

## PODIUM SESSION 1: PROSTATE CANCER SUNDAY, JUNE 24, 12:40-13:40

### PD01.01

#### Assessing individual risk for prostate cancer

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**Introduction and Objective:** There is significant confusion on how to interpret normal and abnormal levels of PSA. New methods to interpret PSA values are needed. We constructed a comprehensive nomogram to estimate individual risk for having prostate cancer for patients who undergo PSA screening, using all risk factors known for prostate cancer.

**Methods:** We conducted a case-control study of 3108 men who all underwent a prostate biopsy for prostate cancer detection which included a subset of 408 volunteers with normal PSA levels. Factors including age, family history of prostate cancer, ethnicity, urinary voiding symptoms, PSA, free:total PSA ratio and DRE were incorporated in a predictive model. A nomogram was constructed to assess risk for any and aggressive prostate cancer (GS 7 or more). Area under the curves (AUC) were examined using receiver operating characteristic (ROC) analysis.

**Results:** Of the 3108 men, 1304 (42.0%) were found to have prostate cancer at biopsy, and 1804 (58.0%) had no evidence of cancer. Among the 408 subset of men with a normal PSA (<4.0 ng/mL), 99 (24.3%) had cancer at biopsy. All risk factors and tumor markers were important predictors for prostate cancer by multivariate analysis (*p* values 0.01 to 0.0001). The AUC for the nomogram in predicting cancer which included age, ethnicity, family history of prostate cancer, urinary symptoms, free:total PSA ratio, PSA and DRE was 0.74 (95%CI: 0.71–0.81) and 0.77 (95%CI: 0.74–0.81) for predicting high grade cancer. This was significantly greater than the AUC for a model that considered using the conventional screening method of PSA and DRE only (0.62, 95%CI: 0.58–0.66 for any cancer; 0.69, 95%CI: 0.65–0.73 for high grade cancer). From ROC analysis, risk factors including age, ethnicity, family history, symptoms and free:total PSA ratio contributed significantly more predictive information than PSA and DRE. In a subgroup of patients with a normal PSA level (<4.0 ng/mL), age was the most important determinant for prostate cancer and not PSA nor the free:total PSA ratio.

**Conclusion:** In a prostate cancer screening program, it is important to consider age, family history of prostate cancer, ethnicity, urinary voiding symptoms and free:total PSA ratio, in addition to PSA and DRE. These factors provide important predictive information that enhance estimates for cancer risk, and we provide a comprehensive nomogram that considers all these factors to individualize cancer risk for primary care physicians.

**Key Words:** prostate cancer, risk factors

### PD01.02

#### Mortality at 120 days after prostatic biopsy: a population-based study of 22175 men

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**Introduction:** Prostate cancer (PCa) is one of the most common male malignancies in North America. Transrectal ultrasound (TRUS) guided biopsy of the prostate represents the diagnostic standard, but its mortality rate has never been examined.

**Methods:** We performed a population-based study of mortality at 120 days after prostate biopsy in 22175 patients, who underwent one or more prostate biopsy sessions between 1989 and 2000. Univariable and multivariable logistic regression analyses were used and a nomogram predict-

ing 120-day mortality after prostate biopsy was developed. Risk variables consisted of patient age at biopsy, the Charlson comorbidity index and of the cumulative number of biopsy procedures. The nomogram was externally validated.

**Results:** Overall mortality at 120 days after prostate biopsy was 1.3%. Of men aged 60 years or less, 0.2% died within 120 days vs. 2.5% of 76–80 year old men. Mortality rate of 0.7% was recorded for patients with Charlson comorbidity index score equal to zero vs. 2.2%, if the score was 3–4. In the multivariable model, increasing age and increasing comorbidity score were associated with higher mortality rate. The first ever biopsy procedures carried a higher mortality risk than subsequent procedures. The nomogram was 79% accurate in predicting the probability of mortality at 120 days and the negative predictive value of 0.5% nomogram cut-offs was 99.7%.

**Conclusions:** Prostate biopsy may be associated with a fatal outcome. Our nomogram can highly accurately identify individuals at negligible risk of mortality at 120 days.

**Key Words:** biopsy, prostate cancer, risk factors

### PD01.03

#### Nomogram predicting 10 year life expectancy after radical prostatectomy or radiation therapy for prostate cancer

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**Introduction:** Candidates for definitive therapy for localized prostate cancer should have life expectancy in excess of 10 years. However, LE estimation is difficult. To circumvent this problem, we developed a nomogram predicting 10 year LE in patients treated with either radical prostatectomy (RP) or external-beam radiotherapy (EBRT) and compared it to an existing tool.

**Methods:** Between 1989 and 2000, 9131 men were treated with either RP (*n*=5,955) or EBRT (*n*=3,176), without any secondary therapy and all deaths were considered unrelated to PCa. Age at treatment and Charlson Comorbidity Index (CCI) predicted 10 year LE in Cox regression models. Two 50% split samples were used for development and validation.

**Results:** Median age was 66 years, median CCI was 1, median follow-up was 5.9 years and median actuarial survival was 13.8 years. Advanced age (*p*<0.001), elevated CCI score (*p*<0.001) and treatment type (EBRT vs. RP, *p*<0.001) were independent predictors of poor 10 year LE. The nomogram predicting 10 year LE after either RP or EBRT was 85.1% accurate in split sample validation and was 2.9% (*p*=0.007) more accurate than the existing tool. A cut-off of 70% or less was 86% accurate in identifying men who did not survive beyond 10 years.

**Conclusion:** Our nomogram can accurately identify those individuals who do not have sufficient LE to warrant definitive PCa treatment and can help optimizing therapy decision-making.

**Key Words:** nomogram, radiation, radical prostatectomy

### PD01.04

#### Natural history of untreated prostate cancer; cohort of 186 men with 5 years follow up

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**Introduction:** Watchful waiting in patients with prostate cancer (Pca) is an established treatment option for selected patients. We present a cohort of patients with 5 years of follow up.

**Methods:** 186 patients with Pca and favorable parameters or refusing treat-

ment were managed with watchful waiting. The decision to treat was based on histological upgrading in repeated biopsy, biochemical progression, or patient preference. PSA level and physical exam were done every 3 to 6 months. The patients were offered re-biopsy annually or if there was a change on DRE or PSA value. Progression was defined as;  $\geq$ T2b,  $\geq$ 3 positive cores,  $>$ 50% of cancer in at least one core or predominant Gleason pattern of 4 in re-biopsy.

**Result:** Mean age at diagnosis was  $69 \pm 6.6$  years. Median PSA at diagnosis was 6.6 ng/dl. Initial Gleason score was  $<$ 7, 3+4, 4+3,  $\geq$ 8 in 131, 25, 9 and 14 patients, respectively. Median follow up was 59 months. 54 patients met the criteria of progression; 28 of whom were treated. Median PSADT of these patients was 64 months compared to 103 months of those who did not progress. 53 patients (28%) were treated; 10 of whom due to patient preference, 41 due to either biochemical or local progression or both and 2 due to distant metastasis. All 9 patients treated with radical prostatectomy had organ confined disease except one. Mean time to treatment was 44.5 months ranging from 7–188 months; 6 patients developed metastasis; 4 of whom refused treatment when recommended by the treating urologist and developed metastasis before treatment or within the first 3 years post-treatment and the other 2 (4%) developed metastasis despite treatment. One patient died of the disease.

**Conclusion:** A significant proportion of patients with prostate cancer on watchful waiting will remain with stable disease for a long time and may not require treatment. A significant proportion of them will also have a negative PSA velocity.

In patients with favorable prostate cancer, watchful waiting with regular evaluation and repeated biopsies allow treatment when the disease shows signs of progression and should result in low rate of metastasis and death from Pca.

**Key Words:** prostate cancer, prostate volume, prostatitis

### PD01.05

#### Thirty-day mortality after radical prostatectomy in over 9000 patients: validation of a predictive nomogram

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**Introduction:** Thirty-day mortality associated with radical prostatectomy (RP) ranges from 0.5% to 0.64%. It is influenced by age, comorbidities and possibly surgical volume (SV). To date there is no tool assessing the combined effects of these variables to predict the probability of 30 day mortality.

**Methods:** We assessed 30-day mortality after RP in a population-based cohort of 9208 consecutive patients treated between 1989 and 2000. Univariable and multivariable logistic regression analyses were used and a nomogram predicting 30-day mortality after RP was developed and internally validated with 200 bootstrap resamples. Patient age at RP, the Charlson Comorbidity Index (CCI) and the annual SV of the urologic surgeon represented predictors.

**Results:** Overall 30-day mortality was 0.52%. Of men aged  $<$ 69 years,

0.44% died within 30 days vs. 0.97% aged 69 years or older. Thirty-day mortality increased with increasing CCI score (0.23% if CCI score = 0 vs. 3.3% if CCI score  $>$ 6). Surgical volume dichotomized as  $>$ 27 RPs (0.07% 30-day mortality) vs.  $<$ 27 RPs (0.6% 30-day mortality) represented the most informative SV cut-off. The CCI demonstrated the highest predictive accuracy (64.8%) vs. age (64.3%) vs. SV (60%). In multivariable analyses, age, CCI and SV represented independent predictors of 30-day mortality. The nomogram was 76.4% accurate and had a 99.7% negative predictive value, when a 0.5% cut-off was used.

**Conclusion:** There is a non-negligible risk of short term mortality after RP. The nomogram can accurately identify those at an over-average risk of 30-day mortality. Alternative treatment options may be more actively pursued in those patients.

**Key Words:** prostate cancer, radical prostatectomy, risk factors

### PD01.06

#### Comparing PSA triggers for treatment for men with prostate cancer on active surveillance

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**Background:** Active surveillance is becoming an accepted management option for men with localized prostate cancer. PSA metrics are the most commonly used triggers for starting treatment. The objective of this study is to compare commonly used PSA triggers.

**Methods:** A prospective phase II study of patients with favorable clinical parameters (stage T1b-T2b N0M0, Gleason score  $\leq$  7, PSA  $\leq$  15 ng/ml) on active surveillance with selective delayed intervention (AS) was initiated in 1995. Those who had a PSA<sub>dt</sub>  $\leq$  3 y, grade progression on rebiopsy or doubling in size of a clinical nodule were offered radical intervention. The remaining patients were closely monitored and formed the cohort for this study. The proportion and frequency of patients who would have been offered treatment based on the following PSA<sub>dt</sub> triggers were calculated: i) PSA threshold (PSAt) of 10 ng/ml for patients with an initial PSA  $<$  10; ii) PSAt of 20; iii) a linear regression of ln(PSA) vs time  $<$  2y for all PSA values (LR-PSAdt); iv) ln(PSA) vs time  $<$  2y using the first and last PSA on record (FL-PSAdt); v) actual PSA velocity (aPSAv)  $>$  2y over last year; vi) calculated PSA velocity  $>$  2y (cPSAv); and vii) a general linear mixed model (GLMM) of ln(PSA).

**Results:** 231 patients had more than 6 mo follow-up; 134(58%) remain on AS and form the cohort for this study. As of March 2006, the median follow-up was 4.9 y (1.0–9.6 y). No patient has died of prostate cancer or had metastatic disease; 14 (10.4%) have died of other causes. The following proportion patients would have received treatment for the various definitions: 14.9%, PSAt  $>$  10; 10% PSAt  $>$  20; 39% LR-PSAdt  $<$  2y; 39% FL-PSAdt  $<$  2 y; 49% aPSAv  $>$  2y; 49% cPSAv  $>$  2y. No patient had a PSA<sub>dt</sub>  $<$  2y using GLMM.

**Conclusion:** Patients followed on AS may be overtreated if the PSA<sub>dt</sub> is calculated using PSAt  $>$  10, PSAt  $>$  20, LR-PSAdt, FL-PSAdt, aPSAv  $>$  2y or cPSAv  $>$  2y.

**Key Words:** prostate cancer, PSA, surveillance

## PODIUM SESSION 2: PROSTATE CANCER SUNDAY, JUNE 24, 14:40-15:30

### PD02.01

#### High surgical volume is associated with lower rate of secondary therapies after radical prostatectomy for localized prostate cancer

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**Introduction:** Surgical volume (SV) defined as the number of radical prostatectomies (RP) performed within one calendar year may represent an important determinant of cancer-control. We assessed the relationship between SV and the rate of use of secondary therapies after RP.

**Methods:** The cohort consisted of 7937 men treated with RP between 1989 and 2000. Median follow-up was 6 years. All were treated by 130 surgeons who had an average individual annual treatment volume of 16.6 cases (median 13, range 1–52). Secondary treatment was defined as radiotherapy or hormonal therapy or orchiectomy. Univariable and multivariable Cox regression analyses targeted the rate of secondary treatment after RP. SV was coded as a cubic spline. Age and Charlson comorbidity index at RP represented covariates.

**Results:** Secondary treatment was delivered to 1982 (25%) of 7937 patients. The median failure-free survival was not reached (mean 11.8 years). The average SV was 16.6 (median 13) RP. SV was indirectly related to the use of secondary treatment and represented independent predictor of secondary treatment use after RP ( $p=0.02$ ). Multivariate cubic spline analyses showed that the rate of secondary treatment sharply decreased with increasing SV. This trend persisted up to SV of 24 RP per year.

**Conclusion:** Surgical volume is a determinant of treatment-failure, evidenced by the use of secondary therapies. Surgeons performing 24 RPs per year had the lowest rate of secondary treatment use.

**Key Words:** prostate cancer

### PD02.02

#### Androgen deprivation therapy is associated with high prevalence of metabolic syndrome and diabetes mellitus

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**Introduction:** Androgen deprivation therapy (ADT) is the main therapeutic approach for men with locally invasive or metastatic prostate cancer. Several studies in patients on ADT suggest an increased prevalence of metabolic syndrome (MetS) and increased insulin levels, both of which are associated with an increased risk for cardiovascular events. We evaluated patients on ADT for incidence of new, previously not diagnosed MetS and diabetes mellitus type 2 (DM2).

**Methods:** We reviewed the charts of consecutive patients on androgen deprivation therapy, and first determined the prevalence of diabetes mellitus and hyperlipidemia. Patients without any these diagnoses underwent an evaluation, including measurement of blood pressure and waist circumference, and a laboratory evaluation (fasting cholesterol profile and glucose tolerance test). The presence of MetS was diagnosed according to the revised NCEP/ATPIII criteria (2005), DM2 was diagnosed based on a glucose tolerance test (GTT).

**Results:** Thirty-five charts were reviewed, 2 patients were excluded because of adrenal insufficiency and chronic renal failure. DM2 was present in 7 patients, 3 of these had been diagnosed after the initiation of ADT. Five patients were taking a statin, indicating dyslipidemia. Of the remaining 21 patients, 12 agreed to undergo evaluation. The median age (range)

was 75 (63–90) years, ADT was given for 50 (0–120) months. A new diagnosis of MetS was made in 5 (42%) patients, and of DM2 in 2 patients.

**Conclusion:** In this small group of patients on androgen deprivation therapy, we found a high prevalence of previously undiagnosed MetS and DM2. Prospective studies are required to determine if the relation between ADT and these metabolic changes is associative or causative, and if proper management of MetS and DM2 decreases the high risk for cardiovascular events.

**Key Words:** diabetes, hormone therapy, prostate cancer

### PD02.03

#### Androgen deprivation therapy for prostate cancer treatment: the role of the time of exposure on the risk of bone fractures

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**Introduction:** Recent reports highlighted the increase in the rate of bone fracture in patients (pts) subjected to androgen deprivation therapy (ADT) for prostate cancer (PCa). We tested the hypothesis that the ADT exposure and its magnitude may affect the rate of bone fractures in PCa pts.

**Methods:** Within a large cohort, 5715 (38.5%) PCa pts were treated with ADT (defined as orchiectomy or GnRH inhibitor) at various times after PCa diagnosis. Conversely, 9124 PCa pts were never exposed to any kind of hormonal therapy. Univariable and multivariable Cox regression analyses addressed the association between ADT and fracture rate. Age and baseline comorbidities, administration of anti-androgens and ADT exposure were used as covariates in multivariable analyses.

**Results:** Median age was 68 years (range 29–97) and the median number of baseline comorbidities was 2 (range 0–14). Of 5715 pts, 238 (4.2%) pts received ADT for less than 3 months, 3032 (53.1%) pts for 3–24 months and 2445 (42.8%) pts for more than 24 months. In univariable analyses, ADT was associated to a 1.74-fold increase in the risk of bone fracture ( $p<0.001$ ). After adjusting for age, number of comorbidities and delivery of anti-androgen therapy, ADT remained associated to a 1.67-fold increase in the risk of bone fracture ( $p<0.001$ ). When the time of exposure was added to the multivariable model, independently from the length of the exposure, ADT was associated to a higher risk of bone fracture (HR 1.45–2.01) compared to pts who never received any hormonal treatment ( $p<0.001$ ).

**Conclusion:** Our findings confirm the increase in the risk of fractures related to ADT in PCa patients. Moreover, even brief exposures increase the risk.

**Key Words:** androgen, prostate cancer

### PD02.04

#### Disease outcome of patients with a PSA $\geq$ 20 NG/ ML treated by radical prostatectomy: analysis of 185 patients

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**Introduction:** Patients with high PSA levels have often been recommended treatment with either radiation therapy or androgen deprivation because of the high risk of metastasis. We reviewed our experience in patients treated by radical prostatectomy (RP) in order to identify favourable prognosis variable as well as disease free survival in patients with a serum PSA  $\geq$ 20. Furthermore, we evaluated the effect of adjuvant hormone and external beam radiation therapy on the pathological stage and risk of biochemical failure.

**Methods:** Between January 1989 and December 1999, 185 patients with

a median age of  $62.5 \pm 6$  years and having a preoperative PSA  $\geq 20$ , underwent a RP. None of these patients had distant metastasis on radiological exam. Pathological and clinical data (staging, Gleason score, recurrence, neoadjuvant and adjuvant treatment) for each patient was examined. The Kaplan-Meier method was used to analyze the disease-free survival for PSA and clinical recurrence.

**Results:** Median PSA was  $42.06 \pm 46.48$ . 89 (48%) had a PSA between 20 and 30, while 82 (33%)  $\geq 40$ . With a median follow up of 7.41 years 29 (16%) patients died from prostate cancer, 17 (9%) developed bone metastasis and 92 (50%) remained biochemical free with or without radiation and / or androgen deprivation treatment.

**Conclusion:** These results suggest that radical prostatectomy has a role in treating select patients with a preoperative serum PSA  $\geq 20$ . While surgery alone is not sufficient, the adjunct of radiation and / or androgen deprivation may prolong survival.

**Key Words:** prostate cancer, PSA, radical prostatectomy

### PD02.05

#### Clinical T3 prostate cancer treated with radical prostatectomy: pathological and long-term outcomes

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**Introduction:** Locally advanced prostate cancer (cT3) is found in up to 5 percent of newly diagnosed men. However, the role of radical prostatectomy (RP) in these patients is controversial. We assessed the rate of favorable pathology at RP and of BCR-free survival in men with cT3.

**Methods:** Of 15,767 patients, 208 (1.3%) were cT3, and were treated with RP at 6 different institutions in North America and Europe. Statistical analyses addressed pathological stage at RP and Kaplan-Meier analyses addressed the rate of BCR after RP.

**Results:** Mean age was 61 years (range 39–79) and mean PSA was 13.8 ng/ml (range 0.12–47.3). Of all cT3 patients, 87 (41.8%) had favorable pathological findings at RP manifested by 9.1% OC stage or specimen confined (32.7%) disease (ECE positive, negative SVI, negative LNI and negative surgical margins), or pathological Gleason sum 2-6 regardless of pathological stage (7.2%). The overall actuarial median time to BCR was 2.8 years and at 5 years 73 (35.2%) patients were BCR-free (Fig. 1). As shown in figure 2, the actuarial median time to BCR was 5.6 vs. 1.8 years, respectively for those with favorable outcomes vs. the others ( $p < 0.001$ ). At 5 years, 120 (57.9%) patients were BCR-free vs. 42 (20.3%) for those with unfavorable pathology ( $p < 0.001$ ).

**Conclusion:** Despite clinically adverse presentation (cT3), almost half of these patients show favorable pathological characteristics at final pathology and 57.9% of those with favorable pathology are BCR-free at 5 years. These findings suggest that RP is a valid treatment option for patients with cT3 PCa.

**Key Words:** prostate cancer, relapse, stage

### PD02.06

#### Salvage therapy with bicalutamide 150 mg in patients with psa failure under LHRH therapy or surgical castration for advanced prostate cancer

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**Introduction:** The objective of the current study was to evaluate the potential benefit of sequential introduction of Bicalutamide 150 mg therapy in patients with rising PSA under definitive LHRH therapy or surgical castration for advanced prostate cancer

**Methods:** The cohort comprises 27 patients in which 4 received definitive therapy with LHRH or a surgical castration for metastatic cancer and in 23 prostatectomy patients with positive lymph nodes or locally advanced cancer initiated immediately after surgery or upon first evidence of PSA failure. A retrospective analysis of the management evaluated the duration of response initial to hormone therapy and prior use of anti-androgen alone or in combination. All patients received Bicalutamide 150 mg in addition to their LHRH therapy when PSA failure was confirmed by at least three consecutive rises in the serum value. A decrease of more than 50% of the PSA value was considered a partial response and the duration of this response was assessed until PSA rose back to the pre-treatment level.

**Results:** A partial or complete response was observed in 17/27 (63%) patients. The duration of response ranged from 6 to 72 months with a mean of 22 months and a median of 18 months. In four patients, two secondary responses were observed with the sequential introduction of first Bicalutamide 50 mg resulting in a response lasting between 8 to 43 months and an additional 8 to 29 month response when increasing the dose to Bicalutamide 150 mg after failure of the 50 mg regimen. It is of note that all 10 patients who showed no response to Bicalutamide 150mg therapy had prior therapy involving the use of an anti-androgen for variable lengths of time either as neoadjuvant or adjuvant. In all cases the use of anti-androgen was stopped several months and more often years before the introduction of Bicalutamide 150 mg. Interestingly, 11/17 responding patients had received prior anti-androgen therapy during the course of their disease.

**Conclusion:** Bicalutamide 150 mg appears to be an effective second line therapy that can provide a significantly lengthy response averaging 1 fi to 2 years in patients with PSA failure under definitive hormone therapy.

**Key Word:** PSA

# PODIUM SESSION 3: RENAL CANCER AND MINIMALLY INVASIVE SURGERY

## MONDAY, JUNE 25, 13:00-13:50

### PD03.01

#### Robot-assisted laparoscopic radical prostatectomy at a Canadian institution: initial experience at the University of Western Ontario

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**Introduction:** Robot-Assisted Laparoscopic Radical Prostatectomy (RALRP) is an accepted surgical option for localized prostate cancer. This technique offers the advantages of laparoscopic surgery while adding the benefits of enhanced vision, intuitive movements and greater degrees of freedom. Thus far, experience with this technique has been limited in Canada, primarily due to high operating costs. We present our experience with 72 cases of RALRP at The University of Western Ontario.

**Methods:** From April 2004 to November 2006 we performed RALRP in 72 patients with localized prostate cancer. With institutional approval we prospectively collected baseline demographics including age, serum PSA, prostate volume, clinical stage and biopsy Gleason score. Intraoperative outcomes including operative time, estimated blood loss (EBL), usage of nerve-sparing technique, and open conversion rates were recorded. Complications, pathologic stage, margin status and pathologic grade were collected postoperatively.

**Results:** Average patient age was 60.6 years with an average prostate volume of 38.6g. Clinical stage was T1c (68.1%), T2a (23.6%), T2b (5.5%), T2c (1.4%) and T3a (1.4%). Average preoperative PSA was 6.51 with biopsy Gleason scores of 5(3%), 6 (70%) and 7 (27%). The mean operative time was 272 minutes and the mean blood loss was 432 mL. Nerve-sparing technique (either unilateral or bilateral) was utilized in 47 (65.3%) patients. Conversion to open surgery was required in 5 patients however this was primarily in the early stages of the program. Eighteen patients had perioperative or postoperative complications with the majority being minor in nature. Overall, 25 (34.7%) patients had positive surgical margins with higher rates in pT3 patients (50.0%) vs. those with pT2 disease (31.5%). One surgeon collected continence data using the UCLA PCI questionnaire in 27 patients with 20 (74.1%) using 0-1 pads per day by 3 months.

**Conclusion:** RALRP is a safe and effective operation with minimal morbidity. The results of our study correspond with the initial outcomes from several other centres utilizing this technique. With increasing surgical volume, we expect to see continued improvement in outcomes with decreased operative times, EBL and rate of positive surgical margins. Further analysis of both mid and long term outcomes is required.

**Key Words:** laparoscopy, prostate cancer, robotics

### PD03.02

#### The natural history of small renal masses: a prospective multi-center Canadian trial

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**Introduction:** The incidence of asymptomatic renal masses is increasing, in part due to widespread imaging. This has led to a stage and grade migration in new renal cell carcinomas (RCC) to small, lower grade tumours, which have limited growth potential. To better define the nat-

ural history of small renal masses presumed to be RCC, we evaluated patients newly diagnosed with T1aN0M0 renal tumors who elected conservative management with surveillance.

**Methods:** Eight Canadian centers prospectively enrolled 100 patients with 121 renal tumors (99 solid and 22 complex cystic masses) from 2002 until 2006. Patients were eligible if elderly, had comorbidity or refused treatment. They were invited to undergo percutaneous biopsy for pathological diagnosis, genomic analysis and tissue banking. Active surveillance with serial imaging was scheduled at 3 months intervals in year 1 and 6 months in year 2 or until progression occurred (increase to 4 cm or volume doubling in <12mo). Pathologically benign tumors were imaged annually. The study endpoints were the time to and rate of tumour progression.

**Results:** The mean tumor diameter at diagnosis was 2.1 cm (range 0.4–3.9 cm; mean volume 6.4 cm<sup>3</sup>). Forty-four biopsies were performed which confirmed malignancy in 56% of the specimens. Of the remaining 34%, 11 were normal kidney, 2 angiomyolipoma and 1 oncocytoma. Four biopsies were not diagnostic. Over a mean follow-up of 10 months, the average growth rate was 0.14 cm/year, and did not differ statistically from zero growth ( $p=0.07$ ). Two patients met out criteria for tumor progression but continue to be followed conservatively due to the presence of comorbidities. Only one patient died from an unrelated cause, and no patient developed metastatic disease. Molecular studies of prognostic factors for progression are in progress.

**Conclusion:** A number of studies have demonstrated that most but not all small renal masses are RCC and most appear to grow slowly and have limited potential for metastases in the short term. This is the first multi-centre prospective study and the first to involve routine needle biopsy. Initial active surveillance with serial imaging and delayed surgery for progression appears to be a safe option in short term in our population. Delayed treatment for tumor progression is unlikely to adversely affect long-term outcomes.

**Key Words:** renal cell carcinoma, surveillance

### PD03.04

#### Watchful waiting strategy for selected patients with renal masses: updated results and long-term follow up

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**Introduction:** The aim of this study was to evaluate the outcome of watchful waiting strategy in patients with renal masses.

**Methods:** Medical records of patients with renal masses diagnosed between January 1992 and May 2006 were reviewed retrospectively. We identified 45 patients with renal masses under observation. Of these 45 patients, 35 with 44 renal masses smaller than 4 cm in diameter at the time of diagnosis and followed for at least 6 months were included in this review. Patients elected for observation because of age, co-morbidity, mass in solitary kidney or bilateral renal masses with fear of dialysis. Medical records were reviewed to determine size and volume changes as well as clinical progression requiring treatment, development of metastatic disease or death.

**Results:** 35 patients (21 men and 14 women) with 44 renal masses were observed. Mean age of these patients was 71.8 years. The majority of these patients (31 of 35) were asymptomatic at the time of diagnosis. Average initial tumor diameter was 2.2 cm ranging from 0.5 to 4 cm with median diameter of 2.1 cm. Mean and median follow-up were 44.3 and 36

months, respectively. Of the 35 patients 2 (5.7%) were lost follow up, 8 (22.9%) underwent surgical resection, and 8 (22.9%) died of other causes. Mean size growth rate of 0.21 cm/year ranging from -0.03 to 1.9. Mean and median volume growth rate was 2.7, and 1.4 cc/year, respectively. Progression to metastatic disease was identified in two patients (5.7%).

**Conclusion:** Most renal masses will grow if observed and may require treatment. Initial tumor size cannot predict the natural history of renal cancer. A risk of developing metastatic disease exists in this patient population. Further research should focus on the role of biopsy and on identification of prognostic parameters allowing more accurate prediction of tumor growth and metastasis.

**Key Words:** renal cell carcinoma, surveillance, watchful waiting

### PD03.05

#### Teaching laparoscopic radical prostatectomy in academic and private hospitals: the mentored approach

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**Introduction:** We developed a novel teaching and mentoring method called "block" surgery to simplify and improve time efficiency and safety while maintaining acceptable oncological and functional outcomes during the learning curve of laparoscopic radical prostatectomy (LRP).

**Methods:** Videos of a LRP were analyzed and broken down into 10 key "blocks" assigned different levels of difficulty. Mentorees progressed gradually through each "block". We compared the clinical outcomes when the mentoree did <50% of the case (group I), >50% of the case (group II), 100% of the case (group III) and when the mentor did the case alone ( $\pm$  fellow or resident) (group IV). This was a multi-center study.

**Results:** Prior to the study all mentorees had at least 100 laparoscopic cases completed and the mentor had completed 62 LRPs. A total of 230 cases (Group I – 32 cases, Group II – 26 cases, Group III – 38 cases, Group – 134 cases) were completed. There were no significant demographic differences between the 4 groups and no differences were noted between group I, II, III and IV with respect to the following parameters: median blood loss (225, 300, 350, 200 mL), mean morphine use post-op (3.14, 1.55, 0.18, 0.5 mg), length of stay (36, 48, 24, 42 hrs), conversion rate (0 in all groups), complications, staging and positive margins. A difference was noted in the mean operative time (219, 232, 213, 180\*,  $p < 0.05$ ). At 6 months, 129 subjects were available for continence and erectile functional assessment. For continence 80% were using no pads and 20% were using 1-2 pads. For erectile function, return of erections were similar in all 4 groups.

**Conclusion:** LRP surgery minimizes some of the morbidity associated with open surgery but it's complex and requires advanced laparoscopic skill sets. Participation in our "block" surgery mentorship programme has diminished the learning curve and has allowed safe implementation of a LRP programme with acceptable oncological and functional outcomes.

**Key Words:** education, laparoscopy, prostate cancer

# PODIUM SESSION 4: PEDIATRIC UROLOGY

## MONDAY, JUNE 25, 15:20-16:10

### PD04.01

#### Competence in pediatric urology upon graduation from residency: perceptions of residents, program directors and pediatric urologists

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**Purpose:** To clarify the scope of pediatric urologic interventions that Canadian Urology Residents should be competent to perform upon graduation.

**Methods:** A web and paper based survey was conducted from April 05 – June 06. Senior Urology Residents (SUR), Urology program directors (UPD), and Pediatric Urologists of Canada (PUC) members from all 12 Canadian training Programs were surveyed. Questions focused on which of 23 pediatric urologic procedures the 3 study groups felt that Residents would be competent to perform and which they would perform upon completion of residency without further fellowship training. Procedures were based upon the “A”, “B” and “C” lists of procedures (least complex to most complex) as outlined in the Royal College of Physicians and Surgeons of Canada (RCPSC) objectives of training for Urology.

**Results:** Response rates were 78%, 100% and 78% for SUR, UPD and PUC respectively. Exposure to pediatric urology during residency was uniform (average 5 months total time) and considered sufficient by 71% of UPD and 69% of SR, but only 45% of PUC members. Overall, the 3 groups agreed upon the level of competence and probability of performing level “A” and “C” procedures. However, there was significant disagreement between PUC members and UPD ( $p=0.005$ ) as well as between PUC members and SUR ( $p=0.004$ ) regarding competence in the “B” list of procedures which are defined in the RCPSC objectives as “should know how to do...but may not have actually done independently during residency.” PUC members tended to rate competence much lower than program directors and senior residents for these procedures.

**Conclusions:** Perceived ultimate competence is consistent between Residents, Program Directors and PUC members for procedures at the extremes of complexity. Fellowship trained Pediatric Urologists perceive Canadian residents’ exposure to Pediatric Urology as insufficient and their competence for procedures of moderate complexity as inadequate. Ongoing assessment of the RCPSC objectives for training in Pediatric Urology is required.

**Key Words:** education, pediatric, residency

### PD04.02

#### Failed pyeloplasty in children: comparative analysis of retrograde endopyelotomy vs. re-do pyeloplasty

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**Purpose:** To compare retrograde endopyelotomy (RE) to open re-do pyeloplasty for treatment of failed pyeloplasty in children.

**Methods:** 478 patients underwent pyeloplasty between 1997 and 2005. Of these, 30 (6.3%) had a secondary UPJO which was managed by retrograde endopyelotomy in 18 and re-do pyeloplasty in 12. Age, operative findings, stent placement and type at initial pyeloplasty, presentation of secondary UPJO, hospital stay, complications and success rate (SR) were compared between the 2 groups. Success was defined as radiographic relief of obstruction, as determined by ultrasound or diuretic renography at the latest follow-up (F/U). An indwelling ureteral stent was placed in all patients and removed 8-12 weeks post-operatively.

**Results:** Mean F/U after primary surgery was 15.8 (3–60) mo for RE and 47 (3–108) for RP. Mean age at RE was 7.4 (2–14) yrs and at RP 7.3 (1–17).

Mean F/U after RE was 47 (15–132) m and after RP 33.1 (12–78). RP was performed through a flank incision (10 dismembered/ 2 ureterocalycostomy). RE technique consisted of laser and cautery wire balloon in 10 and 8 pts respectively. RP was successful in all pts, while RE failed in 55.6% of cases (4- stricture >1cm / 4- age <3 yr at surgery). Cautery wire balloon endopyelotomy had a SR of only 12.5% ( $p=0.05$ ). After failed RE ( $n=10$ ), 3 pts underwent RP (SR=100%), 2 antegrade endopyelotomy (AE) (SR=50%) and 5 repeated RE (SR=40%). The child who failed AE underwent RP and was cured. Of the 3 pts who failed a 2nd RE, 1 had RP, 1 AE and 1 a 3rd RE. All children remain free of obstruction at last F/U.

**Table 1. Abstract PD04.02**

Variables	RE $n=18$ (%)	RP $n=12$ (%)	$p$
Age < 3 yrs	4 (22.2)	4 (33.3)	NS
Crossing vessels	2 (11.1)	1 (8.3)	
Type of stent at pyeloplasty			
Internal/external stent	3 (16.6)	3 (25)	
No stent	5 (27.7)	2 (16.6)	
Double J	10 (55.5)	7 (58.3)	
Presentation 2ndary UPJO			
Pyelonephritis	4 (22.2)	3 (25)	
Obstruction	18 (100)	12 (100)	
Abdominal pain	9 (50)	5 (41.6)	
Hospital stay (days)	1.3	2.9	<0.01
Complications	0	1 (penrose leakage)	
Success rate	8 (44.4)	12 (100)	0.005

**Conclusion:** Single RE had a significantly lower success rate than RP after failed pyeloplasty in children. We speculate that age less than 3 yrs, long stricture at the UPJ and use of cautery wire balloon are bad prognostic factors for success of RE in the management of secondary UPJO.

**Key Words:** obstruction, pediatric, ureteroscopy

### PD04.03

#### Blunt renal trauma in a tertiary pediatric trauma center: management, outcome and complications

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**Introduction:** Renal injuries accounts for 1.3% of the traumas in the pediatric population. It is usually managed conservatively. Higher grades of renal trauma have a greater likelihood of morbidity. We review the management, outcome and complications of these injuries in children.

**Material and methods:** Retrospective analysis of the patients with blunt renal trauma seen at a pediatric tertiary trauma center from 1996 to 2005.

**Results:** 86 patients, 67 boys, median 14 years of age, right kidney trauma in 43 (50%) cases. Gross hematuria in 65/86 (76%), microhematuria in 19/86 (24%) and 2 had no blood in the urine. The Table shows clinical parameters and imaging findings. Mechanism of trauma: sports 42/86(49%), playground activity 17/86(20%), MVA 13/86(15%), bike 10/86 (12%), others: 4/86(4%).

**Table 1. Abstract PD04.03**

Blood pressure (mm/hg)	Mean (SE): 122(11.7)/69(9.7)
Hemoglobin (mg/dl)	Mean (SE): 132(3.54)
CT Grades* (n=51)	I: 27 (52%), II: 11 (22%), III: 6 (12%), IV: 3 (6%) and V: 4 (8%).
US Findings (n=35)	18/35 (51%) with perinephric and sub-capsular hematoma.
Associated injuries 16% (14/86)	Liver in 3, spleen in 3, lung 1, bones 7.
Early complications 7% (6/86)	Urinoma 2, delayed bleeding 2, pleural effusion 1, blood transfusion 1, persistent fever 1.
Delayed complications 19% (16/86)	Renal scar 15, hypertension 1, DMSA with decrease in ipsilateral renal function 6, renal cyst 2.

\*CT graded using the American Association for the Surgery of Trauma Organ Injury Scale.

All patients were managed conservatively. One patient needed a double-J stent for urinary extravasation. Mean stay in hospital was 3.4 days, mean follow up 8.1 months (1–72).

Sixteen children (19%) had delayed complications, and amongst them 56% (9/16) were class I to III.

**Conclusion:** Blunt renal trauma in pediatric population can be safely managed conservatively. All 86 patients were followed clinically and only one case needed a double J stent. Early complications were more common in high grade (IV, V), but interestingly 56% (9/16) of those with delayed morbidity were low-grade lesions. Further studies are necessary in this subgroup of children, meanwhile it seems to be important to consider counseling the parents about the potential morbidity of classes I-III renal trauma.

**Key Words:** kidney, pediatric, trauma

#### PD04.04

##### Laparoscopic extravesical ureteral reimplantation in children

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**Introduction:** Laparoscopic extravesical ureteral reimplantation in children is technically demanding with sparse literature to aid in mastering the learning curve. We present a video demonstrating our current technique and lessons learned after 20 cases in children 4–15 years of age.

**Methods:** We utilize a 4 port transperitoneal technique with the patient in the supine position and the bladder controlled with transurethral irrigation. We find it useful for learning purposes to divide the case into 4 segments: 1. access 2. uretero-vesical junction exposure 3. detrusor tunnel dissection 4. tunnel suturing. Megaureters, duplicated ureters and bilateral high grade reflux are relative contra-indications initially.

**Results:** 1. Access is obtained under direct vision at the umbilicus with a 5mm 00 degree telescope. Three other 5mm ports are placed at the level of the anterior-superior iliac spine. 2. Initially we exposed the ureter at the pelvic brim and followed it down to the bladder but have since moved to open the peritoneum directly adjacent to the bladder. The assistant

holds the ureter with a vessel loop to facilitate mobilization up to the pelvic brim. The detrusor tunnel is measured and marked in a straight posterior-anterior line and exposed with 2 percutaneous traction sutures. 3. The superficial detrusor tunnel is scored with electrocautery. The deeper detrusor tunnel is dissected with a combination of sharp dissection with scissors and cutting current with a right-angled electrocautery. 4. The tunnel is closed with back-hand, interrupted 5-0 PDS sutures on a RB1 needle, controlled with 3 mm forceps and needle driver (KOH micro, Storz). **Conclusion:** The learning curves for ureter exposure and tunnel suturing are quite reasonable and these segments are efficient when performed methodically. The tunnel dissection remains a challenge, especially in thick walled or thin walled bladders where mucosal perforation becomes a nuisance, with time lost for mucosal repair. Improvements in right-angle electrocautery technology would facilitate this portion of the procedure. Though not perfected, the technique remains an alternative for those seeking a minimally invasive, yet durable option.

**Key Words:** laparoscopy, pediatric, vesicoureteric reflux

#### PD04.05

##### Prospective comparative study of polymethylsiloxane vs hyaluronic acid injection for treatment of vesicoureteral reflux

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**Introduction:** Endoscopic treatment of vesicoureteral reflux (VUR) with subureteral injection of a bulking agent is becoming the first line of treatment for low grade VUR. We prospectively recorded our results to compare efficacy of two products commercialised in Canada for VUR.

**Methods:** Between January 2003 and December 2006, 94 patients (24 males, 70 females) followed for primary VUR were prospectively enrolled in a comparative study to be endoscopically treated with subureteral injection of either polydimethylsiloxane or hyaluronic acid. 160 ureters were injected. A total of 116 ureters were treated with Macroplastique™; their grade was I in 12 ureters, II in 34, III in 46, IV in 21 and V in 3. 44 ureters were injected with Deflux™; their grade was I in 5, II in 16, III in 15, IV in 6 and V in 2. Surgical indications were breakthrough urinary tract infection (65%), persistent reflux (20%) or renal scars (15%). Duplex systems were present in 21 refluxing units (13%). The procedure was performed by a single surgeon on an outpatient basis, with the patient under general anesthesia. Patients were followed with renal ultrasonography and voiding cystourethrography 3 months after the surgery.

**Results:** Based on their characteristics, both groups were equivalent. For Macroplastique™, vesicoureteral reflux was fully corrected in 98 (84%) of 116 ureteral units and was ameliorated in 3 injected ureters. However, complete resolution of VUR was only recorded in 28 (64%) of 44 ureters treated with Deflux™. Obstruction was found in 2 ureters injected with polydimethylsiloxane and in 1 with hyaluronic acid. Univariate and multivariate analyses were performed and did not allow the identification of any characteristics of our population that could explain the significant difference in the success rate between the two groups.

**Conclusion:** Subureteral injection of polydimethylsiloxane is an effective treatment for vesicoureteral reflux and gives a better success rate than hyaluronic acid injection. The rate of resolution obtained with Deflux™ was lower than the level recorded by other groups due to the inclusion of high grade VUR. The lower cost of polydimethylsiloxane makes it an interesting product to use for the correction of VUR.

**Key Words:** pediatric, vesicoureteric reflux

## PODIUM SESSION 5: LUTS AND INCONTINENCE TUESDAY, JUNE 26, 09:15-10:05

### PD05.01

#### The adjustable continence therapy (ACT®) system: preliminary results of the North America ACT clinical study group

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**Introduction and Objective:** The management of stress urinary incontinence (SUI) associated with intrinsic sphincteric deficiency can be challenging, particularly after failed therapies. The Uromedica Adjustable Continence Therapy system (ACT) is a new device that provides bulk at the bladder neck with balloons to improve urethral coaptation and bladder neck support. The objective of this study is to determine the clinical efficacy, safety, adjustability and technical feasibility of the ACT system for treatment of female SUI.

**Materials and Methods:** The study population involves female patients with recurrent S.U.I. with or without urethral hypermobility. Baseline and follow-up tests were performed at 6 weeks, 3 months, 6 months, 9 months, 12 months and annually thereafter including urinalysis, a 3-day voiding diary, provocative pad weight tests, direct visual stress test, Stamey score and questionnaires to assess the degree of stress incontinence, voiding dysfunction, sexual function and quality of life.

**Results:** A total of 82 subjects have been implanted and followed through 12 months. The mean age is 67.6 years (31-94 years). Improvement in Stamey score of at least 1 grade was reported in 78% of patients at 12 months (N=62). Improvement in quality of life as measured by the Incontinence Quality of Life Questionnaire score suggests improvement in quality of life at 12 months ( $p<0.001$ ); mean baseline score of 52.42 (SD 20.02) compared to 85.30 (SD 22.32) at 12 months. Regarding the provocative pad weight tests, the average pad weight at twelve months was 11.6 grams compared to 56.2 at baseline. The mean number of adjustments in balloon volume through 12 months was 2.0 (range 0-6). Regarding technical feasibility of implanting the ACT device, 63% of procedures were rated as mild difficulty, 29% as moderate difficulty, while 8% were rated as severe difficulty. 49% percent (N=40) have experienced at least one complication related to device or implant procedure. The main device or procedure complications include pain/discomfort (N=9), port erosion (N=10), balloon erosion (N=8), urinary retention (N=6) balloon migration (N=11) and bladder perforation at the time of implant (N=4) 0.81% percent of reported complications were considered to be of mild severity.

**Conclusion:** The preliminary data suggest the Uromedica ACT system is an effective and simple procedure for recurrent stress urinary incontinence. Balloons can be easily adjusted to enhance urethral coaptation and bladder neck support. Complications are usually of mild severity. Longer follow-up is needed to evaluate the durability of the ACT system in managing SUI

**Key Words:** incontinence, QOL, urinary stress incontinence

### PD05.02

#### Prevalence of overactive bladder: Canadian results from the EPIC study

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**Introduction:** Overactive bladder (OAB) is defined as urinary urgency, with or without urge urinary incontinence (UUI), usually with frequency and nocturia. The purpose of this study was to ascertain the prevalence of OAB in Canada and to determine to what extent UUI or other types of incontinence coexist with OAB.

**Methods:** A cross-sectional population-based survey of people aged  $\geq 18$  years in Canada was undertaken. Telephone interviews were conducted with a geographically stratified random sample of the population. The 2002 International Continence Society definition of OAB and incontinence types were used to classify participants. Age and gender prevalences were calculated by adjusting for the age and gender distributions within Canada at the time of the survey.

**Results:** A total of 4499 participants (mean age, 47 years) were included in the analysis. The prevalence of OAB for the population aged  $\geq 18$  years was 9.4% (8.5% men; 10.2% women). The prevalence increased with age in both genders. For the following age groups 18-39, 40-59 and 60 and more, the prevalences of OAB were 5.5% (4.3% men; 6.7% women), 9.3% (9.0% men; 9.5% women) and 16.6% (16.3% men, 16.9% women), respectively. Based on these prevalences, it is estimated that approximately 2.3 million people suffer from OAB in Canada. Among participants who reported having OAB, 12.8% (11.6% men; 13.8% of women) were found to have UUI. Considering any type of urinary incontinence (UUI, stress, mixed and other urinary incontinence), 51.1% of OAB respondents were found to suffer from incontinence (41.2% men; 58.8% women).

**Conclusion:** The overall prevalence of OAB in Canada was 9.4%, or almost 1 in 10 adults. Half of OAB adults also suffer from some type of incontinence. OAB was more prevalent in women than men across all age groups. However, the differences tend to disappear with increasing age. Over the years, a fourfold increase in the prevalence of OAB in men was observed. The results confirm that OAB is a common condition in both men and women in the general adult population and that OAB may or may not be associated with incontinence.

**Key Words:** detrusor, incontinence, overactive bladder

### PD05.03

#### Male sling for moderate to severe stress urinary incontinence: efficacy and mechanism

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**Introduction:** Stress urinary incontinence (SUI) after prostate surgery has significant impact on patient's quality of life. Recently, bulbourethral sling has gained popularity for the treatment of this condition. We present further evaluation of the male sling procedure using objective, subjective measurements and dynamic magnetic resonance imaging (MRI).

**Methods:** A total of 33 consecutive men (mean age 68) underwent the bulbourethral bone anchored sling for post prostatic surgery SUI. The procedure was performed with the AMS InVance™ male sling kit. Pre and postoperative evaluation consisted of AUA symptoms score, incontinence/quality of life questionnaire, UCLA/RAND, cystoscopy, ICS1H pad test and videourodynamic study. Reassessment was done 2, 6, 12 months after the surgery and yearly thereafter. One third of the patients were randomly selected to have a pelvic dynamic MRI before and 6 months after the male sling.

**Results:** The median follow-up time was 20.6 months. Incontinence was described as moderate (2-3 pads per day) by 14 (42.4%) and severe (more than 3 pads) by 19 (57.6%). ICS1H pad test done 6 months after the

surgery was negative in 72.7% of the patients. Seventeen (51.5%) were dry, 11 (33.3%) used 1 to 2 pads and 5 (15.1%) used more than 3 pads. Post operative videourodynamic demonstrated unobstructed voiding patterns. Mean results reported on the visual analogic scale about discomfort caused by SUI were 75.8% and 20.0% before and after the male sling respectively. Twenty six patients (83.9%) said to be satisfied/very satisfied from the surgery and 22 (71%) said to be cured/almost cured. Outcomes were not significantly affected by the degree of SUI neither by adjunctive radiotherapy. Dynamic MRI and fluoroscopic images did not show any difference in bladder neck position or mobility. Instead, the mesh seemed to dynamically compress and elevate the posterior bulbar urethra by creating a kink at this level.

**Conclusion:** This study shows that bone anchored male sling appears to have high success rate, both subjectively and objectively in patients with moderate to severe SUI. Mechanism of action could be dynamic posterior compression with a secondary elevation of the bulbar urethra, allowing better transmission of intra-abdominal pressure.

**Key Word:** incontinence

### PD05.04

#### Prevalence of lower urinary tract symptoms (LUTS) in men: Canadian results from the epic study

S. Herschorn<sup>1</sup>, L. Valiquette<sup>2</sup>, D. Irwin<sup>3</sup>, J-P Roussy<sup>4</sup>, I. Defoy<sup>4</sup>

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**Introduction:** Lower urinary tract symptoms (LUTS) are categorized as storage symptoms, voiding symptoms, and postmicturition symptoms. The purpose of this analysis was to evaluate the prevalence of LUTS in the general population of men in Canada.

**Methods:** A cross-sectional population-based survey of people aged  $\geq 18$  years in Canada was undertaken. Telephone interviews were conducted with a geographically stratified random sample of the population. LUTS was classified according to the 2002 International Continence Society definitions. Storage symptoms included urgency; frequency; nocturia; and urgency, stress, mixed, and other types of incontinence. Voiding symptoms included intermittency, slow stream, straining, and terminal dribble. Postmicturition symptoms included incomplete emptying and postmicturition incontinence. Age-specific prevalences were calculated by adjusting for the age distribution within Canada at the time of the survey.

**Results:** 1750 men (mean age, 47 years) were included in this analysis. Overall prevalence of LUTS in the population of men aged  $\geq 18$  years was 67.1%. The percentage of men reporting any storage, voiding or postmicturition symptoms increased with age, ranging from 53.4% in the 18–29 years group, to 84.7% in the 70+ years group. Storage symptoms were present in 59.7% of participants whereas voiding and postmicturition symptoms were present in 24.3% and 18.5%, respectively. Among respondents, 19.3% reported both storage and voiding symptoms, 15.1% reported both storage and postmicturition symptoms, 11.6% reported both voiding and postmicturition symptoms and finally, 10.1% reported having all 3 symptoms (storage, voiding, postmicturition). The most commonly reported storage symptom was nocturia (56.4%), followed by urgency and frequency (8.5% each). Intermittency was the most common voiding symptom (10.7%) and incomplete emptying (13.3%) was the most frequently reported postmicturition symptom.

**Conclusions:** LUTS is prevalent, experienced by almost 7 out of 10 men

in the general population. The prevalence of storage symptoms was higher than that of both voiding and postmicturition symptoms. Storage and voiding symptoms were the 2 symptom types that occurred together most often. All categories of symptoms increased with age.

**Key Words:** BPH, incontinence

### PD05.05

#### Finasteride monotherapy maintains stable urinary symptoms (IPSS) in men newly diagnosed with benign prostatic hyperplasia for 9 months after 9 months of combination therapy using both an alpha-blocker and finasteride

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**Introduction:** It may not be necessary to continue alpha-blockade indefinitely in patients diagnosed with BPH who are on combination therapy with an alpha-blocker and finasteride. This Canadian multicenter extension study evaluated the efficacy of continuing monotherapy with finasteride for a total of 9 months after cessation of combination therapy, on symptom improvement in patients newly diagnosed or on watchful waiting with moderate benign prostatic hyperplasia (BPH) in a "real-life" setting.

**Methods:** This "equivalence design" study tested the maintenance of therapeutic symptomatic effect with 9 months of finasteride alone after 9-months' combination therapy using finasteride with an alpha-blocker. Equivalence was defined as a change of  $\geq 2.0$  IPSS points.

**Results:** Of the 124 males who participated in the extension phase of the main study, 78 (62.9%) were initially naïve to alpha-blocker treatment and constitute the population of this sub-study. Mean age was  $65.6 \pm 8.4$  years, baseline IPSS was  $19.4 \pm 5.2$  and IPSS-Quality of Life (QoL) was  $3.9 \pm 1.2$ . At the time of this preliminary analysis, 66 subjects (84.6%) had completed the extension study per-protocol. Data was pending for 10 subjects and 2 subjects had early discontinuation. Intent-to-treat analyses (LOCF) were performed, except for pending data. Interim results show that the IPSS after 9 months of monotherapy phase was not statistically different from the end of the combination period ( $11.8 \pm 6.5$  vs  $11.0 \pm 6.5$ ,  $p=0.1669$ ). Mean IPSS change remained well below the equivalence criteria (mean difference  $-0.788$ ; 95% CI  $-1.727$ – $0.151$ ;  $p<0.0001$ ). In addition, monotherapy was associated with a trend toward improvement in quality of life ( $p=0.0501$ ). PSA levels were reduced from baseline ( $p<0.0001$ ) and then remained stable ( $p=0.7874$ ). A total of 81 NSAEs occurred in 34 of the 78 subjects (43.6%) enrolled in the extension study (mean =  $2.38 \pm 1.67$  NSAEs per pt); 67.9% of all NSAEs occurred during the combination therapy, 6.1% leading to discontinuation of study medication. Of all NSAEs, 25.9% were "urinary/sexual" and 72.8% were definitely or probably unrelated to study medication. Six SAEs occurred (33.3% during the monotherapy period) and only one was considered related to study medication (dizziness during combination therapy).

**Conclusion:** This study demonstrates that, in newly diagnosed/watchful waiting patients with moderate to severe symptoms of BPH never treated with an alpha-blocker before the study start, finasteride therapy alone for 9 months maintains the same urinary symptom control and improvement obtained after an initial 9 months of combination therapy.

**Key Word:** BPH

## PODIUM SESSION 6: Renal Cancer TUESDAY, JUNE 26, 14:00-14:40

### PD06.01

#### A multidisciplinary clinic for metastatic renal cell carcinoma: a streamlined approach to care

SE Pautler<sup>1,2</sup>, E. Winquist<sup>1</sup>, G. Bauman<sup>1</sup>, JI Izawa<sup>1,2</sup>, L. Riehl<sup>1</sup>, C. Johnson<sup>1</sup>, M. Mackenzie<sup>1</sup>

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**Introduction:** Metastatic renal cell carcinoma (mRCC) remains a challenging problem for clinicians. Historically, treatment options have been limited for these patients, and this often resulted in delayed referral and consultation. Three years ago, we established a multidisciplinary clinic (MDT) to improve both access and care of mRCC patients. Herein, we review the initial experience.

**Methods:** A multidisciplinary model of assessment and care for mRCC was developed including a monthly MDT for initial consultation that included a primary oncology nurse, and at least one medical, radiation, and surgical oncologist. All patients were reviewed by the MDT team. Subsequent care and followup disposition was determined by subspecialty in accordance with the treatment plan. Patient demographics, disease characteristics, and treatment were recorded prospectively.

**Results:** From June 2004 to November 2006, 149 patients were seen in the mRCC MDT. Thirty patients were candidates for palliative radiation therapy with the most common indications being painful bony lesions, obstructive bronchial tumors, and brain metastases. Eight patients were candidates for surgery with 6 cytoreductive nephrectomies, 1 brain resection, and 1 lung metastasectomy. Sixty five patients received systemic therapy (3 after a course of radiation) as follows: 15 sunitinib, 17 sorafenib, 14 clinical trial drug therapy, 7 bisphosphonates, 6 high dose interleukin 2, and 6 interferon alpha. Nineteen patients underwent palliative/supportive measures or required no treatment (no metastases present). Seven patients did not have mRCC based on pathology review and were treated with appropriate systemic chemotherapy.

