Poster Session 6: Prostate (II)
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MP-06.01
A comparison of morbidity of ablative energy based whole gland salvage treatments for radio-recurrent prostate cancer

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Introduction: Treatment of radio-recurrent prostate cancer (RRPC) poses a unique challenge. Energy based salvage treatment options such as High intensity focused ultrasound (HIFU) and Cryotherapy (CRYO) can ablate the prostate with minimal side effects. We report our experience comparing the morbidity of both salvage treatment modalities over a 17 years period.
Methods: 283 patients from 1995 to 2014 underwent either salvage CRYO (n=187, from1995 to 2004) or salvage HIFU (n=96, from 2004 to 2014). In 2004, we transitioned from CRYO to HIFU as the salvage ablative technique. Patients were divided into 3 groups, only patients having at least one year follow-up. Complications reported after 90 days of treatment were compared. Group I had the first 65 patients treated with CRYO between 1995 and 1998, Group II was composed of the last 65 patients treated with CRYO from 2002 to 2004 and Group III contained 65 patients who underwent HIFU from 2004 to 2012. This group-wise comparison was designed to elucidate the impact of the learning curve and technologic transit without inter-operator and inter-institutional variability.
Results: The mean pre-salvage Prostate Specific Antigen level in Group I was higher (p=<0.001, one way ANOVA test). Details of other complications are summarized in the Table. HIFU was associated with either equivalent or lower complication rates across all categories compared to CRYO. Overall Improvement in complication rates was seen between our early experience with CRYO and our late experience (88 vs. 56), although statistical significance was not reached (p=0.469). The global improvement in complication rates with after more experience in CRYO use likely signified a learning curve with this procedure. No difference in recto-urethral fistula was seen amongst the three groups with rates of 1.5% - 3% (p=0.817 (Table 1).
Conclusion: HIFU is promising in the management of radio recurrent prostate cancer. It is associated with a low rate of fistula formation and significantly lower rates of incontinence and retention as compared to CRYO.

Table 1. MP-06.01

	Group 1 Cryotherapy (1995–1998) (n=65)	Group 2 Cryotherapy (2002–2004) (n=65)	Group 3 HIFU (2004–2011) (n=65)	*p* value (One-way ANOVA)
Pre-salvage PSA	9.38±7.03	3.25±2.33	3.86±3.01	<0.001*
Median pre-salvage Gleason score	7	7	7	1.00
Incontinence mild to moderate	32 (49%)	20 (31%)	2 (3%)	<0.001*
Severe	1 (1.5%)	3 (5%)	2 (3%)	0.601
Incontinence requiring surgery	1 (1.5%)	1 (1.5%)	1 (1.5%)	1.00
Perineal pain	12 (18%)	7 (10%)	3 (5%)	0.044*
Recto-urethral fistula	1 (1.5%)	2 (3%)	2 (3%)	0.817
Urinary retention	18 (27%)	14 (21%)	1 (1.5%)	<0.001*
Gross haematuria	8 (12%)	5 (7%)	4 (6%)	0.437
Bladder neck contracture/ stricture	7 (10%)	1 (1.5%)	2 (3%)	0.038
Urinary tract infection	8 (12%)	3 (5%)	3 (5%)	0.148

MP-06.02
The effect of wide resection during radical prostatectomy on surgical margins

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Introduction and Objectives: Radical prostatectomy studies do not uniformly identify an association between nerve sparing and a positive surgical margin. The purpose of this study was to determine the risk of a positive surgical margin if a wide prostate resection is performed compared to nerve preservation.
Methods: A consecutive single surgeon patient cohort between 2011 and 2014 was evaluated. Lobe-specific nerve spare or wide resection was documented in the operative report. Wide-resection included dissection posterior to Denonvillier's fascia and incision on to the perirectal fat lateral to the neurovascular bundles. Lobe-specific margin status and tumour stage were obtained by synoptic pathology reports. The primary predictor was wide resection compared to nerve spare technique. The primary outcome was a positive surgical margin from the ipsilateral lobe. Associations were adjusted for patient age, PSA, Gleason sum, prostate volume, tumour volume, extraprostatic extension, and year of surgery.
Results: Of the 388 prostate lobes, wide resection was performed in 105 (26%) and nerve sparing in 283 (74%). Of the 273 lobes without extraprostatic extension, 0 of 52 had a positive margin if a wide resection was performed compared to 20 of 221 (9%) if a nerve spare was performed (p=0.01). Of the 115 lobes with extraprostatic tumour extension, 11 of 53 (21%) had a positive margin if a wide resection was performed compared to 28 of 62 (45%) if a nerve spare was performed (p=0.005). In adjusted analysis, the risk of a positive margin was less if a wide resection was performed compared to a nerve spare (RR 0.42; 95%CI 0.25 to 0.73; p=0.001).
Conclusions: Achieving negative surgical margins for patients with extraprostatic extension may be increasingly important as more patients with high risk cancer choose surgery. Using a standardized wide prostate excision surgical technique, the risk of a positive surgical margin was greatly reduced compared to nerve preservation.

MP-06.03

Patient understanding regarding end-of-life prostate cancer and perspectives regarding cost/benefit of current treatment paradigms

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Introduction and Objectives: Many new compounds are available which extend life for patients with castration resistant prostate cancer (CRPC). Excluding Docetaxel, annual costs vary from 40,000$-93,000$ for mean survival extensions of 2.1-4.8 months. This study aims to elucidate patients understanding of CRPC, opinions on costs/benefit of marketed CRPC drugs and assess if/when patients would forego CRPC drug therapy. We also sought out to see if patients would agree to deny treatment in lieu of a one-time end of life premium of $50,000.

Methods: We conducted a survey on prostate cancer (PCA) patients with various clinical disease states. Our survey collected patient demographics, PCA status, opinions on CRPC drug efficacy (based on hypothetical scenarios) and perspective changes if CRPC drug costs moved from funded to "out-of-pocket" expenditures. A novel treatment was proposed: opt out of life-prolonging drug treatment for a financial pay-out of $50,000 . Chi-squared , Fisher's exact, and T –testing was used when appropriate.

Results: In total, 103 patients completed the survey. CRPC was not understood by 79% of respondents. Most felt Abiraterone was helpful and should be offered to all (71%). Most felt Enzalutamide should be offered for Abiraterone failures despite evidence (65%). A minority felt Alpharedin was helpful to all (30%). Most felt combination drugs should be given and funded despite evidence, exceeding $250,000 (58%). Interestingly, If patients had to pay, only 29% were willing to exceed $40,000. When asked if they would forego therapy for $50,000, a majority agreed/considered (60%). Marital, children and PCA status did not correlate to opinions on drugs or financial stipends whereas education and income status did (p=0.03 and 0.04) with higher educated/income patients more likely to undervalue CRPC drugs or take the end-of life premium.

Conclusion: Patient understanding of CRPC prognosis and drug value is poor. Canadian patients overvalue drugs when paid by third parties but see less value if they have to pay "out-of-pocket". Interestingly, patients with high education/income are more likely to undervalue the benefit of new drugs and more likely to accept an end-of-life premium. More realistic discussions between CRPC patients and their doctors about benefits of CRPC drugs is needed.

MP-06.04

An examination of prostate cancer trends in Canada and other English speaking nations

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Introduction and Objectives: To compare prostate cancer incidence and mortality rates in Canada, USA, Australia and England and quantify the gap between observed prostate cancer deaths and expected deaths across all 4 countries, using USA mortality rates as a baseline.

Subject/patients (or materials) and Methods: Analysis of age standardised prostate cancer incidence and mortality rates, using routinely available data, in four similarly developed countries and joinpoint regression to quantify the changing rates (annual percentage change: APC) and test statistical significance. Expected prostate cancer deaths, using USA mortality rates, were calculated and compared to observed deaths in Canada, Australia and England.

Results: In all four countries, incidence rates initially peaked between 1992 and 1994 but a second higher peak occurred in Australia in 2009 (188.9/100,000), rising at a rate of 5.8% (1998-2008). Mortality rates in the USA (APC -2.9%; 2004-2010), Canada (APC -2.9%; 2006- 2011) and England (APC -2.6%; 2003-2008) decreased at a faster rate compared to Australia (APC: -1.7%; 1997-2011). In 2010, mortality rates were highest in England and Australia (23.8/100,000 in both countries). The mortality gap over the 17-year period saw an excess 6,319 prostate cancer deaths in Canada, 10,895 in Australia, and 28,060 in England in comparison to USA data.

Conclusions: When compared to the USA, the death rate due to prostate cancer in Canada, Australia, and England appears to be higher than it should be. Prostate cancer incidence rates are likely heavily influenced by Prostate Specific Antigen testing, but the fall in mortality occurred too soon to be solely a result of testing. Greater emphasis should be placed on addressing system-wide differences in the management of prostate cancer to reduce the number of men dying from this disease.

The mortality gap between the USA and comparison countries has increased, with a total of 6,319 excess prostate cancer deaths in Canada, 10,895 in Australia, and 28,060 in England between 1994-2010, had rates been the same as USA data.

MP-06.05

Oncological outcomes of salvage high intensity focused ultrasound of radio-recurrent prostate cancer: Results of a prospective phase II clinical trial

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Introduction and Objective: Salvage high intensity focused ultrasound (s-HIFU) is a potentially curative minimally invasive treatment for radio-recurrent prostate cancer (rr-PCA). Aim of this phase II trial was to prospectively assess effectiveness, morbidity and oncological outcomes of s-HIFU.

Materials and Methods: Men aged 40-85 with biopsy-proven non-metastatic rr-PCa underwent s-HIFU (Sonablate-500) and TRUS biopsy(Bx) at 6 months. Treatment failure was identified by biopsy positive for PCa and/or biochemical failure, as per Phoenix criterion. Primary endpoint was persistence of disease at 6 months Bx. Secondary endpoints included QoL, biochemical recurrence-free (BRFS), metastasis-free (MFS), overall (OS) survivals and progression to ADT. Survival analysis was carried out according to Kaplan-Meier.T-student and $\chi 2$ tests were used for continuous and grouped data, respectively (SPSSv.17, $p<0.05$).

Results: 78 men underwent 82 procedures with median operative time of 135 min. Prior to HIFU, 17 men (21.7%) received ADT. At 6 months, of 71 men who underwent Bx, 24 (33.8%) had residual disease. With a mean follow-up of 47.8 months, 48.7% of men did not require additional therapies, whereas 41 (52.8%) have failed s-HIFU due to residual disease at histology (24) and/or to biochemical failure (17). ADT following s-HIFU was initiated in 21 cases (26.9%) at a median of 11 months. Overall, 5 patients (6.4%) died during follow-up from PCa (1) or other causes (4), and 4 (5.1%) are alive with bone metastases. BRFS, MFS and OS at 5yr were 65.5%, 93% and 96.5% respectively. IPSS score significantly increased (7.3vs11.7, $p<0.001$) while IIEF-5 score decreased (8.6vs5.4, $p<0.001$) at 6 months. There were 3 Clavien IIIb (recto-urethral fistulas, 3.8%) and 1 Clavien IVa (bladder rupture requiring laparotomy, 1.3%) events.

Conclusions: S-HIFU is a viable treatment option for rr-PCa even for men who are aged and with comorbidities, providing relatively good local disease control.

