A COMPARISON OF MRI/FUSION-TARGETED PROSTATE BIOPSY IN BIOXY-NAÏVE AND PRIOR BIOXY-NEGATIVE MEN

Yash Khandwala, Zachary Hamilton, Unwanaobong Nseyo, Natalie M Schenker-Ahmed, David Karow, Christopher Kane, A. Karim Kader, Brittney Cotta, and J. Kellogg Parsons

Introduction: Evidence-based clinical guidelines recommend consideration of prostate MRI for men at-risk for prostate cancer who have had a prior negative biopsy, but not for biopsy-naïve men. However, it remains unclear whether cancer detection for MRI/fusion-targeted prostate biopsy (TB) differs between those who have and those who have not undergone prior biopsy.

Methods: Between 2014 and 2016, we identified 103 men without prostate cancer who underwent TB of MRI-detected lesions at our institution: 53 biopsy-naïve and 50 with at least 1 prior negative biopsy. We compared cancer detection on TB between groups. We defined clinically significant disease as Gleason ≥ 3+4 = 7.

Results: Compared to the biopsy-naïve group, the prior negative biopsy group had higher mean prostate volume (59.4 vs. 46.8 cm³, p= 0.04). There were no significant differences in age (65.7 vs. 65.8 years, p= 0.96), median PSA (8.6 vs. 6.9, p= 0.20), median number of targeted cores (3 vs. 3, p= 0.85), proportion with MRI-detected PI-RADS ≥ 4 (43% vs. 50%, p=0.15), proportion with anterior lesions (13% vs. 24%, p=0.18) and median duration of time between MRI and TB (26 vs. 38.5 days, p= 0.09). Among men with at least 1 prior biopsy, the median number of prior negative biopsies was 2. Of all men, 68 (66%) were diagnosed with cancer and 42 (41%) with clinically significant cancer. Cancer was detected less frequently in the prior negative biopsy men (56% vs.75%, p=0.04). The detection of clinically significant disease did not differ significantly between groups (43% vs 38%, p=0.60). In multivariable regression, prior negative biopsy men were 73% less likely (95% CI 0.10-0.74, p=0.01) to be diagnosed with cancer, but there was no significant difference in detection of clinically significant cancer (OR: .45, 95% CI 0.16 to 1.30, p=0.14) between groups.

Conclusion: Among men undergoing diagnostic TB, those with at least 1 prior negative biopsy are less likely to have cancer and equally likely to have clinically significant cancer compared to biopsy-naïve men. These data suggest that clinical guidelines for MRI in prostate cancer early detection merit reconsideration and refinement.
Introduction And Objectives: Prostate cancer (PCa) diagnostics would greatly benefit from more accurate, non-invasive techniques for the detection of clinically significant disease, leading to a reduction of over-diagnosis and over-treatment. Multiparametric MRI (mpMRI) is being used increasingly and has proven to be a valuable addition to the PCa diagnostic pathway. A novel biomarker-based risk score (SelectMDx) assessing urinary HOXC6 and DLX1 mRNA expression levels combined with traditional clinical risk factors, was recently developed to predict high-grade PCa (Gleason score >/=7) upon prostate biopsy and to reduce the number of unnecessary biopsies. The aim of this study was to investigate the correlation between the risk score and mpMRI outcomes.

Methods: The patients in this retrospective observational cohort were previously included in the validation study of the SelectMDx risk score, in which urine was collected after digital rectal examination (DRE) from men undergoing prostate biopsies based on an elevated serum PSA level (/>=3.0 ng/ml) and/or suspicious DRE. A subset of patients underwent an mpMRI after prostate biopsies were performed (n=174). The indications for performing MRI were based on persistent clinical suspicion of PCa after negative prostate biopsies or staging after PCa was found upon biopsy.

Results: 102 of 174 patients (59%) had PCa detected upon prostate biopsy, of which 54 (53%) had high-grade disease and a significantly higher SelectMDx risk score (p<0.001). The median SelectMDx risk score was also significantly higher in patients who had a suspicious lesion on MRI (p<0.001). For 81 mpMRI's the PIRADS classification was reported and there was a positive correlation observed between the risk score and the PIRADS classification (Figure 1). A Kruskal-Wallis test indicated a statistically significant difference in SelectMDx risk scores between the different PIRADS groups (p<0.001).

Conclusions: The novel urinary biomarker-based risk score is a promising tool in PCa detection. This study showed promising results regarding the correlation between the SelectMDx risk score with MRI outcomes. This risk score could potentially guide clinicians in selecting patients at risk for significant PCa for mpMRI.

Source of Funding: MDxHealth
DEVELOPMENT AND VALIDATION OF A NOVEL GENOMIC CLASSIFIER TO PREDICT AGGRESSIVE PROSTATE CANCER FROM DIAGNOSTIC BIOPSY TISSUE

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(Presentation to be made by Dr. Ewan Gibb)

Introduction: Increased clinical adoption of genome-wide expression analysis in urology practice provides an opportunity to prospectively collect massive amounts of genomic data. We have previously shown how these data can be used to further refine our understanding of the genomic landscape of prostate cancer on a population level. Here, we show how these data may also be used to develop a novel genomic classifier that further improves prediction of aggressive prostate cancer.

Methods: Genome-wide expression profiles from 10,917 localized PCa patients were extracted from the Decipher GRID registry (NCT02609269). The training cohort of radical prostatectomy (RP) tumor sample profiles included 545 cases from a retrospective cohort with long-term follow up and 1,939 from prospective clinical utilization of Decipher (GC1, 22 genes). A generalized linear model was trained to predict a composite genomic-pathologic endpoint (GC1≥0.7 and Grade Group ≥4) in the prospective cohort resulting in a final 60 gene model (GC2). Model characterization was performed in an additional 6,739 and 1,694 prospective RP and biopsy samples. The association of Decipher with individual clinico-pathologic variables was assessed using the Spearman’s rank correlation coefficient. Model validation was conducted on 253 biopsy samples from a retrospective cohort of men treated with RP. GC1 and GC2 models were compared using area under ROC curves, uni- and multi-variable logistic regression for the prediction of high-grade (Grade Group ≥3) and high-stage (≥pT3b) endpoints for aggressive disease.

