Performance of a clinically validated urine exosome gene expression test to predict high grade prostate cancer in men with a prior negative biopsy

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Introduction:
The over-diagnosis of low grade, indolent prostate cancer (PCa) initiates significant patient anxiety regarding treatment options and health risk. To address this clinical need, we developed and subsequently validated a noninvasive, easy to administer, supportive diagnostic test (ExoDx™ Prostate (IntelliScore), EPI) to guide the initial prostate biopsy decision process for men with PSA 2-10 ng/ml. (1) The EPI test is a urine exosome gene expression assay to discriminate high-grade prostate cancer (HGPCA, ≥ GS 7 PCA / ISUP 2) from low-grade PCa (GS 6 / ISUP 1) and benign disease, thereby potentially reducing the number of unnecessary biopsies (Figure 1). As many men have had prior negative biopsies, we sought to understand the performance of EPI in this selected population.

Results:

Notably, EPI in the initial biopsy setting had a sensitivity of 92 vs. 87% and an NPV of 91 vs 90%, for the ≥ GS7 PCa (ISUP 2). EPI achieved an AUC of 0.68 vs. AUC 0.59 for the PCPT (i.e. GS6 (ISUP 1) and 12% median PSA 6.1 ng/mL, 22% positive family history, 15% African American; 32% positive biopsy rate: 20% characteristic curve (AUC).

Methods:

Utilizing men with prior negative biopsies from two clinical trials we evaluated performance of the EPI test with respect to subsequent biopsy outcomes. We used the previously validated and alternative EPI cutpoints. Performances of EPI are compared against the Prostate Cancer Prevention Trial (PCPT) Risk Calculator (PCPTRC) version 2 [2] and PSA by area under the ROC curve (AUC).

Table 1:  Histological Definition of the ISUP System

<table>
<thead>
<tr>
<th>ISUP</th>
<th>Benign</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gleason</td>
<td>6(3+3)</td>
<td>3+4</td>
<td>4+3</td>
<td>5+3</td>
<td>7+3</td>
<td>7+4</td>
</tr>
</tbody>
</table>

Conclusions:

The EPI test is a noninvasive, first-catch, non-DRE gene expression array that accurately discriminates low-grade and benign biopsy outcomes from high-grade prostate cancer. The test performs well in both the initial and prior negative biopsy patients and has the potential to reduce the overall number of unnecessary biopsies in both settings.

References:
