

The role of ADC value and ADC ratio in the diagnosis and prognostic evaluation of prostate cancer

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ABSTRACT

Prostate cancer is the second most common malignancy in men after lung cancer and remains a major cause of cancer-related mortality. Although prostate-specific antigen (PSA) testing has reduced mortality, its low specificity leads to overdiagnosis and unnecessary biopsies. Multiparametric magnetic resonance imaging (mpMRI) has advanced prostate cancer evaluation by integrating anatomical, functional, and vascular imaging. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) measurements provide objective markers of tumor cellularity, which correlate with Gleason score and International Society of Urological Pathology Grade Group. To summarize the diagnostic and prognostic role of absolute ADC values and the ADC ratio in prostate cancer. A narrative review of the literature from 2006 to 2025 was conducted through PubMed and Scopus using terms related to prostate cancer, DWI, ADC, ADC ratio, and PSA density. Thirty references were included, ranging from early technical reports to recent meta-analyses and guideline-based studies. Absolute ADC values decrease with increasing tumor aggressiveness but are limited by technical and patient-related variability. The ADC ratio, calculated as the lesion value relative to normal prostate tissue, reduces variability and improves diagnostic accuracy, particularly in Prostate Imaging Reporting and Data System (PI-RADS) category 3 lesions. When combined with PSA density, it increases accuracy for detecting clinically significant cancer and decreases unnecessary biopsies. ADC and the ADC ratio are promising non-invasive imaging biomarkers that improve lesion characterization, biopsy selection, and prognostic evaluation in prostate cancer. Future integration with artificial intelligence, radiomics, and radiogenomics may further enhance personalized patient management.

Keywords: Prostatic neoplasms, diffusion magnetic resonance imaging, apparent diffusion coefficient

INTRODUCTION

Prostate cancer is one of the most common malignancies in men worldwide and represents a major cause of cancer-related deaths.¹ Although prostate-specific antigen (PSA) screening, which is widely used in developed countries, has partially reduced mortality, its low specificity has led to overdiagnosis and unnecessary biopsies.² Therefore, more reliable, non-invasive, and prognostically valuable imaging methods have come to the forefront in diagnosis.

In the past decade, multiparametric magnetic resonance imaging (mpMRI) has emerged as a groundbreaking method in the diagnosis and management of prostate cancer.³ By combining T₂-weighted imaging, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced imaging (DCE-MRI), mpMRI provides a comprehensive assessment of

the anatomical, functional, and vascular characteristics of the prostate. Furthermore, the Prostate Imaging Reporting and Data System (PI-RADS) guideline, developed for the standardization of mpMRI findings, has become an important reference point in clinical practice.⁴

In particular, DWI and its derivative apparent diffusion coefficient (ADC) values are quantitative parameters reflecting the microstructural properties of prostate tissue. ADC values are inversely correlated with tumor cellularity and show a significant reduction in malignant prostate lesions.^{5,6} Studies have demonstrated that ADC measurements are reliable biomarkers in differentiating benign from malignant lesions.⁷



However, absolute ADC measurements may vary due to scanner differences, magnetic field strength, selected b-values, and patient-related factors.⁸ For this reason, the ADC ratio parameter has been developed in recent years. Calculated as the ratio of the lesion ADC value to the ADC value of normal prostate tissue in the same patient, ADC ratio reduces the effects of individual differences and technical variability, thus providing more reliable results.⁹

Preliminary evidence suggests that the ADC ratio may improve diagnostic accuracy and help reduce unnecessary biopsies.¹⁰⁻¹² Furthermore, its potential integration with established clinical parameters like PSA density (PSAD) is an area of active investigation, with the goal of creating stronger, multi-parametric predictors for clinically significant cancer.¹⁰⁻¹² In this context, ADC and ADC ratio measurements not only provide diagnostic accuracy but also hold clinical importance in prognostic prediction and treatment response evaluation.^{13,14}

