

Unmoderated Posters Oncology: Prostate

UP-15

Correlation of Low Urine Prostate Cancer gene 3 (PCA-3) Levels and Prostate Magnetic Resonance Imaging (MRI) Findings Among Patients on Active Surveillance (AS)

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Background: MRI is increasingly being offered as an adjunct to AS in order to minimize risk of disease progression. PCA-3 has also been reported as associated with amount and grade of cancer at biopsy. We set out to determine if prostate MRI held any utility among men with low (<35) PCA-3 test result.

Methods: Men on Active Surveillance (AS) were offered PCA-3 testing and prostate MRI's. All men had very low risk prostate cancers (PSA <10, T1C, Gleason 6 and less than 4 cores with no core >50% involved by length). The fates of men with positive and negative PCA-3 were then correlated with MRI findings. MRI was done on a 3 Tesla unit using endorectal coil and multi-parametric assessment by an experienced radiologist (MH).

Results: We studied 27 patients on AS with both PCA-3 and MRI. 18 patients tested positive for PCA-3 and 9 were negative. Among the 18 positive PCA-3 patients, 9 had completed MRI scans and 5 of those (55.5%) had evidence of MRI detectable larger volume cancers (>1 cm). Conversely, among the 9 patients with negative PCA3 tests, none (0%) had evidence of MRI detectable tumours ($p=0.002$).

Conclusions: Among patients on AS with very low risk prostate cancers, PCA-3 tests are normal in approximately one-third of patients. If normal, MRI appears to add little utility in terms of discovering hidden larger tumours.

UP-16

The Role of FSH in Castration Induced Adipogenesis: Highlighting Differences Between Orchiectomy, GNRH Agonists and Antagonists

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Introduction: Androgen deprivation therapy (ADT) induces weight gain and development of metabolic syndrome. Different ADT modes have different effects on serum FSH levels. Adiposity accompanies the incremental increase in serum FSH levels in menopause. We hypothesized that castration-induced FSH levels elevation can similarly result in adipogenesis and that GNRH antagonists which lower FSH levels will associate with reduced adiposity as compared to GNRH analogues and orchiectomy.

Methods: Adipocyte differentiation and intracellular lipid accumulation were examined in the presence of FSH (0-1000 IU/L). Lipogenesis was assessed by image analysis (oil red staining) and by immunoblotting for fatty acid synthase (FAS). C57Bl/6 mice (n=30) were divided to: orchiectomy + vehicle, sham procedure + vehicle, orchiectomy + GNRH antagonist (degarelix 50 mg/kg in vehicle), sham + degarelix, orchiectomy + GNRH analogue (enantone 2 mg/kg in vehicle), and sham + enantone. Serum testosterone, LH and FSH levels and differences in animal weight and visceral fat mass were determined at 6 weeks. BMI was measured as weight (gr) divided by the distance between the tail root and the lower incisors (cm²).

Results: Mean lowest and highest FSH levels were recorded in mice treated with Degarelix vs. orchiectomy (2.48 and 227 ng/mL). Mean lowest and

highest testosterone levels were in mice treated with orchiectomy+degarelix vs. sham control (0.12 and 13.1 ng/ml). Mice treated with degarelix had significantly lower BMI compared to enantone ($p=0.02$). Visceral fat accumulation was significantly lower in mice castrated by degarelix as compared to enantone ($p=0.035$). Addition of degarelix or enantone to orchiectomy increased differences in visceral fat and BMI between the two groups (0.12gr vs. 0.47gr and 3.73 vs. 4.29 gr/cm²). In vitro, FSH increased lipid accumulation and FAS expression.

Conclusions: Higher FSH levels during ADT promote fat accumulation and weight gain in preclinical models.

UP-17

Novel Laparoscope Defogging and Cleaning Device for Robot-assisted Laparoscopic Prostatectomy (RALP)

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Introduction and Objectives: Maintaining efficiency and optimal visualization are critical components of robot-assisted cases, where removal of the laparoscope to defog or clean the lens requires time and can be cumbersome. We evaluate the Advanced Laparoscopic "Care Kit" (New Wave Surgical, Coral Springs, FL) as a novel set of accessories that defogs and cleans the laparoscope during RALP.

Methods: Laparoscope warming and cleaning equipment were replaced in our operating suite with the Care Kit for 60 consecutive patients who underwent transperitoneal RALP. Our observations and the features of the Care Kit are reviewed.

Results: The Care Kit includes a defogging device that heats an internal reservoir of surfactant based alcohol-free anti-fog solution to 120F. The device remains heated for 5 hours. The surfactant acts as a soap that can remove dried debris from the lens. Because the device is self-contained and hand held, it can be brought to the laparoscope with minimal displacement of the laparoscope from the trocar. The Care Kit also includes microfiber cleaning pads that avoid scratching the delicate lens. A trocar cleaning sponge for removing debris inside the trocar cannula is also supplied. Subjectively, the Care Kit was simple to use by the bedside assistant and effective at maintaining optimal laparoscope visualization. Transfer of the laparoscope to the back table for warming intraoperatively was not required in all 60 cases. The Care Kit protects the laparoscope while it is initially lying on the back table from the dangers of scratching and falling associated with using traditional laparoscope warmers.

Conclusions: The Care Kit was effective in preventing fogging of the laparoscope during RALP. It has the potential to minimize delays that can result from laparoscope defogging and cleaning, thereby reducing operative times.

UP-18
Opioid-free Analgesia Following Robot-assisted Laparoscopic Prostatectomy (RALP)

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Introduction and Objectives: Opioid analgesia following abdominal/pelvic surgery has potential adverse events and can delay return of bowel function. To minimize its use, we utilized scheduled intravenous (IV) acetaminophen and ketorolac for perioperative analgesia following RALP.

Methods: Prospectively collected data from hospital records of consecutive transperitoneal RALP patients using perioperative IV acetaminophen and ketorolac for analgesia were reviewed. All procedures were performed under general anesthesia utilizing a balanced technique. The balanced anesthetic was not standardized with the exception that patients received acetaminophen 1000mg IV over a 15 minute infusion and ketorolac 30mg IV prior to extubation. Acetaminophen 1000mg IV was administered q6 hours post-surgery, while ketorolac 30mg IV was administered at q8 hour intervals. Patients were provided a clear liquid diet and ambulating the evening of surgery. Following passage of flatus and tolerating a regular diet, patients were discharged home.

Results: 44 patients had a mean age of 61.8±6.4 years and an American Society of Anesthesiologists (ASA) class of 2.7±0.5. Mean operative time was 90.4±22.8 minutes and estimated blood loss was 68.4±22.3 mL. Patients had a bilateral (33), unilateral (5) or non (6) nerve-sparing RALP. Mean hospitalization and urethral catheter duration were 21.3±4.7 hours and 5.0±2.0 days, respectively. 14 (31.8%) patients received parenteral opioid medication in the PACU, but did not require opioid medication on the hospital floor; while 27 (61.4%) patients did not require administra-

tion of parenteral/oral opioid analgesia in the PACU/hospital floor. No immediate/delayed adverse events were noted.

Conclusions: Perioperative scheduled IV acetaminophen and ketorolac are effective for pain management following RALP. This regimen has the potential to decrease the need for postoperative opioid analgesia, thereby lowering the risk of opioid-associated adverse events.

UP-19
The Impact of Patient Demographics on Prostate Cancer Treatment Choice

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Introduction and Objectives: Many factors can influence prostate cancer treatment choice, and these are not limited simply to clinical disease characteristics. Prostate cancer affects men within a diverse age, ethnic, and socioeconomic cohort. The purpose of this study was to identify demographic characteristics associated with treatment choice within a large managed care organization.

Methods: From March 2011 to September 2012, all men with biopsy-proven prostate cancer were asked to participate in a quality of life study at 12 regional hospitals at Kaiser Permanente Southern California, the largest managed care organization in California. Men were subsequently counseled and underwent surgery, external beam radiation therapy (EBRT), brachytherapy, active surveillance, watchful waiting, or hormone therapy. Select demographic and clinical parameters were compared between treatment groups using chi-squared and ANOVA tests.

Results: A total of 1698 men were enrolled in the study, of which 739 (43.5%) had surgery, 198 (11.7% total; 8.1% EBRT, 3.6% brachytherapy) underwent radiation treatment, 469 (27.6%) chose active surveillance or watchful waiting, and 292 (17.2%) received hormone therapy. Significant demographic factors identified included age, marital status, and regional education and income levels ($p<0.05$) (Table 1). Ethnicity and primary language distributions were similar in all treatment groups. The majority of clinical factors studied, apart from body mass index (BMI), varied significantly as well.

