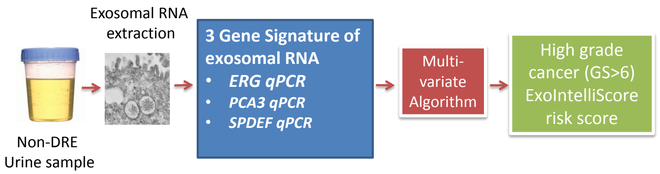
2016 ASCO GU
Abstract #:42

# Extended analysis of a validated urine-exosome signature to predict high grade prostate cancer on initial biopsy maintains performance across multiple sub-groups.

**Michael Donovan (1), Stefan Bentink (2), Mikkel Noerholm (2), Vince O'Neill (3), Johan Skog (3);**

*(1) Icahn School of Medicine at Mount Sinai, New York, NY; (2) Exosome Diagnostics GmbH, Martinsried, Germany, (3) Exosome Diagnostics, Cambridge, MA*

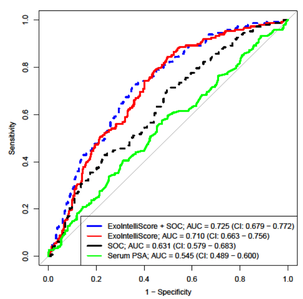
***Introduction*:** We recently completed a prospective observational clinical trial of a first-catch urine exosome gene expression signature ExoIntelliScore Prostate (formerly known as EXO106) to predict high-grade prostate cancer, HGPCA ( > / = GS7) on initial biopsy. The assay accurately predicted HGPCA with an NPV > 90% for an intended use population: men > / = 50 years with an equivocal PSA of 2-10 ng/mL presenting for their first biopsy. Given the current high prostate biopsy rate and potential impact of race we sought to further understand performance of the assay by constructing sub-cohorts from the validation study.




***Methods*:** Utilizing the ExoIntelliScore Prostate result and clinical data from the 519 patient intended use clinical validation cohort (IU) we constructed several sub-groups including: i. prior negative (A, n = 149), ii. combined prior negative + initial biopsy (B, n = 668) and African Americans, AA (C, n = 87). Area under the curve (AUC), NPV, PPV, sensitivity and specificity with validated cut-point assess performance.

***Results***: There was demographic comparability between the initial intended use (IU; Figure 1) and various subgroups, i.e. prior negative (A; Figure 2), combined prior negative and initial biopsy (B; Figure 3) and African Americans (C; Figure 4) with some exceptions observed (bold) for AA patients; family history (IU, 23%; A: 27%, B: 24%,C: **30%**; positive biopsy rate (IU,48%; A: 34%, B: 45%, **C:52%**; and > / = GS7 (IU, 28%; A: 13%, B: 27%; C: **34%**). The AUC range for ExoIntelliscore Prostate + standard of care (i.e. age, race, PSA and family history) between IU and A, B subgroups was 0.72-0.74; AUC for AA was 0.62, except for prior negative biopsy AA patients, AUC 0.80; supporting importance of prior negative biopsy. Of note, applying the ExoIntelliscore Prostate cut-point, A, B yielded an NPV of 91%; including NPV of 89% for AA (initial biopsy) and NPV of 91% for AA with initial + prior negative biopsy.

Figure 1. Intended Use (**IU**) Initial biopsy cohort, serum PSA 2-10 ng/mL; n=519
Discrimination for High Grade Cancer; SOC=Age, PSA, Fam History, Race)




**ExoIntelliScore + SOC:**
**AUC: 0.725**

**ExoIntelliscore:**
**AUC: 0.711**

**SOC:**
**AUC: 0.631**

**PSA:**
**AUC: 0.545**

**$AUC_{(EXO106+SOC)}$ > $AUC_{(SOC)}$ P < 0.00004**

Figure 2. Group **A**: Repeat Biopsy, serum PSA 2-10ng/mL; n=149

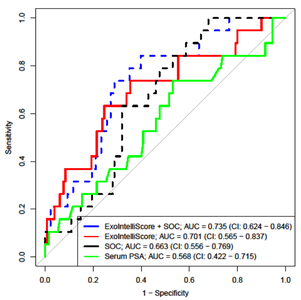



Figure 3. Group **B**: Initial + First Biopsy, serum PSA 2-10ng/mL; n=668

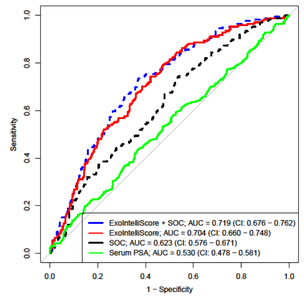



Figure 4. Group **C**: African American, initial biopsy, serum PSA 2-10ng/mL; n=87

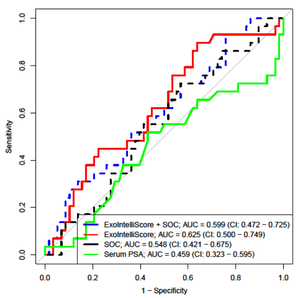



Table 1. Comparison of Intended use cohort with various sub-groups.

| Cohorts | N | HGP | TP | TN | FP | FN | NPV | PPV | SENS | SPEC |
|---|---|---|---|---|---|---|---|---|---|---|
| **IU** - Initial biopsy, (PSA 2-10) | 519 | 28.5 | 136 | 126 | 245 | 12 | **91.3** | 35.7 | 91.9 | 34.0 |
| **A** -Repeat Biopsy; (PSA 2-10) | 149 | 12.7 | 16 | 33 | 97 | 3 | **91.7** | 14.2 | 84.2 | 25.4 |
| **B** - First and Repeat Biopsy (PSA 2-10) | 668 | 25.0 | 152 | 155 | 346 | 15 | **91.2** | 30.5 | 91.0 | 31.0 |
| **C** - African-American; Initial Biopsy (PSA 2-10) | 87 | 33.3 | 27 | 16 | 42 | 2 | **88.9** | 39.1 | 93.1 | 27.6 |

HGP, high Gleason grade (>/-GS7) prevalence; TP, true positive; TN, true negative; FP, false positive, FN, false negative; NPV, negative predictive value; PPV, positive predictive value; SENS, sensitivity; SPEC, specificity.

***Conclusions:*** The ExoIntelliScore Prostate performed equally well in men with or without a prior negative biopsy with comparable results also seen for African Americans. Additional confirmatory studies with more patients are necessary to confirm initial observations

***References:***


- Miranda KC, Bond DT, McKee M, Skog J, Paunescu TG, Da Silva N et al. Nucleic acids within urinary exosomes/microvesicles are potential biomarkers for renal disease. Kidney Int. 2010;78:191-199.
- Donovan MJ, Noerholm M, Bentink S, Belzer S, Skog J et al: A molecular signature of PCA3 and ERG exosomal RNA from non-DRE urine is predictive of initial prostate biopsy result. Prostatic Diseases and Prostate Cancer. 2015, in press
- He J, Schepmoes AA, Shi T, Wu C, Fillmore TL, Gao Y et al. Analytical platform evaluation for quantification of ERG in prostate cancer using proteins and mRNA detection methods. J Transl Med. 2015;54:1-14.
- Klotz L. Active Surveillance for Low-Risk Prostate Cancer. Curr Urol Rep 2015; 16: 1-10.
- Nilsson J, Skog J, Norstrand A, Baranov B, Mincheva-Nilsson L, Breakefield XO, Widmark A; Prostate Cancer-Derived Urine Exosomes; A Novel Approach to biomarkers for Prostate Cancer; British Journal of Cancer (2009) 100, 1603-1607


**Contact: michael@exosomedx.com**