

## Multiparametric Prostate Magnetic Resonance Imaging Before Radical Prostatectomy: Can it Predict Histopathology?

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**Purpose:** We aimed to investigate the histopathological correlation of the suspected prostate malignancy detected in multiparametric prostate magnetic resonance imaging (mpMRI).

**Materials and Methods:** The data of 93 patients who underwent radical prostatectomy and had preoperative mpMRI were examined. Age and pre-operative Prostate-Specific Antigen values were retrospectively collected from patient files. The pathology specimens were examined again and post-operative ISUP grade group, other pathological findings (seminal vesicle invasion, lymph node involvement, and extraprostatic extension), pre-operative mpMRI were re-examined and PIRADS score, extracapsular extension, seminal vesicle invasion, neurovascular bundle invasion, lymph node involvement, and ADC values were recorded.

**Results:** 151 (92,07%) of 164 lesions detected in mpMRI were histopathologically correlated. 80% of patients with seminal vesicle invasion ( $P < 0.001$ ), 28.8% of patients with extracapsular extension ( $P < 0.052$ ) and 42.9% of patients with lymph node involvement ( $P = .001$ ) in mpMRI were histopathologically correlated. A significant relationship was found between PIRADS scores and ISUP grade groups ( $P < 0.001$ ). There was a negative correlation between ADC values and ISUP grade groups ( $P < 0.001$ ).

**Conclusion:** Our study showed that the lesions detected by mpMRI showed a high histopathological correlation.

**Keywords:** correlation; diagnosis; histopathology; prostate cancer; multiparametric prostate mri

## INTRODUCTION

Prostate cancer (PCa) is considered as one of the most important health problems encountered in male population. In Europe, PCa, which exceeds the number of colorectal and lung cancer, has been the most common solid neoplasm<sup>(1)</sup>. However, PCa is the second most common cause of cancer death in men<sup>(2)</sup>. Since PCa has a heterogeneous structure, two or more graded tumors may coexist in the same disease. Therefore, the Gleason grading system, defined by Donald Gleason in 1966 and later modified, is used for the grading of prostate adenocarcinoma<sup>(3)</sup>. In 2014, the International Society of Urological Pathology (ISUP) prostate carcinoma Gleason grading conference brought a new interpretation to the Gleason score. The ISUP grading system has been introduced to describe in detail the clinically important distinction between Gleason score 7 (4+3) and 7 (3+4) prostate adenocarcinoma<sup>(4)</sup>. Magnetic Resonance Imaging (MRI) has been used for the non-invasive assessment of the prostate gland and surrounding structures since the 1980s. Initially, prostate MRI was based solely on morphological evaluation using T1-weighted and T2-weighted sequences, and its primary role was local staging in the patients with PCa proven by biopsy. Advances in technology have led to the development of multiparametric MRI (mpMRI)

which combines T2 weighted imaging with functional and physiological evaluation through techniques such as diffusion weighted imaging (DWI), and its variations like diffusion coefficient (ADC) and dynamic contrast-enhanced imaging (DCI). In 2012, Prostate Imaging and Reporting and Data System (PIRADS) version 1 (v1) was released by the European Society of Urogenital Radiology (ESUR). As a result of the increase in experience and rapid progress in this field, some limitations of this scoring system have emerged. PIRADS v2 has been published in 2014 to make the standardization more acceptable<sup>(5)</sup>. However, further efforts are underway to improve it and overcome its shortcomings. The PIRADS v2 uses a 5-point scale based on the combination of mpMRI findings in T2W, DWI, and DCI which is associated with the presence of a clinically significant cancer for each lesion in the prostate gland<sup>(5)</sup>. PIRADS v2 segmentation model is adapted from the European Consensus Meeting and the ESUR 2012 Prostate MRI Guidelines<sup>(5)</sup>. The use of this map; enables radiologists, urologists, and pathologists to localize the findings described in MRI, and is a valuable visual aid for discussions with patients about biopsy and treatment options.

