Original Investigation

A Novel Urine Exosome Gene Expression Assay to Predict High-grade Prostate Cancer at Initial Biopsy

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Editorial page 867

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IMPORTANCE Overdiagnosis and overtreatment of indolent prostate cancer (PCA) is a serious health issue in most developed countries. There is an unmet clinical need for noninvasive, easy to administer, diagnostic assays to help assess whether a prostate biopsy is warranted.

OBJECTIVE To determine the performance of a novel urine exosome gene expression assay (the ExoDx Prostate IntelliScore urine exosome assay) plus standard of care (SOC) (ie, prostate-specific antigen [PSA] level, age, race, and family history) vs SOC alone for discriminating between Gleason score (GS)7 and GS6 and benign disease on initial biopsy.

DESIGN, SETTING, AND PARTICIPANTS In training, using reverse-transcriptase polymerase chain reaction (PCR), we compared the urine exosome gene expression assay with biopsy outcomes in 499 patients with prostate-specific antigen (PSA) levels of 2 to 20 ng/mL. The derived prognostic score was then validated in 1064 patients from 22 community practice and academic urology clinic sites in the United States. Eligible participants included PCA-free men, 50 years or older, scheduled for an initial or repeated prostate needle biopsy due to suspicious digital rectal examination (DRE) findings and/or PSA levels (limit range, 2.0-20.0 ng/mL).

MAIN OUTCOMES AND MEASURES Evaluate the assay using the area under receiver operating characteristic curve (AUC) in discrimination of GS7 or greater from GS6 and benign disease on initial biopsy.

RESULTS In 255 men in the training target population (median age 62 years and median PSA level 5.0 ng/mL, and initial biopsy), the urine exosome gene expression assay plus SOC was associated with improved discrimination between GS7 or greater and GS6 and benign disease: AUC 0.77 (95% CI, 0.71-0.83) vs SOC AUC 0.66 (95% CI, 0.58-0.72) ($P < .001$). Independent validation in 519 patients' urine exosome gene expression assay plus SOC AUC 0.73 (95% CI, 0.68-0.77) was superior to SOC AUC 0.63 (95% CI, 0.58-0.68) ($P < .001$). Using a predefined cut point, 138 of 519 (27%) biopsies would have been avoided, missing only 5% of patients with dominant pattern 4 high-risk GS7 disease.

CONCLUSIONS AND RELEVANCE This urine exosome gene expression assay is a noninvasive, urinary 3-gene expression assay that discriminates high-grade (≥GS7) from low-grade (GS6) cancer and benign disease. In this study, the urine exosome gene expression assay was associated with improved identification of patients with higher-grade prostate cancer among men with elevated PSA levels and could reduce the total number of unnecessary biopsies.

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Prostate cancer (PCA) is the most common solid malignant disease and second leading cause of cancer death in men worldwide, with over a million new cases and approximately 300 000 deaths in 2014.[1,2] The United States Preventive Services Task Force (USPSTF) guidance against prostate-specific antigen (PSA) screening and the conflicting outcomes of 2 randomized clinical trials of PSA screening have created uncertainty in the use of PSA in clinical care.[3-5] With a dramatic increase in PCA detection after the inception of PSA testing in the United States, treatment rates increased and a fall in PCA mortality ensued. Nonetheless, evidence strongly suggests that most cancers detected, especially low-grade (LG) tumors, will remain indolent for the patient's lifetime.[6-8]

The strongest evidence of mortality reduction in PCA is in intermediate- to high-risk, generally high-grade (HG) cancers (with Gleason scores [GS] of 7-10, hereafter ≥GS7) in which randomized clinical trials show benefits of therapy with radiotherapy or surgery.[9-11] The aggregate of these large studies suggests that optimal PCA early detection methods would preferentially identify patients with HG tumors for biopsy while avoiding biopsy in men without cancer or with LG tumors.

