Unmoderated Poster Sessions: Oncology – Prostate
June 19, 2011–June 21, 2011

UP-001
Aberrant Fer/STAT3 Signaling Favors Prostate Cancer Progression to the Androgen-Refractory Stage

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Introduction and Objectives: Mechanisms underlying prostate cancer (Pca) progression from an androgen-responsive to a refractory (castration-resistant) stage prove to be challenging and still poorly understood. Heterogeneity regarding tumor cell sensitivity to androgens may play an important role. Indeed by responding to diverse growth-promoting factors such as interleukin (IL)-6, tumor cells expressing the androgen receptor (AR) may adapt while subsets of AR(-) cells may concomitantly be selected. We identified Fer as the major tyrosine kinase implicated in the IL-6-mediated activation of STAT3 (the signal transducer and activator of transcription) that controls growth of human metastatic Pca cell lines, both AR(+) and AR(-). Moreover, Fer is implicated in cross-talks between IL-6 and AR signaling pathways in AR(+) tumor cells and controls AR-dependent genes. Since Fer is up-regulated in Pca, the aim was to test the hypothesis of an active pathway implicating pairs such as Fer/pSTAT3, Fer/AR, pSTAT3/AR in prostate cancer tissues from patients with advanced disease.
Methods: Paraffin-embedded blocks of prostate tissues obtained by TURP from hormone-treated patients (n=29) were retrieved from pathology. Consecutive sections were processed to stain Fer, pSTAT3, and AR by immunohistochemistry. Tumor cell staining was quantified by percentage and intensity and used to calculate H scores. Significance of correlations was analyzed through the Spearman Rho's method.
Results: Each TURP case was of good quality for immunohistochemistry. All three markers were primarily found in the nucleus. Overall, 97% (28/29) of cases were AR(+), 86% (25/29) of cases were Fer (+) and 83% (24/29) of cases were pSTAT3(+). A single case was AR(-), while positive for Fer and pSTAT3. Within each case, a majority of tumor cells were AR(+). Yet single cell analysis revealed the tumor heterogeneous nature with respect to AR. Indeed, all specimens contain AR(-) cells, the mean being 17%, interspersed among AR(+) cells. The analysis of pairs of markers revealed no correlation between AR and pSTAT3, and between Fer and AR. Nonetheless, Fer and pSTAT3 were strongly correlated, in both percentages of stained cells ($p<0.01$) and H score ($p<0.0001$), and regardless of the tumor cell AR status. In the end, Fer was expressed along with pSTAT3 in both AR(+) and AR(-) cells in 79% of cases.
Conclusion: The co-expression of Fer and activated STAT3 in advanced prostate cancer supports that aberrant Fer signaling favors adaptation and selection of tumor cells during progression towards hormone-refractory disease.
Supported by Prostate Cancer Canada.

UP-002
Measurement of Periprostatic Fat on Ultrasound: A New Risk Factor for Prostate Cancer

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Introduction and Objectives: Diet and obesity are known to be associated with prostate cancer. Recent evidence suggests that adipokines released from periprostatic fat may be important in prostate cancer aggressiveness. We set out to determine if the amount of periprostatic fat estimated on transrectal ultrasound (TRUS) is associated with prostate cancer or high grade (HG) disease.
Methods: A prospective cohort of 1041 patients undergoing prostate biopsy for cancer suspicion at the Princess Margaret Hospital in Toronto was utilized. From this cohort all TRUSs were retrospectively reviewed and the distance between the prostate and the pubic bone was recorded as a rough index of periprostatic fat quantity. These measurements in combination with other prostate cancer risk factors were evaluated against prostate cancer and HG prostate cancer outcome with univariable and multivariable logistic regression and receiver operating characteristic curve area under the curve (AUC) analysis.
Results: Among this cohort 47% of patients were diagnosed with prostate cancer and 23% were diagnosed with high grade disease. In multivariable logistic regression analysis age, NSAID use, positive family history, elevated BMI, African ethnicity, lower prostate volume, positive DRE, nodule on ultrasound (US), elevated PSA and increasing periprostatic fat measurement were associated with prostate cancer diagnosis. The AUC and odds ratio for the independent association of periprostatic fat with prostate cancer was 0.58 and 1.15, respectively ($p=0.01$). For HG disease, age, elevated BMI, positive DRE, US nodule, low prostate volume, PSA and increasing periprostatic fat measurement were independently associated with HG PCa. The AUC was 0.59 and the OR was 1.28 for the association of periprostatic fat with HG PCa ($p<0.01$).
Conclusions: Fat surrounding the prostate can be estimated with TRUS and is an additional predictor of prostate cancer at biopsy.

UP-003
PDK1 and Prostate Cancer Progression

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Introduction and Objective: Early detection of aggressive prostate cancer (PCa) is necessary for an intervention at a curable stage of the disease. From that emerges the need for molecular prognostic markers that are specific, reliable and objectively measured. Previous gene expression profiling data have shown the AKT survival pathway to be overexpressed in metastatic compared to primary tumours. PDK1, which activates the AKT pathway, was found to be highly expressed through amplification of chromosome 16p13. A non-catalytic function of PDK1 was recently linked to cell motility, and the 16p13 amplicon remains uncharacterized in PCa. Our goal is

to establish the prognostic value of 16p13 amplification, and the role of PDK1 in prostate cancer progression.
Methods: A fluorescent *in situ* hybridization (FISH) probe, specific to the chromosome 16p13, was successfully developed to survey tissue microarrays of formalin fixed paraffin embedded prostate tumours for amplification at this locus. FISH was applied to 7 primary tumours and their matched metastases and to a cohort of 47 patients with primary tumours. In PCa cell lines, PDK1 levels of expression were knocked down using siRNA and the effects on proliferation and motility were measured by MTT and wound healing assays respectively.
Results: In the 7 pairs of primary and matched metastasis samples, 3 of the 7 patients harboured the 16p13 amplification in their metastasis and 2 of these 3 cases had the alteration in their matched primary sample. In patients with primary tumours (n=47), the amplification was detected in 19.1% of cases and there was a trend towards an association between high Gleason grade and the presence of the amplification (χ^2 test, n=47, p=0.11), pointing to the prognostic potential of the amplification. *In vitro*, reduced PDK1 levels by siRNA significantly decreased migration of three different PCa cell lines (PC3, DU145 and LNCaP) assessed by wound healing assay (p<0.01), while cell proliferation remained unaffected.
Conclusions: We showed that PDK1 affects PCa cell motility *in vitro* and that 16p13 amplification could be successfully retrieved in archived primary tumours. To further explore the prognostic role of the amplification, more patients will be examined, and the correlation with other clinical-pathological features will be measured. The role of PDK1 in PCa motility will be also further characterized. Establishing the prognostic value and the role of PDK1 amplification in metastatic progression could be crucial for effective clinical management, and meaningful for therapeutic applications.