**Conclusion:** Our multidisciplinary approach has shortened the time from referral to consultation, improved care for patients with mRCC at our centre, and increased clinical trial accrual. The timing of this initiative was also fortuitous as it also facilitated access to tyrosine kinase inhibitor therapies for these patients.

**Key Words:** cancer, kidney, treatment delay

### PD06.02

#### Prediction of the probability of metastatic disease after nephrectomy for renal cell carcinoma: validation of a multi-institutional nomogram

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**Introduction:** Presence of metastatic disease changes the treatment paradigms in patients with renal cell carcinoma (RCC). However, some patients may harbour radiographic changes that are non-specific and a clear distinction between M0 vs. M1 disease may be difficult. To address the difficulty in accurate M stage assignment, we examined the association of locoregional tumour characteristics with the presence of distant metastases.

**Methods:** Analyses were performed on two different cohorts. One served for model development (2570 patients from five institutions) and the other for external validation (1377 patients from five other institutions). Logistic regression analyses assessed the association between predictors and the

outcome which was defined as presence of radiographically confirmed distant metastases. Predictors consisted of age, gender, T and N stages, tumor size, Fuhrman grade, histological subtype and symptom classification (asymptomatic vs. local vs. systemic symptoms). The most informative predictors were included in a nomogram. The nomogram accuracy was tested in the external validation cohort.

**Results:** Of 2570 patients in the development cohort, 334 (13%) had confirmed MRCC. T ( $p<0.001$ ) and N ( $p<0.001$ ) stages, Fuhrman grade ( $p=0.01$ ) and symptom classification ( $p<0.001$ ) were independent predictors of MRCC in multivariate analyses. A nomogram predicting the likelihood of MRCC based on these variables was 90% accurate in the external validation cohort.

**Conclusion:** We developed and externally validated a highly accurate (90%) nomogram capable of predicting the presence of metastatic disease in patients treated with nephrectomy for renal cell carcinoma. This tool may be useful in distinguishing between non-specific changes and true metastatic disease in patients subjected to nephrectomy for RCC.

**Key Words:** kidney, nephrectomy, renal cell carcinoma

### PD06.03

#### Surgical experience with renal cell carcinoma and inferior vena cava thrombus

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McGill University Health Center, Montréal, QC

**Objective:** Renal cell carcinoma (RCC) with caval thrombus is a technical and oncological challenge. The technique including the need for cardiopulmonary bypass (CBP) or deep hypothermic circulatory arrest (DHCA) and oncological efficacy of caval thrombectomy are controversial.

**Methods:** A Retrospective analysis of 74 patients with RCC and tumor thrombus that were treated in our institution, 45 of them underwent radical nephrectomy and IVC thrombectomy.

**Results:** Mean age was  $59\pm 11$  years. The thrombus was supra-diaphragmatic in 8 patients with 6 (13%) extending to the right atrium. Planned CBP was used in 1 patient. 2 patients underwent DHCA. In 4 patients (9%) the thrombus was retracted back into the renal vein followed by completion of the nephrectomy. Cavotomy and direct thrombectomy was performed in 31 patients (69%). Right atriotomy was added to cavotomy in 3 patients with atrial extension to assist in thrombus dissection. One patient underwent limited caval resection and reconstruction with PTFE graft. The infra-renal IVC was ligated in 2 patients. Intra-operative tumor spillage from the IVC thrombus occurred in 4 patients. Peri-operative morbidity included massive bleeding in 2 patients; one of them developed acute tubular necrosis. One patient developed Post-operative deep venous thrombosis and another patient had minor cerebro-vascular accident. One patient died within 30 days of surgery (2%). Post-operative local recurrence and/or metastases occurred in 29 patients (64%). Median time to recurrence was 10 months. Five patients developed local recurrence post resection, 3 of which (60%) had supra-diaphragmatic thrombus. Sites of metastases included: lungs, liver, bone, adrenal glands, brain in 10,6,5,2, 1 patients, respectively. Post-operative 5-year overall survival rate for patient with caval thrombus was 45% compared to 55% for those with renal vein thrombus. The level of caval thrombus was not predictive of survival.

**Conclusion:** Surgical excision of renal cell carcinoma with caval thrombus is relatively safe procedure. Although the level of the thrombus might affect the rate of local recurrences, the rate of metastases and overall survival seems to be independent. Revision of the surgical technique or addi-

tion of peri-operative adjunctive therapy might be necessary in cases with thrombus extending above the diaphragm for control of local recurrence.

**Key Word:** nephrectomy

#### PD06.04

##### **A multicenter, randomized, phase 3 trial of a novel autologous therapeutic vaccine (vitespen) vs. observation as adjuvant therapy in patients at high risk of recurrence after nephrectomy for renal cell carcinoma**

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**Objective:** Vitespen (formerly HSPPC-96) is a novel, autologous, patient-specific, tumor-derived heat shock protein (gp96)-peptide complex vaccine preparation. This trial investigated the efficacy of vitespen in renal cell carcinoma (RCC) patients (pts) at high risk for recurrence postnephrectomy.

**Methods:** Eligible pts had AJCC (1997/2002) stage IB, II (clinical tumor size  $\geq 5$  cm; Fuhrman grade 3/4), stage III or stage IV (M0) RCC, clear cell carcinoma ( $\geq 25\%$ ), ECOG PS 0/1 and  $\geq 7$  g viable tumor tissue for vaccine production.

Randomization was 1:1, nephrectomy vs. nephrectomy + vitespen. Pts were stratified by ECOG score, nodal status and histological grade. Vitespen was administered intradermally once weekly x 4 w, then every 2 w until vaccine depletion. Pts were imaged at 3, 6, 9, 12, 18, 24, 30, 36 m postsurgery, then annually for  $\leq 6$  y, with independent radiological review at final analysis. Primary and secondary endpoints are recurrence-free survival (RFS) and overall survival (OS), respectively.

**Results:** Of 818 pts randomized, 728 pts were eligible. Analysis was planned for a target of 214 investigator-reported events. Following independent Clinical Events Committee (CEC) assessment, 149 pts were identified as recurrences, and 124 pts were identified with baseline metastatic/residual disease. Early analysis of RFS in pts without baseline disease (n = 604) shows a trend in favor of vaccine: HR 0.869, P = 0.384. In patients with better prognostic factors (n = 361; stage I/II high grade, III T1, T2, T3a, low grade) data show significant benefit (HR 0.567, P = 0.018). Updated OS data currently show no difference between the two arms (HR 1.098, p = 0.600). In better-prognosis patients there appears to be a signal for potential survival improvement (HR 0.676, P = 0.242). Vaccine was well tolerated; no vaccine-related grade 3-4 AEs were identified.

**Conclusion:** This represents the largest randomized study to date in RCC in the adjuvant setting. The protocol-specified number of events needed to initiate final analysis of RFS had not been reached. However, early analysis shows an apparent clinically significant benefit of vitespen in a subset of pts with better prognostic factors. This group of better-prognosis pts closely correlates with "intermediate risk" pts, a definition currently being utilized by the Eastern Cooperative Oncology Group (ECOG) in a large ongoing RCC adjuvant study. Pts continue to be followed for RFS and OS.

## PODIUM SESSION 7: OUTCOMES WEDNESDAY, JUNE 27, 09:50-10:30

### PD07.01

#### Success of erectile dysfunction treatment in men after radical prostatectomy, radiation therapy or both for prostate cancer

SB Radomski, J. Chung, P. Kudlow

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**Introduction:** Patients that have radical surgery or radiation therapy for prostate cancer often develop erectile dysfunction (ED). Furthermore, in many of these patients treatment for their ED is less than satisfactory. Our aim was to assess the success of ED treatment in those men who have had either a radical prostatectomy (RP) or radiation therapy (RT) or both for prostate cancer treatment.

**Methods and Material:** From July 1/1996 until May 1/2006 we retrospectively reviewed 421 men with ED who presented to our specialized ED clinic in our cancer institute after radical prostatectomy ( $n=267$ ), radiation therapy ( $n=111$ ) or radical prostatectomy and radiation therapy (RPRT) ( $n=43$ ). Patients on hormonal therapy were excluded. The mean age of the RP group was 61.6 years (range 42–79), RT group 68.2 years (range 36–80) and RPRT group 64.5 years (range 47–79). All 3 groups had similar medical problems except that cardiac disease was significantly higher in the RT group (36.9%) in comparison to the RP group (13.5%) and the RPRT group (9.3%).

**Results:** The mean duration of their ED was 26.3 months in the RP group, 30.8 months in the RT group, and 45.7 months in the RPRT group. Prior to coming to our ED clinic 81.3% of those that had a RP, 52% that had RT and 67.4% that had RPRT had tried some form of ED treatment. At the initial visit inability to penetrate was 86.5% in the RP group, 72.1% in the RT group and 83.7% in the RPRT group. 88% of the RP group, 43% of the RT group and 81.4% of the RPRT group were on some form of ED treatment when they were last seen in the clinic. The mean follow-up from 1st to last visit was 15.9 months for the RP group, 12.6 months for the RT group and 12.2 months for the RPRT group. Patients felt their treatment for their ED was successful (ability to have sexual intercourse) in 11.2% of the RP group, 43.2% of the RT group and 23.3% of the RPRT group.

**Conclusion:** The success of treatment of ED as determined by the patients after prostate cancer treatment was poor. Patients who had radiation therapy alone had significantly better success. Patients who had radical surgery had very poor results. Effective treatment for ED after prostate cancer treatment needs to be improved.

**Key Words:** erectile dysfunction, radiation, radical prostatectomy

### PD07.02

#### Examination of the relationship between prostate inflammation, clinical prostatitis-like symptoms, BPH-related lower urinary tract symptoms and sexual dysfunction: baseline data from the REDUCE trial

JC Nickel<sup>1</sup>, CG. Roehrborn<sup>2</sup>, MP O'Leary<sup>3</sup>, DG Bostwick<sup>4</sup>, MC Somerville<sup>5</sup>, RS Rittmaster<sup>5</sup>

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**Introduction:** All men in REDUCE trial were biopsied prior to study entry, enabling the relationship between prostate inflammation, prostatitis-like symptoms, BPH-related LUTS and sexual dysfunction at baseline to be examined.

**Methods:** Inflammation was scored across all cores for a given individual as none (0), mild (1), moderate (2), or marked (3). The CPSI and IPSS were used to assess prostatitis-like symptoms and LUTS, respectively while sexual function (sexual activity, impotence, decreased libido) was scored as present/absent.

**Results:** This database (>8,200 men) is the largest to examine these questions. Very weak correlation was found between total CPSI score and chronic inflammation (CI) ( $p=0.043$ ), but not for pain (subscore or severity) or clinical prostatitis. Correlation was only shown between urinary ( $p=0.049$ ) and QoL subscores (0.043) of the CPSI. Statistically significant, but very weak, correlations were found between CI and IPSS variables (0.057;  $p<0.0001$ ). In linear regression, both age and CI were significant after adjustment for other covariates; for both variables, higher values were associated with higher IPSS scores. There was a high degree of correlation between most symptom components of the IPSS and the CPSI (for example, correlation between total CPSI and IPSS was 0.728;  $p<0.001$ ). There were also statistically significant associations between the IPSS and pain on the CPSI, although the correlations were weaker (0.137–0.283;  $p<0.001$ ). Impotence and decreased libido were statistically significantly associated with higher CI at baseline ( $p=0.0007$  and 0.0037, respectively). Logistic regression results demonstrated that age, BMI, and IPSS (all  $p<0.001$ ), but not inflammation ( $p=0.12$ –0.24), had statistically significant relationships with sexual function components.

**Conclusion:** These data do not confirm a relationship between histological inflammation and clinical prostatitis but do suggest a relationship between the degree of LUTS and the degree of chronic inflammation in the REDUCE population. Men with more severe LUTS are more likely to experience pelvic pain as part of their symptom complex. The apparent association between sexual dysfunction and chronic inflammation was not significant after adjustment for other relevant covariates. Longitudinal 4-year follow-up will determine the impact of baseline prostate inflammation and dutasteride therapy on progression of prostate inflammation, prostatitis-like symptoms, LUTS, LUTS-associated complications and sexual dysfunction.

**Funding:** Glaxo-Smith-Kline

**Key Words:** BPH, inflammation, sexual activity

### PD07.03

#### Impact of treatment delay in bladder cancer patients managed with partial cystectomy in Quebec: a population-based study

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McGill University Health Center, Montréal, QC

**Introduction:** Treatment delays have been associated with adverse outcomes in bladder cancer patients treated with radical cystectomy. We sought to evaluate the impact of treatment delay on recurrence of disease in patients with bladder cancer treated with partial cystectomy.

**Methods:** We obtained the billing records of all patients who underwent partial cystectomy for bladder cancer in Quebec from 1983 until 2005. The analysis included age, gender, year of surgery, surgeon's age, hospital type, preoperative and postoperative visits with accompanying diagnoses, dates of TURBT, partial cystectomy, and salvage radical cystectomy, and date of death.

**Results:** A total of 714 patients underwent partial cystectomy for invasive bladder cancer were included in this study. Median patient age was 70 years. Of these, 52 (7.3%) required salvage radical cystectomy. Patients who underwent salvage radical cystectomy post partial cystectomy had significantly shorter overall survival than patients who underwent upfront radical cystectomy (HR 1.6,  $p<0.01$ ). Median delay from TURBT to partial cystectomy was 28 days. Patients who had a treatment delay > 28 days had a higher incidence of salvage radical cystectomy compared to those who did not (HR 2.3,  $p=0.005$ ). The risk of requiring salvage radical cystectomy progressively increases as treatment delay increases (HR

3.0 if >84 days, and HR 4.2 if >210 days,  $p < 0.0001$ ).

**Conclusion:** Treatment delay in bladder cancer patients managed with partial cystectomy is associated with adverse prognosis and higher rate of salvage radical cystectomy.

**Key Words:** bladder cancer, cystectomy, treatment delay

#### PD07.04

##### Non risk-adapted surveillance management for clinical stage I nonseminomatous testis tumors

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University Health Network, Princess Margaret Hospital, University of Toronto, Toronto, ON.

**Introduction and Objective:** Active surveillance is an established treatment option for clinical stage I nonseminomatous germ cell testicular tumor (NSGCTT). We have evaluated our experience with non risk-adapted active surveillance with delayed treatment for relapse.

**Methods:** From January 1981 to August 2004, all 305 patients with clinical stage I NSGCTT were prospectively placed on an active surveillance protocol. Patients were not stratified by their risk of disease progression. Additional treatment was reserved for those who subsequently relapsed. Recurrence rates and time to relapse, risk factors predictive

for failure, burden and value of treatment delayed until progression, disease specific and overall survival were assessed.

**Results:** Median time of follow-up was 6.3 years (range 0.1-24.3). Progression was detected in 77 (25%) patients, with a median time to relapse of 0.6 years (range 0.2-12.4). In all but 3 patients (4%), recurrence occurred within 2 years from initial diagnosis. The presence of lymphovascular invasion and/or pure embryonal carcinoma (<100% was not in the primary tumor were significant risk factors for disease recurrence in multivariate analyses ( $p < 0.05$ ). Of the 305 patients, 228(75%) were cured by the orchiectomy alone and underwent no further treatment, 19 (6%) were salvaged by retroperitoneal lymph node dissection alone, 20(6.5%) by chemotherapy only, and 38(12.5%) received a combination of different therapeutic modalities. Overall, 8 deaths occurred: 2(0.6%) of testis cancer (one of them refused further treatment offered for second relapse). Disease specific and overall survival rates were 99.4 % and 97.5 % respectively.

**Conclusions:** An active surveillance without any risk stratification is a highly effective treatment for all clinical stage I NSGCTT and can now be recommended as a standard management option. Nearly 100 % of those who are destined to progress can be salvaged with delayed therapy, with an acceptably low morbidity. Finally, overtreatment of patients cured by orchiectomy is avoided.

**Key Words:** germ cell tumor, surveillance, testis cancer

# MODERATED POSTER SESSION 1: PROSTATE CANCER

## Monday, June 25, 09:00-10:30

### MP01.01

#### High volume provider is associated with lower rate of secondary therapies after definitive radiotherapy for localized prostate cancer

C. Jeldres<sup>1</sup>, QD Trinh<sup>1</sup>, J. Walz<sup>1</sup>, G. Hütterer<sup>1</sup>, F. Saad<sup>1</sup>, M. McCormack<sup>1</sup>, L. Valiquette<sup>1</sup>, P. Perrotte<sup>1</sup>, F. Montorsi<sup>3</sup>, PI Karakiewicz<sup>1</sup>

<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>Vita Salute University, Milan, Italy

**Introduction:** The relationship between provider volume and cancer control has not been studied in the setting of definitive radiotherapy. We examined the effect of the average annual number of treated patients on the rate of use of secondary therapies after definitive external-beam radiotherapy (EBRT) for localized prostate cancer.

**Methods:** The cohort consisted of 3907 patients treated with definitive radiotherapy between 1989 and 2000. Median follow-up was 6.2 years. All were treated by 72 radiation oncologists who had an average individual annual treatment volume of 13.9 prostate cancer cases (median 10.0, range 1–39). Secondary treatment was defined as hormonal therapy after definitive EBRT. Univariable and multivariable Cox regression analyses targeted the rate of secondary treatment after initial radiotherapy. Provider volume was coded as cubic spline. Age at definitive EBRT and Charlson comorbidity index at EBRT represented covariates.

**Results:** Secondary therapy was recorded in 731 (18.7%) patients. The median failure-free survival was not reached (mean 11.2 years). Provider volume was a significant univariable predictor of secondary therapy-free survival after EBRT ( $p=0.02$ ). Moreover, in multivariate Cox regression models, provider volume achieved independent predictor status ( $p=0.01$ ). Multivariate cubic spline analyses showed that the rate of secondary treatment decreased markedly when provider volume exceeds 13 cases per year.

**Conclusion:** High provider volume exerts a protective effect on secondary therapy-free survival after definitive radiotherapy for clinically localized prostate cancer. Lower rates of secondary treatment become evident when provider volume exceeds 13 cases per year.

**Key Words:** localized prostate cancer, prostate cancer, radiation

### MP01.03

#### Age is an independent predictor of bone metastasis in patients diagnosed with prostate cancer

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<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>Vita-Salute University, Milan, Italy

**Introduction:** We hypothesized that age may be associated with the rate of bone metastasis (BM) in patients diagnosed with prostate cancer (PCa). We examined the distribution of metastatic bone disease at diagnosis according to age, after controlling for PSA clinical stage and biopsy Gleason.

**Methods:** Clinical and pathological data were available for 1107 patients from a single referral center, diagnosed with PCa between 2002 and 2006. All patients were routinely subjected to bone scan, independently from their clinical characteristics. Patients with PSA > 50 ng/mL were excluded from the analyses. Univariable and multivariable logistic regression analyses addressed the rate of BM at diagnosis. Covariates consisted of pre-treatment PSA, primary and secondary biopsy Gleason, clinical stage and age at diagnosis. Age was assessed as a continuous as well as a categorical variable.

**Results:** Mean age was 65.7 (46-85) and mean PSA 8.98 (0.1-50.0). Clinical stage was T1c, T2 or T3 in 604 (54.6%), 468 (42.3%) and 35 (3.2%)

patients, respectively. Primary biopsy Gleason was  $\leq 3$  or  $\geq 4$ , in 971 (87.7%) and 136 (12.3%) patients, respectively. Secondary biopsy Gleason was  $\leq 3$  or  $\geq 4$ , in 780 (70.5%) and 327 (29.5%) patients, respectively. 86 (7.8%) patients were 75 or older. At diagnosis, 50 (4.5%) patients had a BM documented by bone scan. In logistic regression models, age coded as a continuous variable was an independent predictor of BM ( $p=0.004$ ). Similarly, when age was categorized according to 75 year cut-off, independent predictor status was also confirmed ( $p<0.001$ ). In multivariable analyses, a patients age 75 or older were at 4.4-fold higher risk of having BM at diagnosis than younger men, despite adjusting for PSA, clinical stage and biopsy Gleason (OR 4.42).

**Conclusion:** Older age, above 75 years, appears to predispose to a higher risk of harboring BM. This may be explained by higher affinity of PCa for BM in older men. Conversely, this finding may be also associated with a lead time bias, whereby PCa is diagnosed at a more advanced stage in older men. This cannot be fully accounted for by PSA, clinical stage and biopsy Gleason in statistical analyses.

**Key Words:** bone metastases, prostate cancer, risk factors

### MP01.04

#### Pre-operative staging of prostate cancer using surface-coil magnetic resonance imaging

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<sup>1</sup>Division of Urology and <sup>2</sup>Department of Radiology, University of Ottawa, Ottawa, ON

**Introduction:** Pre-operative prostate cancer staging impacts prognosis and surgical planning. Endo-rectal coil magnetic resonance imaging (MRI) is effective in detecting tumour within the prostate and peri-prostatic tissue. The purpose of this study was to review the efficacy of surface-coil MRI in pre-operative staging of prostate cancer.

**Methods:** All prostatectomies performed by two urologists were reviewed to determine if pre-operative pelvic MRI were performed. The images of identified patients were reviewed by one radiologist who was blinded to clinical information. The radiologist reported presence or absence of tumour within each lobe of the prostate. Extracapsular extension, seminal vesicle invasion and lymph node metastasis was also reported. The same data were extracted and compared from original pathology reports.

**Results:** From January 2000 to September 2005, 320 prostatectomies were performed. Of these, 19 had pre-operative pelvic MRI performed. Pathologically, 29 of 38 (76%) lobes contained tumour, 9 (24%) lobes had associated extracapsular extension, 5 (13%) seminal vesicles and 3 (8%) sets of lymph nodes contained cancer. MRI sensitivity and specificity were, respectively, 86% and 89% for tumour location, 44% and 97% for extracapsular extension, 40% and 100% for seminal vesicle invasion and 100% and 100% for lymph node involvement.

**Conclusion:** MRI appears to be effective in detecting tumour within the prostate and pelvic lymph nodes. In addition, approximately half of extracapsular extension and seminal vesicle involvement was identified. Surface-coil MRI likely has a role in pre-operative staging and surgical planning of intermediate and high-risk prostate cancer.

**Key Words:** imaging, localized prostate cancer, lymph nodes, neoplasm, radical prostatectomy, stage

### MP01.05

#### Prediction of prostate cancer in patients with prostatic intraepithelial neoplasia or atypical small acinar proliferation

M. Amin, S. Jeyaganth, N. Fahmy, L. Begin, S. Aronson, S. Jacobsen, S. Tanguay, A. Aprikian

McGill University Health Center, Montréal, QC

**Introduction:** To evaluate the predictors of prostate cancer in follow up of patients diagnosed on initial biopsy as high-grade prostatic intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation (ASAP).

**Methods:** We studied 201 patients with HGPIN and 22 patients with ASAP on initial prostatic biopsy among 2265 patients and who had subsequent prostatic biopsies for evaluation. The mean time of follow up was 17.3 (range from 1 to 62) months; the mean number of biopsy sessions was 2.54 (range from 2 to 6), and the median number of biopsy cores was 10 (range from 6 to 14).

**Results:** On subsequent biopsies, the rate of prostate cancer was 21.9% (44/201) in HGPIN patients. Of these, 72.7% (32), 20.5% (9) and 6.8% (3), cancer was found on the first, second and third follow up biopsy sessions, respectively. In ASAP patients the cancer detection rate was 72.7% (16/22), all of who on the first follow-up biopsy. Multivariate analysis showed that the independent predictors of cancer diagnosis were PSAD and number of biopsy cores of more than 10 (odd ratios of 3.05 and 3.15) ( $p < 0.006$  and  $0.04$ ), respectively. 38.6% (17/44) of cancer cores were found at the same site as that of HGPIN on initial biopsy. On the other hand, in ASAP patients none of these variables were found to be predictors of cancer diagnosis, while 50% (8/16) of cancer cores were found at the same site as that of ASAP.

**Conclusion:** ASAP is strong predictive factor associated with cancer. However, HGPIN on initial biopsy is associated with cancer on follow-up biopsy in the minority of cases. The factors predictive of cancer on follow-up biopsy are elevated PSAD and greater than 10 core-biopsy. When cancer is found, it is in the same site as the original HGPIN in only one-third of cases. As the cancer rate on repeated biopsy of HGPIN patients is the same like that of patients without HGPIN, perhaps the standard reflex of repeat biopsy in all patients with HGPIN should be revisited.

**Key Words:** ASAP, PIN, prostate cancer

### MP01.06

#### Outcome of repeat transrectal ultrasound prostate biopsy positive patients with HPIN and/or ASAP

DL Lim, M. Abdelhady, D. Downey, J. Izawa, J. Chin

University of Western Ontario, London Health Sciences Center, London, ON

**Introduction:** Follow-up of patients with a diagnosis of high-grade prostatic intraepithelial neoplasia (HPIN) and/or atypical small acinar proliferation (ASAP) based on transrectal ultrasound guided biopsy (TRUS Bx) is an important clinical issue. We reviewed the pathological features associated with detection of prostate cancer (CaP) on subsequent biopsy and the detection rates with each entity.

**Methods:** A total of 610 men (mean age 61 yrs, range 48-67) underwent repeat TRUS-guided 8-10 core prostate biopsy between 1/2003 and 12/2004. Of the whole cohort, Group 1 (G1) consists of 343 men who underwent repeat TRUS Bx for rising prostate specific antigen (PSA) levels and/or abnormal digital rectal examination (DRE) but no previous HPIN/ASAP; while 128 had previous HPIN only (G2), 89 men with previous ASAP only (G3), and 50 men had HPIN + ASAP in previous biopsies (G4). In men with positive repeat biopsy, further analysis of Gleason score was done to evaluate if the presence of previous HPIN and ASAP is associated with lower or higher grade CaP.

**Results:** CaP detection rate on repeat bx was 29.5% for group 1, 14.8% for group 2, 42.7% for group 3, and 30.0% for group 4. The cancer detection probability was higher for the ASAP group than the other 3 groups (Table 1). Furthermore, patients with previous HPIN and/or ASAP when they were diagnosed with CaP, their tumors were of lower Gleason score (Table 2). Out of these patients, 31 underwent radical prostatectomy. On final pathology, only 3 out of the 22 patients with Gleason score  $< 7$  on TRUS biopsy were upgraded to 7. While 5 out of 9 patients with Gleason score  $\geq 7$  were downgraded to 6, only 1 patient with Gleason score of 7 was upgraded to 8.

**Conclusion:** Patients with ASAP had a higher risk of CaP detection on repeat biopsy. Both HPIN and ASAP were more likely to be associated with CaP of Gleason score 6 or less. Vigilant follow-up with earlier repeat biopsies especially for patients with previous ASAP would be warranted for earlier detection of CaP.

**Key Word:** prostate cancer

**Table 1. Abstract MP01.06. Cancer detection probability according to the presence of HPIN and/or ASAP in previous biopsies**

	n positive biopsy (%)	P value
Repeat Biopsy (n = 610)		
No previous PIN/ASAP (n = 343)	101 (29.5)	0.52
Previous HPIN (n = 128)	19 (14.8)	0.002
Previous ASAP (n = 89)	38 (42.7)	0.001
Previous HPIN + ASAP (n = 50)	15 (30)	0.49

**Table 2. Abstract MP01.06. Gleason score outcome in positive patients with previous HPIN and/or ASAP**

Positive repeat biopsy (n = 72)	Gleason score (%)		P value*
	$< 7$	$\geq 7$	
—			—
Previous HPIN (n = 19)	15 (79)	4 (21)	0.09
Previous ASAP (n = 38)	27 (71)	11 (29)	0.44
Previous HPIN + ASAP (n = 15)	11 (73)	4 (27)	0.15

\* Probability of detecting Gleason score of  $\geq 7$ .

### MP01.07

#### Risk of prostate cancer detection on repeat transrectal ultrasound guided biopsy

M. Abdelhady, D. Lim, D. Downey, J. Izawa, J. Chin

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**Introduction:** By utilizing sextant biopsies, 19%–23% of men who underwent second set prostate biopsies (Bx) are diagnosed with prostate cancer (PCa). We reviewed our experience with repeat Bx and compared the clinical, biochemical and pathological features of patients diagnosed with PCa with those with no malignant findings on repeat Bx.

**Methods:** Repeat transrectal ultrasound guided biopsies (TRUS Bx) were done in our institution for 610 men during the years 2003 and 2004. The indications for repeat Bx were rising PSA or finding of high-grade prostatic intraepithelial neoplasia (HGPIN) or atypical small acinar proliferation (ASAP) on previous biopsy. Patient's age, family history of PCa, DRE findings, PSA, prostate volume, PSAD, TRUS appearance (graded 1–5 based on level of suspicion), number of cores obtained, number of previous Bx done, and history of HGPIN or ASAP on previous Bx were reviewed according to Bx results. Univariate and multivariate stepwise logistic regression analyses were used for statistical analysis.

**Results:** Out 610 men, 173 patients diagnosed with prostate cancer. Of these, 31.5% (140/444), 20.9% (22/105) and 18% (11/61) were diagnosed with PCa after 1, 2,  $\geq 3$  repeat biopsies, respectively. On univariate analysis, all the variables tested were significant except family history of prostate cancer, but only patient's age, TRUS findings, number of cores and 1/prostate volume continued to show significance in multivariate analysis.

**Conclusions:** Extended multicore Bx protocols are advised on repeat Bx. Men with larger prostates and history of previous negative Bx seems to be at lower risk of detecting PCa on repeat TRUS Bx.

**Key Words:** biopsy, risk factors, ultrasound

### MP01.08

#### MRI directed trans-rectal ultrasound biopsies in patients at risk for prostate cancer

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**Introduction:** We evaluated whether performing an erMRI prior to TRUS biopsies of the prostate increases the yield for cancer in a high-risk population. In a subset analysis, we also compared the yield with high field MRI (3 T) versus lower field (1.5 T).

**Methods:** Between March 2003 and November 2005, 26 consecutive patients underwent erMRI prior to their TRUS biopsy of the prostate. Median age was 62 years (range 32–76). Median PSA value was 8.40 ng/mL (range 2.1–85.9). All patients had at least 1 prior negative prostate biopsy (Median 3, range 1–12). Twenty-three patients had at least 1 risk factor for prostate cancer (family history, high PSA velocity, low percent-free PSA, PIN or ASAP on prior biopsy). MRI studies consisted of T2-weighted and DCE imaging studies.

**Results:** There was a high degree of correlation between T2-weighted and DCE images (84.6% agreement,  $p < 0.0001$ ). Neither T2-weighted nor DCE imaging correlated with a higher yield for cancer on final biopsy (T2: PPV=20.0% NPV=14.2%,  $p=0.21$ ; DCE: PPV=20.6% NPV=14.8%,  $p=0.26$ ). Combining the two modalities did not improve cancer yield. There was no significant difference in the probability of cancer based on 1.5T or 3T imaging (16.7% vs.15.6%,  $p=0.88$ ).

**Conclusion:** Although MRI prior to TRUS biopsies trended toward higher cancer yields in our population, this did not reach statistical significance. Reasons for this may include suboptimal localization of the MRI finding and the biopsy location. Better methods for fusing MRI and TRUS images are presently being developed at our institution to allow higher targeting accuracy.

**Key Words:** biopsy, imaging, prostate cancer

### MP01.09

#### Impact of extended prostate biopsy on minimization of the volume-grade bias in prostate cancer detection

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**Introduction and Objective:** The Prostate Cancer Prevention Trial revealed a higher number of high-grade cancers among men who were randomized to finasteride and underwent predominantly sextant prostate biopsies. We have recently shown that these results may have arisen due to a previously unknown association between prostate volume and sextant-biopsy derived grade. A basic tenet of measurement theory is that repeated or additional measurement improves validity of the underlying construct. This study examines the impact of extended prostate biopsy on cancer detection and histological grade.

**Methods:** We reviewed 679 patients (median: age 62 yrs, PSA 5.3 ng/mL, prostate volume 46.8 cc) in our center who underwent systematic 10 core or more biopsies with negative TRUS and PSA < 10. Since specimens were separately labeled, we were able to compare results from the first 6 cores to the extended pattern. The association between histological grade, prostate volume and the number of cores (extended vs. sextant) was examined using McNemar's and Cochran–Armitage tests. Prostate volume was divided into tertiles.

**Results:** Prostate cancer detected using a 6-core technique revealed 179/679 (26.4% 95% CI: 23.1–29.9) cancers vs. 240/679 (35.4% 95% CI: 31.8–39.1) using the extended core technique ( $p < 0.001$ ). The marginal cancer detection rate increased significantly as prostate volume increased. Cancer detection rates for first, second and third tertiles of prostate volume were increased by 16/227, 17/226 and 28/226, respectively ( $p=0.05$ ). Upgrading of Gleason score from 6 to 7 was observed in 14 patients (7.9%  $p < 0.001$ ) due to the additional procured cores. There was no association between upgrading and prostate volume;  $p=0.87$ .

**Conclusions:** Although more high-grade cancers are detected by additional prostate sampling, there is no differential upgrading with respect to prostate volume. Based on these observations, extended prostate sampling within clinical trials of agents that reduce prostate size will have minimal impact on volume grade associations.

**Key Words:** biopsy, prostate cancer, prostate volume

### MP01.10

#### Impact of negative re-biopsy in a cohort of prostate cancer patients managed with watchful waiting

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**Introduction:** Watchful waiting in patients with prostate cancer is an established management option for patients with favorable parameters. We have examined the impact of negative re-biopsy after diagnosis in a cohort of watchful waiting prostate cancer.

**Methods:** 186 men with prostate cancer with favorable parameters or refusing treatment were conservatively managed with watchful waiting. 108 of them had at least one biopsy after diagnosis. Patients were followed every 3 to 6 months with PSA and physical exam and were offered rebiopsy annually or if there was change on physical exam or PSA value. Progression was defined as having one or more of the following criteria on follow up after diagnosis;  $\geq$ cT2b,  $\geq$ 3 positive cores, >50% of cancer in at least one core or predominant Gleason pattern of 4 in re-biopsies.

**Results:** Mean age at diagnosis was 69±6.6 years. Initial Gleason score was <7, 3+4, 4+3,  $\geq$ 8 in 131, 25, 9 and 14 patients, respectively. Median follow up was 59 months. 46,25,13,10,2 patients had 2,3,4,5,6 biopsies, respectively. A total of 185 re-biopsies were done after the diagnosis. 126/185 biopsies were done routinely, of which 14 (8%) showed histological progression; 52/185 biopsies were done for increase PSA, change in DRE or both, and 26 (50%) of these showed histological progression,  $p < 0.0001$ .

Of the 108 patients who had at least one repeated biopsy, 54 (50%) had at least one negative re-biopsy. Of these 54 patients; 33 had persistent negative biopsies subsequently, of whom one patients (3%) developed progression. At diagnosis, 33 (100%) of those patients had clinical stage  $\leq$ T2a, 31(94%) had PSA of  $\leq$ 10, 31(94%) had  $\leq$ 2 positive cores for cancer. The median amount of maximal percentage of cancer per core at diagnosis was 6%. Their median PSADT was 154 months. Of the 41 patients with persistently positive re-biopsy; 22 (54%) had histological or clinical progression. Their median PSADT was 64 months.

**Conclusion:** Negative re-biopsy in patients with prostate cancer on watchful waiting is associated with low volume disease and low PSA at diagnosis. It is also associated with limited risk of progression.

**Key Words:** prostate cancer, prostate volume, prostatitis, PSA

### MP01.11

#### Second treatment rates in prostate cancer patients treated for cure in the USA and Canada

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**Introduction:** Second treatment after therapy with curative intent denotes failure of primary treatment, and has significant morbidity. The purpose of this study was to determine if second treatment rates differed between the USA and Canada (Ontario) and if there were significant predictors of treatment failure.

**Methods:** CaPSURE (Cancer of the Prostate Strategic Urologic Endeavor), a national disease registry of men with various stages of prostate cancer, was screened to identify patients treated for cure. The Canadian database, Co-morbidity and Initial Treatment in Prostate Cancer Patients Treated for Cure was created from a stratified random sample of patients from Canada's most populous province. The time period for the enrollment of patients was the same: 1990–1997, to ensure adequate follow-up time afterwards. Multivariate logistic regression was completed to determine the factors which impacted receipt of second therapy.

**Results:** CaPSURE contributed 2616 patients and the Canadian database had 1444 patients eligible for study. Over 5 years, the survival from second treatment was slightly higher for CaPSURE patients (75%) than Ontario patients (72%) (Wilcoxon  $p$  value =0.003). Higher D'Amico risk categorization and radiation as initial treatment (HR 1.3 [95% CI 1.1–1.4]) were predictive for receipt of second treatment. Nation of treatment did not predict for second treatment in multivariate analysis. When

radiation and surgical patients were compared separately, higher BMI was predictive of second treatment for surgical patients, but not for radiotherapy patients.

**Conclusion:** Patients treated in the US and Canada had higher rates of second treatment if they received radiotherapy or were intermediate or high-risk patients. While Canada appeared to have a higher rate of second treatment failure, this was explained once treatment type was included in the model. Overall, this population based study which accounts for disease and patient characteristics found country of treatment did not affect second treatment rates.

**Key Words:** localized prostate cancer, relapse, statistics

**MP01.12**  
**Drivers of treatment selection in prostate cancer patients treated for cure in an American database and a Canadian database**

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<sup>1</sup>Queen's University, Kingston, ON; <sup>2</sup>University of California San Francisco, CA

**Introduction:** It is known that selection of prostate cancer treatment for cure differs between the US and Canada despite geopolitical similarities. The purpose of this study is to determine the relevant variables that guide patients in their decision making and if they account for the disparity in the treatment delivered between regions.

**Methods:** CaPSURE (Cancer of the Prostate Strategic Urologic Endeavor), a national disease registry of prostate cancer patients, was screened to identify those treated for cure. The Canadian database, Co-morbidity and Initial Treatment in Prostate Cancer Patients Treated for Cure is a stratified random sample of patients from Ontario. The time period for the data sets is the same: 1990–1997. Both clinical and sociodemographic data were analyzed in multivariate logistic regression to determine the odds ratio for receiving radiation stratified by region.

**Results:** CaPSURE contributed 2616 patients and the Canadian database had 1444 patients eligible for study. The first definitive treatment received by Americans was surgery for 67.4%, external beam radiotherapy (EBRT) for 26% and 6.7% received brachytherapy. For Canadians, 41% received surgery, 59% EBRT and there was almost no use of brachytherapy in this cohort. Sociodemographic variables were statistically but not clinically significantly different. Multivariate logistic regression was completed to determine the different variables' relative contribution to decision making. Examining region of origin and treatment decision, it was found that Americans had a 3.8 times higher propensity to select surgery as compared to Canadians. While D'Amico risk category, Body Mass Index and relationship status had statistically significant impact on treatment decision making, age was found to impact the odds ratio the greatest amount. Younger age increased the propensity to select surgery to 4.3 times over radiation for Americans. An unexpected finding was that risk category did not change the odds ratio at all when added to the model.

**Conclusion:** Patients treated in the US selected surgery at a vastly higher rate than patients treated in Canada, even after controlling for important disease and patient characteristics. Social, cultural and resource issues that are not measured but components of nationality are likely responsible for the different treatment paradigms between regions.

**Key Words:** localized prostate cancer, radical prostatectomy, statistics

**MP01.13**  
**A cross sectional study of health related quality of life (HRQOL) in men treated with radical prostatectomy or external beam radiotherapy for localized prostate cancer**

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**Introduction:** To compare the long-term health-related quality of life outcome in patients with localized prostate cancer (PCa) treated with radi-

cal prostatectomy (RP) or external beam radiotherapy (EBRT) using a validated questionnaire.

**Methods:** The Expanded Prostate Cancer Index Composite (EPIC) questionnaire was mailed to patients with PCa and treated with RP or EBRT in our institution between the years 1998–2004. HRQOL was compared among the 2 groups of patients

**Results:** 1775 questionnaires were mailed out to patients who were diagnosed with prostate cancer and underwent RP or EBRT as primary treatment in our institution. The response rate for RP was 72% (633/883) and 66% (592/892) for EBRT. RP patients showed better long-term HRQOL outcome than patients after EBRT in most of the domains studied except for urinary incontinence domain when RP patients showed a lower score, as expected. Both groups showed poor scores in sexual domain and equal scores in the mental component of SF-12 domain.

**Table 1. Abstract MP01.13. Mean score of different EPIC Domains in RP and EBRT groups**

HRQOL domain	Radical Prostatectomy (n = 633)	External Beam Radiotherapy (n = 592)	P value
General HRQOL	mean	mean	
SF-12: mental component summary	54.1	54.8	0.24
SF-12: physical component summary	50.7	44.9	<0.0001
Domain-specific prostate cancer HRQOL: EPIC summary scores			
Urinary irritative	85.1	76.7	<0.0001
Urinary incontinence	72.3	82.9	<0.0001
Bowel	91.2	81.1	<0.0001
Sexual	29.8	24.4	0.0001
Hormonal	87.2	80.4	<0.0001
Obstructive voiding, AUA-SI	6.2	9.1	<0.0001

**Table 2. Abstract MP01.13. Mean score of different EPIC Domain in RP and EBRT groups**

HRQOL domain	Radical Prostatectomy (n = 633)	External Beam Radiotherapy (n = 592)	P value
General HRQOL	mean	mean	
SF-12: mental component summary	54.1	54.8	0.24
SF-12: physical component summary	50.7	44.9	<0.0001
Domain-specific prostate cancer HRQOL: EPIC summary scores			
Urinary irritative	85.1	76.7	<0.0001
Urinary incontinence	72.3	82.9	<0.0001
Bowel	91.2	81.1	<0.0001
Sexual	29.8	24.4	0.0001
Hormonal	87.2	80.4	<0.0001
Obstructive voiding, AUA-SI	6.2	9.1	<0.0001

**Conclusions:** Although most PCa are currently diagnosed in the localized stages with good 5 years survival rates, our results may give the patients a view of the long-term HRQOL after RP or EBRT for Pca.

**Key Words:** QOL, radiation, radical prostatectomy

**MP01.14**

**Health related quality of life (HRQOL) outcome after salvage cryosurgery of the prostate: comparison with outcome after primary radiotherapy**

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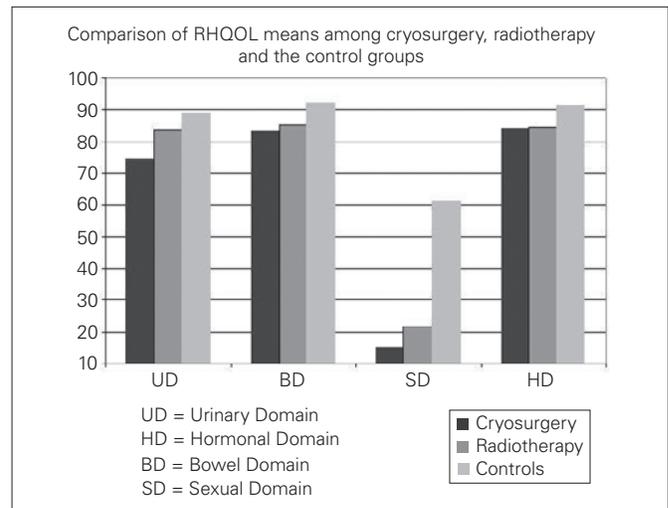
**Introduction:** Currently, with updated technology and improved patient selection, cryosurgery is being used as one of the main salvage procedures for local failure after radical radiation therapy for prostate cancer with successful long-term salvage in approximately 35%. With the earlier concerns about the poor quality of life (QOL) in these patients, we aimed to evaluate the QOL after contemporary salvage cryosurgery and assess the most affected domains of a validated questionnaire in comparison to the scores of patients who had undergone radical radiotherapy for prostate cancer.

**Methods:** EPIC questionnaires were mailed to prostate cancer patients who received primary radiotherapy (n=996) or salvage cryosurgery (n=155) in our center between the years 1998–2004. T test was used for statistical analysis to compare between the means of scores in each group

**Results:** The over all response rate was 66% (68% and 64% for cryosurgery and radiotherapy groups respectively). Patients after salvage cryosurgery showed statistically significant deterioration of the urinary (p<0.0001) and sexual (p= 0.0039) domains when compared to the means of radiotherapy group, while the means for the bowel and hormonal domains showed no statistically significant difference (graph 1). On looking at the AUA symptom score for both groups, the cryosurgery group showed higher score than in the radiotherapy group (11.07 vs. 8.25, p=0.0005). Finally,

there was no difference in the satisfaction mean score for both groups (75.27 vs. 79.02, p=0.21)

**Conclusions:** Although patients after salvage cryosurgery of the prostate may experience further deterioration of their urinary and sexual function, they are usually satisfied with that modality of salvage treatment. Quality of life scores have improved since the earlier days of salvage cryoablation with improvement in patient selection and in cryo-technology and operative techniques. Together with the accepted rate of complications and reasonable reported 8-year biochemical disease free rate of 37% in some groups of patients, our data supports the use of cryosurgery as a salvage treatment modality after failure of primary radiotherapy treatment for prostate cancer.



**Key Words:** cryotherapy, QOL, radiation

# MODERATED POSTER SESSION 2: MALE HEALTH

## Monday, June 25, 09:00-10:30

### MP02.01

#### In vivo brain-derived neurotrophic factor (BDNF) expression and timing patterns in aged rats following cavernous nerve axotomy

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University of California San Francisco, CA

**Introduction:** Advanced age is a powerful predictor of compromised erectile function following radical prostatectomy, even with nerve-sparing advancements. The timing pattern and expression of potential neuromodulatory growth factors following cavernous nerve injury is incompletely understood, as are effects of aging. We report in vivo findings for the endogenous brain-derived neurotrophic factor (BDNF) response in young and aged rats.

**Methods:** 36 male Fisher 344 rats (3 and 24 months,  $n=18$  per group) underwent bilateral cavernous nerve transection. The major pelvic ganglion and penis with attached cavernous nerve segment were removed at 0, 12 and 24 hours, as well as 5 and 12 days after axotomy. Protein, messenger RNA (mRNA), and immunohistochemical analysis was performed. BDNF expression was quantified and timing of endogenous response established.

**Results:** BDNF response in young and aged rats is time-dependent, with maximal levels attained within 24 hours and returning to baseline within 5 days. mRNA and protein expression of BDNF was upregulated in the penis after injury in both groups, although maximal expression differed with significantly decreased expression in aged animals ( $p<0.05$ ). The JAK/STAT pathway (BDNF target) was activated in the MPG after transection, although to a lesser extent in the aged group ( $p<0.05$ ).

**Conclusion:** Endogenous release of BDNF has previously demonstrated neuroregenerative potential. Decreased levels observed in aged animals may contribute to poorer peripheral nerve regeneration or neuroprotection after injury. BDNF activity occurs within a well-defined time period and potential translational applications for cavernous nerve recovery after radical prostatectomy are dependent upon the increased understanding of the neurobiological response to injury.

**Key Word:** erectile dysfunction

### MP02.02

#### Early experience with the new AMS 700™ with MS pump™ series inflatable penile prosthesis

AJ Bella<sup>1</sup>, TF Lue<sup>1</sup>, S. Phonsombat<sup>1</sup>, WO Brant<sup>1</sup>, A. Nehra<sup>2</sup>

<sup>1</sup>University of California San Francisco, CA; <sup>2</sup>Mayo Clinic, Rochester, MN

**Introduction:** A new single button deflation momentary squeeze pump for the AMS 700™ Inflatable Penile Prosthesis (IPP) series has been developed in order to further improve patient ease-of-use. We report our early experience with this new device.

**Methods:** An ongoing prospective, multicenter study is being conducted at 3 investigative sites. Primary outcome measures include a 17-item questionnaire specific to inflation and deflation of the IPP, changes in pre- and postoperative erectile function as measured by the International Index of Erectile Function (IIEF) and posttreatment satisfaction profiles using the Erectile Dysfunction Inventory of Treatment Satisfaction instrument (EDITS).

**Results:** 50 patients have undergone implantation with the AMS 700™ with MS Pump™. Patients report no difficulties inflating the IPP or finding the deflation button. Deflation occurs with a single press of the button for 2–4 seconds, and accidental inflation has not been noted. The IIEF erectile function domain score improved significantly (mean 10.5). EDITS data were collected at 6 months following surgery and initial results indicate high patient satisfaction (ongoing accrual).

**Conclusion:** The MS Pump™ allows for ease of inflation and defla-

tion, including one-handed operation by some patients. This modification provides benefit for patients and physicians and seems to improve ease-of-use over the previous AMS 700™ series pumps.

### MP02.03

#### Potential mechanisms for erectile rehabilitation after radical prostatectomy: indirect effect of sildenafil on neurite outgrowth

AJ Bella, TX Minor, G Lin, C-S Lin, N Hayashi, TF Lue  
University of California San Francisco, CA

**Introduction:** Oral phosphodiesterase-5 inhibitors are a common treatment for erectile dysfunction following nerve-sparing radical prostatectomy, including contemporary post-operative penile rehabilitation programs. The recovery effect of sildenafil therapy is believed to be mediated, at least in part, by neuronal regenerative and neuroprotective properties. Increased delivery of growth factors and modulation of local oxygen tension levels preventing hypoxia-induced cavernous smooth muscle fibrosis may represent alternative mechanism(s) of action. We examined the neurotrophic effects of arterial or venous blood versus sildenafil upon neurite outgrowth from the major pelvic ganglion (MPG) of the rat.

**Methods:** MPGs were microdissected to isolate regions expressing neuronal nitric oxide synthase. Tissue cultures were incubated with rodent arterial or venous serum (1:10), incremental concentrations of sildenafil (range 12.5–100  $\mu$ m), or phosphate-buffered saline (control). Digitized images of stained ganglia were quantified at 24 and 48 hours to determine the maximal lengths of neurite sprouting.

**Results:** Arterial serum enhanced neuronal fiber outgrowth from MPG, followed closely cultures to which venous blood was added ( $p<0.05$  vs. controls). Sildenafil did not confer a direct effect on neurite outgrowth ( $p>0.05$  vs. controls).

**Conclusion:** In clinical studies, treatment with sildenafil has been shown to confer an advantage for recovery of erectile function in some men. Based on these results, it appears that sildenafil does not modulate neuronal regeneration directly; rather, increased blood flow to the penis provides increased levels on neural and vascular growth factors essential to the neuromodulation microenvironment (indirect mechanism). Further basic science and clinical studies are required to define sildenafil's mechanism(s) of action in this role, and to identify patient subgroups in whom this approach yields optimal benefit.

**Key Word:** erectile dysfunction

### MP02.04

#### Liquid microparticle delivery of intracavernous growth differentiation factor-5 therapy enhances the recovery of erectile function in a rat model of cavernous nerve injury

AJ Bella, TM Fandel, G Lin, K Tantiwongse, TF Lue  
University of California San Francisco, CA

**Introduction:** To determine whether intracavernous injection of growth differentiation factor-5 (GDF-5) improves erectile function after cavernous nerve (CN) injury in the rat.

**Methods:** 48 male Sprague-Dawley rats were randomly divided into 6 equal groups: one group underwent sham operation (uninjured controls), while 5 groups underwent bilateral cavernous nerve crush. Crush-injury groups were treated at the time of injury with liquid microparticles containing no GDF-5 (vehicle), 0.4 mg (low-concentration), 2 mg (intermediate-concentration), or 10 mg GDF-5 (high-concentration) injected into the right corpus cavernosum. One untreated group served as injured controls. Erectile function was assessed by CN electrostimulation at 4 weeks. Total RNA was isolated from penile tissue samples for real-time PCR. Expression

levels of TGF- $\beta$ , eNOS, iNOS, and nNOS were determined. **Results:** Untreated nerve injury significantly decreased erectile function. GDF-5 treatment significantly enhanced erectile recovery in the low- and intermediate-concentration groups. The low-concentration group demonstrated the most significant preservation of function, as the intracorporeal pressure increase did not differ significantly from uninjured controls. High-concentration GDF-5 did not confer meaningful recovery. CN injury resulted in significant changes of mRNA expression for TGF- $\beta$ , eNOS, iNOS, and nNOS compared to uninjured controls. Treatment with 0.4 mg GDF-5 significantly reversed the changes in mRNA expression for all factors measured, while 2 mg and 10 mg GDF-5 reversed injury-induced changes in mRNA levels for TGF- $\beta$  and nNOS.

**Conclusion:** Intracavernous injection of low- (0.4 mg) or intermediate-concentration GDF-5 (2 mg) significantly preserved erectile function. Low-concentration GDF-5 was most promising to reverse mRNA changes in the penis after CN injury.

**Key Word:** erectile dysfunction

**MP02.05**  
**Comparison of Kruger strict morphology among fertile and infertile males**

ED Grober, SP Stroup, RC Walters, M. Khera, DS Crain, DJ Lamb, L. Murthy, M. Lopez-Perdomo, LI Lipshultz  
 Scott Department of Urology, Baylor College of Medicine, Houston, TX and The Naval Medical Center, San Diego, CA

**Introduction:** Considerable uncertainty surrounds the clinical utility of strict morphology (SM) in the evaluation of the infertile male. Kruger's original cut-off of 4% normal forms was determined based on fertilization outcomes among couples undergoing in vitro fertilization. While Kruger's strict criteria is currently the most commonly used method to evaluate sperm morphology, the range of values found in a control population of fertile men attempting natural conception have not been reported. The primary objective of the current study was to prospectively compare SM results between infertile males presenting for evaluation to those of men of proven fertility.

**Methods:** Subjects included men from two groups. Group 1 consisted of men with a history of natural paternity presenting for elective vasectomy. Men greater than 40 years of age or with evidence of a clinical varicocele (past or present) were excluded from analysis. Group 2 consisted of a random sample ( $n = 100$ ) of age-matched men with sperm concentrations  $> 20$  million/ml. presenting for infertility evaluation. Semen samples were obtained by masturbation following a minimum of 2 days abstinence. Semen analyses were performed and values reported relative to W.H.O. limits of adequacy for semen volume, sperm concentration, % motility, and forward progression. Trained andrologists, blinded to semen analysis results, determined SM levels using Kruger's strict criteria. Direct comparisons of SM results were made between the fertile and infertile male subjects.

**Results:** Fifty-four fertile men with a mean age of 32 years and an average of 2.2 children provided semen samples for analysis. Table 1 com-

pares the mean % SM between the fertile and infertile male subjects at the 25th, 50th, and 75th percentiles.

**Conclusions:** Men with proven fertility have a high frequency (56%) of abnormal SM according to Kruger's criteria that is not significantly different from infertile males. Strict morphology likely represents a non-specific surrogate or a more global measure of sperm dysfunctional fertilization capacity. Accordingly, couples should be counseled with caution to pursue assisted reproductive technologies based solely on SM.

**Key Words:** infertility, sperm

**MP02.06**  
**Extracorporeal shock-wave lithotripsy is not supported by evidence-based medicine for first line treatment of Peyronie's disease**

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**Introduction:** Extracorporeal shock-wave lithotripsy (ESWL) has been described for non-surgical first-line therapy for men with Peyronie's Disease (PD). We critically review the evidence supporting ESWL for this purpose.

**Methods:** Extracorporeal shock-wave lithotripsy (ESWL) has been described for non-surgical first-line therapy for men with Peyronie's Disease (PD). We critically review the evidence supporting ESWL for this purpose.

**Results:** Level I evidence does not exist to support ESWL for PD treatment. All studies reviewed contain methodological errors, specifically for primary endpoints and metrics utilized to measure patient improvement. An ideal randomized, placebo controlled double blind study using objective measures of efficacy, including improved erectile/sexual function, and a large population followed for an appropriate amount of time is unavailable. Some studies have shown improvement for penile pain, and occasionally for angulation. Plaque change is uncommon.

