2022 Clinical Abstract

Title
Refinement and External Validation of a Novel Multiplex Urine Test for High-Grade Prostate Cancer

Introduction and Objective
The MyProstateScore (MPS) test employs the long non-coding RNA PCA3 and the TMPRSS2:ERG (T2:ERG) gene fusion to detect clinically-significant (Grade Group [GG]≥2) prostate cancer (PCa). To build upon MPS, we analyzed RNA-seq data from a PCa compendium, identifying 50 additional cancer- and high-grade cancer-specific markers. In total, 54 transcripts were measured by multiplex qPCR in 1504 urine biospecimens. The current study sought to develop and validate a novel urinary test for improved detection of GG≥2 PCa.

Methods
The 54-marker qPCR panel was assessed in a development cohort of men undergoing biopsy at the University of Michigan. The development cohort was divided into four subsets over ten iterations for *glmnet* modeling, identifying 17 markers independently contributing to discriminative accuracy. Acknowledging varying availability of patient-level clinical data (c) and prostate volume (v) in clinical practice, three novel MyProstateScore 2.0 models were developed: i) markers-only (MPS2), ii) markers and clinical data (MPS2c), and iii) markers, clinical data, and prostate volume (MPS2cv). The locked MPS2 models were provided to external analysts for validation in a blinded, multi-institutional NCI-EDRN biopsy cohort.

Results
Model development included 761 men with PSA 3-10 ng/ml, of whom 293 (39%) were found to have GG≥2 cancer on biopsy. The existing MPS test provided an area under the receiver operating characteristic curve (AUC) of 0.73, while the MPS2, MPS2c, and MPS2cv models yielded cross-validated AUC values of 0.78, 0.80, and 0.82, respectively. In the external validation cohort of 743 men with PSA 3-10 ng/ml, of which 151 (20%) were found to have GG≥2 cancer, the existing MPS test yielded an AUC of 0.73. The MPS2, MPS2c, and MPS2cv models yielded AUC values of 0.75, 0.81, and 0.82, respectively. At test thresholds providing 95% sensitivity, MPS provided 17% specificity, while the novel MPS2cv model provided 38% specificity.

Conclusions
Incorporating novel transcripts associated with high-grade cancer, we externally validated a 17-marker urinary panel for detection of GG≥2 PCa. Compared to the clinically-available MPS test, the MPS2cv model improved diagnostic accuracy (AUC) by nearly 10% and increased specificity by 21% at clinically-actionable, highly-sensitive thresholds. These findings suggest that the MPS2 test meaningfully improves detection of GG≥2 PCa relative to current diagnostic tests and could contribute to a more optimal contemporary diagnostic pathway.

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Tables/Graphs
None.

Name*	Institution*	Disclosures
Nathan L Samora	Vanderbilt University Medical Center	
Yuping Zhang	University of Michigan	Consultant – LynxDx.
Lanbo Xiao	University of Michigan	
Heng Zheng	University of Michigan	
Cassie Xie	Fred Hutchinson Cancer Research Center	
Bruce J Trock	Johns Hopkins University Brady Urological Institute	Consultant: Emmes Corporation Myriad Genetics, Inc. Research funding: MDxHealth, Inc.
Javed Siddiqui	University of Michigan	Advisor/Consultant – LynxDx.
Lakshmi P Kunju	University of Michigan	
Yashar S Niknafs	University of Michigan	Investment (Equity) Interest – LynxDx.
Zoey Chopra	University of Michigan	
Grace Herron	University of Michigan	
Neil Vaishampayan	University of Michigan	
Kumaran Arivoli	University of Michigan	
Simpa S Salami	University of Michigan	
Todd M Morgan	University of Michigan	
Ganesh S Palapattu	University of Michigan	
Yingye Zheng	Fred Hutchinson Cancer Research Center	
John T Wei	University of Michigan	
Arul M Chinnaiyan	University of Michigan	Owner, advisor – LynxDx.
Jeffrey J Tosoian	Vanderbilt University Medical Center	Owner, advisor – LynxDx.

- Board Member/ Officer/Trustee
- Consultant/Advisor
- Employee
- Investigator
- Investment Interest
- Meeting Participant/Lecturer
- Owner
- Scientific Study/Trial
  Other

Yashar's email address: yniknafs@med.umich.edu

Characters: 2217.