Table 1. UP-19

Demographic factor	Surgery (%)	BT (%)	EBRT (%)	AS/WW (%)	HT (%)	p value
Age						<0.0001
40 to <50	52 (77.6)	1 (1.5)	1 (1.5)	9 (13.4)	4 (6.0)	
50 to <60	250 (60.2)	13 (3.1)	11 (2.7)	113 (27.2)	28 (6.8)	
60 to <70	357 (47.4)	33 (4.4)	58 (7.7)	221 (29.4)	84 (11.2)	
≥70	80 (17.3)	14 (3.0)	67 (14.5)	126 (27.2)	176 (38.0)	
Marital status						<0.0001
Partnered	573 (48.8)	43 (3.7)	92 (7.8)	274 (23.3)	192 (16.4)	
Single	139 (40.5)	15 (4.4)	28 (8.2)	103 (30.0)	58 (16.9)	
Ethnicity						0.17
Black/African American	109 (42.1)	8 (3.1)	22 (8.5)	68 (26.3)	52 (20.1)	
White/Caucasian	331 (40.9)	31 (3.8)	70 (8.6)	238 (29.4)	140 (17.3)	
Latino/Hispanic	213 (51.3)	15 (3.6)	27 (6.5)	98 (23.6)	62 (14.9)	
Asian/Other	86 (40.2)	7 (3.3)	18 (8.4)	65 (30.4)	38 (17.8)	
Primary language						0.11
English	645 (43.2)	53 (3.6)	116 (7.8)	418 (28.0)	260 (17.4)	
Spanish	86 (47.5)	6 (3.3)	15 (8.3)	44 (24.3)	30 (16.6)	
Other						
Education	77.8%	75.3%	75.3%	79.2%	74.5%	0.007
Income	\$73,315	\$65,532	\$68,201	\$73,177	\$65,728	0.0012

BT: brachytherapy; EBRT: external beam radiation therapy; AS: active surveillance; WW: watchful waiting; HT: hormone therapy.

Conclusions: These data suggest that the choice of prostate cancer treatment may be influenced by multiple demographic factors, in addition to common disease parameters. Acknowledging these and other social health determinants may be important in guiding therapeutic decisions for prostate cancer.

**UP-20
Marine Omega-3 Fatty Acids and Risk of Prostate Cancer Progression During Active Surveillance**

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Introduction and Objectives: Marine omega-3 fatty acids, mainly eicosapentaenoic acid (EPA), are suggested to be protective for prostate cancer (PCa) aggressiveness. Many methodological limitations are found in previous epidemiological studies. In particular, no study measured fatty acids in the target prostate tissue. Our objectives were to determine the associations between omega-3-measured in prostate tissue, red blood cells (RBC) and diet-and PCa grade progression during active surveillance. **Methods:** We recruited, in a phase II clinical trial of active surveillance, 59 men diagnosed with Gleason 6 PCa involving less than 6 of 12 cores. At repeat biopsy, 2 additional biopsy cores were snap frozen. Fatty acid profiles were determined by gas chromatography. Diet was measured using a validated food frequency questionnaire. Fligner-Policello test was used to test significance of associations between fatty acids and PCa grade. Logistic regression was used to estimate risk of Gleason 7 upgrade across tertiles of prostate tissue EPA.

Results: At first repeat biopsy session, 17/59 (29%) men had an upgrade to Gleason 7 or more. The prostate tissue of men with Gleason 6-only PCa had a higher level of EPA (mean=0.19% vs. 0.04%, $p=0.00007$) than that of men with Gleason 7 PCa. Differences in EPA levels across grade were progressively less significant when measured in RBC ($p=0.041$) and in diet ($p=0.083$). Compared to men in the lowest tertile of prostate tissue EPA, men in the highest tertile had a decreased risk of Gleason 7 upgrade (OR: 0.05; $p=0.007$).

Conclusions: An elevated marine omega-3 EPA content in the target prostate tissue appears to be protective in a dose-dependent manner against prostate cancer aggressiveness, during active surveillance. The EPA difference across grade was progressively less marked as the EPA measure was more distant from target prostate tissue. This measurement error could be an information bias explaining the controversy of previous epidemiological studies.

**UP-21
A New Knowledge Transfer Strategy for Prostate Cancer Management in Ontario**

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Introduction: Cancer Care Ontario (CCO) Surgical Oncology Program is a provincial agency whose mission is to improve surgical care, minimize practice aberrations and optimize resource usage via clinical practice guideline (CPG) development and community of practice engagement. To increase uptake of CPG recommendations, active implementation strategies with a multifaceted approach are needed. CCO developed a multidisciplinary online list serv discussion forum to enhance dissemination to urologists and pathologists of a CPG on prostate cancer (CaP) surgical and pathological quality performance for radical prostatectomy (RP). (Key surgical recommendations: positive margin rate <20% for pT2, <35% for pT3; transfusion rate <10%; rectal injury rate <1%, detailed clinical information for pathologist). We report the process and feedback of a new knowledge transfer and exchange (KTE) strategy.

Table 1. UP-21. Total 162 prostate cancer list serv respondents

% respondents who read scenarios & followed discussion	100%
Average # hours spent reading/discussing per scenario	2.3 hours
% respondents who posted comments/active discussion	34%
Average # of comments per scenario	37.8
% respondents who read	94%
Evaluation of scenarios	
Response rate for scenario evaluation	17.8%-43% (Taken from breast & colorectal list servs conducted contemporaneously)
% agreed:	80%
Overall final evaluation of list serv initiative and process	
% very satisfied or satisfied with overall list serv initiative	92%
% very satisfied or satisfied scenario format	93%
% very satisfied or satisfied with list serv e-mail format	91%
% very satisfied or satisfied with timelines	88%
Increased Awareness of New/Different Practices:	74%
Will this change or has it changed your practice?	
No, not at all or very little	34%
Yes, somewhat	35%
Yes, to a great extent	19%

Methods: Using an electronic mailing list software app., the “list serv” consisted of 4 clinical scenarios posted online, allowing real-time discussion. For each scenario, highlighted key CPG recommendations, clinical information and questions to stimulate discussion were posted on Weeks 1, 2. Participants posted comments with clinical experts facilitating discussion and addressing questions. Recommendations from the CPG and supporting evidence were posted on Week 3. At the end of each scenario and entire list serv, online participant evaluation was sought.

Results: 162 participants included Urology (58), Radiation (22) & Medical (5) Oncology, Pathology (57) and Others (22). Results of participation and evaluation of process are listed in Table 1.

Conclusions: There was excellent participation and satisfaction with the process and format. Although objective quantitative assessment was not possible, self-reported increased awareness of CPG recommendations and plans for practice change suggest this internet-based tool is an effective knowledge transfer and exchange strategy.

UP-22

PSA Outcome for Permanent Prostate Seed Brachytherapy After Active Surveillance for ≥12 Months

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Introduction and Objectives: We assessed prostate-specific antigen (PSA) outcome after permanent 125Iodine prostate brachytherapy (PB) for localized low or intermediate risk prostate cancer for patients initially on active surveillance.

Methods: We reviewed the medical records of 720 patients treated in our department with either exclusive PB or in combination with external beam radiation therapy. Patients were included if their first biopsy with cancer was at least 350 days before PB. Patients had to have no androgen deprivation therapy and a minimum PSA follow-up of 24 months. The rate of patients attaining a PSA at last follow-up of ≤0.2, ≤0.5 ng/mL and patients with biochemical relapse (nadir+2 ng/mL) was calculated.

Results: Sixty-seven patients met our inclusion criteria. Median follow-up was 43.3 months (range 24.4-79.1). 63% had a follow-up >4 years. Median age at the time of treatment was 66 years (51-78). Gleason score was 7 in 39 % and PSA 10-20 ng/mL in 12 % of patients. 60% of patients had PB only. Reasons for intervention on surveillance were cancer progression (PSA- and/or progression on biopsy) in 67 %, patient preference in 28% and other causes in 5%. Median time from initial positive biopsy to PB was 593 days (350-2311). Most patients (57%) achieved a PSA level ≤0.2 ng/mL and an additional 21 % had ≤0.5 ng/mL at last follow-up. Thirteen patients (19%) had a last PSA of 0.5-3.3 ng/ml. Two patients (3 %) experienced biochemical failure.