**Conclusion:** Available data does not support ESWL for the treatment of PD. Well-designed studies are needed to document a treatment effect, and patients should most likely be treated with ESWL in the context clinical trials. Basic research is required to determine the mechanism of (any) effects of ESWL on Peyronie's plaques.

**Key Word:** meta-analysis

**MP02.07**  
**Relationship between sperm dna fragmentation and sperm density, motility, and abnormal morphology**

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**Introduction:** High sperm DNA damage has been associated with abnormal semen analysis parameters and poor prognosis for in vitro fertilization (IVF) cycles. Our goal is to evaluate the relationship between sperm DNA fragmentation and sperm morphological and functional characteristics.

**Methods:** Semen analysis, sperm penetration assay and sperm DNA damage from 412 patients presenting for evaluation of infertility from July 2002 to January 2004. Semen samples were collected, and routine semen analyses were performed and then evaluated with sperm DNA damage tests. A modified alkaline single cell gel electrophoresis (CometAssay<sup>TM</sup>) was used to assess the level of DNA damage.

**Results:** In the multivariable analysis high sperm DNA damage is associated with low sperm density (22 mill sperm/ml compared to 62 mill sperm/ml,  $p < 0.001$ ), and low motility (35% compared to controls 54%,  $p < 0.001$ ). The mean percentage of sperm head defects was higher (89% among cases compared to controls (85%,  $p < 0.05$ ).

**Conclusion:** This result implies that sperm from patients with high percentage of DNA damage is more likely to display poor sperm density, poor motility, increased abnormal morphology, and associated with defects of the sperm head. Therefore, selection of morphologically normal sperm for the use of IVF and intracytoplasmic sperm injection (ICSI) may improve the pregnancy outcome in infertile couples with high sperm DNA fragmentation.

**Key Words:** infertility, risk factors, sperm

**Table 1. Abstract MP02.05**

	Mean % SM +/- SE*	25 <sup>th</sup> percentile	50 <sup>th</sup> percentile	75 <sup>th</sup> percentile	% abnormal SM (< 4%)
Fertile Males (n=54)	3.7% +/- 0.3	2%	3%	5%	56%
Infertile Males (n=100)	3.5% +/- 0.3	1.5%	3.3%	5%	54%

\* $p = 0.9$

**MP02.09****The effect of male testosterone replacement therapy on untreated female partners: a pilot study**

M. Khera, B. Najari, E. Grober, LI Lipshultz  
Baylor College of Medicine, Houston, TX

**Introduction:** Recent studies have shown that female partners of men treated for erectile dysfunction with vardenafil had a significant improvement in their Female Sexual Function Index (FSFI) scores. The purpose of this study was to evaluate changes in FSFI scores in women whose male partners were treated with testosterone replacement therapy (TRT).

**Material and Methods:** Five hypogonadal male patients, who were initiated on TRT, were asked to complete the Sexual Health Inventory for Men (SHIM) questionnaire (range 1–25), the Androgen Deficiency in Aging Males (ADAM) questionnaire (positive or negative response, with positive response associated with hypogonadism), and a modified ADAM questionnaire. The modified ADAM questionnaire quantified ADAM domains on a Likert scale from 1 (terrible) to 5 (excellent) [range 10–50]. Concurrently, the female partners were administered validated FSFI questionnaires (range 2–36). Both the male and female partners were asked to complete each questionnaire following 4 weeks of TRT.

**Results:** Male patients demonstrated a significant improvement in all three questionnaires after being started on TRT. Average SHIM scores increased from 10.4±6.8 to 19.4±4.6 ( $p=0.04$ ). Prior to TRT, all 5 men had a positive response on the ADAM questionnaire. Following TRT, 3 men continued to have a positive response on the ADAM questionnaire ( $p=0.44$ ). Quantitatively, pre and post-treatment ADAM scores were 7.6±1.1 and 2.8±3.8, respectively ( $p=0.03$ , lower scores suggest a more favorable response). On the modified ADAM questionnaire, pre and post-treatment quantitative scores improved from 27.7±5.29 to 34.4±7.74, respectively ( $p=0.14$ ). In the untreated female partners, FSFI scores significantly improved from 24.7±4.0 to 30.3±1.9 ( $p=0.04$ ). The majority of the domains of the FSFI demonstrated a trend towards improvement, with the greatest improvement seen in female “satisfaction” (Table 1).

**Table 1. Abstract MP02.09. FSFI Domains Before and After Partner TRT**

	Desire	Arousal	Lubri- cation	Orgasm	Satis- faction	Pain
Before	4.1 ±0.6	4.0 ±1.4	4.0 ±2.0	3.4 ±2.0	3.2 ±1.1	6.0 ±0
After	4.8 ±0.5	5.3 ±0.7	4.9 ±1.3	4.7 ±1.7	4.6 ±1.5	6.0 ±0

**Conclusion:** TRT appears to be effective in improving not only erectile dysfunction, but also, as expected, symptoms of hypogonadism (i.e. decreased libido and energy). Moreover, TRT also appears to be effective in improving overall sexual function in untreated female partners. Increasing number of couples are currently being recruited and evaluated to make this data more robust.

§Goldstein et al. Women’s sexual function improves when partners are administered vardenafil for erectile dysfunction: a prospective, randomized, double-blind, placebo-controlled trial. *J Sex Med* 2005;2(6):819-32.

**Key Word:** androgen

**MP02.10****Testosterone is a better indicator than prolactin in predicting a pituitary microadenoma in patients with hyperprolactinemia**

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**Introduction:** Not all infertile male patients with hyperprolactinemia will have a pituitary microadenoma on MRI. Knowing which patients are more likely to have a pituitary microadenoma would allow clinicians to better select which patients should undergo a head MRI.

**Material and Methods:** A retrospective review of all new male infertile patients presenting to a single institution from 2002–2006 was per-

formed. Serum hormone values (LH, FSH, prolactin, testosterone, and estradiol) were measured. Patients with a persistently elevated serum prolactin level (>22 ng/ml) were screened with a pituitary MRI. Serum prolactin and testosterone levels were correlated to pituitary MRI findings.

**Results:** From 2002–2006, 197 men were found to have an elevated prolactin level. Complete data were available for 174 patients. Among these patients, 26 men had a persistently elevated serum prolactin level (>22 ng/ml), had follow-up data, and underwent a head MRI. Nine of the 26 patients (34.6%) were found to have a pituitary microadenoma on MRI. The average size of the adenoma was 4.49 mm (range 3–7mm). There was no significant difference between prolactin values among patients with and without a pituitary microadenoma (47.9 ng/ml and 48 ng/ml, respectively,  $p=0.9$ ). However, the average testosterone values for men with and without pituitary microadenomas were significantly different (223.67 ng/ml and 428.21 ng/ml, respectively) [ $p=0.02$ ].

**Conclusion:** Lower testosterone values in patients with hyperprolactinemia increase the probability that the patient will have a pituitary microadenoma. In this cohort, higher prolactin levels were not correlated with an increased probability of encountering a pituitary microadenoma on head MRI. This information is valuable when deciding when to obtain a costly head MRI in patients with hyperprolactinemia.

**Key Words:** risk factors, screening

**MP02.11****The safety and efficacy of testosterone replacement therapy following radical prostatectomy**

M. Khera, J. Colen, E. Grober, B. Najari, L. Murthy, D. Lamb, L. Lipshultz  
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**Introduction:** There has been much debate in the literature as to when, or if, to start testosterone replacement therapy (TRT) in hypogonadal men following radical prostatectomy (RP). Furthermore, there have been limited studies assessing the efficacy of TRT in these men. The purpose of this study was to evaluate the safety and efficacy of TRT in men following RP.

**Material and Methods:** All hypogonadal men in our department who were initiated on TRT following RP were retrospectively reviewed. Only symptomatic men with low testosterone levels were started on TRT. All men had negative surgical margins on pathology and an undetectable PSA as a requirement to initiate TRT. PSA values before and after RP, and after TRT were evaluated. Similarly, serum testosterone levels before and after TRT were examined. A follow-up telephone survey was performed, during which the Androgen Deficiency in Aging Males (ADAM) questionnaire (positive or negative response, with positive response associated with hypogonadism) and a modified ADAM questionnaire were administered. The modified ADAM questionnaire quantified each ADAM question on a Likert scale from 1 (terrible) to 5 (excellent) (range 10–50). Patients were asked to complete both of these questionnaires comparing their symptoms before and after initiating TRT.

**Results:** Twenty-one men, ages 51 to 80 years (mean 63.1), were identified as having initiated TRT following RP. The average PSA prior to RP was 6.68±3.97, while the average Gleason score at the time of RP was 6.4±0.8. Men were initiated on TRT an average of 54.4 months following RP (range 1–181). Patients were followed an average of 12.0 months following TRT (range 1 to 60 months). The average rise in testosterone before and after TRT was from 275.8±124.9 ng/dl to 440.1±294.6 ng/dl ( $p=0.03$ ). PSA prior to TRT was 0.005±0.015 ng/ml and was 0.005±0.016 ng/ml after TRT ( $p=0.99$ ). None of the men studied had a biochemical PSA recurrence. Eleven men could be contacted for the telephone survey. Prior to TRT, 9 men had a positive response on the ADAM questionnaire. Following TRT, only 1 man continued to have a positive response on the ADAM questionnaire ( $p=0.02$ ). Quantitatively, pre and post-treatment ADAM scores were 4.6±2.2 and 0.9±1.1, respectively ( $p<0.01$ , lower scores indicating a better response). On the modified ADAM questionnaire, pre and post-treatment quantitative scores were 23.7±6.3 and 32.3±5.9, respectively ( $p=0.01$ , higher scores indicating a better response).

**Conclusion:** TRT is not only safe, but also effective in improving symptoms of hypogonadism in men following radical prostatectomy. None of the men on TRT had a PSA recurrence after being followed for an average of 12 months. Although men in this study were initiated on TRT on

average 54.4 months after radical prostatectomy, clinicians may consider initiating TRT at an earlier time in the symptomatic patient.

**Key Words:** androgen, andropause, prostate cancer

**MP02.12**  
**Should patients with decreased prolactin levels be screened differently for prostate cancer?**

M. Khera, E. Grober, L. Murthy, D. Lamb, L. Lipshultz  
 Baylor College of Medicine, Houston, TX

**Introduction:** In prostate cancer and benign prostatic hyperplasia (BPH), there is compelling data to support that prolactin and testosterone both stimulate prostate growth. Morgentaler et al. demonstrated that men with normal Prostate Specific Antigen (PSA) and low testosterone values had a 14% chance of having prostate cancer on their prostate biopsies. These authors also found that men over 60 years of age with low testosterone levels and normal PSAs had a 29% chance of having occult prostate cancer. They concluded that PSA levels were an insensitive indicator of prostate cancer in men with low testosterone levels. Realizing the similarities between testosterone and prolactin and their effect on prostate growth, we evaluated the association between prolactin and PSA values.

**Material and Methods:** A retrospective review of all patients who visited a single institutional practice (B.C.M.) from 2000–2006 was performed. All patients with a PSA as well as serum hormone levels, including FSH, LH, prolactin, and testosterone, were included in the study. Serum prolactin levels were correlated with PSA and hormonal profiles.

**Results:** From 2000 to 2006, 403 patients had a PSA and complete hormone evaluation. Prolactin was significantly correlated with testosterone ( $p=0.001$ ), LH ( $p<0.001$ ), FSH ( $p<0.001$ ), and PSA ( $p=0.001$ ). Using 20 ng/ml as the upper limit of normal for serum prolactin at our center, 384 men had prolactin < 20 ng/ml, and 19 men had a prolactin of > 20 ng/ml. Among men with prolactin levels <20 ng/ml, the average testosterone and PSA was 397 ng/dl and 1.7 ng/ml, respectively. PSA was significantly correlated with prolactin ( $r=0.168$ ,  $p=0.001$ ) and testosterone ( $r=0.147$ ,  $p=0.005$ ) values. Among men with serum prolactin levels > 20 ng/ml, the average testosterone, and PSA were 369 ng/dl and 2.6 ng/ml, respectively. PSA did not correlate with prolactin levels, although there was a trend towards clinical significance ( $p=0.18$ ). Furthermore, testosterone did not correlate with prolactin or PSA in this group of men.

**Conclusion:** In men with prolactin levels <20 ng/ml, PSA directly correlated with both prolactin and testosterone. However, prolactin was not correlated with testosterone. These results suggest that PSA levels could be an insensitive indicator of prostate cancer in men with low prolactin levels. Further studies are needed to assess the correlation between prolactin levels and prostate cancer.

**Key Words:** prognostic marker, prostate cancer, PSA

**MP02.13**  
**Biopsychosocial factors in quality of life in men with chronic prostatitis/chronic pelvic pain syndrome**

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**Introduction:** To explore interactions between psychological, environmental, urinary, and demographic predictors of Quality of Life (QOL) in men with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

**Methods:** Men ( $n=253$ ) previously enrolled in the NIH Chronic Prostatitis Cohort study in North American tertiary care clinical centers (6 US, 1 Canada) self-reported with validated instruments including the Physical (PCS) and Mental (MCS) Component Summary subscales of the SF-12, demographics, urinary symptoms, depression, current pain, pain coping and catastrophizing, pain control, social support and solicitous responses from a partner. Data were collected through a one-time survey. Covariates determined to be significant (in correlation analysis) were entered into a multivariable regression model predicting PCS and MCS.

**Results:** After adjusting for covariates, regression models showed that poorer PCS scores were predicted by worse urinary function ( $p=0.0002$ ) and

increased use of pain-contingent resting as a coping strategy ( $p=0.026$ ). Further, poorer MCS scores were predicted by greater pain catastrophizing ( $p=0.002$ ) and lower perceptions of social support ( $p<0.0001$ ). The helplessness subscale was the primary significant predictor of the catastrophizing scale on follow up regression analyses ( $p=0.0004$ ) while the family and friends subscales of the social support scale were the primary MCS predictors ( $p=0.002$ ;  $p=0.0002$ ).

**Conclusions:** These data support a biopsychosocial model for QOL in CP/CPPS, suggesting that specific coping and environmental factors (i.e., catastrophizing, pain-contingent resting, social support) are significant in understanding CP/CPPS patient adjustment. These data can be utilized to develop specific cognitive-behavioral programs for men with CP/CPPS that are refractory to standard medical therapy.

**Key Words:** pain, prostatitis, QOL

**MP02.14**  
**80 W potassium-titanyl-phosphate (KTP) laser photoselective vaporization prostatectomy (PVP) for symptomatic benign prostatic hyperplasia (BPH)**

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**Introduction:** KTP laser PVP is a relatively new technology for the treatment of lower urinary tract symptoms (LUTS) secondary to BPH. We review our initial experience.

**Methods:** We prospectively evaluated our initial 12-month experience with KTP laser PVP. All had International Prostate Symptom Score (IPSS), American Society of Anesthesiologists (ASA) risk score, serum prostate specific antigen (PSA), complete blood count (CBC) and electrolyte panel, maximum flow rate (Qmax) and post void residual (PVR) determinations and volumetric measurements with transrectal ultrasonography. Under general anesthesia, transurethral PVP was performed using an 80 W KTP side-firing laser system through a 23 Fr continuous-flow cystoscope with normal saline irrigant. Voiding trials were performed 2 hours post surgery; if unable to void, a urethral catheter was replaced. IPSS, Qmax and PVR were evaluated 1, 4, 12, 24 and 52 weeks postsurgery.

**Results:** 160 consecutive patients were identified, having a mean age of  $70 \pm 9$  years. The mean prostate volume was  $72 \pm 50$  cm<sup>3</sup> and the mean ASA score was  $2.4 \pm 0.6$ . Mean laser time and energy usage were  $33 \pm 30$  minutes and  $99 \pm 90$  kJ, respectively. Perioperative serum sodium and hemoglobin did not change significantly. All were outpatient procedures with the majority of patients catheter-free at discharge. Thirty-one patients required catheter drainage for one week. Thirteen patients developed urinary tract infections. One patient required hospitalization after developing pyelonephritis. Thirteen patients had persistent hematuria for over a week. Three patients developed bladder neck contractures requiring intervention. Three patients had persistent urinary retention due to detrusor failure. No urethral strictures or urinary incontinence were noted. All patients were able to discontinue their prostate medications following surgery. Mean IPSS decreased significantly from 27 to 15, 11, 9, 8 and 6 ( $p<0.05$ ) at 1, 4, 12, 24 and 52 weeks, respectively. Qmax and PVR values also showed statistical significant improvement ( $p<0.05$ ).

**Conclusion:** Our initial results demonstrate that KTP laser PVP is safe and effective for the treatment of LUTS secondary to BPH, providing excellent results and minimal morbidity.

**Key Words:** BPH, laser, prostate

**MP02.15**  
**Holmium laser enucleation of the prostate (HoLEP): long-term results**

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 McGill University, Montréal, QC

**Purpose:** to evaluate long-term outcomes of Holmium Laser Enucleation of the Prostate (HoLEP) for patients with symptomatic enlarged prostate, including the learning curve.

**Materials and Methods:** a retrospective analysis of 118 patients who underwent HoLEP between March 1998 and February 2001 at our institution. This represented our initial experience with the technique reflecting our

learning curve. The voiding outcome parameters, operative duration time, enucleation time, morcellation time, eucleated tissue weight, catheterization time, hospital stay and complications were recorded.

**Results:** The mean patient age was 76.5 years (range 59–93 years) and the mean preoperative prostate volume was 59.3 cc (range 20–172 cc). The mean catheter time and hospital stay was 1.3 and 1.5 days, respectively. At 6 years postoperatively, mean peak flow rate ( $Q_{max}$ ) increased from 6.3 to 16.2 ml/sec and mean postvoid residual urine (PVR) decreased

from 232 to 41.2 ml ( $p < 0.0001$ ). Mean International Prostate Symptom Score (IPSS) improved from 17.3 to 5.6 ( $p < 0.0001$ ). Bladder neck contracture and urethral stricture developed in 0.8% and 1.7% of patients, respectively. The reoperation rate for recurrent BPH obstruction was 4.2%. **Conclusions:** HoLEP represents a safe and effective treatment for patients with symptomatic enlarged prostate. The improvement in outcome parameters is durable and the late complications and reoperation rate are very low. **Key Word:** LUTS

## MODERATED POSTER SESSION 3: MISCELLANEOUS TOPICS

### Monday, June 25, 09:00-10:30

#### MP03.01

##### One year follow up of autologous muscle derived cell injection to treat stress urinary incontinence

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**Introduction and Objective:** Prior studies have shown that injection of muscle-derived cells (MDC) into periurethral muscle resulted in increased leak point pressures in an animal model of stress urinary incontinence (SUI). We now report 1-year follow up on the initial 8 women in North America with SUI treated with MDC periurethral injections.

**Methods:** Eight women at Sunnybrook Health Sciences Centre entered this trial. In the first North American trial of this kind, the injection technique evolved during the initial set of patients. A dosage of 18–22 x 106 autologous MDC was used for all injections. The first three women received a transurethral injection with a Williams Cystoscopic 8 mm Injection Needle. The next two women received a transurethral injection with a longer 10 mm Injection Needle. The last 3 received the injection periurethrally using a 1fi" 25 gauge needle. Additionally, 3 of these patients received a re-injection using the periurethral approach. Pre and post injection pad weights, bladder diaries, and quality of life measures were utilized to assess outcome.

**Results:** Mean and median follow up in this group was 16.5 and 17 (range 3–24) months. Five women had 1 injection and 3 had 2 injections. Improvement in SUI was seen by objective and/or subjective measures in 5 of 8 women with 1 achieving total continence. Onset of improvement was noted between 1–8 months after injection. Cure or improvement continues at a median of 10 months. No serious adverse events were reported. Cystoscopy at study exit and surgical exploration in 2 patients at the time of midurethral tape surgery did not demonstrate any appreciable tissue change. Subsequent midurethral tape placement and outcome was not negatively impacted upon by previous MDC injection. The periurethral injection route or transurethral route utilizing a longer 10-mm needle appeared to be associated with increased success.

**Conclusion:** Pure cellular therapy with MDC can lead to durable objective and subjective improvement of SUI. Onset of improvement is delayed following injection, suggesting that restoring muscle function may be the mechanism of action unlike standard bulking agents. Deeper delivery of MDC into the external sphincter appears to be important for successful outcome.

**Funding:** Cook MyoSite, Inc

**Key Word:** urethra

#### PD03.02

##### Peer reviewed publications by the CUA membership: then and now

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**Objective:** To assess changes in the quantity, quality, authorship characteristics, and funding sources of scholarly publications by CUA members over a 10 year period.

**Methods:** A PubMed single-citation search was performed. All publications by active CUA members during the periods Jan 93-Dec 94 and Jan 03-Dec 04 were reviewed. Data recorded were author demographics, type of publication, financial support, journal and associated impact factor.

**Results:** In the 93-94 era there were 486 active members, of whom 145(30%) published a total of 624 manuscripts (483 clinical, 141 basic science). External funding was acknowledged in 27% (8% industry, 92% peer

reviewed). Types of publication included 218/624 (35%) observational studies, 124/624 (20%) review articles, 66/624 (11%) case reports, 18/624(3%) case series, and 18/624 (3%) randomized controlled trials. In the 03-04 era there were 475 active members, of whom 144 (30%) published 775 manuscripts (658 clinical, 117 basic science). External funding was acknowledged in 31% (24% industry, 76% peer reviewed). 260/775 (34%) were observational studies, 126/775 (16%) review articles, 55/775 (7%) RCT's, 55/775 (7%) case reports and 48/775 (6%) case series. Of those members publishing, intensity increased to an average of 2.7 manuscripts annually for the most recent era, compared to 2.15 manuscripts annually a decade ago. Median impact factor of journals was 2.8.

**Conclusions:** Scholarly activity has remained robust over the last decade with 30% of active CUA members continuing to contribute to the peer reviewed literature. The percentage of funded manuscripts has remained constant, although the proportion with industry funding has increased. The level of evidence hierarchy has increased with a greater proportion of randomized controlled trials. CUA members should be proud of their academic productivity.

**Key Words:** education, statistics

#### MP03.03

##### HATS: health advocacy in training survey

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**Introduction:** Health advocacy is a well-defined core competency by medical education and licensing bodies, encompassing health promotion, disease prevention, resource access and identification and modification of the determinants of health at the patient and community level. Health advocacy is stressed as a critical component of physician functioning in his or her community, and also in evaluation of performance during residency training. We sought to assess surgical residents' perceptions and attitudes toward health advocacy in residency training and practice.

**Methods:** A survey was distributed to all Canadian chief residents in urology. The survey was closed-ended and employed a 5-point Likert scale and was designed to assess familiarity with the concept of health advocacy and its application and importance to training and practice. This was compared to the availability of formal training and resident participation in activities involving health advocacy.

**Results:** There was a 93% response rate from the chief residents. Most residents were well aware of the role of health advocate in urology (57% agreed or strongly agreed), and 68% believe it to be important in residency training and in the urologist's role in practice. This is in contrast to described participation and formal training in health advocacy. 14–21% or trainees had participated in health promotion or disease prevention activities prior to residency. 7–25% agreed that formal training or mentorship in health advocacy was available at their institution, and 21–39% have employed its principles in the clinic or community. Only 4–7% or residents surveyed were aware of or had participated in local urologic health advocacy groups.

**Conclusion:** Despite knowledge and acceptance of the importance of the health advocate role, there is a perceived lack of formal training and a dearth of participation during urologic residency training.

**Key Words:** education, residency

#### MP03.04

##### Percutaneous nephrolithotripsy for staghorn calculus: a single centre's experience

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**Introduction:** The percutaneous management of staghorn calculi may be one of the more challenging endourological procedures. Various techniques have been described and complications rates vary widely in the literature. Reported blood transfusion rates vary between 14% and 45%. The purpose of this study is to evaluate the outcomes and complications with PCNL for staghorn calculus in a large group of patients in a tertiary stone centre.

**Methods:** Between July 1990 and December 2005, all patients at a single centre scheduled for PCNL were prospectively reviewed. In 1338 patients, 509 PCNL procedures for partial or complete staghorn calculus defined as stone burden involving the renal pelvis and at least 2 calyces. Various intracorporeal lithotripters were utilized including, ultrasound, pneumatic, electrohydraulic and Holmium:YAG laser. Data collection included procedure time, hospital length of stay, number of access tracts, transfusion rates, major complications and stone free status.

**Results:** Mean age was 53.8 (range 4–84) years. The average procedure time was 104 minutes. Sixteen percent of the cases were done with multiple access tracts (range 2–5). The lower calyx was most commonly used (64.1%), followed by the upper in 18.5% and the middle in 17.4%. The blood transfusion rate was 0.8%. There was no statistically significant difference in terms of transfusion rates (0.7%–1.2%,  $p=1$ ) or other major complications between single and multiple tracts, respectively. Major complications included one case of bleeding requiring selective renal artery embolization and 8 patients were found to have a pneumo/hydrothorax. Stone free rates at discharge and at 3 months follow-up were 77.8% and 90.6%, respectively.

**Conclusion:** PCNL is a safe and effective procedure for the management of staghorn renal stones, with outcomes similar to those reported for percutaneous management of smaller volume, non-staghorn stones. The full array of endourologic equipment is essential.

**Key Words:** calculi, kidney, percutaneous

### MP03.05

#### Clinical and radiographic factors predicting shock wave lithotripsy (SWL) success: a view to a nomogram

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**Introduction and Objectives:** Identifying factors predictive of SWL failure would streamline the care of stone patients. The purpose of our study was to examine clinical and radiological factors to determine which had the most significant impact on SWL success.

**Methods:** Patients referred for SWL who had a CT performed at our centre were identified. Patients with intrarenal stones 5–20 mm in diameter were included. CT scans were reviewed to determine stone location, size, density and skin to stone distance (SSD) by an investigator blinded to treatment outcome. Treatment outcome was determined at 2 weeks. Chi square, ANOVA and logistic regression models were performed using SPSS.

**Results:** 111 patients were included with a mean age of 52 (SD±12.5) and a mean stone area of 90.5 mm (SD±78). 44 patients were rendered stone free while 27 had complete fragmentation (asymptomatic fragments < 5mm fragments). Successful treatment was defined as patients rendered stone free and those who had asymptomatic fragments less than 5 mm. Mean stone density was lower in the successfully treated patients at 837HU versus 1092HU in the failed treatment group ( $p<0.001$ ). The mean SSD was also significantly different between successfully treated patients and treatment failures at 9.6 cm versus 11.1 cm, respectively ( $p<0.001$ ). Multivariate logistic regression analysis examining stone size, body mass index, stone density and skin to stone distance revealed the later two factors to be predictive of treatment failure ( $p<0.001$  and  $p<0.026$  respectively). SSD greater than 9.0 cm was associated with failure of SWL therapy yielding an odds ratio of 2.768 (95% CI: 1.079–7.194). Stone density greater than 900 HU was more strongly associated with SWL failure with an odds ratio of 6.1 (95% CI: 2.4–15.4). Patients were then stratified into 4 risk groups; those with density < 900 HU/SSD < 9.0 cm, density < 900 HU/SSD > 9.0 cm, density > 900 HU/SSD < 9.0 cm and density > 900 HU/SSD > 9.0 cm. Success

rates were 90.5%, 78.8%, 58.3% and 40.9% respectively ( $p<0.0001$ ). Patients with either stone density > 900 HU, a SSD > 9 cm or both were at higher odds of treatment failure (odds ratio 6.2; CI: 2.54–15.08).

**Conclusions:** Stone density more than 900HU and SSD greater than 9 cm independently predict failure of SWL in multivariate analysis. Both of these factors will be considered important in the prospective design of an SWL treatment nomogram at our center.

**Key Words:** CT, lithotripsy, ureteroscopy

### MP03.06

#### Long term indwelling catheters: an RCT of catheter flush vs standard care

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**Introduction:** Blockage, encrustation and urine bypassing associated with long term indwelling catheters are common problems and costly for the urologist, homecare nurse and patient. The potential quality of life and economic impact is significant if an effective strategy can be found to manage these issues but currently no randomised controlled trials (RCTs) evaluate the options. In this study, we assess whether a "catheter maintenance solution" used widely in the UK is beneficial in maintaining catheter patency.

**Methods:** This is a 2 centre, 3 group RCT in progress in patients who have an indwelling catheter in situ greater than 30 days and who have blocked catheters requiring changes more than 1 time a month. Subjects are randomized to an 8 week, once weekly, 5-minute protocol with 50 ml of saline or 50 ml acidic solution (Suby G) or to weekly surveillance. Primary outcome: number of changes over the 8-week period; secondary outcomes: staff and subject satisfaction with the protocol, cost, incidence of symptomatic UTI, haematuria, pyuria, and urine pH.

**Results:** To date, 59 subjects have been randomized; 40 (68%) have complete data. Preliminary results suggest a drop in the number of catheter changes per month from 2.5 to 1.0 ( $p<0.001$ ) in the irrigation groups compared to the standard care group. No adverse events have occurred. A complete analysis based on a sample of 20 per group will further described in the presentation.

**Conclusion:** If routine catheter flushes can prolong catheter life and reduce the number of changes required, significant savings in healthcare dollars may be realised.

**Funding:** Alberta Heritage Foundation for Medical Research

**Key Words:** bladder, catheter

### MP03.07

#### Long-term surgical outcomes of ileocystoplasty with continent abdominal stoma

D. Hajek Provost, M. Saltel, S. Herschorn

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**Introduction:** To describe a 26-year experience with bladder augmentation with continent abdominal stoma in patients with refractory incontinence.

**Methods:** We performed a chart review of all adults undergoing ileocystoplasty with a continent abdominal stoma at our institution since 1982. The procedure involved detubularized augmentation with an ileal segment combined with an intussuscepted nipple valve for continence. Urethral continence procedures or bladder neck closure were carried out as required.

**Results:** Sixty-five patients (55 women and 10 men) underwent surgery at a mean age of 37.2 years (range 19–75). Fifty-eight were neurologically impaired, and 55 were wheelchair-bound. The most frequent diagnoses were spinal cord injury (28 patients), spina bifida (12), and multiple sclerosis (6). Four of 10 men underwent a concomitant bladder neck procedure (fascial sling plus tapering in 2, and bladder neck closure in two). Forty-five of 50 women underwent a concomitant bladder neck procedure (fascial sling in 24, fascial sling plus tapering in 13, and bladder neck closure in 8). Patients were followed for a mean of 6.4 years (range 3 mo to 16.5 yr). Fifty-five patients (85%) were continent from both the

urethra and stoma at last follow-up. Mean bladder capacity improved from 222 ml preoperatively to 435 ml postoperatively ( $p < 0.05$ ). Mean pressure at capacity decreased from 34.4 cm of H<sub>2</sub>O to 10.2 cm of H<sub>2</sub>O ( $p < 0.05$ ). Seven patients had hydronephrosis preoperatively, and this improved in all. Thirty-three patients (51%) required re-operation, included 18 procedures for bladder stones, 9 valve revisions, 6 stoma revisions, 2 injections of collagen into the valve, 2 parastomal hernia repairs, 1 bladder neck closure, and 1 ileal conduit.

**Conclusion:** Follow up of this group of patients reveals high rates of continence and significant improvement in urodynamic storage parameters. Despite a high rate of reoperation over the long-term, ileocystoplasty with a continent abdominal stoma is an effective option for patients requiring augmentation, who are unable to perform urethral catheterization or have severely compromised bladder outlets.

**Key Word:** reconstruction

### MP03.08

#### Dyspareunia response in interstitial cystitis patients treated with intravesical lidocaine, bicarbonate, and heparin

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**Purpose:** Dyspareunia occurs in as many as 87% of patients with interstitial cystitis/painful bladder syndrome (IC/PBS). A recent study showed improvement in voiding symptoms and pain in IC/PBS patients treated with intravesical lidocaine, heparin, and bicarbonate (therapeutic solution). We test the dyspareunia response of IC/PBS patients treated with intravesical therapeutic solution.

**Methods:** Consecutive IC/PBS patients that were sexually active treated with intravesical therapeutic solution were studied. All patients were diagnosed on the basis of a suggestive history and physical examination, urinalysis and urine culture negative for infection or hematuria, urine cytology negative for cancer, elevated PUF scores, and voiding diary showing frequent small voided volumes. Cystoscopy was performed when indicated. Patients were asked to complete the portion of the female sexual function index (FSFI) related to the pain domain (questions 17–19). Patients were treated with intravesical instillations 3 times per week for 3 weeks. Patients were asked to return to clinic 3–4 weeks later and were re-evaluated with history and exam, PUF, and FSFI questionnaires (questions 17–19). Patients rated their response using a PORIS score.

**Results:** There were 21 patients. The ages were  $39 \pm 12$  years (range 22–63). The PORIS changes were  $54 \pm 38\%$ . Thirteen patients (62%) reported PORIS improvements of  $>50\%$ . All patients reported dyspareunia at the outset. After therapy, if patients reported no dyspareunia, their PORIS scores were  $82 \pm 16\%$ , versus patients who still had dyspareunia reported PORIS scores of  $16 \pm 18\%$ ,  $p < 0.001$ . Pre- and posttherapeutic instillation nocturia was  $4 \pm 2$  vs.  $2 \pm 1$ ,  $p < 0.001$ , daytime frequency (minutes) was  $60 \pm 35$  vs.  $101 \pm 58$ ,  $p < 0.001$ , voided volumes (cc)  $91 \pm 58$  vs.  $158$  vs.  $76$ ,  $p < 0.001$ , PUF  $22 \pm 6$  vs.  $15 \pm 6$ ,  $p < 0.001$ , and FSFI pain domain  $1.9 \pm 0.9$  vs.  $3.7 \pm 1.6$ ,  $p < 0.001$ .

**Conclusions:** Intravesical therapeutic solution provides relief of voiding symptoms, pain, and dyspareunia in IC/PBS patients. A randomized, prospective trial is warranted.

**Key Words:** bladder dysfunction, interstitial cystitis, sexual activity

### MP03.09

#### Urethrovaginal fistula repair: long-term experience

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**Introduction and Objective:** The Urethrovaginal fistula is not a highly prevalent problem in North American urologic practice but is one that deserves attention. There are few large descriptive series of urethrovaginal fistula repairs in the literature. Our objective was to review our data from repairs over 20-year period with regard to risk factors, etiology, surgical techniques, success, and long-term lower urinary tract symptoms (LUTS).

**Methods:** Between January 1986 and June 2006, a total of 24 urethrovaginal fistulas were repaired. Charts were reviewed to record etiology, loca-

tion, presentation, previous attempt at repair, surgical approach, complications and overall cure rate. All fistulas were closed in 3 or more layers. The fistula tract was routinely not excised. A variety of flaps were used as needed. A suprapubic catheter was left for 4–6 weeks.

**Results:** Mean patient age was 46.73 (range 21–81). 8 (33.3%) of patients had been long-time smokers. 2 patients had a history of urethral diverticulum and 2 had previous pelvic malignancies. 20 (83.3%) patients had undergone prior pelvic surgery. The most common etiology was an incontinence procedure in 9 patients (37.5%). Other causes were forceps delivery (5 patients, 21%), chronic intermittent catheterization (3 patients, 12.5%), malignancy (2 patients, 8.3%), urethral diverticulum repair (2 patients, 8.3%), cystectomy and neobladder (2 patients, 8.3%), and vaginal surgery (1 patient, 4.2%). 19 fistulas were closed via a transvaginal approach. 2 fistulas were approached transabdominally. Three fistulas were closed with a combined abdominal and vaginal approach. Thirteen repairs were done with flaps including Martius in 10 and one each with omentum, gracilis muscle, and vaginal wall. The overall repair success rate was 95.8%. Mean follow-up time was 34.72 months (range 0.33–207.33). Long-term LUTS included frequency in 8 (33.3%), urgency in 7 (29.2%), urge incontinence in 6 (25%), and stress incontinence in 4 patients (16.7%).

**Conclusions:** The management techniques that optimized outcome included selection of appropriate surgical access, optimal tissue conditions, multiple layers closures with or without flaps, and postoperative suprapubic drainage. Tailoring the procedure to the individual patient circumstances appeared to be of benefit.

**Key Word:** reconstruction

### MP03.10

#### Treatment-related improvement in sleep disturbances in patients with interstitial cystitis/painful bladder syndrome (IC/PBS)

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<sup>6</sup>Statistical Consultants, Norwalk, CT

**Introduction:** We describe the sleep disturbances, evaluate impact on work and Quality of Life (QoL), and determine any relationship between symptom reduction and improvements in sleep and missed workdays in patients with IC/PBS.

**Methods:** Patients in a multidose pentosan polysulfate (PPS) clinical trial (Nickel et al 2005) with a diagnosis of IC/PBS who were randomized to 300 mg PPS/day completed the IC Symptom Index (ICSI), MOS Sleep Scale, SF-12 QoL, and Work Productivity (WP) questionnaires at weeks 8, 16, 24 and 32. The MOS Sleep Scale evaluates sleep disturbance via 6 questions (none to all of the time) for a range of 0–100 (higher scores reflect better sleep functioning). The WP measures days missed from work. Treatment responders were defined as those achieving a  $\geq 30\%$  reduction in ICSI from baseline to study endpoint. An intent-to-treat last-observation-carried-forward analysis was performed.

**Results:** Mean baseline ICSI, SF-12 (physical and mental components) and MOS Sleep scores (range) were 12.4 (5–20), 41.7 (16–60), 46.3 (12–64), and 57.9 (3–93), respectively. Positive correlation was observed between MOS Sleep and SF-12 QoL physical and mental components (0.426 and 0.370, respectively; baseline,  $N=122$ ;  $p < 0.0001$ ). Patients showed statistically significant improvement in ICSI and MOS Sleep at weeks 8, 16, 24 and 32. At week 32, among all patients, mean change in MOS Sleep from baseline was  $6.0 \pm 19.3$  (compared to baseline  $p=0.0011$ ). Patients achieving a  $\geq 30\%$  reduction in ICSI ( $n=48$ ; 43% responders) had a mean change in MOS Sleep of  $11.8 \pm 22.4$  while nonresponders ( $n=64$ ; 57%) had a mean change of  $1.6 \pm 15.7$  (between groups  $p=0.0055$ ). Reduction in ICSI score positively correlated ( $r=-0.33$ ;  $p=0.0003$ ) with improvement in MOS Sleep from baseline to study endpoint. Positive correlations were observed between ICSI and missed workdays at weeks 16, 24 and 32 ( $r=0.36$ ,  $p=0.0078$ ; week 32) and between MOS Sleep and fewer missed workdays at weeks 24 and 32 ( $r=-0.31$ ;  $p=0.0284$ ; week 32).

**Conclusions:** Sleep disturbances are moderate to severe in patients with IC/PBS and may impact QoL. Reduction in IC/PBS symptoms may be associated with patient-reported improvement in sleep and fewer missed work-days.

**Funding:** Ortho-McNeil Pharmaceuticals

**Key Words:** cystitis, interstitial cystitis, pain

### MP03.11

#### Analysis of videourodynamic results and the utility of leak point pressure as a measure for intrinsic sphincter deficiency in women with stress urinary incontinence

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**Introduction:** History, symptoms and urodynamic findings were correlated in a cohort of women undergoing videourodynamic testing (VUDS) for stress urinary incontinence (SUI). The clinical utility of leak point pressure (LPP) to predict intrinsic sphincter deficiency (ISD) without hypermobility (Type III) was also determined.

**Methods:** 2230 women underwent 2510 studies. After standardized history, VUDS was performed according to International Continence Society recommendations. Upright SUI testing was according to Blaivas (Types I, IIA, IIB, III and 0). Data analyzed included symptoms, presence of detrusor overactivity (DO) and type of SUI. LPP was analyzed by SUI type and receiver-operator characteristics (ROC) curves to determine clinical utility.

**Results:** 86% of patients had storage symptoms, and 77% had urgency incontinence (UUI). DO was more common in those with storage symptoms ( $p<0.05$ ). Distribution of SUI types was: 18.8% Type I, 25% IIA, 15.7% IIB, 11.6% III and 28.9% Type 0. Storage symptoms were more common in Type III than in I and IIA ( $p<0.05$ ). Mean LPP was lowest for Type III (67 cm water) and highest for IIA (87 cm water) ( $p<0.05$ ), whereas I and IIB had similar LPP results. The areas under the ROC curves of LPP were significantly larger for Types III and IIA than for I and IIB ( $p<0.0001$ ). The best LPP cutoff for predicting Type III was  $<78.5$  cm water (sensitivity 0.62, specificity 0.61). In our sample (Type III prevalence 16.3%), the positive predictive value of this LPP cutoff was 0.24, with a likelihood ratio of 1.33. Lower cut-off LPP values yielded higher positive predictive values up to 0.294, but had lower specificities.

**Conclusion:** Most patients had storage symptoms and hypermobility, with DO primarily associated with storage symptoms. LPP was poor in predicting for Types I and IIB, but had some predictive value for IIA and III. The best LPP cutoff for predicting ISD ( $<78.5$  cm water) had a low positive predictive value, and hence was of limited value in detecting Type III over other types of SUI. These results suggest that the clinical utility of LPP alone is very low for predicting for ISD without hypermobility (Type III).

**Key Words:** bladder dysfunction, incontinence, urinary stress incontinence

### MP03.12

#### The effects of Triclosan on uropathogen sensitivity to clinically relevant antibiotics

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**Introduction:** Several studies have shown varying levels of Triclosan (Tcn) resistance among several uropathogens, namely *P. aeruginosa* and *E. faecalis*. However, these studies involved rich conditions favorable to organism survival and may not be clinically relevant. Mechanisms such as the expression of a Tcn-resistant FabK protein, mutations in the FabI protein and expression of efflux pumps enable this resistance. Furthermore, high-level Tcn resistance is associated primarily with efflux pump expression, which can be metabolically costly to bacteria. Our objective is to

characterize resistance patterns of common uropathogens to Tcn using clinically relevant media and determine whether the stress and metabolic load of Tcn improves susceptibility to common antibiotics.

**Methods:** Using multiple strains from seven uropathogenic species, we carried out 24 hour growth experiments in human pooled urine, artificial urine and bacterial media. Each strain was exposed to escalating doses of Tcn and growth curves were established via 3 independent experiments to assess the dose response and minimal inhibitory concentration (MIC50) of each strain. Based upon the calculated MIC50s, Tcn will next be added to agar plates and broth cultures in combination with several clinically relevant antibiotics to determine the effect on uropathogen susceptibility.

**Results:** As expected, *S. epidermidis* and *S. aureus* were the most susceptible to Tcn while *E. faecalis* and *P. aeruginosa* demonstrated moderate and high level resistance respectively. While strains of *K. pneumoniae*, *E. coli* and *P. mirabilis* demonstrated dose-dependent Tcn growth inhibition, they were not as susceptible as the staphylococci. From this data we will characterize Tcn MIC50s and carry out plate and broth antibiotic susceptibility assays. Interestingly, analysis of the data suggests that several strains including *K. pneumoniae* and *S. aureus* are more susceptible to Tcn in urine than in bacterial media.

**Conclusion:** The Tcn dose response curves generated for all uropathogens are consistent with previous studies. Use of human and artificial urine will offer more clinically relevant results concerning the growth effects of Tcn, since earlier studies were carried out strictly using bacterial media. We expect that under more physiological conditions, Tcn will work synergistically with other antibiotics and urinary constituents to eradicate uropathogens.

**Key Words:** antibiotics, infection, UTI

### MP03.13

#### Assessment and correlation of urinary symptoms and urodynamic findings in multiple sclerosis patients: do they correlate?

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**Introduction and Objectives:** Multiple Sclerosis (MS) patients commonly complain of urinary symptoms. Urodynamic findings are also commonly found in these patients. We retrospectively reviewed all of our MS patients seen over the last 18 years who were referred for lower urinary tract symptoms to assess if there was any correlation of their symptoms and urodynamic findings.

**Methods and Materials:** From July 1988 to July 2006, 284 patients (330 studies) with MS, who were referred for storage and voiding symptoms, underwent multichannel urodynamics (79 non-video, 251 video). Mean age was 51 years old (range 16–82). There were 182 females and 102 males.

**Results:** The most common symptoms reported were urgency (68%), urge leakage (57%), hesitancy (36%), sensation of incomplete emptying (24%) and retention (14%). The most common urodynamic finding was detrusor overactivity (DO)(72%) and poor emptying, 52% had a postvoid residual (PVR) $>75$ cc and 34% had a PVR $>150$ cc. When we examined those patients with DO, only 49% complained of urgency and/or urge incontinence. Furthermore, in those patients with PVR $>75$ cc and those with PVR $>150$ cc, only 28% and 43% complained of hesitancy or a sensation of incomplete emptying or retention respectively.

**Conclusions:** DO (72%) and poor emptying (52%) were the most common urodynamic findings in those patients with MS referred for voiding dysfunction. However, there was a poor correlation of these findings with the patient's symptoms. Despite this, we believe all patients who have MS and have voiding complaints should undergo multichannel urodynamics. Treatment is guided by the clinical picture derived.

**Key Words:** bladder dysfunction, incontinence, overactive bladder

## MODERATED POSTER SESSION 4: BASIC SCIENCE

### Monday, June 25, 15:20-17:20

#### MP04.01

##### Dendritic cells pulsed with bladder tumor promote anti-tumor effects

Jl Izawa<sup>1</sup>, CY Nguan<sup>2</sup>, JP Deng<sup>1</sup>, A. Elmaadawi<sup>1</sup>, J. Xuan<sup>1</sup>, PJ O'Connell<sup>1</sup>, PPW Luke<sup>1</sup>

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**Introduction:** The most effective prevention of superficial bladder cancer recurrence is accomplished through immunotherapy. Our objective was to assess the ability of the most potent antigen presenting cells, dendritic cells (DC), to promote tumor death.

**Methods:** DC were enriched from the bone marrow of C3H mice through culture in IL-4 and GM-CSF. After pulsing DC with sonicated MBT2 cells, in vitro assessment of MBT2 uptake by DC using confocal microscopy, T cell stimulation by mixed lymphocyte reaction and IFN gamma production was performed. As well, assessment of tumor growth, angiogenesis and necrosis was performed using a subcutaneous (sc) bladder cancer model after sc injection of tumor-bearing mice with pulsed DC.

**Results:** According to flow cytometry analysis, enrichment techniques yielded > 80% purity of DC. Confocal microscopy indicated that DC took up sonicated MBT2 fragments. MLR showed that these DC were capable of stimulating C3H T-cells, as indicated by increased 3H incorporation after three day one-way MLR, as well as augmented IFN-gamma production (ELISPOT, flow cytometry). In vivo, tumor-bearing mice that received weekly sc injection of MBT2-pulsed DC had reduction of tumor growth, as well as promotion of significant necrosis in all tumors analyzed vs. none in controls. Additionally, immunohistochemical assessment of microvessel density, VEGF, FGF-2 and IL-8 of tumor specimens indicated significant inhibition of angiogenesis after a 3-week period.

**Conclusion:** We conclude that DC vaccine is capable of preventing bladder cancer development through upregulated immune response. Its role in association with BCG therapy is continuing to be assessed.

**Key Word:** bladder cancer

#### MP04.02

##### Over-expression of ROM induces inflammatory cytokine expression in hormone-dependent prostate cancer cells

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**Introduction:** Elevated cytokine levels in serum have been associated with advanced stage metastasis-related morbidity in prostate cancer. Several studies have shown that inflammatory cytokines can accelerate the growth of human prostate carcinoma cell lines. We recently observed the induction of I kappa-B kinase-epsilon (ROM) expression by the tumor necrosis factor (TNF)-alpha in LNCaP cells as well as elevated expression of IKKe in the androgen-independent DU145 and PC-3 cells, which exhibit constitutive NF kappa-B activity. Because previous studies, in murine embryonic fibroblasts, have shown that ROM-deficiency results in the reduction of lipopolysaccharide-induced expression of cytokines, we hypothesized that deregulation of ROM expression may be linked to inflammatory cytokine secretion and progression of prostate cancer to a hormone-independent status.

**Methods:** Hormone-sensitive LNCaP and 22Rv1 cells were used to study cytokine secretion in parallel with iKKe expression upon stimulation with TNF-alpha. The pUNO-ROM plasmid was also used to over-express iKKe in these hormone-sensitive cells to levels observed in the androgen-independent cell lines PC-3 and DU145. Cytokine secretions were characterized using ELISA assays. Expression of IKKe was meas-

ured by immunoblot assays which were also used to study the status of NF-kappa-B in cells which over-express ROM.

**Results:** We observed increased inflammatory cytokine secretion in LNCaP and 22Rv1 cells transfected by the pUNO-ROM plasmid. In these cells, over-expression of IKKe was detected without the activation of the NF-kappa-B pathway which is thought to control the expression of several cytokines. On the other hand, stimulation of ROM expression and NF-kappa-B nuclear translocation using TNF-alpha failed to induce a similar NF-kappa-B dependent cytokine secretion in hormone-sensitive prostate cancer cells.

**Conclusion:** Our results show, for the first time, evidence that over-expression of iKKe is closely linked to cytokine secretion. Moreover, the increase in inflammatory cytokine expression is not dependent on NF-kappa-B in prostate cancer cells that over-express ROM. Further studies will be needed in order to determine the mechanism involved in the deregulation of inflammatory cytokine secretion with regard to ROM over-expression and prostate cancer progression toward a hormone-refractory status.

**Key Words:** androgen receptor, inflammation, prostate cancer

#### MP04.03

##### Targeting chemoresistant prostate cancer with HTI-286, a synthetic analogue of the marine sponge product hemiasterlin

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**Introduction:** The development of therapeutic resistance is the underlying basis for most cancer deaths and novel drugs and therapeutic strategies that target the molecular basis of resistance to androgen withdrawal and chemotherapy are urgently required. Although the taxanes currently represent the most active chemotherapeutic agents for first line treatment of metastatic HRPc, most patients eventually progress because of inherited or acquired drug resistance. In contrast to taxanes, HTI-286 does not stabilize but depolymerizes existing microtubules and binds to the tubulin dimer at a unique site.

**Methods:** Androgen-dependent and androgen-independent prostate cancer cell lines including a newly generated docetaxel-resistant PC-3 cell line (PC-3R) were treated with HTI-286 and submitted to in vitro cell growth and apoptosis studies. Gene array profiling was carried out on LNCaP cells to screen for changes in gene expression induced by HTI-286. In vivo, four groups of 10 nude mice with established PC-3 or PC-3R xenografts respectively were given 1.5 mg/kg HTI-286 or vehicle control i.v. at t3 doses, 4 days apart.

**Results:** HTI-286 was a potent inhibitor of proliferation (mean IC50 = 1.9 ± 1.2 nM). Flow cytometry showed significant treatment-induced increases in the apoptotic subG0 phase in all cell lines. Microarray studies identified higher expression levels in several genes known to play roles in survival pathways like BCL2, GADD45, and Clusterin but not in tubulin. In vivo, HTI-286 significantly inhibited tumor growth in mice and demonstrated no cross-resistance to taxanes. Experiments with mice bearing LNCaP tumors and tissue microarray construction are underway to confirm the gene array data and to design combination therapy of HTI-286 and targeted gene knock-down.

**Conclusion:** HTI-286 showed excellent activity both in androgen-independent and in taxane-resistant tumor models. These findings provide pre-clinical proof-of-principle for the use of HTI-286 in second line treatment strategies in multimodal therapy for chemoresistant prostate cancer.

**Key Words:** cancer, chemotherapy, prostate cancer

#### MP04.04

##### C-reactive protein is the foremost predictor of renal cell

**carcinoma-specific mortality: a study of 313 patients**QD Trinh<sup>1</sup>, M. Soubra<sup>1</sup>, PI Karakiewicz<sup>1</sup>, J. Tostain<sup>2</sup>, JJ Patard<sup>3</sup><sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>St-Étienne University, St-Étienne, France; <sup>3</sup>Rennes University, Rennes, France**Introduction:** C-reactive protein (CRP) represents a promising prognostic variable in patients with sporadic renal cell carcinoma (RCC). We hypothesized that CRP can improve the prognostic ability of standard RCC-specific mortality (RCC-SM) predictors in patients treated with nephrectomy for all stages of RCC.**Methods:** Radical nephrectomy was performed in 314 patients from 2 European centers. Life table, Kaplan-Meier and Cox regression analyses addressed RCC-SM. Covariates included age, gender, TNM stage, tumor size, Fuhrman grade and histological subtype.**Results:** The median survival of the cohort was 19.9 years. Age ranged from 10 to 77 years. Most patients were male (69%). T stages were distributed as follows: T1-121, T2-45, T3-140, T4-7. CRP values ranged from 1.0 to 358. mg/L (mean 40.9, median 11.0 mg/L). In multivariable analyses, CRP was an independent predictor of RCC-SM ( $p=0.003$ ). The consideration of CRP in the multivariable model increased the predictive accuracy by 3.7% ( $p<0.001$ ). Moreover, the model with CRP performed 2.4 and 4.6% better than the UCLA Integrated Staging System (UISS) at respectively 2 and 5 years.**Conclusion:** CRP represents a highly accurate predictor of RCC-SM. Its routine use could allow better risk stratification and risk-adjusted follow-up of RCC patients.**Key Words:** cancer, kidney, nephrectomy**MP04.05****Novel markers of aggressiveness in renal cell carcinoma generated from an in vitro model**J-B Lattouf<sup>1</sup>, B Peruzzi<sup>2</sup>, D.P. Bottaro<sup>2</sup><sup>1</sup>CHUM, Montréal, QC; <sup>2</sup>Urologic Oncology Branch, NCI/NIH, Bethesda, MD**Introduction:** Prognostic markers of aggressiveness in renal cell carcinoma (RCC) are lacking. We used proxies of aggressiveness in clear cell RCC derived from an in vitro model, namely cellular branching and invasion (which have been extensively validated in the literature), in order delineate differentially expressed genes in the aggressive state.**Methods:** Our in vitro model consisted of three cell lines: 1- the renal cell carcinoma cell line 786-0, which has a documented VHL mutation, 2- 786-0 with an added ectopic expression of VHL and 3- 786-0 VHL+ with an ectopic expression of a non-degradable form of beta-catenin (S37A+). These 3 cell lines have been shown to differentially manifest branching and invasion with or without hepatocyte growth factor (HGF) stimulation (published data, Peruzzi B et al PNAS, 2006). A gene probe micro-array analysis of these three cell lines was carried out. Differential gene expression between the branching/invasive and non-branching/invasive cell lines was assessed using class comparison analysis and scatter plot analysis (BRB-ArrayTools).**Results:** branching and invasion were shown to correlate positively with a limited set of genes. As already reported, genes regulating cell cycle and division as well as cell-cell interactions were found to be modulated by VHL. Further analysis using reverse modulation between the 3 different cell lines according to combinatorial models confirmed that some of these genes may also regulate branching and invasion. Surprisingly, the set of modulated genes also comprised multiple candidates derived from the BRCA/Fanconi anemia pathway, which may for the first time establish a link between the latter and the VHL pathway.**Conclusion:** We have identified a set of genes that may be related to aggressiveness in clear cell RCC and we believe further validation of this set of genes is warranted. These may prove to be promising candidates for outcome and treatment response prognostication, as well as targets for molecular therapeutics strategies.**Key Word:** molecular marker**MP04.06****VHL gene mutations in sporadic renal cell carcinoma**

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**Introduction:** VHL mutations are ubiquitous in patients with sporadic renal cell carcinoma (RCC). They occur relatively early and disrupt critical pathways in kidney tumorigenesis. The identification of VHL mutations will more accurately characterize kidney tumors, and serve as invaluable prognostic makers in kidney cancer, especially early stage small renal masses.**Methods:** Kidney tumor tissue was obtained from 26 patients undergoing radical or partial nephrectomy for sporadic RCC. Percutaneous needle biopsy cores were also obtained from patients on a conservative surveillance protocol for the management of small renal masses (< 4 cm). DNA was extracted from tumor tissue and amplified by PCR for sequencing to identify variations in nucleotide sequence or splicing errors. Quantitative PCR was carried out to detect amplifications or deletions in allelic copy number. Methylation-specific PCR was also done to detect hypermethylated DNA promoter regions. The association between the presence of somatic VHL mutations in clear cell RCC phenotype were compared with wild VHL genotypes and related to various clinical and pathological parameters.**Results:** In the extirpated clear cell RCC specimens, the VHL mutation detection rate was 75%; over 2/3 were point mutations detected by sequencing and 1/3 were loss of heterozygosity. Wild VHL genotype was found in normal kidney parenchyma, benign renal tumors, papillary and chromophobe RCC. Molecular analysis of the small renal tumor specimens is ongoing.**Conclusion:** The detection of a VHL mutation may predict the biological behavior of small renal tumors. By combining a set of molecular markers with defined pathological parameters we hope to preemptively select out patients for early surgical intervention versus conservative surveillance, providing new opportunities for personalized patient care.**Key Words:** DNA, molecular marker, renal cell carcinoma**MP04.07****Low CAIX expression and absence of VHL gene mutation are associated with tumor aggressiveness and poor survival in patients with renal cell carcinoma (RCC)**QD Trinh<sup>1</sup>, M. Soubra<sup>1</sup>, PI Karakiewicz<sup>1</sup>, P. Fergelot<sup>2</sup>, N. Rioux-Leclercq<sup>2</sup>, RA Figlin<sup>3</sup>, JW Said<sup>3</sup>, AS Belldegrin<sup>3</sup>, AJ Pantuck<sup>3</sup>, JJ Patard<sup>2</sup><sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>Rennes University, Rennes, France; <sup>3</sup>David Geffen School of Medicine at UCLA, Los Angeles, CA**Introduction:** VHL gene mutations induce the expression of CAIX and previous studies have shown that low CAIX results in worse prognosis for RCC. We attempt to further describe the relationship between CAIX expression, VHL gene mutations and tumor characteristics.**Methods:** Radical nephrectomy was performed in 100 patients at 2 centers. Genomic DNA was extracted from frozen tumor samples using the QIAmp® DNA mini kit. Four amplicons covering the whole coding sequence of the VHL gene were synthesized by PCR and sequenced by Big Dye. Mutation bearing sequences were confirmed by a second round of sequencing. The monoclonal antibody M75 was used to score the expression of the CAIX protein. Life table, Kaplan-Meier and Cox regression analyses addressed RCC-specific mortality (RCC-SM).**Results:** VHL mutations were identified in 58 patients (58%) and CAIX tumor expression ranged from 0% to 100%. Low CAIX expression (<85%) was associated with absence of VHL mutation ( $p=0.02$ ), larger tumors ( $p=0.002$ ), higher T stage ( $p=0.007$ ), nodal metastases ( $p=0.001$ ) and higher Fuhrman grade ( $p=0.006$ ). Absence of VHL mutation was associated with worse ECOG ( $p=0.005$ ), higher T stage ( $p=0.01$ ) and presence of nodal ( $p=0.03$ ) and distant metastases ( $p=0.02$ ). Categorically-coded, CAIX was a statistically significant predictor of RCC-SM ( $p=0.002$ ), while VHL mutation approached statistical significance ( $p=0.08$ ) and a trend was observed for worse survival when VHL was not mutated. Patients with both high CAIX and VHL mutation had better survival (95.9% 1 year and 6 year median survival) than their counterparts with low CAIX expression and absence of VHL mutation (62.9% 1 year and 1.5 year median survival) ( $p<0.001$ ). In Cox regression analyses, neither CAIX ( $p=0.06$ ) nor

VHL ( $p=0.4$ ) achieved independent predictor status, when adjusted for age, gender, TNM stage, tumor size, Fuhrman and ECOG.