Results: GC2 achieved an AUC of 0.92 on 10-fold cross validation to predict the composite endpoint. In prospective biopsy and RP cohorts, both GC1 and GC2 similarly had weak-moderate correlations with NCCN risk groups, tumor grade and pathologic stage (all p<0.001). In the retrospective biopsy validation cohort both models had an AUC of 0.75 to predict high-stage disease at RP. In a subset of 174 men with biopsy Grade Group 1-2 disease, the AUC for high-grade disease at RP was 0.62 and 0.67 for GC1 and GC2, respectively. In a multivariable model adjusted for age, pre-treatment PSA and percent positive cores, only the GC2 model remained significant in predicting high-grade disease with an odds ratio of 1.4 (95% CI 1.1-1.8) for every 10% increase in score (p=0.005).

Conclusion: This study has demonstrated for the first time how genomic data collected prospectively through the clinical use of a first-generation genomic test may be used to train a new and improved second generation risk model for prediction of aggressive disease.

Source of Funding: GenomeDx Biosciences Inc.
SELECTMDX™ URINE TEST IMPROVES LIKELIHOOD OF DIAGNOSING HIGH GRADE PROSTATE CANCER AT BIOPSY

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Introduction and Objective: There is a significant unmet clinical need for non-invasive methods that can accurately identify patients at increased risk for high-grade (HG) prostate cancer (PCa). The SelectMDx urine test provides the likelihood of detecting PCa and HG PCa upon subsequent biopsy. The test measures the mRNA levels of the homeobox C6 (HOXC6) and distal-less homeobox 1 (DLX1) biomarkers in urine samples. Higher expression levels of HOXC6 and DLX1 are associated with an increased probability for HG PCa. We investigated the clinical performance of this test using histopathological data of patients opting for template-guided transperineal mapping biopsy (MB) as the reference.

Methods: In this retrospective study, patients chose MB to confirm the histopathological findings of their initial TRUS biopsies. Post-DRE, first-void urine specimens were collected from each patient prior to MB. Histopathology of MB was independently read by a genitourinary pathologist. PCa patients with HG disease have tumors of Gleason Score (GS) ≥7 with Gleason grades 4 & 5. MB histopathology data was compared against SelectMDx™ test results for probability of PCa and HG PCa at biopsy. Likelihood of diagnosing PCa and HG PCa at biopsy is reported as a probability (p) between 0 – 100%.

Results: A total of 69 patients were included in this study with mean age of 62.8 ± 8.2 (34 - 78) yrs and PSA 7.52 ± 9.0 (0.32 - 41.82) ng/mL. MB identified 20 patients with benign pathology and 49/69 (71%) patients with PCa including 23/49 (47%) with GS ≥ 7 and 12/23 (52%) with GS ≥ 4+3 tumors. Performance results of SelectMDx™ test are summarized in the table. Sensitivity and NPV of the test is low for the likelihood of PCa at biopsy due to 28/49 (57%) patients with cancer indicated as p = 0. Accuracy improved for the likelihood of GS ≥ 7 (3+4) tumors with only 6/23 (26%) patients with HG tumors indicated as p = 0. Sensitivity and NPV reached 100% when the test was limited to patients with GS ≥ 4+3 tumors with an AUC of 0.92. However, 6/20 (30%) patients without PCa were indicated as p > 0.

Conclusions: SelectMDx urine test demonstrated high accuracy for discriminating between patients with HG PCa vs. patients with low-grade or benign disease at biopsy. Hence, SelectMDx may represent an important new method to better select men with HG PCa for prostate biopsy and thereby reducing over-detection of indolent disease.

Source of Funding: The study was supported in parts by the Bingham Research Fund and MDx Health
MULTIPARAMETRIC MRI AND THE 17-GENE PANEL IN THE SETTING OF INTERMEDIATE RISK PROSTATE CANCER

(Presentation to be made by Dr. Amir Salmasi)

Objectives: Active Surveillance (AS) may be an option for some patients with Intermediate-Risk Prostate Cancer (IRPCa). Multiparametric Magnetic Resonance Imaging (mpMRI) and tissue-based molecular assays may be helpful in selecting IRPCa patients suitable for AS. We explored synergies between GPS and mpMRI for prediction of adverse pathology (AP, pathological GS > 4+3 and/or pT3+) in men with IRPCa.

Methods: A cohort of men with IRPCa who were managed with radical prostatectomy (RP) was identified from a clinical database. Patients were required to have had a simultaneous mpMRI-guided and systematic biopsy and to have undergone RP within 6 months. Biopsy tissue of the highest Gleason pattern was used for calculation of a 17-gene Oncotype Dx® Genomic Prostate Score™ (GPS). Two analyses were conducted. The first analysis was prediction of AP in men with IRPCa. A second analysis was prediction of AP in the subset of men with favorable IRPCa (FIRPCa, defined as <50% of cores positive, biopsy Gleason score [bGS] ≤3+4, and only a single intermediate risk factor). Logistic regression models were fit to evaluate the relationship between AP and both GPS (per 20 units), high risk mpMRI (defined as UCLA MRI Score of 4 or 5), and clinical variables.

Results: 112 men with IRPCa (84% of total cohort) met criteria for the primary endpoint. Median age was 63 years (range 46 to 77). bGS 3+3, 3+4 and 4+3 was present in 4%, 80% and 16% of men, respectively. GPS was associated with AP (OR 5.1, 95% CI 2.5 to 11.5, p<0.001) in univariable analysis. After adjustment for highest bGS, clinical stage, and mpMRI, GPS remained significantly associated with AP (OR 4.0, 95% CI 1.9 to 9.4, p<0.001). High risk mpMRI trended towards significance for prediction of AP (OR 2.1, 95% CI 0.9 to 4.8, p=.08). GPS was also a significant predictor of AP in 67 patients with FIRPCa (OR 3.8, 95% CI 1.6 to 11.2, p = 0.002).

Conclusions: GPS provides independent prognostic information in the setting of mpMRI-guided biopsies. The combination of mpMRI for biopsy guidance and GPS for molecular analysis of biopsy tissue may optimize prediction of AP in men with IRPCa; this information may help improve shared decision making for patients with IRPCa.
USING PSA DENSITY, ULTRASOUND STAGING, MRI AND KALLIKREIN PANEL TO IMPROVE EARLY DETECTION OF HIGH GRADE PROSTATE CANCER

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(Presentation to be made by Dr. Adam Gadzinski)

Objectives: There are limitations in the accuracy of prostate specific antigen (PSA) testing for early detection of clinically significant prostate cancer. We aim to evaluate the value of multiparametric MRI (mpMRI) and Kallikrein panel (4K panel) alone and in combination in predicting clinically significant prostate cancer in men with PSA ≥ 3 ng/ml.

