Refining Risk Stratification in Grade Group 2 Prostate Cancer: The Role of Multiparametric MRI in Detecting Cribriform and Intraductal Carcinoma

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Background. Cribriform morphology and intraductal carcinoma (IDC) of the prostate are adverse histologic features associated with early metastasis and poor outcomes. Noninvasive detection of these patterns (together called unfavorable histology prostate cancer, uhPC) could improve risk stratification and guide surveillance eligibility, especially in patients diagnosed with grade group (GG) 2 prostate cancer (PC) on biopsy. This group represents an intermediate-risk category where clinical management decisions—such as active surveillance versus definitive treatment—are often uncertain, making improved risk stratification particularly valuable. At the patient level, we evaluated the ability of both qualitative MRI — specifically the Prostate Imaging Reporting and Data System (PI-RADS) — and quantitative MRI, using the Restriction Spectrum Imaging restriction score (RSIrs), to detect uhPC diagnosed on biopsy.

Methods. Participants received multiparametric MRI for suspected or known PC at University of California San Diego, University of California San Francisco, Massachusetts General Hospital, University of Rochester Medical Center, University of Texas San Antonio or University of Cambridge between January of 2016 and June of 2025. Participants were included if they were biopsy naïve prior to MRI and had a biopsy within 6 months after MRI. Participants were excluded if they had hip implants or received PC treatment before MRI. We evaluated discrimination performance for uhPC and favorable histology PC (fhPC) vs GG1, or benign biopsy using the receiver operating characteristic (ROC) curve. Performance was assessed by computing the area under the ROC curve (AUC) with 95% confidence intervals from 10,000 bootstrap samples.

Results. 1009 patients met the inclusion criteria: 310 benign, 192 GG1, 257 GG2, and 250 ≥GG3. Of the patients that were diagnosed with GG2 disease, 26 had uhPC (cribriform/IDC) on biopsy and 231 had fhPC (no cribriform/IDC). At the patient-level, the AUCs for GG2 uhPC vs. no uhPC were 0.80 [0.72-0.86] for RSIrs and 0.78 [0.67-0.86] for PI-RADS, respectively (n=528). For discrimination of GG2 fhPC vs GG1/benign (n=733), the AUCs were 0.67 [0.63-0.72] for RSIrs and 0.71 [0.67-0.75] for PI-RADS.

Conclusions. mpMRI can discriminate patients with uhPC from benign and GG1 patients. Early detection of unfavorable histology is clinically relevant, as these patterns are associated with an increased risk of early metastasis and worse outcomes. This distinction supports more tailored management strategies—where patients with favorable GG2 disease may be considered for active surveillance, while those with unfavorable features could benefit from earlier intervention. Noninvasive identification of histologically adverse GG2 tumors has the potential to enhance risk stratification and guide more personalized treatment decisions.

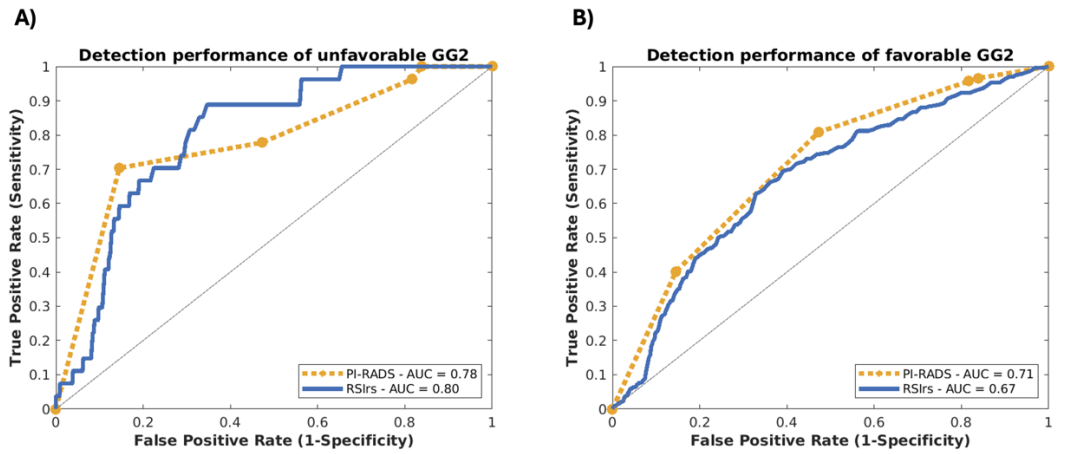

Figure 1. ROC curves for patient-level detection of grade group 2 prostate cancer with and without unfavorable histology using the quantitative biomarker RSIrs and PI-RADS. Patients were included if they were biopsy-naïve at time of MRI and had a biopsy-confirmed diagnosis after MRI. Yellow circles correspond to PI-RADS thresholds. A) ROC curves for discrimination of unfavorable (with cribriform or intraductal carcinoma) GG2 PCa vs no csPCa (n=528). B) ROC curves for discrimination of favorable (without cribriform or intraductal carcinoma) GG2 PCa vs no csPCa (n=733).

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Conflicts of Interest Disclosure Statement
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