MpMRI has recently become more widely used in the

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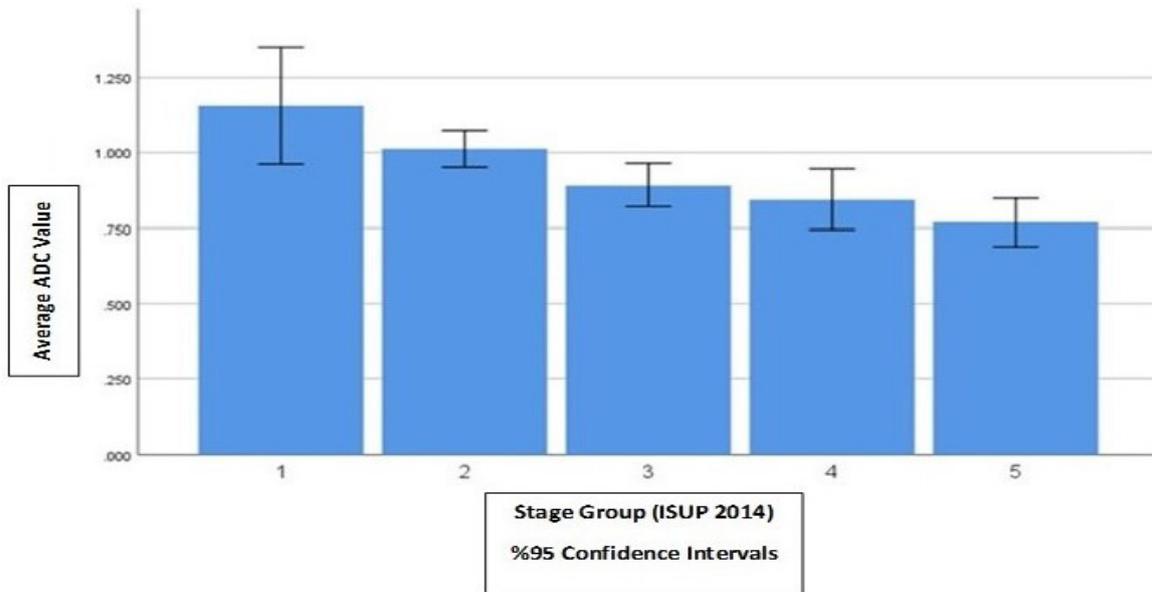
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**Figure 1.** Distribution of average ADC values by grade group

diagnosis and staging of PCa, and its importance has increased with increasing experience and device quality. In this study, we aimed to investigate the histopathological correlation of malignant suspected foci detected in mpMRI.

## MATERIALS AND METHODS

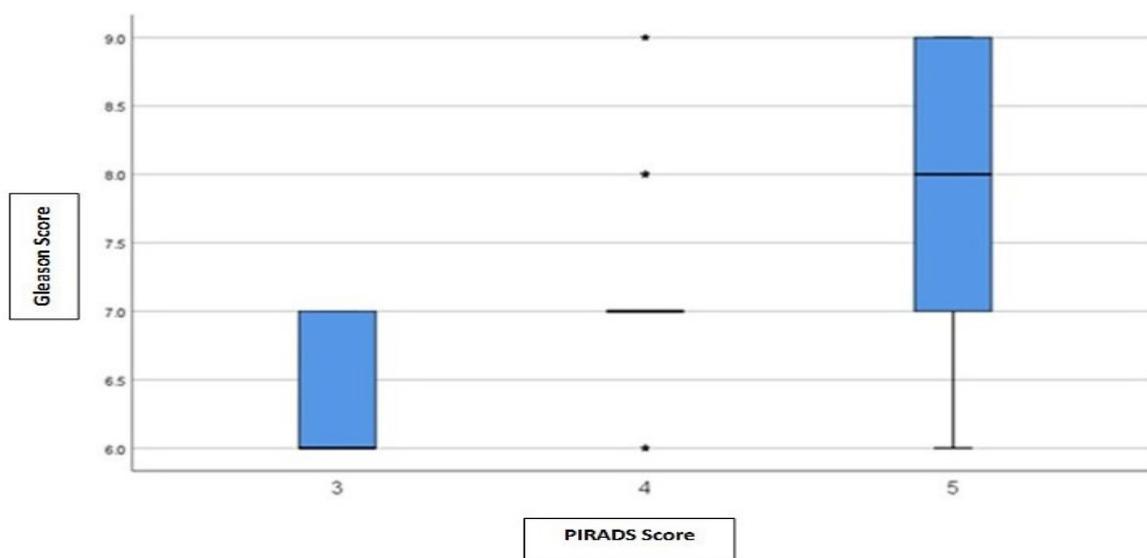
### Study Population

919 patients who underwent radical prostatectomy at a third step urology department between January 2012 and June 2018 were included. Retropubic radical prostatectomy or transperitoneal robot-assisted laparoscopic radical prostatectomy (da Vinci Si System, IntuitiveSurgical®) was performed. Patients who had not undergone mpMRI and had not been recorded according to PIRADS v2 and those who had previously

received radiotherapy and/or hormonotherapy for PCa were excluded.

### Procedures

Gleason scores, lesion localization, capsule invasion, extraprostatic extension, peripheral surgical margin status, seminal vesicle invasion, lymph node involvement, and ISUP grade were evaluated by an experienced uro-pathologist. PIRADS scores, lesion localization, lymph node involvement, capsule invasion, seminal vesicle invasion, and ADC scores of lesions were evaluated by an experienced uro-radiologist. Age and pre-operative PSA data were collected retrospectively from patient files. The Gleason score and ISUP grading were assigned according to the decisions of the international urological pathology consensus conference on the Gleason grading of PCa in 2014. PIRADS scores were assigned ac-



**Figure 2.** Distribution of Gleason scores according to PIRADS scores of lesions

**Table 1.** Demographic, preoperative, perioperative, and histopathologic data for groups 1 and 2

Variables (n = 93)	Number (%)
<b>Seminal Vesicle Invasion (Pathology)</b>	
Positive	14 (15.1%)
Negative	79 (84.9%)
<b>Seminal Vesicle Invasion (MpMRI)</b>	
Positive	15 (16.1%)
Negative	78 (83.9%)
<b>Capsule Invasion (Pathology)</b>	
Positive	20 (21.5%)
Negative	73 (78.5%)
<b>Capsule Invasion (MpMRI)</b>	
Positive	52 (55.9%)
Negative	41 (44.1%)
<b>Lymph Node Involvement (Pathology)</b>	
Positive	8 (8.6%)
Negative	85 (91.4%)
<b>Lymph Node Involvement (MpMRI)</b>	
Positive	7 (7.5%)
Negative	86 (92.5%)
<b>Neurovascular Bundle Invasion (MpMRI)</b>	
Positive	46 (49.5%)
Negative	47 (50.5%)
<b>Extraprostatic Extension (Pathology)</b>	
Positive	40 (43%)
Negative	53 (57%)
<b>Peripheral Surgical Margin (Pathology)</b>	
Positive	20 (21.5%)
Negative	73 (78.5%)
<b>Operation Type</b>	
RRP	43 (46.2%)
RALRP	50 (53.8%)
<b>Gleason Score</b>	<b>n = 248</b>
(3 + 3) 6/10	22 (8.8%)
(3 + 4) 7/10	94 (37.9%)
(4 + 3) 7/10	63 (25.4%)
(4 + 3,5) 7/10	4 (1.6%)
(4 + 4) 8/10	28 (11.2%)
(4 + 4,5) 8/10	5 (2%)
(4 + 5) 9/10	26 (10.4%)
(5 + 4) 9/10	6 (2.4%)
<b>Grade Group (ISUP 2014)</b>	<b>n = 248</b>
1	22 (8.4%)
2	95 (36.4%)
3	66 (25.3%)
4	33 (12.6%)
5	32 (12.3%)
<b>PIRADS Score</b>	<b>n = 161</b>
3	7 (4.3%)
4	66 (41%)
5	88 (54.7%)

**Abbreviations:** MpMRI, Multiparametric prostate magnetic resonance imaging; RRP, Retropubic radical prostatectomy; RALRP, Robot assisted laparoscopic radical prostatectomy; PSA, Prostate specific antigen; ISUP, International society of urological pathology.

according to PIRADSV2. Permission was obtained from all patients for the availability of preoperative data. Ethics committee approval was received (decision number: 18-10.1/7). During the study, the principles of the Declaration of Helsinki were followed and confidentiality of the data was ensured.