**Conclusion:** Low CAIX expression is associated with the absence of VHL mutation and aggressive tumor characteristics, and is a statistically significant predictor of poor prognosis in patients with clear cell RCC.

**Key Words:** kidney, nephrectomy, renal cell carcinoma

#### MP04.08

##### Expression of TMPRSS2:ERG gene fusion in prostate cancer cells is an important prognostic factor for cancer progression

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**Introduction and Objective:** The prostate-specific gene, TMPRSS2, is fused with the transcription factor gene, ERG in a high proportion of prostate cancers. However, the clinical significance of TMPRSS2:ERG gene fusion among prostate cancer patients is unknown.

**Methods:** We assayed for the presence of the TMPRSS2:ERG fusion gene product among 83 patients who underwent surgery for clinically localized prostate cancer using RT-PCR and direct DNA sequencing, and evaluated its prognostic significance. We used biochemical recurrence as the primary endpoint and evaluated whether expression of TMPRSS2:ERG gene fusion was a predictor for recurrence.

**Results:** The fusion gene was present within prostate cancer tumor cells in 39 patients (46.4%). Twenty-five patients (29.8%) experienced biochemical disease relapse (elevated PSA) after a mean follow-up of 23.3 months (range 1–96 mo). Patients with the fusion product had a significantly higher rate of recurrence (5-year recurrence rate 68.4%) compared to patients who lacked the fusion product (5-year recurrence rate 17.1%,  $p=0.0002$ ). After adjusting for grade, stage and PSA level at diagnosis, the hazard ratio for disease relapse for patients with the fusion gene was 4.8 (95% CI: 1.6–14,  $p=0.004$ ) compared to patients without the fusion. From the multivariate analysis, the presence of gene fusion was the single most important prognostic factor.

**Conclusions:** Our study indicates that the expression of TMPRSS2:ERG fusion gene among prostate cancer patients treated with surgery is a strong prognostic factor for disease relapse, and may have important clinical implications.

**Key Words:** prostate cancer, prognostic factors

#### MP04.09

##### Reduction of the cytosolic Cdk11 protein expression in clear cell renal cell carcinoma

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**Purpose:** The PITSLRE kinase (Cdk11) is mapped to 1p36.3, a region frequently deleted in solid tumors. To determine how Cdk11 functions in renal tumorigenesis, we examined Cdk11 expression in 34 cases of primary clear cell carcinoma (ccRCC) and their matched non-tumor tissues.

**Materials and Methods:** ccRCC and the adjacent non-tumor kidney tissues were obtained after surgery. Both tissues were mounted on the same slide for immunohistochemistry staining for Cdk11 expression. Lysate was prepared from the paired ccRCC and non-RCC tissues and analyzed for the expression of Cdk11 and actin. After being normalized against actin, the levels of the Cdk11 protein in ccRCC were compared to those of Cdk11 in the matched non-RCC kidney tissues.

**Results:** In comparison to the paired non-RCC tissues, 44% of ccRCCs (15/34) and 52.9% of ccRCCs (18/34) contain less than 50% and 60% of the Cdk11p110 protein, respectively, when compared to Cdk11 expression in the paired non-tumor kidney tissues. In non-tumor kidney tissues, Cdk11 is largely expressed in the cytosol and nucleus of the proximal tubule epithelial cells. In ccRCC tissues, Cdk11 is predominantly a nuclear protein, suggesting that the process of ccRCC tumorigenesis results in loss of the cytosolic portion of Cdk11p110. The levels of Cdk11 reduction do not correlate with the tumor sizes and grades of ccRCC.

**Conclusions:** Reduction in Cdk11 expression and loss of cytosolic Cdk11 occur in ccRCC.

**Key Words:** cancer, kidney, molecular marker

#### MP04.10

##### Tn expression in localized high-risk prostate cancer

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**Introduction:** Alteration of the glycosylation process is often associated with neoplastic transformation. This results in the expression of various carbohydrate antigens such as blood group-related Tn, T, sialyl-Tn and sialyl-T antigens (family of T antigens). The tumour-associated antigen Tn has been shown to be a promising immunotherapeutic target for the immunotherapy of cancer. The objective of this study was to characterize its expression in high-risk localized prostate cancer.

**Methods:** Immunohistochemical staining was carried out on tissue microarray (TMA) sections using the anti-Tn mAb B1.1. TMAs were built from 116 pT3 prostatectomy specimens, using 6 cores per tumour. Following prostatectomy, patients had no additional treatment until PSA failure.

**Results:** Staining was observed both in tumour cells and in glandular secretions. An average 15% of tumour glands were stained. Seventy-two percent of tumours contained up to 100% of positive glands while 38% contained more than 10% stained glands. Staining was associated with T stage ( $p=0.0015$ ) and Gleason grade ( $p=0.0006$ ) but not with initial PSA ( $p=0.53$ ). The proportion of positive tumours was higher in pT3a and in Gleason  $\leq 7$  tumours. Patients with positive tumours ( $>0$  positive glands) had a 2-fold reduced risk of PSA failure in non-adjusted Cox regression analysis ( $p=0.044$ ) but no significant association was observed after adjusting for stage, Gleason grade and initial PSA.

**Conclusion:** These data show an association of Tn expression with tumour characteristics and confirm its relevance as a target for immunotherapy of prostate cancer, especially in low Gleason grade ( $\leq 7$ ) tumours.

**Key Words:** cancer, molecular marker, prostate

#### MP04.11

##### MAGE-A4 and MAGE-A9 protein expression in renal cell carcinoma

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**Introduction:** Cancer-testis antigens, such as MAGE-As, are ideal targets for immunotherapy of cancers. However, little is known about their expression in renal cell carcinomas (RCCs). The objective of this study was to analyse the expression of MAGE-A4 and MAGE-A9 proteins in a retrospective cohort of RCCs obtained at nephrectomies performed between 1990 and 2000.

**Methods:** Immunohistochemical analysis was performed using mAbs 57B and 14A11, to detect respectively MAGE-A4 and MAGE-A9. The mAbs were tested on tissue microarrays of 227 primary tumours, including 179 (79%) conventional clear cell and 36 (16%) papillary RCCs, and on 20 normal kidney samples. Four 0.6 mm diameter tissue cores taken in the highest grade area of the tumours were used to build the tissue microarrays. Slides scoring was carried out by two independent observers. Clinical data were collected in a database including patient characteristics, TNM staging, biological profile, radiologic workup and treatment outcome with a 6.5 years median follow-up.

**Results:** Expression of MAGE-A4 and MAGE-A9 was not observed in normal kidney but was respectively found in 14% and 18% of clear cell and in 36% and 64% of papillary RCCs. Staining with both mAbs was exclusively observed in the cytoplasm of tumor cells. In the majority of positive cases, less than 75% of tumour cells were stained. However, up to 30% of MAGE-A9-positive tumours contained more than 75% of positive cells whereas only 7% of the MAGE-A4-positive tumours did so. No statistically significant association could be found between marker expression and progression or specific death.

**Conclusion:** MAGE-A4 and MAGE-A9 are predominantly expressed in papillary RCCs. MAGE-A9 constitutes a better target than MAGE-A4 for RCC immunotherapy as its expression is more frequent and is found in a larger proportion of tumour cells.

**Key Words:** immunotherapy, molecular marker, renal cell carcinoma

**MP04.12****Lower plasma adiponectin levels as a potential biomarker for renal cell carcinoma: an update on a continuing study**B. Tisdale<sup>1</sup>, T. Hamlet<sup>2</sup>, J. Lu<sup>2</sup>, A. Gills<sup>1</sup>, O. Moshkin<sup>2</sup>, G. Singh<sup>2,3</sup>, A. Kapoor<sup>1</sup>, J. Pinthus<sup>1,2</sup><sup>1</sup>Institute of Urology, <sup>2</sup>Juravinski Cancer Center Research Institute, <sup>3</sup>Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON

**Introduction:** An increased incidence of renal cell carcinoma (RCC) in overweight and obese male and female patients has been reported by several studies. Adiponectin is a cytokine secreted by adipocytes and accounts for approximately 0.01% of total plasma protein. Unlike other adipocyte products, adiponectin correlates with reduced body mass index or body weight. We report our recent findings correlating the plasma levels of adiponectin and the tumor expression of adiponectin receptor 1 and 2 (AdipoR1, AdipoR2) with the disease characteristics.

**Methods:** Blood samples, collected pre-operatively from 38 patients, were analyzed in triplicates for the levels of plasma adiponectin using specific ELISA assay. All patients had conventional (clear cell) RCC but represented different stages of the disease including 3 cases of metastatic RCC. One pathologist reviewed all pathology slides. Patients were not diabetic and all had normal renal functions. Body weight (kg) and height were measured at diagnosis. The RCC and corresponding normal renal tissue were analyzed comparatively for their AdipoR1 and AdipoR2 expression (immunoblotting) in 10 patients.

**Results:** In the healthy population adiponectin can be found in the plasma at concentrations of 7–12 µg/ml. However, in our RCC cohort 70% and 43% of the patients had adiponectin levels less than 7 µg/ml and 5 µg/ml respectively including all patients with metastatic RCC. The average, median and range of plasma adiponectin levels were 5.9, 5.35 and 1.2–11.7 µg/ml, respectively. A strong inverse correlation was found between the plasma levels of adiponectin and the tumor size with significantly lower levels of adiponectin in tumors  $\geq 4$  cm ( $p < 0.05$ ) with no statistical difference in the BMI of patients with tumors' size smaller or larger than 4 cm. Moreover, the expression of AdipoR2 was found to be lower in the cancerous tissue compared to the same patient's normal kidney tissues in 72% of the cases. The mean and median relative expression of AdipoR2 in the cancer tissue vs. the normal parenchyma was 50% and 59% respectively. Moreover, lower levels of expression for AdipoR2 were associated with tumor grade, size and metastasis. A differential expression of AdipoR1 was also recorded between the cancer tissue and the normal parenchyma. Most of the patients in the cohort had abnormal BMI: 38% had BMI between 25–30 kg/m<sup>2</sup> and 38% had BMI  $> 30$  kg/m<sup>2</sup>. We could not demonstrate an inverse correlation between BMI and adiponectin levels in our cohort however there was a clear trend for more aggressive tumour grade (3 + 4s) for BMI  $> 30$ .

**Conclusions:** Based on this ongoing study, lower blood levels of adiponectin and lower expression of the adiponectin receptor R2 are positively associated with renal cancer pathogenesis and aggressiveness. This suggests that adiponectin could be a potential suppressor of renal cancer in obese individuals. Thus it provides a potential link between obesity and RCC and may shed some new light on the pathogenesis of RCC. We expect to present data on more than 50 patients and also to present experimental data from our lab showing the biological effect of human adiponectin (that we have cloned) on various models of human RCC.

**Key Word:** prognostic marker

**MP04.13****High Ki67 expression is associated, in a multi-variate model, with lower risk of biochemical recurrence in prostate cancer patients following radical prostatectomy**PO Gannon<sup>1</sup>, IH Koumakpayi<sup>1</sup>, C. Le Page<sup>1</sup>, M. Alam Fahmy<sup>1</sup>, A-M Mes-Masson<sup>1,2</sup>, F. Saad<sup>1,3</sup><sup>1</sup>Institut du Cancer de Montréal/CR-CHUM/Hôpital Notre-Dame; <sup>2</sup>Département de Médecine, Université de Montréal, <sup>3</sup>Département de Chirurgie-Oncologie, Université de Montréal, Montréal, QC

**Introduction:** The prediction of disease progression in prostate cancer patients following radical prostatectomy remains problematic. The use of

molecular markers in the diagnostic decision could offer a better stratification of patients more at risk of progressing to advanced stages of the disease. As such, we recently reported that nuclear ErbB3, a growth factor receptor, was associated with Gleason score and hormone-refractory status. The objective of this study was to evaluate whether ErbB3 could predict overall biochemical recurrence (BCR). In addition, we evaluated if three nuclear markers known to be associated with prostate cancer progression (Cyclin D1, Ki67 and androgen receptor) were more significant predictors of BCR than ErbB3 alone or in combination.

**Methods:** Using immunohistochemistry, we analyzed a tissue microarray containing 373 cores from 63 radical prostatectomy specimens. No patient had received hormone therapy prior to surgery and prior to BCR. The quantitative analysis of nuclear staining was measured by 2 independent observers (ErbB3, Cyclin D1 and AR) or with the ImagePro Plus software<sup>TM</sup> (Ki67). Marker expressions were categorized as either positive or negative according to the median expression.

**Results:** Of the four markers analyzed, Ki67 alone was the strongest predictor of overall BCR. In a multi-variate Cox regression model (backward conditional), while controlling for the pre-operative PSA, Gleason score and lymph node invasion at time of surgery, Ki67 was found to be an independent predictor of BCR with a Ki67+ patients having lower risk of BCR (HR = -2.51,  $p = 0.015$ , CI 95%: 1.19–5.29). We then analyzed if different marker combinations could predict BCR. Patients positive for nuclear AR or AR+/Cyclin D1+ double positive were found to have lower risk of BCR (Kaplan-Meier,  $p = 0.047$  and  $p = 0.026$ , respectively). However, in the multi-variate model, the combinations of Cyclin D1+/AR+ (HR = -2.28,  $p = 0.053$ , CI 95%: 0.94–5.49), ErbB3+/Ki67+ (HR = -2.43,  $p = 0.034$ , CI 95%: 1.07–5.52) and AR+/Ki67+ (HR = -2.32,  $p = 0.049$ , CI 95%: 1.01–5.35) could not improve on the predictive value of Ki67 alone.

**Conclusions:** The major new finding of the study is that patients positive for Ki67 expression were at a lower risk of developing BCR, which contrast previously published results, and warrants further investigations.

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**Key Words:** molecular marker, prognostic marker, prostate cancer

**MP04.14****The role of stimulatory ligand expression on prostate cancer cells and evasion of immune effector cell killing**

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**Introduction and Objective:** Escape from immune surveillance is one outcome of neoplastic progression and facilitates proliferation, invasion and metastases of solid tumours, including prostate cancer. It has been previously demonstrated that tumor hypoxia is one mechanism underlying tumour escape. Herein, we determine the mechanisms of prostate cancer evasion of circulating immune cells.

**Methods:** To determine the effect of cancer cell exposure of a hypoxic environment (1% O<sub>2</sub>) on immune cell recognition and killing, two human prostate cancer cell lines PC3 and DU145 were used for cytotoxicity experiments using fresh human peripheral blood lymphocytes (PBL) in a standard chromium release assays. The effect tumour hypoxia on the expression of immunostimulatory ligands on cancer cells, including MIC A/B, was assessed by flow cytometry and ELISA. The role of matrix metalloproteinase (MMP) on MIC expression was determined using pharmacologic inhibitors. The effect of cellular hypoxia on cytokine expression by the cancer cells was measured by ELISA of supernatant.

**Results:** Results of the cytotoxicity assays reveal that culturing cell lines in a low oxygen environment will significantly effect immunosurveillance by decreasing the natural killer (NK) cell activity of circulating PBLs. Exposure of cell lines to a hypoxic environment for as little as 8 hours significantly decreases the expression of the stimulatory ligand MIC A/B by shedding of the ligand from the cell surface. The MMP inhibitors appear to mediate this shedding. Hypoxia also modulates the tumour environment by increasing immuno-modulating cytokines such as TGF-beta.

**Conclusions:** These findings indicate hypoxia leads to cellular adaptive

responses of prostate cancer cells, which interfere with immune effector cell killing. These hypoxia related effects are likely multiple, including modulation of cell surface ligands and immunosuppressive cytokine expression, but demonstrate possible therapeutic targets for immunotherapy protocols for prostate cancer.

**Key Words:** immunotherapy, prognostic marker, prostate cancer

#### MP04.15

##### Prognostic value of tumor-infiltrating dendritic cells expressing CD83 in human superficial bladder cancer

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**Introduction:** The clinical significance of tumor infiltration by dendritic cells (DCs), as marker of the immune response, has been reported in a variety of human cancers. To estimate the importance of their contribution to the response to BCG immunotherapy of superficial bladder cancer, we evaluated tumor infiltration by CD83 positive mature DCs, in resected tumors, prior to Bacillus Calmette-Guérin (BCG) treatment.

**Method:** Immunohistochemical staining was performed with an anti-CD83 monoclonal antibody (clone 1H4b from Novocastra) on 23 superficial bladder tumors from patients who received induction BCG with or without 1 or 2 maintenance BCG treatments, following resection. Scoring of positive cells in the papillary axis, in lymphatic nodules and infiltrated into tumors was carried out by two independent observers.

**Results:** The presence of CD83-positive tumor-infiltrating DCs was associated with a near-significantly increased recurrence-free survival ( $p=0.061$ ). After 36 months, all patients with tumors containing no CD83-positive infiltrated DCs had suffered recurrences while 46% of those showing the presence of such DCs had no recurrence. In a multivariate Cox regression analysis, adjusted for age, number of BCG treatments and stage, presence of CD83-positive cells was associated with a four-fold decreased risk of recurrence ( $p=0.04$ ).

**Conclusion:** We observed a correlation between the presence of CD83-positive infiltrated DCs and recurrence-free survival in BCG-treated superficial bladder tumors. These results suggest that infiltration of tumors by mature DCs may be important in the anti-tumor immune response. Further studies are required to confirm the relevance of these tumor-infiltrating DCs to clinical outcome in larger cohorts.

**Key Word:** immunotherapy

#### MP04.16

##### Low nuclear androgen receptor expression in prostate cancer predicts an early onset of biochemical recurrence

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**Introduction:** Prostate cancer (PCa) is a leading cause of cancer death in North American men. The androgen receptor (AR) has an established role in the progression of this disease; however, it is unclear at what stage it intervenes. It is also uncertain whether the AR can be a useful prognostic marker for PCa. In this study, we assessed AR expression and sub-cellular localization in normal prostate as well as in androgen sensitive and insensitive PCa (AIPCa) tissues, and evaluated the ability of the AR to predict biochemical recurrence (BCR).

**Methods:** We used tissue micro-arrays containing prostate tissue cores obtained from cancer-free patients ( $n=43$ ), AIPCa patients ( $n=36$ ), and patients with hormone-sensitive cancers ( $n=64$ ) from which were collected both cancerous and normal adjacent tissue. Using immunohistochemistry, we stained the tissue micro-arrays with a monoclonal antibody recognizing the AR. Two observers assessed the frequency (0–100%) and intensity (0–10) of both cytoplasmic and nuclear AR staining. AR cytoplasmic (Ci) and nuclear (Ni) indices were calculated by multiplying nuclear staining frequency and nuclear staining intensity. Kaplan–Meier,

and Cox multivariate analyses were done using SPSS.

**Results:** We found that AR Ci increased significantly in AIPCa although a modest but significant increase in PCa Ci was observed compared to normal tissues. In contrast, AR Ni was significantly lower in cancer-free patients as opposed to that seen in normal tissue adjacent to cancer. Similarly, cancerous tissue exhibited higher AR Ni than its adjacent normal tissue ( $p<0.05$ , Kruskal–Wallis). Kaplan–Meier analyses revealed that low AR Ni was predictive of an early onset of BCR (before 3-years) in the sub-cohort of hormone-sensitive patients (LR=6.51,  $p=0.011$ ). Furthermore, low AR Ni remained an independent predictor of BCR before 3-years in a Cox multivariate model controlling for age, pre-operative PSA, lymph node invasion, Gleason score and surgical margin status (hazard ratio=2.28, 95% confidence interval=1.04–5,  $p<0.05$ ).

**Conclusion:** We conclude that increased nuclear AR activity could be a pre-malignant step in PCa progression whereas its role within cancer cells may be more complex, as we also found that low AR nuclear activity was associated to an early onset of BCR. In addition, the observation that cytoplasmic AR is prevalent in AIPCa suggests that cytoplasmic AR functions potentially contribute to the AIPCa phenotype and warrant further investigation.

**Key Words:** androgen receptor, prognostic marker, prostate cancer

#### MP04.17

##### ErbB4 nuclear localization, gamma-secretase and neuregulin expression in prostate cancer: multivariate analysis of prostate cancer patient clinical outcome

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**Introduction and Objective:** Membrane protein ErbB4 is a member of the ErbB growth factor receptor family, which can be activated by neuregulins and other growth factors. ErbB receptor family members are involved in prostate cancer (PCa) progression. Upon neuregulin activation, ErbB4 is cleaved within its transmembrane domain by presenilin gamma-secretase (PSN) to release an intracellular domain that translocates into the nucleus. Although, ErbB4 ligand-dependant translocation of ErbB4 to the nucleus and its nuclear activity has been reported in breast cancer cell lines, there are few reports concerning ErbB4 nuclear localization and its clinical relevance. In this study, we report for the first time the clinical relevance of ErbB4 nuclear localization, neuregulin (NRG), and presenilin 2 gamma-secretase (PSN2) expression in prostate cancer tissues.

**Methods:** Immunohistochemistry using anti-ErbB4, anti-presenilin 2 gamma-secretase and anti-neuregulin antibodies was done on a set of tissue microarrays (TMA) from 140 patients. The TMAs contained, 92 cores of normal prostate tissue obtained from 46 autopsy specimens from young males, 373 tumor and normal adjacent cores from 63 hormone sensitive PCa (HSPCa) patients, and 146 cores from 31 hormone refractory PCa (HRPCa) patients. All statistical analyses were done using SPSS software Version 11.

**Results:** We found a statistically significant increase in the percentage of ErbB4 nuclear localization (68.7% vs. 53.2%,  $p<0.01$ ), NRG expression (2.06 vs. 1.41,  $p<0.001$ ) and PSN2 expression (2.14 vs. 1.53,  $p<0.001$ ) when comparing cancerous tissues to normal tissue found adjacent to cancer. Interestingly, a similar statistically significant increase in nuclear ErbB4 and NRG expression was observed when comparing HRPCa to HSPCa samples ( $p<0.001$ ). In cancerous tissues, a strong correlation was found between ErbB4 nuclear localization and NRG expression ( $r=0.672$ ,  $p<0.001$ ), between ErbB4 nuclear localization and PSN2 expression ( $r=0.51$ ,  $p<0.001$ ), and between PSN2 and NRG expression ( $r=0.71$ ,  $p<0.001$ ). Additionally, nuclear ErbB4 and PSN2 inversely correlated with tumor stage, perineural invasion, lymph node invasion and seminal vesicle invasion. Kaplan–Meier analysis of nuclear ErbB4 (Log rank  $p=0.030$ ) and PSN2 expression (Log rank  $p=0.018$ ) showed an inverse association with biochemical recurrence of PCa patients. In multivariate analyses including these three markers and controlling for clinical parameters, only nuclear ErbB4 remained an independent prognostic marker.

**Conclusion:** Our results suggest that high ErbB4 nuclear localization along with increased PSN2 expression have a protective effect against prostate cancer progression and biochemical recurrence.

Source of funding: Fonds de la recherche en santé Québec, Université de Montréal's Chair in Prostate Cancer and CUOG-AstraZeneca Research Award

**Key Words:** molecular marker, prognostic marker, prostate cancer

#### MP04.18

##### Effect of androgen deprivation on PSP94 expression in prostate cancer cells

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**Introduction:** Prostate secretory protein of 94 amino acids (PSP94) synthesis was demonstrated to show androgen independence. However, immunohistochemistry staining of radical prostatectomy specimens showed that after androgen deprivation PSP94 expression was decreased in grade 3 tumor foci but increased in higher grade lesions. We aimed to examine if longer duration of neoadjuvant hormone treatment (NHT) has any effect on the intensity and extent of PSP94 expression in prostate adenocarcinoma (CAP) cells.

**Methods:** Sixty patients with histologically confirmed CAP underwent radical prostatectomy (RP) in our institution. They were divided into 3 groups: Group 1–16 patients received no NHT, Group 2–25 patients received

3 months of NHT and Group 3–19 patients received 8 months of NHT. Immunohistochemistry staining was done on TRUS-Bx and RP specimens. The intensity and extent of PSP94 expression was reported. Univariate and multivariate statistical analyses were performed to evaluate the predictors of outcome for PSP94 intensity and extent, and for biochemical disease free survival (BDFS).

**Results:** The three groups were similar with regards to age, PSA, TRUS-Bx Gleason score, TRUS-Bx PSP94 intensity and extent. PSP94 intensity was significantly lowered in Group 3. Univariate and multivariate analyses of PSP94 extent and intensity in surgical specimens showed that NHT was the only independent predictor in both models. When we considered BDFS in univariate and multivariate analyses; baseline PSA, biopsy Gleason score and adjuvant radiotherapy were significant in univariate analysis and only adjuvant radiotherapy was the independent predictor of BDFS in multivariate model.

**Conclusions:** Eight months of neoadjuvant hormone treatment seems to affect PSP94 expression in prostate cancer cells. With the advent of protocols involving neoadjuvant taxane-based chemo- and hormone therapy for high risk disease, PSP94 may still have a role in disease course monitoring. Based on the results of this study; we have embarked on a prospective study on the effect of NHT and radical prostatectomy on the serum level of PSP94. Further studies are needed to detect if PSP94 expression would change with longer duration of androgen deprivation and also to find out the level of expression of PSP94 in hormone refractory prostate cancer patients

**Key Words:** androgen ablation, hormone therapy, prostate cancer

## MODERATED POSTER SESSION 5: MISCELLANEOUS ONCOLOGY MONDAY, JUNE 25, 15:20-17:20

### MP05.01

#### Differentiation of renal tumors by diffusion-weighted MRI: utility of the apparent diffusion coefficient

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**Introduction:** Diffusion-weighted imaging (DWI) is a novel MRI technique which measures the degree to which water is free to diffuse within a tissue. The calculated Apparent Diffusion Coefficient (ADC) is a quantitative parameter measuring this diffusion (in mm<sup>2</sup>/s) which can be obtained from DW MR images. One potential use could be in helping differentiate renal cell carcinoma (RCC) from normal parenchyma and benign tumours when standard imaging is inconclusive. The objective of this prospective study was to determine whether DWI could differentiate malignant from normal parenchymal and benign tumour tissues within the kidney.

**Methods:** In total, 66 consecutive patients with renal masses were prospectively evaluated with DWI. 32 patients who underwent subsequent resection and had confirmed pathology were then analyzed. Mean ADC values were obtained for all pathologically malignant and benign tissues as well as unaffected parenchymal tissue. RCC's were then subclassified as predominantly solid, cystic, or mixed. A two-tailed paired t test was used for statistical analysis.

**Results:** A total of 36 tumors had ADC values calculated. Of the 31 RCC lesions, 12 were deemed predominantly solid, 7 were predominantly cystic and 12 were mixed in composition. The mean ADC value for all RCC lesions (1.12) differed significantly from that of benign parenchymal tissue (2.08). This difference remained statistically significant when benign tissue was compared to the sub-groups of RCC, with mean ADC values for predominantly solid, cystic and mixed tumors being 1.15, 1.24 and 1.03, respectively. No significant difference existed between oncocytoma (n=5) and RCC ADC values.

**Conclusion:** This initial study demonstrates that DWI may help in the pre-operative diagnosis of malignant renal masses. A significant difference between the mean ADC values of malignant and benign parenchymal tissues was observed. The significance of this difference was maintained regardless of the over-all distribution of solid and cystic components within RCC lesions. Studies incorporating greater numbers of patients are needed to further assess the ability of DWI to reliably distinguish between RCC and benign solid and cystic tumors. This may allow for a reduction in the rate of surgical intervention for pathologically benign renal masses.

**Key Words:** imaging, kidney, renal cell carcinoma

### MP05.02

#### A phase I/II study of Vicinium™ given by intravesical administration in patients with superficial transitional cell carcinoma of the bladder: phase I final results

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**Introduction:** Vicinium™ is a fusion protein comprised of a humanized scFv, specific for Ep-CAM (epithelial cell adhesion molecule), and a truncated fragment of Pseudomonas exotoxin A. Ep-CAM is highly expressed on carcinoma cells including superficial transitional cell carcinomas (TCC) of the bladder. Vicinium specifically targets and kills Ep-CAM positive tumors. Results from a Phase I/II trial where Vicinium was instilled into the bladders of patients with superficial TCC of the bladder showed the drug to be very well tolerated and showed promising clinical results.

**Methods:** 64 patients with Ep-CAM positive superficial TCC of the bladder, Ta, Tis or T1 Grade 2 or Grade 3, who were refractory or intoler-

ant to BCG therapy, were entered into the study. Dosing comprised a minimum of 3 subjects per dose level through 12 escalating doses. Vicinium was given once/week for 6 consecutive weeks by intravesical administration into the bladder via a catheter at escalating dose levels of 0.1, 0.2, 0.33, 0.66, 1.32, 2.64, 5.28, 10.56, 13.73, 17.85, 23.2 and 30.16 mg/week. All toxicities were assessed according to the NCI CTC AE v3. Blood samples were collected at different times in the study to determine systemic drug exposure and to assess immunogenicity. Efficacy was explored via biopsy, cystoscopy, urine cytology and FISH.

**Results:** Vicinium was very well tolerated at all doses. No maximum tolerated dose (MTD) was reached. Almost all (>98%) of the patients screened were positive for the Ep-CAM antigen. Pharmacokinetic analysis showed no evidence of Vicinium in the circulation of any of the patients. Most patients, in particular at the higher doses, demonstrated a positive clinical benefit following treatment.

**Conclusion:** Vicinium dosed on a weekly basis for 6 weeks was very well tolerated at all dose levels. Moreover, although this study was primarily designed to evaluate safety and tolerability, Vicinium showed promising efficacy results. The early clinical benefit observed with Vicinium strongly supports its development as a promising therapy for superficial transitional cell carcinoma of the bladder.

**Key Words:** bladder, bladder cancer, superficial bladder cancer

### MP05.03

#### Prognostic risk factors for progression in clinical stage I nonseminomatous testicular germ cell tumors managed by surveillance

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**Introduction and Objective:** Clinical stage I nonseminomatous germ cell testicular tumors (NSGCTT) are usually treated according to individual risk assessment for disease progression. Prognostic factors for recurrence have been defined to select the patients who may require treatment for progression. We have evaluated the features of the primary tumor as potential prognostic risk factors.

**Methods:** Between January 1981 and August 2004, all 305 patients with clinical stage I NSGCTT were managed by active surveillance with delayed treatment for progression at our institution. Histopathologic features of the primary tumor that might be predictive of relapse were assessed. The presence of any lympho-vascular invasion (LVI), the percentage of embryonal carcinoma (EC) and pathologic tumor stage (pT) in the primary tumor were considered candidate factors. Statistical analysis using Cox proportional regression model was performed.

**Results:** Progression occurred in 77 (25%) patients. The multivariate analyses indicated that LVI and pure EC (as opposed to any range <100%) were the only significant predictors for recurrence ( $p < 0.05$ ). Therefore, 104 (34.1%) patients with LVI and/or pure EC were classified as high risk group and 201 (65.9%) patients as low risk. At a median follow-up of 6.3 years (range 0.1–24.3), 47.1% (49/104) of the high-risk group relapsed compared to only 13.9% (28/201) of the low risk category. Log rank test indicated that the two groups had significantly different recurrence-free survival curves ( $p < 0.01$ ).

**Conclusions:** Stratification of clinical stage I NSGCTT by high or low risk of relapse using known histopathological features of the primary tumor fails to identify all patients at risk. More than half of patients defined as high-risk will never relapse and would be overtreated with routine adjuvant intervention. Given that nearly 100% of patients that progress can be rescued safely with delayed therapy, initial active surveillance

therapy is an attractive treatment option.

**Key Words:** risk factors, surveillance, testis cancer

#### MP05.04

##### Outcomes of extravesical tumor extension (pT3) in pathological staging of bladder cancer following radical cystectomy

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**Introduction:** The objective of this study was to analyze the long-term outcome of patients with pT3 bladder cancer treated with radical cystectomy in a single institution.

**Methods:** We retrospectively reviewed the data of all patients who underwent radical cystectomy at Vancouver General Hospital, performed by three experienced urologists (LS, SLG and MEG) from November 1984 until February 2006 and had a pathological stage pT3 (TNM 1997). We analyzed the histological type, grade, presence of lymph nodes, presence of carcinoma in situ (CIS), margins status, any adjuvant chemotherapy received and survival. We used Fisher's exact test to analyze the data and the Kaplan-Meier method to evaluate the overall, cancer-specific and disease-free survival.

**Results:** Clinical information was available in 47 patients (30 men and 17 women). Patient's age ranged from 32 to 83 years old (mean, 64.61 years) and they had a follow up ranging from 4 to 169 months (median, 33.5 months). The predominant histological type was transitional cell carcinoma, and high grade group (grades III and IV) was the most common found in this cohort. Association with previously unknown prostate cancer was found in 8 patients (17%) but was not significantly related to worse outcome. Grade four tumors were diagnosed in only 2 patients who died from the disease no later than 6 months after the surgery. No significant difference was found in patient's outcome among histological type, grade and presence of CIS or adjuvant chemotherapy. The finding of positive lymph node was the only predictive factor associated to increased mortality and appearance of metastasis in this cohort ( $p < 0.05$ ). The overall survival at 5, 10 and 14 years was 36%, 31.2% and 24%, respectively. The cancer-specific survival was 42.1%, 39.7% and 37.5%, and the disease-free survival was 39.5%, 37.2% and 35.3%, respectively.

**Conclusion:** Radical cystectomy does have an important role in treatment of extravesical disease, independently of adjuvant chemotherapy. Our results were comparable with other reports in the literature and in this cohort of patients pathological positive lymph node involvement was an independent predictive factor influencing the survival.

**Key Words:** bladder cancer, cystectomy, radical cystectomy

#### MP05.05

##### Disease free and overall survival worse in elderly patients with upper tract urothelial carcinoma despite lower stage disease

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**Introduction:** Information about outcomes in upper tract urothelial carcinoma (UTUC) is sparse and little is known about specific prognostic factors. The goal of this study was to test the hypothesis that patients who are older than 80 at diagnosis do worse in terms of both disease free survival (DFS) and overall survival (OS).

**Methods:** A retrospective review of patients diagnosed with UTUC in the province of Nova Scotia, Canada since 1979 was performed (review up to November 2006). The subjects were divided into two groups based on age at diagnosis and chi-square tests were performed to determine if there was a difference between the two groups in terms of DFS and OS.

**Results:** The cohort consisted of 143 patients, 122 of whom were younger than 80 at time of diagnosis (group A), and 21 who were 80 or older (group B). In terms of DFS, group B did significantly worse than group A. DFS at 1, 2 and 5 years was 22%, 7% and 7% respectively for group B compared to rates of 59%, 38% and 24% among group A ( $p = 0.0008$ ). OS was also worse in group B, with OS at 1, 2 and 5 years being 57%, 52%

and 37% respectively compared to corresponding OS rates of 85%, 67% and 47% for group A ( $p = 0.02$ ). Comparison of disease stage, however, revealed that patients in group B had lower stage disease than group A.

**Conclusion:** Despite having lower stage disease at presentation, patients with UTUC who are 80 years of age or older at diagnosis do significantly worse in terms of both DFS and OS when compared to younger patients. This has important implications for making treatment decisions with elderly patients. Furthermore, anticipating high rates of disease recurrence can aid in the design of optimal follow-up regimens UTUC patients older than 80 at diagnosis.

**Key Words:** cancer, survival, TCC

#### MP05.07

##### Clinical relevance of incidental prostate cancer at radical cystoprostatectomy for urothelial carcinoma

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**Introduction:** Incidental prostate cancer in radical cystoprostatectomy specimens performed for urothelial carcinoma has been reported in the literature. We sought to evaluate the incidence of clinically relevant prostate cancer that may have implications for prostate-sparing radical cystectomy.

**Methods:** We retrospectively reviewed the charts of all men treated from 1993–2004 with radical cystoprostatectomy for invasive urothelial carcinoma at the Montréal General Hospital. Patients who had suspicion of prostate cancer prior to surgery were excluded from the study.

**Results:** A total of 120 men were reviewed; of these, 30 (25%) men with a median age of 67 years, were found to have incidental prostate cancer in the surgical specimen and form the basis of this report. Two (1.7%) men had a history of treated prostate cancer and were thought to be free of disease at surgery. Four (3.3%) men had negative TRUS prostatic biopsies for an elevated PSA. Eight patients (26.7%) had higher grade prostate cancer (Gleason score  $> 7$ ) in the specimen. All 30 patients had pT2 prostate cancer except 1 had pT3 disease. The surgical margin of the surgical specimens was negative in all patients. Of survivors, 1 patients developed bone metastasis due to prostate cancer.

**Conclusion:** Clinically relevant prostate cancer is not uncommon in cystoprostatectomy specimens of patients with urothelial carcinoma. These findings should be taken into consideration when counseling patients for prostate-sparing cystectomy.

**Key Words:** bladder cancer, prostate cancer, radical cystectomy

#### MP05.08

##### Partial cystectomy for bladder cancer in Quebec: a population-based study

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**Introduction:** Partial cystectomy remains a viable alternative to radical cystectomy for the management of invasive bladder cancer in approximately 5% of patients. Our goal was to examine the use and outcomes of partial cystectomy in the province of Quebec.

**Methods:** We obtained the billing records of all patients who underwent partial and/or radical cystectomy performed for bladder cancer in Quebec from 1983 until 2005. The analysis included age, gender, year of surgery, surgeon's age, hospital type, preoperative and postoperative visits with accompanying diagnoses and dates of death.

**Results:** From 1983–2005, 714 patients underwent partial cystectomy. The majority of partial cystectomies (65%) were performed in non-academic institutions. Median patient age was 70 years. Pelvic lymphadenectomy was performed in only 163 (22.8%) patients and ureteral reimplantation was performed in 89 (12.5%) patients. 194 (27.2%) patients had  $> 1$  TURBT prior to partial cystectomy. 167 (23.4%) developed recurrence of disease; of these, 52 (31.1%) required salvage radical cystectomy. The 5-year overall survival for patients with bladder cancer who underwent partial cystectomy versus upfront radical cystectomy was 50% and 42% respectively. Patients who underwent salvage

radical cystectomy post partial cystectomy had significantly shorter overall survival than patients who underwent upfront radical cystectomy (HR 1.6,  $p < 0.01$ ).

**Conclusion:** The rate of partial cystectomy for bladder cancer in Quebec is higher than expected. Pelvic lymphadenectomy appears to be underutilized in conjunction with partial cystectomy. Reasons for the prevalent use of partial cystectomy in Quebec need further evaluation. Data from billing records provide certain limitations in this study.

**Key Words:** bladder cancer, cystectomy

### MP05.09

#### Cystectomy: time and treatment factors affecting tumour progression

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**Introduction:** Intravesical BCG is first line therapy for many patients with high-risk non-invasive bladder cancer and has been shown to significantly decrease subsequent progression. Given the morbidity of a cystectomy, the decision to proceed as primary curative therapy for high-risk disease (T1G3), or to proceed after a failure after one course of intravesical therapy, is difficult. Whether repeated attempts at bladder preservation result in an increased risk of pathologic upstaging and decreased survival remains debatable. The purpose of this study was to determine factors predictive of clinical-to-pathological upstaging, particularly repeated courses of intravesical therapy for bladder preservation.

**Methods:** A retrospective chart review of all patients in a single center who received intravesical therapy for bladder cancer and who subsequently underwent cystectomy between 1990 and 2006 was performed. For the purpose of statistical analysis, clinical and/or pathological states of T2 N0 and less disease were grouped into "low TN stage", and T3 N1 or higher were grouped into "high TN stage."

**Results:** The chart review identified 44 patients who met inclusion criteria, although 6 had insufficient records for analysis. Upstaging following cystectomy was seen in 42% of the cystectomies performed. No association was found between upstaging and age, length of time from first TURBT to cystectomy, number of cycles of intravesical therapy or number of TURBT's. No statistical significance was found between time to recurrence after cystectomy and age, length of time from first TURBT, number of intravesical therapy cycles, or number of TURBT's.

**Conclusions:** Despite an apparent aggressive bladder preservation approach to high-risk non-invasive bladder cancer, we have demonstrated only a 42% upstaging rate at the time of cystectomy, in line with results in the literature. Length of time between first TURBT to cystectomy, number of cycles of intravesical therapy and number of TURBT's do not appear statistically significant in affecting pathological upstaging or time to recurrence following cystectomy.

**Key Words:** BCG, bladder cancer, cystectomy

### MP05.10

#### Treatment of BCG failed non muscle invasive bladder cancer (NMIBC) with intravesical bacille Calmette-Guérin (BCG) and interferon- $\alpha$ 2B (IFN) combination therapy

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Department of Urology, Queen Elizabeth II Health Sciences Centre and Dalhousie University, Halifax, NS

**Introduction:** NMIBC forms a majority of all newly diagnosed bladder cancers. Intravesical BCG as adjuvant treatment fails in 30–40% patients. Before radical surgery, BCG and IFN combination offers an appealing alternative of bladder preserving treatment.

**Methods:** A retrospective review was performed from the Nova Scotia Cancer Centre database. 22 patients from 2003–2006 who had NMIBC with failed BCG or chemotherapy and then received combination BCG and IFN were reviewed. These patients received 6 weekly intravesical treatments of 1/3 dose BCG and 50 million units of IFN. The average age was  $71 \pm 9.6$  years and 68% were male. All had normal upper tracts on initial imaging. 14 patients had T1 disease, 4 had CIS and rest had combination T1 and CIS. 18 patients had high grade disease at initial biop-

sy. Depending on their response they were given maintenance therapy. All data until their last follow up or cystoscopy was recorded and survival curves were analysed using Kaplan–Meier plots.

**Results:** After a median follow up of 16 months (range 3–38), 16 (73%) patients had negative cytology and bladder biopsy on their last follow up. One patient with positive biopsy had low grade disease continued on maintenance therapy. Five patients required intervention, three of whom underwent radical cystectomy. The histology showed T0, T1 and T2 disease respectively. One patient with lung metastasis received chemotherapy and another received radiation. Patients received on average 2.7 maintenance cycles of BCG/IFN. All patients tolerated the intravesical treatments. Two patients had mild fatigue, one each had dysuria and fever for one day. Three patients had nephroureterectomy for upper tract disease during the follow up.

**Conclusion:** BCG and IFN combination in BCG failed NMIBC appears to be a reasonable option which can be offered to patients before embarking on radical surgery. This series is the largest reported Canadian experience to date. Most of the patients who progress can be candidates to undergo curative radical surgery. This treatment is well tolerated by patients with no drop outs due to adverse effects. Longer follow up with a greater patient numbers can effectively answer whether this treatment provides a durable option.

**Key Words:** BCG, bladder cancer, superficial bladder cancer

### MP05.11

#### Cost effectiveness of immediate cystectomy versus BCG for the treatment of high risk T1G3 bladder cancer

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**Introduction:** The optimal management of high risk T1G3 bladder cancer is controversial. Immediate cystectomy offers the best chance for cure but is associated with a potentially impaired quality of life. Initial intravesical therapy with Bacille Calmette-Guérin (BCG) with delayed cystectomy, if indicated, can help maintain quality of life via bladder preservation but may not be as efficacious as immediate radical surgery. Given that bladder cancer is the most expensive malignancy to treat per patient, decisions regarding the optimal treatment strategy for high risk T1G3 tumours must also incorporate the cost considerations. Cost-effectiveness analysis was therefore performed to address the high risk T1G3 controversy.

**Methods:** A Markov Monte Carlo cost-effectiveness model was created to simulate the outcomes of a cohort of patients diagnosed with incident high risk T1G3 bladder cancer. Treatment options included immediate cystectomy versus conservative therapy with intravesical BCG. Movement across health states was guided by probabilities derived from the medical literature. Patient utilities were extrapolated from the literature or generated via expert opinion. Costing data were obtained from the University Health Network Case Costing Centre, a participant of the Ontario Case Costing Initiative. Standard errors for probability, utility and cost estimates were used in probabilistic sensitivity analyses. Outcomes included life years, quality-adjusted life years, total costs and incremental cost-effectiveness ratios.

**Results:** Using probabilistic sensitivity analysis, patients undergoing immediate radical cystectomy had a quality-adjusted life expectancy of 12.83 years (SD: 2.64 years). Those opting for conservative therapy had a quality-adjusted life expectancy of 12.45 years (SD: 1.97 years), a decrease of 0.38 years. The expected per-patient lifetime cost of undergoing immediate cystectomy was \$42400, compared to \$50100 for each individual opting for conservative therapy. Immediate cystectomy was found to be more effective and less expensive than initial intravesical therapy. Discounting costs and health benefits did not alter the results.

**Conclusion:** Immediate radical cystectomy is the dominant strategy for

the treatment of high risk T1G3 bladder cancer. Adoption of initial radical therapy could potentially lead to an improved quality-adjusted life expectancy for many patients with this disease and could yield significant cost-savings at the societal level.

**Key Words:** BCG, radical cystectomy, superficial bladder cancer

### MP05.12

#### Immediate cystectomy versus conservative management with delayed cystectomy for high risk T1G3 bladder cancer: a decision analysis

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**Introduction:** Controversy exists about the most appropriate treatment for high risk superficial bladder cancer. Immediate cystectomy offers the best chance for survival but may be associated with an impaired quality of life compared with conservative therapy. We estimated life expectancy (LE) and quality-adjusted life expectancy (QALE) for both of these treatments for a 60-year-old, otherwise well, potent man with T1G3 bladder cancer.

**Methods:** We evaluated two treatment strategies for high risk, T1G3 bladder cancer using a decision-analytic Markov model: 1) Immediate cystectomy with neobladder creation versus 2) Conservative management with intravesical Bacillus Calmette-Guerin (BCG) and delayed cystectomy in individuals with resistant or progressive disease. Probabilities and utilities were derived from published literature. Extensive sensitivity analyses were conducted to identify variables most likely to influence the decision. Structural sensitivity analyses modifying the triggers for cystectomy in the conservative therapy arm were also explored.

**Results:** The LE of a 60-year-old male was 14.3 years for immediate cystectomy and 13.6 years with conservative management. With the addition of utilities, the immediate cystectomy strategy yielded a QALE of 12.40 years and remained preferred over conservative therapy by 0.38 years. Incorporating utilities did not significantly alter the preferred treatment. Worsening patient comorbidity diminished the benefit of early cystectomy and only altered the preferred treatment for patients over age 65. Sensitivity analyses revealed that patients over the age of 70 or those strongly averse to loss of sexual function, gastrointestinal dysfunction or life without a bladder have a higher QALE with conservative therapy. The results of structural sensitivity analyses did not change the preferred treatment option.

**Conclusion:** Our model demonstrated that younger patients with high risk T1G3 bladder had a higher LE and QALE with immediate cystectomy. The decision to pursue immediate cystectomy versus conservative therapy should be based on discussions that consider patient age, comorbid status and an individual's preference for particular post-cystectomy health states. Patients over the age of 70 years or those who place high value on sexual function, gastrointestinal function or bladder preservation may benefit from a more conservative therapeutic approach.

**Key Words:** immunotherapy, radical cystectomy, superficial bladder cancer

### MP05.13

#### Bone density in patients with prostatic adenocarcinoma treated with GnRHa – a prospective cohort study

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**Introduction:** Androgen deprivation therapy (ADT) is commonly used in the treatment of prostate cancer (CaP). An unintended consequence of ADT is accelerated bone loss. We present the preliminary results of a prospective cohort study examining the rate of and risk factors for bone loss in men receiving gonadotropin releasing hormone analogues (GnRHa) over a 1-year follow-up.

**Methods:** All patients with CaP from a single institution currently undergoing treatment with GnRHa were screened for enrollment. Patients with known bony metastases or comorbidities affecting bone turnover were excluded. Bone mineral density (BMD) was assessed using 2-site dual energy x-ray absorptiometry (DEXA) and serum and urinary markers of bone turnover.

**Results:** Of 169 patients currently undergoing ADT with GnRHa at our institution, 25 patients have been enrolled in this study (14.8%). Here we report data from 22 patients at baseline and 13 at one year follow-up. Patients were 76.8±10.7 years of age, and had been on ADT for 3.73±2.7 years. All patients had castrate levels of testosterone. Overall, 7 patients (31.8%) were found to have osteopenia and/or osteoporosis and one additional patient developed the condition over the follow-up period. Time on ADT was associated with lower BMD. Treatment tertiles demonstrated a reduction in BMD from 1.04±0.15 g/cm<sup>2</sup> to 0.87±0.13 g/cm<sup>2</sup> at the hip and 1.19±0.27 g/cm<sup>2</sup> to 0.96±0.01 g/cm<sup>2</sup> at the lumbar spine ( $p=0.037$  and  $0.056$  respectively). BMI, physical activity level, age, smoking, alcohol consumption and family history did not contribute. Urinary N-telopeptide, a marker of bone resorption, was elevated in 77.3% of patients while bone-specific Alkaline Phosphatase and osteocalcin (markers of bone formation) were elevated in 8.7% and 0% respectively. Markers were not predictive of degree of bone loss. No patients developed osteoporotic fractures or bony metastases over the follow-up period.

**Conclusion:** Men on GnRHa therapy for less than 4 years have a high incidence of bone loss. Duration of therapy is associated with bone loss, while the role of more traditional risk factors over a 1-year follow-up remain less clear. Because identifying men who are at increased risk for bone loss remains problematic, all patients should be targeted for bone-protective strategies.

**Key Words:** bone mineral density, hormone therapy, prostate cancer

### MP05.14

#### Zoledronic acid reduces bone loss from goserelin acetate treatment in men with prostate cancer

Richard Casey

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**Introduction and Objective:** The primary treatment for locally extensive or metastatic prostate cancer is androgen-deprivation therapy (ADT) through surgical castration or pharmacologic means with luteinizing hormone-releasing hormone (LHRH) analogues such as goserelin acetate. Prolonged treatment with LHRH analogues increases the risk of bone loss and fractures. Zoledronic acid prevents and delays skeletal complications in patients with bone metastases from prostate cancer and increases bone mineral density (BMD) during ADT. An open-label, controlled, multicenter study investigated whether zoledronic acid can prevent bone loss in patients with prostate cancer during goserelin-based ADT.

**Methods:** ADT-naive patients with locally advanced prostate cancer were randomized (1:1) to receive 10.8 mg goserelin (control) alone or goserelin plus 4 mg zoledronic acid (treatment) every 3 months for 1 year. The primary endpoint was the percentage change from baseline in lumbar spine BMD with or without zoledronic acid. Secondary endpoints included percentage change from baseline in femoral neck and hip BMD, change in height, and safety.

**Results:** 200 patients were randomized to treatment, and 155 completed the 12-month study. The mean age of patients was comparable between treatment groups. Patients treated with zoledronic acid and goserelin had a mean increase of 3.29% in lumbar spine BMD, compared with a mean decrease of 1.47% in the control group ( $p = 0.0005$ ). Moreover, patients treated with zoledronic acid and goserelin had mean increases in BMD of the femoral neck and total hip BMD of 1.77% and 0.92%, respectively, compared with mean decreases of 1.69% and 1.97% in the control group ( $p < 0.0001$  and  $p = 0.0012$ , respectively). Treatment effects on height were not significant. Overall, the combination of 4 mg zoledronic acid plus goserelin was well tolerated.

**Conclusions:** Zoledronic acid is safe and effective for the prevention of cancer treatment-induced bone loss in men undergoing ADT with goserelin acetate. Further follow-up will evaluate clinical consequences with

regard to fracture rates and development of bone metastases.

**Key Words:** androgen ablation, bisphosphonates, bone mineral density

### MP05.15

#### **Patterns and detection of relapse in clinical stage I nonseminomatous germ cell testis tumors on surveillance: recommendations for follow-up**

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**Introduction and Objective:** Successful active surveillance therapy with delayed treatment of relapse for clinical stage I nonseminomatous germ cell tumors of testis (NSGCTT) depends on early detection of recurrence. The burden of follow-up visits and associated imaging can be substantial and is an important consideration when comparing treatment options. In an attempt to optimize our follow-up, we have evaluated relapse patterns and the role of each follow-up modality in recurrence detection.

