**Running head:** Correlation of mpMRI and prostate histopathology

# Multiparametric Prostate Magnetic Resonance Imaging before Radical Prostatectomy: Can IT Predict Histopathology?

Mehmet Sahin[1*], Fuat Kizilay[1], Ezgi Guler[2], Banu Sarsik[3], Mustafa Harman[2], Serdar Kalemci[1], Adnan Simsir[1], Ibrahim Cureklibatir[1]

1 Departmentof Urology, Ege University Hospital, Izmir 35100, Turkey

2 Department of Radiology, Ege University Hospital, Izmir 35100, Turkey

3 Department of Pathology, Ege University Hospital, Izmir 35100, Turkey

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## ABSTRACT

**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 underwent radical prostatectomy and had preoperative mpMRI were examined. Age and pre-operative Prostate-Specific Antigen value 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.

## 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 [(1)]. However, PCa is the second most common cause of cancer death in men [(2)].

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 [3]. In 2014 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 [4].

Magnetic Resonance Imaging (MRI) has been used for non-invasive assessment of 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 development of multiparametric MRI (mpMRI) which combines T2 weighted imaging with functional and physicological evaluation through techniques such as difusion weighted imaging (DWI), and its variations like difusion 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 [5]. 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 [5].

PIRADS v2 segmentation model is adapted from the European Consensus Meeting and the ESUR 2012 Prostate MRI Guidelines [5]. 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 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 evaluated by an experienced uropathologist. PIRADS scores, lesion localization, lymph node involvement, capsule invasion, seminal vesicle invasion and ADC scores of lesions evaluated by an experienced uroradiologist. 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 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 were analyzed. Histopathological confirmation of seminal vesicle invasion, capsule invasion and lymph node involvement detected in mpMRI were analyzed. The relationship between ADC value and ISUP grade group were analyzed. The relationship between PIRADS score with Gleason score and PIRADS score with ISUP grade group were 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 ± 6,814, and the median pre-op PSA value was 8 ng/mL and 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 specimen. 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 with 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 multipl tests, the difference between PIRADS 3 and 4 was not significant ($P$ .073), PIRADS 3 and 5 ($P< 0.001$) and PIRADS 4 and 5 ($P < 0.001$) were significant. **Figure 2** shows 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 [8-10,15]. General opinion is that radical prostatectomy histopathology is the most valid reference standard. In our study, 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 [6]. 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, oncologic and functional management [7].

Loggitsi et al reported 53% sensitivity and 90.3% specificity for mpMRI by taking radical prostatectomy histopathology as a reference [8]. 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 [9]. In our study, PIRADS score ≥ 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 well differentiated tumors. 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 gleason score ≥ 3+4 7/10 and tumor volume ≥ 0.55 mL [10]. Tumor was confirmed histopathologically in 151 (92.07%) of 164 foci with PIRADS score ≥ 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 ≥ 3 in mpMRI by mpMRI targeted biopsy [11]. 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 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 [12]. 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 [13]. 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 [14]. 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 VonBelow. 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 [15]. 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 about 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, 35.6% of patients with PIRADS 5 lesions were clinically significant (ISUP grade group $\geq$ 2) [16]. 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 [17,18].

The limitations of our study are its retrospective manner and low number of patients because of recently 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 malign (PIRADS 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 improves, the diagnostic ability and objectivity of the test will increase. As the staging accuracy in mpMRI improves, treatment planning or 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.

## ACKNOWLEDGEMENT

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## CONFLICT OF INTEREST

The authors report no conflict of interest.

## REFERENCES

1. Boyle P, Ferlay J. Cancer incidence and mortality in Europe 2004. Ann Oncol 2005 Mar;16:481-8.

2. Jemal A, Siegel R, Ward E et al. Cancer statistics, 2008. CA Cancer J Clin 2008 Mar-Apr;58:71-96.

3. Gleason DF: Classification of prostatic carcinomas. Cancer Chemother Rep 1966, 50:125-8

4. Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of Grading Patterns and Proposal for a New Grading System. Am J Surg Pathol. 2016 Feb;40:244-52.

5. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging - Reporting and Data System: 2015, Version 2. Eur Urol. 2016 Jan;69:16-40.

6. Gupta RT, Faridi KF, Singh AA, et al. Comparing 3-T multiparametric MR Imaging and the Partin tables to predict organ-confined prostate cancer after radical prostatectomy. Urol Oncol 2014 Nov;32:1292-9.

7. Sciarra A, Barentsz J, Bjartell A, et al. Advances in Magnetic Resonance Imaging: How They Are Changing the Management of Prostate Cancer. Eur Urol. 2011 Jun;59:962-77.

8. Loggitsi D, Gyftopoulos A, Economopoulos N et al. Multiparametric Magnetic Resonance Imaging of the Prostate for Tumour Detection and Local Staging: Imaging in 1.5T and Histopathologic Correlation. Can Assoc Radiol J. 2017 Nov;68:379-86.

9. Chan Ho Lee, Ja Yoon Ku, Won Young Park, Nam Kyung Lee, Hong Koo Ha. Comparison of the accuracy of multiparametric magnetic resonance imaging (mpMRI) results with the final pathology findings for radical prostatectomy specimens in the detection of prostate cancer. Asia Pac J Clin Oncol. 2019 Apr; 15:20-7.

10. Radtke JP, Schwab C, Wolf MB, et al. Multiparametric Magnetic Resonance Imaging (MRI) and MRI-Transrectal Ultrasound Fusion Biopsy for Index Tumor Detection: Correlation with Radical Prostatectomy Specimen. Eur Urol. 2016 Nov;70:846-53.