Materials and Methods: We retrospectively reviewed 188 participants referred for biopsy with a PSA ≥ 3 ng/ml. 69 underwent mpMRI-ultrasound fusion biopsy due to 4K panel ≥7% or had PI-RADS score 4/5 on mpMRI or presence of hypoechoic lesion on TRUS. The outcome was defined as Gleason Score ≥ 3+4 prostate cancer (PCa) on biopsy. We compared predictive capabilities of PSA alone (reference model) to a model where we added TRUS findings, mpMRI PI-RADS score, and 4k panel using logistic regression models and the area under Receiver Operating Characteristic (ROC) curve (AUC).

Results: The mean age was 67, median 4K score and PSAD were 16%, and 0.13 respectively. High grade PCa (Gleason score ≥ 7) was detected in 30 (44%), whereas 7 (10%) had 3+3 and 32 (46%) had negative biopsy. In the multivariate model adjusted for PSA, positive lesion on TRUS, and mpMRI PI-RADS 4/5, 4K panel ≥7% (OR: 7.66, 95% CI: 1.31-44.77), p=0.024) was the significant predictor for HG PCa. The AUC for the reference model was 0.494. Adding TRUS findings, 4K panel, and mpMRI PI-RADS to the reference model increased the discriminatory detection of HG cancer to AUC of 0.854 (95% CI: 0.764-0.944) (Figure).

Conclusion: In men with PSA ≥ 3 ng/ml, adding a 4K panel, mpMRI, and TRUS findings to the reference model, improved accuracy of detecting clinically significant cancer and may offer a more personalized approach to biopsy.

Figure
Introduction and Objective: The relationship between testosterone supplementation (TST) and prostate cancer (CaP) has been well established: TST is not linked to an increased risk of CaP. However, the concomitant use of TST in men with untreated CaP is less clearly delineated. We sought to examine differences in CaP treatment pattern for men undergoing TST, specifically focusing on active surveillance patients.

Methods: A retrospective review of men undergoing CaP screening at a single institution from 2008-2015 was performed. Patients were selected from a matched cohort with and without ongoing TST, all of whom had PSA testing and undergone prostate biopsy. Patients were excluded who had a history of CaP prior to initiation of TST. Subanalysis was performed on patients from an institutional active surveillance (AS) database. Statistical significance was determined by p-value < 0.05.

Results: 123 men underwent prostate cancer screening during study period (61 TST and 62 non-TST). PSA at the time of biopsy was lower for men on TST (4.97 vs 6.79, p=0.018). 78 men were diagnosed with CaP during the study period with equivalent rate of CaP detection: 0.59 (non-TST) vs 0.66 (TST). Comparing non-TST and TST groups, no significant difference in CaP profile or initial treatment management was observed (Table 1). Patients with subtherapeutic and supratherapeutic (T<300 or >1000 ng/dL) testosterone levels were more likely to have low-risk disease as compared to eugonadal men who were more likely to have intermediate risk disease (p = 0.063).

In the AS population (TST n = 28, non-TST n =19), patients on TST spent a shorter amount of time on AS (average 3.6 years vs 8.2 years). In addition, of those with disease progression based on Gleason grade, 100% of those on TST and none of the non-TST patients underwent definitive treatment.

Conclusions: Men undergoing TST had equivalent rates of positive prostate biopsy compared to men not receiving TST. While their pathologic characteristics were equivalent, patients on TST were more likely to undergo treatment during AS suggesting treatment bias due to ongoing concern of the effect of exogenous testosterone. Future studies are needed to further explore treatment patterns in AS patients undergoing TST.

Table 1. Prostate cancer diagnosis and treatment outcomes.
PROSTATE CANCER IN VETERANS WITH A PSA < 1.0 NG/ML

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(Presentation to be made by Omar Safar)

Introduction: The benefits of prostate cancer (PCa) early detection through Prostate Specific Antigen (PSA) based screening are unclear. One widely held belief suggests that a low PSA (<1.0 ng/ml) can be used to identify a group of men at an extremely low lifetime risk for clinically significant PCa. Herein we investigate a large veteran database to determine the distribution of clinically meaningful PCa in men below this threshold at any point prior to their PCa diagnosis.

Methods: Using an IRB approved protocol, the VA Informatics and Computing Infrastructure (VINCI) database was queried from January 1, 2000 to December 31, 2015. All men with a diagnosis of PCa with at least 1 PSA measurement prior to diagnosis and known treatment information were included. Exclusions were made for patients with no available Gleason score (~10%), no clinical staging, or no cause of death info (together an additional ~3-5%).

Results: Overall, 52,354 men with PCa were included in this analysis (PSA ≤ 1; 5270, PSA > 1: 47,084). There were no substantial differences between the 2 groups in terms of Gleason Score, stage, metastases at presentation, age at diagnosis, overall and cancer specific survival. Interestingly 62% of the PCas diagnosed in men with PSAs < 1 were of intermediate and high grade. Furthermore, by forgoing screening in these men, 3281 or 12% of intermediate and high grade cancers would be missed.

Conclusions: A substantial number of patients with clinically significant PCa have had a PSA ≤1.0 ng/ml at some point in their lives. Although appealing, using this PSA threshold to withhold PSA screening may be dangerous.

Source of Funding: None

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<th>Covariate</th>
<th>Min PSA ≤ 1</th>
<th>Min PSA &gt; 1</th>
<th>P value</th>
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<tr>
<td>Gleason Score (n, %)</td>
<td></td>
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<tr>
<td>≤ 6</td>
<td>1989 (38)</td>
<td>19681 (42)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>2080 (39)</td>
<td>19175 (41)</td>
<td></td>
</tr>
<tr>
<td>≥ 8</td>
<td>1201 (23)</td>
<td>8228 (17)</td>
<td></td>
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<tr>
<td>T stage (clinical) (n, %)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>1</td>
<td>3528 (67)</td>
<td>32441 (69)</td>
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<td>1630 (31)</td>
<td>13394 (28)</td>
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<td>3</td>
<td>87 (2)</td>
<td>998 (2)</td>
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</tr>
<tr>
<td>4</td>
<td>25 (0)</td>
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<td>T stage (pathologic) (n, %)</td>
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<td>2</td>
<td>815 (74)</td>
<td>7614 (76)</td>
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</tr>
<tr>
<td>4</td>
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<td>54 (1)</td>
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<td>Metastases at presentation (n, %)</td>
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<tr>
<td>Yes</td>
<td>53 (1.2)</td>
<td>774 (1.6)</td>
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<tr>
<td>Age at diagnosis (median, IQR)</td>
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<td>&lt;0.001</td>
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<tr>
<td>65 (61-70)</td>
<td>65 (61-71)</td>
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<tr>
<td>Median follow-up time (years)</td>
<td>4.75</td>
<td>6.28</td>
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Introduction: Since the 2011 U.S. Preventative Services Task Force (USPSTF) recommendation against prostate cancer (PCa) screening, there have been various modifications observed in the practice of urology.[1, 2] We hypothesized that low risk PCa is managed more conservatively secondary to the USPSTF recommendation and sought to evaluate the rates of non-definitive management (NDM) during this era.