UP-004

Office Based Anterior Zone Trans-Rectal Ultrasound Guided Prostate Biopsies for Patients with Elevated Serum PSA Levels and Previous Negative Biopsies: Diagnostic Yield and Limitations

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Background: Patients with previous negative extended prostate biopsies (Pbx) and a persistently elevated PSA present a diagnostic challenge. Recent MRI data suggest the anterior zone (AZ) of the prostate, an area not targeted routinely by extended or saturated trans-rectal ultrasound (TRUS) guided Pbx can harbor cancer. We assessed the value of AZ sampling at the time of repeat TRUS guided saturation Pbx in an office based setting
Methods: 49 patients (mean age 63.9), with at least one previously negative extended TRUS guided Pbx (1-4 previous bx (median 2), mean # of cores 19.6), underwent saturation TRUS guided Pbx under local freezing (n=37) or spinal anesthesia if diagnostic TURP was conducted concomitantly (n=12). 12-21 cores were taken from the peripheral zone (PZ), up to 6 cores from the transitional zone (TZ), and 6-8 cores from the AZ. All suspicious ultrasonic areas were targeted to a total of 17-42 cores (median 26). None had an MRI prior to their biopsy
Results: Overall cancer detection rate was 34.7% (17 patients). AZ cancers were found in 18.3% of cases (9 patients), but in only 2 patients was the AZ the only site of disease. Gleason score of AZ cancers were G8(4+4)x2, G7(3+4)x2, and G6(3+3)x5. Suspicious ultrasonic findings in the AZ were present in 3/9 with AZ cancer. Mean and median PSA levels as well as prostate volume for the entire cohort were 12.1, 10, and 58.9cc, and for cases with cancer 14.1, 12.8, and 55cc, respectively. TZ cancers were uncommon (4.1%), and accompanied PZ cancers. No infectious complications occurred
Conclusions: AZ sampling as part of saturation Pbx is an easily performed and safe office based procedure which results in AZ cancer detection rate of 18%. However, since AZ tumors are usually accompanied by PZ tumors (7/9), the main diagnostic yield (34.7%) likely stems from PZ saturation bx and thus routine AZ bx may not be justified without suspicious MRI. Suspicious ultrasonic findings in the AZ were present in 33% of those with AZ cancer and thus AZ Pbx cannot usually be directed specifically which may reduce their accuracy compared to MRI directed AZ Pbx

Prostate cancer (PCa) incidence varies by geographic location, with developed countries exhibiting higher levels of disease. Some attribute this to 'Westernized lifestyles' of high energy diets and limited physical activity with consequent obesity. Obesity and related diseases like diabetes, cause hyperinsulinemia, which upregulates pro-survival insulin/insulin-like growth factor signalling. Our previous work shows diet-induced hyperinsulinemia enhances PCa tumor growth *in vivo*. Metformin, a diabetic therapy, reduces hyperinsulinemia, and also has direct anti-neoplastic properties. We assessed the potential benefit of combining a standard PCa treatment (androgen ablation therapy with bicalutamide) with metformin *in vitro* and *in vivo*.

Using clonogenic assays we assessed the effect of bicalutamide and/or metformin on colony formation rates in LNCaP, PC3, DU145 and PC3AR2 PCa cell lines. Western blot and cell cycle analyses were used to elucidate any mechanism of interaction between the drugs in androgen receptor (AR) positive (LNCaP) and AR negative (PC3) cell lines. The combination treatment regimen was then assessed *in vivo* using a LNCaP murine xenograft model.

Micromolar bicalutamide or millimolar metformin caused significant dose-dependent reduction in colony formation rates (p<0.001). Combination treatment further significantly reduced colony formation rates (p<0.005). This effect was more marked in AR positive cells. Western blot and cell cycle analyses suggested differing mechanisms of interaction in AR positive and negative cell lines. Following combination treatment, LNCaP cells exhibited altered cell proliferation (decreased PCNA) and perturbed cell cycle kinetics (G1/S arrest). PC3 cells showed evidence of enhanced apoptosis (increased BAX, decreased caspase 3, phospho-Akt). Preliminary *in vivo* results show diminished tumor growth in response to combination treatment, and are subject to ongoing statistical analyses.

Combining bicalutamide and metformin significantly reduces PCa cell colony formation rates further than either monotherapy. In AR positive cells this effect is mediated by reducing cellular proliferation rates, whereas in AR negative cells the combination regimen promotes apoptosis. This combination drug regimen may potentially improve prostate-cancer specific survival via the direct anti-neoplastic properties outlined.

UP-005

Utilizing Metformin to Enhance the Efficacy of Androgen-Deprivation Therapy in the Treatment of Prostate Cancer

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Prostate cancer (PCa) incidence varies by geographic location, with developed countries exhibiting higher levels of disease. Some attribute this to 'Westernized lifestyles' of high energy diets and limited physical activity with consequent obesity. Obesity and related diseases like diabetes, cause hyperinsulinemia, which upregulates pro-survival insulin/insulin-like growth factor signalling. Our previous work shows diet-induced hyperinsulinemia enhances PCa tumor growth *in vivo*. Metformin, a diabetic therapy, reduces hyperinsulinemia, and also has direct anti-neoplastic properties. We assessed the potential benefit of combining a standard PCa treatment (androgen ablation therapy with bicalutamide) with metformin *in vitro* and *in vivo*.

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Combining bicalutamide and metformin significantly reduces PCa cell colony formation rates further than either monotherapy. In AR positive cells this effect is mediated by reducing cellular proliferation rates, whereas in AR negative cells the combination regimen promotes apoptosis. This combination drug regimen may potentially improve prostate-cancer specific survival via the direct anti-neoplastic properties outlined.

UP-006

Utilizing Metformin as a Radiosensitizing Agent in the Treatment of Prostate Cancer

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External beam radiation therapy (EBRT) is a well recognised curative prostate cancer (PCa) treatment modality utilizing ionizing radiation (IR). In addition to mediating DNA damage IR upregulates several intracellular pro-survival pathways, designed to minimize the insult of radiation. Such pathways, which include the insulin-like growth factor (IGF) signaling network, are felt to contribute to the intrinsic radioresistance exhibited by certain tumors. Diabetic patients with PCa experience poorer outcomes following EBRT than their non-diabetic counterparts. Some attribute this to diabetes-induced chronic hyperinsulinemia, causing upregulation of pro-survival insulin/IGF signaling. Indeed previous work by our group showed diet-induced hyperinsulinemia enhanced PCa tumor growth *in vivo*. Metformin, a treatment for diabetes, alleviates hyperinsulinemia, and has also recently been shown to exhibit anti-neoplastic properties. We postulate that pre-treatment with metformin to correct hyperinsulinemia may protect cells from radiation-mediated pro-survival insulin/IGF signaling. Thus we assessed the radiosensitizing potential of metformin using both *in vitro* and *in vivo* PCa models.

Using clonogenic assays we assessed the effect of IR and/or metformin on colony formation rates in LNCaP, PC3, DU145 and PC3AR2 PCa cell lines. The combination treatment regimen was also assessed *in vivo* using a LNCaP murine xenograft model. Western blot and cell cycle analyses are ongoing to try and elucidate a potential mechanism of interaction between metformin and IR, in both androgen receptor (AR) positive (LNCaP) and AR negative (PC3) PCa cells.

Monotherapy with IR (1-8Gy) or metformin (0.01-10.0 mM) caused significant dose-dependent reduction in colony formation rates ($p<0.001$). Combination treatment further significantly reduced colony formation rates ($p<0.03$). This effect was more marked in AR positive cell lines. Preliminary results from our *in vivo* study show significantly diminished tumor growth in response to combination treatment ($p<0.0001$).

Our *in vitro* findings confirm combining metformin with IR significantly reduces PCa cell colony formation rates further than either monotherapy. Recapitulation of these results *in vivo* would provide justification for translating this work into a phase II clinical trial of metformin as a radiosensitizing agent.

UP-007

Low Incidence of Prostate Cancer Identified in the Transition and Anterior Zones with Transperineal Biopsy

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Objectives: To determine the incidence of anterior zone and transitional zone prostate cancers using a transperineal guided biopsy mapping approach.