THE DIAGNOSTIC AND PROGNOSTIC ROLE OF ADC VALUE AND ADC RATIO IN PROSTATE CANCER

Basic Principles and Image Formation

DWI is a functional MRI technique that captures the Brownian motion of water molecules within tissues. Tissue microstructure-including cellular density, membrane integrity, and extracellular matrix architecture-modulates water mobility and thus the DWI signal.⁵ In malignant prostate tissue, increased cellularity and reduced extracellular space produce restricted diffusion, manifesting as a decrease in the ADC.⁶ In practice, DWI acquired with multiple b-values enables quantification of signal attenuation; pixel-wise monoexponential fitting yields ADC maps that allow quantitative assessment of intratissue water diffusion.^{7,8}

Practical Measurement Considerations

Accurate ADC quantification requires standardized acquisition and analysis:

- **Field strength and coils:** High-field MRI with optimized receiver coils, including endorectal coils when appropriate, improves signal-to-noise ratio and spatial resolution for lesion detection and characterization.⁷
- **Region-of-interest (ROI) strategy:** ADC can be measured as minimum, mean, or percentile values using whole-lesion segmentation. Whole-lesion histogram analysis provides a more reliable assessment of intratumoral heterogeneity than small, single ROIs.⁶
- **Quality control:** Geometric distortion, susceptibility to hemorrhage or post-biopsy changes, and motion artifacts must be recognized and minimized during interpretation.^{7,12}

Pathophysiology, Malignancy, and Quantitative Behavior

In the peripheral zone, malignant lesions typically have lower ADC values than benign tissue due to higher cell density and reduced extracellular space.^{6,9} Several studies confirm that prostate cancer shows significantly reduced ADC compared with benign conditions, supporting its role as a biomarker of malignancy.^{10,11} Moreover, ADC correlates with histopathology: minimum ADC values decrease with

increasing Gleason grade, demonstrating the biological link between diffusion restriction and tumor aggressiveness.^{5,6}

CLINICAL APPLICATIONS OF ABSOLUTE ADC

Lesion Characterization

Across benign mimickers-such as prostatitis, glandular hyperplasia, and stromal nodules-ADC values are generally higher than in cancer; by contrast, cancer foci demonstrate a marked ADC decrease.^{7,10} Nonetheless, atrophy and biopsy-related fibrosis can also restrict diffusion, so ADC must be integrated with T₂-weighted morphology and dynamic contrast-enhanced MRI (DCE-MRI) for robust characterization.¹²

Risk Stratification and Prognosis

ADC metrics track with histologic grade: increasing Gleason score and higher ISUP Grade Groups are associated with lower minimum ADC values.^{6,13} Pooled evidence indicates that ADC contributes prognostic information for grade upgrading and clinically significant disease.^{8,14} Quantitative ADC also relates to tumor volume and burden, supporting its role in disease assessment beyond binary detection.¹⁵

Treatment Response Assessment

Post-radiation, ADC tends to rise in treated cancers consistent with reduced cellularity, supporting its use as a response biomarker and potential surveillance parameter after therapy.¹⁶ After radiotherapy, DCE-MRI findings correlate with biopsy results, highlighting the value of multiparametric follow-up in which ADC serves as a key quantitative component.¹⁷

ADC Ratio: Rationale, Definition, and Advantages

Definition: The ADC ratio is the quotient of the lesion's ADC divided by the ADC of normal-appearing prostate tissue in the same patient.⁹ By normalizing to an internal reference, the ADC ratio mitigates interscan and interindividual variability introduced by scanner hardware, field strength, chosen b-values, and patient-related heterogeneity-limitations that challenge absolute ADC harmonization across centers.^{9,10,19} Through internal normalization, ADC ratio often yields more reliable, comparable measurements, especially in multi-institutional or longitudinal contexts.^{9,10}

