ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

# Correlation of multiparametric MRI (PIRADS grading) and apparent diffusion coefficient values in prostate tumor with Gleason score

**Ravina Saini[1], Aditi Vohra[2], Amit Jain[3], Harneet Narula[4], Harneet Kadyan[5], Sanjay Singh[6]**

*[1,5,6]Postgraduate Resident, [2,4]Professor, [3]Associate Professor, Department of Radiodiagnosis, Maharishi Markandeshwar Institute of Medical Sciences and Research, MMDU, Ambala, Haryana, India*

Submission: 20-09-2022 Revision: 29-11-2022 Publication: 01-01-2023

## ABSTRACT

**Background:** Multiparametric magnetic resonance imaging (mpMRI) of prostate is the radiological investigation of choice for the evaluation of prostatic tumors. **Aims and Objectives:** The aim of the present study was to evaluate the efficacy of mpMRI using PIRADS 2.1 grading and apparent diffusion coefficient (ADC) values as a non-invasive investigation in the detection of prostatic tumors and to correlate PIRADS grade and ADC values with Gleason score of prostate cancer (prostate Ca). **Materials and Methods:** Fifty patients above the age of 50 years presenting with signs and symptoms of prostate Ca were enrolled for the study. All patients were subjected to the mpMRI including ADC values and then all underwent transrectal ultrasound-guided biopsies. The post-biopsy Gleason score was correlated with PIRADS grading and ADC values followed by statistical correlation. **Results:** There was a positive linear association between PIRADS score and serum prostate-specific antigen levels (+0.433) and inverse relationship between mean tumor ADC values and Gleason score with correlation coefficient of −0.846 (P<0.001). There was a positive linear association between the PI-RADS score and Gleason score (correlation coefficient of +0.739 with P<0.001). In addition, the positive predictive value of mpMRI was 78.79%, while the negative predictive value was 84.34%. **Conclusion:** Our study concludes that mpMRI with PIRADS grading including ADC values assists in targeting the appropriate biopsy site for better characterization of the prostate Ca as it correlates well with the Gleason score.

**Key words:** Prostate; Multiparametric MRI; Gleason score; Apparent diffusion coefficient

**Access this article online**

**Website:** http://nepjol.info/index.php/AJMS

**DOI:** 10.3126/ajms.v14i1.48514

**E-ISSN:** 2091-0576

**P-ISSN:** 2467-9100



## INTRODUCTION

Prostate cancer (prostate Ca) is one of the most commonly diagnosed malignancies among men. Multiparametric magnetic resonance imaging (mpMRI) has gradually gained importance for timely diagnosis and an accurate characterization of prostate Ca lesions, and is an integral part of the management.[1,2] PIRADS score is used to grade the identified prostatic lesions using mpMRI to identify clinically significant cancer. Sequences included in MpMRI are T2-weighted – T2, diffusion-weighted MRI – DWI, and dynamic contrast-enhanced MRI – DCE-MRI. PIRADS score ranges between 1 and 5, indicating a very low to a very high likelihood that a lesion is malignant. The PIRADS classification has a crucial role in prostate Ca management since its development.[3-5] Evaluation of PIRADS score and ADC values on mpMRI can help predict the stage of the prostatic malignancy and play a role in planning the treatment. The objective of our study was to evaluate the correlation between the PIRADS score and ADC values in the tumor region with post-biopsy Gleason score.

### Aims and objectives

The aim of the present study was to evaluate the efficacy of mpMRI using PIRADS 2.1 grading and apparent diffusion coefficient (ADC) values as a non-invasive investigation in the detection of prostatic tumors and to determine the correlation between PIRADS grade and ADC values with Gleason score of prostate cancer.