Methods: From September 1, 2009 to February 28, 2010, 137 patients with history of previous negative biopsy but had a rising PSA, history of HGPIN or ASAP or abnormal DRE underwent transperineal saturation biopsy of the prostate. The number of biopsy cores was determined by sonographic prostate volume. The cores were taken from specified areas of the prostate. A pre-defined template was used to obtain cores from specific areas of the prostate. The electronic medical records of these patients were reviewed for the patients' clinical and pathological characteristics.

Results: In 41 of 137 patients (31.4%), biopsy was positive for prostate adenocarcinoma. Of the positive biopsies, 11 were from 24 core sampling, 19 from 36 and 11 from 48 core samples. Patients with glands > 45cc had a mean of 1.7 ± 0.8 previous biopsies and a PSA of 9.1 ± 6.0 ng/mL. Corresponding results for glands <30 cc were 1.3 ± 0.9 and 6.3 ± 3.8 ng/mL and those with 30-45cc were 1.4 ± 0.9 and 6.5 ± 3.8 ng/mL. Glands < 45cc had higher number of positive biopsies per total number of cores. 7 patients chose active surveillance as treatment while 34 chose active treatment. 2.2% and 1.5% of the 36 and 48 cores biopsies respectively were positive in the TZ. 1 patient was AZ positive alone, 1 was TZ positive alone and 18 were PZ positive alone. 12 patients had cancer detected in both PZ and TZ. Post-biopsy, 2 patients developed urinary retention and 1 a urine infection.

Conclusions: Trans-perineal saturation biopsy of the prostate is a safe and efficacious method of prostate cancer detection in patients with a previous negative biopsy and high clinical suspicion for cancer. Few cancers were found to originate in the TZ or AZ alone, even in this subset of patients who have undergone previous biopsy. We recommend that initial biopsy templates should ensure robust sampling of the PZ with less focus on the TZ.

UP-008

The Value of Traditional Screening Methods in Highlighting Intermediate and High-Grade Prostate Cancer in an Atlantic Canadian Population

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Introduction and Objectives: Prostate specific antigen (PSA) and Digital Rectal Examination (DRE) are simple, commonly used screening methods for the detection of prostate cancer (PCa). Alone they lack the sensitivity and specificity to predict prostate biopsy results however, studies have shown increased cancer detection rate when they are used together. We know that the presence of hypoechoic lesions on TRUS is indicative of a potential malignancy. Despite this fact, transrectal ultrasonography's current role is prostate biopsy guidance and volume measurement. TRUS lesions play no role in PCa prediction using the PCPT calculator. The purpose of our study was to compare PSA, DRE, and TRUS results between low, intermediate, and high-grade PCa in our population.

Methods: The analysis was performed on prospectively collected data of 1869 men undergoing transrectal ultrasound guided prostate biopsy by two urologists at one institution. The following variables were recorded: age at diagnosis, number of cores taken, PSA value at diagnosis, DRE at diagnosis, TRUS lesions, family history, and prostate volume.

Results: Of the 1869 men who underwent TRUS biopsy 669 (35.3%) were diagnosed with PCa. The average age at diagnosis was 66.6 years old. The median PSA for men with PCa was 5.75. Of the biopsied population diagnosed with cancer 66.8%, 24.9%, 4.6%, and 3.6% were Gleason grade 6,7,8, and 9 respectively. PSA values for low-grade cancer were significantly lower than values of intermediate and high-grade cancer ($p<0.01$;$p<0.001$ respectively). There were more hypoechoic TRUS

lesions in high and intermediate grade cancers than in low-grade cancers (60% high, 39.9% intermediate, 21.2% low p=0.0001, p=0.01 respectively). Our results show that 42.9% of low-grade cancers have palpable DREs whereas 62.8% (p =0.001) of intermediate and 67.2% (p=0.01) of high-grade cancers have palpable lesions. *low-grade = gleason 6, intermediate grade = gleason 7, high grade = ≥ gleason 8.
Conclusion: In our patient population two thirds of diagnosed PCas are low-grade gleason 6 disease. The two screening methods for PCa, PSA and DRE, are significantly more sensitive in highlighting intermediate/high-grade disease than low-grade disease. Based on our data hypoechoic lesions are more likely to be seen in intermediate and high-grade cancers.

UP-009

Wait Times for Prostate Cancer Care in Newfoundland and Labrador

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Background and Objective: Using chart reviews, we measured the wait time intervals for patients seeking urologists' care for suspected prostate cancer. We compared the wait times to benchmarks set by local experts and the recommendations of the Canadian Society for Surgical Oncology (CSSO).
Method: Residents who had a biopsy/TRUS for suspected prostate cancer between April 1, 2009-March 31, 2010 at the Health Science Centre in St. John's, NL were eligible. We calculated median and maximum and minimum waits for the intervals: date of referral to first visit with urologist, decision to biopsy to date of biopsy, biopsy date to notification of patient, and from decision to treat to first treatment. We calculated median (minimum and maximum) waits, and the proportion of patients who met benchmarks.
Results: The 341 eligible patients in the study waited a median of 68 days (0-310) from referral to first visit with urologist, 28 days (0-151) from the decision to biopsy to date of biopsy, 40 days (13-404) from the biopsy date to notification of the patient, and 30 days (0-272) from decision to treat to first treatment. By interval, 13% to 62.5% of men met the local benchmarks (based on expert opinion) for these intervals. Seven percent of men met the CSSO's benchmark for referral to first consultation and 33% of men met the CSSO's benchmark for conclusion of preoperative tests to first treatment.
Conclusion: Few men met local and national wait time benchmarks for suspected prostate cancer care. Study results will be used to identify strategies to improve timelines of specialist care in the province. They will also provide the groundwork for ongoing monitoring and interprovincial comparisons.
Funding: Newfoundland and Labrador Centre for Applied Health Research (NLCAHR), Canadian Institutes for Health Research (CIHR).

UP-010

Short and Intermediate Term Complications following Robot Assisted Radical Prostatectomy in a Prospective Cohort of 305 Consecutive Cases

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Introduction and Objectives: Robot Assisted Radical Prostatectomy (RARP) has emerged in the last decade as an alternative to Open Radical Prostatectomy (ORP) for men with localized prostate cancer. The increased cost of this technique has been justified by its ability to provide improved vision, reduced blood loss, less post-operative pain and more rapid recovery from surgery while maintaining satisfactory oncological and functional outcomes. Given the increasing diffusion of robotic surgical technology within Canada and its associated high capital and operating costs, we report a review of the clinical outcomes and complications from 305 consecutive cases performed at our institution.
Methods: A consecutive cohort of 305 patients with a mean follow up of 902 days was analyzed with institutional ethics approval. All patients were treated and reviewed post-operatively by a single surgeon (SP). The primary aim of the study was to assess the incidence and type of complications associated with RARP in a Canadian setting. Our prospective database captured pre-operative, intra-operative and post-operative data and was maintained by an individual independent of the robotic program. We report complications categorized according to the Clavien system. Multiple complications seen in an individual were recorded separately for the purposes of our analysis.
Results: Three hundred and five consecutive patients (mean age 59.9 years) underwent RARP at our institution between April 2005 and October 2010. A total of 68 complications were identified, with 46 (67.6%) requiring only conservative or pharmacological management (Clavien I-II). Twenty-two patients were found to have a major complication (Clavien III-V) requiring further intervention. Of those patients requiring intervention under general anaesthesia, 3 required emergency treatment with the remainder performed electively. We report an overall pT2 positive margin rate of 10.2%.
Conclusions: RARP has been incorporated at our institution with an acceptably low rate of intra-operative and post-operative complications. We report intermediate term outcome data from our prospective database. The database serves as an effective means of gaining consent from patients who are fully informed with regard to the institution specific risks of RARP.