**Methods:** From January 1981 to August 2004, 305 consecutive patients with clinical stage I NSGCTT were managed by initial surveillance after orchiectomy. Bimonthly history, with focused physical examination, plus markers and chest x-ray, with abdomino-pelvic computerized tomography (CT) every 4 months were done for the first 2 years. The rate, site and timing of relapse, as well as contribution of each follow-up modal-

ity to progression detection were assessed.

**Results:** Median follow-up was 6.3 years (range 0.1–24.3). Overall, 77 (25%) patients experienced 92 recurrences. In 65 patients, a single relapse was detected, 11 progressed twice and 1 recurred 5 times. The retroperitoneum was the premier site of metastases, followed by lung, peripheral lymph nodes and mediastinum in 71 (77%), 16 (17%), 8 (9%) and 3 (3.2%) of recurrences, respectively. Median time to relapse was 0.6 years (range 0.2–12.4). Sixty (78%) of the progressions were observed within the first year and 14 (18%) in the second year of follow-up. Only 3 patients (4% of relapsers) recurred more than 2 years after orchiectomy; 1 at 2.7 years and 2 were detected with symptoms 10 years after initial diagnosis. All 3 were salvaged successfully. History and physical examination, tumor markers, abdomino-pelvic CT and chest x-ray served as an initial indicator of relapse in 25 (27%), 59 (64%), 65 (71%) and 18 (20%) of cases, respectively. Each follow-up modality was the only representative of disease progression in 3 (3.3%), 5 (5.4%), 17 (18.5%) and 0 cases, respectively. New contralateral tumors were detected in 12 (4%) patients, with a mean of 8.4 years (range 0.8–12.0) after their initial diagnosis.

**Conclusion:** History, physical examination, tumor markers and abdomino-pelvic CT are essential follow-up elements. The chest x-ray can be safely deleted from the follow-up protocol. The role for follow-up after 2 years is unclear. However, lifelong follow-up, including regular self-examination is recommended.

**Key Words:** germ cell tumor, surveillance, testis cancer

# MODERATED POSTER SESSION 6: PEDIATRIC UROLOGY

## TUESDAY, JUNE 26, 15:30-17:30

### MP06.01

#### Construction of a tissue engineered genitourinary tubular tissue graft

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**Introduction:** Various urethral conditions such as congenital or traumatic defects often require tissue reconstruction. In a majority of cases, the quantity of urinary tissue and mucosa for an adequate restoration is limited. The aim of this study is to evaluate the possibility of constructing a completely autologous tissue-engineered urethra or ureter graft and to evaluate its mechanical and physiological properties.

**Methods:** Dermal fibroblasts (DF) are extracted from a small skin biopsy. They are expanded and cultured in vitro with sodium ascorbate to form fibroblast sheets. Once the sheets have reached a state allowing manipulation, they are wrapped around a tubular support to form a cylinder. Following adequate maturation, the urothelial cells (UC) are seeded inside the DF tube by perfusion. When the tissue engineered graft is fully mature, burst pressure and compliance are measured using a computerized device developed at the LOEX. This apparatus is capable of submitting the tissue-engineered urethra/ureter to hydrostatic loading while monitoring its internal pressure and external diameter. Immuno-histochemical analysis allows us to determine the architecture and characteristics of the model.

**Results:** The burst pressures of DF constructs were measured after 2 and 3 weeks of maturation and found to be, on average, 539 and 849 mmHg respectively ( $n=5$  for both maturation periods). Real porcine urethras tested with the same apparatus had a maximum recorded burst pressure of 458 mmHg. Following the perfusion of URCs and a 1-week maturation period of the DF+URC constructs in a bioreactor, the mean burst pressure was 783 mmHg ( $n=5$ ). Visual examination of the DF+UC constructs confirmed that all the layers had merged. A pluristratified urothelium could also be identified on the luminal surface of the tube.

**Conclusion:** The tissue-engineering technique used to produce this model seems very promising for bioengineering a urethra/ureter graft. If this solution for creating urinary tissue reveals itself as efficient, it could open a doorway to new possibilities for urethra/ureter reconstruction and solve part of the problem related to insufficient quantities of urinary tissue encountered in the treatment of congenital or traumatic defects.

**Key Words:** reconstruction, ureter, urethra

### MP06.02

#### In vitro construction of a tissue engineered autologous vesical graft by the self-assembly method

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**Introduction:** Augmentation cystoplasty and bladder reconstruction/replacement are major areas of research in urology. The gold standard is to use gastrointestinal segments but this generates well-known complications. Consequently, there are high expectations for the development of new alternatives in the field of tissue engineering. The aim of this study is to develop a new method to produce completely autologous vesical grafts by tissue engineering.

**Methods:** Small human skin biopsies are obtained. Fibroblast cells are extracted from the biopsy and expanded. They are seeded in multiple flasks and cultured in medium containing ascorbic acid. The cells are in culture until a cellular sheet is formed and its resistance can allow manipulation (approx. 1 month). Cell sheets are subsequently superimposed (3

or 6 layers) to form a flexible biological construct and remain in medium for an extra week to allow fusion of the layers. Urothelial cells (UC) are obtained from a small bladder biopsy (cadaveric donor). Extracted and purified UC are then seeded on one side of the biological construct and the new bladder wall model is cultured for 1 week under submerged conditions. The vesical equivalents are then brought to air/liquid interphase for one more week for UC differentiation. Histological examination are performed using Masson's trichrome and characterization of the UC is possible by indirect immunofluorescence assays. Mechanical resistance is also measured by uniaxial tensile testing using a computerized program.

**Results:** The in vitro engineered vesical graft is histologically characterized by the fusion of the fibroblast layers and a pluristratified urothelium coating. Positive marking for cytokeratins 8 and 18 confirmed the presence of a differentiated urothelium. Mechanical resistance for a 3-layer fibroblast construct is suitable for grafting.

**Conclusion:** This new promising model of tissue engineering vesical graft could circumvent the use of scaffolds that are associated with inflammatory responses, which represents a considerable limitation to success. The permeability properties of these tissue engineered bladder walls will be evaluated to document the impermeability of the construct to urine. Furthermore, the completely autologous origin of this model is an important asset that will eventually permit the elaboration of a dog model for long-term implantation.

**Key Words:** bladder, reconstruction, tissue engineering

### MP06.03

#### Parital nephrectomy: does retroperitoneoscopy adversely affect postoperative residual size and function?

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**Introduction:** Although retroperitoneoscopy (RPS) has become a widely used surgical option, recent reports have shown a possible detrimental effect on the residual moiety function secondary to RPS. We hypothesize that RPS is not associated with worse residual moiety function outcome. Our objective is to compare post operative moiety size and function after open vs. RPS partial nephrectomy.

**Methods:** We retrospectively analyzed all cases ( $n=38$ ) of open ( $n=20$ , group 1) and RPS ( $n=16$ , group 2) partial nephrectomy for duplication anomalies that were performed at our institution by 3 pediatric urologists between 2000 and 2006. One case was excluded due to leukemic death and another one due to loss to follow-up. Short- and long-term size and function of residual moiety was assessed post-operatively by renal ultrasound (US) and radionuclide scintigraphy (DMSA), and were compared with the preoperative kidney size and function. Statistical analyses were performed using Kruskal-Wallis nonparametric test.

**Results:** Median age at surgery in group 1 was 5 months and in group 2 was 21 months. Preoperative kidney size and function in group 1 were respectively 6.7 cm and 42%, compared to 7.7 cm and 40% in group 2. Post-operative moiety size and function in group 1 were 4.7 cm and 26% compared to 6 cm and 34% in group 2. There was a significant difference ( $p<0.001$ ) between the pre-and post-operative renal size in group 1. On the contrary, there was no significant change in renal size in group 2. In group 1, only 6 patients had post-operative DMSA available. Although a loss of function was demonstrated, it was not statistically significant. In group 2, there was no significant difference in pre-and post-operative kidney function.

**Conclusion:** There is no significant difference in post operative size and function of the residual moiety after RPS. RPS seems at least as safe as, if not superior to open surgery in preserving the size and function of the residual moiety.

**Key Word:** parital nephrectomy

#### MP06.04

##### Factors influencing the outcome of primary hypospadias repair

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**Introduction:** The incidence of abnormal positioning of urethral meatus and of their surgical repair is increasing. However, the complication rate of hypospadias repair is relatively high and depends on the kind of surgery employed and on the dexterity of the surgeon. We reviewed our experience with hypospadias surgery when tubularised incised plate (TIP) repair was performed.

**Methods:** The medical records of 203 men with hypospadias corrected surgically between August 2002 and November 2006 by a single newly established surgeon were reviewed. All revision surgeries and all repairs different from the TIP urethroplasty were excluded. We analysed the chart of 128 patients treated with TIP repair for primary hypospadias. We recorded initial position of the urethral meatus, presence of chordee, use of stent, age and blood loss. Finally, we evaluated the possible relationship between the characteristics of our population and the different complications encountered.

**Results:** During the last 4 years, 128 men with a median age of 40 months (2 months to 49 years) have undergone a TIP urethroplasty for primary hypospadias. The initial position of the urethral meatus was either distal penile (73%), midshaft (8%) or penoscrotal (12%). Sixty-nine (69) presented with a chordee that was corrected at the time of surgery, 87% being cutaneous and 13% intrinsic. Urethral stent was left in place at the end of the surgery in 93 patients for an average of 10 days. Mean blood loss was 18 ml. Thirty-five (35) complications were reported at follow-up: 12 fistulas (9%), 8 infections (6%), 7 meatal stenosis (5%), 7 cosmetic imperfections (5%) and one significant bleeding (1%). Twenty-one corrective surgeries were performed. Two links were established between the characteristics of our population and the different complications. The risk of fistula was higher as the position of the urethral meatus was more proximal (6 penoscrotal, 2 midshaft). Moreover, cosmetic irregularities were more frequent when the patient was younger than 9 months at the time of the correction. The others characteristics analysed could not help to predict possible complications. The complication rate was significantly higher in the cases performed during the first year of our review.

**Conclusion:** TIP repair is a frequent procedure performed by paediatric urologists with a significant rate of complication. Initial position of the urethral meatus and age at the moment of surgery are two characteristics that may predict possible complications of TIP repair for primary hypospadias. The learning curve is also a predominant factor.

**Key Words:** pediatric, urethra

#### MP06.05

##### Bladder mass after renal transplantation in children

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**Introduction:** A bladder mass after renal transplantation is an infrequent occurrence in the pediatric patient population. Reported lesions are nephrogenic adenoma, transitional carcinoma and rarely a post-transplant lymphoproliferative disorder. We present our experience with 4 cases, highlighting the potential morbidity that can occur despite benign pathology.

**Methods:** Over the last 10 years, 75 renal transplants (59% live donors) were performed at our institution. We identified 4 (5%) patients who developed a bladder mass following transplantation and reviewed their records.

**Results:** Mean age at presentation was 11.5 years (range 7–16 years). The male:female distribution was 3:1. The etiology of end stage renal disease was cystinosis, Bartter's syndrome, renal agenesis with contralateral dysplastic kidney, and ill defined congenital nephrotic syndrome. All 4 cases were recipients of EBV positive live donor kidneys with HLA A2 shared by both donor and recipient. The immunosuppressive regimen included induction with anti-thymocyte globulin followed by prednisone, mycophenolate mofetil and either cyclosporine or tacrolimus. Clinical presentation included hematuria (2), hydronephrosis (2), acute graft

dysfunction (1) and incidental finding (1). Ultrasonography revealed a bladder mass in all cases. At cystoscopy the mass was located at the neoureteral orifice in 3 cases. There was no correlation with the suture used or technique of reimplantation at the time of surgery. Postoperatively all patients had an indwelling Foley catheter for 3–5 days. All patients except one who presented 2 years postoperatively, presented within 2 months of transplantation. All patients underwent a transurethral resection of the lesion due to concerns of obstruction in 2 cases or malignancy in 2. Histopathology was consistent with papillary and polypoid cystitis in all cases. There have been no recurrences to date.

**Conclusion:** Papillary and polypoid cystitis can present as a bladder mass in the pediatric population after renal transplantation. Though benign, endoscopic resection may be indicated to relieve obstruction or rule out malignancy. Whether these patients are at higher risk for urothelial neoplasms in the future is unclear.

**Key Words:** bladder, pediatric, transplant

#### MP06.06

##### The "incidental anaesthetic": an opportunity for the endoscopic management of vesicoureteric reflux

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**Introduction:** Commonly accepted options for the management of vesicoureteric reflux (VUR) include antibiotic prophylaxis or surgery. The endoscopic management of VUR with sub-ureteric injection (STING) has become more popular with the availability of dextranomer/hyaluronic acid copolymer (Deflux). In fact, the low morbidity of the STING procedure as led to some authors advocating its use as a first-line therapy. Many physicians are uncomfortable with this suggestion because of the potential morbidity of general anaesthesia, especially in infants. We present an alternative without added anaesthetic morbidity, that of offering the parents a STING when their child is undergoing an anaesthetic for other surgical indication.

**Methods:** We present an example of a male infant with bilateral VUR, right grade 3 and left grade 4, with left reflux nephropathy and megaureter. At 6 months of age he was scheduled for orchidopexy for a barely palpable cryptorchid testis. The parents were interested in the option of STING because of concerns over chronic antibiotic usage, the potential for repeated invasive imaging and were reassured by the reported 0.7% incidence of hydronephrosis with STING.

**Results:** The child underwent an uneventful orchidopexy and bilateral STING with Deflux. At 3 months postop a nuclear cystogram demonstrated complete resolution of VUR and an ultrasound revealed the bladder implants with improvement of the left megaureter. We have performed STING during anaesthetics administered for various procedures, but the most common application has been during circumcision in an infant with VUR and a breakthrough urine infection.

**Conclusion:** The idea of performing STING during an incidental anaesthetic is a reasonable option which deserves more attention and outcome analysis. In fact, the commonly accepted options of chronic antibiotic prophylaxis or circumcision under general anaesthesia require the same rigorous analysis of safety, cost-effectiveness and efficacy.

**Key Words:** pediatric, vesicoureteric reflux

#### MP06.07

##### Management of pediatric urethral strictures: a review of our experience

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**Introduction:** Urethral strictures are uncommon in the pediatric population. We reviewed our results of direct visual internal urethrotomy (DVIU) for boys with urethral strictures.

**Methods:** IRB approved review of hospital charts of patients with urethral strictures over the past 15 years. Patients treated with DVIU for urethral stricture disease were included. The end point was defined as the requirement of additional post-operative intervention(s) for the stricture. Further intervention included DVIU, urethral dilatation, and open urethroplasty.

**Results:** The median age of the study population was 13.5 years (25th and 75th quartiles: 9.8 and 16.0); 7/14 (50%) of the patients had previous urethral surgery; 6/14 (42.9%) patients had no identifiable cause and 1 patient had a history of repeated urethral trauma. Two patients had previous urethral dilatations prior to their first DVIU. Median follow up was 23.5 months (25th and 75th quartiles: 22 and 69). Initially, 13 (92.9%) patients improved; however, half of the patients eventually failed, requiring further intervention. Of these patients, the average time to the failure was 17.6 months. Three patients required only 1 further intervention which included DVIU, urethral dilation, or urethroplasty. Two patients, who were noted to have idiopathic strictures, went on to have multiple DVIUs. One of the patients failed 4 months after their initial DVIU and the other failed at 13 months.

**Conclusion:** DVIU is appropriate for initial management of urethral strictures in children. Recurrence after initial management was difficult to predict in this series. Those managed with DVIU that failed more than twice, seemed to reoccur repeatedly. This suggests that patients who have more than 2 recurrences are at higher risk of failure if managed further with DVIU. A reasonable therapeutic approach is to manage repeated urethral strictures with open urethroplasty rather than continued DVIU.

**Key Word:** stricture

### MP06.08

#### Comparative analysis of tubularized incised plate vs. onlay island flap urethroplasties for penoscrotal hypospadias

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**Table 1. Abstract MP06.08**

Variables	TIP n=35 (%)	ONLAY n=40 (%)	p
Preop penoscrotal transposition	14 (40)	16 (40)	NS
Preop severe chordee (> 45°)	7 (20)	18 (45)	0.02
Dorsal plication performed	19 (54.3)	27 (67.5)	NS
Mean catheter duration (days)	8.5 (7-10)	10.3 (7-14)	NS
Overall Complication Rate	21 (60)	18 (45)	NS
Fistula/Breakdown	18 (51.4)	10 (25)	0.01
Fistula location (proximal:distal)	13:5 (72:28)	2:10 (20:80)	0.02
Stricture	0 (0)	2 (5)	NS
Meatal stenosis	1 (2.8)	1 (2.5)	NS
Recurrent chordee	2 (5.7)	5 (12.5)	NS
Average flow rate (ml/sec)	3.1 to 13.2	3.0 to 16.0	NS
Flattened uroflow curve	16/24 (66.6)	7/21 (33.3)	<0.01
PVR >30% expected bladder capacity	2/24 (8.3)	0/21 (0)	NS
# pts with >1 re-operations	2 (5.7)	7 (17.5)	NS

**Purpose:** Despite being the dominant technique for repair of distal hypospadias, acceptance of Tubularized Incised Plate (TIP) approach for penoscrotal hypospadias (PSH) remains unclear. We reviewed our experience with PSH, comparing TIP to transverse island flap ONLAY urethroplasty.

**Material and Methods:** A retrospective review of consecutive patients with PSH was performed. 1657 boys underwent hypospadias repair at our institution from 1998 to 2006; 75 comprised our study population: 35 children (TIP), 40 (ONLAY). Preoperative penoscrotal transposition and degree of chordee, type of chordee repair, complication rate, available uroflowmetry in toilet trained-pts., and number of re-operations were compared between the 2 groups.

**Results:** Mean age was 17m (9–91) for TIP and 17.8m (10–58) for ONLAY. Mean follow up was 30m (6–74) and 38.8m (16–80), respectively.

**Conclusion:** The overall complication rate was similar for penoscrotal TIP and ONLAY urethroplasties. The TIP-fistula rate was higher vs. ONLAYS, though catheter duration was the same in both groups. While PVRs were not elevated, more flattened TIP-flow curves may suggest that TIP-urethroplasty is narrower and thus, behaves as a relatively distal “resistance” prompting more proximal fistula formation. Nevertheless, both techniques appear to be equivalent approaches to correct PSH. Longer follow-up may reveal more divergent outcomes for these 2 approaches.

**Key Words:** pediatric, reconstruction, urethra

### MP06.09

#### Complications of the catheterizable channel following continent urinary diversion: their nature and timing

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**Purpose:** To review the incidence and timing of complications related to the catheterizable channel following continent urinary diversion (CUD).

**Methods:** A 5 year retrospective, single centre review was conducted to define a set of predetermined adverse channel outcomes. A total of 65 patients [42 female, 23 male, average age 13 years (1.6-30 years)] underwent CUD by one of two surgeons at British Columbia Children's Hospital during calendar years 2001–2005. The three major diagnoses were meningomyelocele (46), exstrophy (8), and cloacal anomaly (5). Catheterizable channels included 52 Mitrofanoff appendicovesicostomies, 11 Casale ileovesicostomies and 2 Yang-Monti ileovesicostomy channels. Timing of complications was defined as early (<12 months) or late (>12 months) from surgery.

**Results:** At a mean follow up of 29 months (3-62 months), a total of 21 complications were identified in 16 patients (25%). Superficial cutaneous stenosis occurred in 3/65 (5%) of cases as both an early and a late complication. These were initially treated with dilation. Further followup will determine if they will ultimately need surgical revision. Conduit stricture at the bladder-reservoir anastomosis occurred in 4/65 (6%) of patients occurring as an early and late complication, and was treated with operative revision in 2 cases and endoscopic resection in the remainder. Three patients developed stomal prolapse (5%), which was generally a late occurrence and required operative revision in all cases. Channel leakage requiring endoscopic injection of bulking agents occurred in 8/65 (12%); the majority (56%) presented as an early complication.

**Conclusion:** Complications of the catheterizable channel are a challenging problem. Stricture, stenosis and incontinence appear to occur throughout the life of the conduit. Stomal prolapse tends to occur late. Further follow up of these patients is required to assess the performance and durability of continent catheterizable channels in children as they progress to adulthood.

**Key Word:** bladder

### MP06.10

#### Peri-conceptual folic acid use in Nova Scotia

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**Introduction:** Folic acid (FA) supplementation decreases the incidence of neural tube defects (NTDs) by up to 50–70%. The optimal supplement-

tation period is 3 months before conception through the first trimester of pregnancy. Recommended intake is 400 µg/day, but average intake is only 260 µg/day despite grain product fortification. Less than one-quarter of women take FA supplementation before pregnancy.

We aim to determine the prevalence of peri-conceptual FA use in Nova Scotia and identify the sources of knowledge of FA supplementation and risks for low use of supplementation.

**Methods:** Pregnant women undergoing initial evaluation at the IWK Health Centre Perinatal Care Centre answered a 1-page survey including demographic information, FA use and source of knowledge. Exclusion criteria include conditions with high risk of NTD (diabetes, epilepsy, previous pregnancy with NTD). Statistical analysis was performed using chi square test with one degree of freedom.

**Results:** Preliminary analysis of 236 women is reported. Mean age was 28 years (range 15–43 years). 96% knew of FA, 22% did not know why to take FA, and 54% knew FA reduces the risk of birth defects or spina bifida/NTDs. 71% knew the appropriate timing of FA supplementation, but only 58% took FA 3 months prior to pregnancy. Family physicians were the most common source of FA knowledge (38%), followed by family/friends (22%), media (12%), books (8%), and others. 80% of women were advised to take FA by their physician and 75% by family/friends. Most pregnancies were planned (63%). Inappropriate FA supplementation (i.e. not taken 3 months prior to and during the first trimester of pregnancy) was related to unplanned pregnancies, age under 25, single status, low income/pharmaceutical, and lower level of education ( $p < 0.001$ ).

**Conclusion:** Preliminary data indicate women in Nova Scotia use FA supplementation at a higher rate than other areas. Groups at higher risk of inappropriate use include single women, young women, lower socioeconomic status and unplanned pregnancies. Focused educational efforts directed to family physicians to counsel all women of childbearing age to take 400 µg/day may improve peri-conceptual FA use in NS and decrease the incidence of NTDs.

**Key Words:** education, pediatric, prevention

**MP06.11**

**Spongioplasty facilitates postoperative catheterization, if required after non-stented tubularized incised urethral plate (TIP) repair of primary hypospadias**

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**Introduction:** We hypothesize that spongioplasty can provide enough urethral support so that the neourethra can withstand early urethral catheterization without compromising the repair.

**Materials and Methods:** All non-toilet-trained children who underwent TIP repair for primary hypospadias, by one surgeon over a 30-month period were included in the study. In all cases the technique involved mobilization of the divergent spongiosa off the corpora cavernosa. The mobilized spongiosa was then wrapped around the neourethra as well as the hypoplastic distal urethra. A dorsal preputial dartos flap was then utilized to cover the neourethra. At the end of the procedure the urethroplasty was calibrated with an 8-F catheter. If the catheter passed easily, the bladder was emptied and no stent was left. If any difficulty was encountered, a urethral stent was left. Early and late complications were noted.

**Results:** The study included 32 consecutive patients with a mean age of 18±6 months. The defects included 26 (80%) distal and mid-shaft and 6 (20%) proximal-shaft. No difficulty was observed during intraoperative catheterization and all repairs were non-stented. Mean follow-up was 9±6 months. Urinary extravasation was seen in one patient (3%) in the second postoperative day. A urethral catheter was easily inserted and left indwelling for 5 days. One patient presented 6 days after surgery with suspected voiding difficulty. Urethral calibration was easily performed excluding any mechanical obstruction. There were no urinary fistulas and re-operation was not required. An excellent cosmetic appearance was obtained in all patients.

**Conclusion:** Spongioplasty provides good support to the neourethra and to the hypoplastic distal urethra. It facilitates catheterization if required and should be considered with non-stented TIP repairs. Separating the spongiosa off the tunica albuginea decreases tension on the midline

urethroplasty especially during erection. Combined spongioplasty and dartos flap maximize neourthral protection.

**Key Word:** urethra

**MP06.12**

**Intravesical oxybutynin for children with poorly compliant neurogenic bladders: a systematic review**

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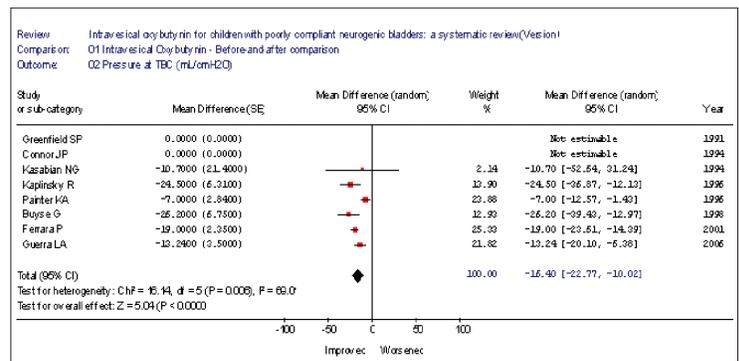
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**Introduction:** Children with neurogenic bladders and poor bladder compliance are usually managed with bladder catheterization and oral anticholinergic medication. They may become non-responders to the drug or present with severe harms.

**Objective:** To evaluate the effectiveness and tolerability of intravesical oxybutynin in children with poorly compliant neurogenic bladders.

**Methods:** Pubmed, Embase, Cinahl, SciELO, ProQuest, Lilacs, Cochrane database, protocol registries and grey literature were searched systematically. Two reviewers independently assessed study quality and extracted data.

**Results:** Eight studies (2 prospective; 6 retrospective), assessed the effectiveness and harms of intravesical oxybutynin in children with neurogenic bladders. Reports were generally of poor quality, with weak study designs (single group before-after evaluations). In total, 297 children started treatment and 22.2% (66/297) discontinued the therapy; 9.4% (28/297) quit due to systemic harms. Mean change in bladder compliance (primary outcome) was reported in only 2 studies (+7.4 and +7.5 ml/cmH<sub>2</sub>O). The pooled mean change in pressure at total bladder capacity (TBC) was -16.4 cmH<sub>2</sub>O (95% CI: -22.77 to -10.02). TBC was not pooled (I<sup>2</sup>=61%; forest plot suggested high inconsistency). Incontinence improved significantly in most studies, with "dry and improved" from 61% to 83%. The funnel plot of pressure at TBC suggested no publication bias.



**Conclusion:** Adjunctive intravesical oxybutynin therapy increased the mean total bladder capacity and decreased bladder pressure in children with neurogenic bladders. However, identified studies offered a low level of evidence; most were poorly reported retrospective case series with potential biases. Although the incidence of harm was lower with the intravesical route, they are still possible and should be discussed with patients and families. The evidence in this review is insufficient to recommend this therapy. Research of more sound study design such as a RCT should be conducted to assess the efficacy and harms of intravesical oxybutynin in children.

**Key Words:** meta-analysis, overactive bladder, pediatric

**MP06.13**

**Long-term functional outcome and satisfaction of patients with hypospadias repaired in childhood**

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**Introduction:** Potential long-term sequelae of hypospadias and its surgical correction include difficulties in voiding, sexual function, psychosexual adjustment, and self-appraisal. These difficulties often evolve long after surgical repair as children grow to adulthood. Despite this, there is limited patient-driven data on long-term functional outcomes and satisfaction, leaving the true success of hypospadias surgery essentially unknown. The aim of this study was to address these deficiencies.

**Methods:** A chart review for all patients operated on by a single urologist from 1981–1988 was conducted. Extensive efforts were made to obtain accurate current address information for patients. A database of patient demographics and pathology, operative details, and complications was created. A 22-item questionnaire was mailed to study subjects. Telephone follow-up by an independent research nurse bolstered response rates. Responses from returned questionnaires were pooled and analyzed.

**Results:** 115 patients were included in the chart review; 100 patients (with address information) were mailed questionnaires and 28 ultimately responded. The chart review group was comparable to other published studies. Despite a slightly higher initial major complication rate (57.2%), respondents reported few long-term complications (11% fistula, 29% persistent chordee, 10% stricture), and excellent urinary and sexual functional results. The most common functional complaints were spraying and hesitancy during micturition. Overall, 86% of patients were satisfied with their surgical result and 52% wished they had been provided longer follow-up.

**Conclusion:** Long-term outcomes data is critical to an honest account of success rates for hypospadias surgery. Obtaining this data remains challenging. In this series, despite high initial complication rates, most patients reported excellent long-term functional results and were quite satisfied with their overall outcome.

**Key Words:** pediatric, QOL, reconstruction

## MP06.14

### Factors associated with mortality in children with Wilms' tumor

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**Introduction:** Wilms' tumor is the most common renal tumor in children (6% of pediatric cancers). Patients at the Centre Hospitalier Universitaire de Québec (CHUQ) are treated following the protocols of the National Wilms' Tumor Study Group (NWTSG). Mortality in our cohort under treatment from 1988 to 2004 is higher (22.5%) than the one reported by the NWTSG (>15%). Potential explanations for this higher mortality must be found in order to improve therapeutic outcomes. Our objectives were to describe factors influencing mortality and relapse in our population and also to compare our population to the corresponding cohorts of the NWTSG.

**Methods:** This retrospective study included all pediatric patients newly diagnosed with Wilms' tumor from January 1st 1988 to December 31st 2004 and followed at the CHUQ afterwards ( $n=40$ ). Medical charts were reviewed with a standardized form. Mortality and relapse risks were calculated in regard to each variable. Distribution of patients according to tumor stage and survival rates at 2 and 4 years were compared to the NWTSG data.

**Results:** The mortality rate is significantly higher in the presence of relapse (RR 2.3 [CI 95% 1.3–4.0]), subtotal resection (RR 3.4 [CI 95% 1.2–9.4]) and anaplasia (RR 3.4 [CI 95% 1.2–9.7]). Older children at the time of diagnosis were associated with higher risk of relapse (6.4 years vs. 2.8 years  $p=0.004$ ). Moreover age at diagnosis is associated with a tendency towards higher mortality (6.2 years vs. 3.6 years). There is no significant difference over mortality in regard to initial therapeutic modality, stage, time to surgery or surgical spillage. In our cohort, the proportion of advanced stages (III, IV, V) was much higher than in NWTSG. By stratification for stage and treatment protocols, we found no difference in survival between our cohort and NWTSG. Average age at diagnosis in our group is higher than what found in literature.

**Conclusion:** Mortality in children with Wilms' Tumor is higher in the presence of relapse, subtotal resection and anaplasia. Higher age at diagno-

sis is associated with more risk of relapse and a tendency towards higher mortality. Global mortality in our cohort can be explained by more advanced stages and older children at the time of diagnosis. More studies are mandatory to explain the prevalence of higher stages and ages in our population compared to NWTSG.

**Key Words:** pediatric, survival, Wilms' Tumour

## MP06.15

### Critical appraisal of the role of ureteroscopy in treatment of pediatric renal and ureteric calculi

S. Dave, L. Braga, AE Khoury, W. Farhat

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**Introduction:** The refinement and miniaturization of ureteroscopes and ancillary instruments has led to an increased application of ureteroscopy in managing ureteric calculi in children. We report our experience with the use of ureteroscopy in managing ureteric and renal calculi and assess the results in relation to stone location and whether ureteroscopy was used as a primary or secondary treatment modality.

**Methods:** A retrospective chart review was performed for 28 patients with 32 stones ranging between 2–16 years (mean 6.9 years) of age who underwent ureteroscopy for treatment of calculi between 1999 and 2004. Data collection included presentation, review of operative details, initial complete radiological clearance and follow up procedures.

**Results:** Follow up ranged between 6–72 months (mean 23 months). Twelve of the 28 children (42%) had an associated metabolic disorder predisposing them to recurrent urolithiasis. Of the 32 stones treated, 18 were located in the upper urinary tract, 6 in the proximal ureter and 8 in the distal ureter. A postoperative ureteric stent was used in all cases. The lithotripsy modality used was the holmium: YAG laser in 25 and electrohydraulic lithotripsy in 3. Overall initial stone clearance was achieved in 85.7% (12/14) of ureteric stones. Stones located in the renal pelvis showed a 53% (7/13) clearance with poor results in those with calyceal extension. Only 1 of the 5 staghorn calculi was cleared with ureteroscopy. The 2 complications in this series were a distal ureteric perforation in 1 and a malpositioned stent with a urinoma in 1.

**Conclusions:** Ureteroscopy and laser lithotripsy achieves good results with minimal complications in treating ureteric calculi and stones located in the renal pelvis. The initial stone clearance achieved in large staghorn calculi or pelvic stones with calyceal extension is poor. Despite the technical challenges and the results in this group of patients it may have a limited role as salvage therapy in children with metabolic disorders who often have large stone burden and recurrent calculi.

**Key Words:** calculi, laser, ureteroscopy

## MP06.16

### Foreskin reconstruction in hypospadias surgery: does our practice reflect parental expectation in North America?

S. Dave, MD Suoub, J. Cerveira, W. Farhat

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**Introduction:** Parental request for foreskin reconstruction has become more common among children who need hypospadias repair. When feasible, we routinely offer foreskin reconstruction for distal hypospadias. Herein we analyze our early experience with specific consideration to the outcome and parental satisfaction.

**Methods:** Between January 2003 and December 2005, 22 (glandular 6, coronal 16) of 158 children with distal hypospadias underwent hypospadias repair with foreskin reconstruction by a single surgeon at our institution. The procedures performed included tubularized incised plate (TIP) urethroplasty in 16, glanular approximation in 2, meatal advancement and meatoplasty in 3 and isolated foreskin reconstruction in 1. The parents were thoroughly counseled regarding the complications of foreskin reconstruction in addition to the postoperative care requirements. Parental satisfaction with the cosmetic outcome was documented in the post-operative clinic visit.

**Results:** Operative time ranged between 30–86 minutes (mean 56 min.). Initial retraction of the foreskin by the surgeon was successful in 15. Of the 7 who failed initial retraction, 6 responded to Betamethasone cream.

Four children underwent redo surgery, which included repair of urethrocutaneous fistula in 3 (18%) children who had undergone a TIP urethroplasty (1 with redo circumcision for foreskin dehiscence) and circumcision for recalcitrant phimosis in 1. Follow up ranged between 4–50 months (mean 17.5 months). The remaining 18 children had an acceptable cosmetic result as documented by parental satisfaction. There was

no significant difference in the age at surgery, type of procedure and post-operative protocol in those who had complications.

**Conclusions:** Hypospadias repair and foreskin reconstruction should be proactively offered to parents. The results of foreskin reconstruction are favorable in a selected group of patients with distal hypospadias.

**Key Words:** phimosis, reconstruction

# MODERATED POSTER SESSION 7: RENAL CANCER

## TUESDAY, JUNE 26, 15:30-17:30

### MP07.01

#### Initial assessment of a screening tool for renal tumor therapy sensitivity using ex vivo invasion assay

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**Objective:** Metastasis secondary to RCC have variable and limited responses to systemic therapy. However, the heterogeneity of tumors has not been assessed against these therapies. Using an ex vivo model of invasion, we assessed the impact of different therapeutic agents on patient's live tumor cells procured during surgical resection.

**Methods and Patients:** Twelve consecutive patients undergoing surgical resection of renal masses were enrolled. A sample of each tumor was removed from the periphery of the tumor as well as a normal piece of kidney. These specimens were placed into a nutrient-rich collagen matrix. Growth and invasiveness were monitored microscopically by measuring the disseminated distance of tumor cells from the origin over 5 days. In the presence of different chemotherapeutic and anti-angiogenic agents (irinotecan, 5-FU, doxorubicin, cisplatin, Taxol, mTOR inhibitor), the invasive capacity of tumors was assessed. All tumors were preserved in paraffin for immunohistochemistry staining to assess cell viability and angiogenesis as well.

**Results:** Among the initial 12 patients, 10 had clear cell RCC, 1 had papillary RCC and 1 had a metanephric adenoma. 7 patients were pT1 and 5 were pT3 among which 3 had metastasis. Samples from the normal kidney samples did not migrate as expected. The cells from the metanephric adenoma migrated up to 110 +/- 84 mm compared with 84 +/- 265 mm in the malignant specimens ( $p < 0.001$ ). When comparing tumors with Fuhrman grade 1/2 with 3/4, growth was 730 +/- 148 vs. 870 +/- 281 mm, respectively ( $p < 0.05$ ). Among the therapeutic drugs, as expected, 5-FU and irinotecan did not reduce migratory capacity. However, taxol, taxotere and doxorubicin were capable of reducing tumor invasiveness by 72%, 75% and 83%, respectively. Cisplatin and mTOR inhibitors had intermediate and variable response with a mean reduction of 46% and 36%, respectively.

**Conclusions:** Initial experience with this ex vivo invasion assay appears to have promise, as there is correlation between tumor grade/ malignant potential and invasiveness. Potentially, it may be able to predict tumor response to therapeutic agents. In the future, we hope to create an index that assesses invasiveness/ angiogenesis/ viability in the hopes of individualizing mono or combination therapy for patients with kidney cancer.

**Key Words:** renal cell carcinoma, screening, stage

### MP07.02

#### The prognostic ability of simplified nuclear grading of renal cell carcinoma

QD Trinh<sup>1</sup>, PI Karakiewicz<sup>1</sup>, M. Soubra<sup>1</sup>, N. Rioux-Leclercq<sup>2</sup>, V. Ficarra<sup>3</sup>, L. Cindolo<sup>4</sup>, A. De la Taille<sup>5</sup>, J. Tostain<sup>6</sup>, R. Zigeuner<sup>7</sup>, JJ Patard<sup>2</sup>

<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>Rennes University, Rennes, France; <sup>3</sup>University of Verona, Verona, Italy; <sup>4</sup>Benevento Hospital, Italy; <sup>5</sup>CHU Henri Mondor, Créteil, France; <sup>6</sup>St-Étienne University, St-Étienne, France; <sup>7</sup>Graz University Hospital, Graz, Austria

**Introduction:** The Fuhrman grading system is an established predictor of survival in patients with renal cell carcinoma (RCC). We tested the predictive accuracy of various Fuhrman grading schemes, with the intent of improving the prediction of RCC-specific survival (RCC-SS).

**Methods:** Analyses targeted 5453 patients from 14 institutions. Univariable, multivariable and predictive accuracy analyses addressed RCC-SS. The statistical significance of the gain in predictive accuracy was quantified with the Mantel-Haenszel test.

**Results:** Median follow-up time was 4.5 years. In both univariable and multivariable analyses, Fuhrman grade achieved independent predictor status regardless of the coding scheme. When Fuhrman grade was not considered in multivariable analyses, predictive accuracy was 83.8%. Addition of Fuhrman grade to the multivariable model resulted in predictive accuracy gains of 0.8% for all three grading schemes tested.

**Conclusion:** Fuhrman grade must to be considered when RCC-SS is assessed. However, modified or conventional Fuhrman grading schemes perform equally well relative to the conventional grading system.

**Key Words:** kidney, nephrectomy, renal cell carcinoma

### MP07.03

#### Anaemia and thrombocytosis do not change the ability to predict renal cell carcinoma (RCC) specific survival: an analysis of 1828 patients

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<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>David Geffen School of Medicine at UCLA, Los Angeles, CA; <sup>3</sup>Rennes University, Rennes, France; <sup>4</sup>St-Étienne University, St-Étienne, France; <sup>5</sup>CHU Henri Mondor, Créteil, France

**Introduction:** Anaemia and/or thrombocytosis were identified as independent predictors of poor survival in renal cell carcinoma (RCC). We tested the extent to which these markers worsen the prognosis in these patients.

**Methods:** Analyses targeted 1828 patients with renal cell carcinoma. Univariate, multivariate and predictive accuracy analyses addressed RCC-specific survival (RCC-SS).

**Results:** In both univariable and multivariable analyses, both platelet count and preoperative haemoglobin were statistically significant predictors of RCC-SS. However, neither platelet count nor preoperative haemoglobin increased the combined multivariable accuracy of established RCC-SS (predictive accuracy gain = 0.3%) predictors.

**Conclusion:** Patients who present with severe anaemia or elevated platelets are at no higher risk of RCC-specific mortality than that related to their stage, grade, histological subtype and performance status.

**Key Words:** kidney, nephrectomy, renal cell carcinoma

### MP07.04

#### Partial nephrectomy using renal artery perfusion for cold ischemia: functional and oncologic outcomes.

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<sup>1</sup>CHUM, Montréal, QC; <sup>2</sup>Krankenhaus der Elisabethinen, Linz, Austria

**Introduction:** We present our series on the safety, oncologic and functional outcomes of laparoscopic partial nephrectomy using renal artery perfusion for cold ischemia.

**Methods:** Of ninety four patients having undergone laparoscopic partial nephrectomy in our center between August 2000 and September 2006, twenty eight were performed using cold ischemia and are included in this review. Mean age was 57.8 years (range 22–80). Mean tumor size was 2.67 cm (range 1.5–5). Five patients had an imperative indication for partial nephrectomy. Eight tumors were hilar. Cold perfusion was achieved through renal artery catheterization followed by intra-operative artery clamping and perfusion with 4°C lactated ringer solution with mannitol. A 2-tailed paired t-test or Wilcoxon test were carried out for pre- and post-operative continuous parameters' comparisons. A  $p$  value inferior to 0.05 was considered statistically significant.

**Results:** Mean ischemia time was 40.8 min (range 25–101). Mean estimated blood loss was 241 mL (range 50–1000). Three patients underwent

open conversion, but their procedure was still completed under cold perfusion. Segmental artery penetration and venous penetration occurred in one patient each. Post-operative complications included one pancreatitis and one pulmonary embolism; none were related to cold perfusion. Functional studies showed mild decrease in renal creatinine clearance with improvement 1 month after surgery. Nuclear scans showed functional kidney moiety in all but one case. Although differential Mag-3 clearance was decreased on the operated side, peak concentration times (PCT) were not different pre- and post-operatively on the operated side. Additionally, no difference in PCT was documented between the operated and non operated side. Oncologic outcome revealed 100% disease specific survival for 45 month median follow-up.

**Conclusion:** Intra-operative cold ischemia for laparoscopic partial nephrectomy using arterial perfusion is safe and feasible. It constitutes a viable alternative for complex tumors where ischemia time would 30 min. We provide proof of principle confirming the protective effect of cold perfusion to prevent parenchymal damage.

**Key Words:** kidney, laparoscopy, partial nephrectomy

### MP07.05

#### Increasing tumor size is associated with increasing nuclear grade in patients with renal cell carcinoma

E. Antebi<sup>1</sup>, QD Trinh<sup>1</sup>, C. Jeldres<sup>1</sup>, A. Gallina<sup>1</sup>, K. Shahrouh, PI Karakiewicz<sup>1</sup>, JJ Patarid<sup>2</sup>

<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>University Hospital, Rennes, France

**Introduction:** Fuhrman is a strong and established predictor of renal cell carcinoma-specific survival (RCC-SS). Previous reports demonstrated higher survival rates for low grade renal cell carcinoma (Fuhrman I and II) compared to high grade RCC (Fuhrman III and IV). However, Fuhrman grade can only be established after pathological examination. We tested the hypothesis that tumor size could accurately discriminate between low and high grade RCC tumors.

**Methods:** Radical nephrectomy was performed in 4794 patients from 18 European centers. Logistic regression analyses addressed the association between tumor size and Fuhrman grade after adjustment for age, gender, TNM stage and histological subtype. Tumor size was analyzed either as a continuous or as a categorical variable. Nuclear grade was defined as low grade (Fuhrman grade I and II) vs. high grade (Fuhrman grade III and IV).

**Results:** Mean age at nephrectomy was 63 (range 10-96) and tumor size range from 0.5 to 23.0 cm (median 5 cm). Most patients were male (67%). Of the entire cohort, 68.4% had low grade RCC, while 31.6% had high grade RCC. In univariable analyses, tumor size coded either as a continuous or as a categorical variable was a statistically significant predictor of nuclear grade ( $p < 0.001$ ). In multivariable analyses, tumor size achieved independent predictor status ( $p < 0.001$ ). For example, tumors greater than 8.0 cm in diameter were associated with a 2.6-fold risk of high grade RCC compared to lesions smaller than 3.5 cm in diameter.

**Conclusions:** Our results show that tumor size is an independent predictor of nuclear grade in patients with RCC. Small tumor size is associated with low nuclear grade.

**Key Word:** renal cell carcinoma

### MP07.06

#### A nomogram predicting renal cell carcinoma-specific survival in patients with nodal metastases is more accurate than any individual variable

E. Antebi<sup>1</sup>, QD Trinh<sup>1</sup>, V. Cloutier-Fournier<sup>1</sup>, A. Gallina<sup>1</sup>, N. Bhojani<sup>1</sup>, PI Karakiewicz<sup>1</sup>, JJ Patarid<sup>2</sup>

<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>University Hospital, Rennes, France

**Introduction:** Outcome of patients with exclusive renal cell carcinoma (RCC) nodal metastases without distant metastases is not extensively described. We developed and validated a standardized nomogram predicting the probability of renal cell carcinoma-specific mortality (RCC-SM) in this subgroup of patients.

**Methods:** Analyses targeted 171 patients with RCC nodal metastases and

absence of distant metastases (TanyN1-2M0). Cox regression analyses were used to develop a prognostic nomogram for prediction of RCC-SM.

**Results:** Median RCC-SS in this subgroup of patients was 2.3 years. In multivariable analyses, symptom classification ( $p < 0.001$ ), Fuhrman grade ( $p = 0.02$ ) and histological subtype ( $p = 0.04$ ) were independent predictors of RCC-SM. The nomogram predicting RCC-SM based on histological subtype, Fuhrman grade, symptom classification, T stage and tumour size was 67.3% accurate and performed significantly better than symptom classification alone, where presence of systemic symptoms represented the strongest predictor of mortality.

**Conclusions:** RCC-SM of patients with exclusive nodal metastases may show important variability. Models predicting RCC-SS in patients with exclusive nodal metastases are not perfectly accurate. However, they systematically combine the available predictors and are significantly better than single variables or chance predictions. We developed and validated a nomogram predicting RCC-SM in this group of patients. This nomogram may assist clinical decisions regarding treatment choice and follow-up as well as identifying patients at high risk of mortality who may benefit from neo-adjuvant and/or adjuvant treatment modalities.

**Key Word:** renal cell carcinoma

### MP07.07

#### Tumor histology is not a predictor of renal cell carcinoma-specific survival in patients with metastatic renal cell carcinoma

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**Introduction:** The effect of histologic variants on renal cell carcinoma-specific mortality (RCC-SM) of patients with either exclusive nodal or distant metastases has received very little attention. Our objective was to assess the prognostic ability of tumour histology in this subgroup of patients.

**Methods:** Our sample size consisted of 574 RCC patients with either exclusive nodal (TanyN1-2M0) or distant metastases (TanyNanyM1). Of these, 92% ( $n = 528$ ) had clear cell RCC, 7% ( $n = 22$ ) had papillary RCC and only 1% ( $n = 4$ ) had chromophobe RCC. We assessed the effect of histology in this cohort using univariable and multivariable analyses. Moreover, we quantified the ability of tumour histology, as well as of all other established predictors by determining their univariable and multivariable predictive accuracy.

**Results:** Clear cell histology predominates in patients with distant metastases (96%) vs. 86% in patients with exclusive nodal metastases. Conversely, the prevalence of papillary (12.9–4.9%) and chromophobe (1.2–0.5%) RCC decrease in patients with distant metastases relative to their counterparts with exclusive nodal metastases. The accuracy of histological subtype in prediction of RCC-SS was 51.3% vs. 50% for a flip of a coin ( $p = 0.7$ ). Conversely, symptom classification (61.3%,  $p < 0.001$ ) and Fuhrmann grade (58.8%,  $p = 0.003$ ) demonstrated higher univariate accuracy. In multivariable analyses, histological subtype contributed only 0.8% ( $p = 0.8$ ) to the combined predictive accuracy of all variables.

**Conclusions:** Tumour histology is not an important clinical determinant of RCC-SS in patients with nodal and/or distant metastases.

**Key Word:** renal cell carcinoma

### MP07.08

#### Presence of systemic symptoms is the foremost predictor of mortality in patients with exclusive nodal metastases

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**Introduction:** Outcome of patients with exclusive renal cell carcinoma (RCC) nodal metastases without distant metastases is not extensively described. We searched for the most important predictors of renal cell carcinoma specific survival (RCC-SS) in these patients.

**Methods:** Analyses targeted 171 patients with RCC nodal metastases and absence of distant metastases. Univariable, multivariable and predictive

accuracy analyses addressed RCC-SS with the intent of identifying independent and most informative predictors of RCC-SS in this cohort of patients. **Results:** Median RCC-SS was 2.3 years. At 10 years, 30% were alive and 40% of asymptomatic patients were alive at 10 years vs. 12% of those with systemic symptoms. In multivariable analyses, symptom classification contributed the most to the combined predictive accuracy of all variables (+4.2%,  $p < 0.001$ ) and was followed by Fuhrman grade (+2.3%) and histological subtype (+1.0%).

**Conclusions:** Renal cell carcinoma specific survival of patients with exclusive nodal metastases may show important variability and is mostly affected by the presence of systemic symptoms. Patients with systemic symptoms may warrant early systemic therapy.

**Key Words:** lymph nodes, renal cell carcinoma, survival

### MP07.09

#### Presence and type of renal cell carcinoma (RCC) related symptoms predict rcc-specific survival after nephrectomy in patients with either nodal or distant metastases

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<sup>1</sup>Université de Montréal, Montréal, QC; <sup>2</sup>CHU Créteil, France; <sup>3</sup>Universitätskrankenhaus Graz, Austria; <sup>4</sup>CHU Rennes, France

**Introduction:** The survival of patients treated with nephrectomy for metastatic renal cell carcinoma (RCC) is highly variable and there are no established criteria indicating when to initiate adjuvant therapy. We tested RCC-specific mortality (RCC-SM) predictors in this group of patients.

**Methods:** Analyses targeted 574 patients who underwent nephrectomy in presence of nodal or systemic RCC metastases. Multivariable Cox RCC-SM models relied on the 2002 TNM stages, tumour size, Fuhrman grade, histological subtype, age, gender and symptom classification.

**Results:** Presence of systemic symptoms vs. local vs. absence of symptoms distinguished between good (median 3.3 years), intermediate (median 1.5 years) and poor survival (median 1.0 year). It represented an independent predictor of RCC-SM ( $p < 0.001$ ) and was the most informative variable of all examined factors (TNM stage, tumour size, Fuhrman grade, age, gender and histological subtype).

**Conclusions:** After nephrectomy, in presence of either nodal or distant metastases, presence and type (local vs. systemic) of symptoms may help stratify between those who warrant immediate or deferred adjuvant treatment.

**Key Words:** lymph nodes, renal cell carcinoma, survival

### MP07.10

#### Follow-up regimens after radical or partial nephrectomy for localized renal cell carcinoma

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**Introduction:** Up to 50% of patients surgically treated for renal cell carcinoma (RCC) will recur with local or distant metastases. There is evidence that a subset of these patients benefit from salvage surgery and/or systemic therapy suggesting that early detection of recurrence may have value. A number of follow-up protocols have been described but have not been validated. We have established a stage-specific surveillance protocol based on the best available literature in an attempt to more accurately define the time, pattern and method of detection of disease recurrence.

**Methods:** From July 2004 until September 2006, 67 patients were prospectively enrolled following partial or radical nephrectomy for pT1-3N0M0 RCC with informed consent. All patients were evaluated with a history, physical, laboratory tests and chest x-ray at each visit. The surveillance regimen for stage T1a entailed annual visits with abdominal ultrasonography (US). For stages T1b, T2 and T3 RCC, the surveillance visits were semi-annual in the first 3 years, then extended to annually thereafter. All the annual visits entailed abdominal imaging with computed tomography (CT) alternating with US. The primary outcome was the contribution of each investigation to the identification of progression. Secondary outcomes were time to recurrence, disease-free and overall survival.

**Results:** The 67 patients with a mean age of 60.1 years underwent radical ( $n=43$ ) or partial ( $n=25$ ) nephrectomy for RCC (76% clear cell, 13% papillary and 10% chromophobe). The pathological stage was T1a in 37 (55%), T1b in 13 (19%), T2 in 11 (16%) and T3 in 6 (9%). After a median follow-up of 13.1 months, 3 patients recurred with distant metastases. The median time to recurrence was 9.7 months, and it was clinically apparent in 2 of the 3 patients. In the patient with T1a RCC, recurrence in the liver and retroperitoneum was apparent only on abdominal US at 12 month postoperatively. All patients with recurrence underwent salvage therapy but the one patient with T2c RCC died of disease 8 months post-operatively.

**Conclusion:** Although follow-up is short and the numbers who were consented to date is small, the use of standardized surveillance protocols for the follow-up of patients after surgery for RCC should be encouraged to reduce variation in practice and to establish if they will yield earlier and a higher detection rate of local or distant recurrences that are amenable to treatment with curative intent.

**Key Words:** renal cell carcinoma, stage, surveillance

### MP07.11

#### Early detection of renal cell carcinoma in asymptomatic patients improves cancer-specific survival in all stages

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**Introduction:** Early detection of renal cell carcinoma (RCC) has received limited attention. We explored the positive benefits related to the detection of RCC at an earlier asymptomatic stage.

**Material and Methods:** Nephron sparing surgery or radical nephrectomy were performed in 4712 patients from 13 European centers. Life table, Kaplan-Meier and Cox regression analyses addressed RCC-specific mortality (RCC-SM) according to either presence or absence of symptoms at diagnosis. Adjustment was made for age at diagnosis, gender, TNM stage, tumor size, Fuhrman grade and histological subtype.

**Results:** Of the whole cohort, 2357 (50.0%) patients were asymptomatic at diagnosis. Of these, 2294 (48.7%) were stage I vs. 541 (11.5%) stage II vs. 1256 (26.7%) stage III vs. 621 (13.2%) stage IV. The overall 5-year and 10-year cancer-specific survival in asymptomatic vs. symptomatic were 90.4 vs. 69.1, and 86.1 vs. 62.7, respectively (log-rank  $p < 0.001$ ). In multivariable Cox regression model, adjusted for all covariates, asymptomatic patients were at a 40% lower risk of RCC-SM ( $p < 0.001$ ). The multivariable survival benefit was 47.8% for stage I, 55.5% for stage II, 22.3% for stage III and 5.4% for stage IV (all  $p < 0.05$ ).

**Conclusions:** Better survival was seen in asymptomatic patients. Substantial survival gain related to absence of symptoms across all RCC stages indicates that early detection or even screening could improve their survival.

**Key Words:** renal cell carcinoma, risk factors, survival

### MP07.12

#### Management of metastatic renal cell carcinoma (mRCC) with tyrosine kinase inhibition (TKI) sorafenib and sunitinib — clinical experience and toxicity management

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**Introduction:** The management of mRCC has undergone a fundamental shift towards use of sorafenib (Nexavar®) and sunitinib (Sutent®) since recent Health Canada approval for these agents in this patient population.

**Methods:** 17 patients were treated with sorafenib 400mg BID po, 5 patients treated with sunitinib 50 mg po x 4 weeks, 2 weeks off, for mRCC from January 2006 to December 2006. Average age for sunitinib-treated patients was 51 (35–62), with metastasis mainly to lung and bone. Average age for sorafenib-treated patients was 62 (50–87), with metastasis mainly to lung and bone. Three patients with brain metastasis (an exclusion criteria for

initial trials) were treated with sorafenib. Two patients with sarcomatoid variant RCC (an exclusion criteria for initial trials) were treated with sunitinib.