Conclusion: Our early results suggest that PB is an effective treatment for patient on active surveillance treated ≥1 year after the initial diagnosis.

UP-23

Matched Cohort Study of Low-risk Prostate Cancer Treated with Standard External Beam Radiotherapy Versus Stereotactic Body Radiotherapy

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Introduction and Objectives: Radiation therapy is a standard treatment option for patients with prostate cancer. The purpose of this study is to evaluate and compare biochemical control and late toxicities of low-risk prostate cancer patients treated with standard external beam radiotherapy

Table 1. UP-23

	STND (n=81)	SBRT (n=84)	Fisher exact test p value
Bowel toxicities			
Hematochezia	21 (25.93%)	21 (25.00%)	0.89
RT related	8 (9.88%)	6 (7.14%)	0.59
Laser coagulation	3 (3.70%)	2 (2.38%)	0.68
Fistula	0 (0.00%)	1 (1.19%)	0.32
Unknown	3 (3.70%)	1 (1.19%)	0.36
Bladder toxicities			
TURP	3 (3.70%)	2 (2.38%)	0.68
Hematuria	1 (1.23%)	0 (0.00%)	0.49

STND: standard external beam radiotherapy; SBRT: stereotactic body radiotherapy; RT: radiotherapy; TURP: transurethral resection of the prostate.

(STND; median 76 Gy in 38 fractions) versus stereotactic body radiotherapy (SBRT: 35 Gy in 5 fractions) at the Odette Cancer Centre.

Methods: A matched cohort study of 165 low-risk prostate cancer patients was conducted. From 2006-2008, 81 patients were treated with STND and medical charts were reviewed retrospectively; during the same period 84 patients were treated with SBRT and followed prospectively. 5 and 1 patients, respectively, were treated with short-term neoadjuvant androgen deprivation therapy and excluded from biochemical analyses.

Results: At baseline, 87% of patients were T1c, 13% T2a; 100% had GS 6; median PSA 6.2 (range 0.5-10) ng/ml. There were more patients in the STND cohort who had T2a disease (21% vs. 6%, $p=0.0055$); all other factors were well balanced. The median follow-up for the STND and SBRT cohorts were 62 and 57 months, respectively. Four patients, 2 in each cohort, had biochemical failure. There was no significant difference in biochemical disease-free survival between the two cohorts (96.9% vs. 97.4% at 60 months, respectively, $p=0.94$). There was also no significant difference in bowel or bladder toxicities experienced by patients in the two treatment groups (Table 1).

Conclusions: SBRT shows equivalent tolerability and effectiveness as STND at our centre. However, SBRT requires fewer patient visits, is more convenient and is less costly to the patient and department than STND. Further prospective studies of SBRT are ongoing.

UP-24

Short-term Androgen Deprivation Therapy is not Associated with Depression: 1-Year Interim Results of a Prospective Cohort Study

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Introduction and Objectives: The presence, timing and magnitude of effect of androgen deprivation therapy (ADT) on anxiety and depression are controversial in prostate cancer (PC) research. This is an interim analysis of a 2-year prospective cohort study investigating the influence of ADT on patient depression and quality of life.

Methods: Three cohorts of men were enrolled: those initiating ADT for advanced PC, those undergoing adjuvant ADT in a combined-modality curative protocol for higher risk cancer, and a control group consisting of patients on watchful waiting. Patients are assessed every 3 months from baseline (i.e., before ADT) for 2 years. Questionnaire data were collected to assess depression and quality of life (QoL) at every time point.

Results: There were no significant group differences at baseline in terms of age ($p=0.15$), marital status ($p=0.26$), depression ($p=0.06$) or mental QoL ($p=0.40$). A 5x3 (Time x Group) Repeated Measures ANOVA examined differences in physical and mental QoL, and depression from the baseline assessment to the 1 year point. Both patient groups on ADT reported poorer physical QoL than controls ($p=0.02$) but there was no effect for time ($p=0.20$) or for the interaction between time and group ($p=0.25$). There was no effect for the time analysis ($p=0.94$), or the group analysis ($p=0.69$) or the interaction ($p=0.60$) for mental QoL. There were changes in depression over time ($p=0.03$; all increased depression) but no group ($p=0.33$) or interaction effect ($p=0.36$). There was a depression spike at 6-months. This was manifest by an increase in depression from 3-6 months ($p=0.05$), followed by a decrease from 6-9 months ($p=0.07$).

Conclusions: In this prospective study, individuals receiving any form of treatment ADT had significant decreases in physical health over time, in comparison to controls. All individuals within this sample appeared to have an increase in depressive symptoms over the course of the year.

UP-25

Salvage Therapy with Bicalutamide 150mg and Tamoxifen in Patients with Rapidly Rising PSA after Radical Prostatectomy

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Introduction and Objective: To evaluate the efficacy of bicalutamide 150 mg plus tamoxifen 20 mg once daily and the duration of prostate-specific antigen (PSA) response after biochemical recurrence in cases of rapidly rising PSA after radical prostatectomy (RP).

Method: This single centre, retrospective study included 86 prostate cancer (PCa) patients treated with RP who had a rapidly rising PSA recurrence. Patients were elected to be treated with daily bicalutamide 150 mg plus tamoxifen 20 mg (to minimize gynecomastia) to preserve their quality of life and libido. Response was defined as positive (decline or stable PSA) or negative (PSA increase). The duration of response is the time from starting treatment to first PSA rise after reaching nadir.

Results: The mean PSA at start of treatment was 2.87±7.55 ng/mL. The mean duration of treatment was 38.9±27 months and the median was 32 months. Of this group, 58 patients reached undetectable PSA. The duration of response was 42.5±25 months for the complete responders compared to 31.5±29.4 months for those that did not reach undetectable PSA ($p=0.07$). Analyses were performed to correlate the duration of response with various baseline parameters such as stage, Gleason score, margin status, nodal status and PSA at the start of treatment. Only Gleason score was significantly correlated with the duration of response: of the 17 patients with Gleason 6 the mean duration was 52±25.8 months compared to 34.6 ±23.5 months for the 61 patients with Gleason ≥7 ($p=0.009$). The main side effect was hot flushes which were managed by reduction of the tamoxifen dose. No patient experienced significant gynecomastia.

Conclusions: Bicalutamide 150 mg plus tamoxifen 20 mg is an effective treatment for biochemical recurrence after RP for men wishing to minimize the side effects of LHRH therapy. Our results indicate that patients with Gleason 6 will have a longer duration of positive response.

UP-26

Capsaicin Enhances the Effect of Radiation in Prostate Cancer Through NFκB and Androgen Receptor Suppression

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Introduction and Objective: Radio-sensitizing agents sensitize cells to the lethal effects of ionizing radiation (IR). This permits use of lower doses of radiation to achieve equivalent cancer control thereby minimizing adverse effects to normal tissues. Given their lack of toxicity compounds occurring naturally in the diet make ideal potential radio-sensitizing agents. Capsaicin, the active compound chilli peppers, has recently been reported to have some anti-carcinogenic potential in vitro. The objective of the present study is to assess the how capsaicin is radio-sensitizing capacity in vitro an in vivo models.

Methods: Using clonogenic assays the effect of IR (1-8 Gy) and/or capsaicin (1-10µM) on colony formation rates was assessed in human PCa cell lines (LNCaP, PC3, PC3AR2, DU145). Western Blot and ICC were performed to look for alterations in AR and NFκB expression. Athymic nude mice were inoculated subcutaneously with human PCa (LNCaP) cells. Once xenografts reached 100 mm³ mice were randomized into 4 groups (15/group); control (no treatment), capsaicin alone (5 mg/kg/d), IR alone (6 Gray) and capsaicin and IR. Treatments were administered over a two-week time period. Tumours were fixed and stained for pathological analyses and IHC evaluation.

Results: There were no differences in food consumption or body weight of mice between groups. Two mice experienced mild to moderate inflammation of the stomach. No other toxicities were observed. Mice treated

with capsaicin or IR alone had a significant reduction in tumour growth overtime ($p<0.001$). Mice treated with capsaicin and IR capsaicin had a reduction in the tumour volume greater than either capsaicin alone ($p<0.001$) or radiation alone ($p<0.03$). IHC analysis revealed a reduction in the proliferative index, AR and NFκB expression, and an increase in apoptosis.

Conclusion: Further studies should be carried out to examine the efficacy for capsaicin as a radio-sensitizing agent in pre-clinical models.

