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EXPLAINABLE AI-BASED MULTIPARAMETRIC MRI RADIOMICS FOR PREDICTING CLINICALLY SIGNIFICANT PROSTATE CANCER

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ABSTRACT

Background

Multiparametric magnetic resonance imaging (mpMRI) is an established component of prostate cancer diagnosis; however, PI-RADS interpretation remains partly subjective, particularly for equivocal lesions. Radiomics can quantify imaging characteristics that may not be readily appreciated visually, while explainable artificial intelligence (XAI) can make machine-learning predictions more transparent.

Methods

A retrospective cohort of 300 men undergoing prostate mpMRI followed by histopathological assessment was hypothetically evaluated. T2-weighted (T2W), apparent diffusion coefficient (ADC), and dynamic contrast-enhanced (DCE) sequences were analyzed according to PI-RADS v2.1. Shape, first-order, and texture radiomic features were extracted following standardized preprocessing. Reproducible features were selected using intraclass correlation, correlation filtering, and LASSO. Logistic regression, random forest, support vector machine, and XGBoost models were assessed. SHAP was used to explain feature contributions.

Results

In the illustrative dataset, 132/300 patients (44.0%) had clinically significant prostate cancer (csPCa; Grade Group ≥2). The integrated PI-RADS, clinical, and radiomics model achieved an illustrative AUC of 0.95 (95% CI, 0.92–0.98), sensitivity of 90.5%, specificity of 88.1%, and accuracy of 89.3% in the test cohort. ADC entropy, T2W texture heterogeneity, ADC percentile measures, DCE texture features, and lesion morphology were among the leading predictors.

Conclusions

An explainable mpMRI radiomics framework may provide complementary quantitative information to PI-RADS and clinical variables for prediction of csPCa. SHAP-based explanations can link model predictions to anatomically plausible imaging characteristics. Prospective multicenter external validation is required before clinical implementation.

KEYWORDS: *Prostate cancer; multiparametric MRI; radiomics; explainable artificial intelligence; PI-RADS.*

1. INTRODUCTION

Prostate cancer is a major cause of cancer morbidity and mortality among men. A central diagnostic challenge is distinguishing clinically significant prostate cancer (csPCa), which is likely to require definitive treatment, from indolent disease that may be safely monitored. Serum prostate-specific antigen (PSA) is useful for risk assessment but lacks sufficient specificity to distinguish clinically important malignancy from benign prostatic conditions.

Multiparametric MRI has become an important imaging examination in contemporary prostate cancer pathways. T2-weighted imaging provides anatomical and zonal information, diffusion imaging and ADC maps characterize water mobility and tissue cellularity, and DCE imaging provides information related to perfusion and vascularity. PI-RADS v2.1 standardizes interpretation and improves communication between radiologists and clinicians. Nevertheless, interpretation remains dependent on visual assessment, and equivocal lesions—particularly PI-RADS 3 lesions—continue to represent a diagnostic challenge.

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Radiomics provides a quantitative approach in which medical images are transformed into large numbers of reproducible numerical descriptors. Shape, first-order intensity, and texture features can characterize lesion morphology and spatial heterogeneity. In prostate MRI, radiomics has shown potential for improving prediction of csPCa and may provide information complementary to PI-RADS.

A major limitation of many artificial-intelligence models is limited interpretability. In clinical medicine, a prediction without an understandable rationale may be difficult to trust or incorporate into decision-making. Explainable AI methods such as SHAP provide feature-attribution values that indicate how individual variables influence a prediction. In prostate MRI, these explanations can potentially connect quantitative characteristics—such as low ADC, increased heterogeneity, or irregular morphology—to recognizable tumor imaging phenotypes.

We hypothesized that an integrated model combining mpMRI radiomics, PI-RADS, and clinical variables would improve discrimination of histopathologically confirmed csPCa compared with conventional variables alone, while XAI would provide clinically interpretable explanations of individual predictions. The primary objective was to develop and internally validate an explainable AI model for prediction of csPCa.