**Results:** Main toxicities in sorafenib group were increased fatigue (40%), hand-and-foot rash (38%), diarrhea (37%), hypertension (15%). Eight patients (mainly older) were dose reduced to 200 mg BID po because of painful hand-and-foot rash. Two patients discontinued drug due to hand-and-foot rash, and one due to diarrhea, despite dose reduction. Main toxicities in sunitinib group were increased fatigue (40%), diarrhea (40%), hand-and-foot rash (20%), hypertension (20%). Neutropenia, anemia, thrombocytopenia were more common in the sunitinib group. No patient discontinued therapy in the sunitinib group, this group was a smaller and younger cohort. Of 3 patients with mRCC and brain metastases treated with sorafenib, one progressed after 3 months and 2 patients have stable disease currently at 5 months.

**Conclusion:** Sorafenib and sunitinib are reasonably well tolerated oral agents for the treatment of mRCC. Toxicity management strategies are crucial to ensure quality of life and targeted dose compliance.

**Key Words:** cancer, chemotherapy, kidney

### MP07.13

#### Cytoreductive nephrectomy in patients with metastatic renal cell cancer: impact of different clinicopathological factors on survival

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**Introduction:** Multimodality treatment of metastatic renal cell carcinoma with immunotherapy and cytoreductive surgery has produced durable responses. Studies have demonstrated increased survival when cytoreductive nephrectomy is performed. In this study we review our experience with cytoreductive nephrectomy and attempt to identify factors predicting survival in these patients.

**Methods:** Medical records of patients who underwent nephrectomy were reviewed. Out of 540 patients we identified 42 patients who underwent nephrectomy for metastatic renal cell carcinoma. Clinical features, pathologic findings, and follow up events were retrieved.

**Results:** Mean Age at nephrectomy was 58 year old. 35 patients (83%) were symptomatic at presentation. Weight loss at presentation was found in 9 patients. Metastatic disease was present in the lung in 35 patients, the bone in 8 patients, and in the liver 4 patients. Multiple synchronous metastatic sites were observed in 37 patients (88%). 35 patients (83%) were found to have conventional histologic subtype. 5 patients (12%) received immunotherapy prior to nephrectomy. Mean follow up was 24 months. At last follow up, 19 patients died of progressive disease, 3 died with disease of other cause, 11 patients were alive with disease, 6 patients lost follow up, and 3 patients were free of disease. Age, sex, symptoms, histologic subtype, pathologic stage, and site of metastatic disease failed to predict survival.

**Conclusion:** Our experience is similar to the published literature. Only few patients will achieve cure with combination of cytoreductive nephrectomy and immunotherapy. The role of cytoreductive nephrectomy prior to multitargeted tyrosine kinase inhibitors remains to be defined.

**Key Words:** clinical pathway, nephrectomy, renal cell carcinoma

### MP07.14

#### Preservation of renal function after partial nephrectomy when compared with radical nephrectomy

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**Purpose:** To compare the preservation of renal function after partial nephrectomy as compared radical nephrectomy using creatinine clearance measurements from 24-hour urine collection.

**Material and Methods:** Creatinine clearance (CrCl) measurements were prospectively obtained by 24-hour urine collection in patients undergo-

ing either a partial nephrectomy (PN) or radical nephrectomy (RN) from 2003 to 2005 at the Ottawa Hospital Civic Campus. Patient's age, sex, presence of hypertension, vascular disease, diabetes, use of ACE inhibitors or ARB, and tumour size, histology and stage were also collected and analyzed. Creatinine clearance was measured at baseline (preoperative), and 3, 6 and 12 months postoperatively. The change in creatinine clearance was then compared between the partial and radical nephrectomy groups. The two groups were compared using a mixed model analysis using the spatial power covariance structure in SAS Version 9.1 and a standard t test.

**Results:** Between 2003 and 2005, 47 consecutive patients with two kidneys, unilateral tumour involvement had preoperative CrCl measured. There were 23 patients in the PN group and 24 patients in the RN group that met the inclusion. The groups were similar with respect to age, sex, presence of hypertension, vascular disease, diabetes mellitus and ACE inhibitor/ARB use. A mixed model analysis showed that the only baseline variable predicting significant change in creatinine clearance was procedure (PN vs. RN,  $p=0.01$ ). The PN group had a lower pre-operative mean creatinine clearance (1.50 mL/min vs. 1.79 mL/min). The partial nephrectomy group had significantly less change in CrCl compared to the radical nephrectomy group at three (-31.8% vs. -5.3%,  $p<0.0001$ ), 6 (-33.0% vs. -4.7%,  $p<0.0001$ ), and 12 months postoperative (-34.6% vs. -5.3%,  $p=0.002$ ).

**Conclusions:** Partial nephrectomy has a significant effect on preserving renal function measured by creatinine clearance relative to radical nephrectomy in this group of patients.

**Key Words:** kidney function, nephrectomy, partial nephrectomy

### MP07.15

#### Dietary habits, genitourinary tract infection and prostate cancer prediction

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**Introduction:** Many studies demonstrated that different macronutrient elements, supplements, body mass index and even infection of the prostate affect the prostate cancer detection. We did this study to evaluate the influence of dietary habits and infections of the genitourinary tract (GU) on prostate cancer detection.

**Methods:** The study was done on 917 patients who planned to have TRUS guided prostatic biopsy based on elevated PSA, rising PSA or abnormal digital examination; all the patients answered a questionnaire including: the marital status, ethnic background, family history of prostate cancer, smoking, dietary profile, the difference in body weight between biopsy time and age of 30 years, medical history of general diseases and local GU diseases. In combination with the pathology data we did univariate and multivariate analyses.

**Results:** Prostate cancer found in 42.09%(386/917) the mean age was  $64.5 \pm 8.3$ ; the mean PSA for prostate cancer and benign prostate patients respectively was  $13.4 \pm 28.2$  and  $7.3 \pm 4.9$  ng/ml. Univariate analysis revealed that the Age, PSA, PSA density, history of sexually transmitted diseases (STDs) including genital warts, syphilis, gonococcal and non gonococcal urethritis, African Canadian ethnic background, diet containing (red meat, hamburger or sausages) increasing the risk of prostate cancer; while fish containing diet and English Canadian background decrease the incidence of prostate cancer. Multivariate analyses revealed that Age, PSA density, history of STDs and diet containing fish were independent predictors of cancer (odds ratio, 1.05, 3.24, 2.28 and 0.77 respectively,  $p<0.04$ ). After age categorization we found that for patients < 65 years old the only independent predictors were history of STDs and PSA density (odds ratio 3.01 and 4.44, respectively,  $p<0.001$ ) while that for patients  $\geq 65$  years the only predictor was PSA density (odds ratio; 2.87,  $p<0.05$ ).

**Conclusion:** Fish containing diet may be a protecting factor against prostate cancer, history of sexually transmitted diseases is an independent predictor of prostate cancer in patients younger than 65 years old. Further studies are needed to evaluate which one of those STDs is more predictor for prostate cancer.

**Key Words:** cancer, infaction, prostate

**MP07.16****Protective effects of non-steroidal anti-inflammatory drugs on prostate cancer progression: a population-based study***DR Siemens<sup>2</sup>, D. Stock<sup>1</sup>, P. Groome<sup>1</sup>*Departments of <sup>1</sup>Epidemiology and Cancer Care and <sup>2</sup>Urology, Queen's University, Kingston, ON

**Introduction:** Pre-clinical investigations have demonstrated a benefit of non-steroidal anti-inflammatory drugs (NSAIDs) by inhibiting oncogenesis and epidemiologic studies have confirmed a possible role of NSAIDs as a chemopreventative agent. However, evidence for a significant effect of this class of drugs on prostate cancer progression is lacking. We determine the effect of NSAID use on indicators of prostate cancer progression in men treated with radical prostatectomy, including the effect on pathologic findings and survival.

**Methods:** Cross-sectional and case-cohort designs were used to assess the effect of NSAIDs on indicators of prostate cancer progression, including grade of disease and disease-specific survival. The study population consisted of 2,009 men treated by radical prostatectomy between 1990 and 1998 and sampled from regional cancer centers in Ontario. It was comprised of 1,619 randomly selected patients (subcohort) and 453 prostate cancer mortality

cases. Ordinal multivariate logistic regression was used to assess Gleason score at diagnosis. Cox Proportional Hazards regression modeling was used to compare disease-specific mortality across NSAID usage.

**Results:** Patients who used NSAIDs prior to diagnosis were more likely to have a Gleason's score of 2–6 relative to 8–10 (adjusted odds ratio (OR): 0.74), though this association was not statistically significant (95% confidence interval [CI]: 0.47–1.17). This trend was more pronounced among a middle tertile age group of 65 to 70 years (OR: 0.43, 95%CI: 0.18 to 1.02). Case-cohort survival analysis did not reveal a protective benefit to having used NSAIDs prior to diagnosis (hazard ratio (HR): 1.01, 95%CI: 0.77-1.31). When inclusion was limited to those that had survived to at least 5 years follow-up, a slight trend towards a reduced risk of prostate cancer death among NSAID users was noted (HR: 0.83, 95% 0.51–1.31).

**Conclusions:** No statistically significant association of NSAID use and disease-specific survival was shown in this population-based study, although there was a trend to a protective benefit on Gleason score for men treated curatively with radical prostatectomy. Further investigation into the protective effect of NSAIDs on prostate cancer progression, particularly on pathologic variables, is warranted.

**Key Words:** prostate cancer, statistics

# MODERATED POSTER SESSION 8: TRANSPLANTATION AND MINIMALLY INVASIVE SURGERY

## TUESDAY, JUNE 26, 15:30-17:30

### MP08.01

#### Safety of penile prosthesis for the treatment of erectile dysfunction in solid-organ transplant patients

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**Introduction:** Contemporary literature suggests that patients previously treated with solid organ transplant are at increased risk of mechanical breakdown or infection if a 3-piece inflatable penile prosthesis (PP) is used for therapy of erectile dysfunction (ED) refractory to 1st or 2nd line treatments. We present a contemporary series of 3-piece PP in this population.

**Methods:** A literature search (1995 to present) identified series' reporting PP in post-solid organ transplant patients. These studies were compared to 5-year follow-up of our series of 28 men (high volume surgical team).

**Results:** Contrary to published literature, infection and mechanical reliability were comparable for both transplant and non-transplant cohorts. Two pts experienced device failure (5 and 7 years) and 1 infection occurred. Reservoir placement did not add to morbidity. No transplant complications were noted. Despite immunosuppression, rates of infection were similar to previously published studies of non-transplant patients.  
**Conclusion:** The 3-piece PP in an important and safe treatment option for men with refractory ED following solid organ transplant. This cohort does not appear to demonstrate an increased rate of short or longer-term complications.

### MP08.02

#### Impact of arterial and arteriovenous renal clamping with and without intrarenal cooling on renal oxygenation and temperature in a porcine model

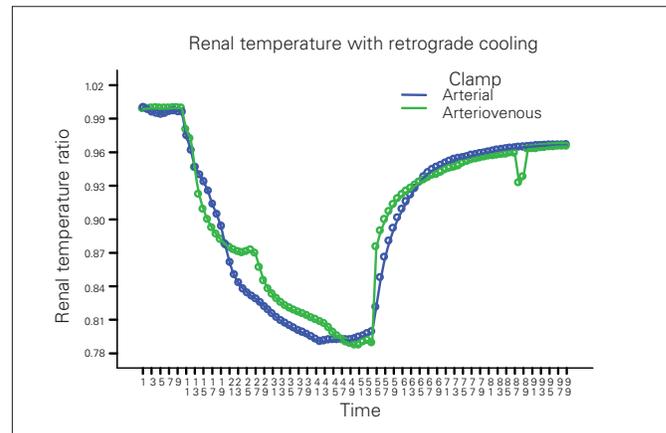
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**Background:** We have previously demonstrated the differential impact of arterial vs. arteriovenous clamping on renal blood flow and oxygenation. We now examine the impact of vascular clamping both without and with retrograde intrarenal cooling.

**Materials and Methods:** Under general anesthesia, laparoscopic access with intra-abdominal pressure of 15 mm Hg to the left renal hilum was obtained. Licox® tissue oxygenation and temperature probes were placed into the kidney transcutaneously; measurements were taken every 30 seconds. After establishing baseline readings, either the artery alone ( $n=18$ ) or the artery and vein ( $n=18$ ) were clamped for 30, 60 or 90 minutes ( $n=12$  each). During vascular clamping, retrograde, intrarenal cooling was performed with ice cold saline infused via a percutaneously placed ureteric catheter in 18 pigs. Changes in renal pO<sub>2</sub> and temperature were analysed with repeated measures ANCOVA in SPSS 13.

**Results:** Retrograde cooling decreased renal parenchyma to 75.8% of baseline temperature (27.9C) within 15min. There were no differences in cooling whether arterial or arteriovenous clamping was used ( $p=0.786$ ). There were no differences in intrarenal pO<sub>2</sub> ratio during vascular clamping in cooled and uncooled animals ( $p=0.70$ ). Following release of the vascular clamps, however, there was a slower recovery of tissue oxygenation in cooled pigs ( $p<0.01$ ); this difference disappeared within 5 minutes. In cooled animals, longer clamp times were associated with more delayed rewarming ( $p=0.04$ ), but did not significantly affect the return of renal pO<sub>2</sub> ( $p=0.508$ ).



**Conclusion:** Retrograde intrarenal cooling can reliably cool the porcine kidney to 28C, regardless of whether arterial or arteriovenous clamping is used. Cooling did not alter intrarenal pO<sub>2</sub> vs. uncooled animals either during vascular clamping or up 30 min post-clamp release.

**Key Words:** laparoscopy, partial nephrectomy, vascular

### MP08.03

#### Ability of carbon monoxide releasing molecules to protect against transplant-related injury

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Significant organ damage may occur as a result of injury during the transplantation process. Carbon monoxide (CO) has previously been shown to reduce damage associated with ischemia reperfusion injury, but is difficult to store and deliver carbon monoxide in a safe, controlled manner. Therefore, we assessed the ability of novel carbon monoxide releasing molecules (CORM) to prevent apoptosis and inflammation in models relevant to the transplant process.

To assess the ability of CORM-2 (tricarbonyldichlorourthenium II dimer) to protect C57BL/6-derived TEC from cytokine-mediated injury, TEC were incubated in 10 ng/ml TNF $\alpha$  and IFN $\alpha$  for 24 hr. Using Annexin V/ 7-AAD staining, cell death was shown to be reduced in TEC after pre-incubation in CORM-2 in a concentration-dependent manner. Similarly, TEC were incubated at 4° C for 12 hr and re-warmed to assess the ability of CORM-2 to protect against temperature-mediated injury. At a concentration of 100 mM, CORM-2 appeared to optimally protect TEC from cytokine and temperature-mediated injury relevant to transplantation. As well, the ability of CORM-2 to modulate endothelial cell pro-inflammatory phenotype was evaluated. CORM-2 prevented activation of NF $\kappa$ B with subsequent downregulation of NF $\kappa$ B-dependent adhesion molecules such as ICAM-1 and E-selectin after induction of inflammation. This translated into reduction of PMN adhesion to endothelial cells (MPO assay). As well, CORM-2 reduced generation of intracellular oxidative stress as indicated by decreased oxidation of DHR123 and nitration of DAF-FM, H<sub>2</sub>O<sub>2</sub> and nitric oxide fluorochromes (iNOS). Interestingly, inducible heme oxygenase (HO-1), which has been identified as a

protective precursor to CO in biologic systems, is upregulated at the protein level.

In summary, we have shown that CORM can protect both endothelial and epithelial cells against temperature and inflammation-related injury. This provides rationale to use CORM in transplant perfusate to protect the organ during cold storage and reperfusion. These studies are ongoing.

**Key Words:** inflammation, prevention, transplant

#### MP08.04

##### Outcomes comparison between third kidney re-transplant versus mate primary transplant

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Third kidney re-transplants have technical and immunologic hurdles that may preclude success. In the face of donor supply/demand issues the outcomes of 3rd kidney transplants were assessed to identify risk of engraftment failure and complications.

A list of deceased organ donors was generated from our center's database that identified donors who had donated one kidney to a third transplant recipient ( $n=21$ ) and the other to a primary renal transplant recipient. The functional and surgical outcomes from the recipients of 3rd kidneys (group 1) were compared with outcomes from first allograft recipients (group 2). Both recipient groups were comparable with respect to age, gender, cold ischemic time and HLA mismatches. As expected, patients in group 1 were more highly sensitized vs. group 2 (%PRA  $23\pm33$  vs.  $7\pm13$ ).

Delayed graft function occurred more frequently in group 1 vs. group 2 (52% vs. 0%,  $p=0.003$ ), despite use of induction therapy in group 1 patients. As well, group 1 patients suffered biopsy-proven rejection twice as often as patients from group 2 (52% vs. 27%). Although patient survival was comparable, there was reduction in graft survival in group 1 (63%, 47% and 43% at 1, 3 and 5 years) vs. group 2 (90%, 83% and 83%). Renal function in patients remaining off dialysis indicated by estimated creatinine clearance was similar in both groups. Operative time and blood loss were significantly higher in group 1 ( $233\pm55$  min and  $540\pm750$  ml) vs. group 2 ( $186\pm54$  min and  $205\pm164$  ml). Overall, there were more surgical and medical complications in group 1 vs. group 2, likely as a result of increased surgical and immunologic complexity in group 1 patients. Allograft survival is reduced and complication rates are higher in 3rd kidney recipients. However, a number of patients receiving their 3rd transplants had excellent long-term renal function.

**Key Words:** kidney function, survival, transplant

#### MP08.05

##### Accurate prediction of delayed graft function after renal transplantation based on recipient weight and cold ischemia time

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**Introduction:** Delayed graft function (DGF) is defined as the need for dialysis in the first week after transplantation. DGF has important clinical and economic consequences. Based on these considerations, we developed and internally validated a model predicting the likelihood of DGF.

**Methods:** Renal transplantation from cadaveric and live donors was performed in 783 patients at one institution. Univariate and multivariate logistic regression analyses addressed DGF. Covariates included age, gender, race and weight of recipient, number of HLA-A, HLA-B and HLA-DR mismatches, maximum and last titer of panel reactive antibodies, donor age and cold ischemia time. Continuously-coded variables were analyzed as is, as well as in a categorically-coded format. The cut-offs were defined according to  $p$  value analyses in univariate Cox regression models.

**Results:** Overall, 129 patients (17%) developed DGF. Age of recipients ranged from 2 to 84 years and most were male (62%) and of Caucasian origin (73%). In multivariable analyses, recipient race ( $p=0.009$ ) and weight

( $p=0.01$ ), donor age ( $p=0.05$ ) as well as cold ischemia time ( $p<0.001$ ) were independent predictors of DGF. After backward variable removal, recipient weight and cold ischemia time were 77.8% accurate in predicting the likelihood of DGF.

**Conclusion:** We developed and internally validated a highly accurate model predicting the likelihood of DGF in patients undergoing renal transplantation.

**Key Words:** kidney, kidney function, transplant

#### MP08.06

##### Immunological and surgical outcomes of extra-capsular vs. intra-capsular allograft nephrectomies

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**Introduction:** To compare the immunologic and surgical outcomes of extra-capsular (ECAN) vs. intra-capsular allograft nephrectomy (ICAN).

**Methods:** Between 1990 and 2004, 96 allograft nephrectomies were performed at one transplant center. 29 procedures were performed within 1 month of the transplant and were therefore omitted from analysis. Overall, the results of 44 ECAN and 23 ICAN were reviewed through evaluation of operative time, estimated blood loss, and peri-operative complications. In addition, an evaluation of the immunological impact of leaving greater amounts of allograft capsule and urothelium behind with ICAN was performed by comparing the change in percent Panel Reactive Antibody (%PRA) after each procedure. In addition the percentage of patients re-listed and re-transplanted was compared.

**Results:** The mean operative times were 110.9 min vs. 130.4 min for ICAN vs. ECAN ( $p=0.02$ ) and estimated blood loss was 226 ml for ICAN vs. 483 ml for ECAN ( $p=0.004$ ). Intraoperative and post-operative complications were low using either technique and differences were not statistically significant. Overall, the pre- to post-operative change in %PRA  $+2.1\%$  for ICAN vs.  $+1.2\%$  for ECAN (NS) at 5.9 months and 8.5 months, respectively (NS). The percentage of patients re-listed was 33.3% vs. 54.3% (NS), and percentage of patients re-transplanted was 22.2% vs. 34.3% (NS) for ICAN vs. ECAN, after a mean follow-up time of 4.5 years and 8.4 years, respectively.

**Conclusions:** Intra-capsular allograft nephrectomies can be performed with shorter operative times and less blood loss vs. the extra-capsular approach. As well, this operative approach does not affect sensitization and the ability to re-transplant the patient.

**Key Words:** nephrectomy, transplant, vascular

#### MP08.07

##### Laparoscopic partial nephrectomy (LPN) with six-year follow-up. Intraoperative ultrasound necessary for oncologic success?

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**Introduction:** Laparoscopic radical nephrectomy has become the standard of care for T1-T2 lesions of the kidney. Laparoscopic partial nephrectomy (LPN) is a more challenging approach to nephron-sparing strategies for small renal masses. Optimal techniques to secure hemostasis are being developed (Lapra-Ty®, Bio-glue®, Tiseel®). The use of intraoperative ultrasound to achieve adequate surgical margins during LPN is debatable. We provide our experience with LPN without the use of intraoperative ultrasound.

**Methods:** Sixty-five (65) patients underwent LPN between 9/2000 – 9/2006 for exophytic solid renal masses between 1 cm–5 cm. The renal hilum was mobilized and either en-bloc clamped with laparoscopic satinsky or renal artery clamped alone with laparoscopic debakey at the time of clamping. The kidney was first stripped of its peri-nephric fat, leaving the fat overlying the exophytic tumor. The normal kidney surrounding the tumor was then scored with cautery, and the hilum clamped. Cold scissors were then used to excise the mass. Gross inspection was done of the tumor base to ensure negative surgical margin. Collecting system, if entered, was closed with 4-0 vicryl. The argon beam was then used to secure hemostasis, and renal parenchyma closed with 2-0 vicryl Lapra-Ty® (Ethicon). The hilum was then unclamped, and Tiseel applied laparoscopically.

**Results:** Average hilar clamp time was 28 minutes (18–53 minutes). Average tumor size with 2.9 cm (1–5 cm). Intraoperative ultrasound, although available, was not used for exophytic tumors. Average blood loss was 50 cc (10 cc–400 cc). Margins were negative in 64 patients. One patient had an intact tumor capsule, but no normal kidney was visible over a small area. This patient underwent re-resection of kidney resection base at same operation with all normal kidney and warm ischemic time of 53 minutes. Final pathology included 54 RCC, 7 AML, 4 benign. No patient to date has experienced tumor recurrence.

**Conclusion:** Laparoscopic Partial Nephrectomy has long-term (up to 6 years in this report) oncologic efficacy. Intraoperative ultrasound does not appear to be necessary for laparoscopic management of exophytic renal masses.

**Key Words:** cancer, kidney, laparoscopy

### MP08.08

#### Laval University experience of 100 cases of laparoscopic pyeloplasties: no difference between primary and non-primary pyeloplasty success rates

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**Introduction:** Laparoscopic pyeloplasty (LP) is a minimally invasive reproducible technique with high success rates that matches open procedures. Criteria used to define success rate vary in literature. We report our experience and compare success rates of primary and non-primary laparoscopic pyeloplasties.

**Methods:** We reviewed retrospectively adult cases of laparoscopic pyeloplasties performed between 2003 and 2006; 72 were done by transperitoneal (TPLP) while 28 by retroperitoneal approach (RPLP) using Anderson-Hynes procedure in 98% of cases. Out of the 100 cases, 10 were non-primary, of which 4 were tertiary. Renal scintigraphic success rates were defined with precise criteria: strict (T1/2 < 10 min), nonobstructive (T1/2 < 20 min) and technical success (improved T1/2). 87% of our patients had a renal scintigraphy before surgery.

**Results:** Indications for surgery were pain (88%), pyelonephritis (5%) and/or stone (9%). Aberrant renal vessel was found in 44% of cases. Average OR time was 129±47 minutes, blood loss was 54±177ml and average post-operative hospital stay was 3.2±1.8 days. 23% of patients had complications, the most frequent being urinary tract infection. Strict success was achieved in 84% of cases, while non-obstructive success and technical success were achieved in 89 and 95%, respectively. Interestingly, strict success was achieved in 80% of non-primary cases, while non-obstructive success and technical success were achieved in 90 and 100%, respectively. Clinical success was achieved in 98% of primary pyeloplasties and in 90% of non-primary. Finally, no statistically significant difference was observed between operative, post-operative characteristics and success rate between RPLP and TPLP.

**Conclusion:** Our series belong to the largest published to date on LP. By defining strict renal scintigraphic criteria, we still obtain a high success rate. Moreover, we show that we can achieve success rates equal to primary Lap approach with non-primary LP.

**Key Word:** laparoscopy

### MP08.09

#### Robot-assisted laparoscopic radical prostatectomy: single surgeon learning curve at a Canadian institution

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**Introduction:** Robot-Assisted Laparoscopic Radical Prostatectomy (RALRP) is an established surgical technique for the treatment of organ-confined prostate cancer. At present the majority of robotic programs exist in the United States, with only 3 da Vinci robots operating in Canada. Implementation of a RALRP program is underway at our institution and we examine the learning curve for a single surgeon using this technique.

**Methods:** We examine the first 50 cases of RALRP at our institution performed by a single surgeon. The surgeon (SP) has fellowship training in urologic oncology and completed a “mini-fellowship” in RALRP at the

University of California, Irvine. Data were collected prospectively from April 2005 to November 2006 with institutional approval. Preoperative factors include patient age, BMI, biopsy Gleason score, PSA, clinical stage and prostate volume. Intra-operative factors include total operative (OR) time, estimated blood loss (EBL), and rate of conversion to open prostatectomy. Pathologic stage, Gleason score, margin status and complication rates were examined post-operatively. We compare the results of the first 25 cases versus the second 25 cases. Statistical analysis was carried out using an unpaired t test, Chi-square or Fisher’s exact test where appropriate. Statistical significance was defined as a *p* value of <0.05.

**Results:** There were no significant differences between the two groups with respect to pre-operative factors. OR time was significantly shorter in the second 25 cases (mean 259 min vs. 233, *p*=0.0334). Statistical significance was also noted for EBL (mean 630 cc vs. 275 cc, *p*=0.0418) but not for rate of conversion or number of nerve sparing procedures. When we analyze the individual portions of the procedure only the time to divide the dorsal venous complex was significant between groups (mean 37 min vs. 25 min, *p*=0.0031). Post-operatively there was no difference between groups for margin status, pathologic stage, Gleason score or complication rate.

**Conclusion:** This study represents a single surgeon experience with RALRP at our centre. Our data support previous studies from other countries and shows that there is improvement in mean OR time and EBL with higher case volume. Further study of the mid and long term outcomes is required.

**Key Words:** laparoscopy, prostate cancer, robotics

### MP08.10

#### A single institution experience with laparoscopic radical prostatectomy for high risk prostate cancer patients

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**Introduction:** Laparoscopic Radical Prostatectomy (LRP) is gaining acceptance as a viable surgical treatment option for localized prostate cancer. The efficacy of LRP for high-risk prostate cancer patients (clinical stage ≥T3, GS ≥8) has yet to be established. We prospectively evaluate the PSM, positive LN rate, and complication rate in a subset of patients that have undergone LRP for high-risk prostate cancer.

**Methods:** Between Nov. 28/06 and Dec. 01/06, 191 patients consecutively underwent LRP by one surgeon (EM). A prospective evaluation of patients with high grade disease, or clinical stage greater than T3 was conducted. Intra-operative outcomes, as well as post-operative pathologic evaluation are reported.

**Results:** Of these, 17 pts (8.9%) had ≥cT3 disease, or GS ≥ 8 on initial prostate biopsy. On pre-operative TRUS guided biopsy, 15 patients were GS 8, and 2 patients were GS 9. One patient (5.8%) was clinically staged as T3. Mean pre-operative PSA was 7.2 ng/mL (3.9–14.0 ng/mL). Mean operative time for LRP on these patients was 300 minutes (120–360 min), with an average blood loss of 376 mL (100–1000mL). On post-operative pathologic evaluation, 6 patients (37.5%) were pT2 and 10 patients (62.5%) were pT3. Specifically, 18.5% were T3a, 25.5% T3b, and 18.5% T3c.

2 patients originally biopsied with GS 8, demonstrated GS 9 on final pathologic evaluation. All underwent a laparoscopic pelvic lymph node dissection at the time of LRP. None of these patients had positive lymph nodes on pathologic evaluation. 6 patients (35.2%) had positive surgical margin (PSM). 5 of these patients were pathologically staged as pT3. 50% of the positive margins occurred at the apex. The mean duration of hospital stay for these patients was 39.6 hours. The mean duration for catheterization was 8.6 days. Regarding post-operative complications, one patient required an incisional hernia repair at the extraction site.

**Conclusion:** LRP can be safely performed for high risk prostate cancer patients. Although a greater number of patients are required to further establish the oncologic efficacy of LRP for high-risk prostate cancer, our initial experience in this subset of patients is encouraging.

**Key Words:** laparoscopy, prostate cancer, radical prostatectomy

**MP08.11****Comparative analysis of transperitoneal and retroperitoneal laparoscopic partial nephrectomies reveals that retroperitoneal approach leads to shorter hospital stay**

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**Introduction:** Laparoscopic partial nephrectomy is a minimally invasive technique that can be achieved by 2 main approaches: transperitoneal and retroperitoneal. Both approaches show little morbidity when compared to open approach. We report here our experience of 128 consecutive cases.

**Methods:** We reviewed retrospectively cases of laparoscopic partial nephrectomy between August 2003 and May 2006. 90 were done by transperitoneal approach (TPLN) while 38 by retroperitoneal approach (RPLN). Beside approach, the techniques were similar in the two groups. Surgeries were done by 2 surgeons and the approach was not dependent on tumour size or location. Each surgeon performed only one of the two approaches.

**Results:** Preoperative characteristics (age, sex, creatinine, BMI, number of previous surgeries) were not statistically significant between the two groups. Tumour size were  $3.2 \pm 1.3$  and  $2.7 \pm 1.3$  cm for TPLN and RPLN ( $p > 0.05$ ). Clear cell carcinoma were diagnosed in 54 and 49% of tumours from TPLN and RPLN, respectively ( $p > 0.05$ ) while benign tumours were found in 20 and 15%. T1 pathological stage represented 84 and 97% of cases. Operative time was  $128 \pm 32$  and  $134 \pm 37$  minutes for TPLN and RPLN ( $p > 0.05$ ). Average blood loss was  $206 \pm 314$  and  $189 \pm 295$  ml ( $p > 0.05$ ). Urological complications or overall complications were not statistically significant between the two groups. However, RPLN showed a shorter hospital stay when compared to TPLN ( $3.2 \pm 1.5$  vs.  $4.5 \pm 3.0$  day,  $p = 0.02$ ). Pain was not responsible for the difference in hospital stay since narcotic use was similar in the 2 groups. Multivariate analysis demonstrated that complications and transperitoneal approach were predictive of longer hospital stay ( $p < 0.05$ ). Finally, we did not find any correlation between BMI or a history of abdominal surgery and operative parameters such as OR time, blood loss or complications.

**Conclusion:** We show that retroperitoneal partial nephrectomy is associated with a significant reduction in hospital stay. This is the third retrospective study and the first analyzing it in a multivariate manner to show this finding. These results should encourage the retroperitoneal approach, especially in posterior and lower pole renal tumours. However, these results should be reproduced in a randomized control trial before establishing that RPLN definitely decrease hospital stay.

**Key Words:** laparoscopy, parital nephrectomy, renal cell carcinoma

**MP08.12****Validated visual grading system for nerve-sparing laparoscopic radical prostatectomy**

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**Introduction:** Despite advances in surgical technique for nerve sparing radical prostatectomy, there exists a wide disparity in reported potency rates following surgery. We hypothesize that the variability may be due to the technical success of the nerve sparing dissection. A visual grading system from 1 to 5 is proposed to grade the quality of the left and right neurovascular bundle (NVB) following laparoscopic radical prostatectomy (LRP). The grading system is illustrated in Table 1.

**Methods:** Twenty-two consecutive patients undergoing LRP for biopsy proven adenocarcinoma of the prostate were followed between July and October 2006. A unilateral, bilateral, or non nerve sparing LRP was performed according to preoperative clinical staging. After removal of the prostate, 3 images of the NVB were taken. The operating surgeon assigned a score to each NVB (baseline score). Digital images were saved and baseline scores were blinded from the primary surgeon and respondents. Six of the original 22 patients were discarded from the study due to technical problems resulting in poor image quality. Technical problems included poor exposure, incorrect resolution, and poor focus. The 48 images were randomized into a slideshow presentation. Fifteen respondents attend-

ed a slide show and were asked to grade each of the 96 NVBs. Intraclass correlation was used to assess the reliability of respondents' scoring.

**Table 1. Abstract MP08.12. Grading Criteria of NVB**

Grade	Mechanical Preservation [% of NVB preserved]	Thermal Injury [% of NVB preserved]
1	0%	0%
2	1-25%	1-25%
3	26-50%	26-50%
4	51-75%	51-75%
5	76-100%	76-100%

**Results:** Six urologists, 5 residents, and 4 medical students participated in the scoring. The mean score was 2.8 and there was no significant difference between rater qualification group. The overall intraclass correlation was 0.78 ( $p < 0.001$ ) indicating good overall reliability. Medical students exhibited the best reliability at 0.81 while urologists showed the greatest variation at 0.76. The intraclass correlation for residents was 0.79. All qualification groups exhibited good reliability.

**Conclusions:** This validated grading tool may serve as a useful instrument to aid in prognostication of patient outcomes. Further study is required to determine whether higher reported grades of nerve sparing correlate with improved patient outcomes post LRP regarding potency, time to return of potency, continence, and more.

**Key Words:** nerve sparing, prostate cancer, radical prostatectomy

**MP08.13****Laparoscopic extraperitoneal radical prostatectomy: experience at a small Canadian community hospital with 100 cases**

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**Introduction:** Laparoscopic prostatectomy has gained popularity in Europe but its application in Canada has been sparse. We present our experience at a small community hospital using the extraperitoneal technique popularized by Stolzenburg.

**Methods:** From June 2004 to November 2006, laparoscopic extraperitoneal radical prostatectomy (LERP) technique was applied to 100 of 102 patients who chose surgery for prostate cancer treatment by one surgeon. Mean patient age was 63.7 (range 47–76). Mean preoperative PSA was 14.8 (range 1.17–690). Patients are divided into 2 groups to highlight the learning curve which we believe is around 40–50 cases.

**Results:** Mean operative time with lymph node dissection was 239 min, 145 min for Groups 1 and 2, respectively. There were 4 conversions in Group 1 and none in Group 2. Transfusion rate was 10% for Group 1 and 2% for Group 2. Post operative day 1 hematocrit was 0.34 and 0.36 for Group 1 and 2. Hospital stay was 1.6 days (range 1 to 6) for Group 1 and 1 day (all patients discharged on postoperative day 1) for Group 2. There was one readmission in group 1 and none in Group 2. Pathological stage was pT2c in 81% and 82%, pT3 in 17% and 16%, pT4 in 2% and 2% respectively in Groups 1 and 2. Positive margin rate for pT2 tumours was 20% and 9.7%, pT3 tumours 50% and 50% for Groups 1 and 2 respectively. Mean catheterization was 11 days for Group 1 and 7 days for Group 2. No patient used morphine in the entire series. Continence rates for the 2 groups at 6 weeks were 34% and 63%, at 6 months 77% and 94%, respectively.

**Conclusion:** Laparoscopic extraperitoneal radical prostatectomy is a challenging laparoscopic procedure with a long learning curve. This series shows the feasibility of adopting the LERP technique in a small Canadian community institution by providing similar oncological results and operative times to the open technique with superior functional results. Further multicenter use of the LERP technique needs to be implemented to assess feasibility in other institutions.

**Key Words:** laparoscopy, prostate cancer, radical prostatectomy

**MP08.14**

**Laparoscopic partial nephrectomy: functional and oncologic outcomes with up to 6 years followup**

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**Introduction:** We present functional and oncologic outcomes of laparoscopic partial nephrectomy from one institution with a follow-up of up to 6.5 years.

**Methods:** Ninety four patients underwent laparoscopic partial nephrectomy between August 2000 and September 2006. Of these, 53 patients with at least one year follow-up were included in this study. Mean patient age was 62.5 years. In 4 (7.5%) of the cases indication for partial nephrectomy was imperative. Mean tumor size was 2.4 cm (range 0.6–4.3). In 46 (86.8%) of the cases, postoperative histo-pathological examination was positive for renal cell carcinoma. A two tailed paired t-test or Wilcoxon signed rank test were carried out for pre- and post-operative continuous parameters' comparisons. A *p* value inferior to 0.05 was considered statistically significant.

**Results:** Median follow-up was 36 months (mean 35.9; range 12–79). Calculated creatinine clearance (CCT) decreased from a mean of 87.0 ml/min preoperatively to 74.5 ml/min in the immediate postoperative period (*p*<0.001). Three months following the surgery, CCT improved significantly to 80.8 ml/min (*p*<0.003). Post-operative nuclear scans showed functional kidney moiety in all but one case. A mean calculated post-operative split MAG-3 clearance was significantly lower on the operated side than on the contra-lateral side (74.0 ml/min vs. 110.7 ml/min respectively; *p*<0.001). However a mean post-operative peak concentration time was similar on the both sides (6.42 min vs. 6.05 min; *p*=0.652). The rate of positive surgical margins was 2.2% (1 patient). No cases of disease progression, local or port-site recurrence were observed. Two patients (3.8%) died 11 and 20 months after the surgery of unrelated causes. Overall survival was 96.2% and disease-free survival 100% at a median of 36 months of follow-up.

**Conclusion:** At a median follow-up of 3 years, laparoscopic partial nephrectomy demonstrates oncologic and functional results similar to that of open surgery.

**Key Words:** kidney, laparoscopy, partial nephrectomy

# POSTER DISPLAY 1: ENDOUROLOGY-LAPAROSCOPY, ONCOLOGY

## SUNDAY, JUNE 24

### DIS01.01

#### Pulmonary embolization of radioiodine seeds following permanent prostate brachytherapy

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**Introduction:** To study the incidence of seed migration to the lungs after prostate brachytherapy, and evaluate treatment-related parameters influencing seed embolization.

**Materials and Methods:** We retrospectively reviewed the charts of ninety-seven consecutive patients with localized prostate cancer treated with radioiodine seed implant between April 2003 and February 2006. Chest x-rays obtained at one month follow-up were examined to document the number and location of seeds in the lungs. CT and MRI scans of pelvis were taken one month after implant to check seed position and postimplant dosimetry. The implant characteristics possibly impacting seed migration were analyzed.

**Results:** Seed embolization occurred in 17 (17.5%) of 97 patients, and in majority of cases (88%) only one seed embolus was documented. 19 (0.23%) of 8082 seeds implanted migrated to the lungs, 11 in left and 8 in right lung respectively. The locations of seeds are 1 each in left and right upper lobes, 2 in right middle lobe, 5 in right lower lobe, and 10 in left lower lobe. In one patient a single seed was identified within the right ventricle of heart. No patients complained of any change in pulmonary symptoms on routine follow-up. We are currently analyzing any correlations between the number of seeds planned for extraprostatic placement and the frequency of seed migration. We do not expect any adverse effect of small proportion of migrating seeds (<0.5%) to the lungs on the postimplant dosimetry results.

**Conclusions:** The incidence of pulmonary seed embolization after prostate brachytherapy observed in our series is very low (0.23%). The lower lobes were mainly the frequent sites (79%). Seed migration to the lungs had no significant clinical or dosimetric consequences in the current study.

**Key Words:** brachytherapy, prostate cancer, surveillance

### DIS01.02

#### Influence of continence on quality of life after radical prostatectomy: a comparison of patients younger and older than 70 years of age

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**Introduction:** Incontinence is a potential complication in therapy of a locally limited carcinoma of the prostate by retropubic radical prostatectomy. Here, we compare the quality of life of patients who are older than 70 years to those of younger men on the basis of early and late status of continence.

**Methods:** From November 2001 to December 2005, 179 patients underwent a retropubic radical prostatectomy in our hospital. We evaluated status of continence and quality of life in patients regarding post-surgical morbidity before missal as well as more than 6 months after surgery. An ICS 24h pad test was performed during hospital stay on day 10 after surgery for status of early continence. Telephone interviews (EORTC-QOL-C30, incl. prostate module) were done to assess late-stage continence more than 6 months after the operation. In the telephone interview, 140 (78.2%) patients had taken part, resulting in an average follow-up of 40 months as of now.

**Results:** From all operated 179 patients 50 (27.9%) were older than 70 years (average: 73.3±2.0a). The average hospital stay (13.2±4.9 days) and

days for tightness of anastomosis (9.8±7.2 days) did not differ significantly between older and younger patients. Regarding status of early continence, 4% of the older patients (>70a) suffered from urine leakage of 5 pads or more (>50 ml) in 24h. However, over 68% of the older patients reported a main consumption of 1 pad (0-2 ml) in 24hrs. These data did not show any significant difference to those obtained from younger patients (<=70a). Here, 71.3% patients showed a satisfying status of early continence (0-1 pad in 24h), and 6.9% had urine leakage requiring more than 5 pads per day. Concerning the status of late continence, 80.1% (>70a) and 87.3% (<=70a) of the patients reported no use of any pads at all at 5 months after surgery. As for the state of health and quality of life, no significant differences were measured between the two groups of patients: 85% (>70a) and 79.3% (<=70a) reported a good to excellent state of health. Further, 62.5% (>70a) and 65.8% (<=70a) certified having an excellent quality of life. In the older patients, 97.5% did not feel impaired at all by bladder symptoms in their lives (vs. 92.1% <=70a).

**Conclusion:** Patients who are older than 70 years reach a good early and late status of continence (>5 months) after retropubic radical prostatectomy in our hospital. Radical prostatectomy does not lead to a significant increase of post-surgical morbidity from incontinence symptoms in the elderly.

**Key Words:** incontinence, prostate cancer, QOL

### DIS01.03

#### Diagnosis and treatment of prostate cancer with radical prostatectomy at an earlier age does not affect the pathological stage

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**Introduction:** Some argue that prostate cancer (PCa) detection and treatment at a younger age may translate into higher rate of clinically insignificant PCa. We assessed the effect of patients age at diagnosis on the pathological stage at radical prostatectomy (RP).

**Methods:** Clinical and pathological data were available for 11975 patients from 3 European and 3 North American tertiary care centers. All RPs were performed between 1987 and 2006. Univariable and multivariable logistic regression analyses addressed the effect of age at RP on the rate of extracapsular extension (ECE), seminal vesicle invasion (SVI) and lymph node invasion (LNI), after controlling for PSA, clinical stage, biopsy Gleason sum and year of surgery. Age at RP was coded as cubic spline to allow non-linear effects.

**Results:** Pathological age only affects the rate of SVI. However, only one in ten men harbored SVI and this percentage may decrease even further with ongoing stage migration. Nonetheless, these data suggest that the removal of seminal vesicles should not be omitted in older men.

**Conclusion:** Pathological age only affects the rate of SVI. However, only one in ten men harbored SVI and this percentage may decrease even further with ongoing stage migration. Nonetheless, these data suggest that the removal of seminal vesicles should not be omitted in older men.

**Key Words:** prostate cancer, radical prostatectomy

### DIS01.04

#### Extended biopsy schemes are associated with similar pathological characteristics but lower biochemical recurrence than sextant biopsy

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**Introduction:** Historically extended biopsy schemes were associated with increased detection of clinically insignificant prostate cancer (PCa). We assessed the difference in pathological stage and the rate of biochemical recurrence (BCR) after radical prostatectomy (RP) according to sextant versus extended (10 or more cores) biopsy scheme, in contemporary patients. **Methods:** Between 2000 and 2006, 4525 patients underwent prostate biopsy followed by RP, at 6 different institutions in North America and Europe (sextant: 2246 [49.6%]; extended scheme: 2279 [50.4%]). Pathological stages were classified according to presence of extracapsular extension (ECE), seminal vesicle invasion (SVI) or lymph node invasion (LNI). Tumor grades were assigned according to the Gleason score. The median follow-up was 6 years. BCR was defined as PSA >0.1 ng/ml and rising.

**Results:** Mean age was 61 years (median 62) and mean PSA was 7.4 ng/ml (median 6). At RP, when Gleason sum was stratified according to sextant vs. extended biopsy schemes. Gleason 7-10 was recorded in 22.0% vs. 23.9% patients. ECE distribution was 22.6% vs. 20.5%, SVI 8.4% vs. 8.2% and LNI 3.8% vs. 3.4%. BCR status was available in 2980 (65.9%) patients. The actuarial BCR-free survival at 5 years was 78.0% vs. 84.9%, respectively for sextant vs. extended biopsy schemes (log rank  $p=0.01$ ) as shown in Figure 1. After adjustment for PSA, clinical stage and biopsy Gleason sum, extended biopsy scheme was associated with lower BCR rate (RR 0.62;  $p<0.001$ ).

**Conclusion:** Extended biopsy scheme is associated with the same rate of high grade PCa, ECE, SVI and LNI as sextant biopsy. However, the rate of BCR is lower in men diagnosed with extended biopsy schemes. Thus, extended biopsy has more favorable natural history despite similar pathological characteristics.

**Key Words:** biopsy, prostate cancer, relapse

### DIS01.05

#### Larger prostate glands are associated with a lower rate of upgrading between biopsy and radical prostatectomy

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**Introduction:** Significant upgrading between biopsy and radical prostatectomy (RP) Gleason sum is a well known phenomenon that affects roughly 30% of patients. We hypothesized that prostate volume may significantly affect the rate of upgrading, where higher rates of upgrading could exist in larger, less extensively sampled glands.

**Methods:** We tested the above hypothesis in 3870 patients from one European and one North-American tertiary academic centers. Significant upgrading was defined as biopsy Gleason 2-6 increase to RP Gleason 7-10 or biopsy Gleason 7 increase to RP Gleason 8-10. Logistic regression analyses tested the association between prostate volume and the rate of significant upgrading, after adjusting for PSA, biopsy Gleason sum, clinical stage and number of biopsy cores.

**Results:** Mean age was 62 years (39-79) and mean PSA was 8.5 ng/ml (median 6.6). Clinical stage was T1c, T2 and T3 in 2543 (65.7%), 1283 (33.2%) and 44 (1.1%), respectively. Biopsy Gleason sum was 2-6, 7 or 8-10 in 2634 (68.1%), 1097 (28.3%) and 139 (3.6%), respectively. A significant upgrading between biopsy and RP was recorded in 1000 (25.8%) patients. In multivariable analyses, increasing prostate volume was associated with a decreased risk of significant upgrading ( $p<0.001$ ; OR 0.99; Figure 1). This implies that for every cc increase in prostate volume, the probability of upgrading decreases by 1%. Thus, the difference in the rate of upgrading between a 40 and a 30 cc gland is 10%. Similarly, the

difference in the rate of upgrading between a 60 and a 30 cc gland is 30%.

**Conclusion:** Prostate volume is inversely associated to the rate of upgrading. Larger glands may be subjected to biopsy due to BPH driven PSA elevations, which lead to the diagnosis of less aggressive PCa that are less frequently upgraded at RP.

**Key Words:** biopsy, prostate cancer, radical prostatectomy

### DIS01.06

#### Digital rectal examination is an independent predictor of gleason 8-10 in patients treated with radical prostatectomy for clinically localized prostate cancer

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**Introduction:** Some investigators questioned the utility of digital rectal examination (DRE) in the diagnosing of prostate cancer in contemporary PCa patients. We hypothesized that DRE may be of crucial importance in identifying high grade PCa (HGPCa) at radical prostatectomy (RP).

**Methods:** Clinical and pathological data were available for 1492 patients. The cohort characteristics were as follows: mean age 62 (39-75), mean PSA 8.4 (0.14-46.7), mean percentage free PSA 14.2% (1.7-75%), mean prostate volume 49.5 (13-240). Biopsy Gleason sum was 2-6, 7 or 8-10 in 984 (65.9%), 455 (30.5%) and 53 (3.6%) patients, respectively. A suspicious DRE was present in 435 (29.2%) patients. Univariable and multivariable logistic regression analyses addressed the presence of HGPCa at RP, defined as RP Gleason sum  $\geq 7$ . Variables consisted of pretreatment PSA, biopsy Gleason sum, prostate volume, percentage free PSA (% fPSA), year of surgery (coded as quartiles) and DRE findings (pos. vs. neg.).

**Results:** At RP, 794 (53.2%) patients harbored HGPCa. After adjusting for PSA, %fPSA, prostate volume, biopsy Gleason sum and year of surgery, DRE was an highly statistically significant independent predictor of HGPCa at RP ( $p<0.001$ ). A positive DRE was associated with a 2.5-fold increase in the risk of detecting a HGPCa at RP. Moreover, when DRE was removed from the whole model, the predictive accuracy decreased from 80.6 to 78.9%.

**Conclusion:** Digital rectal examination is an independent predictor of HGPCa at RP, even in contemporary patients. A positive DRE is associated with a 2.5-fold increase in the risk of harboring a HGPCa at RP.

**Key Words:** DRE, Gleason, localized, prostate cancer

### DIS01.07

#### Is transperitoneal laparoscopic radical prostatectomy associated with a greater presence of small bowel in the planning target volume for adjuvant or salvage radiotherapy?

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**Introduction:** Robot assisted and laparoscopic radical prostatectomy (LRP) is becoming a popular alternative to open retropubic radical prostatectomy. Although extraperitoneal LRP is feasible, there are advantages to a transperitoneal approach. However breaching the peritoneum may facilitate movement of bowel loops into the pelvis, thereby precluding some patients from adequate, full dose, adjuvant radiation. Although this concern is theoretical, it has never been investigated. Our objective was to compare the incidence of small bowel within the planning target volume (PTV) for radiotherapy to the prostate bed for patients post open and laparoscopic radical prostatectomy.

**Methods:** 23 of 115 patients who recently had a LRP for clinically localized prostate cancer prospectively underwent a single radiotherapy planning CT simulation to assess the frequency of small bowel within the PTV for the prostate bed. This was compared to the radiotherapy planning CT scans of 48 patients who had an open RP and received adjuvant or salvage radiotherapy for prostate cancer. For all CT scans, a single blinded observer delineated the distal loops of small bowel, and a single blinded radiation oncologist delineated the superior extent of the clinical target volume (CTV). The superior extent of the CTV was 5mm above the

most superior surgical clip at the level of the vas deferens, or the tip of the seminal vesicles. A 15mm margin was then applied to the CTV to generate the PTV, accounting for organ motion and set-up uncertainty.

**Results:** In the open RP group, 8/48 patients (17%) displayed an overlap between small bowel and PTV for radiotherapy. In comparison, 3/23 (12%) of patients in the LRP group had overlap ( $p = 1.0$ ).

**Conclusions:** There is no difference between transperitoneal LRP and open RP with regards to the incidence of small bowel in the PTV for the prostate bed. Thus, patients undergoing LRP are no less likely to be candidates for standard adjuvant or salvage radiotherapy should they require it.

**Key Words:** laparoscopy, prostate cancer, radiation

### DIS01.10

#### Circulating levels of plasminogen activation inhibitor-1 improve the accuracy of pre- and post-operative nomograms for prediction of prostate cancer recurrence after radical prostatectomy

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**Introduction:** Plasminogen activation inhibitor-1 (PAI-1) plays an important role in signal transduction, cell adhesion, invasion and migration. We tested whether the addition of pre-operative circulating PAI-1 levels improves the accuracy of standard pre-operative and post-operative models for prediction of biochemical recurrence (BCR) in prostate cancer patients treated with radical prostatectomy.

**Methods:** Pre-operative plasma levels of PAI-1 were measured in 429 consecutive patients treated with radical prostatectomy for clinically localized prostate cancer. The patients were randomly divided into a development (67%,  $n=286$ ) and a split sample validation cohort (33%,  $n=143$ ). Cox regression analysis was used to develop prognostic nomograms for prediction of BCR.

**Results:** In standard univariable analyses, categorically coded pre-operative PAI-1 was significantly associated with BCR ( $p<0.001$ ). In standard pre-operative and post-operative multivariable analyses, preoperative PAI-1 was independently associated with BCR ( $p<0.001$  and  $p=0.002$ , respectively). In the split sample validation cohort, the addition of PAI-1 increased the predictive accuracy of the pre-operative multivariate model by 1.2, 7.7, 10.3, 6.7 and 5.4% at 1, 2, 3, 4 and 5 years, respectively. Moreover, the addition of PAI-1 increased the predictive accuracy of the post-operative model by 0.5, 1.1, 4.0, 2.4, and 3.6% at 1, 2, 3, 4 and 5 years, respectively.

**Conclusion:** Preoperative circulating PAI-1 is a powerful predictor of BCR, and it substantially enhances the accuracy of established BCR markers. We developed and validated pre-operative and post-operative nomograms that include circulating pre-operative PAI-1 levels. These nomograms may assist clinical decisions regarding treatment choice and follow-up as well as identifying patients at high risk of BCR who may benefit from neoadjuvant and/or adjuvant treatment modalities.

**Key Words:** incontinence, prognostic marker, prostate cancer, radical prostatectomy

### DIS01.11

#### Demographic analysis: an update of randomized controlled studies in prostatic oncology

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**Introduction:** We examined randomized controlled trials (RCTs) on one of the most researched topics in urologic oncology, prostate cancer. Particular emphasis was placed on newly conducted prospective phase III RCTs.

**Methods:** For urologic malignancies in prostate cancers, MEDLINE® searches for articles for years 2004 through March 21, 2006 with the medical subject headings (MeSH) "prostatic neoplasms" were carried out separately, and then crossed with the MeSHs "Clinical trial.mp. or clinical trial.pt. or random.mp. or tu.xs.", which has been shown to be an optimal search strategy with great sensitivity for detecting RCTs. The search-

es yielded 2306 articles in total for the defined period. These were manually analyzed and excluded by title, abstract or whole article (2113). The qualifying 193 articles were then analyzed based on modality of therapy, cohort size, participating country, principle author and journal type.

**Results:** Using our filter parameters for the MEDLINE® searches, in the majority of RCTs over the above years, even though modalities varied, to shed new light on prostatic oncology most trials commonly examined medical therapies, 43.6%, 37.6% and 83.3% for years 2004, 2005 and for the examined period of 2006 respectively. This was followed by diagnostic and screening studies in most cases. Cohort sizes were generally greater than 100 (33%–62%). Urologists were often the lead investigators of the trials (43%–67%). Articles were usually published in surgical journals (40%–80%) and Europe and the United States are responsible for most of the publications of RCTs.

**Conclusion:** Given that initial searches yielded well over two thousand articles listed as RCTs in prostatic oncology, only a small percentage (9%) of these were actually phase III and thus offered new results not described in review articles or commentaries. The majority of published data were either review articles or commentaries.

It is abundantly clear that new recruitment strategies need to be developed to encourage patients to enrolled in RCTs and that such studies need to be undertaken in urologic oncology to provide definitive answers to the abundant and unanswered questions in this fascinating area.