**Address for Correspondence:**
Dr. Amit Jain, Associate Professor, Department of Radiodiagnosis, Maharishi Markandeshwar Institute of Medical Sciences and Research, MMDU, Ambala, Haryana, India. **Mobile**: +919872643560. **E-mail:** amit.jain.dr@gmail.com

## MATERIALS AND METHODS

A prospective observational study was conducted in the department of radio-diagnosis, at our institute over a period of 2 years. Our Institutional Ethical Committee approved the study protocol. Adult male patients above the age of 50 years, reporting to the urology department with signs and symptoms raising suspicion of prostate malignancy, were enrolled in the study.

The inclusion criteria were: Males above 50 years of age, raised prostate-specific antigen (PSA) levels, hard enlarged nodular prostate on digital rectal examination, subjects willing to participate in the study with informed written consent. The exclusion criteria were: Patients <50 years of age, those with raised PSA levels associated with non-neoplastic etiologies such as catheterized patients, patients with cystitis, and prostatitis, and patients with claustrophobia and MRI incompatible implants. As per the inclusion and exclusion criteria, 50 patients were selected for the study.

All the 50 patients were subjected to mpMRI on Philips Achieva/Philips Multiva (1.5 T) machine in our department using body coil. Sequences taken included axial and sagittal T1W, axial, coronal, and sagittal T2W, STIR coronal, DWI, and DCE. ADC values of all prostatic lesions were determined and recorded. We utilized b values of 0, 500, and 1000 $mm^2/s$ for diffusion-weighted imaging, The MRI scans were reviewed by experienced radiologist and were graded as per PIRADS version 2.1 into PIRADS Grades 1–5.[6]

All 50 patients were subjected to transrectal ultrasound (TRUS) scan with Philips Affinity 50 machine with intracavitary probe in the left lateral position. Systematic 12 core biopsies were taken.

The biopsy samples were analyzed by two faculty members from pathology department of our institute and Gleason scoring was done after histopathological analysis. The tumors were then categorized into three groups – as low grade (Gleason score ≤ 6), intermediate grade (Gleason score 7), and high grade (Gleason score > 7). The PIRADS grading and ADC values were correlated with Gleason score and statistically analyzed in all cases.

### Statistical analysis

Data collected from our study were assessed using a Chi-square test for categorical data and a Student's t-test or ANOVA for continuous data. SPSS 21 and R software were used for statistical analysis.

## RESULTS

Fifty patients were enrolled during the study period as per inclusion criteria. The age of patients' varied from 50 to 85 years. The mean±SD serum PSA level of patients was 54.06±39.93 with a range of 5.5–112 ng/ml.

Patients underwent mpMRI for prostate followed by TRUS-guided biopsy and histopathological analysis. MRI of all patients was graded as per PIRADS 2.1. The T1W and T2W images were also analyzed for seminal vesicle invasion; extracapsular extension (ECE); neurovascular bundle invasion; lymph node involvement; other pelvic organs involvement (urinary bladder/rectal invasion); and bony metastasis.

Out of the 50 patients, PIRADS score of 2 was given to two patients, score of 3 – 4 patients, and scores of 4 and 5 – 22 patients each. There was a positive linear association between PIRADS score and serum PSA levels (+0.520), indicating that a rise in PIRADS score is linked with increased PSA levels. TRUS-guided biopsy was done for all the patients for histopathological analysis.

Gleason scoring was done only for 46 biopsy samples, which were found malignant on histopathological analysis. Two patients with raised PSA levels were given PIRADS score 2 on mpMRI and were confirmed to be benign, having benign prostatic hypertrophy (BPH) on biopsy. There were two false-positive diagnosis of carcinoma on T2W images. Out of these two patients, one patient had features of chronic prostatitis and one had features of BPH on histopathological analysis.

Out of 46 confirmed malignant cases, Gleason score of ≤6, 7, and >7 was given to 8 (17.4%) patients, 16 (34.8%) patients, and 22 (47.8%) patients, respectively (Table 1). Correlation coefficient of +0.739 ($P<0.001$) was found between PIRADS score and Gleason score suggesting a positive linear association between them, indicating that a rise in PIRADS score is linked with an increase in Gleason score. Hence, it reveals that mpMRI can suggest the aggressiveness of malignancy on the basis of PIRADS score. Figure 1 is an example of a case showing MRI images and histopathological analysis.