MP-06.06

Long-term morbidity and oncological outcomes of salvage cryotherapy of radio-recurrent prostate cancer

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Introduction and Objectives: Salvage cryotherapy (s-cryo) of radio-recurrent prostate cancer (rr-PCa) has been reported to achieve 5y DFS rates up to 60%. However, the majority of such data is based on mid-term follow-up outcomes. Aim of this study was to analyze morbidity and oncological outcomes, with median follow-up 10 years, of s-cryo on rr-PCa patients at an academic center.

Materials and Methods: A retrospective analysis from a prospectively maintained database was performed on 187 patients who underwent s-cryo from 1995 to 2004. Two freeze-thaw cycles of transperineal cryo were performed under TRUS guidance by a single surgeon. Complications were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) system v2.0. Recurrence was defined using Phoenix definition (nadir + 2ng/ml) as well as any radiologic/histologic clinical evidence of recurrent PCa. DFS was defined as the time period from s-cryo to date of recurrence. Primary outcome was survival. Secondary outcomes included morbidity and DFS. Statistical analysis was carried out using Kaplan-Meier method for survival and t-student and χ^2 tests for continuous and grouped data, respectively (SPSSv.17, $p<0.05$).

Results: Of 187 patients, 176 (94%) had records available for follow-up. Mean age was 69.6±5.9 yr and mean pre-salvage PSA was 6.6±5.7 ng/ml. Mean follow-up was 123±55 mo. Fifty-three and 11 patients were followed >10 and >15 yr respectively. Overall, 39 patients (20.9%) died during follow-up either due to PCa (9) or other causes (30). DFS at 10 yr was 39%. Four patients (2.1%) developed recto-urethral fistula (successfully repaired), and 13 patients (7%) had bladder neck contracture requiring urethrotomy. Acute urinary retention requiring Foley catheter was observed in 40 cases (21.4%) and severe gross hematuria requiring bladder washout was recorded in 21 (11.2%).

Conclusion: S-cryo is a viable minimally invasive treatment option for rr-PCa. Reasonable long-term DFS with acceptable morbidity can be achieved in a significant portion of patients with rr-PCa.

MP-06.07

Bone turnover marker levels and outcomes in men with prostate cancer and bone metastases treated with bone antiresorptive agents

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Introduction and Objective: Men with prostate cancer (PC) and metastatic bone disease typically have elevated levels of bone turnover markers (BTMs). Antiresorptive agents, such as denosumab and zoledronic acid, can significantly reduce BTM levels. Higher baseline levels of BTMs have been associated with shorter survival. (Fizazi et al. *Eur Urol*. Oct 29 2014) We evaluated the association between BTM levels after treatment with antiresorptive agents and disease progression (DP) and overall survival (OS) in men with PC and bone metastases (mets).

Methods: This post-hoc analysis included data from men with PC and bone mets enrolled in a phase 3 trial randomized to receive either denosumab (120 mg SC) or zoledronic acid (4 mg IV, adjusted for creatinine clearance). The BTMs urinary N-telopeptide (uNTx) and bone-specific alkaline phosphatase (BSAP) were measured at study entry and 3 months. DP and OS were compared in men with BTMs above and below median levels after month 3. For these covariate analyses, a Cox model was used.

Table 1. MP-06.07. Covariate analysis results

Covariate analysis	Point estimate (95% CI)	*P* value*
Disease progression		
uNTx†	1.32 (1.17, 1.50)	<0.0001
BSAP¥	1.83 (1.61, 2.09)	<0.0001
Death from all causes		
uNTx†	2.12 (1.82, 2.48)	<0.0001
BSAP¥	2.81 (2.39, 3.32)	<0.0001

*A Cox model was used, and was stratified by treatment, prior skeletal-related event before month 3, PSA level, and current chemotherapy at randomization.
†Median levels of uNTx at month 3 were 9.60 nmol/mmol; n=764 with uNTx ≥median and n=763 with uNTx <median.
¥Median levelsof BSAP at month 3 were 21.43 ng/mL; n=858 with BSAP ≥median and n=754 with BSAP <median.

Results: Compared with those below the median, men with uNTx levels at or above the median (9.60 nmol/mmol) at month 3 had a significantly greater risk of DP (by 32%) and reduced OS (by 112%; Table 1). Similarly, men with BSAP levels at or above the median (21.43 ng/mL) at month 3 had an increased risk for DP (by 83%) and reduced OS (by 181%) compared with those below the median. Results were maintained after adjustment for risk factors suggestive of more advanced disease. There was no significant difference in DP within bone for men with BTMs above and below the median after month 3.

Conclusions: In general, men with BTM levels at or above versus below the median at month 3 had worse outcomes. Assessment of BTM levels after antiresorptive agent treatment may add to our understanding of which patients are most at risk for DP and decreased survival.

MP-06.08

Enzalutamide (ENZA) in men with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC): Final analysis of the phase 3 PREVAIL study

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Introduction and Objectives: The PREVAIL Study (NCT01212991) was a prospective, randomized, placebo (PBO)-controlled phase 3 clinical trial of enzalutamide (ENZA) in asymptomatic to mildly symptomatic chemotherapy-naïve men with mCRPC. A planned interim analysis at 540 deaths showed a statistically significant benefit of ENZA over PBO, with improved overall survival (OS) (hazard ratio [HR] 0.71; 95% confidence interval [CI] 0.60–0.84; P<0.001) and radiographic progression-free survival (rPFS) (HR 0.19; 95% CI 0.15–0.23; P<0.0001). An Independent Data Monitoring Committee considered the benefit-risk ratio to favor ENZA and recommended stopping the study and crossing PBO patients (pts) to ENZA in an open-label period of the study. On the basis of these results, ENZA was approved for chemotherapy-naïve mCRPC in Europe and the USA.
Methods: Pts were randomized 1:1 to ENZA 160 mg/day or PBO (with the option of ENZA crossover after interim analysis). Planned sample size was 1680 with ≥765 deaths to achieve 80% power to detect a target OS HR of 0.815, with a type I error rate of 0.049 and a single interim analysis at 516 (67%) deaths. All pts were followed in an open-label extension protocol. Data cutoff was 1 Jun 2014 for the final analysis to reach ≥765 deaths.
Results: 1717 men were randomized (1715 treated) between Sep 2010 and Sep 2012. The final analysis at 784 deaths with a median follow-up of 31 months (mo) confirmed the OS benefits of ENZA with a 23% reduction in risk of death (HR 0.77; 95% CI 0.67–0.88; P=0.0002) and a 4-mo improvement in median OS (35.3 mo [95% CI 32.2–not yet reached]) vs. 31.3 mo [95% CI 28.8–34.2]). 42% of ENZA and 49% of PBO pts had died; 52% of ENZA and 81% of PBO pts (including 167 pts who crossed over to ENZA) received ≥1 subsequent life-extending prostate cancer therapy.
Conclusions: With longer follow-up time, ENZA continued to demonstrate a robust improvement in OS in asymptomatic or mildly symptomatic chemotherapy-naïve mCRPC.

MP-06.09
Treatment of castration-resistant prostate cancer in a real-life setting in Quebec
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Introduction and Objectives: Systemic treatment of castration-resistant prostate (CRPC) has evolved considerably in the last decade. Our study aimed to analyze healthcare services utilization, clinical outcomes and survival trends in the Quebec management of CRPC in a current real-life setting.
Methods: The study cohort consisted of 6,927 patients with evidence of CRPC from January/2001 to July/2013, selected from the Régie de l'Assurance Maladie du Québec (RAMQ) databases. Survival was evaluated by Kaplan-Meier and the difference in survival between pre-docetaxel (Doc) and Doc (2002-2005 vs. 2008-2011) era by log-rank test. The association between Doc exposure and survival was evaluated by Cox proportional hazards model adjusted for several co-variables.
Results: In our study cohort, the overall distribution of first line therapy was: 17.6% chemotherapy, 47.5% maximal androgen blockade (MAB) alone, and 3.1% Abiraterone. Androgen targeted therapies (MAB and Abiraterone) were the treatment of choice for the elderly population (mean age 78.8±7 and 78±7, respectively), while chemotherapy was offered to younger patients (mean age 72 ±7.3). The use of chemotherapy was increased in the Doc (23.6%) vs. pre-Doc (15.2%) periods. Survival in the Doc group was significantly improved with an average of 5.89 months increment (p<0.001) and a 59% reduction in the risk of death when compared to the previous standard chemotherapy (HR1.41; 95%CI 1.17-1.77 pre-Doc vs. Doc era).
Conclusions: In our study cohort, age seems to be a strong determinant in CRPC therapy selection. Chemotherapy usage increased after the introduction of Doc, but is still limited to the minority. Survival was improved in the Doc era. These findings are promising and encourage further real-life studies in newly approved CRPC therapies.

MP-06.10
A detectable PSA nadir predicts failure of high-intensity focused ultrasound (HIFU) as salvage therapy for radio-recurrent prostate cancer
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Introduction: Select patients may respond to additional local treatment after experiencing recurrence following primary radiotherapy (RT) for prostate cancer (PCa). Salvage prostatectomy, the standard of care in this disease state, is rarely performed due to its morbidity. Prior studies have demonstrated that high-intensity focused ultrasound (HIFU) may serve as an alternative to salvage prostatectomy with acceptable morbidity. This study investigates the efficacy of HIFU in the treatment of radiorecurrent PCa and the value of a detectable PSA nadir in predicting HIFU failure.
Methods: This institutional review board approved study prospectively accrued patients receiving HIFU for PCa from 2005-2014. Patients were treated with the Ablatherm HIFU device (EDAP, France) and had routine PSA and clinical follow-up. Patients were included if they had recurrence after RT for PCa with biochemical failure (ASTRO Phoenix criteria) and a positive pre-treatment biopsy. Included patients had a negative metastatic evaluation and a minimum of 1-year of follow-up. Patients were excluded from analysis if they had androgen deprivation therapy (ADT) at the time of RT failure or had prior salvage therapy. The primary endpoint was disease recurrence, defined as PSA progression (nadir+2ng/mL), receipt of further salvage therapy, ADT, clinical progression or death from disease. Statistical analysis was performed with Kaplan-Meier survival analysis and multivariate Cox regression analysis.
Results: A total of 24 patients were included. Median pre-treatment PSA was 4.02 ng/mL and the majority of patients had Gleason 7 or higher (21/24) and palpable disease (14/24). Median follow-up was 31.0 months. Median 2-year and 5-year recurrence free survival was 66.3% and 51.6% respectively. Median post-HIFU nadir PSA was 0.04 ng/mL which was reached at a median of 3 months. An undetectable PSA nadir served as a strong predictor of recurrence-free survival on univariate and multivariate analysis (multivariate Cox hazard ratio 15.437 95% CI 1.73-137.726 p=0.014).
Conclusion: Salvage HIFU allows for long term disease control in select patients. An undetectable PSA nadir serves as an early predictor of recurrence-free survival.

MP-06.11
Prostate cancer risk stratification with circulating tumour cells and three-dimensional molecular characterization
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Introduction and Objectives: Circulating tumor cells (CTCs) are emerging as a promising bio-marker in prostate cancer screening and in monitoring of disease progression. We have developed an efficient and reliable method of CTC isolation and characterization. Upon isolation of CTCs, analysis of the three-dimensional (3D) nuclear organization of telomeres can be used to further profile and stratify prostate cancer patients. We show that patients with low, intermediate, and high risk as well as metastatic prostate cancer, display CTCs along with unique telomeric profiles that correlate to their risk stratification.
Methods: CTCs from 50 patients presenting with various prostate cancer risk stratification were isolated using a size based filtration technique.