UP-27

Continence Outcomes Following Robotic-assisted Laparoscopic Prostatectomy: A Single-surgeon, Single-institution Experience

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Introduction and Objectives: Prostate cancer remains a leading cause of morbidity and mortality in the US and worldwide, accounting for 33,000 deaths in the US alone in 2011. Therefore, development of highly effective and minimally invasive treatment methods remains a priority in the clinical management of prostate cancer. Robotic-assisted laparoscopic prostatectomy (RALP) has rapidly become the minimal-invasive surgical modality of choice for the treatment of prostate cancer. The object of the current analysis was to evaluate the importance of predictors of early (6 weeks) continence in patients undergoing RALP.

Methods: We performed a retrospective analysis of continence outcomes at a single high-RALP volume institution performed by a single surgeon (IAT). Patient's demographics and baseline characteristics were assessed. We compared the number of pads used at six weeks after RALP in patients who underwent nerve sparing versus those who had non nerve sparing. The statistical significance threshold was set at $p<0.05$. Analyses were conducted using the STATA 12 statistical package.

Results: From November 2008 until September 2012, 1051 patients underwent RALP. One hundred thirty eight (%13) patients have missing values. Nine hundred and thirteen patients were analyzed. The median number of pads used per day at 6 weeks post-RALP is 1-2 pads, (mean 1.78; SD 1.58). Table 1 shows a comparison between the number of pads in the nerve sparing versus the non-nerve sparing group.

Conclusion: Our analysis shows nerve sparing significantly improves continence at six weeks after RALP. A major strength of our study is that the procedures were performed by a single surgeon at a single institution.

Table 1. UP-027

	No. patients	No. pads		p value
		Mean	SD	
Nerve sparing	786	1.61	1.58	<0.0001
Non-nerve sparing	127	2.81	2.18	

SD: standard deviation.

UP-28**The Impact of Multiple Biopsies on Erectile and Voiding Function After Radical Prostatectomy: A Population-based Assessment**

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Introduction: A previous study showed that a delay in radical prostatectomy (RP) after prostate cancer (PCa) diagnosis is associated with worse functional outcomes postoperatively. Since delay of RP likely results in increased number of prostate biopsies (PBx), we hypothesized that increasing number of PBx prior to RP was associated with higher rates of erectile dysfunction (ED) and urinary incontinence postoperatively.

Methods: Overall, 10,743 men without a baseline diagnosis of ED or incontinence who underwent RP for clinical stage T1–2, low-grade PCa between years 1995 and 2005 within the SEER Medicare-linked database were identified. For each patient, the number of PBx prior to RP was abstracted, and dichotomized as <2 vs. ≥2. Postoperative functional outcomes consisted of urinary incontinence and ED diagnosis/procedure. Univariable and multivariable logistic regression analyses were performed. Covariates consisted of patient age at diagnosis, race, baseline comorbidities, clinical tumour stage, year of diagnosis, Metropolitan areas, marital and socioeconomic status.

Results: Overall, 7739 (71.8%) and 3004 (28.2%) patients had <2 or ≥2 PBx prior to RP, respectively. Patients who received ≥2 PBx prior to RP had higher rates of ED diagnosis (36.6 vs. 31.3%) and procedure (5.8 vs. 4.9%), as well as urinary incontinence diagnosis (31.4 vs. 24.8%) and procedure (24.8 vs. 18.5%, all $p < 0.001$). After accounting for all other confounders, patients with ≥2 PBx prior to RP were respectively 20 and 10% more likely to experience an ED diagnosis and procedure postoperatively (both $p < 0.01$). Similarly, ≥2 PBx was associated with respectively 18 and 23% higher risk of postoperative urinary incontinence diagnosis and procedure, (both $p < 0.01$).

Conclusions: Patients who receive multiple PBx prior to RP for clinically localized PCa may be at risk of higher rates of ED and urinary incontinence postoperatively. Such concerns should be communicated to patients during counseling.

UP-29**Robotic-assisted Radical Prostatectomy in Biopsy Proven High-grade Prostate Cancer: Experience From Two Tertiary Centres with Gleason Downgrading at Final Pathology Assessment**

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Introduction and Objectives: The use of radical prostatectomy as part of the treatment algorithm in high-grade prostate cancer (HGPCa) remains controversial. On the other hand, there are well-known limitations of conventional TRUS-guided biopsy such as insufficient tissue sampling and pathologist experience. Such limitations raise concerns about the accuracy of Gleason grading as a main predictor of PCa aggressiveness. Based on validation by the final pathology assessment of prostatectomized specimens, we searched a cohort of patients with Gleason downgrading regarding association with other pathology characteristics, oncological and functional outcomes.

Methods: Among a total of 965 collective RARP consecutive cases, 59 (6.1%) patients with high-grade PCa underwent RARP at two, high-volume tertiary centres between October 2006 and August 2012. We assessed the rate of pathological Gleason downgrading, status of surgical margins, extracapsular extension, seminal vesicle invasion, lymph node involvement, biochemical recurrence (PSA ≥ 0.20 ng/ml) and recovery of urine continence (0 pads usage).

Results: Median follow-up was 12 months (range 1–24). Sixteen patients (27.1%) had positive surgical margins, majority (70%) where pT3-disease. Nineteen men (32.3%) had extra-capsular extension and eight (13.5%) had seminal vesicle invasion. Six patients (10.1%) did not reach undetectable PSA on initial postoperative visit and were treated with ADT, 3 of which had positive lymph nodes. Overall biochemical recurrence was observed in a total of 7 patients (11.8%) with median time for recurrence 12 months. Only four men had PSA ≥ 0.20, the remaining had early salvage EBRT with PSA < 0.20. Nine patients (15.2%) underwent adjuvant/salvage EBRT +/- ADT. In total, 34 patients (57.6%) were downgraded to Gleason 7 on final surgical pathology, and yet another two patients downgraded to Gleason 5 and 6. Finally, pad-free urine continence at 3 and 12 months were 64.5% and 82.9%, respectively.

Conclusions: In spite of advances in prostate biopsy diagnosis of HGPCa, we observed a significant likelihood for disease downgrading on final pathology. Most patients had organ/ specimen confined disease, adequately served by RARP and avoided ADT, while maintaining known advantages of RARP. Therefore, it should be taken into consideration by robotic surgeons that not necessarily all biopsy proven HGPCa will have these features at final pathology.

UP-30**Is There a Role to Include Prostatic Anterior Zone Sampling as Part of Saturation Trans-rectal Ultrasound Guided Prostate Biopsy?**

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Introduction and Objectives: The prostatic anterior zone (AZ) is not targeted routinely by TRUS guided prostate biopsy (TRUS-Pbx). MRI is an accurate diagnostic tool for AZ tumours, but is often unavailable due to cost or system restrictions. We examined the diagnostic yield of office based AZ TRUS-Pbx.

Methods: 114 men at risk for AZ tumours were studied: Patients with elevated PSA and previous extended negative TRUS-Pbx (group 1, n=70) and actively surveyed low risk prostate cancer patients (group 2, n=44). Biopsy template included suspicious ultrasonic areas, 16 peripheral zone (PZ), 4 transitional zone and 6 AZ cores. Multivariate analysis was used to detect predictors for AZ tumours accounting for age, PSA, PSA density, prostate volume, BMI, number of previous biopsies and cores.

Results: Median PSA was 10.4 (group 1) and 7.3 (group 2). Age (63.8, 64.6), number of previous biopsies (1.5) and cores (17.8, 21.3) and prostate volume (57.3cc, 52.9cc) were similar for both groups. The overall diagnostic yield was 33% (group 1) and 91% (group 2). AZ cancers were detected in 19% (group 1) and 31% (group 2) but were rarely the only zone involved (1.4% and 4.5% respectively). Gleason > 7 AZ cancers were rare (7%) and often accompanied by equal grade PZ tumours. In multivariate analysis only prostate volume predicted for AZ tumours. Patients detected with AZ tumours had significantly smaller prostates (38.2cc vs. 61.9cc $p = 0.01$). Suspicious AZ ultrasonic findings were uncommon (6.1%).

Conclusions: TRUS-Pbx AZ sampling rarely improves the diagnostic yield of extended PZ sampling or changes risk stratification. Patients with AZ tumours had significantly smaller prostate volumes on TRUS.

UP-31**Efficiency and Outcomes of Robotic Surgery During the First Year of Implementation Using a Multi-surgeon Team Approach**

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Introduction and Objectives: To report our multi-surgeon team approach to initiating a robotic surgery program in Canada.