Methods: We performed a retrospective cohort study of 105,295 patients in the National Cancer Database diagnosed with NCCN low risk PCa from 2010-2013. Our primary endpoint was to identify rates of NDM {active surveillance (AS) + watchful waiting (WW)} before and after the USPSTF recommendation against PSA screening in 2011. We performed multivariate logistic regression analysis to evaluate patient specific factors contributing to this form of management. These included age, race, clinical stage, facility volume, facility type, insurance, Charlson comorbidity index, PSA, year of diagnosis, geographic location, and neighborhood income.

Results: Of the 105,295 patients with low risk disease, 15,423 (15%) elected NDM versus 89,872 (85%) who elected active treatment. Of the 15,423 patients who elected NDM, 75% were on AS and 25% on WW. Median age of patients electing NDM versus treatment was 65 and 62 years old, respectively. As shown in Figure 1, the rate of NDM in years prior to the USPSTF recommendation was 10.1% and 12.9% in 2010 and 2011, respectively p<0.001. NDM increased in the years following the USPSTF recommendation of 2011 with the rate of NDM of 17.04% in 2012 (OR 1.92, p<0.001), and increasing to 21.6% in 2013 (OR 2.56, p<0.001). At the current rate of change of 3.85% per year, NDM utilization would reach 50% by the year 2021.

Conclusion: Since the USPSTF recommendation, NDM utilization has significantly increased in patients with low risk PCa. However, this data highlights the continued underutilization of surveillance in this patient population.

Source of Funding: None
DOES EXPOSURE TO AGENT ORANGE (AOE) AFFECT THE CHOICE OF ACTIVE SURVEILLANCE (AS) IN PROSTATE CANCER (PC)?

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(Presentation to be made by Hamed Ahmadi)

Objectives: AOE in Viet Nam Veterans is associated with the detection of aggressive prostate cancer in men undergoing a biopsy. Public awareness of this link creates anxiety about the risk of cancer development and progression and thus may reduce the acceptance of more conservative approaches such as AS for PC. We hypothesized that service-related AOE was associated with reduced rate of acceptance of AS in men with PC.

Methods: Using data from the Veteran Affairs PC Registry, patients with NCCN low- and intermediate-risk PC (PSA < 20 ng/mL, Stage <= T2, Gleason (GS) <= 7) diagnosed between 2003 and 2014 were identified. Using logistic regression, factors including age, clinical stage, GS, AOE, Charlson comorbidity index (CCI) and PSA at time of diagnosis were used to assess the risk of choosing AS versus PC-directed therapy.

Results: Of 1246 patients with low- or intermediate-risk PC, 628 (51%) patients chose AS (53% low-risk and 47% intermediate-risk). Mean age (yrs): 65.5 (IQR: 61.3-69.3), Mean CCI: 1 (IQR: 0-2), mean PSA (ng/mL): 7.2 (IQR: 5.0-8.9). In multivariate analysis, AOE was not associated with selection of PC-directed therapy as compared to AS (p=0.09). Factors that were associated with selection of AS included Age (p=0.003), Stage (p= 0.000) and GS (p=0.000).

Conclusions: AOE is not associated with a reduced rate of acceptance of AS for low- and intermediate-risk PC when adjusting for tumor and demographic factors. Potential biases about the effect of AOE on medical decision making in PC do not appear to reduce the rate of acceptance of AS in appropriate patients.

Source of Funding: Veterans Administration
UTILITY OF MP-MRI AND ONCOTYPE DX ASSAY IN SELECTING MEN FOR ACTIVE SURVEILLANCE OF PROSTATE CANCER

Aims: Management of low risk prostate cancer has shifted towards active surveillance. However, the known rate of underestimation and undersampling after a single prostate biopsy affects up to 25% of patients. Multiple tests have been developed to better stratify risk in patients on active surveillance; however these tests are costly, not always readily available, and their long term utility in predicting cancer progression and mortality remains unclear. We sought to describe our experiences with mp-MRI and the Oncotype Dx gene expression assay (GPS) in patient selection for AS. We specifically sought to study the ability of these tests to predict the pathologic outcome after repeat prostate biopsy and to directly correlate PIRADS lesions found on MRI with Oncotype Dx assay results.

Methods: Single institution retrospective review from 2007 to 2017 of all patients who were placed on the active surveillance protocol. Patients on the protocol who had received both prostate MRI (1.5T with endorectal coil) and Oncotype Dx were selected for analysis. The GPS as well as sub-exams within the genomic test were compared to PIRAD lesions found on MRI as well as Gleason score of the patients’ subsequent biopsy using Spearman correlation.

Results: Sixty one patients on active surveillance were identified who had both MRI and oncoype exams performed within the study period. Average PIRADS lesion was 3.8, median of 4. Average GPS value was 26 (range 8-54). When correlating pathology (Gleason 6 or 7/8) on follow up biopsy with the oncoype DX score, there was no statistically significant correlation in increased GPS score with increased Gleason score. Using Spearman correlation, increased GPS score was positively correlated with PIRADS lesions (P=0.34, p=0.02), while increased PIRADS was negatively correlated with each of the subtests within GPS scoring - likelihood of favorable pathology (P=-0.47, p=0.001), likelihood of low grade disease (P=-0.47, p=0.001), and likelihood of organ confined disease (P=-0.43, p=0.002).

Conclusions: There is a statistically significant correlation between concerning GPS scores and PIRADS lesions. In our data, we were unable to show a correlation between higher Gleason score and higher oncotype Dx assay values.

<table>
<thead>
<tr>
<th>Oncotype Score</th>
<th>Correlation With PI-RADS (Spearman Correlation)</th>
<th>P-Value</th>
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<tr>
<td>Dx GPS</td>
<td>0.34</td>
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<td>LFP</td>
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RATES OF NON-DEFINITIVE MANAGEMENT FOR LOW AND INTERMEDIATE RISK PROSTATE CANCER IN AFRICAN AMERICANS

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(Presentation to be made by Dr. John F. Burns)

Introduction: Disparities exist with respect to race in the management of localized prostate cancer (PCa). We hypothesized that African American (AA) men with low and intermediate risk PCa (LIPCa) were more likely to choose non-definitive management (NDM) as well as less invasive treatment options versus Caucasian (CA) men.