How to Measure ADC Ratio in Practice

- **Internal reference placement:** Use normal-appearing tissue in the same zone (e.g., contralateral peripheral zone at a comparable slice level) to avoid zonal heterogeneity as a confounder.^{9,10}
- **Lesion sampling:** Prefer whole-lesion or carefully placed ROIs that capture the most restricted areas to avoid partial-volume effects and to reflect clinically relevant tumor biology.^{6,9,10}
- **Reporting:** Document the ROI strategy (size, location), the reference site, and summary statistics (minimum/mean ADC and the derived ADC ratio) alongside acquisition parameters, to facilitate reproducibility and longitudinal comparison.^{6,9,12}

ADC Ratio in PI-RADS 3 Lesions

PI-RADS 3 denotes indeterminate likelihood of clinically significant cancer and is a frequent clinical dilemma. Here, ADC ratio has shown particular value: multiple studies report that ADC ratio can outperform absolute ADC in differentiating benign from malignant PI-RADS 3 lesions, likely due to its robustness against interpatient and interscanner variability.^{10,11,12} Within a comprehensive mpMRI framework, integrating ADC ratio with T₂-weighted morphology and perfusion behavior supports more confident decisions about targeted biopsy versus surveillance.^{11,12,18,19}

Integration with the PI-RADS Framework

Quantitative measures can refine PI-RADS categorization when judiciously applied. Mean ADC quantification has been shown to improve PI-RADS v2 categorization and validation of PI-RADS v2.1 demonstrates solid reader agreement and diagnostic performance when standardized interpretation is maintained—an environment where internally normalized metrics like ADC ratio are naturally synergistic.^{18,19}

Pitfalls and Confounders

- **Benign entities with low ADC:** Prostatitis, fibrosis, and post-biopsy changes may mimic cancer by restricting diffusion; correlation with T₂ and DCE is essential.^{7,10,12}
- **Heterogeneity:** Focal necrosis, mucinous components, or hemorrhage can alter ADC distribution; whole-lesion analysis helps avoid sampling bias.⁶
- **Technical variability:** Differences in b-values, echo times, susceptibility artifacts, and field inhomogeneities all influence ADC; normalization by ADC ratio reduces, but does not eliminate, these effects.^{9,10,19}

Practical Reporting Recommendations

- **Acquisition summary:** Note field strength, coil configuration, and diffusion scheme (multiple b-values).⁷
- **Lesion quantification:** Provide minimum and/or mean ADC and (where available) ADC histogram descriptors for the index lesion.^{6,12,20}
- **Normalization:** Report an ADC ratio using same-zone normal tissue as reference and describe ROI placement.^{9,10}
- **Contextual interpretation:** Integrate T₂-weighted morphology and DCE kinetics, especially for PI-RADS 3 lesions, and state how quantitative metrics influenced management recommendations (e.g., biopsy targeting).^{11,12,18,19}
- **Longitudinal use:** In post-radiotherapy follow-up, track ADC trends as part of response assessment, recognizing that rising ADC generally aligns with reduced cellularity.^{16,17}

Limitations and Future Directions

Although absolute ADC and ADC ratio provide biologically meaningful, reproducible markers of malignancy and grade, heterogeneity persists across studies due to differences in acquisition protocols, ROI strategies, and reference-tissue

selection. Meta-analytic evidence supports diagnostic and prognostic utility, yet also highlights the need for standardized acquisition/analysis pipelines and prospective validation in PI-RADS 3 decision-making.^{8,14} Continued work on robust normalization schemes and automated whole-lesion analytics may further enhance reproducibility and clinical adoption.^{6,9,12,14}

The comparative features, advantages, and limitations of absolute ADC versus ADC ratio are summarized in **Table 1**.