There are several blood- and urine-based assays that provide prognostic information regarding risk of high-grade prostate cancer at initial biopsy. These include the US Food and Drug Administration (FDA) approved prostate health index blood test (PHI) (Beckman Coulter, Inc), which combines total PSA, free PSA, and [-2] proPSA and the 4-kallikrein (4K) blood test, which incorporates kallikrein-related peptidase 2 (hK2), intact PSA, free PSA, and total PSA (4K, OPKO).[12,13] The 2 urine tests both require a digital rectal examination (DRE) prior to collection and include the FDA-approved PCA3 assay (Progensa; Hologic), which detects PSA 3 (PCA3) transcript levels and a urine test which combines total serum PSA, the PCA3 assay, and expression of the TMPRSS2:ERG fusion gene (Mi-Prostate Score [MiPS], University of Michigan).[14,15] Using the published receiver operating characteristic curve (AUC) to assess accuracy for predicting high-grade PCA GS ≥7, all of these assays have comparable AUCs ranging from 0.68 to 0.71 with improvement for the MiPS test (AUC, 0.77) when PSA and or the Prostate Cancer Prevention Tool (PCPT) are included in the algorithm.

We have developed an exosome-derived novel gene expression signature derived from normalized PCA3 and ERG (V-ets erythroblastosis virus E26 oncogene homologs) RNA from urine that is predictive of initial biopsy results. The assay is unique in that it does not require precollection DRE nor special handling, and can be easily collected as part of the basic clinical workflow.[16] Exosomes are small, double-lipid membrane vesicles that are secreted from cells. Exosomes encapsulate a portion of the parent cell cytoplasm and are shed into various biofluids, including blood and urine. They are a rich source of cellular protein and RNA, and are promising for profiling RNA expression from tumor cells because they are highly representative of their cell of origin[17] and provide protection for messenger RNA (mRNA) during sample processing.[18-23] Exosomes in post-DRE urine collected from patients with PCA contain both PCA3 and TMPRSS2: ERG mRNA.[18] Using advances in purification techniques, we have isolated urinary exosomal RNA without prostate examination, deriving a molecular signature predictive of PCA. We prospectively validated the stability of the urine exosome signature and predicted for HG PCA at prostate biopsy.

Key Points

Question Can an exosome gene signature from a first catch, nondigital rectal examination (DRE) urine specimen be useful for discriminating high-grade vs low-grade prostate cancer and benign prostatic diseases on an initial biopsy?

Findings A novel urine exosome assay plus standard of care (SOC) (prostate-specific antigen level, age, race, and family history) was statistically more predictive than SOC alone for predicting Gleason score of 7 (GS7) prostate cancer from GS 6 and benign disease.

Meaning Use of a novel urine exosome may reduce and/or delay unnecessary biopsies for most men presenting with an equivocal PSA level and an initial biopsy.

