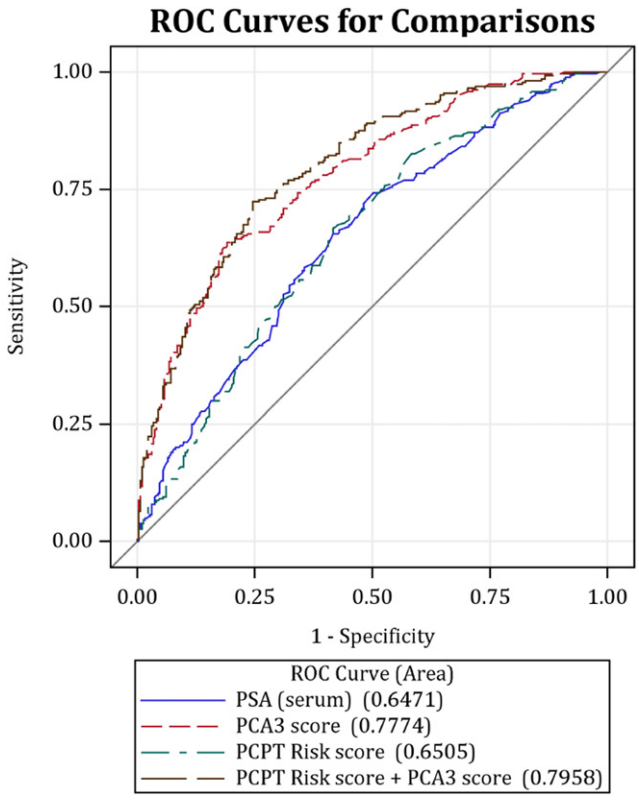

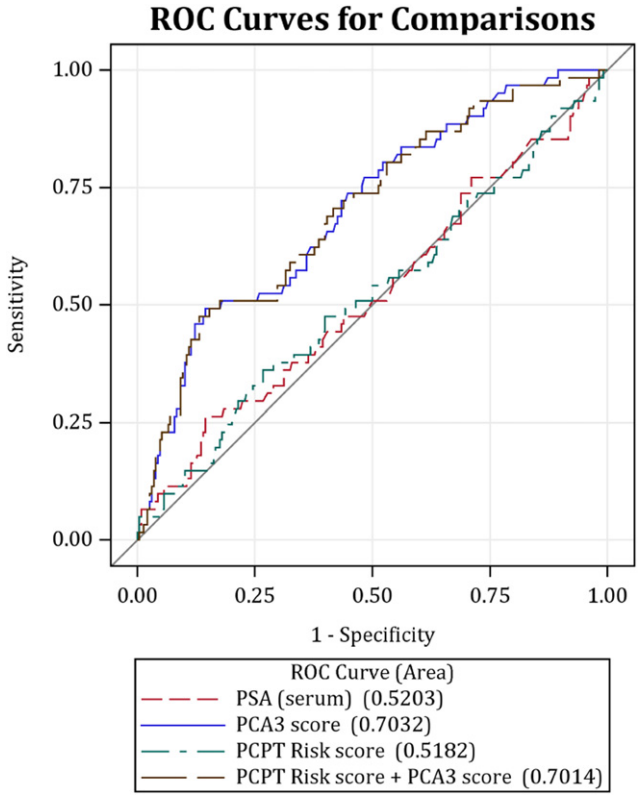

Source of Funding: None

2207

TOTAL SERUM TESTOSTERONE/PCA 3 RATIO: INCREASING THE PROSTATE BIOPSY YIELD

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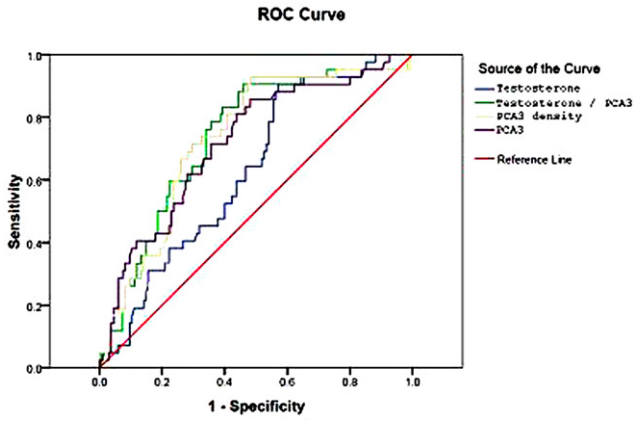
INTRODUCTION AND OBJECTIVES: Early detection of prostate cancer usually requires a prostate biopsy which is a generally safe and well tolerated but does have some associated morbidities. Both hypogonadism and elevated urinary Prostate Cancer Gene 3 (PCA3) levels have been associated with increased detection of prostate cancer. We sought to determine whether the ratio of total serum testosterone to PCA3 density might enhance the positive prostate biopsy yield of prostate cancer in a select population of men undergoing prostate biopsies for 'abnormal' serum prostate specific antigen (PSA) levels.