2. MATERIALS AND METHODS

2.1 Study Design and Population

A retrospective diagnostic prediction study was designed using an illustrative cohort of 300 consecutive men who underwent prostate mpMRI followed by targeted and/or systematic biopsy or prostatectomy. Patients were eligible if they had complete T2W, diffusion/ADC, and DCE sequences, a PI-RADS v2.1 assessment, and histopathological reference data. Patients with previous definitive prostate cancer treatment, incomplete MRI examinations, severe artifacts, or inadequate pathological information were excluded.

For the purposes of this manuscript draft, the numerical results are synthetic and are provided only to demonstrate manuscript structure. They must be replaced with actual measurements before submission.

2.2 MRI Protocol and PI-RADS Assessment

MRI examinations were assumed to be performed on 1.5-T or 3-T systems using institutional prostate protocols. The protocol included multiplanar T2W imaging, diffusion-weighted imaging with ADC maps, and DCE imaging following intravenous gadolinium administration. Lesions were assigned PI-RADS v2.1 scores by an experienced prostate radiologist.

2.3 Histopathological Reference Standard

Histopathological examination of targeted and/or systematic biopsy specimens was used as the reference standard. csPCa was defined as International Society of Urological Pathology Grade Group ≥2, broadly corresponding to Gleason score ≥3+4. Benign tissue and Grade Group 1 disease were categorized as non-csPCa for the primary binary classification.

2.4 Image Preprocessing and Segmentation

DICOM images were converted into a standardized research format. T2W, ADC, and DCE images were spatially registered, and voxel dimensions were standardized before feature extraction. Intensity normalization was applied to reduce acquisition-related variability. Lesion volumes of interest were manually delineated by an experienced radiologist and reviewed by a second reader. Sequence-specific contours were adjusted where required.

2.5 Radiomic Feature Extraction

An IBSI-compatible radiomics workflow was used. Shape features included lesion volume, surface area, sphericity, compactness, elongation, and maximum diameter. First-order features included mean, median, standard deviation, skewness, kurtosis, entropy, energy, and percentile measures. Texture features were derived from gray-level co-occurrence, run-length, size-zone, dependence, and neighboring gray-tone matrices. Features were extracted separately from T2W, ADC, and DCE images.

2.6 Feature Selection

Reproducibility was assessed using intraclass correlation coefficients. Features with ICC ≥0.80 were retained. Near-zero variance and highly correlated features were removed, followed by LASSO-based selection. All feature-selection operations were restricted to the training data to minimize information leakage.

2.7 Machine-Learning Models

The dataset was divided at the patient level into approximately 80% training and 20% independent test cohorts. Five-fold cross-validation was performed within the training set. Logistic regression, random forest, support vector machine, and XGBoost were evaluated. Three model configurations were considered: a clinical model containing age, PSA, PSA density, and prostate volume; a radiomics model; and an integrated model containing clinical variables, PI-RADS, and selected radiomic features.

2.8 Explainable AI

SHAP was used as the primary explainability method. For an individual patient, the model output can be expressed conceptually as $f(x)=\varphi 0+\Sigma\varphi i$, where $\varphi 0$ is the baseline prediction and φi represents the contribution of feature i. Positive SHAP values indicate increased predicted risk and negative values indicate reduced predicted risk. Global SHAP analysis identified features that were influential across the cohort, whereas local SHAP plots explained individual patient predictions.

The clinical interpretation of XAI was performed cautiously. Lower ADC values may be consistent with restricted diffusion and increased cellularity, whereas increased texture heterogeneity may represent spatial variation in cellular density, stroma, necrosis, or vascularity. Irregular shape may reflect infiltrative growth. These associations are biologically plausible but do not establish causality.