The mean ADC value was taken for all prostatic lesions and correlated with post-biopsy Gleason score. As per our study, the mean ADC values for tumors with Gleason score of ≤6, 7, and >7 were $0.85\pm0.03\times10^{-3}$ $mm^2/s$, $0.74\pm0.02\times10^{-3}$ $mm^2/s$, and $0.63\pm0.08\times10^{-3}$ $mm^2/s$, respectively.

As demonstrated in Table 2, the mean, minimum, and maximum ADC value of tumors dropped as Gleason

**Table 1: Comparison of PI-RADS score with Gleason score**

| | PIRADS score | Gleason score group | | | Total | Kappa value | P-value |
|---|---|---|---|---|---|---|---|
| | | ≤6 | 7 | >7 | | | |
| PIRADS (T2W+DWI+DCE) | 3 | 2 | 0 | 0 | 2 | 0.491 | 0.0001 |
| | 4 | 6 | 12 | 4 | 22 | | |
| | 5 | 0 | 4 | 18 | 22 | | |
| Total | | 8 | 16 | 22 | 46 | | |

**Table 2: Comparison of ADC values (in $10^{-3}$ $mm^2/s$) of tumor among Gleason groups**

| DWI/ ADC | Gleason's score | N | Mean ADC value | SD | Std. error | 95% confidence interval for mean | | Minimum | Maximum | F | P-value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Lower bound | Upper bound | | | | |
| | ≤6 | 8 | 0.85 | 0.03 | 0.01 | 0.83 | 0.88 | 0.81 | 0.87 | 48.482 | <0.001 |
| | 7 | 16 | 0.74 | 0.02 | 0.01 | 0.73 | 0.75 | 0.71 | 0.77 | | |
| | >7 | 22 | 0.63 | 0.08 | 0.02 | 0.60 | 0.66 | 0.46 | 0.74 | | |
| | Total | 46 | 0.71 | 0.10 | 0.01 | 0.68 | 0.74 | 0.46 | 0.87 | | |

ADC: Apparent diffusion coefficient, DWI: Diffusion-weighted imaging

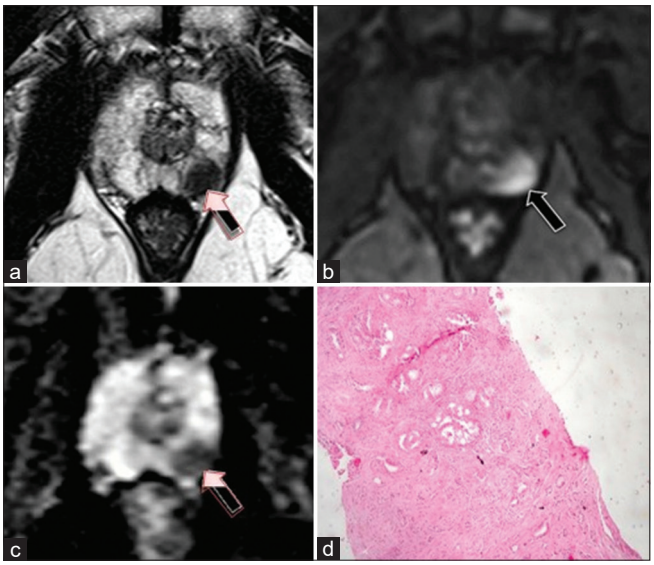


**Figure 1:** (a-d) Case of prostatic adenocarcinoma with PIRADS 4 and Gleason score 7 (4+3). (a-c) MRI axial T2W, DCE, and ADC images show a well-defined focal nodule in the peripheral zone of prostate in the left posterolateral aspect at the level of apex, abutting the capsule but without definite evidence of extraprostatic extension. ADC value: $0.741\times10^{-3}$ $mm^2/s$, (d) histopathological analysis reveals Gleason patterns 4 and 3 with Gleason score of 7. ADC: Apparent diffusion coefficient

score increased thus proving the inverse relationship between mean tumor ADC and Gleason score. Correlation coefficient of 0.846 with P<0.001 was found between mean tumor ADC levels and Gleason score.