Methods

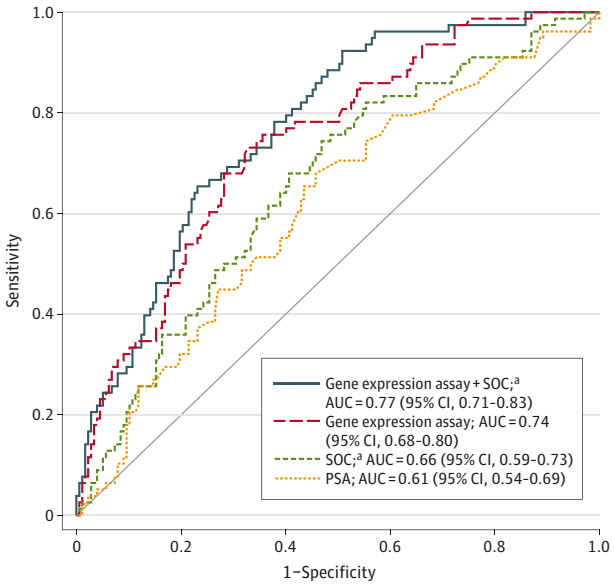
Study Design and Assessments

A prior observational study identified the predictive accuracy of a 3 gene exosome expression signature in discriminating ≥GS7 disease from GS6 and benign histologic findings at prostate biopsy.[16] We subsequently conducted a prospective study, enrolling patients undergoing prostate biopsy at 22 clinical sites in the United States between June 2014 and April 2015 (see eTable 1 in Supplement 1). Eligible participants included PCA-free men 50 years or older, who were scheduled for an initial or repeated prostate needle biopsy owing to a suspicious DRE and/or PSA levels (limit range, 2.0-20.0 ng/mL). Men with a history of invasive treatment for benign prostatic disease within 6 months or taking medications that have an effect on serum PSA levels within 3 to 6 months were excluded. Pathological examination of biopsies, blinded to the urine exosome gene expression assay (ExoDX Prostate IntelliScore, Exosome Diagnostics) result, was performed by urologic pathologists at each study site. The study protocol, provided in Supplement 2, was approved by local institutional review boards; all participants provided written informed consent and they were not compensated for participating.

ExoDx Prostate IntelliScore

First-catch urine samples (25-50 mL) were collected and stored without preservatives at 2°C to 8°C for up to 2 weeks until shipped on ice to a central laboratory (Exosome Diagnostic Laboratory). Samples were filtered through a 0.8-μm syringe filter and stored in 20-mL aliquots at −80°C until processing. Description of the methods used in exosome isolation, RNA extraction, and reverse transcriptase polymerase chain reaction (RT-qPCR) including specimen exclusion are provided in the eMethods, including primer and probe sequence and eTable 2 in Supplement 1.[16] Samples were normalized for RNA levels

Figure 1. Area Under Receiver Operating Characteristic Curve (AUC) for Performance of Gene Expression Assay Score Plus Standard of Care (SOC), Gene Expression Assay Score, or SOC in the Intended Use Training Cohort (N = 255)



The urine exosome gene expression assay in combination with SOC (AUC, 0.77) significantly outperforms SOC alone for predicting high-grade disease (AUC, 0.66, $P < .001$, DeLong test for paired AUC curves).

with SPDEF (SAM pointed domain-containing Ets transcription factor) to derive ERG or PCA3 RNA Ct (cycle threshold) value relative to SPDEF mRNA Ct values. The urine exosome gene expression is represented as a number (range, 1-100) derived from the combination of these 3 genes. The incorporation of a cut point transforms the urine exosome gene expression into a binary predictor of HG PCA.

Statistical Analysis

The primary objective was to validate the accuracy of the urine exosome gene expression assay for predicting HG PCA on initial biopsy for men with a PSA level of 2 to 10 ng/mL in a prospective, multisite trial. In addition to ruling out HG PCA to avoid a first prostate biopsy, we also evaluated model performance for men with a prior negative biopsy result.

We first completed an interim training cohort analysis of 499 patients, focusing on the subset of men presenting for their initial biopsy with a PSA level of 2.0 to 10.0 ng/mL. Standard of care (SOC) variables (PSA level, age, race, and family history of PCA) were modeled by logistic regression as predictors of the biopsy result for PCA and HG PCA (biopsy negative and GS6 vs ≥GS7) (see Supplement 1, Statistical Analysis). Receiver operating characteristics of logistic regression models (AUC-ROC) with and without the urine exosome gene expression as a predictor assessed clinical performance. A binary cut point with a negative predictive value (NPV) of greater than 95% was selected. The results of the DRE were not included in the SOC variables owing to inconsistent clinical site reporting.

The urine exosome gene expression assay and cut point was validated in an independent cohort (see statistical analysis in Supplement 1). The clinical value of the urine exosome gene expression assay was assessed with a decision curve analysis to evaluate the net health benefit of the urine exosome gene expression assay for predicting ≥GS7 disease.[24]

The primary models (with or without the urine exosome gene expression assay) along with inclusion of the Prostate Cancer Prevention Trial Risk Calculator, 2.0[25-27] were compared by fixing the sensitivities for each model at 90% and computing improvements in specificity, positive predictive value (PPV), and NPV. Further analyses included a combined prior and initial biopsy cohort and postrial adjusted cut point to maximize the number of avoided biopsies. A validation sample size of 500 patients was derived from a previous discrimination of AUC training results (ie, validation vs SOC) to achieve a statistical power of 80% and an α significance level of .05.