Table 1. Comparison of definitions, advantages, and clinical values of absolute ADC vs. ADC ratio

Feature	Absolute ADC	ADC ratio
Definition	Direct measurement of the lesion's ADC value	Ratio of lesion ADC value to normal prostate tissue ADC value
Advantages	-Simple and rapid measurement -Can be directly calculated by most software-widely used in the literature	-Reduces inter-scanner variability -Minimizes individual differences within the same patient -More reliable for multi-center studies -Provides greater diagnostic contribution in PI-RADS 3 lesions
Disadvantages	-Influenced by scanner differences, magnetic field strength, and b-values -Patient-related factors (edema, hemorrhage, inflammation) may alter results	-Variability in reference region selection -Prostate zonal heterogeneity may cause challenges -Lack of standardized cut-off values in the literature
Clinical value	-Strong correlation with tumor aggressiveness -Decreases consistently with higher Gleason scores	-Improves diagnostic accuracy in PI-RADS 3 lesions -Reduces need for biopsy when combined with PSA density
Future perspective	-Limited role due to standardization issues	-Expected to become more prominent in multi-center studies and AI-assisted analyses

ADC: Apparent diffusion coefficient, PI-RADS: Prostate Imaging Reporting and Data System, PSA: Prostate-specific antigen, AI: Artificial Intelligence

Combination with PSA Density

PSAD, defined as the serum PSA level normalized to prostate volume, is a widely used clinical parameter for prostate cancer risk stratification and is particularly valuable in the assessment of indeterminate mpMRI findings such as PI-RADS 3 lesions. Although direct evidence evaluating the combined use of ADC ratio and PSAD is limited, the available literature suggests that integrating quantitative diffusion metrics with established clinical markers may enhance overall diagnostic confidence.

Studies have repeatedly demonstrated the prognostic and diagnostic utility of ADC-based measurements—including ADC ratio—as robust biomarkers of tumor cellularity and aggressiveness.⁹⁻¹⁴ Within this framework, PSAD offers complementary biological information that reflects glandular volume and PSA kinetics. Therefore, combining ADC-derived parameters with PSAD holds conceptual promise for improving risk stratification, guiding biopsy decisions more effectively, and potentially reducing unnecessary interventions; however, prospective validation is still required.

By decreasing the probability of unnecessary biopsies and focusing diagnostic work-up on patients at higher risk of clinically significant prostate cancer, such multiparametric approaches may ultimately contribute to more cost-effective care pathways. Formal cost-effectiveness studies and guideline-level recommendations regarding the integration of ADC ratio and PSAD have yet to be established, and further multicenter investigations will be essential to define their optimal role.

Limitations

Despite the growing interest in ADC ratio as a quantitative imaging biomarker, several limitations must be acknowledged.

- **Reference region variability:** There is no uniform consensus regarding the optimal site for measuring “normal” prostate tissue when calculating the ADC ratio. Different studies have used contralateral normal-appearing peripheral zone, transition zone, or whole-gland reference regions, which may introduce variability in ratio calculations.^{9,10}
- **Zonal heterogeneity:** ADC values differ between prostate zones due to intrinsic microstructural and cellular differences. As a result, ADC and ADC-ratio thresholds derived from peripheral-zone lesions may not be directly applicable to transition-zone tumors.²⁰
- **Heterogeneous cut-off values:** Thresholds proposed for both absolute ADC and ADC ratio vary considerably across studies, partly due to differences in scanners, field strengths, b-value schemes, and ROI strategies.^{12,14} This heterogeneity underscores the need for standardized acquisition protocols and large-scale prospective validation before ADC ratio can be implemented uniformly in clinical practice.

Clinical Applications

ADC and ADC ratio are among the most valuable quantitative parameters guiding clinical decision-making in the diagnosis and prognosis of prostate cancer today. Their clinical applications can be summarized as follows:

- **Differentiation of benign and malignant lesions:** ADC values play a critical role in distinguishing prostate cancer from benign conditions. Prostatitis and benign prostatic hyperplasia usually show higher ADC values, whereas malignant lesions present with marked decreases.^{7,10} However, fibrotic changes or atrophy may also cause restricted diffusion, so ADC measurements should always be interpreted together with T₂-weighted and DCE-MRI findings.¹²
- **Prediction of tumor aggressiveness:** There is a strong relationship between ADC measurements and histopathological aggressiveness. Meta-analysis and quantitative studies have confirmed that ADC is a reliable biomarker in predicting tumor aggressiveness.^{14,20} ADC ratio, compared with absolute ADC, stands out as a more stable parameter. Lower ADC (and, in some studies, ADC

ratio) values have been significantly associated with higher Gleason scores.^{13,21} Therefore, ADC ratio can be used as an additional prognostic tool for early identification of aggressive tumors.