Cytokeratin 8,18, 19 immunostaining, androgen receptor staining, and 3D quantative fluorescence in situ hybridization of telomeres was performed on the isolated CTCs followed by 3D image acquisition. Quantitative image analysis was then preformed to obtain 3D telomere profiles and to identify the number of CTCs. Centroid cluster analysis was used to analyze the following statistical parameters: percentage of cells with aggregates, average number of telomeres per cell, average number of aggregates per cell and average nuclear volume.

Results: Our data shows that CTCs are present and can be isolated in each prostate cancer risk group. The telomere profiles of prostate CTCs correlate to their risk stratification when comparing percentage of cells with aggregates, average number of telomeres per cell, average number of aggregates per cell and average nuclear volume with centroid cluster analysis. Cluster analysis of 3D telomere profiles found in CTCs indicates no overlap between risk groups.

Conclusion: This proof of principle study shows that CTCs in each prostate cancer risk stratification group display unique 3D nuclear telomeric profiles. These findings show that prostate cancer CTCs and telomeric analysis have the potential to become a biomarker for tumor stage and progression. These results could add yet another potential robust prognosticator of risk stratification that could be of significant value in predicting both candidates for certain therapies or trials and ascertaining subsequent progression risk.

MP-06.12

Predictors of biochemical failure and outcomes of radical prostatectomy in a contemporary cohort spanning 10 years

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Introduction and Objectives: To analyze a contemporary cohort of patients at risk of prostate cancer (PCa) recurrence after radical retropubic prostatectomy (RRP) for clinically localized disease.

Methods: Data was collected on consecutive patients undergoing RRP over a ten-year period. Information extracted included pre- and post-operative variables, biopsy characteristics, neo-adjuvant therapy, pathology results, biochemical recurrence (BCR), adjuvant treatment, and death. A univariate and multivariate analysis was performed using SAS software. Kaplan-Meier (KM) method was used to illustrate BCR free survival.

Results: 470 consecutive patients underwent RRP with extended bilateral pelvic lymph node dissection from Jan 2003 to Sept 2014 by two urologic oncologists. Overall BCR was 20%. Median values are: follow-up 4.0 years (0.1- 10.7), pre-op PSA 8.1 (0.6 – 98.6), Gleason 4+3, age 61 (38-76), volume 30cc (12-152), and cores positive 42% (5-100%). Overall lymph node invasion (LNI) was 17% and 20% had seminal vesicle invasion (SVI). In the failure group, LNI was present in 26% and SVI in 41% (Table 1). Positive surgical marginal rate was 57% in the failure group versus 39% in the non-failure group. The median number of nodes removed was 12 (2-60). Median time to failure was 11.8 months, and median PSA at failure 0.34 (0.2 to 13.61). 76/469 received neo-adjuvant therapy and 4 deaths from PCa occurred during our study period.

Conclusion: Our cohort represents a relatively high-risk group compared to literature with a 20% BCR (Trock et al. 2009. PMID: 19683280). Pre-operatively PSA >20, high-risk clinical stage, and higher Gleason score were predictive of failure. Post-operatively PSA >20, pT4, and Gleason 4+3 or higher predicted failure. PSA values were significant for stratifying failure. The type of neo-adjuvant therapy received also stratified failure in our cohort, and held true in subgroup analysis of only high-risk patients.

Table 1. MP-06.12.

Variables	No BCR 378 (80%)	BCR 94 (20%)	*p* values
Age at Sx	61	61	0.1065
PSA 0–4	45 (12%)	4 (4%)	
PSA 4.1–10	214 (57%)	35 (37%)	<0.0001
PSA 10.1–20	83 (22%)	32 (34%)	
PSA ≥ 20	34 (9%)	23 (24%)	
Gleason ≤6	85 (23%)	10 (11%)	
Gleason 3+4	112 (30%)	11 (12%)	<0.0001
Gleason 4+3	81 (22%)	31 (33%)	
Gleason ≥4+4	98 (26%)	42 (45%)	
Clinical Stage ≤T2a	312 (83%)	62 (66%)	
Clinical Stage T2b	40 (11%)	16 (17%)	<0.0001
Clinical Stage ≥T2c	22 (6%)	16 (17%)	
Ratio core length/total length	17%	23%	0.0422
Biopsy Max Cancer %	60%	65%	0.9841
Prostate Volume	35 cc	35 cc	0.2841
Medical Tx None	323 (86%)	70 (76%)	
Medical Tx AR blocker	27 (7%)	13 (14%)	<0.0001
Medical Tx LHRH/Chemo	24 (6%)	9 (10%)	

MP-06.13

Is prostate cancer a marker for metabolic syndrome or good health? Analysis of a propensity-score matched population-based cohort

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Introduction: Metabolic Syndrome is associated with an increased risk of prostate cancer (PC) diagnosis. However, it is unclear if the converse is true - whether men with PC have an increased risk of harbouring cardiometabolic abnormalities that predispose them to increased CV risk. Our objective was to compare the risk of CV events and all-cause mortality between men with and without a PC diagnosis.

Methods: Men ages 50-75 diagnosed with PC between 1996 and 2009 were hard-matched and propensity score-matched 1:1 to men without PC diagnosis, based on demographic, socio-economic, co-morbidity measures and CV risk factors, using population-based administrative databases for Ontario, Canada. The outcomes were time to first CV event (composite outcome of cardiac, cerebrovascular, and peripheral vascular events) and all-cause mortality. Competing risks analyses were performed, using Cox-models (cause-specific approach) and Fine and Gray models (sub-distributional approach).

Results: In our cohort of 107,250 men with a median follow-up of 7.9 years, there were 14,395 CV events and 21,367 deaths. Men with PC had a lower rate of CV events (19.6 vs. 21.8 per 1000 person-years, p<0.001) and death (26.9 vs. 30.3 per 1000 person-years, p<0.001) compared to men without PC. PC diagnosis was associated with a lower cause-specific rate of CV events (HR=0.89, 95%CI=0.86-0.92, p<0.001) and simultaneously a lower cause-specific rate of death prior to CV event (HR=0.89, 95%CI=0.86-0.92, p<0.001). Sub-distributional competing risks results were similar. In the subgroup of men who underwent radical prostatectomy, PC diagnosis was associated with an even lower cause-specific rates

of CV event (HR=0.81, 95%CI=0.76-0.87, p<0.001) and death (HR=0.42, 95%CI=0.40-0.44, p<0.001).
Conclusion: Men diagnosed with PC, particularly those selected for radical prostatectomy, appear to be healthier (lower rate of CV events and all-cause mortality) compared to matched counterparts without PC in the general population, even after accounting for numerous demographic, socio-economic, and co-morbidity measures and CV risk factors. In the setting of generally favourable PC-specific outcomes, this may reflect that men with inherently longer life expectancy are being appropriately selected for PC screening.

UP-06.01

Prognostic utility of the neutrophil-to-lymphocyte ratio in a large cohort of 2,407 men undergoing radical prostatectomy for clinically localized prostate cancer

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Introduction: An elevated peripheral neutrophil-to-lymphocyte ratio (NLR), a marker for systemic inflammation, has been associated with advanced tumor stage and poor outcome in various cancers, including metastatic castrate-resistant prostate cancer (PC). Whether NLR also predicts outcome in patients undergoing radical prostatectomy (RP) for clinically localized PC is unknown. We aimed to assess the association between pre-treatment NLR and pathological stage, grade and overall failure in a large cohort of patients undergoing RP.
Methods: Patients undergoing RP for clinically localized PC in a tertiary referral center (2004-2013) were identified using our institutional database. Patients with medical conditions that may influence blood cell lines, or patients undergoing neoadjuvant treatment or salvage RP after failed radiotherapy were excluded. NLR was computed using complete blood counts (CBCs) performed pre-RP. The predictive ability of NLR was assessed using logistic regression and Cox proportional hazards modeling for the following outcomes: Stage (≥pT3 vs. <pT3), Gleason grade (8-10 vs. <8), and treatment failure (biochemical failure (defined as PSA >=0.2) or need for salvage therapy). Additionally, Kaplan-Meier curves and multivariable regression analyses adjusting for known PC risk factors were performed for these outcome parameters using a cut-point for NLR of 2.5.
Results: Our final cohort included 2407 patients; 822 patients (19%) had ≥pT3 disease and 147 patients (6%) had a Gleason score of 8-10. NLR, as a continuous predictor, was neither associated with higher stage (OR 1.01; 95%CI: 0.95-1.08, p=0.71) or grade (OR 0.94; 95%CI: 0.82-1.08, p=0.26) nor with a higher risk of treatment failure (HR:1.01; 95%CI: 0.94-1.09, p=0.76). Accordingly, NLR ≥2.5 was not an independent predictor of higher stage (OR 1.05; 95%CI: 0.86-1.28, p=0.63), higher grade (OR 1.25; 95%CI: 0.87-1.79, p=0.23) or treatment failure (HR:1.16; 95%CI: 0.94-1.43, p=0.18).
Conclusions: NLR was not an independent predictor of pathological stage, grade or overall failure in this large cohort of men undergoing RP for clinically localized PC, in contrast to studies in patients with metastatic castrate-resistant PC. The prognostic utility of NLR in PC may be limited to more advanced disease.

UP-06.02

PCA3 and PCA3/TERG add further predictive value to the PCPT risk calculator amongst non-African American men alone in the Early Detection Research Network (EDRN)

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Introduction and Objective: Prostate-specific antigen lacks specificity to accurately detect prostate cancer (PCa). Biomarkers such as Prostate Cancer Antigen 3 (PCA3) and transmembrane protease, serine 2 and v-ets erythroblastosis virus E26 oncogene homolog gene fusion (T2ERG) have been utilized to improve prediction models such as the Prostate Cancer Prevention Trial Risk Calculator (PCPT RC). Utility of such biomarkers in specific racial groups is unknown. The added utility of PCA3 and/or T2ERG to the PCPT RC was examined amongst African American (AA) and non-African American (non-AA) men.
Materials and Methods: Prospective post-digital rectal exam urine was collected with informed consent from 718 men presenting for trans rectal ultrasound (TRUS) guided biopsy at three academic sites as part of the IRB approved Early Detection Research Network (EDRN) study.
Outcome was defined as the presence of PCa on standard TRUS biopsy. Receiver operating characteristic curves were performed for the two racial groups to compare the predictive capabilities of PCA3, T2ERG, PCPT RC, and their combinations via logistic regression models.
The area under the curve (AUC) was compared to the base model of PCPT RC to delineate the added benefit of PCA3 and/or T2ERG in subgroups.
Results: 72 (10%) men were AA. 324 (45%) men had PCa on biopsy; 194 (27%) had clinically significant (Gleason grade ≥7) PCa (CS PCa). AUCs for PCPT RC for the non-AA and AA groups was 0.64 (95% CI, 0.60-0.68) and 0.75 (95% CI, 0.63-0.87) respectively. Addition of PCA3 or PCA3/T2ERG to the base PCPT RC model increased the AUC for non-AA men to 0.75 (95% CI, 0.71-0.79; p=0.0003) and 0.76 (95% CI, 0.73-0.80; p <0.0001), respectively. In AA men the new AUCs were 0.77 (95% CI, 0.65-0.88; p=0.06) and 0.77 (95% CI, 0.65-0.88; p=0.81), respectively. Patients diagnosed with CS PCa, addition of PCA3 and PCA3/T2ERG to the PCPT RC (CS model) improved diagnostic performance in non-AA men (p=0.01 and p=0.002, respectively) but did not improve performance within the AA cohort (p=0.89 and p=0.72, respectively).
Conclusions: PCA3 and PCA3/T2ERG add predictive value to the PCPT RC in non-AA patients for diagnosing PCa. However, it may not be as beneficial in AA men. Furthermore, use of these two biomarkers adds further utility in for non-AA men with CS PCa but again does not appear to for AA men.