Results

Patient Characteristics

Urine samples were collected from 1563 participants enrolled between June 6, 2014, and April 30, 2015. The first 499 patients represent the training cohort of which 32 patients (6%) were excluded for Qbeta > Ct 32 and 78 patients (15%) with urine volume greater than 49 mL. Of the remaining 395 patients, 255 represented the intended use population: age 50 years or older, no prior biopsy, and PSA levels of 2 to 10 ng/mL. There were 80 patients excluded for prior negative biopsy results in this age and PSA range group. For each participant, exosomal RNA was extracted and RNA copy, Ct values of ERG (including TMPRSS2: ERG), PCA3, and SPDEF were determined. Median participant age was 62 years; median PSA level was 5.0 ng/mL (see eTable 3 in Supplement 1). Risk factors included suspicious DRE (23% of participants), family history of PCA (25%), and African American race, self-reported (19%). PCA was diagnosed in 47% of participants; 30% had ≥GS7.

A total of 1064 patients represented the validation cohort of which 9% (102) were excluded for internal control failure (Qbeta bacteriophage) and 17% (183 patients) for urine volume greater than 49 mL. Of the remaining 793 patients, 519 qualified for the intended use population (see eTable 3 in Supplement 1). A total of 149 patients were excluded for prior negative biopsy result in this age and PSA range group. The training and test groups were not statistically different, including a comparable positive biopsy prevalence (48% vs 47%) and ≥GS7 (31% vs 29%). The median number of prostate biopsy cores was 12. Notably, 455 (58%) of the combined train and test intended use patients expressed total ERG (>1 copy of ERG). It is noteworthy that none of the 22 sites reported the use of a magnetic resonance image (MRI) in the clinical diagnostic biopsy implementation plan.

ExoDx Prostate IntelliScore in the Training Cohort

Exosomal RNA Ct values of ERG, PCA3, and SPDEF were used to derive an urine exosome gene expression assay score for each

Table 1. Performance of Gene Expression Assay[a] in the Training Cohort

	Biopsy Result				
	High Grade	Negative and Low Grade	Total	Performance, % (SE)	(95% CI)
ExoDx Prostate IntelliScore > cut point	76	128	204	Sensitivity, 97.44 (1.79)	(93.93-100)
ExoDx Prostate IntelliScore ≤ cut point	2	49	51	Specificity, 27.68 (3.36)	(21.09-34.28)
Total	78	177	255	PPV, 37.25 (3.39)	(30.62-43.89)
				NPV, 96.08 (2.72)	(90.75-100)
High-grade biopsy prevalence %	30.59	Fraction predicted negative	20.00		

Abbreviations: NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

[a] ExoDx Prostate IntelliScore urine exosome assay (Exosome Diagnostics, Inc).

patient. The performance of the urine exosome gene expression assay signature to discriminate between a negative biopsy result and GS6 vs ≥GS7 prostate cancer was evaluated by AUC and compared with SOC. The urine exosome gene expression assay plus SOC and AUC was superior to SOC alone for predicting ≥GS7 disease ($P < .001$) (**Figure 1**). The AUC of the assay plus SOC was 0.77 (95% CI, 0.71-0.83) vs SOC 0.66 (95% CI, 0.58-0.73) while PSA alone had an AUC of 0.61 (95% CI, 0.54-0.69). By comparison, the ExoDx Prostate IntelliScore gene signature alone had an AUC of 0.74 (95% CI, 0.68-0.80).

