Moderated Poster Session III: Oncology 1
Thursday, October 29, 2015
3:30 – 5:00 p.m.

P32
Pathologic Evaluation Of Non-tumor Renal Tissue Predicts Renal Function Post Radical Nephrectomy

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Background: Recent studies have demonstrated that the evaluation of non-neoplastic renal parenchymal tissue post partial nephrectomy may predict future renal function. We assessed the predictive role of non-neoplastic renal pathology in a cohort of patients with normal pre-operative renal function who underwent radical nephrectomy for a renal mass.
Methods: All patients from our institution with a normal contralateral kidney who underwent radical nephrectomy from 2002 - 2008 were identified. Patients with missing clinical data or pre-operative chronic kidney disease (CKD), defined as Glomerular Filtration Rate (GFR) <60mL/min/1.73m2) were excluded. Pathology slides were re-reviewed by two pathologists (MM & GI) for presence of glomerulosclerosis (GS), interstitial Fibrosis (IF), tubular atrophy (TA), and arterial narrowing (AN) which were correlated with pre and post-op renal function.
Results: 97 patients met inclusion criteria and had tissue available for pathology review. GS, IF, TA and AN was present in 70%, 44%, 44% and 96% of patients, respectively. The presence of IF and TA was associated with relatively reduced renal function both pre-op and at one year ($p<0.0001$). Patients with GS demonstrated significant decline in renal function at 1 year ($p<0.0001$) despite normal pre-operative renal function. Of the assessed clinical conditions, only hypertension and coronary artery disease affected post-op renal function on logistic Regression ($p=0.04$ and 0.04).
Conclusions: Evaluation of non-tumor renal tissue at the time of radical nephrectomy offers valuable predictive information regarding post-operative renal function Our significant data suggest an ongoing role for pathological evaluation of non-neoplastic renal tissue in nephrectomy specimens.

P33
Performance Of CCP Assay In An Updated Series Of Biopsy Samples Obtained From Commercial Testing

E. David Crawford[1], Neal Shore[2], Peter T. Scardino[3], John W. Davis[4], Jonathan D. Tward[5], Lowndes Harrison[6], Brent Evans[7], Lisa FitzGerald[8], Steven Stone[8], Michael K. Brawer[7].
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Background: The cell cycle progression (CCP) score is an RNA–based expression assay, which has improved the prediction of prostate cancer aggressiveness in nine separate retrospective cohorts. In this analysis, we characterized the patient population and CCP score performance in commercial testing.
Methods: Formalin–fixed prostate biopsy samples from 8151 patients were submitted by 1434 physicians to Myriad Genetic Laboratories for CCP test analysis. Patient clinicopathologic data was obtained from the test request form. The CCP score was calculated based on RNA expression of 31 cell cycle progression genes normalized to 15 housekeeping genes. Patients were sorted in to AUA risk categories and assigned a relative classification of cancer aggressiveness based on the CCP score.
Results: Of the 8151 samples that contained sufficient carcinoma (>0.5mm linear extent), 7881 (96.7%) provided quality RNA for analysis. The CCP score distribution ranged from –2.9 to 3.8. Correlation with Gleason score was r=0.36 and the correlation with PSA was r=0.17. Based on the CCP score, 32.7% of men had a less aggressive cancer and 23.5% of patients had a more aggressive cancer than expected based on clinicopathologic prediction.
Conclusions: The CCP test can improve risk stratification for men with prostate adenocarcinoma independent of other clinicopathologic variables. Fifty–six percent of men tested in the commercial assay were assigned to a different risk category than predicted by their clinicopathologic features.

P34
Partial and Hemi-Nephrectomy for Renal Malignancy in Patients with Horseshoe Kidney

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Background: Horseshoe kidney is the most common congenital renal fusion anomaly, with an estimated incidence of 1:400 to 1:1000 patients. Management of localized renal malignancy in a horseshoe kidney may be complicated by abnormal renal location, aberrant vascular anatomy, presence of the renal isthmus, and need to preserve functional renal parenchyma. To date, only individual case reports and small case series have been published on this topic. We present the largest known series of patients with renal malignancy in horseshoe kidneys managed by partial or hemi-nephrectomy with associated outcomes.
Methods: A retrospective review of our institution's electronic medical record was conducted to identify operative reports that contained the key words "nephrectomy" and "horseshoe kidney" over a 15-year period. Pediatric patients and those who underwent surgery for benign indications were excluded from analysis. Data collected included patient demographics, tumor characteristics on pre-operative imaging, intra-operative details, final pathologic analysis, pre- and post-operative renal function, treatment complications and long term oncologic outcomes.
Results: Eight patients with horseshoe kidneys who had undergone partial or hemi-nephrectomy for renal malignancy were identified. Five underwent partial nephrectomy while 3 underwent hemi-nephrectomy with division of the renal isthmus. Seven patients were managed with open surgery while 1 underwent a hand-assisted laparoscopic approach. Mean tumor size was 6.2±3.2 cm. Median Charlson Comorbidity Index was 2 (IQR 2-3). Mean operative time was 214±154 minutes and 2 patients required peri-operative blood transfusion for intra-operative blood loss. Six patients had clear cell renal cell carcinoma (RCC), 1 patient had papillary variant RCC and 1 patient had a renal carcinoid tumor. All patients survived to discharge with a median length of stay of 4 days (IQR 2-6 days). Mean pre-operative and discharge estimated Glomerular Filtration Rates were 82.6±16.3 mL/min and 66.8±27.8 mL/min, respectively, with a mean decrease of 15.8±18.5 mL/min. No patients required acute hemodialysis in the post-operative