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2.9 Statistical Analysis

Continuous variables were summarized as mean ± standard deviation or median with interquartile range, and categorical variables as counts and percentages. Group comparisons used the Student t-test or Mann–Whitney U test for continuous variables and chi-square or Fisher exact tests for categorical variables. Diagnostic performance was evaluated using ROC curves, AUC, sensitivity, specificity, accuracy, positive predictive value, and negative predictive value. Ninety-five percent confidence intervals were estimated by bootstrap resampling. DeLong testing was planned for ROC comparisons, while calibration plots, Brier scores, and decision-curve analysis were used to assess model reliability and potential clinical utility. A two-sided P<0.05 was considered statistically significant.

2.10 Ethical Considerations

The proposed retrospective study would require approval from the institutional ethics committee. Patient confidentiality would be maintained by de-identification of imaging and clinical data. As this draft contains illustrative data, the final manuscript must include the actual institutional ethics approval number and applicable consent waiver or consent statement.

3. RESULTS

The illustrative cohort included 300 patients, of whom 132 (44.0%) had csPCa and 168 (56.0%) had non-csPCa. Patients with csPCa demonstrated higher PSA and PSA density and, on average, smaller prostate volumes. Higher PI-RADS categories were also more frequent among patients with csPCa.

Variable	Non-csPCa (n=168)	csPCa (n=132)	P value
Age, years	64.1 ± 7.8	67.8 ± 7.1	<0.001
PSA, ng/mL	8.4 ± 5.2	15.7 ± 10.8	<0.001
PSA density	0.12 ± 0.08	0.24 ± 0.16	<0.001
Prostate volume, mL	61.3 ± 25.7	49.8 ± 20.4	<0.001
PI-RADS 3	43.5%	18.2%	<0.001
PI-RADS 4	37.5%	43.2%	—
PI-RADS 5	19.0%	38.6%	—

3.1 Diagnostic Performance

The illustrative clinical model achieved an AUC of 0.78. PI-RADS v2.1 achieved an AUC of 0.86, while the radiomics-only model achieved an AUC of 0.91. Combining PI-RADS with radiomics increased the AUC to 0.93. The integrated model containing PI-RADS, clinical variables, and radiomics achieved the highest illustrative performance, with an AUC of 0.95.

Model	AUC	Sensitivity	Specificity	Accuracy
Clinical variables	0.78	72.4%	73.8%	73.3%
PI-RADS v2.1	0.86	82.1%	78.6%	80.0%
Radiomics only	0.91	85.7%	84.5%	85.1%
PI-RADS + radiomics	0.93	87.9%	85.7%	86.9%
Integrated model	0.95	90.5%	88.1%	89.3%

The illustrative integrated model produced a negative predictive value of approximately 92.8%, suggesting potential utility for identifying patients at lower predicted risk of csPCa. These values are hypothetical and require replacement with actual study results.

3.2 Explainable AI Findings

SHAP analysis identified ADC entropy, T2W gray-level non-uniformity, ADC lower-percentile measures, DCE texture contrast, and lesion shape among the most influential variables. Lower ADC percentile values and greater texture heterogeneity contributed toward increased predicted risk. The patient-level SHAP explanation demonstrated how these features shifted the prediction from the cohort baseline toward an individualized probability.

Figure 1 should present the complete study workflow, including patient selection, MRI preprocessing, segmentation, radiomic extraction, feature selection, model development, and SHAP interpretation. Figure 2 should present representative T2W, ADC, and DCE images with lesion segmentation. Figure 3 should present ROC curves. Figure 4 should show the global SHAP feature-importance plot, and Figure 5 should show a patient-specific SHAP waterfall plot.

4. DISCUSSION

This study presents a proposed explainable AI framework for prediction of csPCa using quantitative features derived from prostate mpMRI. The principal finding of the illustrative analysis was that combining radiomic features with PI-RADS and clinical variables produced greater discrimination than conventional clinical variables or PI-RADS alone. Importantly, the objective of the framework is not to replace radiologists but to provide a quantitative second layer of decision support.

The observed pattern is biologically plausible. ADC-derived features were among the strongest predictors, consistent with the established role of diffusion restriction in prostate cancer assessment. Radiomics extends this concept by measuring the spatial distribution of diffusion values rather than relying only on visual assessment or a single average measurement. Increased

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ADC heterogeneity may reflect regional differences in tumor cellularity and extracellular water mobility.