**Key Words:** prostate cancer, screening

### DIS01.12

#### Evaluating the evidence: reporting of comparative observational studies of surgical interventions in the urological literature

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**Introduction:** In the absence of randomized controlled trials, well-designed observational studies comparing surgical interventions potentially provide the highest levels of evidence. Although several methodological criteria have been reported as safeguards against bias, no consensus has yet been reached regarding reporting standards for surgical observational studies. We sought to develop and apply a standardized evaluation system for assessing surgical observational trials in the urology literature.

**Methods:** A standardized evaluation form was developed using questions from the Consolidated Standards for Reporting Trials (CONSORT) statement and previously reported criteria from the surgical literature that were found applicable to observational surgical trials. All parallel design observational trials involving human subjects and an invasive therapeutic surgical procedure published in four leading urology journals in 1995 and 2005 were evaluated. Reporting adequacy was scored in five categories: background, intervention, statistical analysis, results, and discussion.

**Results:** There were 27 articles in 1995 and 62 articles in 2005. The most common topics were endourology (30%), oncology (24%), and reconstruction (24%). Ninety percent of studies were retrospective. From 1995 to 2005, improvements were seen in all categories: background (4.1±1.4 vs. 4.7±1.4 out of 8 possible,  $p=0.043$ ), intervention (4.2±1.9 vs. 5.8±1.5 out of 9,  $p=0.001$ ), statistical analysis (2.3±1.2 vs. 3.1±1.3 out of 9,  $p=0.006$ ), results (5.0±1.7 vs. 5.5±1.6 out of 10,  $p=0.217$ ), and discussion (3.6±1.1 vs. 3.9±0.9 out of 6,  $p=0.106$ ). Overall score increased from 19.1±3.9 to 23.0±4.2 ( $p=0.001$ ) on a scale of 0–42. Regarding individual criteria, studies in both 1995 and 2005 explained scientific background (96% vs. 97%,  $p=0.909$ ) and study hypothesis (85% vs. 87%,  $p=0.808$ ) in a high percentage of published studies. From 1995 to 2005, improvements were seen in description of interventions (59% vs. 87%,  $p=0.003$ ) and reporting of efforts to standardize procedures under investigation (48% vs. 82%,  $p=0.001$ ). Clearly defined primary outcomes (11% vs. 19%,  $p=0.340$ ), reporting of baseline data (59% vs. 73%,  $p=0.213$ ), and discussion of limitations (44% vs. 48%,  $p=0.732$ ) did not significantly improve from 1995 to 2005.

**Conclusion:** This systematic assessment suggests that reporting of observational studies in the urology literature has improved from 1995 to 2005. However, the adequacy of reporting still remains sub-optimal with only approximately half of reporting standards being met in 2005.

**Key Word:** statistics

### DIS01.13

#### Cadaveric study of a novel urethral catheter in the management of posterior prostatic urethral trauma

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**Introduction:** Unsuccessful urethral catheterization due to posterior prostatic urethral trauma (PPUT) is usually the result of previous unsuccessful attempts creating a false passage, an undermined bladder neck post TURP, previous urethral surgery or external traumatic lesions. These situations require either SP catheterization or cystoscopy with catheter-over-guidewire techniques. This study evaluates the use of a simply modified urethral catheter for management in PPUT.

**Methods:** A novel urethral catheter was created using 5 cube NdFeB magnets (0.125 mm) inserted into the distal drainage port of an 18 Fr straight catheter. An external disc NdFeB magnet (5.08 x 1.27 cm) was placed over the pubic symphysis during insertion. Once in the bladder, catheter-over-wire technique would complete intravesical catheterization. Three male cadaveric dissections were completed to recreate a PPUT, specifically, a false passage. Urethral catheterization was then attempted with an 18 Fr straight, an 18 Fr coude, and the 18 Fr novel urethral catheter. Correct positioning in the bladder was confirmed via a dissected anterior bladder window. The anterior surface of one cadaveric bladder was dissected off in order to display the path of each catheter attempt. Digital video was recorded.

**Results:** The 18 Fr straight and the 18 Fr coude were unable to navigate the false passage in all 3 cadaveric specimens. In contrast, the novel urethral catheter was able to be confirmed as being intravesical in all cases. The digital video displaying the path of the novel catheter showed that the catheter hugged the anterior surface of the prostatic urethra and never contacted the posterior prostatic urethra.

**Conclusion:** The novel urethral catheter presented herein was able to be intravesically confirmed where traditional catheterizations failed. The path of the novel catheter suggests that by avoiding contact with the posterior surface of the prostatic urethra, false passages could be reduced. This finding may prove even more advantageous in the frequently catheterized patient, ie CIC's. A prototype catheter with an indwelling magnetic tip using in vivo trials may further elucidate its role.

**Key Words:** catheter, trauma, urethra

### DIS01.14

#### Management of upper urinary tract TCC in patients with HNPCC

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**Introduction:** Hereditary nonpolyposis colorectal cancer (HNPCC) is associated with neoplasms in several sites including upper urinary tract, colon, breast and uterus. Management depends upon early surveillance among the organ systems involved. We report endoscopic diagnosis, treatment and surveillance of upper tract neoplasms in 3 first-degree relatives and 2 unrelated individuals affected with HNPCC.

**Methods:** One family presented through a 70 year-old male with a family history of multiple cancers (colorectal, endometrial, ureteral and breast). The patient had bilateral ureteral transitional cell carcinoma (TCC). A sister had breast cancer at age 70 and transitional cell carcinoma of the renal pelvis at age 74. A son was diagnosed with TCC of the ureter at age 42. Two unrelated patients were found to have upper tract neoplasms after presentation with hematuria. One had a history of carcinoma of the colon, uterus and breast. Genetic study demonstrated mutations of DNA mismatch repair genes in both families. All patients were treated endoscopically and followed on an endoscopic surveillance protocol.

**Results:** All patients are presently free of urothelial neoplasm. A bladder tumor was found in one patient who later developed a ureteral stricture and required nephroureterectomy with diffuse carcinoma in-situ in the specimen. A second patient developed carcinoma in-situ of the bladder during surveillance.

**Conclusion:** Transitional cell carcinoma of the upper tract occurs in patients with HNPCC. Genetic abnormalities should be studied in all patients with

upper urinary TCC and colon cancer. Conservative therapy should be considered strongly to preserve renal units in these patients.

**Key Word:** TCC

### DIS01.15

#### Reference selection bias in major original clinical research papers

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**Introduction:** A concerning trend noted among the latest published original research papers involves the use of increasingly recent cited references to both formulate scientific hypotheses and validate study outcomes. This may be due to the ease of accessing the body of literature online. A selection bias was hypothesized to be influenced by this ease of access. Our study seeks to determine if in fact there is such a trend and if it is significantly associated with being currently available electronically.

**Methods:** 7 clinical journals were identified based on their highest impact factor: urology: BJU, European Urology, Journal of Urology; and general clinical medicine: NEJM, Lancet, JNCI, and JAMA; 10 random articles were identified from the most recent electronic copies of the journals and 10 random articles were identified from the oldest electronic copies (articles  $n = 140$ , references  $n = 5326$ ). Each cited reference's year of publication was recorded in a database. Two sample T tests compared the means of the years passed since publication when cited for each journal. Regression analysis was used to compare an article's availability online as a statistically significant variable influencing its use in present literature.

**Results:** The references from the original research papers of every journal were significantly different according to the studies analyzed: NEJM 2006 vs 1996,  $p < 0.01$  (95% CI: 1.58, 3.78), Lancet 2006 vs. 1995,  $p = 0.018$  (95% CI: 0.33, 3.52), JAMA 2006 vs. 2001,  $p = 0.037$  (95% CI: 0.06, 2.03), JNCI 2006 vs 1999,  $p = 0.022$  (95% CI: 0.12, 1.55), J Urol 2006 vs. 1999,  $p < 0.01$  (95% CI: 1.15, 4.94), Eur Urol 2006 vs 2001,  $p = 0.042$  (95% CI: 0.08, 4.29), BJU 2006 vs. 1996,  $p < 0.01$  (95% CI: 3.11, 6.30). Power calculation for each comparison was  $> 0.80$  in every instance. Availability online was significantly associated with being chosen as a reference in the 2006 cohort of articles on regression analysis ( $p < 0.01$ ).

**Conclusion:** A selection bias was shown to be statistically significant in every journal analyzed by this adequately powered study. Perhaps all years of literature should be electronically available to authors as opposed to an arbitrary year set by the online publisher.

**Key Words:** education, meta-analysis, statistics

### DIS01.16

#### A prospective randomized study of pfannenstiel versus expanded port site incision for intact specimen extraction in laparoscopic radical nephrectomy: preliminary results

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**Introduction:** To evaluate and compare the surgical outcome of intact specimen extraction through a muscle-cutting (expanded port site-EPS) incision or a muscle-splitting (Pfannenstiel -PFN) incision in patients undergoing transperitoneal laparoscopic radical nephrectomy.

**Methods:** Patients with clinically localized renal cancer undergoing transperitoneal laparoscopic radical nephrectomy with intact specimen extraction were recruited from December 2005 onwards. Patients were randomized into Group 1 (Expanded port site: 20) or Group 2 (Pfannenstiel: 20) and followed prospectively. A detailed analysis of the critical intra-, peri-operative, 6-weeks and 6 months follow-up clinical variables was performed. This report is a preliminary assessment of the first 20 patients in each group.

**Results:** Apart from more males in the EPS group and younger patients in the PFN group there was no preoperative demographic difference between the 2 groups. Intraoperatively, PFN associated with a shorter operative time and reduced blood loss. EPS associated with a smaller

extraction incision, and larger specimen size and weight. Both incisions had an equal extraction time. One intraoperative complication encountered in the EPS group not incision related. In the recovery room, both groups had equal pain score and narcotic consumption. Following the first postoperative date, both groups had equal pain score, although EPS group consumed more narcotics. Both had equal timing related to unassisted ambulation, fluid and full diet. PFN patients had less hospital stay (1 vs. 2 day). Postoperative complications related to incision type occurred more frequently in EPS group (5 Vs 3). After 6 weeks postoperatively, both groups showed no difference in pain score or narcotic use. 2 short-term incision related complications encountered in the EPS group. At 2 weeks and 6 months followup, there was no difference between the two groups in overall operative satisfaction or incision related satisfaction.

**Conclusion:** These preliminary results suggest that a Pfannenstiel extraction incision is associated with less operative complications and a shorter hospital stay. No difference was noticed related to postoperative pain or analgesic use. To achieve statistical significance, these findings await the completion of the ongoing study (92 patients).

**Key Word:** renal cell carcinoma

### DIS01.17

#### Infrared ureteric illumination during laparoscopic ureterolysis: a novel approach

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**Introduction:** Retroperitoneal fibrosis is an uncommon cause of ureteric obstruction. Treatment with laparoscopic ureterolysis has been described in the past. We describe a novel technique utilizing infrared emitting ureteral catheters to aid in identification of the ureter during laparoscopic ureterolysis.

**Methods:** We describe a case of a male patient with bilateral ureteric obstruction secondary to idiopathic retroperitoneal fibrosis. A novel technique utilizing the Infravision Ureteral Kit (Stryker Endoscopy) to assist in illumination and identification of the ureter during laparoscopic ureterolysis was conducted.

**Results:** The system consists of a 6 Fr ureteral catheter with an infrared light emitting fibre and a laparoscopic camera, which detects infrared light. The infrared signal can penetrate up to 12mm of tissue. Prior to surgery, ureteral catheters are placed cystoscopically in the usual manner, followed by placement and advancement of the light emitting fibre. A four port transperitoneal approach was used for laparoscopic ureterolysis. During laparoscopy, the light emitting fibre allows for faster and easier identification of the ureter and gonadal vessels, minimizing the risk of ureteral injury.

**Conclusion:** Use of the Infravision Ureteral Kit (Stryker Endoscopy) allows for faster and easier identification of the ureter during laparoscopic ureterolysis. Such technique may reduce the risk of ureteral damage allowing for decreased operative time with improved surgical outcomes.

**Key Words:** catheter, laparoscopy, ureter

### DIS01.28

#### Optimal port placement during laparoscopic radical prostatectomy: avoiding inferior epigastric artery injury

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**Introduction:** The placement of anterior abdominal wall trochars during laparoscopic radical prostatectomy (LRP) can be complicated by inadvertent injury to the inferior epigastric artery (IEA), as well as crossover confliction between midline and lateral ports. We describe technical approach to minimize IEA injury, while allowing for adequate distance between medial and lateral instruments.

**Methods:** 112 consecutive patients underwent a LRP from December 2005, to December 2006. All patients underwent LRP with a standard 5-port approach. 10mm – infraumbilical for camera access, 2 x 10mm for medial ports, and 2x 5mm for lateral ports. Upon insufflation of pneumoperitoneum, the medial ports were placed 5cm from the patients

midline, at half the distance from the pubic symphysis to the umbilicus. Patients were evaluated prospectively based on position of IEA to trochar placement, intra-operative blood loss, and need for conversion to open procedure.

**Results:** 112 consecutive patients underwent a LRP during this time. Mean BMI for these patients was 26.3 kg/m<sup>2</sup> (range: 19 to 35 kg/m<sup>2</sup>). The average operative time was 187 minutes (range: 90–360 minutes). The course of the IEA was found to be lateral to the 5cm mark in all patients. No injury to IEA was sustained in any of these patients. Mean blood loss was 277mL (100 to 1000mL). In addition, no ports required repositioning and no patients required conversion to open prostatectomy due to sub-optimal port placement.

**Conclusion:** The surface anatomy of the IEA is difficult to predict. Medial 10mm port placement 5cm from midline of the patient upon insufflation, will predictably allow for placement of the trochar medial to the IEA. This will minimize IEA injury, allow for adequate instrument manipulation, and minimize the need to reposition ports and risk of conversion to open prostatectomy due to inadequate access.

**Key Words:** laparoscopy, radical prostatectomy, vascular

### DIS01.19

#### Treatment of intermediate sized upper tract calculi at a single Canadian center

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**Introduction and Objectives:** Shock wave lithotripsy (SWL) is routinely used for upper tract stones less than 10mm while it is widely agreed that stones larger than 2cm are best treated by percutaneous nephrolithotomy (PNL). Treatment of stones between these domains is controversial. Advances in technology make retrograde intrarenal surgery (RIRS) as an alternative for non-staghorn intrarenal calculi. Randomized studies examining the treatment of non-staghorn calculi are difficult to conduct owing largely to patient preferences. We reviewed our modern series of RIRS, PNL and SWL outcomes for intermediate sized upper tract calculi.

**Methods:** Patients presenting for RIRS, PNL or ESWL over an 18 months were identified. Upper ureteric and intrarenal non-staghorn stones were included. RIRS and PNL were performed by 2 endourologists. SWL was conducted by several treating urologists on patients referred from the greater Toronto area. Distribution of patients amongst modalities, demographics and outcomes were analyzed using SPSS.

**Results:** 104 patients were referred with non-staghorn upper tract calculi. 70 (62.5%) were referred for SWL, 13 (11.6%) and 29 (25.9%) underwent RIRS and PNL respectively. Mean age of RIRS, PNL and SWL patients was 57, 49 and 56 years of age respectively. Mean body mass index was 27 in all 3 groups. Mean stone size was higher in the PNL group at 29.2mm compared with 27.7mm for RIRS and 27.8mm for SWL ( $p < 0.01$ ). Stone free (SF) status post RIRS and PNL was 54% (7/13) and 79.3% (23/29) while a further 31% (4/13) RIRS and 13.8% (4/29) PNL patients had asymptomatic fragments (AF) less than 5mm. Single treatment success rates (SF+AF) were 85% for RIRS versus 93% for PNL ( $p = 0.58$ ). SF rate after a median of 2 SWL sessions was 22.8% (16/70) with a further 27.1% (19/70) having AF. SWL success (SF+AF) after a median of 2 sessions was 50% (35/70), lower than with RIRS or PNL ( $p < 0.01$ ).

**Conclusions:** SF and overall success rates are higher with single treatment RIRS or PNL compared with SWL for intermediate sized upper tract stones. SWL is a reasonable alternative for patients not fit for or not wishing a general anesthetic provided they will accept a higher number of treatments.

**Key Words:** lithotripsy, percutaneous, ureteroscopy

### DIS01.20

#### Interim analysis of a randomized, double-blinded trial of ketorolac in addition to narcotic patient-controlled analgesia (PCA) following laparoscopic donor nephrectomy (LapDN)

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**Introduction and Objectives:** While LapDN offers a number of advan-

tages over open donor nephrectomy, it remains a completely elective operation with significant post-operative pain and morbidity. We sought to examine the impact of adding intravenous (IV) ketorolac to PCA following LapDN on post-operative recovery and quality of life (QOL).

**Methods:** 37 (of a pre-planned sample size of 74) patients scheduled to undergo LapDN were enrolled and randomized. All patients underwent a transperitoneal, 3 trocar, LapDN performed by two surgeons. All patients received intravenous narcotic PCA post-operatively, in addition to either 10mg IV ketorolac or saline q6h for 48h. Data was collected on analgesic usage, complications, bowel function, serum creatinine, length of stay, time to return to work, and QOL as assessed by the Post-operative Recovery Scale (PRS), a modification of the SF-36 that includes visual analog assessments of pain). Data were analyzed with Chi-square, ANOVA, and repeated measures ANCOVA where appropriate according to our pre-planned blinded interim analysis.

**Results:** 37 patients, 23 were women (59%), with a mean age of 39.9 (SD=12.4), and mean BMI of 25.4 (SD=3.3) were enrolled between September, 2003 and August, 2006. There were no differences between the groups at baseline. Length of stay was similar (96.3 vs. 103.2h,  $p=0.4$ ), but there was a trend to less narcotic usage in group 1 (117.0 vs. 74.6mg morphine equivalent,  $p=0.09$ ). QOL scores were significantly higher in group 1 throughout the immediate post-operative period ( $p=0.043$ ). By 2 weeks post-operatively QOL scores became identical between the 2 groups ( $p=0.6$ ). There were no differences in serum creatinine between the 2 groups ( $p=0.49$ ). Recipient outcomes were identical. Complications were rare: one patient in group 2 experienced an ileus; there were no conversions and no bleeding complications.

**Conclusions:** Ketorolac appears to improve QOL in the immediate post-operative period, with a trend to reducing morphine usage, improved pain control, and no adverse impact on renal function in patients undergoing LapDN.

**Key Words:** analgesia, donor, kidney

### DIS01.21

#### Percutaneous surgery for treatment-resistant biliary calculi

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**Introduction:** Due to extensive experience with percutaneous treatment of renal calculi, patients that have failed open or endoscopic (ERCP) treatment of biliary stones may also be referred to Urologists. Here we report the results of all biliary calculi treated by endourologic methods at a single institution over the past 10 years.

**Methods:** We conducted a retrospective study of all patients that underwent percutaneous, endoscopic treatment of biliary calculi since January 1st, 1996. Both hospital and clinic charts were systematically reviewed. We investigated both the endoscopic technique used as well as type and location of tract as predictors of success. Primary outcomes of interest were symptom and stone free rates, length of hospital stay and complications.

**Results:** Over the past ten years, 15 patients underwent 16 percutaneous treatments of their biliary calculi. Of these, 13 patients had failed prior endoscopic or open attempts at treatment of their stones, while the remaining 2 patients were unable to tolerate a general anaesthetic. The primary location of the stones was: gallbladder (6), cystic duct (2), and common bile duct (8). Overall treatment was judged to be successful in 87.5% of patients. All patients were subsequently followed by the referring general surgeon. Cholecystograms were conducted an average of 20.9 days after treatment and 75% of patients were stone-free. Average length of hospital stay was 1.94 days. One patient experienced prolonged biliary drainage after successful endoscopic treatment of a gallbladder stone. There were no cases of treatment-related sepsis and no other complications were observed.

**Conclusion:** Biliary calculi may be successfully treated using standard endourologic methods with high stone-free rates. Percutaneous treatment is generally well-tolerated and complications are rare.

**Key Words:** calculi, lithotripsy, percutaneous

### DIS01.22

#### Occupational noise exposure in endourology

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**Introduction:** Long-term exposure to loud noise in the workplace is a known cause of hearing loss. There has been limited study on the potential harm related to shock wave lithotripsy (SWL) or intracorporeal devices on patients and operating room personnel.

**Methods:** We used a digital sound meter to measure decibel levels in the operating room during several endourological procedures. The decibel levels were recorded during SWL, percutaneous nephrolithotomy using an ultrasonic lithotripter (Olympus LSU-2, GyruS-ACMI Cyberwand) and during ureteroscopy using Holmium-YAG laser. Three measurements were taken for each device at the patient's head, the urologist's head level and in the SWL control room. Findings were compared with the Occupational Health and Safety Act (OHSA) recommendations on permissible noise levels in the work place.

**Results:** The background sound level in the operating room before the endourological procedure ranged between 58 and 60 dB. In the SWL control room, sound levels ranged from 67 to 75 dB during treatment. The corresponding decibel levels recorded at the patient's head during SWL were between 75 and 83 dB. Measurements of the CyberWand device revealed higher decibel readings of between 89 and 102 dB. The Olympus ultrasound and the holmium laser were quieter. Noise ranges were between 63 and 67 dB with the Olympus and between 60 and 62 dB with the laser.

**Conclusion:** OSHA guidelines recommend an annual audiogram and hearing protection when occupational exposure exceeds 85dB for 8 hours a day or more. In our study, although we found that patients and operating room staff maybe exposed to significant noise levels during endourologic procedures, the duration of exposure is short. The risk to patients and staff appears to be minimal, based on current occupational guidelines.

**Key Words:** calculi, lithotripsy, ultrasound

### DIS01.23

#### Randomized controlled trial comparing a dual probe ultrasonic lithotrite to a single probe lithotrite for percutaneous nephrolithotomy (PCNL)

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**Introduction:** PCNL is the treatment of choice for large and/or complex renal stones. Currently, the choice of commercially available intracorporeal lithotriptors include ultrasonic (US), pneumatic (PN), and combined ultrasonic/pneumatic (combo) energy sources. However, the utility of these devices may be limited by stone size and hardness (US), or device ergonomics and suction port design (combo). To address these limitations, a new dual probe ultrasonic lithotrite, Cyberwand (GyrusACMI, Southborough, MA), has recently been introduced. This dual probe ultrasonic lithotrite design incorporates coaxial high and low frequency ultrasonic probes which provide a synergistic mechanism to improve stone comminution. The purpose of this study is to compare this new device to a standard single probe ultrasonic lithotrite.

**Methods:** A research ethics boards approved multicentre, randomised controlled trial (RCT) to compare the Cyberwand to the Olympus LUS-II (Melville, NY) single probe lithotrite has been initiated. Eligible patients included those undergoing PCNL with a target stone greater than 2 cm. The primary outcome of interest was time to removal of the targeted stone burden. Additional data collected included stone composition, stone free rate and complications.

**Results:** A total of 12 PCNLs (6 Cyberwand and 6 Olympus LUS-II) of the 46 to be enrolled have been performed in 11 patients. There was no statistically significant difference observed between the devices for the

**Table 1. Abstract DIS01.23**

Mean	Cyberwand (n=6)	Olympus LUS-II (n=6)	p value
Target stone surface area (mm <sup>2</sup> )	550	428.8	0.62
Time to clear targeted stone in minutes (seconds)	9.23 (554)	8.28 (497)	0.86
Target stone clearance rate (mm <sup>2</sup> /sec)	1.47	1.74	0.79

parameters listed in the table below. Four of 6 (66%) patients in each group were stone-free following the initial PCNL.

**Conclusions:** The preliminary data in the early stages of this multicentre RCT do not show any statistically significant differences between the dual probe and the single probe ultrasonic lithotrites. Further data analysis as patient enrollment continues will be necessary to confirm or refute these findings.

**Key Words:** calculi, percutaneous, ultrasound

#### DIS01.24

##### Endoscopic assessment of bladder tumours: accuracy of endoscopic staging and grading with fiberoptic and digital cystoscopes

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**Introduction and Objective:** The management of bladder cancer requires accurate tumour staging and grading. Assessment begins and relies heavily on cystoscopy. Recent advances in flexible scopes with digital tech-

nology, image capture, and processing have provided enhanced image quality compared to early generations with fiberoptic technology. Such advances provide a unique opportunity to formally evaluate the inter- and intra-observer reliability of cystoscopy in the assessment of TCC tumor stage and grade, and to compare the accuracy of the cystoscopic technologies (digital versus fiberoptic).

**Methods:** Fifty-nine tumours in 34 patients with urothelial carcinoma of the bladder were evaluated with informed consent immediately prior to TURBT to determine whether tumours can be, 1) staged and graded by experienced urologists at cystoscopy with the same reliability as that provided by histopathology, and 2) more accurately assessed using digital cystoscopes compared with fiberoptic cystoscopes. Studies were done under general anesthesia prior to tumour resection using ACMI instruments sequentially and with video recording for later review by three observers blinded to the tumour information and instrument type. Tumour stage and grade were estimated at the time of surgery and again on later blinded review of recorded images and compared with pathology. Image quality was scored globally for overall quality, clarity, brightness and estimated real life fidelity.

**Results:** Definitive pathologic tumor grade and predicted tumor grade using digital ( $\rho = 0.5$ ,  $p < 0.001$ ) and fiberoptic ( $\rho = 0.4$ ,  $p = 0.002$ ) cystoscopy were significantly correlated. Exact concordance between pathologic grade and predicted tumor grade using digital and fiberoptic cystoscopy was 43% and 44%, respectively. Histologic tumor stage correlated poorly with predicted tumor stage using digital ( $\rho = -0.1$ ,  $p = 0.5$ ) and fiberoptic ( $\rho = 0.06$ ,  $p = 0.7$ ) cystoscopy. Exact concordance between histologic tumor stage and predicted tumor stage using digital and fiberoptic cystoscopy was 57% and 58%, respectively.

**Conclusion:** Inter- and intra-observer comparisons have not been completed but cystoscopic estimation of pathological grade by experience urologists appears to be more accurate than estimation of stage. The comparison of image quality will be reported. This type of methodology can be applied to the assessment of endoscopic and imaging technologies.

**Key Words:** bladder cancer, cystoscope, stage

# POSTER DISPLAY 2: BASIC SCIENCE, INFECTIONS & INFLAMMATORY DISEASES, ANDROLOGY, LUTS/BPH

## MONDAY, JUNE 25

### DIS02.01

#### Adult adipose tissue derived stem cells enhance neurite outgrowth from the major pelvic ganglion of the rat

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**Introduction:** Interest in the development and application of neuroprotective and regenerative strategies using adult-tissue derived progenitor cells has heightened as stem cell biology progresses. We investigate the effects of adult adipose-tissue derived stem cells (ADSCs) upon neurite outgrowth from the dorsal caudal region of the major pelvic ganglion (MPG) of the rat.

**Methods:** 6 and 24 month-old Sprague-Dawley rats,  $n=10$  respectively, were used yielding 40 MPG tissue cultures for each group. For both young and aged rats, groups consisted of MPG and ADSC cultures only and DCR-MPGs to which vehicle solution or ADSCs were added. The maximal neurite length for each tissue culture was measured and the mean maximal length  $\pm$  standard deviation was determined for all groups at 48 and 72 h.

**Results:** ADSCs promoted significant outgrowth of neurites compared to non-treated and vehicle groups. In young rats, mean maximal neurite length (standard deviation) at 48 and 72 h was 588.1 (69.3) and 720.9 (58.2)  $\mu\text{m}$  for ADSC treated cultures, compared to 190.5 (38.4) and 305.46 (44.0)  $\mu\text{m}$  for MPG only, and 186.1 (43.6) and 322.7 (37.7) for vehicle treated MPG ( $p<0.05$ ). Aged ADSC-treated MPG neurite growth was 307.4 (59.2) and 512.1 (60.0)  $\mu\text{m}$ , compared to MPG (120.3 and 185.5  $\mu\text{m}$ ) and vehicle only (131.7 and 197.4  $\mu\text{m}$ ) groups ( $p<0.05$ ). Adipose-tissue derived cells with neuron-like appearance unique to DCR-MPG cultures treated with ADSCs were identified.

**Conclusion:** The addition of adipose-derived stem cells significantly enhanced neurite outgrowth from both young and aged DCR-MPGs. This study provides proof-of-concept for the neuromodulatory potential of ADSCs and identifies a promising novel strategy for cavernous nerve neuroregeneration and/or neuroprotection, warranting further in vivo investigation.

**Key Word:** erectile dysfunction

### DIS02.03

#### Erythrocyte sedimentation rate does not improve the ability to predict renal cell carcinoma-specific survival beyond that of standard variables

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**Introduction:** Erythrocyte sedimentation rate (ESR) was found to be an independent predictor of renal cell carcinoma-specific mortality (RCC-SM). We assessed its role in the prediction of RCC-SM in a cohort of 132 European patients.

**Methods:** Radical nephrectomy was performed in 132 patients. Life table, Kaplan-Meier and Cox regression analyses addressed RCC-SM. ESR was analyzed as a continuously-coded as well as a categorized variable: continuously-coded ESR was converted to 4 categories based on the most informative breakpoints in univariate Cox regression models. Covariates included age, gender, TNM stage, tumor size, Fuhrman grade and histological subtype.

**Results:** The median RCC-specific survival was 14 years. Age ranged from 10 to 75 and most were male (65.2%). Their T stage was distributed as follows: T1-54; T2-21; T3-53; T4-4. Nodal metastases at nephrectomy were identified in 22 patients (16.6%) and established distant metas-

tases were known prior to nephrectomy in 33 patients (25%). The majority had Fuhrman III and IV disease (63%) and 118 (89.4%) had clear cell histology. ESR ranged from 1 to 176. In univariate Cox regression models, ESR was a statistically significant predictor of RCC-SM both as a continuously-coded and categorically-coded variable ( $p<0.001$ ). However, ESR failed to reach independent predictor status in either continuously-coded or categorically-coded format in multivariable analyses ( $p$  values respectively 0.5 and 0.2).

**Conclusions:** ESR does not improve the ability to predict RCC-SM beyond that of standard variables.

**Key Word:** renal cell carcinoma

### DIS02.04

#### Development of a 3-Dimensional (3D) Transrectal Ultrasound System (TRUS) for Prostate Biopsies (Bx): Implications for Clinical Management of Atypical Small Acinar Proliferations (ASAP)

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**Introduction:** TRUS prostate Bx is currently confined to 2D information to both target and record 3D Bx locations. Accurate placement of Bx needles cannot be verified without 3D information, and recording Bx sites in 2D does not provide sufficient information to accurately guide repeat Bx. In cases of ASAP, precise documentation of the initial Bx location, thus facilitating repeat targeting of the same location, will be especially useful. We have developed a 3D TRUS prostate Bx system that augments the current 2D TRUS system, without changing the workflow of the current procedure or significantly adding to the examination time.

**Methods:** The Bx system designed by our group displays a 3D model of the patient's prostate, which is generated intra-procedure from a collection of 2D TRUS images, representative of the particular prostate shape. Prostate boundaries are extracted from each image using a semi-automated segmentation technique and the 3D model surface is constructed by interpolating between the 2D boundaries. Bx targets are selected, needle guidance is facilitated, and 3D Bx sites are recorded within the 3D context of the prostate model. The complete 3D Bx system was validated, in vitro, using agar-gelatin models of patient's prostates, confined within phantom boxes designed to mimic the pelvic anatomy. The surface topology and volume accuracy of our 3D modeling was calculated using prostate models reconstructed from 5 sagittal and 5 transverse images. Sextant biopsies of the prostates were performed, using target points selected pre-biopsy. The accuracy of the needle-guidance, Bx location recording, and 3D model volume and surface topology were validated against a CT gold standard.

**Results:** Each 3D reconstruction added 1 min to the standard TRUS examination. The Bx system successfully reconstructed the 3D prostate models with a mean volume error of 3.8%. Compared to the CT gold standard, the mean error for the surface of the prostate model was  $0.70 \pm 0.90$  mm. Using the 3D system, needles were accurately guided to the pre-determined targets with a mean error of  $3.0 \pm 2.4$  mm and the 3D locations of the Bx cores were accurately recorded with a mean distance error of  $1.07 \pm 1.66$  mm.

**Conclusions:** We have successfully developed a 3D TRUS prostate biopsy system and validated the system in vitro. A pilot study has been initiated to apply the system clinically, especially in cases of ASAP for con-

firmation of diagnosis and serial histologic monitoring.

**Key Words:** biopsy, prostate cancer, ultrasound

### DIS02.05

#### A mouse model for orthotopic bladder cancer using transurethral tumor inoculation and bioluminescence imaging

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**Introduction:** A reliable, reproducible and quantifiable model of superficial bladder cancer is required to test the intravesical instillation of novel therapeutic agents. We describe our technique for transurethral tumour inoculation and bioluminescence imaging.

**Methods:** Female nude mice (6–9 weeks old) were anaesthetized for 3 h with isoflurane. A superficial purse-string suture was placed around the urethral meatus before a lubricated 24 gauge angiocatheter was passed through the urethra into the bladder. After irrigation of the bladder, two million KU7 cells were instilled in 50 µL PBS suspension. The cells were previously transduced with a lentiviral construct containing the firefly luciferase gene. Overdistension of the bladder was avoided to limit vesicoureteral reflux and intrarenal tumour implantation as well as urethral tumours. The purse-string suture was tied with a loop and then removed three hours later. Bioluminescence imaging was performed weekly with the IVIS 200 Imaging System (Xenogen Corp., Alameda, CA). Necropsy was performed at 4 weeks. The whole bladders were fixed in formalin. Ex vivo MRI and step sections with H&E staining were obtained.

**Results:** Tumours were successfully inoculated in 97% of mice with KU7 tumour cells. Luminescence at day 4 can be used to exclude mice with perforations and to distribute mice into treatment groups with equal tumour burden. At 4 weeks the tumours were mostly confined to the mucosa and submucosa (pT1). Ex vivo bladder MRI demonstrated a very good correlation between tumour volume and bioluminescence ( $r=0.96$ ).

**Conclusion:** We have established a reliable and reproducible model of orthotopic bladder cancer that we are currently employing to evaluate various models of intravesical drug delivery, including antisense oligonucleotides, and novel chemotherapeutics. Luminescence imaging allows longitudinal surveillance and quantification of tumour burden.

**Key Words:** bladder cancer, imaging, orthotopic

### DIS02.06

#### Does rapamycin inhibit TGFβ1 induced peritoneal fibrosis and angiogenesis?

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Rapamycin is a novel antirejection agent that has demonstrated anti-angiogenic activity in the setting of tumorigenesis. In order to evaluate the effect of rapamycin on angiogenesis associated with fibrosis, we administered rapamycin in drinking water to mice with peritoneal fibrosis induced by adenovirus mediated gene transfer of transforming growth factor β1 (AdTGFβ1). Forty female C57Bl/6 mice had an intraperitoneal injection with either AdTGFβ1 or a control adenovirus (AdDL). Starting on day 4, animals received either rapamycin (Wyeth, Canada) 2 mg/kg/day or vehicle via drinking water. Animals (5/group) were sacrificed on days 10 or 21 after adenovirus administration. Peritoneal tissue was taken for quantitative histology to assess fibrosis (submesothelial thickening) and angiogenesis. AdTGFβ1 induced a significant fibrogenic and angiogenic response compared to AdDL. Rapamycin had no significant effect on these parameters at day 10. At day 21, AdTGFβ1 / rapamycin treated animals had decreased submesothelial thickness and decreased angiogenic response compared with AdTGFβ1 / vehicle treated animals. A prolonged course of rapamycin appears to inhibit TGFβ1 induced angiogenesis and fibrosis. Further work will elucidate the mechanism of this inhibition.

**Key Words:** immunotherapy, transplant

### DIS02.07

#### The effects of a novel coating (mPEG-DOPA3) on uropathogen adherence

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**Introduction:** Success in the prevention of urinary device biofilms has been elusive, largely due to bacterial attachment strategies and the development of urinary films on the device. We investigate a novel anti-fouling coating based on polyethylene-glycol conjugated to mussel adhesive proteins (mPEG-DOPA3) to resist uropathogens on foreign surfaces bathed in human urine.

**Methods:** TiO<sub>2</sub>-coated silicon wafers (1cm<sup>2</sup>) were sonicated consecutively for 10 min in 5% Contrad, ultrapure H<sub>2</sub>O, and 2-propanol. They were dried in a stream of N<sub>2</sub>, exposed to oxygen plasma for 2 min and immersed in 1.0mg/ml solutions of mPEG-DOPA3 in 0.6M K<sub>2</sub>SO<sub>4</sub>, 0.1M N-morpholinopropanesulfonic acid (pH=6.0) at 50°C for 24h. Finally, the coated surfaces were rinsed with ultrapure H<sub>2</sub>O, dried with N<sub>2</sub> and sterilized via ethylene oxide gas. For bacterial challenge experiments, coated and uncoated surfaces were secured in a dot-blot apparatus and separately challenged with bacterial strains comprising six major uropathogenic species for 24 h at 37°C in human pooled urine. Starting inoculum for each strain was 10<sup>5</sup>/mL and 0.5mL was used perDISk. Following incubation, DISks were rinsed 4 times in PBS to remove non-adherent organisms and scraped using cell scrapers in PBS to DISlodge adherent bacteria. Solutions were sonicated for 5 minutes, vortexed at high speed for 1 minute and dilution plated.

**Results:** Thus far, three experiments have been completed in triplicate for both *Escherichia coli* GR-12 and *Enterococcus faecalis* 23241. Importantly, binding of both strains to mPEG-DOPA3-coated surfaces was reduced by >96% compared to uncoated surfaces. In addition, while uncoated disks demonstrated the appearance of a visible biofilm, mPEG-DOPA3-coated surfaces appeared clean. Although additional experiments are required for the remaining uropathogens, similar trends have been observed.

**Conclusion:** Surfaces coated with mPEG-DOPA3 strongly resisted both bacterial attachment and biofilm formation. Future experiments will involve longer incubation times and the coating of urinary device polymers.

**Key Word:** infection

### DIS02.08

#### Prediction of the response of prostate cancer patients to radiation using surrogate tissues

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**Introduction:** Radiation therapy is standard treatment for prostate cancer (PC). Postulated mechanism of action for radiation therapy is via the generation of reactive oxygen species (ROS). Using the current regimen of high dose conformal radiation, treatment failure occurs in 45% of patients with locally confined disease. It is likely that, in addition to individual patient risk factors, intrinsic differences in cellular radio-sensitivity exist which explains the diversity in response between different patients. In previous work we demonstrated the effects of the individuals' androgenic milieu on the basal levels of ROS (bROS) in the PC that leads to relative resistance to irradiation through the over-expression and increased activity of several stress kinases and that of anti-oxidative enzymes (adaptation molecules). Here we demonstrate for the first time that the same effects can be observed in salivary glands and hair follicles of the same individual with PC.

**Methods:** The salivary glands and hair follicles were selected since both tissues are androgen regulated and since their histological structure and hemostasis are analogous to the prostate. Eighteen adult Sprague Dawley male rats weighing 200-250g were randomized into 3 groups of 6 rats each: Group A (assigned A- to indicate lack of endogenous and exogenous androgens): underwent bilateral trans scrotal orchiectomy. Group B

(assigned A+ to indicate presence of both endogenous and exogenous androgens): underwent sub-cutan implantation of slow release testosterone pellet. Group C (assigned as C had their endogenous production of testosterone i.e. testes left intact) underwent sham procedure. These 3 groups thus represent 3 different levels of host androgens-complete absence (A-), normal range (C) to increase levels (A+). The rats were sacrificed after 48 hours. The tissues (skin, prostate, salivary gland) were removed immediately and cut into two halves for histological examination and for tissue lysate preparation. The fixed tissues were embedded in paraffin and were then reconstructed into a pre-planned tissue microarray (TMA) platform. Tissues were examined for the expression of bROS and oxidative stress adaptation markers using specific immunohistochemistry, immunoblotting and enzymatic assays.

**Results:** The basal redox status in the prostate, salivary glands and hair follicles in the same hosts were affected in a similar manner by the androgenic milieu. Consequently, In each individual host all 3 tissues had the same expression pattern of adaptation markers to radiation such as clusterin, p-p38, catalase and others which was significantly higher in groups B&C as compared to group A. The expression of these markers was shown to influence the response to radiation.

**Conclusions:** The individuals' sensitivity to oxidative stress based therapies is dictated by the individuals' redox status and expression of adaptation molecules. This is an androgen-regulated phenomenon. In each individual with hormone sensitive tumor, the salivary glands and the hair follicles serve as a surrogate tissues to pre-determined ones own potential sensitivity to radiation in a minimally or non-invasive method.

**Key Word:** molecular marker

## DIS02.09

### Inhibition of tumor progression using antisense oligonucleotide targeting Gli2 in androgen independent prostate cancer

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**Introduction:** The two Gli transcription factors, Gli1 and Gli2, mediate Sonic hedgehog signaling, play a crucial role in embryogenesis, and have been implicated in several human malignancies, including prostate cancer. The objectives of this study were to assess Gli2 expression levels in human prostate cancer specimens treated with neoadjuvant hormone therapy (NHT), to test the effect of antisense oligonucleotide (ASO) targeting Gli2 on Gli2 expression in PC-3 cell-line, and to determine whether Gli2 ASO enhances paclitaxel chemosensitivity in-vitro.

**Methods:** Gli2 immunostaining was evaluated in a prostate cancer tissue microarray obtained from patients who had NHT prior to prostatectomy. The effects of Gli2 ASO on Gli2 knockdown, PC-3 cell growth, and paclitaxel chemosensitivity was assessed using real-time PCR, Northern and Western analysis, as well as crystal violet assays and flow cytometry. Oligonucleotide spotted microarray analysis was used to determine alteration in Gli2 co-regulated genes after ASO treatment.

**Results:** Tissue microarray analysis showed Gli2 decreases after androgen ablation in a time-dependent fashion, and becomes highly expressed in androgen-independent tumors. Gli2 is highly expressed in PC-3 cells. Gli2 ASO treatment reduced Gli2 mRNA and protein levels in a dose dependent manner (to 11% and 12% of baseline, respectively). Gli2 ASO monotherapy significantly inhibited PC-3 cell growth in vitro (62% suppression compared to controls,  $p < 0.05$ ). Gli2 ASO also chemosensitized cells to paclitaxel. Flow cytometry showed that the apoptotic sub G0-G1 fraction was significantly increased in PC-3 cells after Gli2 ASO monotherapy and highest after combination therapy of Gli2 ASO with paclitaxel. Gene expression profiles after Gli2 knockdown using oligonucleotide microarray and western blot analysis revealed down-regulation of Bcl2, Bcl-xl and Gli1 and up-regulation of the cytoprotective chaperone, clusterin.

**Conclusion:** Gli2 ASO inhibits prostate tumor growth by inducing apoptosis through the modulation of apoptosis related genes and enhances chemosensitivity to paclitaxel. Further evaluation of Gli2 as a therapeutic target in prostate cancer is warranted.

**Key Word:** antisense

## DIS02.09

### Description of interstitial cells of cajal (ICC) and caveolin-1,2,3 in the renal pelvis and ureteropelvic junction

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**Introduction:** Pyeloureteric peristalsis is likely triggered by pacemaker cells in the renal pelvis. ICC cells have recently been implicated to play a pacemaker role in the initiation and propagation of this peristalsis. Our objective is to determine if interstitial cells of Cajal (ICC) pacing networks are present or absent in renal pelvis in the normal setting and in ureteropelvic junction obstruction (UPJO). Also, to determine if the caveolin-1 (Cav1), caveolin-2 (Cav2), and caveolin-3 (Cav3) proteins are present in ICC as they are in other organ systems.

**Methods:** Subjects undergoing pyeloplasty due to UPJO ( $n=3$ ) were included. Controls ( $n=3$ ) were obtained from nephrectomy subjects with normal UPJ. After tissue was extracted at pyeloplasty, it was fixed with 4% paraformaldehyde, rinsed, and cryoprotected. Tissues were then cut into 6  $\mu$ m sections, attached on slides, and stored at -80°C until immunohistochemical processing. Cryosections were then rehydrated, incubated with monoclonal antibodies against ICC (c-kit), and against Cav1, Cav2 and a polyclonal antibody against Cav3. They were immunolabelled with Cy3 conjugated donkey anti-mouse IgG and FITC conjugated donkey anti-rat IgG. The immunolabelled cryosections were examined by confocal laser scanning microscopy. Electron microscopy was also used to determine the presence of caveolae.

**Results:** c-kit immunoreactive cells indicative of ICC were present in high numbers in the UPJ segments of all controls and cases of UPJ obstruction. Cav1, 2, and 3 were found at the smooth muscle cell in both controls and cases. Cav2 was present in the ICC of both the controls and the cases of UPJO. Surprisingly, Cav1 and Cav3 proteins were found to be absent in ICC in all controls and cases. Through electron microscopy, caveolae were found in the cell membrane of smooth muscle cells, but not in ICC.

**Conclusion:** ICC networks are present in normal controls and in cases of adult UPJO. No differences were detected concerning the presence of ICC between controls and UPJO cases. A unique finding compared to similar studies of gastrointestinal smooth muscle was the fact that Cav1 and Cav3 were absent in ICC. Only Cav2 protein was present. Electron microscopy confirmed the presence of caveolae in the cell membrane of smooth muscle cells, but not in ICC.

**Key Words:** diabetes, kidney, obstruction, pediatric

## DIS02.11

### Urine metabolic changes in rats with partial ureteric obstruction

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**Background:** Urine from partially obstructed kidneys may contain important metabolic information to help with the diagnostic and prognostic issues faced in children with partial urinary tract obstruction. We set out to use well-established metabolomics methodology to compare the urinary metabolic profiles of non-obstructed and partially obstructed rat kidneys. We hypothesized that alterations in the metabolism of renal cells would be demonstrated by distinct urine metabolic profiles between partially obstructed and non-obstructed rats.

**Methods:** Partial ureteral obstruction was produced in six 120 gram Sprague Dawley rats by imbedding the left ureter in the psoas muscle. A control group of six rats from the same cohort underwent a laparotomy and exposure of the left ureter without mobilization. Urine samples from each group were collected every other day for 24 hours over a 3 week period. Urine samples were subjected to 1H NMR spectroscopy using a Bruker Avance DRX 500 spectrometer. Principal component analysis (PCA), a standard method of interpreting metabolomic data, in addition to AMIX and SIMCA-P software were used to compare data in terms of clustering behavior and differences between individual metabolites.

**Results:** No gross or histologic differences were observed between par-

tially obstructed and non-obstructed kidneys, aside from the partially obstructed kidneys having a slightly larger mass. Higher urine output and lower urine osmolality were observed in partially obstructed rats. Of all the metabolites in the urine, there were consistent increases or decreases in several dominant metabolites in the partially obstructed rats compared to the control group. When PCA was performed to assess the overall profile of the urine metabolites, there was a clear difference between the partially obstructed and control group of rats.

**Conclusions:** Different urine metabolic profiles were demonstrated in rats with partial urinary tract obstruction compared to control in spite of absent histologic changes. Perhaps subclinical events take place at the mitochondrial and cellular level before visible alterations in the kidney. Metabolism and mitochondrial changes may precede histologic changes in urinary tract obstruction

**Key Words:** kidney, obstruction, pediatric

### DIS02.12

#### Growth arrest and apoptosis of T-24 bladder cancer cells resulting from the histone deacetylase (HDAC) inhibitor, PDX101

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Histone deacetylase (HDAC) enzyme inhibitors mediate gene expression and chromatin assembly, and induce growth arrest and apoptosis of tumor cells. We have shown that an inhibitor of apoptosis, survivin, is up-regulated in bladder cancer and correlates with a poor prognosis. We studied the effect of a new HDAC inhibitor, PDX101, on cell growth, cell cycle arrest, and survivin levels in T-24 bladder cancer cells. T-24 cells were incubated with the HDAC inhibitor, PDX101, and viable cell count and proliferation curves constructed. Cell cycle analysis was conducted with FACS and changes in apoptosis signaling proteins with Western blot. Treatment of T-24 cells with PDX101 (5  $\mu$ M) for 48 and 72 hours induced a 56.7 + 4.2% and 64.8 + 3.2% (mean + SEM) decrease in proliferation, respectively. PDX101 for 48 hrs increased apoptotic cells (sub-G1 cells) 1.3-2.3 fold, decreased G1 phase cells 41-54%, and increased S and G2/M phase cells 2.5-3.5 fold. PDX101 (24 hrs) decreased survivin protein levels by 58.2 + 6.0%, pro-caspase 2 levels by 40.4 + 11%, and pro-caspase 8 levels by 55.2 + 12.4%, while the Bcl2 related protein, Bak, and caspase 3 levels were unchanged. At 48 hrs, PDX101 treatment (1 and 5  $\mu$ M) decreased survivin and pro caspase 2 and 3 levels, whereas Bak and pro-caspases 8 levels only were decreased with 5  $\mu$ M PDX101. Cleaved (activated) caspase 2, 3, and 8 were visualized at 48 hrs. In T-24 cells, the HDAC inhibitor, PDX101 caused a decrease of cell growth and viability, and a specific G2/M phase arrest, and an increase in apoptotic cells. Decreases in survivin levels, and the appearance of activated caspases with a concomitant decrease in procaspases, indicate that PDX101 may activate survivin sensitive death receptor signaling pathways. The HDAC inhibitor, PDX101, may provide a treatment option for bladder TCC.

**Key Word:** bladder cancer

### DIS02.13

#### Clusterin is involved in NF- $\kappa$ B pathway to confer prostate cancer cell survival

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Clusterin is an anti-apoptotic protein upregulated by androgen ablation and chemotherapy to confer resistance to cell death and accelerate androgen independent progression in prostate cancer. Recently we reported that Clusterin regulates NF- $\kappa$ B transcription activity. However, the molecular mechanism by which Clusterin regulates cell survival in NF- $\kappa$ B pathway remains unknown. Here we show that Clusterin leads to cell survival by interfering with Murr1 and I- $\kappa$ B stabilization thereby releasing NF- $\kappa$ B from its cytoplasmic confinement and enhancing its transcriptional activity. Interestingly, Clusterin enhances the degradation of ubiquitinated proteins and its knockdown by OGX-011 inhibits proteasome activity and leads

to accumulation of ubiquitinated proteins. Moreover, Clusterin is a ubiquitin binding protein that targets Murr1 for proteasomal degradation by forming K48 polyubiquitination chains on Murr1. Clusterin accelerates NF- $\kappa$ B nuclear translocation and enhances transcriptional activity induced by TNF- $\alpha$  by increasing I- $\kappa$ B phosphorylation and degradation. Clusterin knockdown is associated with increased Murr1 levels and decreased levels of phospho-I- $\kappa$ B. Interestingly, Murr1 over-expression chemosensitizes prostate cancer cells to paclitaxel similar to that seen by OGX-011 induced Clusterin knockdown. We propose that elevated levels of Clusterin in human prostate cancer promotes cell survival by reducing Murr1 and I- $\kappa$ B levels leading to increased NF- $\kappa$ B transactivation.

**Key Word:** prostate cancer

### DIS02.14

#### T-shaped cavernosum-glans shunt: a new paradigm for the surgical management of priapism

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**Introduction:** Priapism is defined as an erection lasting longer than 4 hours not associated with sexual stimulation. Conservative management of ischemic priapism is rarely effective except in select circumstances. Interventions may include aspiration of the corpora, injection of vasoconstrictive agents, or surgical procedures. We describe a technique that fulfills several important criteria for the surgical management of ischemic priapism: it creates a reliably patent shunt, it may be performed under local anesthetic in an emergency department or clinical setting, and it is relatively easy to perform.

**Methods:** Records were reviewed for patients treated with the T-shunt in whom ultrasonography was performed.

**Results:** Records were available for review for 10 men who underwent T-shunt in O.R. (2), emergency room (5) or clinic (3) settings. In all cases, priapism had lasted for >24 hours (range: 48–336 h) and previous irrigation and intracorporal administration of sympathomimetics had been unsuccessful. In three cases, the patients had undergone prior unsuccessful cavernous-glanular shunts prior to presentation to our service. The first two cases were performed in an operating room with a combination of local anesthetic and intravenous sedation. The subsequent cases were performed using local sedation or anesthetic only. Cavernosal blood flow was restored post T-shunt in all patients but one (336 h priapism). One pt lost flow after 12h, requiring a second procedure (El-Ghorab). T-shunts resulted in resolution of penile pain in all patients, and recovery of erectile function was not seen if priapism lasted > 48 h.

**Conclusion:** The T-shunt technique results in resolution of pain and detumescence. Ultrasonography has confirmed that, in the majority of cases, blood flow is restored to the previously ischemic corpora cavernosa after the procedure. The T-shaped is simple, reliable, and the access also allows for proximal trans-shunt dilation, facilitating recanalization of corporal circulation and could make proximal shunts obsolete.

### DIS02.15

#### Transglanular prosthesis fixation for “floppy” glans penis

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**Introduction:** Patients with a “floppy” glans penis after penile prosthesis placement often complain of difficulty with vaginal intromission, pain, and pain to their partner. Typically, this occurs in a patient with Peyronie’s disease or a post-priapism prosthesis, with extensive corporal fibrosis leading to difficult safe placement of the prosthetic tip into the glanular corpus. This problem has been approached in a number of ways, usually involving dissection under the glans from a ventral or dorsal approach and placement of one or more horizontal mattress sutures to hold the glans penis in place. However, the dorsal approach, which is more common, risks damage to the dorsal penile arteries and nerves, while the ventral approach risks injury to the urethra. Also, in patients who have had multiple operations, suffer from diabetes, or otherwise have the potential for abnormal healing, approaches through potentially tenuous tissue may predispose to later erosion or fistulae. Here, we describe an alter-

native approach, which is to fix the prosthesis through the well-vascularized glans penis. This tissue, even in brittle diabetics or reoperative cases, is usually healthy and robust, and provides enough bulk to prevent erosion.

**Methods:** Records were reviewed for patients treated with this transglanular approach.

**Results:** Three patients have been treated in this manner (1 bilateral, 2 unilateral). Postoperative pain has been minimal and easily controlled with oral medication. Followup is greater than 9 months, and we have not noted either loss of sensation or abnormal cosmesis of the glans.

**Conclusion:** This procedure allows the use of robust and well-vascularized tissue to cover the tip with decreased risk of injury to either the urethra or to the dorsal neurovascular tissue.

extra of each sample. A peak at 31,2 kDa appeared in most of the aspiration samples.

### DIS02.17

#### Efficacy and safety of dose escalation (10 to 20mg) intralesional verapamil therapy for Peyronie's disease

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**Introduction:** Intralesional verapamil (ILV) injections has reported efficacy in patients with Peyronie's disease. An optimal regimen regarding dosing and frequency of administration remains to be established. Previous work from our center revealed that a significant number of patients (40%) require a dose escalation of ILV for maximal benefit (Shin et al. *J Urol* 2004;171[4S]:333). The primary objective of the current study was to evaluate the efficacy and safety of a dose escalation (10–20mg) regimen of ILV in patients with Peyronie's disease.

Table 1. Abstract DIS02.17

	Baseline	6- Injections	12- Injections	Significance
Mean Degree of Curvature	38	34	26	$p = 0.0001^{\dagger}$
Mean Plaque Volume (mm <sup>3</sup> )	472	555	332	$p > 0.05^*$
% Improved Curvature		43%	68%	
% Improved Plaque Volume		23%	68%	
Patient Self-Assessment:				
Improved Penile Curvature		58%	53%	
Improved Erection		58%	53%	

† Significant improvement from baseline  
 + Significant improvement from 6-injections;  
 \*Clinical trend but NSS

**Patients and Methods:** We report on 25 patients with documented Peyronie's disease who completed a dose escalation (10–20mg) regimen of ILV. The protocol consisted of 10mg of ILV every 2 weeks for the first 6 injections, followed by 20mg of ILV of every 2 weeks for the next 6 injections (24 weeks total therapy). Measures of: i) plaque volume using penile duplex Doppler (mm<sup>3</sup>), ii) degree of penile deformity/curvature using serial protractor measurements from digital photographs following intracavernosal injection of Trimix, and iii) patient self-assessment of penile curve, rigidity, length, girth, pain, and ability to engage in sexual intercourse were evaluated at baseline and at the 6- and 12-injection intervals. Adverse events were documented at each treatment session. Repeated measures ANOVA was used to analyze differences over time.