Methods: We reviewed the first year of robot assisted laparoscopic prostatectomy (RALRP) at our institution, from October 31, 2011 to October 31, 2012. Multiple surgeons performed the procedure, with a consistent surgical team and clinical care pathway. The time to perform each component of the procedure was recorded by the nursing staff. An independent data collector obtained pre- and postoperative information from the medical record.

Results: During the study period, 4 urologists performed a total of 104 RALRPs. The median PSA was 6.0 ng/ml (range 1.8 to 41) and median prostate volume was 32 cc (range 13-75). The Gleason score was 6 in 25 (24%), 7 in 65 (62.5%), 8 in 10 (9.6%) and 9 in 4 (3.9%) patients. Forty (39%) patients had extraprostatic tumour extension. The mean total operative time was 263 (SD 81) minutes with a linear decrease from approximately 338 minutes to 230 minutes (-1.0 minutes/case; $p < 0.001$) during the study period. The time required for anesthesia decreased from approximately 24 to 15 minutes ($p = 0.004$) and the mean surgeon time decreased from approximately 225 to 175 minutes ($p = 0.01$). The mean times required to dock the robot (7+/-3 minutes) and extract the prostate/leave the operating room (31±7 minutes) were consistent over time ($p > 0.05$). There were no intraoperative complications or conversions to an open approach. Postoperatively, 5 had anastomotic leak, 2 received a blood transfusion, 2 had urinary tract infection, 2 required catheter reinsertion, and 1 had pneumonia. The mean hospital stay was 1.45 (SD 0.66) days (range 1-5 days). Thirty-eight (36.5%) patients had a positive surgical margin. Sixty-two (60%) were completely continent at 3-months postoperatively. At last follow-up, 25 of 50 (50%) patients with bilateral nerve preservation had satisfactory return of erectile function for sexual intercourse with or without PDE-5 inhibitors.

Conclusions: Using a multi-surgeon team, RALRP has been safely implemented at our institution. Comparing these results to the single-surgeon experience may help determine the optimal method for initiating robotic surgery programs at other institutions.

UP-32**When Active Surveillance Fails: An Analysis of Manitoba Prostate Centre Surveillance Patients That Undergo Treatment**

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Introduction: PSA screening has resulted in a significant increase in the diagnosis of low risk prostate adenocarcinoma. Treating these cancers would cause significant morbidity with radical treatment. Active surveillance (AS) is an alternative to radical treatment for these cancers and to monitor them with the intent to treat radically once the cancer progresses.

Methods: In this retrospective study, patients treated at the Manitoba Prostate Cancer with an active diagnosis of Prostate Adenocarcinoma with Gleason $\leq 3+4$, multiple biopsies, $\leq 2b$ (with one exception), and PSA < 20 (two exceptions) were analyzed for changes in PSA, PSA doubling time, PSA density, Prostate volume changes, triggers for biopsy, triggers for treatment, types of treatment, changes in Gleason grading, pathological changes such as cores involved, percent minimum and maximum. Further biopsy intervals were assessed, follow-up time, and surgical pathology if available. Consent was obtained.

Results: Manitoba Prostate Centre has 194 patients on Active Surveillance; 64 of whom received treatment. Of the treated patients the median age was 65 with an average follow up of 5.3 years, and average of 2.6 biopsies each. Median interval to first biopsy was 9.5 months, and 12 between all biopsies. Majority of patients had Gleason 3+3 when started on active

surveillance. 68.8 percent had a final Gleason of $\geq 3+4$. 64.6 percent of initial biopsies were triggered by PSA, and 81.3 percent of treatment was triggered by biopsy results, i.e. Gleason progression or volume changes.

Conclusion: The Manitoba Prostate Centre treatment data of Active surveillance are consistent with what is found in the literature. The data collected represent a significant cohort of patients relative to available literature.

UP-33**Quality of Life at the End of Life in Men Diagnosed with Prostate Cancer: Results From the CaPSURE Database**

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Introduction and Objectives: The purpose of this study was to evaluate the impact of local therapies on health related quality of life (QOL) in men dying with a previous diagnosis of prostate cancer.

Methods: We studied patients from CaPSURE, a large longitudinal observational cohort of men that have biopsy proven prostate cancer. Patients were included in the analysis if they were diagnosed with non-metastatic prostate cancer, completed a minimum of 2 QOL questionnaires after diagnosis, and subsequently died of any cause. QOL was measured using the RAND SF-36. The primary outcome was association between prior local therapy and QOL. Men were stratified based on baseline characteristics, primary treatments, and cause of death (prostate cancer vs. other).

Results: 2296 men were diagnosed with non-metastatic disease and have subsequently died. Of these, 1076 (47%) completed a minimum of two QOL questionnaires. The mean age was 71.6 years (SD 8). Local treatment was used in 662 (62%) patients with 292 (27%), 320 (30%), and 50 (5%) undergoing prostatectomy, radiotherapy, or cryotherapy, respectively. Median follow-up after local therapy was 67 months (IQR 42-94). The unadjusted rate of death due to prostate cancer was 10% at 5 years after primary treatment. In univariate analysis, prior local therapy was associated with higher mean SF-36 Physical Function, Vitality, and General Health scores within 5 years prior to death ($p < 0.01$). These associations did not remain significant among men who died of prostate cancer.

Conclusions: Local therapy for prostate cancer may provide benefit in some quality of life domains at the end of life. Further elucidating how quality of life is impacted by disease characteristics and type of local therapy will provide important prognostic information to patients.

UP-34**The Impact of Bone Metastases on Pain: Results From a Phase 3 Denosumab Study in Men with Nonmetastatic Castration-resistant Prostate Cancer**

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Introduction and Objectives: Bone pain is one of the most common symptoms experienced by patients with metastatic castration-resistant prostate cancer (CRPC). In a national survey¹, 47% of patients with metastatic CRPC experienced bone pain daily or continuously. In a recent phase 3 study, denosumab prolonged bone metastasis-free survival by a median

of 4.2 months (HR 0.85; 95% CI 0.73-0.98, $p=0.028$) vs. placebo in men with nonmetastatic CRPC². This post-hoc analysis evaluated pain and analgesic use associated with development of bone metastasis.

Methods: Men with nonmetastatic CRPC (baseline median PSA 12.3 ng/mL, PSA doubling time 5.1 months, ADT duration 47.1 months) were randomized 1:1 to receive monthly subcutaneous denosumab 120 mg or placebo. Pain severity and analgesic use were assessed at baseline (BL) and at each bi-monthly visit before treatment administration. Pain was measured by the Brief Pain Inventory-Short Form (BPI-SF); 0-4=no/mild pain; 5-10=moderate/severe pain, and analgesic use was quantified using the Analgesic Quantification Algorithm (AQA; 0=no analgesics; 7=strong opioids). A 2-point change in BPI or a shift in AQA from ≤ 2 to ≥ 3 represents clinically relevant changes.

Results: Of the 1432 men enrolled, 605 developed bone metastasis. The development of bone metastasis was associated with risk of a clinically relevant (≥ 2 -point) increase from BL in pain worsening (HR 2.87; 95% CI 2.22, 3.71; $p<0.0001$), and risk of pain progression from no/mild pain at BL to moderate/severe pain on study (HR 3.62; 95% CI 2.72, 4.81; $p<0.0001$). The median times to pain worsening (9.3 months vs. 12.9 months; HR 0.83; 95% CI 0.71, 0.96; $p=0.012$) and pain progression (16.9 months vs. 36.8 months; HR 0.74; 95% CI 0.61, 0.90; $p=0.002$) were shorter in patients with bone metastasis than in those without bone metastasis. The shift from no/mild analgesic use (AQA ≤ 2) to strong opioid analgesic use (AQA ≥ 3) was nearly twice as high in patients with bone metastasis as in those without.

Conclusions: In this study of men with high-risk nonmetastatic CRPC, the development of bone metastasis was associated with pain progression and the need for strong opioid use. These observations support the treatment benefit for the delay/prevention of bone metastases.

UP-35

High-dose-rate Brachytherapy Combined with External Beam Radiotherapy for Localized Prostate Cancer: Correlation Between Clinical and Dosimetric Parameters and Late Genitourinary Toxicity

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Introduction and Objectives: Several investigations have revealed that the alpha/beta ratio for prostate cancer is atypically low, and that hypofractionated radiotherapy or high-dose-rate brachytherapy (HDR-BT) regimens using appropriate radiation doses are expected to improve the local control rate for localized prostate cancer. However, the increase in the total biological effective dose (BED) may cause an increase in the severity and incidence of normal tissue complications. The purpose of this study was to investigate if the clinical and dosimetric factors affected the incidence of late genitourinary (GU) toxicity after HDR-BT combined with external beam radiotherapy (EBRT).