UP-011

Prostate Cancer Antigen 3 (PCA3) as a Predictive Marker for Gleason Score

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Introduction and Objective: Prostate Cancer Antigen 3 (PCA3) has shown promise as a new urinary marker for prostate cancer. PCA3 has been shown to have a higher specificity than prostate-specific antigen (PSA) for prostate cancer. We assessed PCA3 scores in patients with prostate cancer, and its value in predicting higher grade Gleason scores was evaluated.
Methods: Using a prospectively maintained, single organization database, we retrospectively identified 1406 consecutive patients who underwent prostate needle biopsy (all ≥12 cores). Of those patients, 1252 patients had a PCA3 assay. A PCA3 value ≥35 was considered positive. Data on age, PCA3, PSA, biopsy result, and Gleason score were collected. For statistical analyses we used a two-sample t-test and a natural logarithm transform on PSA and PCA3. Logistic regression was used to evaluate the probability of having a higher grade Gleason score.
Results: 454 patients had a positive biopsy for cancer. 37% of patients had Gleason ≥7 cancer (n=166), while 63% had Gleason ≤6 (n=288). Mean PCA3 was higher in patients with Gleason ≥7 cancer than Gleason ≤6, (60.52 vs 46.09), and the association was statistically significant (p=0.0122). PSA and Gleason score were also significantly associated, with higher mean PSA in Gleason ≥7 cancer than in Gleason ≤6 (7.99 ng/mL vs 5.6, p<0.0001). On univariable analysis, PCA3 (p=0.0075), PSA (p=0.0012), and age (p<0.0001) were associated with the likelihood of having a higher Gleason score. On multivariable analysis, PCA3 (p=0.0475), PSA (p=0.0341), and age ≥65 (p=0.0041) were independently associated with the likelihood of a higher grade Gleason score.
Conclusions: Higher PCA3 score was significantly associated with higher grade Gleason score in prostate cancer patients. PSA also had a significant association with higher Gleason score. PCA3 may be a useful adjunct in combination with other markers and established risk factors to better identify and stratify patients for prostate biopsy.

UP-012

The Accuracy of Transperineal Template Prostate Biopsy in Detecting Prostate Cancer

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Introduction and Objectives: Current evidence on the efficacy of transperineal template biopsy of the prostate shows an increase in diagnostic yield in patients with suspected prostate cancer. No consensus exists regarding the method of repeat biopsy for those with high PSA after standard and extended (MD Anderson technique) prostate biopsies. An aim of the transperineal approach is to target accurately the prostate to ensure representative sampling and reduce the risk of infection compared with trans-rectal biopsy.

Material and Methods: A retrospective review of saturation biopsy cases conducted over the last 5 years, to assess the cancer detection. The site of tumours and complications were also analysed. The technique involved transperineal biopsy under general anaesthetic using a brachytherapy template. Tissue from the transition and peripheral zones from each lobe were collected separately. The impact of this procedure on improved diagnostic accuracy, by providing a more detailed assessment of the whole gland with respect to tumour load, may gather more precise data to influence patient treatment choice.

Results: 69 cases underwent saturation transperineal biopsies, with mean PSA level of (15.35) ranges (3.7-44.1) and all had had 2 previous biopsies. Thirty nine cases (56%) had prostate cancer in various locations between transition zone, peripheral zone and midline with 30 (43.5%) cases being found in the transitional zone, 32 (46%) cases in the peripheral zone and 9 (13%) cases in the midline. Fourteen (20%) cases were found in a single prostate zone; 5 (7%) cases were in the transitional zone, 6 (8.7%) cases in the peripheral zone and 3 (4.3%) cases in the midline. Gleason sum score ranged from (6-9); with 14 (36%) cases Gleason 6, 15 (38%) Gleason 7, 8 (21%) Gleason score 8 and 2 (5%) Gleason score of 9. There was great variability in the number of cores taken with median 40 cores, mean 45 cores and ranging from 19 – 128. Our complication rates were: 11(16%) cases of urine retention, 3 (4.3%) cases of prolonged haematuria, and 2(2.8%) cases of septicaemia.

Conclusions: Saturation transperineal prostate biopsy did show a greater diagnostic yield than seen with the transrectal route with 56% of cases who had undergone previous prostate biopsies being found to have prostate cancer. The main disadvantage is the need for general anaesthesia, but the associated complication rates are low and the procedure can be for performed as a day case.

UP-013

Prevalence and Predictors of Selenium and Vitamin E Supplementation in a Urology Population

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Introduction and Objectives: In the Selenium and Vitamin E Cancer Prevention Trial (SELECT) investigators concluded that neither selenium nor vitamin E have a significant impact on prostate cancer incidence despite promising pre-clinical data. In this study we aim to investigate the prevalence and predictors for use of these supplements in men with or at risk for developing prostate cancer post-SELECT publication.

Methods: 312 men visiting PMH urology clinics were enrolled in this UHN REB approved questionnaire-based study investigating past and present supplement use, reasons for use and demographic characteristics.

Results: We observed that 13.5% and 20.8% of the participants are currently using selenium and vitamin E, respectively while 10.6% and 15.7% previously used selenium and vitamin E, respectively. Both education (p_{Se}=0.008, p_{vitE}=0.013) and health literacy (p_{SeQ1}=0.023, p_{SeQ2}=0.000, p_{SeQ3}=0.025, $_{vitEQ2}$=0.010, $_{vitEQ2}$=0.006) status are predictors of selenium and vitamin E use on univariate analysis. On multivariate analysis education (p_{Se} =0.044 OR 2.095 CI 1.019-4.305, p_{vitE}=0.045 OR 1.855 CI 1.015-3.338) remains a significant predictor of selenium and vitamin E use. Overall, a larger proportion of men attributed their use of selenium and vitamin E to urologist advice (21%) and family member advice (20%), respectively, as compared to other reasons. Triaging reason for use by education we found that more men with a higher education attributed their use of selenium to urologist advice (24%) and with a lower education attributed their use of selenium to naturopath/homeopath advice (28%).

Conclusions: Many patients continue to use selenium and vitamin E despite publication of the SELECT data. Education and health literacy are important variables in determining the use of these supplements in men with or at risk for developing prostate cancer. Furthermore, men with different education levels have different reasons for taking selenium. This information is important for addressing the needs of the diverse patient population using these supplements for the prevention of prostate cancer.

UP-014

The Ghrelin Receptor as a Novel Imaging Target in Prostate Cancer

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Introduction: Ghrelin is a natural growth hormone secretagogue. The co-expression of Ghrelin and its receptor GHS-R, a G protein-coupled receptor, had been demonstrated in human prostate cancer cell lines. We wished to investigate the Ghrelin receptor as an imaging marker in human prostate cancer.

Methods:

Ghrelin Probe Assembly:

A Ghrelin analogue was synthesized using the APEX 396 peptide synthesizer and labelled with FITC. Purity was determined by RP HPLC.

Ghrelin Probe Imaging in PC-3 Cell line:

Ghrelin probes were incubated with PC-3 cells prior to or after the 4% formaldehyde fixation, to determine the Ghrelin receptor binding fixed cells. 10 times concentration of Ghrelin analogue without FITC was used as blocking reagent for the specific binding test. The signal of Ghrelin probe was amplified with anti-fluorescein antibody and secondary antibody labelled with alexa fluor 647. Intensity of Ghrelin probe signal was quantitative analyzed by Volocity Imaging System.