METHODS: The study population consisted of 177 men undergoing prostate biopsy between March 2008 to July 2011. Morning serum total Testosterone levels (T) were obtained on all men undergoing biopsy. PCA3 urinary levels were obtained after digital exam, immediately prior to twelve core ultrasound guided prostatic biopsy. PCA3 urinary level was divided by prostatic volume to obtain PCA3 density as PCA3 is representative of prostate cancer volume. Testosterone levels were converted from ng/dl to ng/ml by dividing by 100. This value was divided by PCA3 density to obtain the ratio of Testosterone to PCA 3 density.

RESULTS: Cancer was detected overall in 42 (24%) patients. Decreasing total serum Testosterone and increasing urinary PCA3 density were associated with an increased detection of prostate cancer. The Receiver Operating Characteristic (ROC) curve was analyzed for the ratio of Testosterone to PCA3 density. The area under the curve was 0.737 which was greater than that of serum Testosterone (0.631), PCA3 (0.719) and PCA3 density (0.734).

CONCLUSIONS: The ratio of testosterone to PCA3 density demonstrates an association with the results of prostate biopsy in our select group of men undergoing prostate biopsy.



Source of Funding: None

2208

CAN A GLEASON 6 OR LESS MICRO-FOCUS OF PROSTATE CANCER IN ONE BIOPSY AND PROSTATE SPECIFIC ANTIGEN LEVEL < 10 NG/ML BE DEFINED AS ARCHETYPE OF LOW-RISK PROSTATE DISEASE?

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INTRODUCTION AND OBJECTIVES: Prostate cancer (PC) remains the most common cancer in men and its prevalence in men aged > 50 years has been estimated to be as high as 40%. PC still represents the third leading cause of male cancer-related death, after lung and colorectal cancer but the majority of cases are non-lethal.

Although it is true that radical treatment significantly decrease the risk of death from PC, it is also true that 19 men need to be treated to benefit one man. This arises from the prostate-specific antigen (PSA) screening Era, although the helpfulness of PSA screening still remains debated.

Here we investigate whether a single micro-focus of PC at the biopsy (graded as Gleason ≤ 6 or less, $\leq 5\%$ occupancy in one biopsy core) and the Prostate Specific Antigen (PSA) < 10 ng/ml can define the archetype of low-risk prostate disease.

METHODS: 4500 consecutive patients who underwent extended prostate biopsies were enrolled in the present study. Among them, 134 (2.9%) patients who underwent nerve-sparing retropubic radical prostatectomy (RRP) for a single micro-focus of PC were followed-up and the parameters influencing the biochemical relapse (BR) analyzed.

RESULTS: Of the 134 patients, 94 (70.15%) patients had clinically significant disease, specifically in 74.26% of the patients with PSA < 10 ng/ml. Positive surgical margins and the extra-capsular invasion were found in 29.1% and 51.4% patients, respectively. BR was observed in 29.6% of the patients. Cox regression underlined a correlation between the BR and Gleason grade at the RRP ($HR=2.94$; $p<0.009$), capsular invasion ($HR=3.56$; $p<0.006$) and the presence of positive surgical margins ($HR=6$; $p<0.001$). Multivariate Cox regression showed a correlation between the presence of surgical margins at the RRP and BR ($p=0.006$).

CONCLUSIONS: Considering a single micro-focus of PC at the biopsy and PSA serum level <10 ng/ml as the archetype of low risk disease, clinically significant disease was found in 74.26% patients. Among the investigated parameters, only positive surgical margins are useful for predicting the BR.

Source of Funding: None

2209
ULTRA HIGH-RESOLUTION TRANSRECTAL ULTRASOUND: A NOVEL TECHNIQUE FOR ENHANCED PROSTATE CANCER IMAGING

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INTRODUCTION AND OBJECTIVES: Prostate cancer is the only solid malignancy for which no reliable imaging modality exists. Ultra high-resolution transrectal ultrasound (UHR-TRUS) provides enhanced image definition by utilizing a unique transducer with a center frequency of 21 MHz. We report the results of an initial utilizing UHR-TRUS for the detection of human prostate cancer.