UP-06.03

Long term follow-up in patients with initial high-grade prostatic intraepithelial neoplasia and benign prostate biopsies

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Introduction and Objectives: Limited data exist on long-term pathological outcomes in patients with initial prostate biopsies showing either high-grade intraepithelial neoplasia (HGPIN) or benign findings, who are subsequently diagnosed with prostate cancer (PCa).
Methods: Pre-operative characteristics of patients showing either HGPIN or benign initial prostate biopsy, were compared in patients with and without a subsequent diagnosis of PCa. Biopsy and prostatectomy findings in patients with PCa were further evaluated. Patient characteristics were compared using the Wilcoxon rank-sum test for continuous variables and Chi-square test for categorical variables.
Results: We evaluated 161 and 85 consecutive patients with initial HGPIN and benign prostate biopsies, respectively, who had a subsequent biopsy in our institution. After a median follow-up of 11 years, PCa was detected in 26.7% patients after HGPIN and in 22.3% patients after initial benign biopsy. On follow-up biopsy, Gleason score (GS) 6 disease was detected in 86% and 58% of patients with initial HGPIN or benign biopsies, respectively. Of 35 patients who underwent prostatectomy (22 after initial HGPIN biopsy and 13 after initial benign biopsy), all had node negative,

organ-confined disease; 86% and 54% patients had GS 6 disease, with ≤5% tumor volume found in 91% and 62% of the HGPIN and benign group, respectively.
Conclusion: Patients with initial HGPIN or benign biopsies preceding a diagnosis of PCa usually show favourable pathological outcomes on follow-up biopsy and prostatectomy, most commonly exhibiting low volume and low grade disease. These findings may help clinicians risk-stratify patients who may benefit from conservative management options including active surveillance.

UP-06.04

Quantitative method for predicting therapeutic response using a sub-millimeter ex-vivo tumor sample: A step towards personalized care for mCRPC

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Introduction and Objectives: The lethal form of prostate cancer (PC) is the castration resistant state that develops when patients progress while on androgen deprivation therapy. New strategies based on targeted drugs are increasingly gaining clinical acceptance, and may be appropriate throughout PC progression. However, an important consideration is matching the most appropriate drug to a patient's tumor characteristics. Recent developments in engineering have permitted the design and production of a new generation of microfluidic devices, a low cost high throughput empirical testing platform capable of trapping micrometer-size tumor samples and maintaining their viability over several days. We hypothesize that these devices are particularly well suited to meet the challenges of pre-clinical drug testing.
Material and Methods: For the xenograft biopsy model, 22Rv1 or PC3 cells were mixed with matrigel and injected sub-cutaneous into the flank of male SCID mice. Cylindrical micro dissected tumors (MDT) (300x500 µm) were obtained from the xenograft by vibrotome slicing and punching. The MDT was loaded on microfluidic chip. To follow the MDT response to treatments, we stained the MDT with CellTracker Green dye (live cell) and 7AAD (dead cell). MDT were observed directly in the microfluidic device by confocal microscopy. The mortality fraction (dead cells/total cells) was determined using an image-processing program (Matlab). Samples were removed from microfluidic chip, analyzed by FACS to study cell viability.
Results: Our microfluidic chip has 5 independent microfluidic channels, can hold up to 25 MDT in designated traps (5 MDT per channel) in which they can be exposed to five distinct therapeutic agents or five different doses of the same agent. We were able to maintain high cell viability of MDT ex-vivo on chip (60% to 95%) for up to seven days. We also demonstrated the feasibility of drug testing in our microsystems by the treatment of 22Rv1 and PC3 MDT using different doses of docetaxel (1 nM to 100 nM).
Conclusion: With an increasing armature of various therapeutic agents, it is essential to stratify patients based on sound instruments and data when choosing a drug treatment, to maximize clinical responses while minimizing cost and treatment toxicities to the patient. Testing patient biopsy material should allow for direct empirical evaluation of therapeutic responses to a wide concentration and variety of agents. This should eventually lead to a more rational approach in therapeutic strategies and clinical decisions for individual patients.

UP-06.05

Neoadjuvant androgen deprivation prior to brachytherapy: A retrospective review

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Introduction: Brachytherapy, placement of ^{125}I radioiodine seeds, is an effective treatment of localized prostate adenocarcinoma. Neoadjuvant androgen deprivation therapy (NADT) has been shown to decrease prostate volume prior to brachytherapy, facilitating optimized radiation planning, seed placement and decreased dose prescription. There is no consistent agreement in current literature on the impact of combining NADT with brachytherapy on long term morbidity and mortality. The aim of this study was to determine the impact of neoadjuvant androgen deprivation therapy on patients undergoing brachytherapy.
Methods: 217 patients were identified in a retrospective fashion in an 8-year period between 2003 and 2011. 155 patients received no NADT while 62 received NADT. Outcomes are stratified based on disease, patient and treatment factors such as: initial PSA, Gleason score, disease extent, planning target volumes and clinical target volumes, prescribed radiation dose, length and type of androgen deprivation therapy, age, lifestyle factors, co-morbid conditions, treatment side effects, and time to progression were included in the analysis.
Results: The average prostate volume on transrectal guided ultrasound was found to be roughly equal between the two groups (32.3cc vs. 32.2cc in the NADT group). Pre-ADT volume on CT was found to be roughly equal as well (31.4cc vs. 27.4cc in the NADT group) and there was no significant difference in the planning target volumes (59.4cc vs. 51.1cc in the NADT group). The D90 was similar in both groups (138.8 Gy vs. 132.48 Gy in the NADT group). The post-implant PSA was expectedly lower in the NADT group (0.82 vs. 1.76) and lower PSA at 12-month follow-up (0.98 vs. 0.69 in the NADT group) but there was no difference in the rate of biochemical failure (5% vs. 2% in the NADT group) and there was no difference in over-all survival (96% vs. 95.3% in the NADT group).
Conclusion: No previous studies have identified ADT as having any benefit to disease specific or overall survival in any stratified population. Currently, our data does not suggest this to be any different. There is a suggested impact on biochemical progression-free survival with lower average PSA during follow up. With longer follow-up, there could be a difference seen in the rate of biochemical failure.

UP-06.06

Early and late continence after open bladder neck sparing prostatectomy

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Introduction: Urinary incontinence has been a well-recognized side effect of radical prostatectomy with between 2.5-57% of men reporting incontinence post radical prostatectomy (Robert et al. *The Journal of Urology*, 1992;188:2:502-6). It has been demonstrated that laparoscopic and robotic prostatectomy result in improved early return to continence via a bladder neck sparing (BNS) technique (Chłosta et al. *Videosurgery Miniinv 7,* 2012; 89-95). This study aims to report our initial experience with bladder neck preservation in open radical retropubic prostatectomies and the effect on post-operative urinary continence and to determine the effect, if any, on potential oncologic outcomes.
Methods: Radical retropubic prostatectomy with and without a bladder neck sparing technique were carried out between April of 2013 and October of 2014. 76 patients were identified, 22 of had a BNS technique. Data analyzed include age, stage, grade of tumour, pathologic stage, positive margin rate, immediate, early, and late continence, measured by use of incontinence pads. Tumor pathology and surgical margins were observed and correlated to margin positivity rates.
Results: The results indicate that BNS patients showed improved early return to continence at 3 months (72.7% vs. 41.7%) and 6 months (92.3%

vs. 68.4%). However, no change in over-all continence at 1 year was observed with 90% of BNS patients achieving one pad or less per day and 86% of the non-BNS patients achieving similar levels of continence. In terms of oncologic outcomes, extra-capsular extension was observed in 53% of non-BNS patients versus 33.3% in the BNS group. Positive surgical margins at the prostate base were observed less frequently as well (3.7% in the BNS cohort vs. 8.2%)

Conclusion: This study clearly demonstrates faster initial return of urinary continence with bladder neck sparing surgery but does not demonstrate a long-term benefit. While a common criticism of BNS surgery is the risk of higher positive margin rate (Steiner et al. *The Journal of Urology*, 1991;145:512-15), this study demonstrated the opposite. The bladder neck sparing approach to open radical prostatectomy is safe in organ-confined disease in the appropriately selected patient. Further prospective, randomized studies are required.

UP-06.07

Prognostic value of CD1a+, CD83+ and CD209+ tumor-infiltrating dendritic cells in human prostate cancer

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Introduction and Objectives: Prostate cancer (PCa) is a heterogeneous disease that shows considerable variation in disease recurrence, treatment response and disease-specific death between individuals despite similar clinicopathological characteristics. There is growing evidence that exhaustive analysis of tumor infiltrating immune cells may help predict the evolution of cancers. Dendritic cells (DCs) are key players in the immune response, acting as an interface between innate and acquired response. Here we analysed prostate tumor infiltration by different subsets of DCs to evaluate their prognostic potential.

Methods: Formalin-fixed paraffin-embedded prostatectomy specimens from 96 patients were analyzed. Immunohistochemistry staining was performed on 5µm sections using monoclonal antibodies against immature DCs (CD1a and CD209), and mature DCs (CD83). The density of DC infiltration in tumor, normal, stromal areas, and in lymphoid aggregates was determined by two independent observers in a blinded manner.

Results: There was no infiltration by CD1a+ DCs in the PCa specimens. CD83+ and CD209+ DC subsets displayed different patterns of distribution. While the majority of CD83+ DCs were found in the stroma, CD209+ DCs were found in both stromal and epithelial areas. Lymphoid cell aggregates were highly infiltrated by CD83+ DCs whereas infiltration by CD209+ DCs was low. CD83+ infiltration showed no association with baseline characteristics or prognostic. In univariate Cox regression analysis, CD209+ cell infiltration in the stroma was associated with biochemical recurrence (HR=1.12, p=0.0046), metastasis (HR=1.28, p=0.0023), and specific death (HR=1.25, p=0.014). Furthermore, multivariate Cox regression analysis, showed that CD209+ cell infiltration in the stroma was significantly associated with a higher risk of death (HR= 6.139, p= 0.0080).

Conclusion: Infiltration by immature CD209+ DCs may have a prognostic impact in PCa.

UP-06.08

Improved diagnostic rate for high-risk prostate cancer with targeted multiparametric transrectal ultrasonography-guided biopsy

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Introduction and Objective: To improve the diagnostic rate for high-risk prostate cancer of transrectal ultrasonography (TRUS)-guided biopsy by comparing the standard systematic vs. targeted TRUS-guided biopsy.

Methods: We reviewed the medical records of patients who underwent prostate biopsy performed by the same urologist at the Centre Hospitalier Universitaire de Québec between September 2011 and June 2013. 259 biopsies with available ultrasound and histopathologic reports were identified. Before each biopsy, multiparametric TRUS was done to identify suspicious lesions. Targeted TRUS-guided biopsy was performed when a suspicious lesion was observed otherwise standard systematic TRUS-guided biopsy with the sextant approach was used. We compared the diagnostic rate for high-risk cancer (Gleason ≥7) between these two techniques.