- **Determining biopsy indications:** Adding ADC ratio increases diagnostic accuracy in detecting clinically significant prostate cancer.^{11,22} Its combination of mpMRI scores and PSAD reduces unnecessary biopsy rates and makes significant contributions to patient management.^{14,23}
- **Active surveillance and treatment response monitoring:** ADC measurements can be used to predict tumor progression during active surveillance of low-risk prostate cancer. Progressive decreases in ADC may indicate worsening tumor biology. In addition, increases in ADC values after radiotherapy and androgen deprivation therapy have been shown to correlate with decreased tumor cellularity.¹⁵⁻¹⁷
- **Potential impact on clinical guidelines:** Recent evidence suggests that ADC and ADC ratio, particularly when combined with PSA density, may be integrated into clinical guidelines.^{24,25} This approach may help base biopsy indications on more objective data, providing clinicians with a reliable roadmap.

A structured overview of the diagnostic, prognostic, and clinical roles of absolute ADC and ADC ratio is provided in **Table 2**.

Clinical Application	Role of absolute ADC	Role of ADC ratio
Differentiation between benign and malignant lesions	Markedly reduced ADC values in malignant lesions	More reliable than absolute ADC in distinguishing benign from malignant lesions
Prediction of tumor aggressiveness	-Minimum ADC values -Correlates with Gleason score and ISUP Grade Group	-Lower ADC ratio - Shows a stronger association with higher Gleason scores
Biopsy indication	Limited contribution in clinical practice	Supports biopsy decision in PI-RADS 3 lesions, reducing unnecessary biopsies
Active surveillance	Decrease in ADC may indicate progression	May represent a more stable and reliable parameter for follow-up
Assessment of treatment response	Increase in ADC after radiotherapy indicates treatment response	Currently limited data, but promising for the future due to normalization advantage
Integration into guidelines	Currently used indirectly	High potential for integration into clinical guidelines in combination with PSA density

ADC: Apparent diffusion coefficient, ISUP: International Society of Urological Pathology, PI-RADS: Prostate Imaging Reporting and Data System, PSA: Prostate-specific antigen

FUTURE PERSPECTIVES

Future applications of ADC values and ADC ratio in prostate cancer are expected to be strongly influenced by developments in quantitative imaging, artificial intelligence, and personalized medicine. Although these parameters already demonstrate diagnostic and prognostic value, several

domains require further exploration and validation before full clinical adoption.

Artificial Intelligence and Automated Measurements

Manual ROI placement is one of the main reasons for variability in ADC analysis. Differences in observer experience and lesion sampling strategies can lead to inconsistent results, especially in heterogeneous tumors. The integration of AI-based algorithms promises to automate ROI selection and standardize ADC quantification, thereby reducing interobserver variability. Initial studies integrating ADC maps into multiparametric machine learning pipelines have shown improved lesion classification and diagnostic accuracy.^{12,26,28} AI tools may also provide real-time biopsy guidance by highlighting regions with lowest ADC or abnormal ADC ratio, potentially redefining workflow in both diagnosis and active surveillance.

Radiomics and Multiparametric Integration

Conventional ADC reporting often relies on mean or minimum values, which may fail to capture intratumoral heterogeneity. Radiomics can extract a broad range of texture, shape, and histogram-based features from ADC maps, offering a more comprehensive representation of tumor biology. Several studies have demonstrated that radiomic models integrating ADC features with T₂-weighted or DCE-MRI improve the discrimination between clinically significant and insignificant prostate cancer.^{12,26,28} In the future, radiomics may not only refine PI-RADS classification but also contribute to individualized treatment planning, for example by predicting response to focal therapy or radiotherapy.