METHODS: Men with prostate cancer and gland size <60cc by LR-TRUS who were scheduled for radical prostatectomy (RP) were prospectively recruited into a clinical trial comparing UHR-TRUS and standard low-resolution TRUS (LR-TRUS). Patients were preoperatively imaged transrectally using both modalities in an attempt to identify foci of altered echogenicity $>$ 5mm in maximum diameter in each sextant area of the prostate. Actual areas of prostate cancer $>$ 5mm in maximal diameter at sagittally-sectioned RP specimen were correlated to abnormal foci previously noted on sagittal LR- and UHR-TRUS cine-loops. Complications, adverse events, and pain scores using LR-TRUS or UHR-TRUS were recorded. Sensitivity and specificity analysis were performed for each imaging modality. UHR-TRUS equipment was provided by Imagistx Inc. and LR-TRUS was using a standard Aloka system.

RESULTS: 20 men were prospectively recruited into the trial. There were no complications or adverse events. Pain scores using LR- and UHR-probes were low and not significantly different. Among the 56 pathologically identified cancerous foci, LR-TRUS identified 23 and missed 33. HR-TRUS identified 36 and missed 20. Sensitivity was 41.1% for LR-TRUS and 64.3% for UHR-TRUS. Specificity was 59.4% for LR-TRUS and 71.9% for UHR-TRUS. Agreements between LR-TRUS vs. pathology and UHR-TRUS vs. pathology were compared using McNemar's test; UHR-TRUS was significantly superior to LR-TRUS ($p=0.01045$) for cancer detection.

CONCLUSIONS: UHR-TRUS appears to be a safe and promising imaging modality for prostate cancer detection. Our initial experience suggests superiority to LR-TRUS for the detection of cancerous foci. Based on these promising results, planning of a clinical trial of UHR-TRUS in the biopsy setting is underway.

Source of Funding: Imagistx Inc.

2210
DETECTION OF THE SECRETED PROSTATE CANCER BIOMARKER AGR2 IN VOIDED URINE

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INTRODUCTION AND OBJECTIVES: Prostate cancer is currently screened by an imperfect test of measuring the blood level of prostate-specific antigen (PSA/KLK3). This test has a false positive rate of nearly 75% with the result that many men would have to undergo an unnecessary biopsy. PSA is not a good cancer biomarker because it is not cancer-specific. Better markers are needed. Comparative transcriptomics between sorted $CD26^+$ cancer cells and $CD26^+$ luminal cells identified AGR2 (anterior gradient 2) as one of the highest up-regulated genes encoding secreted proteins in cancer. Overexpression in primary tumors was verified by tissue microarray analysis: AGR2 expression was absent in non-cancer ($n=111$) and BPH ($n=288$) *vs.* elevated in cancer ($n=659$) and PIN ($n=68$). AGR2 encodes a 19-kDa secreted protein that might be found in voided urine.

METHODS: Mouse monoclonal antibodies (mAbs) were generated against recombinant AGR2. One antibody pair, P1G4 (IgG1) to capture and P3A5 (IgG2a) to detect, showed good performance characteristics in a sandwich ELISA. This assay could measure AGR2 at sub ng/ml quantities.

RESULTS: AGR2 was detected in tissue digestion media of tumor specimens (and not that of non-cancer specimens) and culture media of AGR2-secreting prostate cancer cell lines. Specificity of the newly obtained mAbs was validated by immunoprecipitation, frozen tissue immunohistochemistry, and Western blot analysis. An AGR2 ELISA was developed with P1G4 and P3A5. Voided urine samples were collected from pre-operative cancer patients, and urinary protein was desalted and concentrated by spin filtration. The amount of AGR2 detected was scored as pg/100 μg urinary protein, and then converted to pg/ml urine. This ELISA was able to detect AGR2 in urine, ranging from 3.6 to 181 pg/ml, in an initial cohort of samples. Higher values appeared to correlate with tumor size. AGR2 was not detected in the urine of healthy control and a bladder cancer patient as bladder cancer cells do not overexpress AGR2.

CONCLUSIONS: For prostate cancer, an AGR2 urine test could be used for diagnosis and screening. The data showed that developing such a test for clinical application is viable because AGR2 is specific to cancer cells, and is secreted into urine. Since urine is a waste product, large volumes can be collected repeatedly and concentrated for testing.

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2211
BETTER PERFORMANCE OF PLASMA VOLUME THAN BODY MASS INDEX FOR HIGH-GRADE PROSTATE CANCER DETECTION AT EXTENDED BIOPSY IN JAPANESE MEN

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INTRODUCTION AND OBJECTIVES: A number of papers have reported that body mass index (BMI) is associated with prostate cancer (PCa) risk in biopsy. It has been speculated that the larger