Results: Among the 259 biopsies available, 90 (34.7%) were targeted and 169 (65.3%) were done using the standard systematic approach. Overall cancer diagnostic rate was similar between targeted and systematic biopsy (55.6% vs. 56.8%). High-risk cancers were identified in 33.3% of the targeted biopsy and in 21.3% of the standard systematic biopsy (Fisher's exact test p=0.04). Multivariate logistic regression shows that the lesions characterised as being "really suspicious" by the urologist were significantly associated to the diagnostic of high-risk cancers (OR 10.03; 95% CI, 1.52-90.32; p=0.02) but lesions characterised as being "moderately suspicious" (OR 2.18; 95% CI, 0.46-12.68; p=0.35) and "slightly suspicious" (OR 0.51; 95% CI, 0.09-3.24; p=0.46) were not.

Conclusions: These results show that the use of a multiparametric TRUS approach to identify and target suspicious lesions can increase the diagnostic rate of high-risk prostate cancer. This needs to be validated in a larger cohort and between multiple urologists.

UP-06.09

Metformin use is not associated with oncologic outcomes among diabetic men undergoing radical prostatectomy

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Introduction and Objectives: Our group has previously shown that metformin use is associated with lower all- cause and prostate cancer (PC)-specific mortality in diabetic men diagnosed with PC using population-based data. The objective of the present study was to evaluate whether metformin use is associated with pathological stage, grade and risk of treatment failure among diabetic men undergoing radical prostatectomy (RP) for clinically localized PC.

Methods: Our prospectively maintained institutional cohort of men undergoing RP (2004-2013) was used. Salvage RPs and those receiving neo-adjuvant therapies were excluded. Medication use was ascertained at pre-operative visits. Outcomes were PC stage (intra vs. extra-prostatic), grade (Gleason 6 vs. 7 vs. 8-10) on final RP pathology and RP treatment failure, defined by a post-RP serum PSA >0.2, or use of salvage therapies (radiation or androgen deprivation therapy.) Subjects were censored upon use of adjuvant radiotherapy. Multivariable ordinary and ordinal logistic regression models, Kaplan-Meier analyses, and Cox-proportional Hazards models were used.

Results: In our cohort of 2389 men, 227 (9.5%) had diabetes of whom 153 (67.4%) used metformin. Among men with diabetes, 91 (40.1%) had extra-prostatic disease, while 41 (18.1%), 173 (76.2%) and 13 (5.7%) had Gleason 6, 7 and 8-10 disease, respectively. There were 35 men whom had biochemical recurrence or required salvage therapy following RP. In univariate and multivariable logistic regression analyses, metformin use was not associated with stage (OR=1.89, 95%CI=0.92-3.87, p=0.08) or grade (HR per 1 category increase=0.87, 95%CI=0.40-1.89, p=0.72) of PC. In Kaplan Meier analyses, there were no differences in the probability of failure over time following RP between diabetic metformin users versus non users (p=0.56). In multivariable Cox models, metformin use was not associated with risk of overall failure (HR=1.01, 95%CI=0.36-2.82, p=0.99).

Conclusions: In our cohort, there were no significant differences in PC stage, grade or risk of treatment failure following RP between diabetic metformin users and non-users. This may be because men with clinically localized disease undergoing RP have excellent outcomes, and metformin has little opportunity to make an appreciable difference in outcomes.

UP-06.10

Prediction of prostate volume: Which measurement is more accurate when MRI and TRUS volume estimates disagree?

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Introduction and Objectives: Prostate volume is an important clinical factor in diagnosis, treatment planning, and monitoring therapeutic responses in patients with prostate cancer. Volume has traditionally been estimated with transrectal ultrasound (TRUS) and more recently, magnetic resonance imaging (MRI). Studies comparing volume estimation by MRI and TRUS demonstrate conflicting results, and recommendations for interpretation if results are disparate are unclear.

Methods: We reviewed radical prostatectomy patients who had both preoperative MRI and TRUS. Prostate volume was estimated by applying the ellipsoid formula to TRUS and MRI images. These estimates were compared to each other and to the volume of the prostatectomy specimen (referent standard).

Results: During the study period, 318 patients met the study criteria. The average prostate volumes as calculated by TRUS, MRI and pathological specimen were 34.4 cc, 39.2 cc and 37.3 cc, respectively. On average, MRI overestimated prostate volume (1.4 cc) and TRUS underestimated prostate volume (-3.4 cc). MRI was slightly more accurate than TRUS based on interclass correlation (0.83 versus 0.74) and absolute risk bias (higher proportion of volumes accurate within 5, 10 and 20cc of pathologic volume). The average difference between MRI and TRUS volumes compared to pathological specimens was 4.81 cc ($p<0.001$). As estimates became increasingly divergent between MRI and TRUS (11-20cc, >20cc), MRI was more accurate than TRUS at estimating volume relative to pathology. On average, presence of a median lobe resulted in volume overestimation (6.9 vs. 1.1 cc) and increased variability.

Conclusions: Prostate volume can be accurately estimated using either TRUS or MRI. MRI demonstrated better correlation with radical prostatectomy specimen volume and is more often accurate when TRUS volume and MRI volumes are disparate. For both imaging modalities, the presence of a median lobe was associated with less measurement accuracy.

UP-06.11

Can serum adipokines predict the outcome of prostate biopsies?

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Introduction and Objectives: Adipokines are produced by the adipocytes and are increased in their serum levels in obesity. We aim to study the association between serum adipokines and outcome of prostate biopsies alone and in combination with clinical parameters.

Methods: Clinical data and serum adipokines were retrieved from three retrospective cohorts at the University Health Network in Toronto - Canada: 1. The Genitourinary Biobank men (subjects with no prior biopsies), 2. The placebo arm of the REDUCE trial (subjects with prior negative biopsies) 3. Placebo arm of the REDEEM trial (subjects with low risk prostate cancer on active surveillance). Adipokines investigated were: Resistin, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), monocyte chemoattractant protein-1 (MCP-1), hepatocyte growth factor (HGF), and nerve growth factor (NGF). The primary outcome was the absence of prostate cancer on biopsy and the secondary outcome was the diagnosis of low risk prostate cancer fitting the criteria for AS. We used univariate and multivariate logistic regression to assess statistical significance.

Results: 2,404 patients were included in the study. In the first cohort, IL-6 was found to be a statistically significant predictor for the outcome of prostate biopsies on univariate analysis (OR 1.17. 95%CI=1.05-1.30, p=0.007). This association lost its statistical significance on multivariate analysis. In the second cohort, none of the adipokines assessed were found to be statistically significant predictors for the outcome of prostate biopsies on multivariate analysis. In the third cohort, MCP-1 and Resistin were statistically significant predictors for the outcome of subsequent biopsies on multivariate analysis (OR 1.00 95%CI: 0.99-1.00, p=0.0257 and OR 1.0 95%CI: 1.00-1.00, p=0.0073).

Conclusions: Our findings do not support a role for adipokines for predicting the outcome of prostate biopsies. More studies are required to validate their roles in clinical practice.

UP-06.12

Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: A retrospective analysis of intraoperative and postoperative complications

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Introduction and Objectives: Extended pelvic lymphadenectomy is the gold standard for detecting occult lymph node metastases in patients undergoing radical prostatectomy. Current literature suggests that due to higher complication rates, this procedure should be reserved for men with medium to high-risk disease. The objective of this study is to determine which variables serve as risk factors for intraoperative and postoperative complications in this patient population.

Methods: A total of 470 patients with prostate adenocarcinoma underwent radical prostatectomy with extended bilateral pelvic lymphadenectomy from January 2003 to March 2014. Preoperative clinical variables (PSA, Gleason sum), pathological variables (pathological stage, node positivity, margin positivity, total core length) and intraoperative variables (operator) were collected. Of the 470 patients, 30 were excluded for lack of data. Complications were recorded and organized using the Clavien classification system. Univariate and multivariate analyses were conducted using SAS software.

Results: Of all subjects analyzed, the rate of complication was 28.2% (124 of 440). When organized using Clavien classification, our series demonstrated 11 Clavien I, 84 Clavien II, 42 Clavien IIIA, 5 Clavien IIIB and 2 Clavien IVA complications. No Clavien IVB or V complications were encountered. The incidence of lymphocele formation, neurovascular injury, thromboembolic events, and ureteral injury was 0.68% (3), 0.23% (1), 1.14% (5) and 0.45% (2) respectively. Univariate and multivariate analyses determined that operator/surgeon ($p<0.0001$) was the only statistically significant variable in terms of predicting complications.

Conclusions: With the exception of operator/surgeon, our data suggests there are no preoperative, pathological, or intraoperative variables that can reliably predict complication rates in patients undergoing radical prostatectomy with extended pelvic lymphadenectomy.

UP-06.13

International prostate symptom score improves in all men following robotic prostatectomy even in those with mild baseline lower urinary tract symptoms, 2 years postoperatively

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Introduction and Objective: Many reports suggest that men with moderate or severe lower urinary tract symptoms (LUTS) experience significant symptom improvement after open radical prostatectomy, whereas patients with mild LUTS do not seem to derive a significant benefit. LUTS have not been well studied after robot-assisted radical prostatectomy (RARP), particularly beyond one year postoperatively. We report the natural his-

tory of LUTS in men who underwent RARP as assessed by international prostate symptom score (IPSS) for 2 years postoperatively.
Methods: We reviewed charts of 678 patients who underwent RARP between 2006 and 2014. Data was collected prospectively and IPSS questionnaire was completed at baseline and at 1, 3, 6, 9, 12, 18 and 24 months postoperatively. Patients were grouped according to preoperative IPSS as having mild (0-7), moderate (8-19) or severe (20-35) LUTS. Paired two sample t-tests were used to compare change in IPSS for each group at 6, 12, and 24 months.
Results: Baseline LUTS were mild (group 1), moderate (group 2) and severe (group 3) in 397 (58.6%), 236 (34.8%) and 45 (6.6%) patients, respectively. Patients in group 3 were older, had higher baseline PSA and larger prostates, had more median lodes, and lower baseline SHIM scores ($p<0.05$). Other clinical and pathological parameters were not statistically different. Median IPSS scores (IQR) at baseline, 6, 12, and 24 months for group 1 were 3 (2-5), 3 (2-4), 2 (2-4), 2 (2-3.5), respectively ($p=0.02$, between baseline and 24 months). For group 2 results were 11 (9-14), 3 (2-4), 3 (2-5), and 3 (2-7), respectively ($p < 0.001$, between baseline and each time point). For group 3 scores were 24 (21-26), 2.5 (2-4.7), 3 (3-5), and 3 (2-6.5), respectively ($p < 0.001$, between baseline and each time point).
Conclusions: All men experienced a statistically significant improvement of LUTS post RARP 2 years after surgery. However, only men with moderate and severe symptoms had a clinically significant improvement that was sustained from 6, 12 to 24 months postoperatively. This benefit of surgical therapy should be considered when patients are weighing risks and benefits of various treatment options for localized prostate cancer.