For HG (≥GS7) disease, a binary urine exosome gene expression assay with a cut off of 15.6 demonstrated an NPV of 0.96 and PPV of 0.37 for prediction of HG (≥GS7) PCA (**Table 1**). Using a urine exosome gene expression assay score >15.6 to prompt a biopsy, 20% of prostate biopsies could have been avoided while missing only 2% of all ≥GS7 PCA, and missing no tumors with primary pattern GS4.

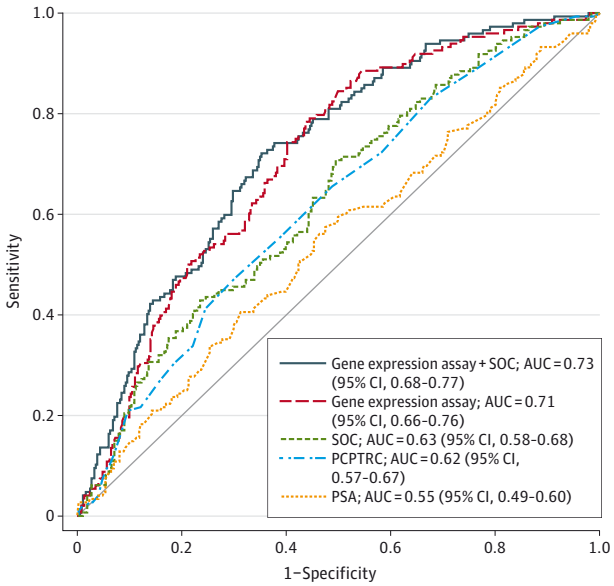
In an extended cohort that included both patients undergoing initial and repeat biopsies, PSA level range 2.0 to 10.0 ng/mL (n = 335), urine exosome gene expression assay plus SOC (AUC 0.78; 95% CI, 0.72-0.83) vs SOC alone (AUC 0.70; 95% CI, 0.63-0.76) also discriminated ≥GS7 cancer from GS6 and benign disease ($P < .001$).

Trial Validation Primary End Point

The urine exosome gene expression assay when combined with SOC (AUC 0.73; 95% CI, 0.68-0.77) was more predictive than SOC alone (AUC 0.63; 95% CI, 0.58-0.68) for discriminating ≥GS7 PCA from GS6 and negative biopsy results ($P < .001$) (**Figure 2**). The urine exosome gene expression assay without SOC had an AUC of 0.71 (95% CI, 0.66-0.75), while PSA level alone had an AUC of 0.55, suggesting that the performance of the test is driven by the gene signature. We also evaluated the Prostate Cancer Prevention Trial Risk Calculator 2.0 (PCPTRC), which yielded an AUC of 0.62 (95% CI, 0.57-0.67).

In addition to the population with an initial biopsy and a PSA level of 2 to 10 ng/mL, we also evaluated performance of the assay in men with a PSA level range of 10 to 20 ng/mL. Although the patient number is small (n = 55), the AUC was 0.72 (95% CI, 0.58-0.86) and when patients undergoing initial and repeated biopsies were combined (n = 93), the AUC was 0.75 (95% CI, 0.65-0.86), supporting comparable performance of the test in a population with elevated PSA levels.

Figure 2. Area Under Receiver Operating Characteristic Curve (AUC) for Performance of Gene Expression Assay Score Plus Standard of Care (SOC), Gene Expression Assay Score, or SOC in the Intended Use Validation Cohort (N = 519)



Additional comparison of Gene Expression Assay with the PCPTRC (Prostate Cancer Prevention Trial Risk Calculator) and PSA alone demonstrated improved performance of Gene Expression Assay.

Trial Validation Secondary End Points

With a cut off of greater than15.6, the urine exosome gene expression assay demonstrated good clinical performance in predicting ≥GS7 PCA, and avoiding 27% of biopsies (**Table 2**). With an NPV of 91% and a sensitivity of 92% the assay missed only 12 of 148 (8%) ≥GS7 cancers, of which 9 patients (75%) had less than one-third of cores involved, and 3 (5%) had dominant GS pattern 4. The clinical characteristics of these 12 patients are included in eTable 4 in Supplement 1.