Methods: We performed a retrospective cohort study of 219,862 patients diagnosed with LIPCa in the National Cancer Database from 2010-2013. Our primary endpoint was rates of NDM {active surveillance (AS) + watchful waiting (WW)} by AA men versus CA men. Our secondary endpoint was to identify the differences in treatment modalities between these two races. We performed multivariate logistic regression analysis that controlled for age, race, clinical stage, facility volume, facility location, facility type, insurance, Charlson comorbidity index, PSA, year of diagnosis, and geographic location.

Results: Of the 219,862 patients with LIPCa, 105,295 patients had NCCN low risk PCa and 114,567 patients had NCCN intermediate risk PCa. 179,372 (82%) were CA men, 31,358 (14%) AA men, and 9,132 (4%) Other men. The median age for AA men, CA men, and Other men was 61, 64, and 63 respectively. 21,544 (9.8%) of patients elected NDM and utilization by AA men was similar to CA men (OR = 1.09) p < 0.001. As shown in Figure 1 and 2, Radical Prostatectomy (RP) was the most utilized treatment modality across all races but AA men were less likely than CA men to utilize this treatment (OR = 0.86), respectively, p < 0.001. In addition, AA men were more likely to choose radiotherapy (RT) versus CA men (OR = 1.22), p < 0.001.

Conclusion: AA men with LIPCa choose NDM at similar rates to CA men, however this rate is relatively low at 9.8%. Notably, AA were more likely to choose RT and less likely to choose RP compared to CA men.

Source of Funding: None
IMPACT OF THE GENOMIC PROSTATE SCORE AT DIAGNOSIS ON OUTCOMES DURING ACTIVE SURVEILLANCE
Selma Masic, Janet E. Cowan, June M. Chan, Matthew R. Cooperberg, Peter R. Carroll

Introduction: Genomic profiling with tissue-based assays may help to discriminate prostate cancer (PCa) aggressiveness and refine management strategies for men who are considering active surveillance (AS). We evaluated the impact of the genomic prostate score (GPS) at the diagnostic or confirmatory biopsy on outcomes during AS.

Methods: We retrospectively reviewed patients enrolled in our AS cohort between 2012 when GPS became available and 2017. Patients with Gleason 3+3 and 3+4 who had a GPS with their diagnostic or confirmatory biopsy were included, and time zero was assigned to the time of the GPS-associated biopsy. Life tables and Kaplan Meier curves were used to estimate upgrade-free survival (any upgrade defined as increase in Gleason grade ≥3+4, major upgrade as Gleason ≥ 4+3) and treatment-free survival. Multivariate Cox proportional hazards regression was used to determine risk factors for upgrade and treatment with GPS as the exposure. Models were adjusted for age, race, PSA (prostate specific antigen), PSA density (PSAD), total number of biopsies, and percentage of cores positive at diagnosis.

Results: A total of 138 men met inclusion criteria and had a GPS at the time of their diagnostic or confirmatory biopsy (67% 3+3 and 34% 3+4.) Mean age was 63 years, median PSA was 5.7 ng/ml (4.4-7.5), and clinical CAPRA risk score was low (0-2) for 74% and intermediate (3-5) for 26% of men. Median initial GPS was 23 (IQR 17-32) for the entire cohort, 22 (IQR 16-29) for men diagnosed with Gleason 3+3 and 29 (IQR 19-35) for those with Gleason 3+4. At 2 years, any upgrade-free survival was 82%, major upgrade-free survival 98%, and treatment-free survival 71%. GPS at diagnosis was not associated with any biopsy upgrade (HR 0.98 95% CI 0.9-1.0) in univariate or multivariate models. Unadjusted GPS was associated with risk of treatment (HR 1.02 95% CI 1.001-1.048) on AS but GPS was no longer significantly associated after adjustment for age, clinical factors, and total number of biopsy sessions. There were too few major upgrade events for analysis.

Conclusions: The initial GPS at diagnosis was not independently associated with risk of upgrade and the relationship between GPS and risk of treatment on AS was mediated by clinical factors in this moderate-sized cohort of men with limited follow up. The score alone should not guide treatment decisions, but may help to refine the complete clinical picture for men on AS.
IMPACT OF SUBSEQUENT PROSTATE BIOPSIES ON HEALTH RELATED QUALITY OF LIFE

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(Presentation to be made by Dr. John F. Burns)

Introduction: Active surveillance (AS) allows low-risk prostate cancer (PCa) patients to delay curative treatment and maintain their health related quality-of-life (HRQoL). We have shown previously that HRQoL was similar in patients on AS versus those with a history of previous negative prostate needle biopsy (PNB). The aim of this study was to identify the effect of subsequent PNB on HRQoL in patients on AS for low-risk PCa and in a comparable group of men without PCa.

Methods: Since 2007, the Center for Prostate Disease Research (CPDR) multi-center national database has enrolled patients undergoing PNB for suspicion of PCa into a prospective study of HRQoL. For this study, patients diagnosed with low-risk PCa and choosing AS, and patients without cancer and a history of negative PNB were included for analysis. All patients complete the Expanded PCa Index Composite (EPIC) and the RAND 36-Item Short Form Health Survey (SF-36) surveys at baseline and at regular follow-up intervals. Mean HRQoL was compared over time between patients who did and did not undergo subsequent PNB following baseline.

Results: Of the 509 patients with history of PNB included for analysis, 420 (82.5%) did not have a diagnosis of cancer and 89 (17.5%) had PCa on AS. Mean follow up was 34.7 (SD ± 16.9) and 31.6 (SD ± 14.6) months for patients with a history of PCa and those without cancer, respectively. 114 (27.1%) of patients without cancer had subsequent PNB, while 54 (60.7%) of PCa patients had subsequent PNB. We did not identify a significant impact on HRQoL in men undergoing secondary PNB over a five year period as shown in Figures 1 and 2.

Conclusion: Alternatives to secondary PNB include imaging modalities such as multiparametric MRI as well as other biomarkers to predict presence of cancer. However, secondary PNB is required in most AS protocols as well as in those with persistent suspicion of PCa. Our analysis shows that secondary PNB does not significantly impact HRQoL in this subset of men.

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DEFINING AND VALIDATING AUTOMATED PERFORMANCE METRICS FOR ROBOTIC SURGERY

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Introduction: Solid evidence suggests surgical performance directly influence clinical outcomes. With the “dVLogger” provided by Intuitive Surgical, surgeon performance on the da Vinci robot console and synchronized video can be captured and objectively evaluated for the first time. Herein, we present an initial construct validation (expert vs novice) of automated surgical performance metrics during select steps of the robotic radical prostatectomy (RRP).