period. One patient developed a post-operative urine leak requiring percutaneous drain placement and ureteral stenting. One patient progressed to metastatic disease. Median follow-up period was 38.5 months, with a cancer-specific survival of 87.5% and an overall survival of 62.5%.
Conclusions: Partial and hemi-nephrectomy for renal malignancy can safely be performed in patients with horseshoe kidney with acceptable operative and oncologic outcomes.

P35
A Multi-center Comparison Of A 17-gene Genomic Prostate Score (GPS) As A Predictor Of Outcomes In African-american (AA) And Caucasian (CA) Men With Clinically Localized Prostate Cancer (PCa)

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Background: For clinical adoption of predictive cancer assays, it is imperative to demonstrate that they have equivalent performance in different racial groups. GPS is a tissue-based RT-PCR assay clinically validated to predict the likelihood of aggressive PCa (adverse pathology - AP, and biochemical recurrence - BCR). The assay measures the expression of 12 cancer related genes, representing 4 biologic pathways (stromal response, androgen signaling, cellular organization and proliferation), and 5 reference genes. We assessed the clinical performance of the test in different racial groups.
Methods: We compared GPS results (scale 0-100) and individual gene group scores in specimens from 138 AA and 957 CA patients in 4 independent cohorts (3 biopsy-based - CPDR, PCaP, and UCSF and one RP-based - CC) with clinically low to intermediate risk PCa. In 3 cohorts (CPDR, CC, UCSF), the association between GPS, race and outcomes were assessed using logistic regression and Cox PH models as appropriate.
Results: Although each cohort had different baseline risk distributions (as reflected by different median GPS), within each cohort median and interquartile ranges of GPS were similar between AA and CA men and were not statistically different (Table 1). Individual gene group expression patterns were similar between the two racial groups and not statistically different. In each of the 3 cohorts with AP endpoints, race was not predictive of outcome; in the CPDR study, race was not predictive of BCR. In a multivariable model with GPS, NCCN risk group and race in the CPDR and UCSF studies, only GPS was significantly ($p<0.001$) associated with clinical outcomes. In the CPDR study, GPS was strongly predictive ($p<0.05$) of clinical outcomes in both racial groups.

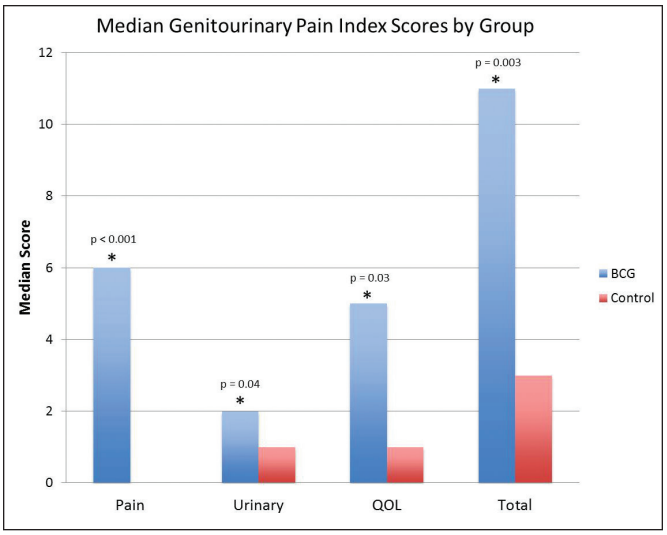

Fig. 1. P36.

Conclusions: The tumor biology measured by GPS is similar between AA and CA men. AA and CA patients had comparable clinical outcomes in these cohorts. In the largest cohort (CPDR), GPS was predictive of AP and BCR in both racial groups.

