East/Southeast Asians and the general population in all patients undergoing radical prostatectomy at the Prostate Centre in the last 27 years (March 1981 to August 2008). The following variables were compared between populations: height, weight, BMI, preoperative PSA, IPSS, biopsy Gleason score, post-operative PSA, pathological Gleason score, positive surgical margins rates and biochemical recurrence of disease.

**Results:** Within a population of 5172 patients, a total of 302 were found to be of ESA descent. ESAs were found to have significant differences in PSA and the Gleason grade at time of presentation of prostatic cancer. PSA in ESAs was increased at 12.59 compared to 11.25 in general population (*p* = 0.0092). Biopsy Gleason scores were higher in ESAs at 6.83 compared to 6.50 in general population (*p* = 0.0021). Recurrence post-radical prostatectomy was found to be lower in Asians (2.4%) compared to the general population (4.6%). Body habitus (BMI), IPSS scores, age at time of surgery and postoperative PSA values were also found to be different between populations.

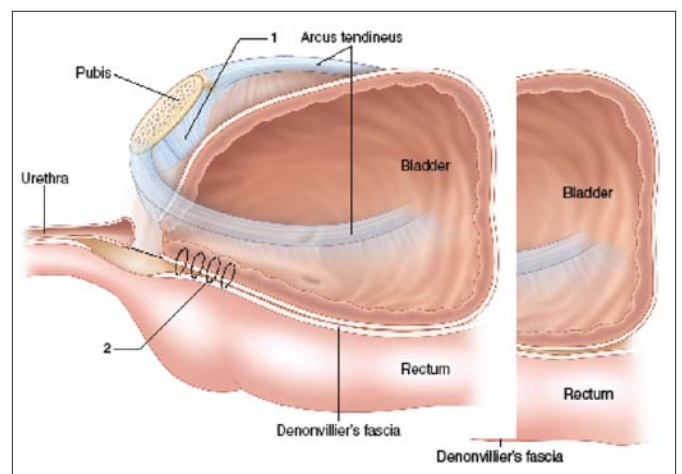
**Conclusion:** Eastern/Southeast Asians presented with statistically significant elevated values of PSA and biopsy Gleason grade. Despite having higher risk PSA and Gleason at time of presentation, recurrence rates of prostate cancer were found to be lower in the ESA population compared to the non-ESA population.

**UP-72**

**Optimizing anastomotic healing and continence mechanism support during robotic radical prostatectomy**

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**Introduction and Objective:** We present our experience with a biomechanics-based paradigm for augmenting continence recovery following robotic radical prostatectomy. Our anatomic restoration technique is aimed at providing circumferential dynamic suspensory support for the urethral sphincter complex, attenuating pelvic prolapse and downward pressure of the bladder on the healing anastomosis during micturition, and relieving tension at the anastomosis for improved healing (Fig 1).

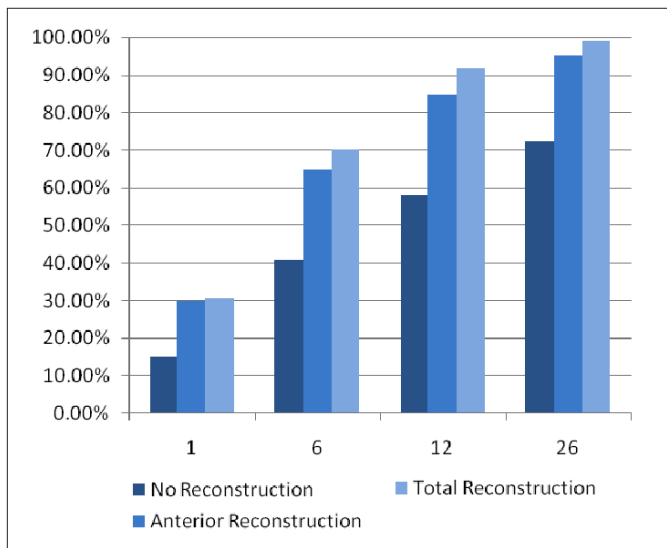


**Fig. 1.**

**Materials and Methods:** Between Jan. 1, 2005, and July 30, 2008, 1294 consecutive patients underwent da Vinci robotic-assisted radical prostatectomy (RARP) by a single experienced high-volume surgeon. Of these, 214 underwent conventional vesicourethral anastomosis (CA), 303 men underwent anterior reconstruction (AR) only and 777 men underwent total anatomic restoration (TR). Continence was defined as zero pad usage. Patients were followed up at 1-, 6-, 12- and 26-week intervals via third-party telephone interviews, and their data entered into a HIPAA-compliant database. Chi-square and Fisher exact tests were used for analysis of categorical variables.