### Evaluations

Histopathological correlation of suspicious foci detected in mpMRI and radiological correlation of foci detected in pathology was analyzed. Histopathological confirmation of seminal vesicle invasion, capsule invasion, and lymph node involvement detected in mpMRI was analyzed. The relationship between ADC value and ISUP grade group was analyzed. The relationship between PIRADS score with Gleason score and PIRADS

score with ISUP grade group was analyzed.

### Statistical analysis

Statistical analysis was performed using SPSS for Windows 22.0. Chi-square, ANOVA, McNemar, Kappa, Mann-Whitney-U, Kruskal-Wallis, and logistic regression tests were used for statistical analysis.  $P < 0.05$  was considered statistically significant.

## RESULTS

The mean age of patients was  $65.38 \pm 6.814$ , and the median pre-op PSA value was 8 ng/mL and the interquartile range of pre-op PSA was 10.935 ng/mL.

MpMRI and histopathologic data of the patients are shown in **Table 1**.

One hundred and fifty one (92.07%) of 164 lesions detected in mpMRIs of 93 patients were confirmed with radical prostatectomy specimens. 151 (60.88%) of 248 lesions detected by a pathologist were confirmed by a radiologist.

We investigated the histopathological correlation of patients with seminal vesicle invasion, capsule invasion, and lymph node involvement in mpMRI. Both methods were shown to be significantly similar in detecting seminal vesicle invasion and lymph node involvement. Histopathological correlation of patients with seminal vesicle invasion, capsule invasion, and lymph node involvement in mpMRI is shown in **Table 2**.

We found a negative correlation between ADC value and ISUP 2014 groups using ANOVA test. We determined that the ADC value decreased as the ISUP grade group increased. ( $P < 0.001$ ) Spearman's rho correlation coefficient was 0.432.

The relationship between ADC value and ISUP 2014 grade group is shown in **Figure 1**.

A positive correlation was found between PIRADS score and Gleason score with Kruskal Wallis test. ( $P < 0.001$ ) Spearman's rho correlation coefficient was 0.449. We showed that with using Bonferroni correction for multiple comparisons, the difference between PIRADS 3 and 4 was not significant ( $P .073$ ), while the difference between PIRADS 3 and 5 ( $P < 0.001$ ), and PIRADS 4 and 5 ( $P < 0.001$ ) were statistically significant. **Figure 2** shows the distribution of Gleason score according to PIRADS scores of lesions.

## DISCUSSION

There are studies investigating the rate of accurate diagnosis of PCa by taking random transrectal ultrasound (TRUS) guided biopsy, transperineal template prostate mapping biopsy, MRI-targeted TRUS biopsy, and radical prostatectomy specimen histopathology as the standard reference diagnostic method<sup>(8-10,15)</sup>. The general opinion is that radical prostatectomy histopathology is the most valid reference standard. In our study, the radical prostatectomy specimen was accepted as the reference.

With the emerging role of mpMRI, the current paradigm of PCa staging is changing, with greater emphasis on the inclusion of mpMRI in clinical staging<sup>(6)</sup>. Before definitive treatment, staging can be performed with mpMRI. Significant staging data may be obtained with mpMRI to guide definitive treatment. Using mpMRI may improve surgical, oncological, and functional management<sup>(7)</sup>.

Loggitsi et al. reported 53% sensitivity and 90.3% specificity for mpMRI by taking radical prostatectomy his-

**Table 2.** Histopathological Correlation of Patients with Seminal Vesicle Invasion, Capsule Invasion and Lymph Node Involvement in mpMRI.

Variables <sup>a</sup>	Histopathologic Correlation	Kappa Value	P-value
Seminal Vesicle Invasion	12 of 15 (80%)	.796	< 0.01
Capsule Invasion	15 of 52 (28.8%)	.154	.052
Lymph Node Involvement	3 of 7 (42.9%)	.348	.001