**Results:** Mean patient age was 55 years. Improvements were demonstrated in both degree of penile curvature and plaque volume over the course

of the dose escalation protocol, with the most dramatic favorable changes occurring after 6-months of therapy (Table 1). One patient experienced transient dizziness with 20mg ILV.

**Conclusions:** A dose escalation regimen of 10 to 20mg of ILV therapy appears to be safe and effective in reducing penile curvature and plaque volume in patients with established Peyronie's disease. A treatment period of greater than 6-injections is necessary to maximize efficacy. Further studies are in progress to determine if initial treatment at the 20mg dose can shorten the duration of treatment or whether a dose escalation is a necessary treatment precondition.

**Key Words:** erectile dysfunction, sexual activity

### DIS02.18

#### Efficacy of testosterone gel substitution (AndroGel® or Testim®) among sub-optimally responsive hypogonadal men

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**Introduction:** Increasing awareness surrounds the benefits of testosterone replacement in hypogonadal men. Once daily testosterone gel preparations represents a safe and effective method of hormonal replacement. Occasionally, hypogonadal symptoms and/or serum testosterone levels fail to improve with the initial testosterone gel selection. The primary objective of the current study was to evaluate the efficacy of testosterone gel substitution among sub-optimally responsive hypogonadal men.

**Methods:** The records of all hypogonadal men on testosterone gel replacement therapy (Testim® or AndroGel®) were reviewed to identify men who underwent a brand substitution in testosterone gel treatment due to initial sub-optimal response, adverse side effects or patient preference. Total serum testosterone, free testosterone, hematocrit, and the presence of hypogonadal symptoms (libido, energy levels, and erectile function) were compared pre- and post-substitution for each form of testosterone gel therapy.

**Results:** Of the 370 hypogonadal men identified on testosterone gel replacement therapy, 70 (19%) underwent a brand substitution in testosterone gel treatment. Eighty-one percent, with a mean age of 60 years, switched from AndroGel to Testim. Nineteen percent, with a mean age of 51 years, switched from Testim to AndroGel. Prior to gel substitution, among patients initially treated with AndroGel, the mean total and free testosterone levels were 313.6ng/dl and 10.2pg/ml, respectively. Total testosterone levels were below 300ng/dl in 57% of these patients. Among patients initially treated with Testim, the mean total and free testosterone levels were 444.0ng/dl and 14.6pg/ml, respectively. Total testosterone levels were below 300ng/dl in 18% of men. Following testosterone gel substitution, the mean increase in total and free testosterone was 174.1ng/dl ( $p = 0.003$ ) and 3.3pg/ml ( $p = 0.14$ ), respectively among men switched to Testim, and 1.0ng/dl ( $p = 0.9$ ) and 0.3pg/ml ( $p = 0.9$ ), respectively among men switched to AndroGel. Hypogonadal symptoms (libido, energy, and erectile function) improved in 76% of men who underwent a brand substitution following an initial suboptimal biochemical or symptomatic response.

**Conclusions:** A significant proportion of men on testosterone gel replacement therapy (19%) have a sub-optimal response to initial gel therapy. Total serum testosterone levels increase significantly following a switch from AndroGel to Testim, but not from Testim to AndroGel. Hypogonadal symptoms improve in a significant proportion of patients (76%). Testosterone gel substitution among initially unresponsive hypogonadal men is justified prior to abandoning or considering more invasive testosterone replacement therapy.

**Key Words:** androgen, andropause, sexual activity

### DIS02.19

#### Increasing incidence of priapism secondary to intracavernosal injection in HIV positive males

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**Introduction:** Priapism is a relatively rare urological emergency. We anecdotally noted an increasing incidence of priapism at our institution, and so we retrospectively reviewed all cases of priapism presenting to our emergency department over a 3-year period.

**Methods:** A 3-year retrospective analysis of patients with priapism presenting to the emergency department at St. Michael's Hospital, Toronto, Ontario, Canada (a tertiary care, academic teaching hospital, and regional trauma centre) was performed.

**Results:** A total of 18 episodes (16 patients, mean age 44) of priapism were identified. All represented ischemic (low-flow) disease. Thirteen emergency visits (72%) occurred within the last year of the three years analyzed. Duration of tumescence ranged from 5 to 44 hours, with a mean of 20 hours. The majority of episodes (83%) were secondary to intracavernosal injection, and of these, 73% occurred in HIV (human immunodeficiency virus) positive men. Most episodes of priapism resolved with cavernosal aspiration and/or phenylephrine injection. Operative intervention for detumescence was required in three cases (17%).

**Conclusion:** A dramatic increase in the incidence of priapism secondary to intracavernosal injection in HIV positive males is described. This represents the first description of an association of priapism and HIV-positivity to our knowledge.

**Key Word:** sexual activity

## DIS02.20

### Triclosan-eluting stents in chronically-stented patients

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**Introduction:** Long-term use of ureteral stents is prevented by biofilm-related infection and encrustation, mandating stent changes every few months. Triclosan is a broad-spectrum antimicrobial in numerous products including toothpaste and surgical scrubs and has been incorporated into a ureteric stent. Our previous work using a rabbit model demonstrated the ability of this stent to inhibit device-related biofilm formation and facilitate clearance of a *Proteus* cystitis. We sought to determine the clinical effects of a triclosan stent in patients requiring chronic ureteric stenting.

**Methods:** Eight long-term stented patients were enrolled prospectively and received a control stent for 3 months and 1 week of levofloxacin following stent placement. Urine cultures were obtained at time of stenting and weekly for 6 weeks and then bi-weekly for the next 6 weeks. After 3 months, the control stent was removed for assessment of adherent bacteria and a triclosan eluting ureteral stent was placed for 3 months following the same protocol. Antibiotics were prescribed only if urine cultures were positive and patients requested it.

**Results:** All 8 patients with 10 ureteral stents in total successfully completed the 24 week study. Twenty one (1 yeast, 20 bacteria) urinary isolates were obtained collectively from all patients during control stenting, plus 3 instances of unidentified/mixed organisms detected. Twenty (1 yeast, 19 bacteria) isolates were obtained from patients during triclosan stenting, plus 1 instance of unidentified organisms. Twenty-five antibiotic prescriptions were written to patients with an indwelling control stent compared to 10 prescriptions while a triclosan stent was indwelling (Average: 3.1 and 1.25 prescriptions per patient during control and triclosan stenting, respectively). Importantly, no bacterial isolates developed resistance to any antibiotics during triclosan stent placement, despite repeated exposure to triclosan and antibiotics simultaneously. All strains isolated from the triclosan stents were also isolated from the control stents. There was no difference in the number of stents with adherent bacteria (5/10 controls vs. 6/10 triclosan).

**Conclusions:** All chronically stented patients had positive urine cultures. Triclosan-eluting ureteral stents did not induce any antibiotic-resistant organisms. Overall, the rate of bacteriuria was no different between control and triclosan stents.

**Key Words:** antibiotics, ureter, UTI

## DIS02.21

### Treatment of chronic radiation cystitis with sodium hyaluronate (Cystistat): a report of three cases

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**Introduction:** Chronic radiation cystitis (RC) is a common cause of morbidity among men who have received external beam radiation therapy for adenocarcinoma of the prostate. The therapeutic options available for the treatment of this condition are limited. To date, there is no description in the literature, of the use of sodium hyaluronate (Cystistat) intravesically as a treatment for RC.

**Methods:** We describe a series of three cases of chronic radiation cystitis post external beam radiation therapy for prostate cancer that were treated with sodium hyaluronate. All three were Caucasian men between the ages of 68 and 82. The major presenting symptoms were hematuria, urgency and frequency, which were refractory to other treatment modalities. We instilled 50cc (40mg) of sodium hyaluronate intravesically once weekly for 6 to 10 weeks followed by monthly maintenance instillations.

**Results:** Each of the 3 had dramatic improvement in urinary frequency and urgency when compared with pretreatment symptoms. Furthermore, longterm control of refractory gross hematuria was achieved.

**Conclusion:** Our cases suggest that sodium hyaluronate should be considered as a treatment option for intractable, chronic radiation cystitis. This merits further investigation.

**Key Words:** cystitis, prostate cancer, radiation

## DIS02.22

### Complications in patients requiring anticoagulation undergoing transurethral prostatectomy

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**Introduction:** Long-term anticoagulation is commonly used in patients with atrial fibrillation, a history of veno-thromboembolism and mechanical heart valves. Many patients with these medical conditions also have urologic conditions requiring transurethral prostatectomy (TURP). While withholding anticoagulants decreases bleeding risk, it increases the risk of thromboembolic events. There is currently no consensus on the optimal peri-operative management of these patients.

**Methods:** We performed a retrospective case-control study of 26 men on chronic anticoagulation therapy referred to our peri-operative anticoagulation clinic who underwent TURPs within an eighteen month period (January 2005–June 2006). The administration of anticoagulants in the peri-operative period was based on risk of venothromboembolism and involved exchange of warfarin with low molecular weight heparin followed by recommencement of warfarin. These men were compared to 26 non-warfarinized age-matched controls during the same time interval. Clinical endpoints included thromboembolic events, bleeding-related events and death. Pre-operative patient characteristics, pathological data, and post-operative outcomes were obtained through a chart review.

**Results:** There was no significant difference in age, concomitant use of aspirin, preoperative hemoglobin, operative time, or the weight and diagnosis of the pathological specimen demonstrated between the two groups. There was no significant difference in the length of stay ( $p=0.36$ ) or the length of catheterization ( $p=0.08$ ) between the two groups. There were significantly higher repeat emergency room visits for clot retention or gross hematuria ( $p=0.01$ ; 36% vs. 8%) and repeat operative procedures ( $p=0.01$ ; 22% vs. 0%) in the anticoagulated group. No deaths or thromboembolic events were observed in either group.

**Conclusion:** Peri-operative anticoagulation results in increased morbidity following TURP. Patients should be counseled accordingly.

**Key Words:** BPH, LUTS, TURP

## DIS02.23

### Making heads or tails out of heads with short tails at the time of vasectomy reversal

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**Introduction and Objective:** The identification of sperm parts in the intravasal fluid at the time of vasectomy reversal presents a challenge to reproductive surgeons in determining the method of reconstruction—vasovasostomy (VV) or epididymovasostomy (VE)—will maximize outcomes. The primary objective of the current study was to evaluate patency

rates following microsurgical vasectomy reversal among patients demonstrating sperm heads and short tails (sperm parts) in the intravasal fluid at the time of reconstruction.

**Methods:** From 2001 to 2006, 428 consecutive patients underwent microsurgical vasectomy reversal by a single surgeon (L.I.L) at our center. Intravasal fluid was evaluated for sperm and fluid quality in all patients. Among these patients, 23 demonstrated only sperm heads and short tails bilaterally in the intravasal fluid at the time of reconstruction, and 19 underwent bilateral vasovasostomy. Post-operatively, patency (evidence of motile sperm in the ejaculate or biochemical pregnancy) was correlated with intravasal fluid quality at the time of vasectomy reversal.

**Results:** Mean patient age and obstructive interval was 44 years (range: 31–58) and 10 years (range: 1–33), respectively. Among patients who underwent bilateral vasovasostomy, patency was 95% (18/19). The isolated case of a non-patent anastomosis was associated with a thick and pasty intravasal fluid at the time of vasectomy reversal.

**Conclusions:** Microsurgical vasovasostomy yields excellent patency rates and is indicated among patients demonstrating only sperm heads and short tails (sperm parts) in the intravasal fluid at the time of vasectomy reversal. Epididymovasostomy should be considered if thick and pasty intravasal fluid is found at the time of reconstruction as this predicts for poor outcomes if only a vasovasostomy is used.

**Key Words:** microsurgery, sperm

## DIS02.24

### The association of hyperprolactinemia and impaired sperm motility: is there a role for dopamine agonist therapy?

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**Introduction:** There have been several small studies showing the relationship between hyperprolactinemia and impaired sperm motility. However, the benefit of Dopamine Agonist Therapy (DAT) in these patients is questionable. The purpose of this study was to determine the association between hyperprolactinemia and impaired sperm motility and to assess if DAT is effective in improving sperm motility.

**Material and Methods:** A retrospective review of all new infertility patients presenting to a single institution from 2002 to 2006 was performed. A semen analysis and hormone evaluation consisting of an FSH, LH, testosterone, prolactin, and estradiol were obtained on all men. Men that did not have a semen analysis and a hormone evaluation were excluded from the study. Semen parameters and hormone profiles were compared pre- and post-DAT therapy.

**Results:** Of the men that initially presented to the infertility clinic from 2002 to 2006, 197 men were found to have an elevated prolactin level. Of these men, complete follow-up data was available for 175 patients. The mean serum prolactin level was 31 ng/ml. Hyperprolactinemia was significantly correlated with a decrease in semen volume ( $r = -1.4$ ,  $p = 0.02$ ) and a decrease in sperm motility ( $r = -1.3$ ,  $p = 0.036$ ). Serum prolactin levels did correlate with serum testosterone levels and approached statistical significance ( $r = -0.13$ ,  $p = 0.06$ ). Serum testosterone levels did not correlate with sperm motility ( $r = 0.04$ ,  $p = 0.6$ ). Fourteen patients with hyperprolactinemia were started on cabergoline, a dopamine agonist. The average duration of DAT was 9 months. Mean sperm motility before and after DAT was 24% and 30%, respectively. Although this was not statistically significant, a trend towards improvement in motility was observed ( $p = 0.09$ ).

**Conclusion:** Hyperprolactinemia is significantly correlated with a decrease in sperm motility. A clinical trend towards improved sperm motility in hyperprolactinemic men was observed with DAT. The fact that serum testosterone levels did not correlate with sperm motility indicates that the improvement in sperm motility following DAT was not a testosterone effect. More patients need to be evaluated to further assess the efficacy of DAT on sperm motility.

**Key Word:** sperm

## DIS02.25

### Indications of vasoepididymostomy in vasectomy reversal in presence of bilateral intravasal azoospermia

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**Introduction:** Unrecognized epididymal obstructions represent an important cause for vasectomy reversal failure. However, there is still a debate in Canada and North America as to when a vasoepididymostomy (VE) should be performed in vasectomy reversal. Thus, we wanted to identify predictive factors of poor outcome for vasovasostomy in presence of bilateral intravasal azoospermia and determine indications of vasoepididymostomy in such cases. During follow-up, alpha-glucosidase is known as a good indicator of epididymal dysfunction, but its specificity has not been proved after vasovasostomy in a case of intra-op bilateral intravasal azoospermia.

**Methods:** We conducted a retrospective study of 417 patients with first vasectomy reversal done between 1995 and 2004 by one single surgeon. We selected 43 patients with bilateral intravasal azoospermia and evaluated if obstructive intervals and quality of intravasal liquid would influence the outcome. Then we compared post-op levels of alpha-glucosidase for patent and non-patent groups.

**Results:** The overall patency rate is 50%. The mean obstructive interval (OI) in the patent group is significantly lower than in the non-patent group ( $p \geq 0.05$ ). 88% of our patent cases had an obstructive interval (OI) of 10 years or less. With an OI of more than 10 years, the odd ratio of failure was 14 (1.54–127) ( $p = 0.02$ ). All patent cases had bilateral clear or opalescent vasal fluid and 74% of clear / opalescent fluids were patent. A majority of cases in non-patent group showed bilateral thick and pasty fluid. Both groups showed low post-op levels of alpha-glucosidase.

**Conclusions:** During first vasectomy reversal, a vasoepididymostomy should be performed, in presence of bilateral intravasal azoospermia, when the intravasal liquid is pasty and thick or when the obstructive interval is longer than 10 years. Alpha-glucosidase is a good indicator of epididymal dysfunction.

**Key Word:** infertility

## DIS02.26

### Differential sperm DNA fragmentation rate in the ejaculate and testicular extracted sperm

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**Introduction and Objectives:** Sperm DNA damage (fragmentation) may contribute to male factor infertility. One study has shown that ejaculate sperm has more DNA damage than testicular sperm and is associated with lower pregnancy rates with intracytoplasmic sperm injection (ICSI). However, the specimens were collected and tested on separate days, often months apart. We studied whether ejaculate and testicular sperm obtained on the same day would show a similar pattern of differences in DNA damage rates as described in samples collected on different days, since sperm DNA fragmentation rates may vary with time. We also ventured to determine if there may be factors (including patient age and the presence of varicocele), which might affect the testicular and ejaculate sperm DNA fragmentation rates. We therefore studied the effect of these factors on the rates of sperm DNA damage in the ejaculate and the testis.

**Methods:** Men with sperm DNA fragmentation (by Sperm DNA Integrity Assay) > 30% (after 3 months of therapy with multi-vitamins and anti-oxidants) and who were about to undergo ICSI were entered into the study. Testicular and ejaculate sperm samples were obtained on the same day and analyzed for DNA fragmentation by a standard terminal deoxynucleotidyl transferase-mediated dUTP nick-ended labeling (TUNEL) assay. Differences in sperm DNA fragmentation rate were evaluated and the rates were correlated with patient factors.

**Results:** Lower rates of positive TUNEL sperm DNA fragmentation in testicular compared to ejaculated sperm was seen in all of the 10 men entered into the study. Overall, TUNEL positivity was significantly lower in the testicular sperm compared to the ejaculate sperm (21.41% vs. 37.48%,  $p = 0.011$ ). Sixty percent of men had testicular TUNEL positive sperm within normal range (<20%). Clinical factors, including age and

the absence of varicoceles did show a trend towards lower rates of DNA fragmentation in testicular sperm but did not reach statistical significance due to the limited sample size.

**Conclusions:** This study supports the idea that sperm retrieved from the testicle has lower DNA damage than ejaculate sperm suggesting that sperm DNA damage is progressive as the sperm transits through the male reproductive tract. However, it remains unclear if it is preferable to use testicular compared to ejaculated sperm for ICSI in men with high rates of sperm DNA damage as pregnancy outcomes in patients undergoing ICSI with sperm retrieved by either technique are still pending.

**Key Words:** DNA, ICSI, infertility

### DIS02.27

#### Semen analysis variables and their association with sperm penetration assay and DNA fragmentation

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**Introduction:** Infertile couples undergoing routine in vitro fertilization (IVF) as well as intra-uterine insemination (IUI) procedures were approximately 2.0 to 7 times more likely to achieve a pregnancy/delivery if their sperm DNA fragmentation was <30%. The null hypothesis was that sperm fertilizing capacity was independent of sperm DNA integrity. The purpose of this study will help clinicians determine the prognosis and significance of patients with different DNA fragmentation parameters.

**Methods:** From July 2002 to January 2004, semen analysis, sperm penetration assay and sperm DNA damage from 411 consecutive patients presented for evaluation of male infertility were examined. Semen samples were collected, and routine semen analyses were performed. Aliquots of the specimen were then sent for sperm penetration assay (SPA) using hamster eggs, and sperm DNA fragmentation tests using a modified alkaline single cell gel electrophoresis technique (CometAssay™). Logistic regression analysis was performed using SAS/STAT software version 13 (SAS Institute Inc. Cary, NC).

**Results:** Of the 411 men, cases were defined as patients with sperm capacitation index (SCI) value less than 5 (273 men/66.4%) and controls (138/33.5%) with SCI >5. When cases were compared to controls significant differences between means was found for motility ( $p < 0.001$ ), density ( $p < 0.001$ ), and DNA fragmentation ( $p < 0.001$ ). After adjusting for age, semen volume, forward progression, density, morphology, head, neck, and tail defects the odds ratio for poor SCI were significant for low sperm motility (OR 1.04  $p = 0.001$ ) and low sperm density (OR 1.01  $p = 0.026$ ). The adjusted odds ratio for sperm DNA fragmentation showed a trend of 0.96 ( $p = 0.077$ ) which did not reach significance.

**Conclusion:** Low sperm density and motility are the most important predictors of lower oocyte penetration capacity. Sperm DNA fragmentation

may be related to poorer oocyte penetration, which leads to lower success rate in routine/classical IVF cycles. Intracytoplasmic sperm injection (ICSI) may be considered as the primary approach in couples with high sperm DNA fragmentation in the setting of assisted reproductive technology.

**Key Words:** infertility, risk factors, sperm

### DIS02.28

#### 120 W potassium-titanyl-phosphate (KTP) laser photoselective vaporization prostatectomy (PVP) for symptomatic benign prostatic hyperplasia (BPH)

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**Introduction:** KTP laser PVP is a relatively new technology for the treatment of lower urinary tract symptoms (LUTS) secondary to BPH. We review our initial experience using the 120 W KTP laser system.

**Methods:** We prospectively evaluated our initial experience with KTP laser PVP. All had International Prostate Symptom Score (IPSS), Sexual Health Inventory for Men (SHIM) score, American Society of Anesthesiologists (ASA) risk score, serum prostate specific antigen (PSA), maximum flow rate ( $Q_{max}$ ) and post void residual (PVR) determinations and volumetric measurements with transrectal ultrasonography. Peri-operative antibiotics were provided. Under general anesthesia, transurethral PVP was performed using a 120 W KTP side-firing laser system through a 23 Fr continuous-flow cystoscope with normal saline irrigant. Laser and operative times and energy usage were recorded. Voiding trials were performed two hours post surgery; if unable to void, a urethral catheter was replaced. IPSS, SHIM,  $Q_{max}$  and PVR were evaluated 1, 4 and 12 weeks post surgery.

**Results:** 67 consecutive patients were identified, having a mean age of  $69 \pm 9$  years. The mean prostate volume was  $76 \pm 46$  cm<sup>3</sup> and the mean ASA score was  $2.3 \pm 0.6$ . Mean laser time, operating time and energy usage were  $12 \pm 7$  minutes,  $29 \pm 19$  minutes and  $84 \pm 46$  kJ, respectively. All were outpatient procedures with 37/67 (55%) patients catheter-free at discharge. Four patients required catheter drainage for one week. One patient developed a urinary tract infection. Ten patients had hematuria for over a week. Two patients had persistent urinary retention due to detrusor failure. No urethral strictures or urinary incontinence were noted. All patients were able to discontinue their prostate medications following surgery. Mean IPSS decreased significantly from 25 to 11, 9 and 9 ( $p < 0.05$ ) at 1, 4 and 12 weeks, respectively.  $Q_{max}$  and PVR values also showed statistically significant improvement ( $p < 0.05$ ). The SHIM score did not change postoperatively.

**Conclusion:** Our initial results demonstrate that 120 W KTP laser PVP is safe and effective for the treatment of LUTS secondary to BPH, providing excellent results and minimal morbidity.

**Key Words:** BPH, laser, prostate

## POSTER DISPLAY 3: ONCOLOGY, PEDIATRIC UROLOGY, STONES, TRANSPLANTATION, INCONTINENCE & OAB TUESDAY, JUNE 26

### DIS03.01

#### Are megacystis-microcolon-intestinal hypoperistalsis and prune belly a spectrum of the same syndrome?

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**Introduction:** Prune belly syndrome (PBS), the triad of abdominal wall laxity, urinary tract dilation and bilateral cryptorchidism is frequently associated with gastro-intestinal malformations. Similarly, megacystis-microcolon-intestinal-hypoperistalsis syndrome (MMIHS) is a fatal cause of functional intestinal obstruction in the newborn, associated with abdominal distension and urinary tract dilation. Herein we report a case of concurrent MMIHS and PBS, and present the idea of a possible common pathogenesis for both syndromes.

**Methods:** Chart review and review of the literature.

**Results:** A male fetus with megacystis and oligohydramnios underwent vesicoamniotic shunting. Postnatally he was found to have the triad of PBS. Bilious vomiting led to findings of gut malrotation on imaging. At laparotomy a microcolon was found and loop ileostomy performed. Lack of output from the stoma prompted further studies which confirmed aperistalsis of the stomach and small intestine, necessitating total parenteral nutrition. Literature review reveals one reported case of concurrent PBS and MMIHS. One report exists of a female case of MMIHS with her brother affected with PBS and argues for a shared genetic pathogenesis. Most reported cases of MMIHS are female and the only element of the PBS triad lacking is cryptorchidism. The first description of masculine MMIHS reports a patient who also had an intra-abdominal testicle. Similarly, there are reports of female PBS and incomplete variants labelled pseudo-PBS. Constipation is a frequent issue in PBS and has been blamed on the abdominal wall laxity, yet a milder motility disorder has not been studied. Reduced numbers of interstitial cells of Cajal in the bowel and bladder of patients with MMIHS has been reported, supporting the theory of a common disorder of peristaltic activity.

**Conclusion:** We present the second known case of concurrent PBS and MMIHS. The shared clinical features together with evidence of familial and histologic overlap supports the idea of a common pathogenesis. We propose that a spectrum exists from pseudo-PBS to PBS to PBS with gut abnormalities and finally MMIHS. It may be that gender influences whether gut or urinary tract motility will be most impaired. These rare cases should be pooled to allow in depth study.

**Key Words:** bladder, pathology, pediatric

### DIS03.02

#### Expression of various cellular markers in genitourinary rhabdomyosarcoma: immunohistochemical study using TMA methodology

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**Background:** Rhabdomyosarcoma (RMS) is the most common sarcoma in the pediatric age group, with 20% of the cases involving the genitourinary tract. These tumors are often characterized by rapid growth, local extension as well as by early metastatic spread. Multimodality therapy has therefore been introduced with ongoing efforts to improve characterization of various prognostic factors, in order to diminish the therapeutic burden and minimize side effects. In accordance, the use of immunohistochemical analysis of the expression of various cellular markers in tumoral cells may enable to better design the therapeutic schedule according to individualized risk-based data and may even define specific therapeutic targets in RMS. The aim of this study was to evaluate the extent of expression of various cellular markers in RMS, using tissue microarray (TMA) technique.

**Methods:** TMA paraffin embedded block was constructed of 8 samples of RMS from different patients operated between 1995–2005. Each tumoral sample was presented in the block by several cores, 2 mm in diameter, containing tumoral tissue with adjacent transitional epithelium and normal detrusor, which served as positive and negative controls. After serial slicing of 4- $\mu$ m thickness, the histological slides were stained with hematoxylin&eosin (H&E) and immunostained with antibodies against Erb-B2, p53, c-kit, Ki 67, Caspase 3, EGFR, N-CAM, TOPO-II and BCL-10. The immunostaining was graded semiquantitatively by the percent of positive cells and the intensity of stain.

**Results:** Four cellular markers were expressed in RMS including Erb-B2, Ki 67, EGFR and N-CAM. Significant positive staining (grades 2-3) for at least one of these markers was noted in 5 of the cases.

**Conclusions:** The expression of Erb-B2, Ki 67, EGFR and N-CAM in genitourinary RMS may have potential therapeutic implications. Our preliminary results may promote further studies to assess the potential role of these markers to serve as therapeutic targets for specific therapeutic agents and thus decrease the overall treatment burden in children suffering from genitourinary RMS.

**Key Word:** pathology

### DIS03.03

#### Expression of various drug resistance proteins in Wilms' tumor: immunohistochemical study using TMA methodology

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**Background:** The multidrug resistance-related protein (MRP-1), lung resistance-related protein (LRP) and topoisomerase-II (TOPO-II) are associated with drug resistance against various chemotherapeutics and protect cells against toxic compounds. Their expression in cancer cells may result in altered membrane transport (MRP-1, LRP) and altered enzymatic activity (TOPO-II). The aim of this study was to evaluate the extent of MDR-related protein expression in Wilms' tumor (WT) using tissue microarray (TMA) technique.

**Methods:** TMA paraffin embedded block was constructed from normal renal tissue, 14 samples of WT from different patients, and from xenografts derived thereof. Each tumoral sample was presented in the block by several cores, 0.06 mm in diameter. After serial slicing, of 4- $\mu$ m thickness, the histological slides were stained with hematoxylin & eosin (H&E) and immunostained with antibodies against MRP-1, LRP and TOPO-II.

The immunostaining was graded semi-quantitatively by the percentage of the stained cells and the intensity of stain.

**Results:** All the normal kidney tissue samples expressed MRP-1 and were weakly stained or negative for LRP and TOPO-II. Samples of WT were universally stained for MRP-1 (only in the tubular component of the tumor), no expression of LRP was detected and various distribution of TOPO-II was observed. The xenografts' varied regarding MRP-1 and TOPO-II expression and exhibited weak or negative staining of LRP.

**Conclusions:** Our study presents the expression of various multidrug resistance proteins in WT, indicating that only MRP-1 might have a potential clinical role. The differences between the expressions of those proteins in the authentic tumors and in their related xenografts might explain differences in response to chemotherapy comparing original tumors and related animal models.

**Key Word:** chemotherapy

### DIS03.04

#### Botulinum toxin A for the treatment of refractory idiopathic bladder overactivity in elderly women

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**Introduction:** Botulinum Toxin A (BTA) has been successfully used for refractory neurogenic detrusor overactivity. Most of these patients already perform self catheterization (CIC) and thus the potential side effect of urinary retention is not a concern. Much less is known about the success of BTA in idiopathic bladder overactivity (IBO) especially in elderly women who often have coexistent poor bladder emptying. Acceptance of the need to perform CIC as a result of BTA injections may be a significant deterrent for elderly women considering this therapeutic option. The purpose of this study was to examine success and retention rates in elderly women receiving BTA for IBO.

**Methods:** The charts of the first consecutive 15 women, aged over 60 years, treated with BTA for refractory IBO were analyzed.

**Results:** Mean and median age were 73 and 76 years, respectively (range 63–80). Injections were given between 9 04 and 11 06. UDS showed IDO (6), mixed IDO and stress incontinence (3), decreased compliance (1), and normal (3). The largest PVR pre BTA was 100cc, with a median of 25cc. 13/15 had urge incontinence (UI) and 2 had overactive bladder (OAB) dry. Doses ranged from 100 units (9 patients, 11 injections), 200 units (4 patients, 7 injections), or 300 units (2 patients). PVRs measured at 7 days by ultrasound were <100cc (6), >100cc (5), and >250cc with need to CIC (4). Both of the 300 unit injections required catheterization and the other 2 women in retention received 100 units. Requirement for catheterization was 3-6 months. Subjective improvements in frequency, nocturia, and UI occurred in 12/15 women for a median duration of 6.5 months (range 1-15). Failures had potential negative prognostic variables: radiation (1), superficial bladder cancer decreased compliance (1), and normal pre BTA UDS (1).

**Conclusions:** BTA is an effective treatment for refractory OAB in elderly women, but retention is a definite risk and the procedure should be undertaken only in those that are capable of CIC. Higher doses of BTA (300 units) appears to have an increased risk of retention, but even 100 units resulted in retention in 2 women with normal pre BTA PVRs.

**Key Word:** overactive bladder

### DIS03.05

#### Electromotive drug-administration (EMDA): a minimal-invasive treatment of therapy-resistant urge incontinence

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**Introduction:** Electromotive drug-administration (EMDA) represents a minimal-invasive method for intravesical instillation of therapeutic agents. We examined the therapeutic effect of EMDA in patients suffering from therapy-resistant urge incontinence regarding urodynamic values and micturition frequency.

**Methods:** Patients suffering from urge symptoms with and without urge incontinence (OAB wet/OAB dry) non-responding of oral anticholinergics

underwent EMDA therapy (Lidocain-HCl 4% [2000 mg] 2ml, Epinephrin [1: 1000 (2mg)] 2ml, Dexamethason-21-dihydrophosphat [40 mg] 10ml and Ampuva 100ml). From 1/2004 to 3/2006, 42 patients (age 64.3±10.6 years; 36 female) with urodynamically-proven detrusor overactivity were treated with EMDA. Following urodynamic measurements and protocol of fluid intake and micturition over 48h we performed EMDA once in four weeks for a period of three months. Patients kept on documenting drinking and micturition data during this time. Before each EMDA session we measured urodynamic parameters. Values are shown as average±s.e.m. and repeated measures ANOVA following a test for a linear trend and in relation to the values before the treatment was used to assess statistical significance.

**Results:** All treated patients suffered from urge symptoms (36% OABwet, 23% OABdry and 41% mixed urge and stress incontinence). Mean frequency of micturition was 14.1±7.5 per day and 4.9±5.3 per night before EMDA. After two EMDA sessions, micturition frequency decreased to 9.3±3.9 per day ( $p<0.0001$ ) and 2.8±1.7 per night ( $p=0.0035$ ). The use of pads could be lowered from 4.5±4.2 per 24h to 2.7±2.9 ( $p=0.0074$ ). First urge assessed by urodynamic started at 88.3±61.6ml prior to treatment begin and decreased to 155.8±78.7ml ( $p=0.0064$ ) after two sessions. Strong urge was felt with 137.1±75.7ml filling of the bladder; after two EMDA sessions, this was reduced to 219.0±97.5 ml ( $p=0.01$ ). Functional bladder capacity increased to 235.8±107.4ml ( $p=0.018$ ) from 188.3±107.4ml in the untreated state. Patients documented an increase in micturition volume from 197.4ml to 234.2ml ( $p=0.043$ ). 57% of the patients reported to be satisfied with the results of EMDA treatment, while 43% complained about an insufficient decrease of urge related symptoms. 26.7% of patients did not continue therapy after 2 sessions.

**Conclusion:** EMDA significantly improves urodynamic values concerning detrusor overactivity and urge incontinence-related symptoms and reduces use of pads in patients.

**Key Word:** overactive bladder

### DIS03.06

#### Vesicovaginal fistula repair: 20 years' experience

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**Introduction and Objective:** The commonest cause of vesicovaginal fistulas (VVF) in Canada and the U.S. is abdominal hysterectomy. Controversy still exists regarding optimal timing of repair. The role of interpositional flaps in uncomplicated fistulas is also unclear. Our objective was to review data from our fistula repairs with regard to risk factors, etiology, surgical approach, success rate, and litigation rate.

**Methods:** Between January 1986 and June 2006, 47 vesicovaginal fistulas were repaired. Charts were retrospectively reviewed for etiology of fistula, location, presentation, surgical approach, long-term complications, litigation rate, and cure rate. The abdominal approach was to enter the plane between the bladder and vagina. The bladder was not bi-valved. Multiple layer closure was carried out with omental interposition. The transvaginal approach involved a similar multi-layer closure with flap interposition as required. Suprapubic catheters were left indwelling for 4–6 weeks. Outcome was determined by cystogram and symptoms.

**Results:** Mean patient age was 43.11. Etiology of the fistula was hysterectomy in (32 patients, 69.6%) and C-section (7 patients, 15.2%). Mean fistula size was 8.79 mm. Mean time from fistula occurrence to repair was 6.9 months (range 2–22). Fistula location was posterior to the trigone in 30 patients (65.2%), trigone in 11 patients (23.9%), and bladder neck in 6 patients (13.0%). Out of 47 VVF's, 38 were complicated (80.85%). 26 (55.3%) of the VVF repairs were performed using an abdominal approach and 19 (40.4%) using a transvaginal technique. We used tissue flaps in all abdominal and combined repairs and 4 (21.0%) of the vaginal repairs. Mean hospital stay was 5.72 days. Mean follow-up time was 20.15 months (range 0.17-132.93). All fistulas were successfully repaired. At follow-up 7 (15.2%) experienced urge incontinence, 6 (13.0%) stress incontinence, 5 (10.9%) urgency, 3 (6.5%) frequency, and 1 (2.2%) chronic pain. 23.4% of patients, who had fistula repairs at our institution, initiated litigation against a previous physician.

**Conclusions:** Abdominal and vaginal VVF repairs are highly successful.

Management techniques include multi-layer closure, flap interposition as deemed necessary, and suprapubic drainage. There does not appear to be a mandatory wait time between time of injury and repair, provided the tissues appear to be healthy. The litigation rate from VVF is very high suggesting a profoundly negative impact on quality of life.

**Key Words:** bladder, incontinence, QOL

### DIS03.07

#### Repair of post radical prostatectomy rectourethral fistulas via the posterior approach

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**Introduction:** Rectourethral fistulas (RUF) are estimated to occur after 1.7% of radical prostatectomies with half failing conservative management and requiring surgical repair. We treated 3 post-radical prostatectomy RUFs with rectal advancement flaps by the posterior approach. The three main types of posterior repairs, which are rarely reported in the literature, are: 1) posterior-sagittal (York-Mason), 2) transanal partial thickness (the modified Latzko technique) and 3) transanal full thickness (the Park technique).

**Methods:** All patients underwent colostomies and suprapubic tubes prior to the procedures. The patients were placed in the prone jack-knife position with exposure facilitated by a ring retractor. The bladder and urethra were dissected away from the rectum and closed in 2 layers. The rectum was then closed with a flap that was mobilized superiorly. Case 1 was a 71 year old who had a prior radical perineal prostatectomy and a later failed retropubic RUF repair. He presented at 23 months postoperatively. Case 2 was 53 year old who presented 13 months post radical retropubic prostatectomy. Case 3 was a 64 year old with a post radical perineal prostatectomy RUF who presented at 8 months postoperatively.

**Results:** Cases 1 and 2 underwent transanal repairs. The first underwent a full thickness anterior rectal flap (Park procedure) and the second a partial thickness rectal mucosa flap (modified Latzko procedure). Case 3 was repaired with a posterior-sagittal approach with a York-Mason type transsphincteric repair. Cases 1 and 2 have been free of recurrence of RUF after 14 and 17 months. The third case is in the early phase of recovery. No postoperative complications were encountered.

**Conclusion:** The posterior approach provides excellent visualization and direct access for the repair of RUFs. It appears to be a safe and effective alternative to traditional abdominal or perineal approaches for repair of RUFs. Urinary and fecal diversions are still required. Low fistulas can be accessed transanally whereas higher or larger fistulas may be accessed by incising the anal sphincter. The posterior approach is a worthwhile addition to the urologic armamentarium.

**Key Words:** radical prostatectomy, reconstruction, urethra

### DIS03.08

#### How does functional capacity and first sensation during cystometrogram relate to nocturia?

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**Introduction:** The measurement of functional capacity and first sensation are common parameters assessed during a cystometrogram (CMG) for a variety of voiding complaints. Unfortunately, the relationship between patient symptoms and CMG findings has been poorly explored. In this study we attempted to discover the relationship between patient reported nocturia versus functional capacity and first sensation determined by a cystometrogram.

**Methods:** We have electronic charts on all patients who have undergone urodynamic (UD) testing from 1996-2006 at our institution contained in an urodynamics (UD) data base. Using the UD data base functional capacity and volume at first sensation was cross-referenced with the degree of nocturia reported by patients. The amount of nocturia was graded from 0 to 3. With 0, 1, 2 and 3 corresponding to 0 times/night, 1-2 times/night, 3-4 times/night and >4 times/night respectively. The mean and standard deviation for functional capacity and first sensation were then determined for each level of nocturia. A 1-way ANOVA was then applied to each level of nocturia to determine if the observed dif-

ferences in their respective functional capacities and first sensations were statistically significant. In addition, those individuals who described no nocturia and those who described nocturia were then compared to determine statistical significance using a 2-tailed unpaired *t* test.

**Results:** There were 3499 patients identified in the urodynamics database who had the above parameters identified. The mean functional capacity for nocturia 0, 1, 2, and 3 were 338.9, 294.9, 258.7 and 239.9 respectively. The mean first sensation for nocturia 0, 1, 2 and 3 were 216.8, 177.5, 161.5 and 150.8, respectively. When the unpaired *t*-test and ANOVA was applied to the data there was a statistically significant difference both between nocturia levels and between those that had described some degree of nocturia and those that did not, for both functional capacity and first sensation.

**Conclusion:** This study of almost 3500 patients demonstrates that individuals with nocturia have a significant decrease in functional capacity and an earlier first sensation as their nocturia worsened. This suggests that functional capacity and not nocturnal polyuria is a major factor contributing to nocturia in patients.

**Key Word:** LUTS

### DIS03.09

#### Acute page kidney: a complication of allograft biopsy requiring urgent recognition

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The Page kidney phenomenon occurs as a consequence of external compression of renal parenchyma leading to renal ischemia and hypertension. However, it has been poorly described in renal transplant literature. We report our series of acute Page Kidneys as a consequence of allograft biopsy-induced subcapsular hematomas.

Between 10/2000 and 10/2006, 418 kidney transplants and 606 allograft biopsies were performed at our center. Among them, 2 adult female patients developed a clinical picture of acute anuria. Emergent doppler ultrasounds were performed demonstrating absence of diastolic flow as well as a subcapsular hematoma at the biopsy site. Prompt surgical exploration with allograft capsulotomy was performed in both cases. Immediately after capsulotomy, doppler ultrasound demonstrated robust return of diastolic flow. The bare regions of the renal parenchyma were covered with Surgicel and Tisseel for hemostasis and generous pieces of Marlex Mesh were used for abdominal fascial closure to provide compression-free coverage of the swollen kidneys. Clinical improvement followed in the immediate post-operative period. After 450 and 50 days post-capsulotomy, both patients have functioning renal transplants with serum creatinine values of 127 and 134  $\mu\text{mol/L}$ , respectively.

We conclude that the acute Page Kidney phenomenon is a rare but serious complication that may result from a renal transplant biopsy. The findings of subcapsular hematoma and acute absence of diastolic flow on doppler ultrasound should be considered to be pathognomonic of this complication. All renal transplant physicians and surgeons should be able to recognise this complication, since immediate surgical decompression can salvage the allograft.

**Key Words:** biopsy, transplants, ultrasound

### DIS03.10

#### Impact of laparoscopic donor nephrectomy on graft perfusion, early graft function and acute rejection in pediatric recipients

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**Introduction:** Delayed graft function (DGF) and acute rejection (AR) following transplantation of kidneys procured laparoscopically in pediatric recipients are concerning events. We routinely perform an intra-operative Doppler study following renal transplantation. Herein we retrospectively review the recipient outcomes comparing our first 11 LDN recipients with 11 preceding age, sex and weight matched open donor nephrectomy recipients (ODN).

**Methods:** Data collected included the intraoperative Doppler ultrasound results, serum creatinine values and creatinine clearances preoperatively, at 24 hours following transplant and at last follow up or at 1 year post-transplant and the incidence of AR episodes.

**Results:** Follow up duration post transplantation was a mean of 10.3 months in the LDN group and 26.2 months in the ODN group. The intraoperative average RI of the transplanted kidney ranged between 0.37 and >1 (mean 0.59) in the ODN group and was between 0.54 and 0.77 (mean 0.66) in the LDN group. None of the LDN group recipients had an abnormal RI of < 0.5 or > 0.8 in our study. Postoperatively, there was a 73.9% (56–88 %) fall in the serum creatinine value in the first 24 hours in the ODN recipient group as compared to 78.8% (42–97%) fall in the LDN recipient group. The mean serum creatinine was lower in the LDN group at 1 week, 1 month and at last follow up as compared to the ODN group. The creatinine clearance was a mean of 100, 91 and 84 ml/1.73 m<sup>2</sup>/min. respectively in the LDN group as compared to 79, 76 and 63 ml/1.73 m<sup>2</sup>/min. respectively in the ODN group at these same follow up points. Four patients in the ODN group had episodes of biopsy proven AR at 1–4 months following transplantation as compared to 1 at 2 months in the LDN group.

**Conclusions:** Laparoscopic donor nephrectomy did not show any adverse impact on recipient outcomes in short term follow up. All grafts demonstrated good perfusion and function in the early postoperative period. Long term follow up of these patients is required to assess the incidence of rejection episodes and graft survival.

**Key Words:** imaging, laparoscopy, transplant

### DIS03.11

#### Predictors of post-partial nephrectomy renal function using 24-hour urine creatinine

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**Introduction:** Partial nephrectomy for primary renal tumours is indicated for preservation of overall renal function. The most accurate calculation of creatinine clearance (CrCl) utilizes 24-hour urine creatinine levels, however, previous reports have only used serum creatinine (sCr) to estimate renal function in partial nephrectomy patients. This is the first study to use 24-hour urine collection to calculate CrCl in this patient population.

**Methods:** All partial nephrectomies performed by one urologist from November 2003 to June 2006 were reviewed. Serum creatinine and 24-hour urine samples were collected pre-operatively and at 3, 6 and 12 months postoperatively. Computed tomography or magnetic resonance imaging was used to determine tumour size, tumour depth and renal volume. The volume of the kidney that contained tumour was divided by the overall renal volume to calculate the ratio of effected renal volume (ERV). CrCl was calculated using a standard formula (CrCl = [24-hour urine creatinine x 24 hour urine volume] / [sCr x 86400sec/day]). Mixed model analysis was performed to determine the pre-operative characteristics that predicted post-operative CrCl.

**Results:** Of 26 patients, 18 (69%) were male, 3 had solitary kidneys and average patient age was 60 (range 30–78). Average tumour size was 2.7±1.3 cm and average tumour depth was 1.6±0.9 cm. Fourteen (54%) of the tumours involved a pole of the kidney and 12 (46%) were in the mid-pole region. Average renal volume was 172.4±64.8 cm<sup>3</sup> on the right and 169.2±63.3 cm<sup>3</sup> on the left. Average pre-operative sCr (n=26) was 101±36 mmol/L and sCr at 3 (n=23), 6 (n=19) and 12 (n=15) months post-operatively were 111±39 mmol/L, 117±51 mmol/L and 116±37 mmol/L, respectively. Corresponding CrCl were 1.46±0.50 ml/sec pre-operatively, 1.36±.47 ml/sec at 3 months, 1.38±.62 ml/sec at 6 months and 1.39±.57 ml/sec at 12 months. Predictors of post-operative CrCl were pre-operative CrCl (0.95±0.04; p<0.0001) and ERV (-0.33±.14; p=0.03). Age (p=0.17), tumour depth (p=0.88), tumour size (p=0.9) and tumour location (p=0.95) were not predictors of post-operative renal function. Post-operative CrCl did not significantly change over time, however, at all post-operative time points, CrCl was less than pre-operative rates (p<0.01).

**Conclusion:** Partial nephrectomy results in a small but significant decrease in overall renal function. The size of the tumour-bearing kidney, compared to the overall renal volume, may be an important predictor of post-operative renal function.

**Key Words:** kidney, kidney function, neoplasm, nephrectomy, partial nephrectomy, renal failure

### DIS03.12

#### Collecting duct renal cell carcinoma: a matched analysis of 41 cases

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**Introduction:** Collecting duct renal cell carcinoma (CDRCC) is a rare, but reportedly aggressive histological subtype. We assessed the stage and histological features of CDRCC patients. Moreover, we compared cancer-specific mortality in CDRCC and matched clear cell renal cell carcinoma (CRCC) patients.

**Methods:** Forty-one (0.6%) patients with CDRCC and 5246 CRCC patients were identified within a cohort of 6608 patients treated with either radical or partial nephrectomy for renal cancer. Within the 5246 CRCC cases, 105 were matched with CDRCC cases for grade, tumor size, as well as T, N and M stages. Kaplan-Meier and life table analyses addressed RCC-specific survival.

**Results:** Of all CDRCC patients, 76% had pT3 disease at nephrectomy vs. 37% for CRCC. The predominant Fuhrman grades were 3 (56%) and 4 (22%) vs. II (42%) and III (28%) for CRCC. Moreover, 49% of CDRCC patients were pN1-2 vs. 8 % for CRCC. Of CDRCC patients 19% had distant metastases at nephrectomy vs. 14% for CRCC. Finally, 73% of CDRCC had either local or systemic symptoms vs. 56% for CRCC. After matching, the RCC-specific mortality of CDRCC patients was no different from CRCC patients (RR=1.1; p=0.8). One- and 5-year CDRCC specific survival was 86% and 48%, respectively vs. 86% and 57% for matched CRCC controls.

**Conclusion:** CDRCC patients present with more advanced stage and with more aggressive disease vs. CRCC. After nephrectomy, when CDRCC cases were matched with CRCC, the same cause-specific survival was seen. The similarity in tumor biology may indicate that CDRCC patients could respond equally favourably to novel targeted therapies.

**Key Words:** kidney, nephrectomy, renal cell carcinoma

### DIS03.13

#### SWL outcomes with new vs. re-used electrodes: a prospective comparison

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**Introduction:** In an effort to reduce the cost of SWL, electrodes are frequently used beyond their recommended 100 percent limit.

**Methods:** This retrospective study analysed the performance of the ELCO124 electrode. 216 patients with a simple previously untreated radio-opaque stone located within the renal collecting system, were treated on the Phillips LithoTron using either new (N), or used once (RE) electrodes, and were followed with KUB's to assess stone area and stone free status. Stone-free status was confirmed with either renal tomography,

**Table 1. Abstract DIS03.13**

	ALL	N	RE	p-value
Success rate at 3 months, n (%)	136 (67.0)	104 (63.8)	32 (80.0)	0.05
Complication rate, n (%)	34 (15.8)	29 (17.3)	5 (10.6)	0.27
Ancillary procedure, n (%)	60 (29.3)	52 (31.7)	8 (19.5)	0.17

non-contrast spiral CT scan, or ultra-sound. Success rate was defined as stone free or adequate fragmentation (asymptomatic fragments <5mm), or sand (fragments = or < 2mm), at 3 months post-treatment.

**Results:** The groups were similar on gender, age, BMI, stone location, side, stent insertion and stone size. SWL success rates were greater in patients treated with RE electrodes (see table) and there was a trend to lower complication rates and fewer ancillary procedures. Patients treated with RE electrodes required fewer shocks (2302 vs. 2675,  $p=0.01$ )

**Conclusions:** Re-used electrodes appear to provide better fragmentation than do new electrodes on the Phillips LithoTron. As a result, cost-savings and improved outcomes can be realized by reusing electrodes between patients.

**Key Words:** kidney, lithotripsy, nephrolithiasis

### DIS03.14

#### Comparison of fast versus slow extracorporeal shockwave lithotripsy rate in the treatment of urinary stones performed by the same urologist at vancouver general hospital

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**Introduction:** Increasing interest in Shock Wave Lithotripsy (SWL) treatment at a slow rate of delivery (60–80 shocks/minute) has revitalized SWL research. The goal of this study is to compare the fragmentation efficacy of SWL using a slow or fast rate of shock wave delivery.

**Methods:** We retrospectively analyzed all cases of SWL performed by a single practitioner (SLG) between July 2005 and March 2006 at a referral lithotripsy centre using a Dornier Doli S Lithotripter. Slow rate of shock wave delivery was defined as 80 shocks per minute (spm), and fast rate defined as 120spm. Data was collected on rate of delivery, stone location, maximal size, procedure time, and patient BMI. Patients were imaged at least 30 days post-procedure. Treatment success was defined as the absence of stone or an asymptomatic residual stone fragment less than 4mm. The results were analyzed using the Fisher's Exact method.

**Results:** A retrospective review of 101 cases was performed (67 kidney stones and 34 ureteric stones). Seventy cases were treated using a fast rate of delivery and 31 using a slow rate. The mean age was 56.2 (22 to 95) years old for the renal stones group and 54.4 (23–84) for the group with ureteric stones. The cases were stratified by rate of shock wave delivery and stone location; defined as kidney and ureteral stone groups. They were also further categorized according to stone size, intensity level and number of shocks. The overall success rate for combined renal and ureteral stones treated at a fast rate of shock wave delivery was 67.1% (47 cases) versus 71.0% (22 cases) in the slow rate group ( $p=0.8181$ ).

**Conclusion:** The current use of slow rate lithotripsy is safe and doable. Although the slow rate of shock wave delivery showed slightly better fragmentation than the fast rate in our series, no significant difference was observed which may be due to the small sample size in this study. Future collection of data on post-procedure complications and related symptoms in a larger series as well as prospective randomized controlled trials may be helpful in determining the better treatment approach.

**Key Words:** calculi, nephrolithiasis, ureter

### DIS03.15

#### The results of reduced dietary salt intake in hypercalciuric stone formers in a referral kidney stone clinic

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**Introduction:** A large proportion of hypercalciuric stone formers have high normal/high urine sodium on 24-hr urine collection. Dietary salt restriction is considered the first step in reducing urinary calcium in the setting of elevated urine sodium. Whether a single dietitian counseling

session is adequate enough to reduce dietary salt intake to instill a change in 24 hr urine variables has been questioned. The objective of this study was to determine the effect of a single dietitian counseling session on reducing urine sodium and calcium at our center.

**Methods:** Consecutive recurrent hypercalciuric (>7.5 mmol/day) calcium stone formers with high normal/high urinary sodium levels (>150 mmol/day) were reviewed. Patients on diuretics were excluded. Two sets of 24-hr urine collections were obtained pre-counseling. All patients then attended a single 45-minute counseling session with a registered dietitian with general recommendations for stone prevention outlined with an emphasis on reduced sodium intake. A 24 hour urine specimen was subsequently collected for comparison. Paired *t*-tests were used to compare 24 hour urine results pre- and post-intervention.

**Results:** Of 23 consecutive patients, 8 were female and 15 were male. Average age was 51 years. Mean follow up was 2 months. There was no significant difference in urine volume pre- or post-treatment (2.348 vs. 2.567 liters;  $p=0.21$ ) possibly reflecting attendance at a dedicated kidney stone clinic. Sodium (236 vs. 191 mmol/day;  $p=0.047$ ) was significantly lower after a single-visit counseling session by a dietitian. Unfortunately, no statistically significant reduction in urinary calcium (9.55 vs. 9.28 mmol/day;  $p=0.72$ ) resulted to parallel the reduction in urinary sodium.

**Conclusion:** Counseling by a dietitian on salt restriction during a single visit resulted in a significant reduction in urinary sodium in our hypercalciuric stone patients. However, this urinary sodium reduction was not statistically sufficient to affect urine calcium. With a larger sample a change in urinary calcium may become apparent. Further research into dietary counseling with multiple dietitian visits and monitoring of compliance with repeated food diaries is warranted.

**Key Word:** calculi

### DIS03.16

#### Cost analysis of non-elective endourological management of urolithiasis—a case for scheduled urgent definitive care

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**OBJECTIVE:** To analyse the costs associated with non-elective endourological management of urolithiasis within The Ottawa Hospital.

**Methods:** A review of a single urologist's computerized billing database identified patients admitted to a tertiary care center for urgent endourological management of urolithiasis. Patients admitted and operated on for pain secondary to urolithiasis were included in the analysis. Exclusion criteria included patients who underwent endourological management for urolithiasis-related complications, such as infection, renal insufficiency, or retained ureteral stent. Patient demographics, stone characteristics, operative procedure and preoperative length of stay (LOS) awaiting non-elective, after-hours operating room availability were reviewed.

**Results:** From July 2002 to January 2006, a total of 152 cases were performed non-electively after regular operating hours; 129 cases were performed for the indication of pain. Number of pre-operative days awaiting operating room availability totalled 233, with the mean (SD) pre-operative admission stay of 1.91 days (1.88 days). Per diem cost for standard ward accommodation is \$1700 (CAD) resulting in a mean cost projection for pre-operative LOS of \$3,247 per patient. Cost of preoperative LOS awaiting non-elective operating room availability over the study period totalled \$396,100.

**Conclusion:** Significant costs are associated with inpatients awaiting access to urgent non-elective operating room availability. Patients admitted for urgent endourological management of pain secondary to urolithiasis possibly represent a cohort of patients that could be managed in a scheduled, urgent operating room. Further feasibility studies are required to assess the potential for an urgent endourological operating room designed to provide definitive stone management to all patients in The Ottawa Hospital.

**Key Words:** lithotripsy, nephrolithiasis, ureteroscopy