Methods: The records of 115 patients with localized prostate cancer treated by HDR-BT combined with EBRT between November 2004 and December 2008 were analyzed. The fractionation schema for HDR-BT and EBRT was prospectively changed. The distribution of the fractionation schema used in the patients was as follows: 9 Gy \times 2+2 Gy \times 20 (BED₃=139 Gy) in 57 patients (Group 1); and 9 Gy \times 2+3 Gy \times 13 (BED₃=150 Gy) in 58 patients (Group 2). The median follow-up duration was 68 (range 48-97) months. The clinical and dosimetric factors affecting the incidence of late Grade 2 or worse GU toxicity were analyzed by univariate and multivariate analyses.

Results: Forty-two (36.5%) and 13 (11.3%) patients developed late Grade 2 and 3 GU toxicity, respectively. There were no statistically-significant differences between Group 1 and Group 2 in the incidence of late Grade 2 or 3 GU toxicity (42.1% and 53.4%, respectively, $p=0.1513$). In the clinical factors, prior transurethral resection of the prostate (TURP) was the only factor related to late Grade 2 or 3 GU toxicity ($p=0.0046$). None of the dosimetric factors were related.

Conclusions: Careful follow-up is needed for patients with a prior history of TURP who were treated with HDR-BT combined with EBRT.

UP-36

Fresh Frozen Prostate Tissues in the PROCURE Quebec Prostate Cancer Biobank Meet High Pathological and Biochemical Standards of Quality

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Introduction and Objectives: Well-characterized, high-quality fresh-frozen prostate tissue is required for prostate cancer research. As part of the PROCURE Prostate Cancer Biobank launched in 2006, 4 University Hospitals in Quebec joined to bank fresh frozen prostate tissues from radical prostatectomies (RP). As the biobank is progressing towards allocation, the nature and quality of the tissues were determined.

Methods: RP tissues were collected by standardized alternate mirror image or biopsy-based targeted methods and frozen for banking. Clinical/pathological parameters were captured. For quality control, two presumed benign and two cancer frozen banked tissue blocks per case (10/site) were randomly selected. In a consensus meeting, 4 pathologists (one/site) blindly evaluated slides ($n=160$) and graded quality, Gleason score (GS), and size of cancer foci. Quality of tissue RNA (37/40 cases) was assessed by RNA Integrity Number (RIN).

Results: The bank included 1819 patients of mean age: 62.1 years; serum PSA: 8 ng/ml; prostate weight: 47.8 g; GS: 7; pathological stage: T2 in 64.5%, T3A in 25.5% and T3B in 10% of cases, without difference between sites. Of the 157 evaluable slides, 79 and 78 had benign and cancer tissue, respectively, with no cancer detected in 3, resulting in a yield of cancer banking of 92.5%. GS for the 37 cancer positive cases were: 6 in 9, 7 in 18 and >7 in 10 and, in most instances, in concordance with final GS. In 40% of slides containing cancer, foci occupied $\geq 50\%$ of block surface and 42% had a diameter ≥ 1 cm. Tissue RNA was of very good quality, with RIN ≥ 7 for 97% of cases (mean=8.7 \pm 0.7).

Conclusions: This study confirms the high quality of randomly selected benign and cancerous fresh-frozen prostate tissues of the PROCURE Quebec Prostate Cancer Biobank. These results strengthen the uniqueness of this large prospective resource for prostate cancer research.

UP-37

Development and Validation of an Algorithm to Map the Prostate Cancer Index to the Patient Oriented Prostate Utility Scale (PORPUS)

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Introduction and Objectives: The Prostate Cancer Index (PCI) is frequently used to measure quality of life (QOL) in prostate cancer (PC) patients. It provides 6 subscale scores: urinary, sexual, and bowel function and bother. The Patient Oriented Prostate Utility Scale (PORPUS-U) measures utility, a global measure of QOL, on a scale where 0=dead and 1=full health, for use in population surveys, clinics, clinical trials, and decision analyses. Our objective was to develop a function to predict PORPUS-U utilities from PCI scores.

Methods: We used patient-level data from two previous studies which administered the PORPUS-U and PCI concurrently. Study 1 included 248 PC outpatients interviewed 3 times within 12 months. Study 2 included 676 community-dwelling PC survivors surveyed by mail. Study 2 data were used to fit three linear regression models, which were validated using study 1 data (3 time periods). One model used original PORPUS-U scores, and two used log-transformed PORPUS-U scores, one with a hierarchy constraint and one without. All were tested with and without age as a

covariate. Models were selected using stepwise selection and 5-fold cross validation. The predictive abilities of the models were assessed.

Results: The best-fitting model used the log-transformed PORPUS-U with no hierarchy constraint, without age. The R-squared was 0.72. The root mean squared error ranged from 0.041 to 0.061 for the 3 validation datasets. The overall mean predicted and observed utilities were similar (e.g., 0.956 vs. 0.955) but predicted utilities slightly overestimated the lowest 5% of observed PORPUS-U scores and underestimated the highest observed scores.

Conclusions: Our algorithm can estimate PORPUS-U utility scores from PCI scores, thus supplementing descriptive QOL with utility scores for a variety of populations and applications.

UP-38

A Calgary Experience in Active Surveillance: Prostate Specific Antigen Level but not Rate Affected Timing of Repeat Biopsies

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Introduction and Objective: Active surveillance protocols, which monitor prostate specific antigen (PSA) levels and histological grading, have been developed as a less invasive alternative to curative procedures in patients with low risk prostate cancer. Active surveillance guidelines have been established, but the experience of urologists and their patients can differ greatly. We aimed to describe in detail the experience in an active surveillance cohort of 114 patients. PSA levels and rates were compared with biopsy intervals to quantify the influence of PSA levels and rates on the timing of repeat biopsies.

Methods: A chart review was conducted on 114 patients who undertook active surveillance between 2001 and 2012. Biopsy intervals and PSA intervals and values were extracted from patient charts. Pre-biopsy PSA rates and levels were compared to biopsy intervals using Pearson correlation analysis (Prism software).

Results: Of 114 patients on active surveillance 53 underwent 2 or more biopsies, 44 patients had 2 or more PSA levels recorded between biopsy 1 and biopsy 2. The average biopsy interval was 16.5 months (range: 3-37). The mean PSA rate between 1st and 2nd biopsies was 0.9/month (range: -1.19-1.3) and the average pre-biopsy PSA level was 5.19 (range: 0.3 - 10.9). Pearson's correlation coefficient between PSA rate and biopsy interval for 44 subjects was 0.06 ($p=0.7161$). However, a strong relationship between pre-biopsy PSA level and biopsy interval was demonstrated (52 subjects); Pearson's correlation coefficient was -0.4383 ($p=0.012$).

Conclusion: The rate of change of PSA levels did not correlate with biopsy interval, which was 4.5 months greater than CUA suggested guidelines. However, PSA level was strongly related to the timing of the second biopsy. Therefore PSA values influenced the physician/patient to obtain a repeat biopsy sooner, but the rate of PSA increase did not impact this decision.

UP-39

Concordance Between Trans-rectal Ultrasound Guided Biopsy Results and Radical Prostatectomy Final Pathology: Are We Getting Better at Predicting Final Pathology?

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Introduction and Objectives: Inaccuracy in biopsy (Bx) Gleason scoring poses a risk to men who may then receive inappropriate treatment. We sought to evaluate if there was a shift in discordance rates between Bx and radical prostatectomy (RP) at our institution in recent years while considering the implementation of active surveillance and the shift in pathological grading of Bx scores caused by the 2005 International Society of Urologic Pathology update to Gleason scoring protocol.

Methods: We retrospectively reviewed patients who underwent RP at our institution between May 2004 and April 2011. We analyzed clinical and pathological correlates of upgrading in three subgroups: GS6/6, GS6/7,

and GS7/7, where the first score belongs to the biopsy and the second to the RP. We applied the log-rank test and Cox model to a Kaplan Meier analysis of biochemical recurrence in the subgroups, and also mapped GS6/7 discordance over time.