UP-06.14

Predictors of positive surgical margin (PSM) following robotic-assisted radical prostatectomy (RARP): Results from the largest Canadian prospective cohort

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Introduction and Objective: PSM is strongly associated with biochemical recurrence (BCR). We though to identify preoperative predictors of PSM in patients treated with RARP for localized prostate cancer.
Methods: 1000 patients underwent RARP between 2006 and 2014. 748 patients had complete data. Preoperative clinical characteristics were collected, included age, BMI, PSA, Gleason sum, clinical stage and TRUS prostate volume. Groups were compared using two-sided t-test. 5-years Kaplan-Meier BCR-free survival curves were derived. Multivariate logistic regression analyses were performed to assess various preoperative predictors of PSM status.
Results: Of 748 patients, 196 (26%) had PSM. Patients with PSM had higher median PSA (6.9 vs. 5.2; $P<0.001$), smaller TRUS prostate volume (34 vs. 37 g; $P=0.02$), higher clinical stage ($P<0.001$) and biopsy Gleason score (G7-10: 73.9% vs. 60.9%; $P<0.001$). For pathological characteristics, patients with PSM harbored more advanced pathological stage ($P<0.001$) as well as higher Gleeson score (G8-10: 18.4% vs. 6%; $P<0.001$). The 5-years freedom from BCR was 75% for patients with PSM compared to 95% for negative margins ($P<0.001$). In multivariate logistic regression analyses, higher PSA (OR: 1.06; $P=0.004$), clinical stage ≥ T2a (OR: 3.01; $P=0.01$), biopsy Gleason sum 7 (4+3) (OR: 2.1; $P=0.02$) and Gleason 8-10 (OR: 2.5; $P=0.01$) were independent predictors of PSM. Conversely, larger TRUS prostate volume was protective against PSM (OR: 0.98; $P=0.007$).
Conclusions: In our series of RARP, PSA, TRUS prostate volume, biopsy Gleason sum and clinical stage are predictors of PSM following RARP.

UP-06.15

Aspirin and anti coagulant impact on prostate cancer detection in a cohort of Atlantic Canadian patients

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Background: Evidence from previous studies has suggested that Aspirin (ASA) & NSAIDS (non-steroidal anti-inflammatories) may reduce the risk of epithelial malignancies such as prostate cancer (Pca). There are many theories regarding the chronic inflammatory component to Pca, but overall the link is poorly understood. Additionally there have been reports that Warfarin may carry an "anti neoplastic" effect on Pca tumor cells. To our knowledge, there is no literature directly comparing Pca risk on Warfarin to ASA & NSAIDS. The aim of this study is to evaluate if the regular use of NSAIDS, ASA, or Warfarin alter the risk of Pca on biopsy relative to non-users.
Methods: Men who were referred to our regional center for prostate cancer evaluation between 2005-2010 were identified using a prospectively gathered database. Patients were categorized in terms of use of ASA, NSAIDS, Warfarin, or none. The primary outcome was the detection of any Pca. Secondary outcome was detection of Gleason ≥ 7 Pca. Analysis was conducted using Chi Sqaure and multivariate logistic regression analysis. Variables such as age, PSA levels, and family history of Pca were controlled during multivariate analysis. All patients on finasteride or dutasteride were excluded.
Results: 2039 patients were identified: ASA 629 (31%), NSAIDS 156 (8%), Warfarin 41 (2%), and none 1213 (59%). In total 791 (39%) of Pca cases were found. Multivariate regression analysis failed to show any significant difference in the odds of detection of any Pca between non-users and those on ASA, NSAIDS, or Warfarin. Of those Pca cases, 284 (14%) were Gleason ≥ 7. Compared to non-users, those on Warfarin were more likely to have Gleason ≥ 7 Pca ($p=0.017$). Logistic regression analysis revealed that the odds of Gleason ≥ 7 Pca for Warfarin users was 2.20 times that of non-users [OR=2.20 (1.06, 4.57; 95% CI)].
Conclusions: Contrary to previous reports in the literature, our cohort of patients on ASA, NSAIDS or Warfarin did not have any significant difference in the odds of detecting any Pca on biopsy relative to non-users. However, when isolating analysis to only Gleason ≥ 7 Pca, Warfarin users had 2 times the odds of Pca detection compared to nonusers. This is despite controlling for underlying cofounders such as age, PSA levels, and family history of Pca. Therefore, the regular use of Warfarin can potentially be taken into account when screening for underlying Pca.

UP-06.16

Radiation therapy after radical prostatectomy: Trends in referral and treatment practices over the last decade

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Introduction and Objectives: Our objective was to assess whether referral and treatment practices changed since the publication of the SWOG trial S8794 in 2009, which was the first randomized study to demonstrate an overall survival advantage for adjuvant radiation therapy (RT) after radical prostatectomy (RP).
Methods: We retrospectively revised all charts of men treated at our institution by radiation therapy between 2004 and 2014 following RP by a single radiation oncologist (DT). We divided the cohort in two groups according to first referral date before/after January 1st, 2010.
Results: Medical charts were available for 161/165 patients (97.6%). RP was performed at the same institution in 58% of the cases. Only 6 patients were treated within 120 days after surgery, and 20 patients were treated within 180 days after surgery. Upon analyzing trends between

the 2 groups, post-RP patho-clinical features were comparable (pT-stage (p=0.74), Gleason score (p=0.10), PSA-doubling time (p=0.21). Median time between surgery and first referral for radiotherapy decreased significantly from 672 days (IQR 295-1449) before 2010 to 300 days (IQR (225-1023) after 2010 (P = 0.04). This trend was also associated with a lower median PSA at radiotherapy referral [0.26 µg/l (IQR 0.17-0.48) vs. 0.46 µg/l (IQR 0.25-90) respectively; P = 0.001]. The use of androgen deprivation therapy with RT nearly tripled over time from 13% before 2010 to 37 % after 2010 (P = 0.003). Throughout the study period, the time interval between surgery and initiation of radiotherapy was positively correlated with pT-stage (P = 0.001), Gleason (P = 0.005) and PSA doubling time (P < 0.001).

Conclusions: At our tertiary-referral, academic institution, post-RP men are notably referred earlier for RT and with lower PSA when compared to men treated prior to the year 2010. Further study is necessary to evaluate this impact on biochemical recurrence-free survival.

UP-06.17

Neutrophil count is associated with survival in localized prostate cancer

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Introduction and Objective: The prognostic value of leukocyte counts was previously reported in metastatic prostate cancer. The purpose of this study was to investigate the influence of readily available markers of systemic inflammation such as leucocyte counts and metabolic co-morbidities on overall survival (OS) after curative radiotherapy for localized prostate cancer.

Methods: We conducted a retrospective study of patients with localized prostate cancer treated with definitive external beam radiotherapy or brachytherapy. Univariate and multivariate cox proportional hazards models were used to investigate the influence of age, comorbidities associated with inflammation such as cardiac history, diabetes and use of a statin, in addition neutrophil and lymphocyte count and neutrophil-to-lymphocyte ratio (NLR) were evaluated, as well as Cancer of the Prostate Risk Assessment (CAPRA) score on OS was estimated. A forward selection of variable based on the Akaike information criterion (AIC) was used for multivariate analysis.

Results: In total, 1971 pts were included; comorbidity data was available for 1792 pts and blood count for 950 pts. Median age was 68 years (range 44-87). Actuarial 5 years OS and BFRS were 93% and 95%, respectively, with a median follow-up of 44 months (1-156). On univariate analysis, neutrophil count (p=0.04), cardiac history (p=0.008), age (0.001) and CAPRA (p=0.0002) were associated with OS. Lymphocytes, NLR and comorbidities other than cardiac history were not associated with mortality. On multivariate analysis, neutrophil count (HR=1.18, 95%CI: 1.02-1.37, p=0.029), age (HR= 1.06, 95%CI: 1.01-1.1, p=0.008) and CAPRA (HR=1.16, 95%CI: 1.03-1.31, p=0.015) were independent predictors of OS.

Conclusion: Neutrophils, as possible markers of systemic inflammation, appear to be an independent prognostic factor for overall mortality in localized prostate cancer. A validation cohort is needed to corroborate these results.

UP-06.18

When is the best time to give Akt inhibitor therapy in advanced prostate cancer?

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Introduction and Objectives: Preclinical studies support co-targeting the PI3K/Akt and AR pathways in prostate cancer (Carver BS et al. *Cancer Cell* 2011;**19**:575-86) (Marques RB et al. *Eur Urol* 2014. Sept 11 [epub ahead of press]) However, the optimal timing of using PI3K/Akt pathway inhibitors remains to be fully understood. Using the well characterized LNCaP xenograft model and the enzalutamide-resistant MR49F model, we evaluate the combination AKT and AR blockade at different time points to model different prostate cancer disease states.

Methods: LNCaP cells were inoculated into nude mice which were castrated when PSA reached 50ng/mL. AZD5363 37.5mg/kg BID was given to inhibit the Akt pathway and enzalutamide(ENZ) 10mg/kg once daily was given to inhibit the AR pathway. Treatments were given 5 days per week. Tumour growth and PSA responses were assessed when the combination was given at time of castration and when the PSA recurred to pre-castration levels(CRPC). Comparator arms at time of CRPC included AZD5363 and ENZ monotherapy. To model ENZ-resistance, AZD5363 was given with or without ENZ to LNCaP-derived ENZ-resistant MR49F cells inoculated into castrate mice.

Results: In the LNCaP model, AZD5363 + ENZ resulted in a dramatic regression of tumours and suppression of PSA when given both at castration and at time of castration of CRPC. Regression of tumour size was not seen with castration alone or with ENZ or AZD5363 monotherapy at time of CRPC. The mean PSA nadir was lower with combination therapy vs. vehicle when given at castration (51-fold change, p=0.064) compared to AZD5363 + ENZ given at time of CPRC vs. ENZ treatment (12-fold change, P=0.065). On discontinuation of combination therapy after near complete regression of tumours treated at time of castration, a similar rising PSA velocity compared to control mice was observed. In the MR49F model, ENZ induced an agonist effect *in vivo*, complicating evaluation of the combination approach. Nonetheless, AZD5363 showed a dose-dependent response in MR49F xenografts, but even without ENZ progressive tumour growth did eventually occur in all cases. Tumour progression during AZD5363 + ENZ treatment was not observed in the LNCaP model.

Conclusions: These preclinical results suggest that Akt inhibitor therapy in combination with ENZ may be more effective when given earlier in the course of disease.

UP-06.19

Endothelial stabilizer SAC-1004 enhances intratumoral perfusion and potentiates docetaxel chemotherapy in prostate cancer

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Introduction: Since tumor requires excessive oxygen and nutrients due to their rapid growth, tumor is generally vascular. However, tumor vasculature is not physiologic but leaky, dilated, and tortuous. The inefficiency of tumor vessels in terms of perfusion induces hypoxic stress that makes the tumor more aggressive. Here, we investigated the role of a novel endothelial stabilizer SAC-1004 on tumor vascular normalization and its effects on tumor growth in prostate cancer.