<sup>a</sup>Variables were compared by Mc Nemar test

topathology as a reference<sup>(8)</sup>. Lee et al. reported 46% sensitivity for mpMRI and 77.7% specificity for index lesions using radical prostatectomy histopathology as a reference for detecting clinically significant PCa<sup>(9)</sup>. In our study, PIRADS score  $\geq 3$  lesions in mpMRI were reported in 151 (60.9%) of a total of 248 foci with cancer detected by pathology. This may be due to the smaller size of these foci or the presence of well differentiated tumors. The diagnostic value of MRI decreases in lesions  $< 5$  mL and poorly differentiated tumors are more easily detected by MRI. In the study of Radtke et al., the cancer detection rate of mpMRI was significantly increased in lesions with a Gleason score  $\geq 3+4$  7/10 and tumor volume of  $\geq 0.55$  mL<sup>(10)</sup>. Tumor was confirmed histopathologically in 151 (92.07%) of 164 foci with PIRADS score  $\geq 3$  lesions reported in mpMRI. Since our study was a correlation study, there were no false positive results of pathology. Therefore, specificity could not be calculated. The sensitivity was 60.9%. Bonekamp et al. reported that clinically significant cancer was detected in 97% of the foci with a PIRADS score  $\geq 3$  in mpMRI by mpMRI targeted biopsy<sup>(11)</sup>. They also reported that only 18% of foci detected by mpMRI were false. In our study, the rate of cancer in foci indicated by mpMRI was 92.07%. In addition, 97 of 248 foci (39.1%) reported by pathology could not be detected by mpMRI. The difference may be due to the use of MRI biopsy like in the study of Bonekamp et al. Ruprecht et al. reported 77.78% sensitivity and 92.86% specificity for histopathological confirmation of seminal vesicle invasion in mpMRI<sup>(12)</sup>. In our study, 85% sensitivity and 96% specificity were detected. This difference may be due to the fact that radiologist interpreting mpMRIs in our study is experienced and 3 Tesla MRI was used in our study.

For the confirmation of extraprostatic extension in mpMRI by pathology, in a meta-analysis conducted by Salerno et al, 50% sensitivity and 85% specificity have been reported for extraprostatic extension in mpMRI<sup>(13)</sup>. Similar to these meta-analysis data, we found 49.3% sensitivity and 75% specificity in our study.

In the study of VonBelow et al. on confirmation of lymph node invasion detected by MpMRI, they reported 55% sensitivity, 90% specificity, and 75% accuracy for lymph node involvement in mpMRI<sup>(14)</sup>. In our study, 37.5% sensitivity and 95% specificity were detected. The difference may be fact that all patients have undergone extended lymph node dissection and included patients with moderate to high-risk PCa only by Von-Below. In our study, extended lymph node dissection was not performed in all patients and low-risk patients were also included.

In the study of Gaur et al., a negative correlation was found between ADC values and ISUP grade group. In the same study, a negative correlation was also found between PIRADS scores and ADC values<sup>(15)</sup>. In our

study, a negative correlation was found between ADC values and ISUP grade groups in accordance with the literature.

In the study of John et al. On the probability of detecting clinically significant PCa with increasing PIRADS score; 11.1% of patients with PIRADS 3 lesions, 42.9% of patients with PIRADS 4 lesions, and 35.6% of patients with PIRADS 5 lesions were clinically significant (ISUP grade group  $\geq 2$ )<sup>(16)</sup>. In our study, clinically significant PCa was detected in 42.3% of PIRADS 3 lesions, 91.8% of PIRADS 4 lesions, and 98.8% of PIRADS 5 lesions. The difference was due to the fact that the patients in our study were previously diagnosed with TRUS biopsy and radical prostatectomy was performed and TRUS/MRI cognitive fusion biopsy was performed in patients without a previous diagnosis in the study of John et al. Similar results have been obtained in other studies; mpMRI findings were correlated with biopsy results and PIRADS score was correlated with ISUP grade group and Gleason score<sup>(17,18)</sup>.

The limitations of our study are its retrospective manner and the low number of patients because of recent utilization of mpMRI in our institute.

## CONCLUSIONS

Based on these results, we concluded that the rate of malignancy diagnosis was found to be very high in the lesions reported as mpMRI was likely malignant (PI-RADS score  $\geq 3$ ). On the other hand, almost 40% of the malign foci could not be detected by mpMRI. As the experience and knowledge of radiologists and mpMRI technique, equipment, PIRADS scoring system improve, the diagnostic ability and objectivity of the test will increase. As the staging accuracy in mpMRI improves, treatment planning or the priority of the patients may change. There may also be decision changes including the operating methods and techniques. The role of mpMRI in the diagnosis of PCa can be better demonstrated with prospective studies including larger patient populations.

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## CONFLICT OF INTEREST

The authors report no conflict of interest.

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