Ghrelin Probe Imaging in Human Prostate Tissue:

Prostate core biopsy samples were collected from fresh surgery specimens of 20 patients undergoing radical prostatectomy, and continuous frozen sections were made for both HE staining and Ghrelin probe imaging. Prostate tissue was categorized into prostate cancer (PCa), prostate intraepithelial neoplasia (PIN) or benign tissue based on the pathological changes in HE staining. Ghrelin staining was quantitatively analyzed within the different tissue types.

Results: The binding of our Ghrelin probe to its receptor is specific and can be blocked by the competitive binding from Ghrelin analogue (p=0.007).

Ghrelin probe signal intensity varied with different histological findings.. The mean signal intensity in PCa, PIN and benign tissue is 671.1 RFU/Pixel, 598.6 RFU/Pixel and 276.8 RFU/Pixel respectively. Independent sample T-test manifested the statistical significance of the signal difference between different groups (PCa vs Benign, $p<0.01$; PIN vs Benign, p=0.017; PCa vs PIN, p=0.001)

Conclusions: The binding of Ghrelin probe to its receptor is specific and leads to low signal intensity in benign tissue and significantly increased expression in PIN and Prostate cancer. Ghrelin receptor labeling needs further investigation as aa novel imaging marker for prostatic neoplasms in both localized and metastatic disease.

UP-015

CD151 as a Prognostic Indicator Prostate Cancer

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Introduction: CD151 is a tetraspanin protein linked to cellular growth and motility. Previous work has suggested that CD151 may play a role in metastases in a variety of cancers and may predict a worse prognosis in prostate adenocarcinoma (PCa) although the mechanism for this is unclear. We wished to check the expression of CD151 in both radical prostatectomy (RRP) specimens as well as biopsy specimens from patients with known metastatic disease to look for any association with disease progression and survival.

Methods: Tissue was attained from 99 patients who had undergone RRP for PCa (mean follow up 12.4 years) and from 36 patients with known metastatic disease. Tissue sections were taken from paraffin embedded slides and imunohistochemical staining performed for mAb 1A5 as a marker for CD151. Histological sections from corresponding levels were stained with H&E and compared for CD151 positivity. A database of patient's demographic factors, disease factors and relevant survival information was generated and correlated with disease-free progression and survival.

Results: There was a statistically significant difference in CD151 expression between malignant tissue and benign tissue around (p=0.01) and away the tumour (p<0.01) in RRP specimens in addition CD151 was associated with earlier biochemical failure (p=0.022). The diagnostic biopsy specimens showed that CD151 staining was associated with earlier overall metastasis (p<0.01), earlier bone metastasis (p=0.01) and the development of hormone resistance (p<0.01).

Conclusions: Patients with PCa specimens that stained positively for CD151 were more likely to develop disease recurrence. This study was probably underpowered to show that Gleason score and tumour stage can predict recurrence suggesting that CD151 positivity may be a more sensitive indicator or risk of recurrence in patients following RRP. We speculate that CD151 may have a clinical role in predicting those who may benefit from adjuvant treatment following RRP. CD151 positivity in patients with known prostate cancer metastases was able to predict early metastases and bone metastases. Interestingly CD151 was able to predict hormone resistance amongst a patient group all with known metastases, this may be the result of simple a greater bulk of disease in this patients but warrants further investigation.

UP-016

Late Toxicity, Urinary Symptom, and Sexual Function Profiles after Image Guided Radiation Therapy, with Daily Cone Beam CT, for Localized Prostate Cancer

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Introduction and Objective: High-dose, intensity modulated radiotherapy (IMRT) for prostate cancer warrants optimal image guidance to maximally reduce toxicity. We evaluated pre- and post-treatment trends in urinary and sexual function, and post-tx toxicity, in a cohort treated with modern image guided radiation therapy (IGRT), using daily cone beam CT (CBCT) for treatment guidance.

Methods: This is a retrospective analysis of 298 men with localized prostate cancer, treated using daily CBCT IGRT with RapidArc IMRT (77.4Gy–81Gy). Patients completed the International Prostate Symptom Score (IPSS) and 5-item International Index of Erectile Function (IIEF-5) prior to treatment start, and at 1 yr post-tx. Gastrointestinal (GI) and genitourinary (GU) toxicity were graded by Common Terminology Criteria for Adverse Events (CTCAE v4.0).

Results: For all 298 men (median tx age = 69; range 46–84), none had GI or GU toxicity above CTCAE Grade 2 at 1 yr follow-up. Urinary toxicity was seen in 3.4% (n=10): 8 men at Grade 1; 2 men at Grade 2. Rectal toxicity was seen in 6.7% (n=20): 14 men at Grade 1; 6 men at Grade 2. GU plus GI toxicity was present in 2 men. 288 men completed pre- and post-tx IPSS. The median pre- v. post-tx IPSS was 7 (range 0–32) v. 6 (range 0–31), with significance toward lower post-tx IPSS (p<.05, Wilcoxon signed ranks test). Same or improved post-tx IPSS was seen in 185/288 (64.2%) men; worsened post-tx IPSS was seen in 103/288 (35.8%) men. ΔIPSS (post- minus pre-tx IPSS) was calculated, with ΔIPSS <0 indicating urinary symptom improvement. Higher pre-tx IPSS was associated with larger negative ΔIPSS values (p=.01, Spearman rank correlation). 203 men completed pre- and post-tx IIEF-5. The median pre- vs post-tx IIEF-5 was 16 (range 2–25) vs 12 (range 5–25), with significant trend toward lower post-tx scores (p<.05). However, only 59 men had pre-tx scores ≥22 (no erectile dysfunction). From this group, 6/59 (10.2%) had post-tx scores of 5–7 (severe ED). Mild ED was defined as IIEF-5 scores of 17–21. 100 men had pre-tx IIEF-5 ≥17 (mild or no ED); post-tx IIEF-5 scores of 5–7 were noted in 17/100 (17%) of these men.

Conclusions: Daily CBCT IGRT shows low GI and GU toxicity, and favorable post-tx IPSS characteristics, at 1 yr follow-up. Post-tx IIEF-5 scores generally worsened from baseline, but stratification indicates that decline from pre-tx mild or no ED, to post-tx severe ED was low.

UP-017

Meat and Related Meat Mutagen Consumption and Risk of Advanced Prostate Cancer

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Introduction: Dietary consumption of various meats has been associated with the development of prostate cancer, presumably through the release of carcinogenic heterocyclic amines and polyaromatic hydrocarbons, which occur when cooking or grilling meat at high temperatures. We examined the consumption of various meat types, meat doneness and related meat mutagens in the development of advanced prostate cancer.

Methods: This was a nested case control study involving 469 aggressive incident prostate cancer cases and 508 controls, recruited from major medical institutions in Cleveland, Ohio, between 2001 and 2004. All subjects were given a self-administered food frequency questionnaire to provide information on meat consumption, methods of preparation and meat doneness level. We estimated odds ratios and 95% confidence intervals for risk of advanced prostate cancer with increasing amounts of meat consumption.