T2W and DCE texture features also contributed substantially. Malignant lesions can demonstrate heterogeneous tissue composition and vascular characteristics. Texture features may therefore capture subtle spatial differences that are difficult to quantify visually. However, radiomic features are mathematical descriptors and may also be influenced by acquisition parameters, preprocessing, voxel size, segmentation, and scanner characteristics.

The relationship between the proposed radiomics model and PI-RADS is best considered complementary. PI-RADS summarizes imaging findings using a structured clinical framework, whereas radiomics provides quantitative measurements. An AI model could potentially be particularly valuable for equivocal cases, including PI-RADS 3 lesions, in which clinical uncertainty remains substantial.

The use of XAI is a central feature of the proposed approach. A conventional prediction might report only that a lesion has an 85% probability of csPCa. SHAP can additionally identify the variables responsible for moving the prediction toward or away from that probability. This creates an opportunity for the radiologist to assess whether the model is responding to plausible lesion characteristics rather than irrelevant imaging artifacts.

For example, a prediction driven by low ADC percentile, increased ADC entropy, T2W heterogeneity, and irregular morphology is more readily interpretable because these characteristics can be localized to the lesion and related to recognized imaging manifestations of tumor biology. Conversely, an explanation dominated by unexpected features may alert clinicians to a potential model failure. XAI should therefore be regarded not merely as a visualization technique but as a tool for model auditing and clinical safety.

4.1 Comparison With Existing Literature

Previous prostate MRI radiomics studies have reported promising diagnostic performance, particularly for PI-RADS 3 lesions and models combining radiomics with clinical variables. However, reported performance varies substantially between studies. Multicenter and multivendor investigations have shown that radiomics does not always provide a significant incremental benefit over PI-RADS and clinical information. This discrepancy highlights the importance of external validation and standardized feature extraction.

The present framework therefore emphasizes IBSI-compatible radiomics, rigorous feature selection, patient-level splitting, leakage prevention, calibration, and decision-curve analysis. A high internal AUC alone should not be considered sufficient evidence of clinical readiness.

4.2 Clinical Implications

If externally validated, the model could support biopsy decision-making, risk stratification of equivocal lesions, and radiologist second-reading. A high negative predictive value could be particularly useful for identifying patients unlikely to harbor csPCa. However, implementation should only occur after prospective evaluation demonstrating that the system reduces unnecessary procedures without increasing clinically meaningful missed cancers.

4.3 Limitations

Several limitations should be considered. The retrospective design may introduce selection bias. A cohort of 300 patients may still be relatively small for a high-dimensional radiomics problem. Scanner and protocol heterogeneity may reduce reproducibility. Manual segmentation introduces observer variability. Internal validation cannot establish generalizability. Furthermore, SHAP describes model behavior but does not demonstrate biological causality. Finally, the numerical results in this draft are illustrative and cannot be used as clinical evidence.

4.4 Future Research

Future studies should include prospective multicenter cohorts, independent external validation, standardized acquisition protocols, automated or semi-automated segmentation, and calibration across institutions and MRI vendors. Integration with PSA density and validated clinical risk calculators should also be investigated. Correlation with whole-mount histopathology may provide an opportunity to examine whether radiomic signatures correspond to tumor grade, cellularity, vascularity, and spatial heterogeneity. Ultimately, prospective decision-impact studies will be necessary to establish whether explainable AI improves clinical outcomes.

5. CONCLUSION

An explainable AI model integrating multiparametric MRI radiomics, PI-RADS, and clinical variables represents a promising approach for predicting clinically significant prostate cancer. Quantitative T2W, ADC, and DCE characteristics may provide complementary information to conventional visual assessment, while SHAP can make individual predictions more transparent by identifying the imaging features that drive model output. The proposed framework may be particularly valuable for equivocal lesions and biopsy risk stratification. Nevertheless, rigorous external and prospective validation is essential before clinical implementation or claims of diagnostic superiority.

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