The sensitivity and specificity of the association between mpMRI-based PIRADS and Gleason score were about 60.61% and 83.33%, respectively. In addition, study revealed the positive and negative predictive value to be 78.79% and 84.34%, respectively.

## DISCUSSION

MRI is a common imaging technique for identifying and staging prostate Ca (MRI). The rise in the number of indolent tumors, as well as the development of more conservative treatment options, has raised the need for improved tumor aggressiveness categorization to choose the appropriate treatment plan.

Advanced imaging techniques such as diffusion-weighted imaging, ADC mapping, and dynamic contrast-enhanced imaging, are employed to detect and categorize prostate Ca in multiparametric prostate studies. The only imaging method that can estimate proton molecule transport *in vivo* while simultaneously giving data on tissue biological properties is diffusion-weighted imaging and ADC values. Diffusion-weighted imaging takes less time and is less subjective as compared to other MR techniques such as T2W and contrast-enhanced imaging. Another advantage is that it has less partial volume effects than with MR spectroscopy.

As we looked at the relationship between ADC value and tumor aggressiveness, we observed that when Gleason's score rises, ADC value drops dramatically. This is in agreement with the previous studies. When matched to the biopsy Gleason's score, our data reveal an inverse association between ADC value and tumor aggressiveness. Wu et al., in 2016, have compared min ADC values and normalized ADC values ($ADC_{ratio}$) and found that these have inverse relationship with Gleason score.[7] Manetta et al., in 2019, observed that mean ADC values decreased with increasing Gleason score and they correlate well statistically. $ADC_{ratio}$ is a better method as compared to mean ADC values as it is independent of b-values.[8] According to Zelhof et al.,[9]

high-grade tumors have high cellular density which results in limited water molecule transport and hence decreased ADC values. However, Aliukonis et al., in 2017, did not find any significant relation between ADC values and Gleason score.[10] Woodfield et al.,[11] discovered that as the percentage of tumor involvement increased, mean tumor ADC values decreased. The reduction in ADC values is attributed in part to better visualization of larger lesions on DWI, allowing for bigger and more precise ROI placement on ADC maps.

Correlation coefficient of +0.739 was found between PIRADS score and Gleason score suggesting positive linear association. This indicates that as the PIRADS score increases, there is relative increase in Gleason score of the lesion. Thus, MP-MRI helps to characterize the lesion with regard to the aggressiveness. Park et al.,[12] in 2016, found that PIRADS 2.0 score correlated well with clinically significant cancer (Gleason score ≥7, ECE, and increased tumor volume of >0.5 $cm^3$). Kizilay et al., have also confirmed significant correlation of Gleason score and PIRADS score.[13] Pripatnanont et al., in 2021, have concluded that PIRADS 5 was found to be highly associated with Gleason score ≥7 with odds ratio of 6.67.[14] However, Slaoui et al., in 2017, have concluded that PIRADS was not associated with significant difference regarding Gleason score distribution within target.[15]

mpMRI has a high specificity, meaning that it has the ability to exclude biopsy in patients which would otherwise yield negative result. As a result, by utilizing mpMRI, undesired and unneeded biopsies can be avoided, minimizing patient suffering and needless health-care costs.

As per our study, we conclude that mpMRI PI-RADS has a positive correlation with Gleason score and that ADC values have a negative correlation with Gleason score. The sensitivity and specificity are high with good predictive values. Hence, mpMRI can be used as a pre-biopsy screening test in addition to providing valuable diagnostic information in large and aggressive lesions.

It may be concluded that mpMRI PI-RADS score and ADC values can play an important role not only in prostate Ca screening but also in diagnosis, therapy, and prognosis.