Of note, in a combined initial and repeat biopsy group (n = 668) (see eTable 5A and eTable 5B in Supplement 1 for complete demographics and test performance), the 15.6 cutoff had a comparable performance (NPV, 0.91), supporting a potential role in men with prior negative biopsy result. Unfortunately the population with prior negative biopsy results alone

Table 2. Performance of Gene Expression Assay in the Validation Cohort

	Biopsy Result				
	Biopsy High Grade	Biopsy Negative and Low-Grade	Total	Performance, % (SE)	95% CI
ExoDx Prostate IntelliScore > cut point	136	245	381	Sensitivity, 91.89 (2.24)	(87.49-96.29)
ExoDx Prostate IntelliScore ≤ cut point	12	126	138	Specificity, 33.96 (2.46)	(29.14-38.78)
Total	148	371	519	PPV, 35.70 (2.45)	(30.88-40.51)
				NPV, 91.30 (2.40)	(86.60-96.01)
High-grade biopsy prevalence %	28.52	Fraction predicted negative	26.59		

Abbreviations: NLR, negative likelihood ratio; NPV, negative predictive value; PLR, positive likelihood ratio; PPV, positive predictive value.

was insufficient (n = 149) for evaluation. A 90% fixed sensitivity analysis on the initial biopsy results of primary intended use population maintained an NPV of 0.90 (see eTable 6 in Supplement 1).

We also assessed the clinical value of the urine exosome gene expression test using a decision curve analysis[24] by comparing urine exosome gene expression results with SOC across a range of probabilities for which a patient would opt for a biopsy. The net benefit is determined by summing the true-positives (benefits) and subtracting the false-negatives (harms) across different probability thresholds for biopsy (see eFigure in Supplement 1). In this analysis, the urine exosome gene expression assay vs SOC had the highest net benefit across the 10% to 40% decision threshold, demonstrating a significant clinical utility when compared with current clinical methods.

Impact of Adjusted Cut Point on Biopsy Rate

To further understand a range of performance surrounding the validated cut point, we reevaluated the urine exosome gene expression score in the 519-patient validation cohort and identified a cut point of 20 (vs 16), which accurately predicted ≥GS7 with an NPV of 90, sensitivity of 87% while avoiding 37% of biopsies (vs 27% of biopsies using the original cut point). The assay missed 19 of 148 (12%) patients with ≥GS7; 13 (68%) of which were 3 + 4, low-volume disease (<33% of cores were positive), 2 patients with 3 + 4 (>33% positive cores), and 4 with dominant pattern 4 (6%). **Figure 3** displays a waterfall plot illustrating both the trial validated and adjusted cut points.