P36
Use of the Genitourinary Pain Index (GUPI) to Quantify Symptoms Associated with Bacillus Calmette-Guerin Treatment for Non-Muscle Invasive Bladder Cancer

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Background: Intravesicle Bacillus-Calmette-Guerin (BCG) treatment for non-muscle-invasive bladder cancer often results in irritative voiding symptoms that may diminish quality of life and limit overall compliance with therapy. To date, no consistent method for quantifying these symptoms has been described. We aim to utilize the Genitourinary Pain Index (GUPI), previously validated for a variety of urologic pain conditions, to quantify symptoms in patients undergoing BCG treatment.
Methods: Patients diagnosed with high grade non-muscle-invasive bladder cancer, including bladder carcinoma in situ (CIS), previously treated by transurethral resection and undergoing either a six-week induction course or three-week maintenance course of BCG were included in this study. One week following office intravesical instillation of BCG for a period up to two hours, patients were asked to complete the nine-question

Table 1. P35. Distribution of GPS Between AA and CA Patients

Variable	Study	Race	Percentage (%)	GPS Values					Wilcoxon Rank-Sum Test *p* value
				Median	Q1	Q3	Min	Max	
GPS	CPDR (n = 387)	AA	21	30	23	38	12	64	0.73
		CA	79	30	23	40	2	87	
	UCSF (n = 372)	AA	3	22	17	27	13	38	0.27
		CA	97	24	18	33	1	65	
	PCaP (n = 23)	AA	57	35	32	42	26	100	0.80
		CA	43	33	30	46	25	85	
	CC BX (n = 166)	AA	17	29	22	41	8	65	0.13
		CA	83	25	16	36	0	62	
	CC RP (n = 313)	AA	14	28	17	40	6	70	0.90
		CA	86	25	19	35	1	100	

GUPI questionnaire. The GUPI includes three subsets describing pain (maximum score of 23), urinary dysfunction (maximum score of 10) and quality of life (QOL) (maximum score of 12). A total sum (maximum score of 45) was also calculated. The GUPI questionnaire was also administered to a control group of patients undergoing surveillance for high grade non-muscle-invasive bladder cancer but not receiving BCG treatment for comparison.
Results: Fifty-four patients completed the GUPI questionnaire, 29 in the BCG treatment group and 25 in the control group. There were no significant differences between the groups in age (67.4 vs 69.7 years, p=0.42), gender (76% vs 80% male, p=0.72) or tumor stage (34% Ta, 42% T1, and 24% CIS vs 28% Ta, 60% T1, and 12% CIS, p=0.34) respectively. The BCG treatment group had significantly higher median scores in all three GUPI subscale categories compared to the control group; pain (6 vs 0, p<0.001), urinary dysfunction (2 vs 1, p=0.04) and QOL (5 vs 1, p=0.03) respectively. The BCG treatment group also had a significantly higher median total GUPI score compared to the control group (11 vs 3, p=0.003) (Fig. 1).
Conclusions: The Genitourinary Pain Index is a valuable tool to quantify the irritative symptoms associated with BCG treatment for non-muscle-invasive bladder cancer. We plan to validate this tool, which may serve as a consistent standard questionnaire in this patient population to analyze response to specific treatments aimed at symptom reduction.

P37
Clinical and Pathological Implications of Cautery Artifact Associated with Transurethral Resection of Large Bladder Tumors
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Background: Transurethral resection of bladder tumor (TURBT) is a key step in the treatment and staging of urothelial cancer. Cautery artifact is found in the majority of bladder specimens with use of monopolar and bipolar electrocautery. At times, cautery artifact can obscure the appearance of tumor cells infiltrating the muscularis propria, a critical problem in accurately staging this cancer. Currently, it is not known whether cautery artifact is clinically significant.
Methods: We queried our institution's billing data to identify patients who underwent TURBT for large bladder tumors >5cm (CPT 52240) by two urologists at a high volume academic center from January 2009 through April 2013. TURBT cases that involved only cold cup resection of tumors for large lawns of suspected CIS or superficial-appearing papillary growths were excluded. Pathological reports were reviewed for tumor type, presence of muscularis, grade, depth of invasion, number of separate pathological specimens per TURBT, and presence of cautery artifact. Surgeon operative reports were reviewed for type of electrocautery, tumor size, and whether additional cold cup biopsies were taken from the tumor bed. Slides were re-reviewed by a genitourinary pathologist to verify the presence of "clinically significant" cautery artifact, which we define as cautery artifact that precludes an accurate determination of presence of cancer, tumor type, grade of cancer, or depth of invasion.
Results: We identified 190 TURBT cases of large tumors using either monopolar or bipolar electrocautery. Cautery artifact was mentioned in 15/190 (7.9%) pathological reports. After re-review by a genitourinary pathologist, clinically significant cautery artifact was seen in 5/120 (4.2%) cases of monopolar resection and 7/70 (10%) cases of bipolar resection. There was no difference between the rate of clinically significant cautery artifact when comparing monopolar and bipolar resection (p=0.22). Tumor size, number of separate pathological specimens sent, grade, tumor type, and clinical stage were not associated with clinically significant cautery artifact (all p>0.05). Additional cold cup biopsies of the tumor bed did not overcome the damaging effects of electrocautery in either the monopolar or bipolar group (p=0.34 and p=0.99, respectively).
Conclusions: In the present study, we identified clinically significant cautery artifact that precludes an accurate diagnosis in up to 6% of all TURBTs with electrocautery resection of large bladder tumors. An inaccurate pathological diagnosis on initial staging TURBTs can necessitate repeat TURBTs. Reducing clinically significant cautery artifact may be an avenue for minimizing the morbidity and health care costs associated with the management of non-muscle invasive or muscle invasive urothelial cancer.