Results: Our search yielded 1,717 patients that met our inclusion criteria. Bx results are concordant with final pathology in only 65% of patients. The three subgroups had significantly different mean PSA, patient age, tumour volume, margin status, pathologic stage, prostate weight, TRUS volume, and rate of progression ($p<0.05$) while core number and BMI were not significantly different ($p=0.6$ and $p=0.3$, respectively). We noted a rising discordance initially, a fall during 2006, and an increasing trend thereafter. However there was no sustained increase or decrease over the study period taken as a whole ($p=0.06$).

Conclusions: Despite that no sustained trend was observed, the falling discordance in 2006 may reflect the accommodation to the 2005 update while the gradual adoption of active surveillance may have led to the otherwise increasing trends. However the observed may also be spurious Bx sampling errors.

UP-40

Re-assessment of 30-, 60- and 90-day Mortality Rates in Non-metastatic Prostate Cancer Patients Treated Either with Radical Prostatectomy or Radiation Therapy

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Introduction and Objectives: It is customary to define a death that occurred within 90 days of surgery as caused by that surgery. However, such practice may not be entirely valid and may overestimate the true short-term mortality rates (SMR) after radical prostatectomy (RP). SMR may be influenced by treatment unrelated events. Our objective was to assess most unbiased RP-specific excess SMR.

Material and Methods: We performed a retrospective analysis of a population-based cohort of 59010 patients (RP n=28281, 48%; external beam radiation therapy (EBRT) as reference group, n=30729, 52%) treated between 1998 and 2005 for non-metastatic prostate cancer (PCa). Descriptive analyses for assessing the rates of 30-, 60- and 90- day mortality were performed. To estimate the most unbiased RP-specific excess mortality rates after RP, we defined the difference between RP SMR and EBRT SMR.

Results: Thirty-, 60- and 90-day mortality rates were, respectively, 0.2, 0.5 and 0.6%, and 0.1, 0.4 and 0.6% for RP and RT patients. After consideration of SMR after EBRT, the most unbiased short-term RP-specific excess mortality rates were 0.1, 0.1 and 0% at 30, 60 and 90 days. In sickest (CCI>2) and oldest (>75 year) patients the differences were as high as 0.5 and 2.3%.

Conclusions: SMR after RP and EBRT are virtually the same. This suggests that in a large-scale epidemiologic database most deaths after RP are not directly related to the surgery itself. Instead, other factors may be at play. However, the differences are substantially more significant in older (>75 year) and sicker (CCI>2) patients.

UP-41

CellSearch EPCAM+ CK+ Subclasses Are Not Prognostic for Advanced Prostate Cancer Status

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Introduction and Objectives: The presence of circulating tumour cells (CTCs) in patient blood represents the onset of metastatic disease in prostate cancer disease progression. Its enumeration by the CellSearch Instrument offers a prognostic means of assessing disease progression but CTC criteria is rigorous and does not include dead CTCs or fragments of CTCs. Previous studies show that there are low CTC counts in localized prostate cancer (PCa) patients whereas various forms of dead circulating tumour cells are abundant in patient plasmas and could offer prognostic information. We expand the CellSearch criteria for CTCs and enumerate several subclasses of EpCAM+ and CK+ events, ranging from intact dead cells to micron-sized cell fragments. We hypothesize that EpCAM+CK+microparticle events are prognostic for localized and metastatic PCa patients and correlate with other clinical markers such as prostate specific antigen.

Methods: Patients were recruited into two different cohorts; localized PCa and metastatic PCa (N=18, 21 respectively). Blood was collected into CellSearch vacutainers and analyzed by the CellSearch instrument. Several different EpCAM+ CK+ DAPI± CD45- event subclasses were enumerated for all patients. Operator bias was eliminated during blinded enumeration of subclasses by randomizing all samples prior to analysis.

Results: There was no difference in all CellSearch subclasses between localized and metastatic PCa patients (Table 1). However, when correlated to PSA, the small and large tumour cell fragment subclasses in the localized PCa patient cohort were the only subclasses to positively correlate with PSA (N=18, R=0.677, 0.792 respectively) whereas all other subclasses did not correlate with PSA.

Conclusions: No significant differences in CellSearch EpCAM+ CK+ event subclasses between localized and metastatic PCa patients was observed. Hence, the clinical utility of CellSearch is questionable.

UP-42

Influence of Body Fat Distribution on Prostate Cancer Aggressiveness and Urinary Symptoms

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Introduction and Objectives: To examine the influence of adipose tissue distribution on prostate volume and prostate cancer stage in patients receiving brachytherapy for localized prostate cancer.

Methods: We analyzed a cohort of 117 patients treated with permanent seed brachytherapy for localized prostate cancer. Adipose tissue distribution was measured on computed tomography (CT) images at four different sites: periprostatic adipose tissue (PPAT), visceral adipose tissue (VAT), subcutaneous adipose tissues (SCAT) at level of iliac crest and symphysis pubis. We realized that a consensus on determining PPAT was missing and decided to include only PPAT outside of the levator ani sling because that tissue depends on rectal filling. Clinical factors were analyzed over tertiles of the different adipose tissue measurements using nonparametric tests.

Results: Measurements depend on the definition of PPAT and whether to included tissue in the levator ani sling. PPAT was the only adipose tissue measurement that was not strongly correlated with BMI (Pearson correlation coefficient $r = 0.27$); the other three were all significantly correlated ($r = 0.58 - 0.7$). The tertile of visceral adipose tissue had a borderline influence ($p = 0.06$) on prostate volume. No differences were found between the other adipose tissue measurements and prostate volume, Gleason score, PSA density or T-stage. BMI was weakly correlated to the IPSS before brachytherapy ($r = 0.20$, $p = 0.029$) and when categorized into normal, overweight and obese, it showed a weak trend ($p = 0.081$) towards an influence on having an IPSS >7. Adipose tissue distribution did not show any influence on pre-treatment IPSS.

Conclusions: PPAT was found to be less dependent of BMI than other measured adipose tissue. A consensus on the delineation of PPAT is needed in the nascent field.

UP-43

Decisional Regret After Robotic-assisted Laparoscopic Prostatectomy: The Role of Race

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Introduction and Objectives: Longitudinal studies report racial disparities in prostate cancer (PCa) including greater incidence, more aggressive tumour biology and increased cancer specific mortality in black men. Regret concerning primary treatment selection is under-evaluated in PCa patients. We investigated the relationships between clinicopathologic variables across racial and socioeconomic lines following robotic-assisted laparoscopic prostatectomy (RALP).

Methods: We assessed treatment decisional regret using a validated questionnaire in a total of 484 white and 72 black PCa patients followed for a median of 16.6 months post-RALP. Socioeconomic status (SES) was aggregated from 2010 U.S. census ZIP code data. Clinicopathologic characteristics and functional outcomes were compared between groups.

Table 1. UP-41

	Counts in localized PCa (counts/uL plasma; mean±SE)	Correlation to PSA (R-value)	Counts in metastatic PCa (counts/uL plasma; mean±SE)	Correlation to PSA (R-value)
CTCs	0.11±0.07	0.0009	7.45±5.45	0.0012
Granular CTCs	1.57±0.48	0.01	1.07±0.39	0.007
Large tumour cell fragment	43.9±7.89	-0.311	28.1±4.38	0.0005
Small tumour cell fragment	29.6±6.11	-0.32	26.6±4.56	-0.248
Large tumour microparticle	20.2±6.12	0.677	25.7±8.34	0.105
Small tumour microparticle	83.9±15.4	0.792	96.6±12.3	0.273

PCa: prostate cancer; CTCs: circulating tumour cells; SE: standard error.

Univariate and multivariate regression analyses were used to evaluate the influence of race, aggregate SES, and other clinical and demographic characteristics on decisional regret.

Results: 87.7% of the population was not regretful of their decision to undergo treatment. However, a greater proportion of black vs. white patients were regretful (20.6% vs. 11.3%, $p=0.03$). White and black men were similar on all functional, clinical and pathologic features with the exception of age. Black men were significantly younger than whites (56 vs. 60 years, $p<0.001$). There were significant differences in SES by race ($p<0.001$), although regret did not differ by SES. Race, surgical complications, postoperative sexual dysfunction, continence and length of hospital stay, however, were significantly associated decisional regret.

Conclusions: Black men were more regretful than white men, even after adjusting for clinicopathologic characteristics and postoperative functional outcomes.