Results: When comparing the highest category of meat consumption with the lowest, both red and white meat consumption showed and increased risk of advanced prostate cancer (Red: OR 1.54 95% CI 1.06-2.26; p-trend= 0.007, White: OR 1.55 95% CI 1.13-2.12; p-trend= 0.006). With respect to meat mutagens we saw an increased risk with 2-amino-3,8-Dimethylimidazo-[4,5-f]Quinolaxine (MelQx) and 2-amino-3,4,8-trimethylimidazo(4,5-f)qunioxaline (DiMelQx), when comparing the forth quartile intake with the first (MelQx: OR 1.69 95% CI 1.08-2.64;p-trend=0.02, DiMelQx: OR 1.53 95% CI 1.00-2.35; p-trend=0.005), however this association was not seen with 2-amino-1-methyl-6-phenylimidazo-[4,5-B]Pyridine or Benzoapyrene. With respect to meat doneness, high consumption of well done or very well done red meat had an increased risk of advanced prostate cancer compared to a low consumption of rare or medium cooked red meat (OR =2.02, 95% CI: 1.29-3.16), however, a low consumption of well or very well done red meat did not show an increased risk of advanced prostate cancer

Conclusion: In conclusion, we found that high consumptions of both red and white meat were associated with increased risk of advanced prostate cancer. High consumption of well and very well done red meat produced an increased risk of advanced prostate cancer.

UP-018

In Potent Men, Does the Need for Phosphodiesterase Inhibitors (PDEI) Have an Impact on Sexual Bother Scores?

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Introduction: Treatment of prostate cancer with radical prostatectomy is known to have an impact on sexual function (SF). Potency following surgery is most commonly defined as having successful erections with or without the use of PDEI. No study, to our knowledge, has determined whether or not this inclusive definition is valid. The goal of present study is to characterize the effect of PDEI use on sexual bother (SB) scores in men who report good SF following surgery for prostate cancer.

Methods: Within the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE™) database, patients who were potent both before and after treatment, diagnosed between 1995 and 2005, underwent radical prostatectomy, and had sufficient follow-up (baseline and at least 2 assessments in 2 years post-treatment) comprised the study population. Disease specific quality of life data was evaluated by the UCLA Prostate Cancer Index (PCI) survey. Potency was defined as having an erection firm enough for intercourse. The relationship between changes in SF and SB and use of PDE-5 over time was evaluated by mixed model analysis controlling for age, clinical risk group, relationship status, and time of PCI assessment.

Results: 258 patients met the study criteria. Within this group, 105 (40.7%) reported PDEI use at some point after treatment. In the mixed model analysis, PDEI use was not associated with improved SF, which was expected given our inclusion criteria of baseline and post treatment potency. Adjusted mean SF scores over the 24 months of follow-up for PDEI users and non-users were 59.1 and 59.2 (p<0.90), respectively. Furthermore, PDEI use was not associated with a change in SB (p=0.25). Adjusted mean SB scores over the 24-month follow up period for PDEI users and non-users were 68.3 and 70.4, respectively. Both SF and SB were significantly associated with time of assessment (p<0.0001) and age (p<0.0001 and p=0.016, respectively) and SF and SB each improved over time. In addition, SB was significantly associated with relationship status (p=0.006).

Conclusion: In this analysis, there was no difference in SB scores between men who are potent without or with the use of PDEI. This suggests that the current, inclusive, definition of potency is valid

UP-019

Short-Term Androgen Deprivation Therapy is Not Associated with Depression: Interim Results of a Prospective Cohort Study

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Introduction and Objective: The presence, timing and magnitude of effect of androgen deprivation therapy (ADT) on anxiety and major depressive illness are controversial. This is an interim analysis of a 2-year prospective cohort study investigating the influence of ADT on depression and mental quality of life.

Methods: Three cohorts of men were enrolled in this prospective, longitudinal study: those initiating ADT for advanced prostate cancer, those undergoing adjuvant ADT in a combined-modality curative protocol for higher risk cancer, and a control group consisting of patients on a watchful waiting approach. Patients are assessed every 3 months from baseline (i.e., before the onset of ADT) for 2 years. Questionnaire data was collected to assess depression (CESD) and mental and physical Quality of Life (QoL; SF-36) at every time point.

Results: The mean age of patients was 71.53 ± 7.55 years in this an interim analysis of short-term (3 months) ADT. There were no significant group differences at baseline in terms of age (F=1.68, p=.20), marital status (F=1.12, p=.34), depression (F=1.42, p=.25), mental QoL (F=.59, p=.56) or physical QoL (F=3.51, p=.04) indicating time comparisons across groups was appropriate. A 2x3 (Time x Group) Repeated Measures ANOVA was employed to determine if there were group differences in depression, mental QoL and physical QoL from baseline. Results show no significant main effects for time (F=2.34, p=.14), group (F=9.78, p=.39) or the interaction (F=.34, p=.71) on depression. Similarly, no significant main effects were found for time (F<.00, p=.95), group (F=1.3, p=.29), or the interaction (F=1.80, p=.12) on mental QoL. Lastly, no significant main effects were found for time (F=.32, p=.58), group (F=1.10, p=.35) or the interaction (F=.87, p=.43) on physical QoL.

Conclusions: In this prospective, detailed analysis there was no demonstrable effect of ADT on developing depression in the short-term. Although these results may be subject to change overtime, they provide novel information in regard to the onset of depression in patients following initial stages of ADT. Future reports will monitor and report on longitudinal changes across patient groups.

UP-020

The Impact of Statins and Anticoagulants in Prostate Cancer Aggressiveness

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Introduction and Objectives: Statins and anti-coagulants (AC) are both independently associated with a less aggressive prostate cancer and a better outcome after treatment for localized prostate cancer. Results of these studies might be confounded by the fact that patients might often take both medications at the same time. We investigated their respective influence on prostate cancer aggressiveness at initial diagnosis.

Methods: We analyzed 402 patients treated with either external beam radiation therapy or brachytherapy for either low (n=155), intermediate (n=152) or high-risk (n=95) localized prostate cancer. Statin and AC (antiplatelet therapy or warfarin) use were noted before treatment. Univariate and multivariate logistic regression analysis were used to investigate an association between these drug classes and National Comprehensive Cancer Network (NCCN) risk class, PSA level, Gleason scores and T-stage. We tested whether the concomitant use of Statin and AC had a different effect than that of either AC or statin use alone.

Results: 185 patients (46%) were taking statins and 162 (40.3%) AC. 118 (29.4%) patients used both. There was a strong association between the use of both (6.9 95% CI, 4.5, 10.9; p<0.0001).

In the univariate analysis, statin users were less likely to have a PSA >20 ng/mL (OR 0.45, 95%CI, 0.22, 0.88; p=0.0202). AC use was associated with risk group (p<0.0001), PSA (p=0.009) and Gleason score (p=0.002). In the multivariate analysis, statin use was not associated with risk group (p=0.3074), but age (p<0.0001) and AC use were (p=0.0117). The use of AC was associated with double the risk of being in either the intermediate and high risk group compared to the low risk group.

Conclusions: The influence of AC on prostate cancer aggressiveness is much more important than the one of statins which might be limited to PSA only, highlighting the importance of considering AC use in the studies of cancer aggressiveness.