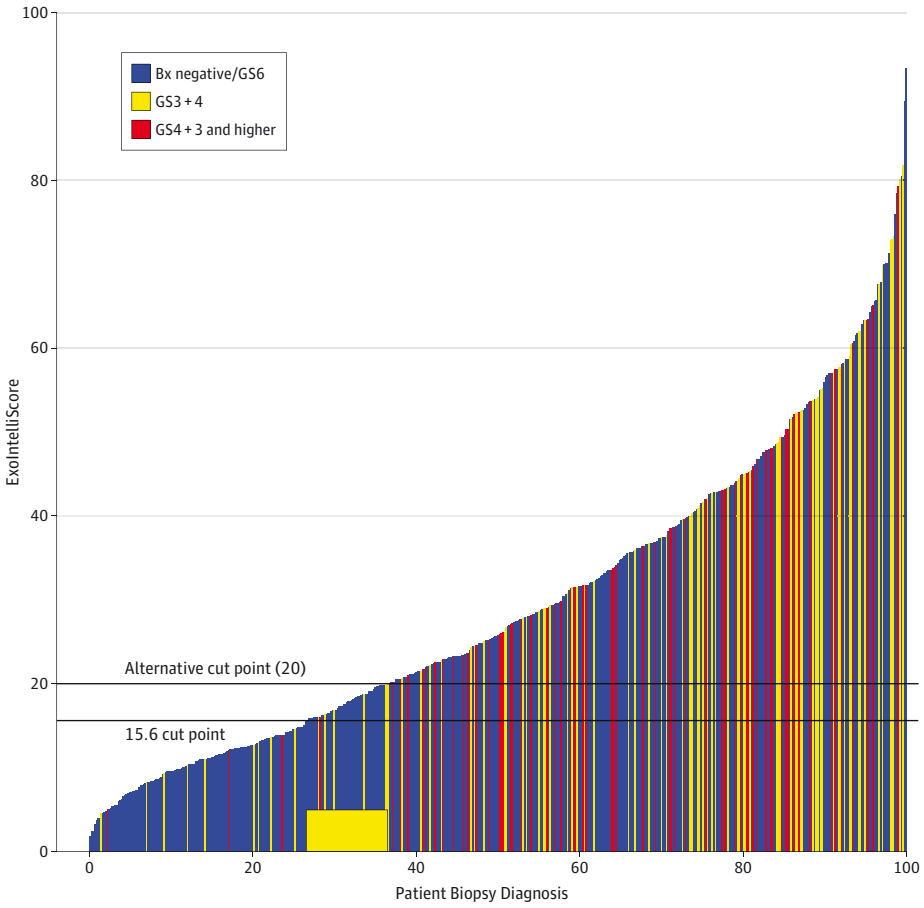
Discussion

Approximately 2 million transrectal ultrasonography-guided prostate biopsies (TRUS-Bx) are performed each year in the United States and Europe.[28] While suspicious DRE, in combination with other SOC factors, such as age, race, family history, and ethnicity, occasionally prompts TRUS-Bx, in most patients it is triggered by a PSA level of 4.0 ng/mL or higher.[29] The procedure is costly, painful, and has an increasing risk of infection and sepsis.[30-32] While clinical assessment tools, such as the PCPTRC, have value in assessing risk, improvements in patient selection for biopsy can dramatically reduce cost and complications.[33] In this study, both the PCPTRC and SOC had relatively poor performance (AUC 0.62 and AUC.63, respectively) for predicting HG PCA in patients undergoing initial biopsy. Additional biomarkers have the potential to improve the identification of patients with HG PCA, targeting these patients for TRUS-Bx.

While the European randomized clinical trial of PSA screening demonstrated a reduction in prostate cancer mortality, and since the inception of screening in the United States, prostate cancer mortality has fallen significantly. Most of the reason for the 2012 USPSTF recommendation against PSA testing was owing to the detection and treatment of LG PCA, a tumor that is often indolent. With the PSA screening pendulum swinging away from testing, there is a risk that successes in reducing prostate cancer mortality will be lost. A screening strategy that preferentially targets HG PCA and avoids detection of LG disease has the potential to maintain the mortality reduction while reducing harm from overdetection of indolent PCA.[33-36] Two recent studies have reported on a decline in the incidence of early-stage prostate cancer[37] and a reduced rate of PSA screening, specifically in men younger than 75 years, after the 2012 USPSTF recommendations,[38] respectively. An additional consideration is the impact of urologist variation in treatment selection based on grade, risk classification, and life expectancy.[39] A test that is able to reduce the "diagnosis" of low-grade and/or low-risk disease should have a positive effect on individual urologist practice pattern variability.

We found that a gene signature within exosomes analyzed from voided urine was predictive of HG (≥GS7) PCA with an NPV of 91%; PPV, 36%; sensitivity, 92%; and specificity, 34%. The urine exosome gene expression assay gene signature is derived from genes known to play a role in prostate cancer initiation and progression including ERG, PCA3, and SPDEF.[40-50] To compensate for tumor heterogeneity we evaluated total ERG levels, including the TMPRSS2: ERG fusion product, to construct the final score.[48-50] We studied men 50 years or older presenting for an initial biopsy with a PSA level of 2 to 10 ng/mL because they represent most men undergoing PSA testing and prostate biopsy. Several commercially available assays, including the Progensa PCA3 (Gen-Probe Inc), Prostate Health Index (PHI) (Beckman Coulter), and the 4K Score (OPKO Inc) have demonstrated varying efficacy to predict HG PCA but are potentially limited by cohort composition, inherent specificity issues of the kallikrein family (eg, PHI, 4K), specifically in the equivocal serum PSA range, or require DRE prior to collection and special specimen processing (Progensa). Furthermore, there has been limited evidence for current assays to support effective discrimination of GS7, 3 + 4 vs 4 + 3, on initial