P38
Four Birds One Stone to Inhibit 5androstane-3α,17β-diol Conversion to DHT
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Background: Almost all men who present with advanced prostate cancer (CaP) and some men who fail therapy are treated with androgen deprivation therapy (ADT). ADT is not curative and CaP recurs as the lethal phenotype. One mechanism that may contribute to CaP resistance to ADT is intracrine metabolism, the conversion of weak adrenal androgens to testicular androgens, testosterone (T) or dihydrotestosterone (DHT). Previous work from our laboratory and others has demonstrated that CaP cells can use the primary (progesterone as substrate) or secondary (androstenedione [ASD] as substrate) backdoor androgen metabolism pathways to produce DHT. The backdoor pathways generate DHT without using T as an intermediate substrate. The final step in the primary backdoor pathway involves the conversion of 5androstane3α,17β-diol (androstanediol) to DHT performed by 4 enzymes. These enzymes are HSD17B6, RDH16, DHRS9 or RDH5. The goal is to inhibit the enzymes responsible for the conversion of androstanediol to DHT. Inhibition of the step immediately proximate to intracrine metabolism of DHT should lower DHT more effectively than inhibitors of 5α-reductases and/or CYP17A1, which act earlier in intracrine metabolism pathways.
Methods: Bioinformatics tools were used to analyze the protein sequences of these 4 enzymes to determine if these enzymes shared common catalytic amino acid residues. Site-directed mutagenesis and liquid chromatography tandem mass spectrometry (LC-MS/MS) were used to test the catalytic significance of the common catalytic amino acid residues and if mutation of these catalytic residues inhibited androstanediol conversion to DHT.
Results: The NCBI Constraint-based Multiple Protein Alignment Tool (COBALT) showed that these 4 enzymes share catalytic amino acids residues. LC-MS/MS confirmed that these 4 enzymes convert androstanediol to DHT and androsterone to androstanedione. Enzymes catalytic residues were mutated using site-directed mutagenesis. LC-MS/MS showed that single, double and complete catalytic deletion of the common catalytic amino acids impaired enzyme activity. Furthermore, the impaired catalytic mutants combined with dutasteride decreased CaP cell line DHT levels more than dutasteride alone. These results demonstrate that a new treatment directed against the terminal steps in the primary backdoor pathway may decrease DHT levels better than ADT alone.
Conclusions: Further reduction of tissue DHT levels by inhibiting the last step in intracrine metabolism may improve response to ADT or induce re-remission of castration-recurrent CaP and improve survival of men with advanced CaP.

P39
Does Dose Reduction of Neoadjuvant Chemotherapy Impact Perioperative Outcomes after Robot-Assisted Radical Cystectomy?
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Background: Despite the survival benefit of neoadjuvant chemotherapy (NAC), some patients fail to complete the full NAC dose. In this study we sought to assess whether failure to complete NAC affects perioperative outcomes following robot-assisted radical cystectomy (RARC) or not.
Methods: A retrospective review of Roswell Park Cancer Institute Quality Assurance database was performed to identify patients who received NAC between 2005 and 2014. The 90-day perioperative outcomes of patients who received full dose of NAC were compared with those who received only a reduced dose.

Results: We identified 64 patients (18%) who received NAC, 52 (81.3%) were males. Both groups were comparable in terms of demographics and primary pathology. Among those who received NAC, 50 patients (78%) received a full dose while 14 (22%) received a reduced dose. Mean time to RARC was shorter for the reduced NAC group, although this did not reach statistical significance (69 versus 84 days, p=0.54). No statistically significant difference was observed with regards operative time, pathological T-stage, soft tissue margins, lymph node yield or N+, or length of hospital stay. The 2 groups showed no significant difference in terms of complications.
Conclusions: Patients who had received a reduced dose of NAC showed comparable 90-day perioperative outcomes, complication rates and pathological outcomes when compared to the full dosage group.

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A Randomized, Double-blind, Phase 2 Efficacy And Safety Study Of Enzalutamide Versus Bicalutamide In Metastatic Castration-resistant Prostate Cancer: The TERRAIN Trial