**Results:** Continence rates at 1, 6, 12 and 26 weeks following robotic-assisted radical prostatectomy was 15.2% versus 29.9% versus 30.8%, 40.8% versus 64.9% versus 70.0%, 58.2% versus 84.7% versus 91.8%, and 72.30% versus 95.2% versus 99.1% in the CA, AR and TR groups, respectively ( $p < 0.001$ ). Clinically significant leaks occurred in 2.3% versus 1.0% versus 0.3%, and anastomotic strictures occurred in 3.7% versus 1.3% versus 0.6% in the CA, AR and TR groups, respectively.

**Conclusion:** Our approach of providing circumferential anatomic support to the continence mechanism delivers significantly improved anastomotic healing and earlier return of continence following robotic prostatectomy (Fig. 2).



**Fig. 2.** Continence rates at 1, 6, 12 and 26 weeks following robotic-assisted radical prostatectomy using 3 different techniques of bladder neck reconstruction.

**UP-73**

**Validation of the clinical target volume for radiotherapy to the prostate bed after radical prostatectomy based on magnetic resonance imaging voxel probability of gross local recurrence**  
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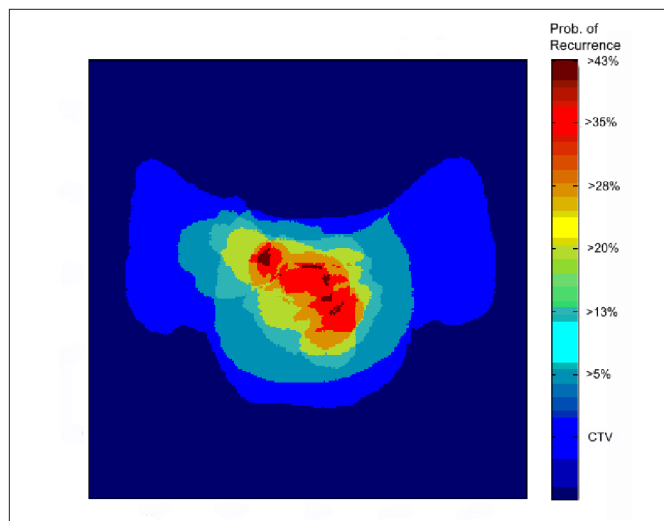
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**Introduction and Objective:** Despite evidence supporting adjuvant and salvage radiotherapy (RT) after radical prostatectomy (RP) in selected patients, optimal dose and volume selections remain at issue. Consensus definitions for anatomic boundaries of the clinical target volume (CTV) at risk of microscopic disease have recently been published by our group and others. We aim to further investigate the validity of our consensus definition by analyzing the spatial probability of gross local recurrences visualized on MRI after RP relative to CTV anatomic boundaries.

**Materials and Methods:** Seventeen patients with gross local recurrences visualized on MRI after RP were prospectively enrolled on a clinical trial ( $n = 7$ ), or retrospectively identified ( $n = 10$ ). For each patient, the CTV and gross tumour volumes (GTV) were delineated on MRI (Pinnacle<sup>3</sup>, Philips). GTVs were deformably registered to a common reference CTV using a nonlinear 3D-registration algorithm (Morpheus) based on finite element methods. Probability of gross recurrence was determined for each reference image voxel within the CTV for the cohort.

**Results:** All patients underwent RP a mean of 5.9 (range 0.8–13.7) years prior to MRI, at a mean age of 65 (range 57–81) years and with a measurable PSA (mean 4.5, range 0.1–22.7 ng/mL) at the time of MRI. GTVs (mean volume 4.71 mL, range 0.09–39.5 mL) were centred in the following regions: retrovesical (47.1%), perianastomotic (41.1%), within retained seminal vesicle, or at anterior or lateral surgical margins (5.9% each). Probability of recurrent tumour was greater than 20% in 8% of voxels within the CTV, and 0% in 59% of the voxels within the CTV.

**Conclusion:** The majority of tumour recurrences were found in the retrovesical and perianastomotic regions. More than half of the CTV never corresponded to locations of grossly recurrent disease. Future work will expand the study cohort, defining sub-regions within the CTV at increased risk of recurrence for potential dose-escalation (Fig. 1).



**Fig. 1.** Tumour recurrence probability density — sum of axial planes.