Methods: Human vascular endothelial cell (HUVEC) was used to evaluate the effects of SAC-1004 on endothelial cells. Immunocytochemical staining and immunofluorescent confocal imaging was performed for E-cadherin expression in HUVECs. MTS assay was performed to assess cell proliferation of HUVECs and PC-3 cells after SAC-1004 treatment. Immunohistochemical staining with anti-CD31 and anti-SMA antibodies was performed to assess vasculature in vivo. PC-3 subcutaneous xenografts were developed to evaluate the effects of SAC-1004 on tumor

vasculature and tumor growth in prostate cancer. Magnetic resonance images were taken to assess vascular perfusion in xenografts. SAC-1004 was administrated via tail vein once a day for 7 days. Docetaxel was administrated intravenously once a week.
Results: SAC-1004 restored junction protein E-cadherin in vitro in endothelial cells and significantly reduced VEGF-induced retinal vascular leakage. SAC-1004 promoted proliferation of HUVECs in vitro in a dose-dependent manner. However, proliferation of cancer cells was not significantly affected by SAC-1004 treatment. Reduced vascular leakiness was found in PC-3 xenografts treated with SAC-1004 treatment and magnetic resonance imaging after SAC-1004 treatment for 7 days confirmed improved perfusion in the PC-3 xenografts treated with SAC-1004 compared with control. Interestingly, SAC-1004 treatment suppressed tumor growth in PC-3 xenografts but SAC-1004 followed by intravenous docetaxel treatment showed the most potent tumor suppression compared with control in PC-3 xenografts.
Conclusions: SAC-1004 restored abnormal leak vasculature of tumor by restoring endothelial cell junction in prostate cancer. Vascular normalization by SAC-1004 induced tumor regression and combination with docetaxel following vascular normalization potentiated anti-tumor effects of docetaxel in prostate cancer.

UP-06.20

Extra-radical prostatectomy with extended pelvic lymph node dissection (ePLND) for the management of high-risk prostate cancer (PCa)

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Introduction and Objectives: Radical prostatectomy is being performed increasingly on men with high-risk PCa. These high-risk patients undergoing RP have adverse pathologic features including positive margin rates as high as 46%. (Laird et al. *BJU Int.* 2014) We have adopted an 'extra-radical' prostatectomy (ERP) surgical approach in managing these patients. We describe surgical and intermediate-term oncologic outcomes in patients undergoing ERP.
Methods: We report outcomes on 26 consecutive patients who underwent ERP and ePLND for high-risk PCa by a single surgeon between 2007-2014. Descriptive analyses assessed patient demographics, histology, intermediate-term oncologic data, and complications.
Results: The median age was 64 (53-79) years and the median pre-op PSA was 11.1 ng/dL (4.2-33.8). 14 patients were clinical stage (CS) 1, 9 CS 2, 5 CS 3, and 4 unknown. On biopsy 3, 5, 11, and 7 patients had gleason grade (GG) 6, 7, 8, and 9 respectively. Post RP pathology showed 5 patients with GG 7, 5 GG 7 tertiary pattern 5, 4 GG 8, and 11 GG 9. 77% had extraprostatic extension and 23% seminal vesicle invasion. Nodal disease was found in 3/26 (12%) with a median lymph node count of 20.5 (11-32). Margins were positive in 8/26 (31%) of which 63% were focal. 64% of patients had an undetectable first post-op PSA. Adjuvant radiation was given to 7/25 (28%) and to date 28% have required salvage radiation. At a median follow-up of 27 (3-88) months, 68% of patients are free of biochemical recurrence. Perioperative complications occurred in 31% of patients, all were Clavien 3.
Conclusions: We demonstrate that, in spite of disease severity, a modified surgical approach can provide a very high negative margin rate, immediate undetectable PSA, and a prolonged biochemical-free recurrence. This series compares favorably with published high-risk surgical outcome data. (Laird et al. *BJU Int.* 2014) We believe that surgical technique should be adjusted based on the patient's pre-operative risk profile. Long-term oncological outcomes are awaited.

UP-06.21

Design and development of a mobile health survivorship solution for prostate cancer patients

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Introduction and Objectives: Prostate cancer [PCa] survivors face isolation and anxiety during survivorship. Mobile health (mHealth) tools may empower patients in this setting for effective self-management. Leveraging the permeation of technology among patients, our objective was the design and development of an mHealth survivorship solution for PCa patients.
Methods: The development phase was divided into 2 steps. The app was designed with a user-centered process with semi-structured interviews with patients and physicians. Phase 1a was an Iterative process and continual formative evaluation involving human factors and high-fidelity prototypes. The design utilized wireframes and usability testing to inform the design. 9 patients and 6 physicians [2 radiation oncologists, 1 medical oncologist, and 3 urologists] were used for phase 1a. Phase 1b used an Agile development/design method, which incorporated feedback from phase 1a usability testing. 9 patients and 8 providers were used in this step. The development adhered to ISO 13485 Medical Device Quality Management Standards, making it available on all platforms with a WebKit-based browser.
Results: The process revealed strong support among all patients and providers, and overwhelming support for the idea of receiving their own PSA results via the app. Physicians supported this with concerns about PSA-related anxiety. Patients wanted a validated symptom reporting method and found excellent utility in EPIC and FACT-P. Both groups did not support the use of online communities, but desired portals to alleviate online searching concerns. Communication tools were integrated and the app was linked to the Ontario Laboratory Information System.
Conclusion: We developed a mHealth PCa survivorship application, which links providers and patients and is the first mHealth app to source health information [PSA] from a provincial information system. It is an integrative solution, which collects patient-reported outcomes, and can prompt treatment change or to inform regarding trends in health outcomes. Patients experience augmented survivorship while validated health outcome measures are used in routine practice. The application is currently the subject of a multi-institutional phase-2 validation trial.

UP-06.22

Health services utilization in the end-of-life phase of patients dying of prostate cancer in Quebec between 2001 and 2013

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Introduction and Objectives: The study objective was to describe health services utilization at the end-of-life phase in castration-resistant prostate cancer (CRPC) by type of initial treatment (radiotherapy (RT) or radical prostatectomy (RP)) received for localized disease.
Methods: The study cohort consists of patients between 60 and 75 years that received medical or surgical castration treatment, became castration-resistant and died from CRPC between January 2001 and July 2013 in Quebec. For each patient in the study cohort, healthcare services use, hospitalisations and associated direct medical costs specific to each intervention, medical visits and treatments related to PCa were identified from

RAMQ and Med-Echo databases in the 2-year period prior to death. The Kaplan-Meier method was used to evaluate the overall survival by initial treatment. The general linear model was used to compare direct medical cost and number of days of hospitalisation by initial treatment.
Results: A number of 681 and 692 patients died of prostate cancer in the study period and had received RT or RP as initial treatment respectively. The median survival were 80.7 months (95%CI: 76 to 85) in the RT group and 85.1 months (95%CI: 78 to 88) in the RP group. In the RT group 26.8% of patients received chemotherapy only, 2.6% received abiraterone without prior chemotherapy and 51.4% received palliative radiation without prior chemotherapy or abiraterone. In the RP group, the figures are: 32.3%, 1.8% and 31.6% respectively. Over the last 2-year period of life, an average of 39 days (RT) and 35 days (RP) of hospitalisation were observed (p=0.07). In addition, the mean direct medical cost was $5,647 and $5,019, respectively (p=0.0008).
Conclusion: Several variations of clinical practice over the end-of-life period have been observed between the RT and RP groups.

UP-06.23

Clinical predictors for upgrading of biopsy Gleason sum 3+4 prostate cancer

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Introduction and Objectives: Gleason sum 3+4 prostate cancer (PCa) has a more favourable prognosis compared to Gleason sum 4+3 or higher tumours. The purpose of this study was to identify predictors for upgrading of biopsy Gleason 3+4 prostate cancer.
Methods: Consecutive patients with Gleason 3+4 on biopsy were identified. Patients who chose radical prostatectomy were included in this analysis. Age, PSA, PSA density (PSAD), % of core biopsies with Gleason pattern 4 and overall % of cancer that was pattern 4 were recorded from the medical record. The primary outcome was Gleason 4+3 or higher on prostate pathologic evaluation.
Results: Of the 73 patients, 25 (34%) were upgraded to GS 4+3 or higher. There was no significant difference in age (p=0.61), PSAD (p=0.09) or % of core biopsies with Gleason pattern 4 (p=0.39) between groups. PSA (p=0.02) and overall % of cancer that was pattern 4 at biopsy (p=0.001) were higher in patients who were upgraded. On a full multi-variable model, only overall % of cancer that was pattern 4 at biopsy was predictive of upgrading (β=9.5, p=0.007). 24 (33%) of patients had >25% Gleason pattern 4 at biopsy. Using a >25% Gleason 4 threshold had a sensitivity of 84.2% and specificity of 55.9% for predicting upgrading.
Conclusion: In patients diagnosed with Gleason 3+4 prostate cancer, higher proportion of pattern 4 predicts Gleason upgrading in the prostate specimen.

UP-06.24

Denosumab treatment for bone loss in men receiving androgen deprivation therapy for nonmetastatic prostate cancer: 5-year safety follow-up

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Introduction and Objectives: Androgen deprivation therapy (ADT) can result in bone loss and increased fracture risk in men with prostate cancer. A phase 3 study demonstrated that denosumab (DMAb) inhibited bone loss and reduced fracture risk. The safety of DMAb was further evaluated in an international, multicenter, single-arm, 2-year open-label extension (OLE) study of patients who completed the pivotal trial. We report here the 5-year safety experience with DMAb.
Methods: Eligible subjects, who completed the treatment phase (placebo [PBO] or DMAb 60mg, subcutaneous [SC] every 6 months [Q6M] for 3 years) and had been followed off-treatment for an average of 25.4 (SD, 3.8) months since their last dose of DMAb or PBO, were enrolled in the OLE study and received DMAb (60mg SC Q6M) for up to 2 years. Safety was assessed in all subjects that received ≥1 dose.
Results: A total of 384 subjects enrolled in the OLE study, (199 previously received DMAb [DMAb/DMAb];185 had received PBO [PBO/DMAb]). 289 subjects (75%) completed the extension study. The type and incidence of adverse events (AEs) are shown in Table 1. The majority of subjects experienced ≥1 AE, most of which were mild or moderate in severity. The most common AEs were constipation, urinary tract infection, arthralgia, back pain, and nausea, each of which occurred in <9% of subjects. Osteonecrosis of the jaw (ONJ) occurred in 1 DMAb/DMAb subject who had received zoledronic acid (4 mg every 4 weeks) for approximately 7 months during the study, and had a tooth extracted approximately 3 months prior to ONJ onset. ONJ resolved approximately 4 months after onset. Some subjects in each group experienced fatal AEs, none of which were considered by investigators to be treatment related.
Conclusions: In men with nonmetastatic prostate cancer undergoing ADT, overall safety and tolerability was similar with long-term (up to 5 years) and shorter-term (up to 3 years) DMAb administration, and consistent with the molecule's safety profile.

UP-06.25

Bone metabolism biomarkers in men with advanced prostate cancer and bone metastases treated with denosumab versus zoledronic acid

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Introduction and Objectives: Denosumab, compared with zoledronic acid (ZA), has recently demonstrated significant benefits in preventing skeletal-related events (SREs) in a double-blind, phase 3 study of men with castration-resistant prostate cancer (PC) and bone metastases (N=1901). This post hoc analysis was performed to determine if key bone metabolism biomarker levels correlated with time-to-first SRE.
Methods: Time-to-Grade ≥2 increase in total serum alkaline phosphatase (ALP) was assessed for correlation with time-to-first SRE. Levels of urinary N-telopeptide (uNTX) and serum bone-specific alkaline phosphatase (BSAP) markers were measured at baseline and study week 13, and correlations with time-to-first SRE were assessed. Covariate analyses were performed using a Cox proportional hazards model, stratified by treatment group or (for baseline analyses) with treatment group as the independent variable.
Results: Analysis of the relationship between time-to-Grade ≥2 increase in ALP and time-to-first SRE demonstrated that Grade ≥2 increases in ALP of PC patients were associated with a higher risk of first SRE (hazard ratio [HR] 1.838, 95% confidence interval [CI] 1.559, 2.167; $P<0.0001$). In dichotomized analyses (< vs. ≥ median), a higher level of uNTX and BSAP (at baseline or week 13) was correlated with an increased risk of first SRE (Table 1). In baseline covariate analyses, treatment benefit for denosumab was maintained after adjusting for either baseline uNTX (HR 0.818, 95% CI 0.703, 0.951; $P=0.0091$) or BSAP (HR 0.813, 95% CI 0.700, 0.943; $P=0.0061$).
Conclusions: Higher levels of uNTX or BSAP at baseline or week 13 were associated with worse SRE outcome in men with advanced PC and bone metastases. Denosumab was more efficacious for preventing or delaying SREs compared with ZA, regardless of baseline bone-related biomarker levels.