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Background: The phase 2 TERRAIN trial (NCT01288911) compared the efficacy and safety of enzalutamide versus bicalutamide in patients with metastatic castration-resistant prostate cancer who have progressed on luteinizing hormone-releasing hormone agonist/antagonist therapy or after bilateral orchiectomy, while maintaining castration therapy during the study.
Methods: In this double-blind study in North America and Europe, patients were randomized 1:1 to enzalutamide 160 mg/day or bicalutamide 50 mg/day. The primary endpoint was progression-free survival (PFS), defined as the time from randomization to centrally confirmed radiographic progression, skeletal-related event, initiation of new antineoplastic therapy, or death from any cause, whichever occurred first.
Results: A total of 184 patients were randomized to enzalutamide and 191 patients to bicalutamide. North American sites enrolled 154 (41.1%) patients and European sites enrolled 221 (58.9%) patients. At baseline, 73.6% of patients had an Eastern Cooperative Oncology Group performance score of 0, median prostate-specific antigen (PSA) was 21 ng/mL, and bone metastases were present in 82% of patients. The data cut-off date was October 19, 2014, with 240 events for the primary efficacy endpoint.The study achieved its primary objective of a statistically significant increase in PFS for enzalutamide compared with bicalutamide (hazard ratio [95% confidence interval] 0.44 [0.34, 0.57]; p<0.0001). Median PFS was longer for enzalutamide patients compared with bicalutamide patients (15.7 versus 5.8 months, respectively). Median time to PSA progression was prolonged on enzalutamide (19.4 months) versus bicalutamide (5.8 months [HR 0.28]; p<0.0001). A ≥50% PSA response was achieved in 82.1% of enzalutamide-treated patients versus 20.9% in bicalutamide. The median time on enzalutamide treatment was 11.7 months, compared with 5.8 months on bicalutamide. Serious adverse events were reported in 31.1% and 23.3% of patients on enzalutamide and bicalutamide, respectively. Grade ≥3 cardiac adverse events were observed in 5.5% and 2.1% of patients on enzalutamide and bicalutamide, respectively. Two seizures were reported with enzalutamide and one with bicalutamide. The most common (≥10%) adverse events reported more frequently with enzalutamide than bicalutamide were fatigue (27.9% versus 20.1%), back pain (19.1% versus 18.0%), hot flush (14.8% versus 11.1%), hypertension (14.2% versus 7.4%), diarrhea (11.5% versus 9.0%), weight decrease (10.9% versus 7.9%) and pain in extremity (10.9% versus 5.3%). Adverse event rates were not adjusted for time on treatment.
Conclusions: Enzalutamide had significantly greater efficacy than bicalutamide, with respect to both PFS and PSA response. The safety profile was consistent with previous reports.

P41

Oncological Outcomes of Salvage High Intensity Focused Ultrasound for Radio-recurrent Prostate Cancer: Results Of A Prospective Phase II Clinical Trial

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Background: 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.
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 χ^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.

P42

Long-Term Morbidity and Oncological Outcomes of Salvage Cryotherapy for Radio-Recurrent Prostate Cancer

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Background: Locally radio-recurrent prostate cancer (rr-PCa) can offer a chance of cure albeit with potential morbidities. Current salvage treatment options include radical surgery and minimally-invasive ablative modalities such as HIFU and cryosurgery (s-cryo). Current data suggests that s-cryo can achieve disease-free survival (DFS) rates up to 60% at 5yr. However, the majority of data is based on retrospective analysis with mid-term follow-up and there is still paucity of data on long-term outcomes. The 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
Methods: A retrospective analysis was performed on 187 patients who underwent s-cryo at our center for biopsy-proven rr-PCa from 1995 to 2004. Two freeze-thaw cycles of transperineal cryo were performed under TRUS guidance by a single surgeon. Patients' preoperative, perioperative, and postoperative features were reviewed from a prospectively maintained database. Complications were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) system v2.0. Recurrence was defined using the Phoenix definition (nadir + 2ng/ml) as well as any radiologic, histologic, or 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 $\chi 2$ tests for continuous and grouped data, respectively (SPSSv.17, p<0.05).

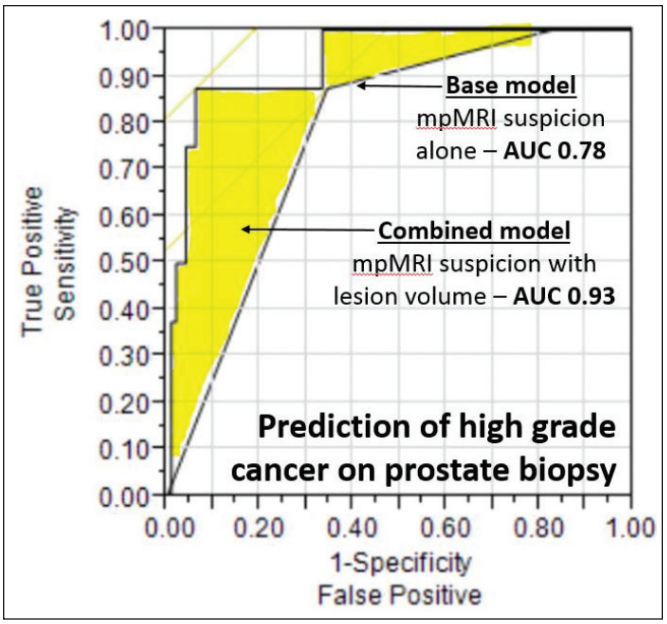

Fig. 1. P43.

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%).
Conclusions: 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.

