

## **A Multi-Institutional Study finds that combining the 4Kscore and mpMRI reduces prostate biopsy more than either test alone.**

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**Introduction and objective:** mpMRI and new biomarkers have emerged as popular alternatives prior to prostate biopsy (Bx). We sought to investigate a combination of 4Kscore and mpMRI to improve diagnostic performance, and potentially further reduce Bx rates compared to the individual tests alone.

**Methods:** This was a retrospective, five-center study of men who underwent a 4Kscore, mpMRI, and Bx. Results from mpMRI were reported using PIRADS and categorized into low (PIRADS 1-2), intermediate (PIRADS 3) and high (PIRADS 4-5). The 4Kscore is reported as a continuous probability of high-grade GG2 or higher cancer (HG), here categorized into low ( $\leq 7\%$ ), intermediate (8%-32%), and high ( $\geq 33\%$ ) risk. The primary endpoint was to evaluate potential Bx reduction, sensitivity, negative predictive value (NPV), and undetected HG cancers when using Single Test or Combination Test strategies for Bx decision-making. We evaluated using either test alone, versus both tests in sequence. With Single Test, patients were stratified with low risk results avoiding a Bx and intermediate or high risk getting a Bx. With Combination Test, high-risk patients by the first test would receive a Bx and low risk would not. For intermediate risk patients, the second test would be used for determining if a Bx would occur (Fig. 1).

**Results:** The final cohort included 407 men, of which 114 were found to have a HG cancer. Using a 4Kscore or MRI alone, resulted in a 25-27% biopsy reduction, with 8-12 men having an undetected HG. Combination strategies yielded higher specificities, leading to larger biopsy reductions in the range of 38-41%, while 11-15 men had an undetected HG. Sensitivity and NPV did not appreciably differ between strategies (Table 1). Similar results were found in the category of men with a PSA of 2-10 and 3-10 ng/mL.

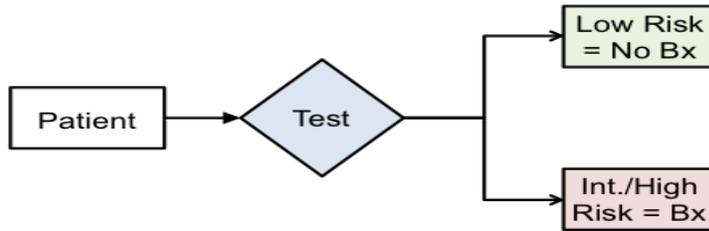
**Conclusions:** Combining 4Kscore and mpMRI to make prostate Bx decisions could further reduce Bx rates, while improving specificity for high-grade cancer, with minimal changes to NPV and sensitivity.

Table 1. Comparison of the Single and Combination Test strategies.

Test	Bx Reduction (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Undetected GG2+ Ca (vs biopsy all)
4Kscore (Single Test)	24.8	93.0	31.7	34.6	92.1	8
mpMRI (Single Test)	27.0	89.5	33.4	34.3	89.1	12
4Kscore = Test 1 mpMRI = Test 2 (Combination Test)	41.0	88.6	52.6	42.1	92.2	13
mpMRI = Test 1 4Kscore = Test 2 (Combination Test)	37.6	86.8	47.1	39.0	90.2	15

Figure 1. Single and Combination Test Strategies

Single Test Strategy



Combination Test Strategy

