Evaluation of AI-based and Genomic Prognostic Markers for the Prediction of Grade Progression in the Prostate Cancer Active Surveillance Setting

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Background
Active surveillance (AS) is a preferred strategy for men with very-low, low, or favorable-intermediate risk prostate cancer, but accurately predicting which patients will experience grade progression remains a critical challenge. Gleason grading is limited by sampling error and interobserver variability. Genomic assays and MRI provide additional insights, yet robust biopsy-based predictors are lacking. We evaluated PATHOMIQ_PRAD, a slide-based AI histology score, and compared it to the Decipher genomic classifier for prognostic prediction in the Miami Active Surveillance Trial (MAST).

Methods
MAST prospectively enrolled 205 men with very-low to favorable-intermediate risk prostate cancer. All diagnostic and confirmatory biopsies were digitized. Of these, 147 patients had PATHOMIQ_PRAD scores, and 106 had both PATHOMIQ_PRAD and Decipher genomic classifier results. The primary endpoint was Gleason grade progression (GG1→≥2 or GG2→≥3), with treatment for volume progression modeled as a competing risk. Associations were assessed using Fine–Gray regression. Cutoff analyses (0.55 for PATHOMIQ_PRAD, 0.60 for Decipher) and multivariable models including age, PSA density, and PI-RADS were performed.

Results
Median age was 62 years (IQR 56–68), median PSA was 5.0 ng/mL (IQR 3.7–7.0). PATHOMIQ_PRAD was independently associated with grade progression (sHR per SD: 1.74, 95% CI: 1.28–2.37, p<0.001). High-risk patients by PATHOMIQ_PRAD cutoff had a nearly three-fold greater hazard of upgrade (sHR: 2.74, 95% CI: 1.61–4.95, p<0.001). In multivariate models including Decipher, PATHOMIQ_PRAD remained an independent predictor (sHR: 1.91, 95% CI: 1.03–3.65, p=0.049). PATHOMIQ_PRAD achieved 72.7%

accuracy in identifying patients harboring occult higher-grade disease when restricted to GG1+2 biopsies.

Conclusions

PATHOMIQ_PRAD, a biopsy-based AI histology score, provides clinically meaningful, independent prognostic information in the AS setting and complements MRI and genomic testing. Incorporation of PATHOMIQ_PRAD may refine biopsy scheduling, guide earlier intervention for higher-risk men, and improve precision in AS management. Multicenter prospective validation is ongoing.

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Conflicts of Interest Disclosure Statement

Some authors are affiliated with PATHOMIQ Inc. and have financial interests in the development of AI-based pathology tools. All other authors declare no conflicts of interest.