P43
Size Does Matter: Improving The Diagnostic Value Of Prostate Multiparametric MRI (mpMRI) With The Consideration Of Lesion Volumes

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Background: Prostate mpMRI and its lesion suspicion (via Likert, PIRADs, etc) has emerged as an excellent predictor of cancer detection. However, the PPV of mpMRI remains imperfect and is dependent on somewhat subjective factors (ie radiologist suspicion). We sought to review our institutional experience with prostate mpMRI and targeted biopsy to identify improved predictors of biopsy histopathology. As tumor size has long been known to be linked to aggressiveness, we sought specifically to address the predictive value of this objective finding on imaging.
Methods: Following IRB approval, we reviewed men from 11/13-11/14 who had 3T mpMRI (Anatomic, DCE, and DWI) with endorectal coil and underwent subsequent fusion MR/US biopsy. All lesions were characterized with MRI suspicion level (Likert and PIRADs), lesion location, and volumetric analysis. Volumes were calculated following individual segmentation utilizing the Dynacad platform.
Results: A total of 52 men, harboring 104 lesions, were studied. Indications for mpMRI were initial biopsy (N=5), prior negative biopsy (N=29), active surveillance (N=16), and suspicion of recurrence (N=2). On univariable analysis, both MRI suspicion and lesion volume were strong predictors of lesion specific cancer detection (P<0.001 for both). ROC analysis revealed MRI suspicion to have AUC of 0.75, 0.79, and 0.78 for all cancers, relevant cancers (GS>6), and high grade cancers (GS>7), respectively. AUC for lesion volume was 0.81, 0.84, and 0.94, respectively. A multivariable model including both lesion suspicion and volume maintained both as significant predictors of cancer. The combined model had improved detection over MRI suspicion alone with AUC of 0.86, 0.89, and 0.93, respectively. To control for spatial accuracy for smaller lesions, prediction models were repeated including the results of the paired systematic biopsy, which again revealed both lesion suspicion and volume to be significant (p<0.001) with the combined model demonstrating AUC of 0.75, 0.80, and 0.92 respectively. Of note, 10 men had high grade disease, all of whom (100%) had lesions 1 mL or greater (p<0.001) (Fig. 1).
Conclusions: Lesion volume is an objective and powerful predictor of cancer and may be combined with more conventional MRI suspicion schemes to improve cancer detection.

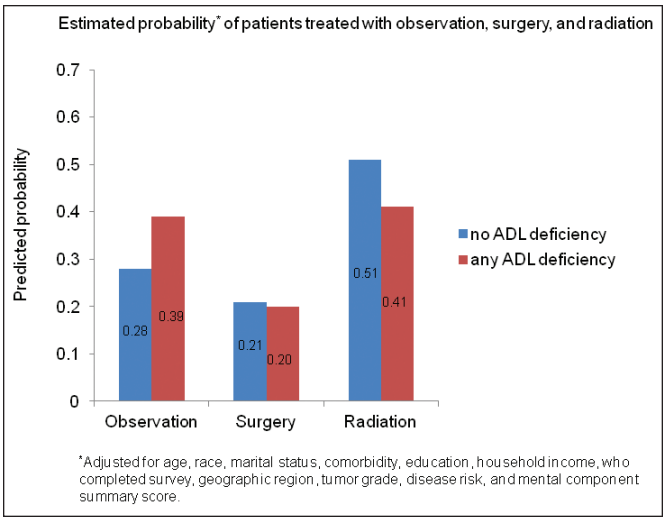

Fig. 1. P44.

P44
The Association Of Functional Status And Treatment Choice Among Older Men With Prostate Cancer

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Background: Prostate cancer is a common disease with a variety of effective treatment options. To what extent a patient's functional status factors into the treatment decisions is unknown. We sought to examine the association of functional status with the receipt of observation, surgery, or radiation among older men with prostate cancer.
Methods: We conducted a retrospective cohort study of men aged 65 or older diagnosed with prostate cancer between 1998 and 2009, using Surveillance, Epidemiology, and End Results-Medicare Health Outcomes Survey (SEER-MHOS) data. We restricted analyses to those who also completed a survey within 1 year prior to diagnosis. Our primary outcome was the use of observation, surgery, and radiation (mutually exclusive categories) within one year of diagnosis. We explored four measures of functional status: activities of daily living (ADL) deficiency (categorized as no ADL deficiency or any ADL deficiency), proxy survey response, and the Medical Outcomes Study Short Form 36 (SF-36) and subsequently the Veterans RAND 12-Item Health Survey (VR-12), broken into physical component summary score (PCS) and mental component summary score (MCS). We fit a multivariable multinomial logistic regression adjusted for a variety of patient, clinical, and regional characteristics. Findings are presented as odds ratios with 95% confidence intervals (CIs) and the predicted probability of treatment type by presence of ADL deficiency.