Figure 3. Waterfall Plot of the Gene Expression Assay Score Across the Validation Cohort



Each colored bar represents an individual patient's gene expression assay score and true biopsy diagnosis, increasing left to right, (0-100 scale). Blue indicates biopsy benign or low grade (Gleason score 6); Yellow, biopsy Gleason score 3 + 4; Red, dominant Gleason score 4 or greater. Two black horizontal lines represent the trial validated 15.6 cut point and the posttrial alternative cut point of 20, with the horizontal yellow bar indicating the number of patients reclassified as negative with the new cut point; the number of avoided biopsies would increase from 27% to 37% with slight decrease in negative predictive value (NPV) (91% to 90%) and a small increase in false-negative rate (dominant pattern 4) from 5% to 6%.

biopsy.[51] Finally, additional factors, such as cost and ease of implementation, must also be considered.

In the 519 men undergoing initial biopsy, a urine exosome gene expression assay score greater than 15.6 would have avoided biopsy in 138 men while missing 12 men with ≥GS7 PCA; 75% of these men, however, had ≤ 1/3 of cores that were positive for GS3 + 4 PCA, a tumor that is often indolent.[52,53] The ability to discriminate GS7 into 3 + 4 vs 4 + 3 categories has important clinical implications for disease management and prognosis.[54] The view that all GS7 cancers are the same is no longer an accepted PCA phenotype. Furthermore, there is evolving understanding that disease in patients with low-volume GS3 + 4, specifically a GS4 component of less than 10%, behaves similarly to that of patients with GS3 + 3 cancer, and these patients may even be appropriate candidates for active surveillance.[55] Only 3 patients with GS4 + 3 or higher grade disease were missed with the current approach. By missing less than 5% of patients with dominant GS4 disease, the assay was able to provide an overall net benefit when compared with standard clinical tools. Although the adjusted cut point requires independent validation, the results suggest an overall comparable performance, with clinical utility and performance studies planned for future cohorts.

The current study has limitations, including the inability to include the DRE and free PSA as part of the standard of care variables. The limited accuracy of the DRE and the observed AUC's for blood-based assays that incorporate free-PSA suggests that the absence of these variables should not have a detrimental impact on overall performance of the exosome assay. Another limitation is that we did not use a central pathology review; however, our objective was to evaluate the assay in a broad academic and community practice setting where individual pathology networks are the acceptable standard. Future efforts will compare the exosome test with some of the currently available blood-based assays (when feasible), assess the impact of advanced imaging studies, which include MRI targeted biopsy assessment, and evaluate performance with respect to the pathologic abnormalities in the prostatectomy specimen. In addition, we will also explore the role of the ExoDx Prostate IntelliScore in men enrolled in active surveillance protocols.

Conclusions

The ExoDx Prostate IntelliScore is a validated, easy to administer, noninvasive urine exosome gene expression assay with the potential to reduce the total number of biopsies performed in men with a suspicion of prostate cancer.

ARTICLE INFORMATION

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Study concept and design: McKiernan, Donovan, O'Neill, Bentink, Noerholm, Belzer, Skog, Partin, Thompson.
Acquisition, analysis, or interpretation of data: McKiernan, Donovan, O'Neill, Bentink, Noerholm, Belzer, Skog, Kattan, Partin, Andriole, Brown, Wei, Carroll.
Drafting of the manuscript: McKiernan, Donovan, O'Neill, Bentink, Noerholm, Skog, Partin.
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