Methods: Surgical performance metrics from da Vinci Si systems of training (<100 console cases) and expert (≥100 cases) surgeons conducting 4 RRP steps were studied: bladder mobilization (BM), seminal vesicles dissection (SVD), anterior vesicourethral anastomosis (AA) and right pelvic lymph nodes dissection (RLD). These metrics include kinematic data, such as, step completion time, instruments economy of motion, and instrument moving velocity. System events data, such as, frequency of camera control, master clutch usage, energy application were also captured. These metrics were compared between expert and training groups using statistical mixed effect models.

Results: We studied 70 cases of RRP. Nine experts (median 810 (100-2000) console cases experience) and 9 novices (median 35 (5-80) cases) participated. For all 4 steps, experts outperformed trainees in step completion time (12 vs 28 min, 10 vs 18 min, 8 vs 17 min, 14 vs 24 min respectfully, p<0.01), and total distance traveled by all instruments (27.7 vs 49.3 m, 17.3 vs 25.2 m, 13.7 vs 22.8 m, 28.1 vs 41.2 m respectfully, p<0.01). For all four steps, experts moved instrument controlled by their dominant hand faster than trainees (2.9 vs 2.3 cm/s, 2.2 vs 1.8 cm/s, 1.8 vs 1.4 cm/s, 2.9 vs 2.0 cm/s respectfully, p<0.01). During BM, SVD and RLD, experts adjusted camera position more frequently (10.2 vs 7.2 times/min, 5.4 vs 4.8 times/min, 7.2 vs 5.4 times/min respectfully, p<0.05) and used third arm more often (2.4 vs 1.8 times/min, 7.2 vs 6.6 times/min, 1 vs 0.2 times/min respectfully, p<0.05) than trainees. Experts applied energy more often during BM and SVD (10.8 vs 7.2 times/min, 7.2 vs 5.4 times/min, p<0.01).

Conclusion: Experts were more efficient and directed in their movement. Further correlation of metrics to clinical outcomes would further validate their clinical significance. This data can also help establish standardized metrics for surgeon assessment, credentialing, and workflow efficiency.

Figure. 3D tracing of instruments and camera movement during anterior vesicourethral anastomosis (AA).
HOW INFORMED IS OUR CONSENT? PATIENT AWARENESS OF RADIATION AND RADICAL PROSTATECTOMY COMPLICATIONS
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(Presentation to be made by Dr. Ziegelmann)

Introduction: Surgery and radiation (RT) are the two common treatments for prostate cancer (CAP), and each modality comes with inherent risks. Patients rely on appropriate counseling by their physicians in order to make an informed decision. However, many patients do not recall or state they were not informed that certain adverse effects were possible. Here, we sought to assess patient recall of pre–treatment CAP counseling.

Methods: A retrospective review of all patients presenting to our reconstructive urology clinic for management of CAP–treatment complications was conducted over a 2 year period. Patients treated with only surgery or only RT were included in the study. As part of a standard patient history, patients were asked a series of questions to assess their recall of pre−CAP treatment consent and their recollection of whether or not the complication they experienced was discussed prior to their treatment.

Results: From January 1, 2015 to December 31, 2016 we identified 604 male patients treated for complications following CAP treatment. Of those, 206 patients met the inclusion criteria. 153 patients (74%) had a history of prostatectomy alone while 53 patients (26%) had received RT alone. Median age at presentation was 72 years in the surgery group and 75 years in the RT group. In the surgery group, 119 (78%) recalled being counseled that the adverse effect they were experiencing was a risk of treatment compared with only 5 (9%) in the RT group (p<0.0001). Mean time since treatment was 8.8 years in those that recalled being counseled and 9.9 years in those who did not recall counseling (p=0.21). 117/153 patients (76%) who underwent surgery reported that their treating physician was aware of their current complication, compared with 16/53 (30%) patients who were treated with radiation (p < 0.0001). Moreover, the surgical group’s treating physicians were more likely to know they were being seen for management of their treatment related complication (46 vs 17%, p<0.0001).

Conclusions: Patient recall of potential complications with prostate cancer treatment is poor and may be related to selective memory loss or inadequate counseling from providers. Regardless, it is clear that many patients are unaware of the potential for serious treatment-related complications.
**SURGICAL FLOW DISRUPTIONS DURING ROBOTIC-ASSISTED RADICAL PROSTATECTOMY**

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**Introduction:** We sought to apply the principles of human factors research to robotic-assisted radical prostatectomy to understand where training and integration challenges lead to suboptimal and inefficient care.

**Materials and Methods:** Thirty-four robotic-assisted radical prostatectomy and bilateral pelvic lymph node dissections over a twenty-week period were observed for flow disruptions (FD) - deviations from optimal care that can compromise safety or efficiency. Other variables - physician experience, trainee involvement, robot model (S vs. Si), age, body mass index (BMI), and American Society of Anesthesiologists (ASA) physical status - were used to stratify the data and understand the effect of context. Effects were studied across four operative phases - entry to insufflations, robot docking, surgical intervention, and undocking. FDs were classified into one of nine categories.

**Results:** An average of 9.2 (SD=3.7) FD/hr were recorded, with the highest rates during robot docking (14.7 [SD=4.3] FDs/hr). The three most common flow disruptions were disruptions of communication, coordination, and equipment. Physicians with more robotic experience were faster during docking (p<0.003). Training cases had a greater FD rate (8.5 vs 10.6, p<0.001), as did the Si model robot (8.2 vs 9.8, p=0.002). Patient BMI and ASA classification yielded no difference in operative duration, but had phase-specific differences in FD.

**Conclusions:** Our data reflects the demands placed on the OR team by the patient, equipment, environment and context of a robotic surgical intervention, and suggests opportunities to enhance safety, quality, efficiency, and learning in robotic surgery.
INTRA-OPERATIVE OPTICAL IMAGING UTILIZING ANTI-PSMA (PROSTATE SPECIFIC MEMBRANE ANTIGEN) FLUORESCENT ANTIBODY DURING ROBOT ASSISTED RADICAL PROSTATECTOMY (RARP)

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(Presentation to be made by Dr. Chennamsetty)

Introduction: Identification of prostatic tissue from non-prostatic tissue can help preserve potency, continence, as well as decrease positive margins. PSMA, a transmembrane glycoprotein expressed by neoplastic prostate epithelium, is a possible target for identification of prostate tissue. MDX1201, an investigational new drug (IND) composed of fully human IgG with conjugated fluorescent marker (Alexa™488) with specificity against PSMA was safely administered in mice models. The antibody-fluorescent dye complex was shown to bind to cells expressing PSMA demonstrating significant staining of prostatic adenocarcinoma. We performed the first in-human FDA-approved phase I 3+3 dose finding study of intravenously (IV) administered MDX1201 in intermediate- to high-risk patients undergoing RARP and extended lymph node (LN) dissection.