UP-021

Implication of Parp-1 Expression in Prostate Cancer Progression

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Introduction: Prostate cancer (PCa) is the leading cancer diagnosed in men, with one out of seven developing PCa and a quarter of those progressing to an advanced stage of the disease. Intense research is ongoing to be able to predict the probability of disease progression. As current nomograms are solely composed of clinico-pathological factors, the inclusion of molecular markers may potentially increase their precision. The over-expression of poly(ADP-ribosyl) polymerase-1 (PARP-1) is associated

with colorectal cancer progression as well as a poor prognosis in ovarian and breast cancers. We hypothesized that the proportion of PARP-1 positive (+) nuclei would increase with PCa progression. The present study evaluated the value of PARP-1 in predicting biochemical recurrence (BCR) in PCa patients.
Methods: We analyzed the nuclear localization of PARP-1 in prostate tissues by immunohistochemistry on tissue microarrays. Our cohort consisted of radical prostatectomy tissues from 62 patients with long follow-up operated at the Centre Hospitalier de l'Université de Montréal (CHUM). We analyzed the percentage of PARP-1+ nuclei using the Aperio software and the IHC Nuclear algorithm (v8.001) in both malignant and non-malignant (normal adjacent to the tumor, prostatic intra-epithelial neoplasia) tissues. Statistical analyses were performed using SPSS software (v.11).
Results: We observed increased PARP-1+ nuclei in malignant tissues compared to non-malignant tissues (Wilcoxon, p=0.001). We found that the percentage of PARP-1+ nuclei in malignant tissues correlated with BCR (Spearman correlation, r=0.389, p=0.002). Also, in a univariate COX regression model, the percentage of PARP-1+ nuclei predicted BCR (p=0.001). A multivariate COX regression determined that the percentage of PARP-1+ nuclei was a predictor independent of the clinico-pathological factors used in Kattan's nomogram (p=0.048).
Conclusion: Our analysis suggests that the percentage of PARP-1+ nuclei increases with PCa progression and that it can predict BCR independently of current clinico-pathological factors. Considering the predictive potential of PARP-1 in this cohort, we are expanding this analysis to a larger cohort to fully assess the predictive value of PARP-1 in PCa.
Source of Funding: Terry Fox Foundation; Sanofi Aventis; RRCancer; Université de Montréal's Chair in Prostate Cancer; Université de Montréal Urology Associates; ICM; Défi Candérel.

UP-022

Minimally Invasive Radical Prostatectomy Hold No Advantage over Open Radical Prostatectomy with Regard to Complication Rates: Population-Based Data from the United States

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Introduction and Objectives: To date, studies suggest a benefit of minimally invasive radical prostatectomy (MIRP) over open radical prostatectomy (ORP) when complication rates are compared. We examined intraoperative and in-hospital complication rates as well as blood transfusion rates after either MIRP or ORP within a contemporary population-based sample from the United States.
Methods: Within the Health Care Utilization Project Nationwide Inpatient Sample (NIS) we focused on patients in whom radical prostatectomies were performed between 2001 and 2007. We relied on previously validated methodology to quantify rates, trends and in-hospital morbidity and transfusion rates. Univariable and multivariable logistic regression analyses were used. Adjustment was made for age, race, baseline Charlson Comorbidity Index (CCI), annual hospital volume tertiles (AHV) and hospital academic status.
Results: A total of 89970 radical prostatectomies were performed during the study period. Of those, 4389 were MIRPS (4.9%). The intraoperative complication rate was 1.3% for MIRP vs 1.4% for ORP (p=0.8). The overall in-hospital complication rates were 9.9 vs 11.4%, respectively (p=0.003). Blood transfusion rates were 1.8 and 6.5% for MIRP and ORP (p<0.001). In multivariable analyses, relative to ORP, MIRP was not associated with lower rates of intraoperative (odds ratio [OR]: 1.1, p=0.6) and in-hospital complications (OR: 1.1, p=0.1). Conversely, MIRP exerted a protective effect on homologous blood transfusion rate (OR: 0.41, p<0.001).
Conclusions: Despite the existence of reports suggesting more favourable complication outcomes after MIRP relative to ORP, our national population-based sample failed to show a benefit of MIRP when complications were defined as the main outcome. Conversely, fewer transfusions were recorded in MIRP patients.

UP-023

Important Racial Disparity Exists with Respect to the Use of Minimally Invasive Radical Prostatectomy in the United States

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Introduction and Objectives: Race represents an established barrier to healthcare access in the United States and elsewhere. We examined whether race affects the rate of use of minimally invasive radical prostatectomy (MIRP) in a population-based sample of individuals from the United States.
Methods: Within the Health Care Utilization Project Nationwide Inpatient Sample (NIS) we focused on patients in whom MIRP and open radical prostatectomy (ORP) were performed between 2001 and 2007. We assessed the proportions and temporal trends in race distributions between MIRP and ORP. Multivariable logistic regression analyses further adjusted for age, baseline Charlson Comorbidity Index (CCI), annual hospital volume tertiles (AHV) and hospital academic status.
Results: Overall, we identified 3581 patients treated with MIRP (5.5%) and 61567 patients treated with ORP (94.5%), after exclusion of 24822 patients for whom race information was unavailable. Of patients treated with MIRP, 18.4% were non- Caucasians vs 21.1% for ORP (p<0.001). The proportions of non-caucasian patients treated with MIRP were 19.1, 10.7, 17.8, 13.6, 23.0, 19.9 and 18.6% respectively from 2001 to 2007 (p=0.1) vs 20.2, 21.6, 21.8, 20.9, 20.7, 22.4 and 21.9% respectively in ORP treated patients during the same study years (p=0.01, increase of 1.2% per year). In multivariable analysis for prediction of MIRP status, non-caucasian race failed to reach independent predictor status (odds ratio [OR]: 0.9, p=0.2). All analyses were then repeated to compare African Americans to other patients. Of patients treated with MIRP, 8.6% were African Americans vs 11.5% for ORP (p<0.001). The proportions of African American patients treated with MIRP were 4.1, 4.0, 6.4, 8.0, 7.5, 11.4 and 8.6% respectively from 2001 to 2007 (p=0.004, increase of 3.8% per year) vs 11.3, 11.5, 11.8, 12.3, 10.5, 11.4 and 11.8% respectively in ORP treated patients during the same study years (p=0.9). In multivariable analysis for prediction of MIRP status, African American achieved independent predictor status (OR: 0.81, p=0.001).
Conclusions: Our results indicate that in the United States non-caucasians have equal access to MIRP. Conversely, African American may have unequal access to MIRP according to the NIS.

UP-024

Capsaicin, a Novel Radio-Sensitizer, Acts via a TRPV6 Mediated Mechanism

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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, a compound found in the *Capsicum sp.* of plants, is a widely consumed food additive in areas with low PCa incidence. Traditionally capsaicin is used to treat chronic pain syndromes; however, recently evidence using *in vitro* PCa models describes its anti-carcinogenic potential. The transient receptor potential vanilloid-receptor (TRPV)-1 and TRPV6 cation selective channels are thought to be partly responsible for mediating these effects. TRPV-1 and TRPV-6 expression is up-regulated in PCa tissue correlating directly with increasing tumor grade. This suggests capsaicin-mediated interventions in PCa patients. As IR and capsaicin both promote

apoptosis and inhibit cell cycle progression *in vitro* we hypothesize an at least additive effect of combining these two therapies.
Methods: Using clonogenic assays we assessed the effect of ionizing radiation (1-8 Gy) and/or capsaicin (1-10 μM) on colony formation rates in 4 human PCa cell lines (LNCaP, PC3, PC3AR2, DU145). Proliferative, apoptotic, TRPV-6 protein markers were assessed using Western blot analyses.
Results: Exposure of cells to capsaicin (1-10μM) or IR (1-8Gy) caused significant dose-dependent inhibition of colony formation ($p<0.001$). Combining capsaicin with IR resulted in further significant inhibition of colony formation rates ($p<0.001$). Western blot analyses showed LNCaP cells treated with capsaicin and/or IR to have increased expression of pro-apoptotic proteins BAX and Bad, tumor-suppressor proteins p21 and p27 and reduced androgen-receptor. Additionally, capsaicin mono-therapy caused a dramatic alteration in TRPV1 and TRPV6 expression.
Conclusion: These studies confirm the radio-sensitizing capacity of capsaicin in PCa cells *in vitro*. Ongoing studies using are further delineating the mechanism of interaction of these treatment modalities.

