Evaluating direct correlations between genomic classifier and digital pathology based mutli-modal AI biomarkers in castration-sensitive prostate cancer: localized and oligometastatic disease spaces

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Background

Prostate cancer is the most common malignancy in men and a leading cause of cancer death in the United States. The Decipher Genomic Classifier (GC) and the Artera multimodal artificial intelligence (MMAI) platform are robustly validated prognostic biomarkers with level I evidence for risk stratification. Whether these assays are interchangeable or complementary remains unclear.

Methods

We analyzed two cohorts of men who underwent both GC and MMAI testing. Cohort 1 included a prospective registry of116 patients with localized prostate cancer treated at a single institution (May 2024–May 2025). Cohort 2 comprised an international multi-institutional retrospective evaluation of 122 patients with oligometastatic castration-sensitive prostate cancer with ≤ 5 metastases. GC scores (low <0.45; intermediate 0.45–<0.6; high >0.6) were derived from microarray or RNA-sequencing. MMAI scores (low <0.27; intermediate 0.27–<0.50; high ≥0.5) were calculated from a machine learning model integrating digitized histopathology with clinical variables; a short-term ADT (stADT) biomarker was also reported. Correlation was assessed with Pearson's coefficient and concordance with Fisher's exact test.

Results

A total of 238 patients were included (116 localized, 122 metastatic). Median age was 68.3 years (localized) and 62.9 years (metastatic). Median PSA at initial diagnosis was 7.5 ng/mL and 9.9 ng/mL, respectively. In localized disease, >90% were Gleason grade group 2–3; the metastatic cohort included 42% grade group ≥4 and 51% T3 disease. Median GC scores were 0.52 (localized) and 0.61 (metastatic); 40% and 53% were GC high-risk, respectively. Median MMAI scores were 0.20 and 0.52, classifying 1.7% of localized and 68% of metastatic cases as high-risk. Correlation between GC and MMAI was moderate (localized r=0.43, R^2=0.19; metastatic r=0.41, R^2=0.17). Risk group concordance was 39.7% in localized (54.3% favorable intermediate vs 31.2% unfavorable intermediate) and 49% in metastatic disease (61% synchronous vs 47% metachronous). Fisher's test showed significant association in localized (p=0.0011) but not metastatic disease (p=0.064).

Conclusion

GC and MMAI demonstrated moderate correlation but low categorical concordance across localized and metastatic prostate cancer. These assays appear to provide complementary rather than interchangeable insights, which has implications for clinical decision-making and biomarker-driven trial design. Future work should evaluate the prognostic performance of combined stratification particularly for patients with discordant results.

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Conflicts of Interest

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