UP-44 Metabolic Syndrome in Robotic-assisted Laparoscopic Prostatectomy

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Introduction and Objectives: Metabolic Syndrome (MetS), the constellation of obesity and related risk factors for cardiovascular disease, is an expanding epidemiological concern in the United States and the developed world. However, the relationship between MetS and prostate cancer remains to be definitively assessed. We evaluated the association between obesity and MetS with pathologic and functional outcomes after robotic-assisted laparoscopic prostatectomy (RALP).

Methods: 2639 patients underwent RALP between March 2003 and July 2012. 186 patients met criteria for MetS as defined by the presence of obesity ($BMI \geq 30$ kg/m²) in conjunction with 2 or more of the following: hypertension (HTN), dyslipidemia (D) and diabetes (DM). Additionally, reference cohorts of 1) 663 non-obese men without HTN, D, or DM, 2) 184 obese patients without HTN, D or DM, and 3) 211 obese men with solitary risk factors were identified for comparison. Demographic, histopathologic, and perioperative clinical parameters were compared.

Results: In comparison to patients without MetS, patients with MetS had larger prostates (OR=1.609, 95% CI=1.04-2.49), increased blood loss (OR=1.592, 95% CI=1.15-2.21) and surgical complexity (OR=4.940, 95% CI=2.29-10.69). No statistical difference was observed between these groups in regard to complication rates, pathologic grade, stage, postoperative continence or erectile function. With the exception of larger prostates found among men with MetS, men with obesity-alone and one additional risk factor appeared similar to those with MetS.

Conclusions: Patients with MetS had similar perioperative, histopathologic, and functional outcomes compared with reference cohorts undergoing RALP. RALP is safe, feasible, and efficacious in men with MetS.

UP-45 Predictors of Gleason Score Upgrading and the Influence of Treatment for Benign Prostate Hyperplasia

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Introduction and Objectives: To examine factors associated with Gleason score upgrading after adjusting for the use of medications known to modify prostate size and PSA level.

Methods: We analyzed 998 patients with biopsy Gleason 6 prostate cancer (PCa) treated with robot-assisted laparoscopic prostatectomy. We tested for correlations between prostate size and preoperative log-transformed PSA among those taking 5- α reductase inhibitors (5- α RI) and α -blockers in 1) the entire study population, 2) men with a prior history of BPH, and 3) men with prostates in the top quartile for size. We used logistic regression to compare known clinical characteristics associated with upgrading in a series of nested models, with and without adjustment for BPH and its treatment.

Results: Men taking α -Blockers had significantly larger prostates than unexposed patients, regardless of having a diagnosis of BPH ($p<0.01$). However, neither drug was crudely associated with upgrading. The likelihood of upgrading increased with age (OR 1.04, 95% CI 1.02-1.06), BMI (OR 1.04 95% CI 1.01-1.08), PSA (OR 6.91, 95% CI 3.36-14.21), % tumour in any biopsy core (OR 1.02, 95% CI 1.01-1.03), number of positive biopsy cores (OR 1.21, 95% CI 1.09-1.34), and decreased with total number of biopsy cores (OR 0.96 95% CI 0.93-0.99), and prostate size (OR 0.98, 95% CI 0.95-0.98). Further adjustment for BPH diagnosis and treatment with 5- α RI or α -blockers yielded ORs for clinical characteristics associated with upgrading that were nearly identical to the unadjusted estimates.

Conclusions: Among men with biopsy Gleason 6 PCa, clinical factors associated with the likelihood of upgrading after prostatectomy were unchanged after further adjustment for BPH and treatment with drugs known to alter prostate size and PSA.

UP-46 Do Asian and Caucasian Men Develop High Grade (Gleason ≥ 7) Prostate Cancer at the Same Age? An Autopsy Study

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Introduction and Objectives: We have previously demonstrated that PCa prevalence is similar between Russian Caucasians and Japanese Asian men. We had chosen a Caucasian population in Russia with low penetrance of PSA screening. Autopsy data in North America and Western Europe would have been contaminated due to opportunistic PSA screening. Screening in Japan is uncommon. We aimed to compare the prevalence of Gleason ≥ 7 PCa on autopsy in Caucasian and Asian men.

Methods: 320 prostate glands were prospectively collected during autopsy from men who died from causes other than PCa in Moscow (Russia $n=220$)-(CAU) and Tokyo (Japan $n=100$)-(ASI). The same harvesting methodology was followed in both sites. Prostates were removed en-block with the seminal vesicles within 24 hours of death and analyzed in toto (perpendicular sections at 4 mm intervals) by an experienced uro-pathologist. We compared across the ASI and CAU populations, the prevalence of GS ≥ 7 PCa over the various age groups.

Results: 37 out of 117 tumours (31.6%) were GS ≥ 7 , with a significantly higher proportion in ASI men (51.4%) compared to CAU men (23.2%, $p=0.003$). Fig. 1 shows the prevalence of GS ≥ 7 PCa in ASI and CAU men

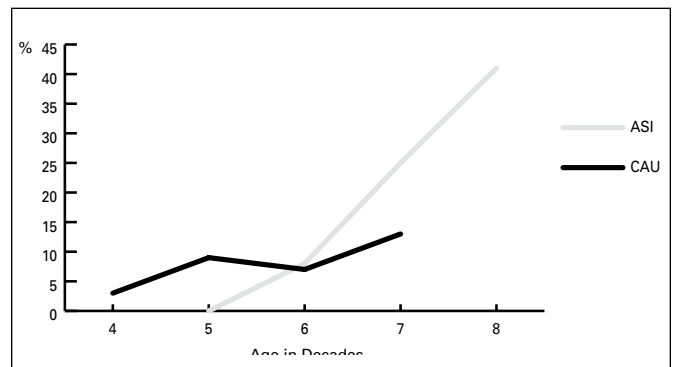


Fig. 1. UP-46.

according to age. Compared to CAU, a higher prevalence of GS \geq 7 PCa was observed at a later age among ASI with a steeper increase in prevalence by the decade. Breaking down GS7 into (3+4) or (4+3), among 14 GS7 in ASI, 13 were 3+4 and 1 was 4+3. Among 16 CAU with GS7, 10 and 6 were 3+4 and 4+3, respectively, ($p=0.086$). Limitations include small population size and the absence of Caucasian men aged 80+.

Conclusion: A higher proportion of autopsy detected PCa in Asians is GS \geq 7 compared to Caucasians. Asian men seem to have a higher prevalence of GS \geq 7 PCa at a later decade in life compared to Caucasians. A hypothesis is that in Asian men, the grade progression is much faster than in Caucasian men. The alternative hypothesis would be a de novo origin of GS \geq 7 instead of grade progression.

UP-47

Prevalence of Inflammation, BPH and Prostate Carcinoma in Asian and Caucasian Men: An Autopsy Study

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Introduction and Objectives: Prostate cancer (PCa) and benign prostatic hyperplasia (BPH) are extremely common in adult men. Data have sug-

gested that prostatic inflammation is involved in the pathogenesis and progression of both conditions. We aimed to investigate the prevalence of inflammation, BPH and PCa in Asian and Caucasian men in autopsy specimens.

Methods: Prostate glands were prospectively obtained during autopsy from men who died from causes other than PCa in Moscow (Russia)-(CAU) and Tokyo (Japan)-(ASI). The same harvesting methodology was followed in both sites. Prostates were removed en-block with the seminal vesicles within 24 hours of death and analyzed in toto (perpendicular sections at 4mm intervals). Identification of PCa, Gleason score (GS), acute inflammation (grade 0-3), chronic inflammation (grade 0-3) and BPH (stage 0-3) was assessed by an experienced uro-pathologist. We used the Cochran Armitage, Spearman correlation, the chi-square and Wilcoxon tests for statistical analyses.

Results: 320 prostates were collected, 220 from CAU and 100 from ASI men. BPH score increased as age increased ($p<0.001$). There was a significant association between BPH and chronic inflammation found on autopsy – higher BPH scores were associated with more chronic inflammation (Spearman correlation 0.55, $p<0.001$) and a much weaker association between acute inflammation and BPH (Spearman 0.28, $p<0.001$). Chronic inflammation was strongly associated with older age, acute inflammation, and BPH (all $p<0.001$). There was no evidence of an association between acute inflammation and PCa nor ethnicity. We observed a significant association between GS \geq 7 PCa and chronic inflammation ($p=0.015$).

Conclusion: Chronic inflammation is associated with both BPH and PCa and interestingly with cancers presenting with aggressive features (GS \geq 7). No evidence of a causal relation can be proven at this stage but this topic clearly deserves scrutiny and additional research.