Methods: Patients received a single intravenous infusion of MDX1201 four days prior to RARP to allow for safety evaluation. A 488 nanometer laser was attached to the da Vinci Si surgical robot camera at the time of RARP to allow for visualization of fluorescent dye marking presence of prostatic cancerous tissue. 5 mg dose was given to the first 3 patients, and then the dose was escalated to 15 mg provided safety considerations permit. Patients with prior prostate cancer treatment were excluded.

Results: MDX1201 was successfully administered to 5 patients, with no adverse events observed. Initial 5 mg dose failed to show visualization of fluorescent dye in first 3 patients. Of the 15 mg dose patients, patient #4 demonstrated fluorescence ex vivo within the sectioned prostate that correlated with pathological findings, while patient #5 demonstrated fluorescence in-vivo with mild prostatic fluorescence at the right apex, left apex, left mid, and also moderate fluorescence demonstrated at the right external iliac LNs. For patient #5, histopathologic examination confirmed tumor to the mid right lobe (dominant nodule), with a minor focus in anterior left lobe near the base. There was no LN metastasis in this patient (pT2cN0). In the five patients (median PSA 9.5, 80% intermediate-risk, 100% > pT2c), the median LN yield was 18 with no LN involvement in any patient. No positive margins were detected.

Conclusion: We demonstrate the first in human study using an anti PSMA antibody demonstrating fluorescence in the prostate. Identification of prostatic tissue using a conjugated fluorescent marker with specificity against PSMA may help guide preservation of critical structures.

Source of Funding: None
Introduction and Objectives: In a recent clinical validation study, the biopsy-based GPS assay (scaled 0-100) was shown to be a significant independent predictor of mets and PCD in surgically treated men with clinically very low (VL), low, intermediate and high risk PCa. We performed additional analyses to examine the clinical relevance of low (<20) and high (>40) GPS cut-point values.

Methods: A cohort sampling study from an eligible population of 6,284 PCa patients was performed within Kaiser Permanente Northern California Health Care System (Van Den Eeden, AUA 2017) where 279 patients were tested for GPS; Data were analyzed to establish the risk of mets and PCD associated with GPS cut-points of 20 and 40 when treated as dichotomized variables. Statistical analyses were based on Cox proportional hazards models and Kaplan-Meier estimations accounting for sampling weights.

Results: The final cohort consisted of 259 patients with valid GPS results and median follow-up 9.8 years. In this study the percentages of patients with GPS <20 within each NCCN subgroup were: VL/low, 38% (n=13), intermediate, 18% (n=18) and high 3% (n=3). No patients with VL, low and intermediate risk PCa and a GPS<20 developed mets or PCD at 10 years. On the other hand, in univariable analysis, a GPS value >40 was associated with a high risk of mets and PCD: HR/20 GPS units for mets 4.86 (95% CI 1.77-13.32; p=0.002), HR/20 units for PCD 4.13 (95% CI 2.12-8.05; p<0.001). Among 160 NCCN intermediate risk patients, 24% (n=52) had GPS > 40; these patients had a 5-year risk of mets similar to NCCN high risk patients.

Conclusions: GPS is a very strong predictor of risk of mets and PCD in men with clinically localized PCa who are treated by prostatectomy. Patients with NCCN very low, low and intermediate risk PCa and GPS <20 have a very low likelihood of harboring aggressive disease, and may be excellent candidates for active surveillance. Patients with NCCN intermediate risk disease and GPS >40 appear to have poor outcomes consistent with high risk patients and may need more aggressive therapy.

Source of Funding: Genomic Health, Inc.
ASSOCIATION BETWEEN RACIAL DISPARITIES AND ONCOLOGIC OUTCOME FOLLOWING RADICAL PROSTATECTOMY FOR CLINICALLY ORGAN CONFINED PROSTATE CANCER: A LONG TERM FOLLOW-UP STUDY FROM USC

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(Presentation to be made by Dr. Erfan Amini)

Objectives: Few studies have evaluated prostate cancer aggressiveness and oncologic outcomes in different ethnic groups following radical prostatectomy for clinically organ-confined disease. Existing studies lack long term post-treatment data. We conducted a long term follow up study to assess the impact of racial differences on risk profile and oncologic outcomes in a large, ethnically-diverse cohort of patients with prostate cancer who underwent radical prostatectomy with curative intent.

Methods: Using our institutional review board-approved prostate cancer database at University of Southern California, we retrospectively reviewed the records of all patients who underwent radical prostatectomy in our institution between 1987 and 2009. Patients with missing data of interest as well as those who underwent salvage radical prostatectomy after radiation therapy were excluded. The final cohort consisted of 3437 patients. Based on ethnicity, patients were divided into three groups comprising Asian American (n=133), African American (n=155) and Caucasians (n=3149). Baseline characteristics and oncologic outcomes including biochemical recurrence free survival (BCRFS), clinical recurrence free survival (CRFS) and overall survival (OS) were compared between the study groups.

Results: A total of 3437 patients with a mean age of 63±9.8 years and median follow-up period of 8.7 (range 0.1-24.1) years after radical prostatectomy were included in the analysis. Median diagnostic PSA value was higher in Asian American (7, IQR: 5.1-12) compared to Caucasian (6.1, IQR: 4.5-9.4) or African Americans (6.4, IQR: 4.7-12.1) (P=0.002). Pathologic stage and the frequency of poorly differentiated prostate cancer (Gleason score 8-10) was higher in Asian Americans; however, margin status did not differ significantly between different ethnic groups. Moreover, oncologic outcomes were comparable between study groups (table 1). In multivariate analysis, both pathologic stage and grade were independent predictors of BCRFS, CRFS and OS, but race was not.

Conclusions: In this large, ethnically diverse, long term follow up study, we noted that Asian Americans are more likely to have higher risk prostate cancer at diagnosis; however, race was not an independent predictor of oncologic outcome following radical prostatectomy with curative intent.