Table 1. UP-06.24.

	2-year OLE		3-year PBO Control*	
	DMAb/ DMAb	PBO/ DMAb	DMAb	PBO
	N = 199	N = 185	N = 731	N = 725
Completed Study	145 (72.9%)	144 (77.8%)	467 (63.6%)	445 (60.6%)
Overall AEs	138 (69.3%)	123 (66.5%)	638 (87.3%)	627 (86.5%)
Treatment-related AEs	9 (4.5%)	11 (5.9%)	62 (8.5%)	65 (9.0%)
Serious AEs	51 (25.6%)	45 (24.3%)	253 (34.6%)	222 (30.6%)
Fatal AEs	14 (7.0%)	12 (6.5%)	44 (6.0%)	46 (6.3%)
AEs of interest				
Hypocalcemia	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
ONJ	1 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infections and infestations	38 (19.1%)	39 (21.1%)	257 (35.2%)	226 (31.2%)
Cataracts	10 (5.0%)	7 (3.8%)	34 (4.7%)	9 (1.2%)

*3-year PBO-control data: Smith MR, et al. N Engl J Med. 2009; 361:745, and Amgen data on file

UP-06.26

The critical role of IL-23 in regulating metastatic prostatic cancer through STAT3/ROR-γ signaling

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Introduction: Interleukin-23 (IL-23) plays an important role in expanding the Th17 cell population and induces STAT-3 to up-regulates the expression of Retinoic Acid Receptor-Related Orphan Receptor Gamma-T (ROR-gamma). STAT-3 regulates the expression of a variety of genes in response to cellular stimuli, and thus plays a key role in cell growth and apoptosis. Furthermore, recent studies identified a critical role for ROR-gamma in lineage specification of uncommitted CD4+ T helper cells into Th17 cells. The goal of this study is to evaluate prospectively the prognostic importance of circulating IL-23 in patients with metastatic prostate cancer through downstream signaling.

Methods: The study involved 140 men diagnosed with stages I-IV prostate cancer and 120 healthy controls. IL-23 serum concentration measure by a quantitative enzyme immunoassay technique associated with clinical-pathological variables. Blocking IL-23 with anti-p19 Ab in mice inoculation with two types of metastatic prostate cancer cell lines (LNCaP, and DU-145) to study the pathway of IL-23 in vivo by using western blot and Real-time RT-PCR.

Results: We found a statistically significant higher systemic IL-23 level in the metastatic group in comparison with non-metastatic group (19.32±5.35 pg/ml vs. 7.25±3.42 pg/ml, P<0.05). Patients with shorter overall survival presented higher IL-23 levels, suggesting a negative prognostic correlation. Furthermore, systemic delivery of blocking Abs directed against IL-23 completely inhibited STAT3/ROR-gamma levels in mice.

Conclusions: These results demonstrate that STAT3/ROR-gamma, is a downstream mediator for IL-23–induced prostate metastasis in murine mice. IL-23 may represent an attractive therapeutic target or a biomarker in metastatic prostate cancer by blocking downstream effects. However, further studies are needed in larger samples to better investigate the implications of IL-23 in prostate cancer.

Table 1. UP-06.25. Relationship of covariance to time to first SRE

Covariate anaylses*	Hazard ratio (95% confidence interval)	*p* value
Baseline		
uNTX	1.402 (1.202, 1.635)	<0.0001
BSAP	1.572 (1.347, 1.834)	<0.0001
Week 13		
uNTX	1.186 (0.998, 1.409)	0.0532
BSAP	1.786 (1.489, 2.142)	<0.0001

BSAP: bone-specific alkaline phosphatase; uNTX: urinary *N*-telopeptide
*Dichotomozed by ≥median vs. <median

UP-06.27

Do rectal swab and the use of targeted antibiotic prophylaxis reduce the incidence of prostate biopsy sepsis?

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Introduction and Objective: Prostate cancer is the most common cancer in men in the UK and it is the second leading cause of cancer-related death in men with an estimated deaths in 2012 (Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62 :10). Across the globe transrectal ultrasound guided prostate biopsy (TRUS-Bx) is used as a diagnostic procedure for prostate cancer (Simsir A et al, Urol Int. 2010; 84(4):395). Common complications related to prostate biopsy are infection, bleeding, urinary retention and sepsis (Akduman B et al, Urology 2011;78:250). Antibiotic prophylaxis is effective in preventing these infectious complications (Zani EL et al, Cochrane Database Syst Rev. 2011 May 11;(5):CD006576) but there is no evidence based standardized regimen for peri-procedural antibiotic prophylaxis (Shandera KC et al, Urology. 1998; 52:644-646). The American Urology Association recommends the use of one or more of the following fluroquinolones, cephalosporins, aminoglycoside and Metronidazole as prostate biopsy prophylaxis. Despite of use of these antibiotics there is a noticeable rise in fluroquinolone resistant infections (Dalhoff A et al, Interdiscip Perspect Infect Dis 2012; 2012:976273) (Feliciano J et al, J Urol 2008;179:952-5;discussion 955). On average 72,500 biopsies was performed in England and Wales in 2008 of which 2.15-3.6% were readmitted with infectious complications, resulting an annual cost of £ 7.7-11.1 million (Batura D et al, J Antimicrob Chemother 2013 Feb; 68(2):247-9). After finding E.Coli resistnat strain in prostate biopsy patients admitted with sepsis we decided to conduct this study.

Materials and **Methods:** This was a prospective, non-randomized, comparative and observational study conducted over a period of four months (March-June 2014) at urology departments of two trust hospitals 100 patients in each group. Study includes residents of South London, underwent a prostate biopsy.Pre biopsy risk factors assessment through a questionnaire and midstream urine sampling. Group A: received single dose of intravenous Gentamicin 240 mg and Metronidazole 500 mg before biopsy. Post biopsy oral Ciprofloxacin 500mg twice a day for five days. Group B: At the time of the decision to proceed for a biopsy a rectal swab is taken via a proctoscope, antibiotic prophylaxis according to rectal swab results. Data collected from A&E records,out patient and telephonic follow-up. Statistical analysis through descriptive statistics and paired student t test.

Results: Showed noticeable reduction in prostate biopsy sepsis and hospital admissions in rectal swab group patients.

Conclusions: Targeted prophylactic antibiotics reduce the risk of sepsis following a prostate biopsy. 28,170.

UP-06.28

Feasibility of planned mini-laparotomy and adhesiolysis at the time of robotic-assisted radical prostatectomy in patients with prior major abdominal surgery: Preliminary results

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Introduction and Objective: Robotic assisted radical prostatectomy (RARP) has overwhelmingly been used and many surgeons have abandoned the open approach. Herein we report our experience on the feasibility of completing radical prostatectomy robotically at time of planned open adhesiolysis for prior major abdominal surgery with lower midline scar.

Methods: We searched our prospectively collected RARP database of 250 patients performed by a single surgeon (AEH) for patients who underwent planned open mini-laparotomy at time of RARP. We included all demographic, intraoperative and perioperative data. Descriptive analysis was used.

Results: A total of 5 patients (group 1) had planned open mini-laparotomy and adhesiolysis at time of RARP among 250 RARP patients (group 2). All patients had prostatectomy completed robotically. The mean values (ranges) of patients' demographics for group 1 versus 2 were as follows: Age 61.8 years (54-69) vs. 60.2 years (41-74); PSA 5.2 ng/ml (1.75-7.90) vs. 7 (0.7-26.4); BMI 30.7 (24.3-45.3) vs. 27.9 (19.5-46); prostate volume 41.5 cc (30.8-54) vs. 35.8 (12-101). Mean operative time (skin to skin) was 245 min (190-280) compared to 224 min , estimated blood loss 410 ml (300-650) compared to 317 ml (50-1000), and hospital stay was 2.8 days compared to 1.2 days in group1 and 2, respectively. There were no intraoperative complications in group 1. Postoperatively, there were one prolonged ileus which resolved spontaneously and one myocardial infarction treated medically.

Conclusion: Robotic completion of radical prostatectomy after open adhesiolysis is feasible. This approach maintains the minimally invasive advantages of RARP, despite a slightly longer hospital stay. Furthermore it precludes the need to refer patients with previous major abdominal surgery for radiation therapy or to surgeons with more experience in open radical retropubic prostatectomy.

UP-06.29

The Centre hospitalier de l'Université de Montréal (CHUM)'s initial experience with the alpha-emitter Radium-223 in metastatic castrate resistant prostate cancer

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Introduction: Radium-223 dichloride (Rad-223) is an alpha emitter that selectively targets bone metastases. The ALSYMPCA study, a phase 3 trial involving more than 900 patients with mCRPC, which randomized patients to six injections of radium-223 vs. placebo has shown improved overall survival. It has also shown a benefit of Rad-223 as compared with placebo in all main secondary efficacy end points. To date, our institution is the only one in Quebec that has treated patients with Rad-223. We report our experience herein.

Methods: We have participated in the 16216 study and in the STEP Program, which were both established in order to treat mCRPC patients with Rad-223. All patients had either received, were not eligible to receive, declined or progressed under chemotherapy (docetaxel or cabazitaxel). Other treatments such as Abiraterone or Enzalutamide were also used prior to Rad-223 but not concomitantly except in one patient. Patients were scheduled to receive six injections of Rad-223 at a dose of 50 kBq per kilogram of body weight intravenously administered every 4 weeks.

Results: From October 2013 to August 2014, 13 patients were treated at our center. Median age at treatment was 68 years (58-89). The mean PSA at time of treatment was 856,79 ng/mL (SD 1285.7). Mean alkaline phosphatase was 200.77 (SD 214.1). 77% of patients had at least 5 bone metastasis and all patients experienced pain prior to treatment with Rad-223. Five patients had lymph node metastasis or local recurrence in the prostate bed. All but one patient had received prior chemotherapy. Median number of cycles of Radium-223 received was 6, with 10 of 13 patients (77%) completing at least five cycles of Rad-223. Two patients died prior to completing all 6 cycles. Radium-223 was well tolerated by all patients with no patient except one who experienced thrombocytopenia. To date 2 patients have received docetaxel after Rad-223 which was well tolerated. Eleven of 13 patients (85%) experienced some level of pain relief from baseline. Eight patients had reductions of alkaline phosphatase levels during therapy, while two patients had PSA reductions of greater than 50%.

Conclusion: Our initial experience with radium 223 is very encouraging. Tolerability has been excellent. Almost all (85%) patients treated to date have reported some degree of pain reduction.