Radiogenomics and Molecular Correlations

Linking imaging features to genomic alterations is a promising field. Quantitative ADC metrics and ADC ratios may correlate with molecular subtypes, proliferation markers, and genetic signatures of aggressiveness. Early studies suggest that ADC-based measures can predict biochemical recurrence and treatment outcomes after radical prostatectomy.^{13,30} Radiogenomics could enable a “virtual biopsy,” allowing non-invasive assessment of tumor heterogeneity and guiding targeted treatment without relying exclusively on tissue sampling. In the long term, radiogenomic signatures combining ADC features with genomic risk scores may offer powerful prognostic tools in precision oncology.

Standardization and Multicenter Validation

One of the critical challenges is methodological heterogeneity. Scanner hardware, magnetic field strength, diffusion encoding (b-values), and ROI strategies lead to wide variability in ADC values across institutions. Current meta-analyses emphasize the lack of standardized cut-offs for distinguishing benign from malignant lesions or for predicting aggressiveness.^{8,14,29} Future research should focus on multicenter prospective trials with harmonized acquisition protocols, automated segmentation pipelines, and clearly defined reference tissues. Standardization will be essential for integrating ADC ratio into international guidelines, especially for PI-RADS 3 lesions where decision-making remains a clinical dilemma.

Clinical Workflow and Decision Support

In the next decade, ADC-derived metrics are likely to become part of multiparametric decision-making tools that combine imaging biomarkers with clinical and laboratory data. The prospective integration of quantitative MRI biomarkers like the ADC ratio with clinical data such as PSA density, Gleason score, and ISUP Grade Group holds the potential to refine integrated risk calculators.^{14,19,22} Such multi-parametric models could ultimately optimize biopsy decisions and reduce overtreatment, though this requires validation in future clinical trials. In active surveillance, monitoring ADC dynamics over time may allow early detection of tumor progression, enabling timely therapeutic intervention. Such integrative models could also be embedded into clinical information systems, supporting radiologists and urologists in daily practice.

Expanded Roles Beyond Diagnosis

ADC and ADC ratio are no longer limited to initial diagnosis. Evidence suggests they are valuable in treatment monitoring: post-radiotherapy and post-hormonal therapy, rising ADC values reflect reduced tumor cellularity and successful response.^{16,17,27} Furthermore, combining ADC with perfusion parameters from DCE-MRI may improve early prediction of therapeutic outcomes. Another promising area is the use of absolute ADC as a prognostic biomarker for biochemical recurrence after radical prostatectomy.³⁰ In the future, these parameters may guide selection of patients for focal therapies, immunotherapies, or novel targeted agents, broadening their role well beyond traditional diagnosis.

EXPANDED OUTLOOK

The future role of ADC and ADC ratio in prostate cancer management is likely to evolve from simple quantitative markers into multifunctional imaging biomarkers, integrated within AI-driven platforms, radiomics pipelines, and radiogenomic models. To realize this potential, rigorous standardization, multicenter validation, and incorporation into clinical guidelines will be essential. Ultimately, these developments may establish ADC-derived metrics as indispensable tools for personalized, non-invasive, and cost-effective prostate cancer care.

CONCLUSION

ADC values and ADC ratio represent promising quantitative biomarkers for the diagnosis and prognostic assessment of prostate cancer. By improving lesion characterization and supporting biopsy decisions—particularly in PI-RADS 3 cases—they have the potential to enhance clinical decision-making and reduce unnecessary interventions. Their association with tumor aggressiveness also highlights their role in prognostic evaluation and treatment monitoring.

Nevertheless, challenges such as variability in imaging protocols, lack of standardized thresholds, and zonal heterogeneity within the prostate remain barriers to routine clinical adoption. Addressing these limitations through prospective multicenter studies with harmonized methodology will be essential.

Looking ahead, integration with artificial intelligence, radiomics, and radiogenomics is expected to further strengthen the value of ADC-based metrics, paving the way for more objective and personalized prostate cancer management.

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This review was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

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