Table 1. Baseline patient characteristics and oncologic outcomes stratified by race
Objective: Prophylactic pelvic drain placement after prostatectomy has long been an empiric practice despite lack of high-level evidence of clinical benefit. However, with robot-assisted radical prostatectomy and improvements to surgical technique, routine pelvic drainage may not be necessary in the contemporary setting. We determined if eliminating the prophylactic placement of a pelvic drain after robot-assisted radical prostatectomy affects incidence of early (90-day) postoperative adverse events.

Methods: From 2012 to 2016, 189 male patients who underwent robot-assisted radical prostatectomy (RARP) were randomized prospectively to undergo no pelvic drain placement (n=92) or pelvic drain placement (n=97). Patients with prior radiotherapy, prior extensive pelvic surgery and demonstrable intra-operative leakage upon bladder irrigation at the end of the procedure were excluded. Demographic data, preoperative and postoperative results for the two groups were compared. The primary endpoint was overall (Clavien I-V) incidence of 90-day complications in a non-inferiority setting, with a 10% delta margin and an expected event rate of 13%.

Results: No pelvic drain and pelvic drain groups were comparable in median PSA (6.3 vs 5.8 respectively, p=0.5), clinical stage (p=0.8), D'Amico risk classification (p=0.4), median lymph nodes dissected (17 vs 18, p=0.2) and proportion of patients receiving an extended pelvic lymph node dissection (70.7% vs 79.4% respectively, p=0.3). Incidence of 90-day overall and major (Clavien > III) complications in the no pelvic drain group (17.4% and 5.4%, respectively) was not inferior to the pelvic drain group (26.8% and 5.2%, respectively; p=0.0008 and p=0.007 for difference of proportions <10%, respectively). Symptomatic lymphocele rates (2.2% in the no pelvic drain group, 4.1% in the pelvic drain group) were comparable between the two arms (p=0.7).

Conclusions: In this prospective randomized drain study, the incidence of early postoperative adverse events in the no pelvic drain group was not inferior to the group who received a pelvic drain. In properly selected patients, the use of a pelvic drain after robot-assisted radical prostatectomy can be safely withheld without significant additional morbidity.

Source of Funding: None
INTRAOPERATIVE FROZEN PATHOLOGY MARGIN ASSESSMENT DURING NERVE SPARING ROBOTIC RADICAL PROSTATECTOMY USING THE GELPOINT MINI FOR SPECIMEN EXTRACTION

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Objectives: Intraoperative frozen pathology margin assessment during nerve sparing radical prostatectomy has previously been shown to increase nerve sparing and decrease positive surgical margins. With the introduction of robotic prostatectomy, timely intraoperative specimen extraction became technically challenging. Using the GelPOINT Mini (Applied Medical, CA, USA) for intraoperative specimen extraction, we aim to evaluate pathological margins, nerve sparing, and operative time during robotic radical prostatectomy.

Materials and Methods: Patients undergoing robotic radical prostatectomy with clinically localized prostate cancer and preoperative transrectal ultrasound concerning for extracapsular extension were included. We place the GelPOINT Mini using the open Hasson technique. The 12mm camera port is inserted through the GelPOINT Mini (Figure). Nerve sparing radical prostatectomy is performed and the prostate specimen is immediately extracted through the GelPOINT Mini. Areas concerning for extracapsular extension based on pre-operative imaging are inked for frozen pathology. If frozen sections reveal positive margins, additional tissue is taken from the neurovascular bundle. We assessed final margin status, nerve sparing, and operative time.

Results: In 11 patients, the mean age was 63 ± 3 years. PSA 9.59 ± 1.95, Gleason sum 7.1 ± 0.2, prostate volume 30.2 ± 2.3 cc, and sexual health in men score 15.2 ± 3.0. The mean operative time was 235 minutes (compared to our historical average of 227 minutes, p = 0.52) Seven men had probable cT3a disease on ultrasound. Four intraoperative frozen sections had positive margins. Following further resection, all these sites had negative final margins. Five men with negative frozen margins underwent a complete nerve sparing procedure, all had negative final margins. No complications occurred using the GelPOINT Mini.

Conclusion: Intraoperative frozen pathology margin assessment during robotic radical prostatectomy using the GelPOINT Mini for specimen extraction maximizes nerve sparing while reducing positive margins in men at high risk for extracapsular extension with no change in operative time.
CARDIO-METABOLIC EFFECTS ASSOCIATED WITH ANDROGEN DEPRIVATION THERAPY: POTENTIAL MECHANISMS OF ACTION

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Presentation to be made by Dr. E. David Crawford

Introduction: Testosterone reduction in androgen deprivation therapy (ADT) can be achieved with either gonadotropin-releasing hormone/luteinizing hormone-releasing hormone receptor (GnRH/LHRH-R) antagonists (blockade) or receptor agonists (hyperstimulation-mediated downregulation), which reduce secretion of pituitary luteinizing hormone. Retrospective, recent, and ongoing studies indicate metabolic differences between GnRH/LHRH-R antagonists and agonists may be responsible for cardio-metabolic effects associated with ADT. These studies have demonstrated GnRH/LHRH-R agonists and antagonist may have discrete levels of risk due to differences in their mechanisms of action. While the magnitude of testosterone suppression is similar for both drugs, GnRH/LHRH-R antagonists differ from agonists in their ability to consistently suppress serum levels of follicle-stimulating hormone (FSH). The purpose of this review was to elucidate the role of FSH in altering adipose tissue biology, and inflammatory processes associated with cardio-metabolic morbidity.

Methods: To explore the relationships between FSH and undesirable effects of ADT, an in-depth review of pre-clinical and clinical literature in Medline and PubMed was conducted. Articles were selected by a colloquium of world experts on the treatment of prostate cancer and ADT.

Results: Stimulation of the FSH system upregulates genes that promote lipid accumulation in adipose tissue (i.e. lipoprotein lipase and fatty acid synthase), and the accumulation of these altered adipocytes occurs in an FSH concentration-dependent manner. Stimulation of the FSH system also correlates with increased BMI. Altered adipose tissue overexpresses the proinflammatory markers, tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which promote insulin resistance as well as atherosclerosis and plaque instability. Additionally, T cell activation by GnRH/LHRH-R agonists induces phenotypic changes to type 1 T helper (Th1) cells associated with proinflammatory states, which may precipitate adverse cardiac events. These findings and others corroborate the concept that inadequate FSH control during ADT underlies profound metabolic differences between GnRH/LHRH-R agonists and antagonists resulting in cardio-metabolic morbidity.

Conclusion: The model describing FSH effects may foretell its importance as a biomarker when treating patients at risk for adverse cardio-metabolic events with ADT; further insights into the mechanisms underlying these events are being investigated.

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