### Limitations of the study

This research has a few drawbacks. First, TRUS-guided biopsy was used instead of radical prostatectomy specimens for histopathological analysis. These biopsies may miss tiny tumor foci detectable on MR imaging, making diagnosis less precise. Standard sextant biopsy has a high false-negative rate,[16] Second, as the b-value utilized in the MRI investigation has an impact on the ADC result and we have utilized b values of 0, 500, and 1000 $mm^2/s$ in our investigation, the mean ADC values for tumors in our study might differ from studies which have used other b values. Finally, it is a single-center study and the sample size being small could have skewed the findings.

## CONCLUSION

We conclude that mpMRI PI-RADS scoring is an non-invasive investigation having high sensitivity and specificity in detecting carcinoma prostate with good predictive values in characterizing the aggressiveness of the disease.

The study also concluded that PI-RADS and Gleason score have a positive linear correlation and there is a significant negative correlation between mean tumor ADC value and Gleason score.

Mean tumor ADC values are useful in differentiating various grades of tumors (low grade to high grade). This can thus be a useful non-invasive parameter in addition to biopsy to avoid surgery in patients with low-grade tumors where the risk of surgery is high.

## ACKNOWLEDGMENT

We would like to thank our statistician for providing the necessary guidance and analysis of the data collected and the department reception staff and technicians for coordinating with the patients for smooth conduct of the study.

## REFERENCES

1. Sun Y, Reynolds HM, Parameswaran B, Wraith D, Finnegan ME, Williams S, et al. Multiparametric MRI and radiomics in prostate cancer: A review. Australas Phys Eng Sci Med. 2019;42(1):3-25. https://doi.org/10.1007/s13246-019-00730-z
2. Hegde JV, Mulkern RV, Panych LP, Fennessy FM, Fedorov A, Maier SE, et al. Multiparametric MRI of prostate cancer: An update on state-of-the-art techniques and their performance in detecting and localizing prostate cancer. J Magn Reson Imaging. 2013;37(5):1035-1054. https://doi.org/10.1002/jmri.23860
3. Zhao C, Gao G, Fang D, Li F, Yang X, Wang H, et al. The efficiency of multiparametric magnetic resonance imaging (mpMRI) using PI-RADS version 2 in the diagnosis of clinically significant prostate cancer. Clin Imaging. 2016;40(5):885-888. https://doi.org/10.1016/j.clinimag.2016.04.010
4. Cash H, Maxeiner A, Stephan C, Fischer T, Durmus T, Holzmann J, et al. The detection of significant prostate cancer is correlated with the prostate imaging reporting and data system (PI-RADS) in MRI/transrectal ultrasound fusion biopsy. World J Urol. 2016;34(4):525-532. https://doi.org/10.1007/s00345-015-1671-8