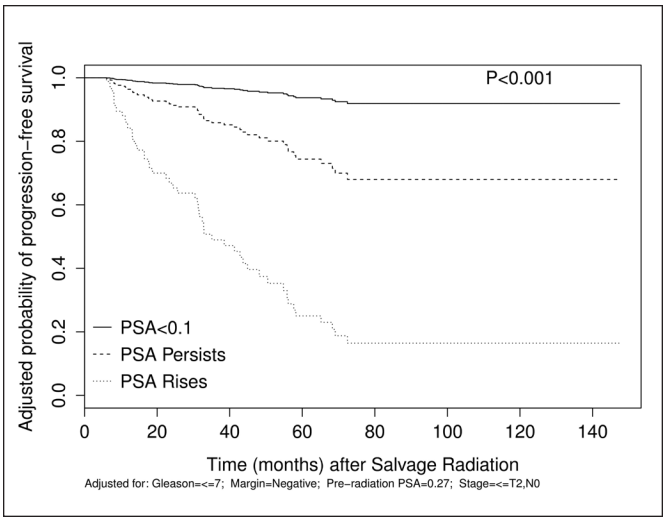

Fig. 1. P45.

Results: There were 961 men who met eligibility criteria. Of these, 297 (31%) underwent observation, 200 (21%) underwent surgery, and 464 (48%) underwent radiation. Proxy survey response, any ADL deficiency, and PCS but not MCS were associated with greater likelihood of observation over surgery or radiation. In a fully-adjusted model, compared to men with no ADL deficiency, those with any ADL deficiency had similar odds of surgery relative to observation (odds ratio [OR] 0.77; 95% confidence interval [CI] 0.48-1.22). However, men with any ADL deficiencies had a lower odds of receiving radiation relative to observation (OR 0.65; 95% CI 0.45-0.94). The predicted probability of observation, surgery, and radiation among patients without any ADL deficiencies versus those with deficiencies was 28% v. 39%, 21% v. 20%, and 51% v. 41%, respectively (Fig. 1).
Conclusions: Functional status is associated with treatment choice for men with prostate cancer, even after adjusting for tumor grade and disease risk. Future research should examine whether this is due to physicians' recommendations or patient preferences or a combination.

P45
PSA Response to Salvage Radiotherapy Predicts Time to Disease Progression
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Background: As many as 25% of men with localized prostate cancer who undergo radical prostatectomy will recur. In this setting, salvage radiotherapy may cure patients with local recurrence, but is ultimately ineffective in those with occult metastatic disease. The objective of this study is to identify factors associated with a durable response to early salvage radiotherapy and, specifically, examine how PSA response to radiotherapy predicts subsequent disease progression.
Methods: Using a prospectively populated database of 3065 men who underwent open radical prostatectomy by a single surgeon, 186 patients (6%) were identified who received salvage radiotherapy without concomitant androgen deprivation for biochemical recurrence. The main outcome was time to disease progression according to initial PSA response after salvage radiotherapy. Patients were stratified into 3 groups based on their PSA response: (1) PSA <0.1 ng/mL, (2) persistently detectable PSA, and (3) rising PSA. Disease progression was defined as initiation of androgen deprivation or radiographic evidence of metastatic disease.
Results: Patients received salvage radiotherapy at a mean PSA of 0.26 ± 0.23 ng/mL. Over a mean follow-up of 42 months, a total of 50 (27%) patients experienced disease progression after salvage radiotherapy, including 37(74%) who were treated with androgen deprivation and 13(26%) who developed distant metastases. On multivariable analysis, both an unchanged PSA (HR 3.66; 95% CI, 1.38-9.73; p=0.009) and a rising PSA (HR 18.22; 95% CI, 7.31-45.45; p<0.001) were associated with increased risk of disease progression compared to those with PSA<0.1 ng/mL after adjusting for several factors, including Gleason score, surgical margin status, stage, and pre-radiotherapy PSA (Fig. 1).
Conclusions: PSA response is associated with the risk of disease progression following salvage radiotherapy. This information can be used to counsel patients on the potential need for additional therapy and identify those at greatest risk for systemic progression.

P46
Pretreatment Peripheral Blood Monocyte Subset Gene Expression Predicts Patient Survival Following Dendritic Cell Vaccination
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Background: Monocytes and macrophages are the most common tumor-infiltrating cells in a majority of tumor types, yet the role these cells play in determining the course of human disease remains an understudied area of investigation. Circulating monocytes, which represent the precursors for tumor-associated macrophages, consist of three main subsets (classical, intermediate, and nonclassical). These monocyte subsets also form the starting material utilized during dendritic cell (DC) vaccination of cancer patients. Since the efficacy of DC vaccines depends on the quality of the cells generated, the goal of this study was to determine if gene expression of monocyte subsets was altered in renal cell carcinoma (RCC) patients treated with DC vaccination and if responders to vaccination could be stratified based upon pretreatment monocyte gene expression analysis.
Methods: Pretreatment peripheral blood monocytes were isolated from healthy donors and RCC patients enrolled in a completed DC vaccination phase II clinical trial (DC + IFNα/IL-2, NCT00085436). Circulating classical (CD14++, CD16-), intermediate (CD14++, CD16+), and nonclassical (CD14+, CD16++) monocyte subsets were isolated from patients prior to therapy using flow cytometry and transcriptional profiles were evaluated by gene expression microarray.
Results: Circulating nonclassical monocytes were increased two to three-fold in complete responders (P<0.05) compared to partial responders, patients with progressive disease or healthy donors. Unsupervised hierarchical clustering analysis of gene expression clearly distinguished the transcriptional profile of classical and intermediate RCC patients from healthy controls. In this respect, classical monocytes from healthy donors were more similar to healthy donor intermediate monocytes than to classical monocytes from RCC patients. Further analysis revealed that classical monocyte subset had the most genes (1100) that were significantly changed (P<0.05, log fold change > log2 (1.5)) when comparing RCC to healthy donor monocytes. Interestingly, 47% of these genes were uniquely changed in the classical subset and were not altered in intermediate or nonclassical monocytes from RCC patients. In contrast, only 7% of the differentially expressed genes between healthy donors and RCC patients were unique to the intermediate monocyte subset. Finally, unsupervised