UP-025
Early Urethral Catheter Removal following Robot-Assisted Laparoscopic Prostatectomy (RALP)
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Introduction and Objectives: Typical urethral catheter duration following radical retropubic prostatectomy (RRP) and RALP is 7–10 days. We review our RALP experience to determine if urethral catheter removal following office cystography performed within the first post–operative week is feasible.
Methods: Using an anterior approach, a bladder neck sparing dissection was preferentially performed. The urethrovesical anastomosis was completed using a double–armed 3–0 monocryl suture ± bladder neck tailoring when appropriate. A 20 Fr urethral catheter was placed. On postoperative day (POD) 5 or 6 (clinic logistics), the urethral catheter was removed following normal cystography.
Results: 219 patients were identified. 104/219 (47.5%) patients, with a mean age of 61.9 ± 8.8 years and PSA of 5.4 ± 3.6 ng/mL, had their urethral catheter removed on POD 5. 67/219 (30.6%) patients had their urethral catheter removed on POD 6 (clinic logistics). Time to urinary continence without pads was 10.0 ± 8.1 weeks. Mean hospitalization was 1.0 ± 0.2 days. 1 (1.0%) pTx, 17 (16.3%) pT2a, 3 (2.9%) pT2b, 70 (67.3%) pT2c and 13 (12.5%) pT3 cancers were reported, having a mean prostate volume of 41.7 ± 14.5 mL. Adverse events included 2 (1.9%) bladder neck contracture, 5 (4.8%) temporary urinary retention and 1 (1.0%) urinary tract infection.
Conclusions: Early urethral catheter removal following RALP is feasible and does not increase patient morbidity in those without urinary extravasation on office cystography.

UP-026
Is Prostate Cancer Pathology following Robot-Assisted Laparoscopic Prostatectomy (RALP) Accurately Predicted by Transrectal Ultrasonographic (TRUS) Guided Biopsy Specimens?
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Introduction and Objectives: Discrepancy between Gleason grade on TRUS biopsy and final pathology may impact management disposition of clinically localized prostate cancer. Pathologic upgrading and downgrad-

Table 1. Clinical and Pathological characteristics of population stratified by BMI. UP-027

Characteristics	<25 Kg/m² Normal Weight	25-29.9 Kg/m² Over Weight	30-34 Kg/m² Mildly Obese
No. Patients (%)	169 (47)	187(51)	7(2)
Age (yr)	60.76±6.25	61.43±6.06	63.00±6.00
BMI Kg/m²	22.70±1.10	26.89±1.50	33.10±2.11
Pre-PSA (ng/mL)	6.90±3.34	6.94±3.22	7.79±2.30
Biopsy Gleason (%)			
≤6	97 (57)	112 (60)	3(42)
7	62 (37)	58 (31)	2 (29)
≥ 8	10 (6)	17(9)	2(29)
Clinical Stage(%)			
T1c	119(70)	125(67)	4(57)
T2a	50(30)	62(33)	3(43)
Pathological Gleason (%)			
≤6	67(40)	78(41)	1(14)
7	87(51)	91(49)	5(72)
≥8	15(9)	18(10)	1(14)
Prostate Weight (g)	41.60±16.81	45.79±13.59	46.81±15.69
% Tumor Involvement	14.5±11.5	15.10±10.00	15.16±11.85
Tumor Volume (cc)	6.90±6.35	7.30±8.86	9.14±6.23
Positive surgical margins (%)	35(21)	49(26)	5(71)
Blood Lost	263.39±203	317.22±216.47	330.00±215.00

ing occurs in 20-40% and 10-20% of cases, respectively. We review the findings in our cohort of RALP patients.
Methods: Consecutive patients who underwent transperitoneal RALP by a single surgeon (CW) were reviewed. Using an anterior approach, a bladder neck sparing procedure was preferentially performed. Unilateral or bilateral nerve sparing prostatectomy was performed when appropriate. TRUS guided biopsy specimens and final prostate pathology were compared.
Results: 219 patients were identified. At baseline, their mean age was 61.9 ± 8.4 years, body mass index (BMI) was 28.3 ± 3.9 kg/m2, PSA was 6.0 ± 4.5 ng/mL and TRUS volume was 43.1 ± 13.8 mL. The mean number of biopsy cores sampled was 11.3 ± 5.1. Clinical stage included 206 (94.1%) T1c and 13 (5.9%) T2a, having a mean Gleason score of 6.5 ± 0.8. 185 (84.5%) had bilateral, 19 (8.7%) had unilateral and 15 (6.8%) did not undergo nerve sparing prostatectomy. 2 (1.0%) pTx, 31 (14.2%) pT2a, 13 (5.9%) pT2b, 144 (65.7%) pT2c and 29 (13.2%) pT3 cancers were reported, having a mean prostate volume of 44.8 ± 12.7 mL. The mean Gleason score was 6.5 ± 1.0. 36 (16.4%) patients had positive surgical margins. Upgrading on final pathology occurred in 30 (13.7%), downgrading in 35 (16.0%) and 154 (70.3%) prostate specimens remained unchanged. The independent variables of preoperative age, BMI, digital rectal examination, PSA, TRUS volume, Gleason sum, number of positive biopsy cores and final pathology were not predictive of whether pathologic upgrading or downgrading would occur.
Conclusions: Our incidence of pathologic upgrading and downgrading following RALP is consistent with that reported in the literature. Whether a TRUS guided biopsy specimen will change on final pathologic evaluation appears to be difficult to predict preoperatively.

UP-027

Body Mass Index as Predictive Factor of Tumor Aggressiveness in Patients with Localized Prostate Cancer: Hormonal Implications

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Introduction and Objective: Obesity is a ubiquitous problem, affecting 1 in 3 adults in North America. It has been related with higher insulin levels and lower androgens levels, which may influence prostatic tissue and cancer growth. It has been associate with increase risk of positive surgical margins (PSM) and biochemical recurrence. These findings support the hypothesis that obesity may be related to aggressive tumor biology and may present some additional challenges during Radical Prostatectomy (RP). The objective of this study was to determine the association between body mass index (BMI) (Kg /m2) and tumor pathological characteristics in patients (pts) with clinically localized PC submitted to RP.
Methods: We retrospectively analysed 363 pts submitted to RP for localized PCa. Patients were stratified by BMI in: <25 (Normal weight), 25-29.9 (Over-weight), 30-34.9 (Mildly obese), >35 (Severely obese). Clinical and pathological characteristics among BMI groups were compared using analysis of variance Kruskall-Wallis for continuous variables, and linear and logistic regression were performed. Statistical package (Graphad Instat 310, Chicago IL, USA), was used.
Results: There were 169 (47%) pts with normal weight, 187 (51%) overweight and 7 (2%) mildly obese. Medina follow-up was 4.0 yrs. See Table 1 for results. At univariable analyses, higher BMI was significantly associated with higherTV, PSM ($p \leq 0.001$), high grade disease ($p=0.006$) and greater % of prostate involvement ($p=0.003$). At multivariable analysis, BMI was an independent predictive factor for TV ($p \leq 0.001$). Three (3%), 18 (9%) and 1 (14%) presented with biochemical recurrence respectively
Conclusions: Our results showed that patients with higher BMI were associated with larger tumor, more aggressive characteristics, higher rates of PSM and biochemical recurrence. These findings support the hypothesis that obesity may be related to aggressive tumor biology, as hormonal metabolism may have an active role in prostate biology.