5. Baldisserotto M, Neto EJ, Carvalhal G, de Toledo AF, de Almeida CM, Cairoli CE, et al. Validation of PI-RADS v.2 for prostate cancer diagnosis with MRI at 3T using an external phased-array coil. J Magn Reson Imaging. 2016;44(5):1354-1359.
https://doi.org/10.1002/jmri.25284
6. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, et al. Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. Eur Urol. 2019;76(3):340-351.
https://doi.org/10.1016/j.eururo.2019.02.033
7. Wu X, Reinikainen P, Vanhanen A, Kapanen M, Vierikko T, Ryymin P, et al. Correlation between apparent diffusion coefficient value on diffusion-weighted MR imaging and Gleason score in prostate cancer. Diagn Interv Imaging. 2017;98(1):63-71.
https://doi.org/10.1016/j.diii.2016.08.009
8. Manetta R, Palumbo P, Gianneramo C, Bruno F, Arrigoni F, Natella R, et al. Correlation between ADC values and Gleason score in evaluation of prostate cancer: Multicentre experience and review of the literature. Gland Surg. 2019;8(Suppl 3):S216-S222.
https://doi.org/10.21037/gs.2019.05.02
9. Zelhof B, Pickles M, Liney G, Gibbs P, Rodrigues G, Kraus S, et al. Correlation of diffusion-weighted magnetic resonance data with cellularity in prostate cancer. BJU Int. 2009;103(7):883-888.
https://doi.org/10.1111/j.1464-410X.2008.08130.x
10. Aliukonis P, Letauta T, Briedienė R, Naruševičiūtė I and Letautienė S. The role of different PI-RADS versions in prostate multiparametric magnetic resonance tomography assessment. Acta Med Litu. 2017;24(1):44-50.
https://doi.org/10.6001/actamedica.v24i1.3462
11. Woodfield CA, Tung GA, Grand DJ, Pezzullo JA, Machan JT and Renzulli JF 2nd. Diffusion-weighted MRI of peripheral zone prostate cancer: Comparison of tumor apparent diffusion coefficient with Gleason score and percentage of tumor on core biopsy. AJR Am J Roentgenol. 2010;194(4):W316-W322.
https://doi.org/10.2214/AJR.09.2651
12. Park SY, Jung DC, Oh YT, Cho NH, Choi YD, Rha KH, et al. Prostate cancer: PI-RADS version 2 helps preoperatively predict clinically significant cancers. Radiology. 2016;280(1):108-116.
https://doi.org/10.1148/radiol.16151133
13. Kızılay F, Çelik S, Sozen S, Ozveren B, Eskiçorapçı S, Ozgen M, et al. Correlation of prostate-imaging reporting and data scoring system scoring on multiparametric prostate magnetic resonance imaging with histopathological factors in radical prostatectomy material in Turkish prostate cancer patients: A multicenter study of the urooncology association. Prostate Int. 2020;8(1):10-15.
https://doi.org/10.1016/j.prnil.2020.01.001
14. Pripatnanont W, Opanuraks J, Prasopsanti K, Santi-ngamkun A, Ratchanon S, Tantiwongse K, et al. A correlation of PI-RADS score and pathological grading outcome post radical prostatectomy: A retrospective review. Insight Urol. 2021;42(2):110-116.
https://doi.org/10.52786/isu.a.32
15. Slaoui H, Neuzillet Y, Ghoneim T, Rouanne M, Abdou A, Lugagne-Delpon PM, et al. Gleason score within prostate abnormal areas defined by multiparametric magnetic resonance imaging did not vary according to the PIRADS score. Urol Int. 2017;99(2):156-161.
https://doi.org/10.1159/000468947
16. Serefoglu EC, Altinova S, Ugras NS, Akincioglu E, Asil E and Balbay MD. How reliable is 12-core prostate biopsy procedure in the detection of prostate cancer? Can Urol Assoc J. 2013;7(5-6):E293-E298.
https://doi.org/10.5489/cuaj.11224

**Authors Contribution:**
**RS-** Study design, data acquisition, data analysis, data interpretation, manuscript writing, and manuscript editing; **AV-** Concept, study design, data analysis, data interpretation, manuscript editing, and manuscript finalization; **AJ-** Concept, study design, data analysis, data interpretation, manuscript writing, manuscript editing, and manuscript finalization; **HN-** Study design, data interpretation, manuscript writing, and manuscript editing; **HK-** Data acquisition, data analysis, and manuscript writing; and **SS-** Data acquisition, data analysis, and manuscript writing.

**Work attributed to:**
Department of Radiodiagnosis, Maharishi Markandeshwar Institute of Medical Sciences and Research, MMDU, Mullana (Ambala), India.

**Orcid ID:**
Dr. Ravina Saini - https://orcid.org/0000-0003-4586-2408
Dr. Aditi Vohra - https://orcid.org/0000-0002-8770-1234
Dr. Amit Jain - https://orcid.org/0000-0002-7840-5812
Dr. Harneet Narula - https://orcid.org/0000-0003-1737-3375
Dr. Sanjay Singh - https://orcid.org/0000-0002-0216-2914

**Source of Support:** Nil, **Conflicts of Interest:** None declared.