Table 1. P47. T stage and number of cases T stage number of cases

T Stage	No. cases
T1a	22 954
T1b	12 279
T2	6223
T3a	5557
T3b	4565
T3c	171
T4	493

hierarchical cluster analysis of the nonclassical monocytes revealed that long-term (>10 years) survivor monocytes could be clearly segregated by gene expression analysis.
Conclusions: These findings demonstrate that the status of gene expression in monocyte subsets may be an important prognostic tool for immune-targeted therapies. Future studies will investigate whether gene expression differences in tumor-conditioned monocytes influence monocyte biology and the function of monocyte-derived dendritic cells.

P47
Contemporary Utilization Of Lymph Node Dissection For RCC: Are We Accepting The Randomized Trial?
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Background: The controversy of RPLND during surgery for RCC has been addressed in a RCT (Blom et al, 2009, epub 2008) revealing a low yield of node positive disease and no survival advantage. However, some continue to perform LND in select patients. This study aims to examine RPLND utilization over the past decade and evaluates the influence of the above RCT on practice patterns in the US.
Methods: SEER-18 registries database was queried for all patients surgically treated for RCC from 2004-2011. Patients with unknown stage or non-cortical RCC were excluded from analysis. Patients were separated into cohorts based on T stage and then divided by year of diagnosis. The regression was calculated over the course of the study period.
Results: T1a tumors were the most common T stage at diagnosis (Table 1). Both T1a and T1b cohorts had a trend towards decreased frequency of lymphadenectomy from 2008 on (consistent with the RCT data dissemination), (r^2=0.66 and 0.61, respectively; $p<0.05$ for decrease in RPLND after 2008). There was no clear trend seen for any other stage tumors. As stage increased, patients had a higher likelihood of undergoing RPLND with 21%, 21%, 35%, 55%, and 45% for T2, T3a, T3b, T3c, and T4 tumors respectively.
Conclusions: RPLND are now rarely being performed for patients with T1 RCC. This supports the dissemination of the randomized trial in urologic practice. A similar trial design may be beneficial for patients with higher stage tumors as RPLND are inconsistently performed in this patient population.

P48
Utility of Preoperative Imaging for the Prediction of Prostate Adenocarcinoma Disease Burden
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Background: Magnetic resonance imaging (MRI) of the prostate is becoming increasingly utilized prior to radical prostatectomy (RP). However, the predictive ability of MRI to detect disease burden varies significantly in the literature. Following its introduction at a single institution, we evaluated the capability of MRI to determine extent of disease.
Methods: Between September 2011 and April 2014, fifty-four, consecutive patients who underwent multi-parametric MRI or computed tomography (CT) imaging prior to RP were retrospectively reviewed. All MRI or CT scans were reviewed and correlated with final pathologic specimens. The sensitivity and specificity of MRI and CT in predicting tumor location, extracapsular extension (ECE), seminal vesicle invasion (SVI), and lymphadenopathy was calculated.
Results: Fifty-four patients with a median age, PSA, and Gleason score of 59.7 years, 17.84, and 4+4=8 respectively underwent a radical prostatectomy with pre-operative imagining. Twenty-one (87.5%) patients had carcinoma of the prostate accurately identified on MR imaging. On final pathology the rate of positive lymph nodes, ECE and SVI was 29.6%, 48.1%, and 22.2% respectively. MRI was superior to CT scan in predicting tumor location, with a sensitivity of 87% compared to 2.6%. CT was unable to accurately predict positive lymph nodes in any patients, resulting in a sensitivity of 0%. MRI had a sensitivity of 10% and a specificity of 92.3% for detecting lymphadenopathy, reflecting a high rate of false negatives. CT was inferior to MRI in for ECE, with a sensitivity of 4.5% compared to 41.7%. MRI had a high false negative rate of 30.4% in determining ECE. Both CT and MRI were unable to determine SVI in any patients; however, CT had a higher specificity for SVI than MRI (100% versus 88.2%), due to a higher false positive rate with MRI.
Conclusions: The ability of MRI to accurately predict ECE, SVI, and lymphadenopathy is superior to CT but remains limited. However, prostate MRI can provide valuable information for treatment decisions and operative planning.