The Single Parameter, Structure-Based IsoPSA Assay Demonstrates Improved Diagnostic Accuracy for Detection of Any Prostate Cancer and High Grade Prostate Cancer Compared to a Concentration-Based Assay of Total PSA

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Background: IsoPSA™ is a serum based assay that predicts prostate cancer (PCa) risk by simultaneously partitioning of isoforms of prostate-specific antigen (PSA) with an aqueous two phase reagent. The assay reports results using a single composite index without a priori assumptions regarding the overall structural composition of PSA.

Methods: Multicenter prospective study of 261 men scheduled for prostate biopsy at five academic and community centers in the U.S enrolled between August 2015 and December 2016. Frozen plasma samples were blindly processed by the IsoPSA™ assay in Cleveland, Ohio. Discrimination power was evaluated using Receiver Operating Characteristics (ROC). Outcome of the IsoPSA assay was transformed into risk probability using logistic regression. Decision Curve Analysis (DCA) was used to compare the net benefit of IsoPSA against other clinical protocols.

Results: The overall prevalence of any PCa and high grade PCa was 53% and 34%, respectively. The area Under the Curve (AUC) was 0.79 for any cancer vs. none and 0.81 for high grade PCa vs. low grade cancer/benign histology. Superior net benefit of IsoPSA by DCA was demonstrated against no biopsy, all biopsy, and the modified Prostate Cancer Prevention Trial Risk Calculator 2.0. At a cutoff selected to recommend biopsy, IsoPSA demonstrated a 48% reduction in the false positive biopsy rate; at a cutoff selected to identity men at low risk for high grade disease, there was 45% reduction in the false positive rate.

Conclusions: Structure-based IsoPSA outperformed concentration-based PSA, and provided net benefit against other protocols. High performing single parameter assays are inherently statistically robust, operationally simpler, and easier to implement in clinical settings. Once validated, clinical use of IsoPSA could significantly reduce unnecessary biopsies while identifying patients needing treatment.

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