11. Bonekamp D, Schelb P, Wiesenfarth M, et al. Histopathological to multiparametric MRI spatial mapping of extended systematic sextant and MR/TRUS-fusion-targeted biopsy of the prostate. Eur Radiol. 2019 Apr;29:1820-30.

12. Oliver Ruprecht, Philipp Weisser, Boris Bodelle, Hanns Ackermann, Thomas J Vogl. MRI of the prostate: interobserver agreement compared with histopathologic outcome after radical prostatectomy. Eur J Radiol. 2012 Mar;81:456-60.

13. Salerno J, Finelli A, Morash C, et al. Multiparametric magnetic resonance imaging for pre-treatment local staging of prostate cancer: A Cancer Care Ontario clinical practice guideline. Can Urol Assoc J. 2016 Sep-Oct;10:332-9.

14. Von Below C, Daouacher G, Wassberg C et al. Validation of 3 T MRI including diffusion-weighted imaging for nodal staging of newly diagnosed intermediate- and high-risk prostate cancer. Clin Radiol 2016 Apr;71:328-34.

15. Gaur S, Harmon S, Rosenblum L, et al. Can Apparent Diffusion Coefficient Values Assist PI-RADS Version 2 DWI Scoring? A Correlation Study Using the PI-RADSv2 and International Society of Urological Pathology Systems. AJR Am J Roentgenol. 2018 Jul;211:33-41.

16. John S, Cooper S, Breau RH, et al. Multiparametric magnetic resonance imaging - Transrectal ultrasound-guided cognitive fusion biopsy of the prostate: Clinically significant cancer detection rates stratified by the Prostate Imaging and Data Reporting System version 2 assessment category. Can Urol Assoc J. 2018 Jun 19;12:401-6.

17. Hofbauer SL, Maxeiner A, Kittner B, et al. Validation of Prostate Imaging Reporting and Data System Version 2 for the Detection of Prostate Cancer. J Urol. 2018 Oct;200:767-73.

18. Mehralivand S, Bednarova S, Shih JH, et al. Prospective Evaluation of PI-RADS™ Version 2 Using the International Society of Urological Pathology Prostate Cancer Grade Group System. J Urol. 2017 Sep;198:583-90.

*Corresponding author:

Mehmet Sahin, MD

Department of Urology, Ege University School of Medicine, Izmir 35100, Turkey

Tel: +90 505 900 57 02 Fax: + 90 (232) 374 65 52 E-mail: dr.mehmetsahin@hotmail.com

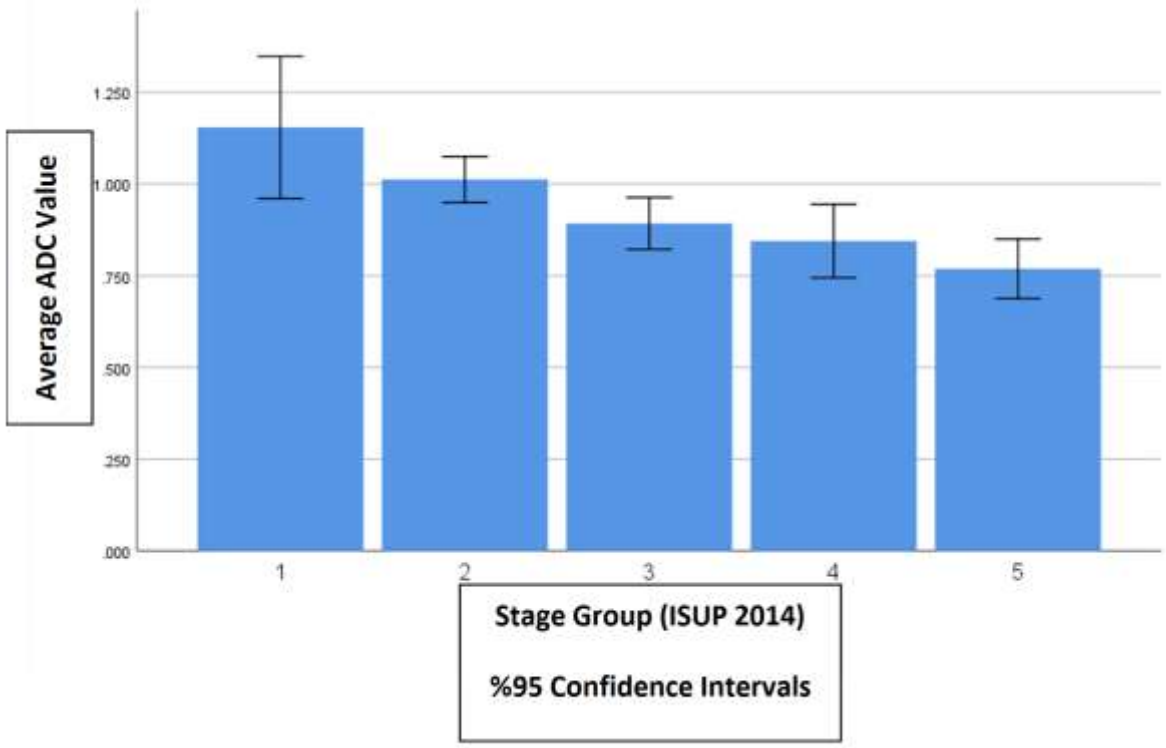


Figure 1: Distribution of average ADC values by grade group

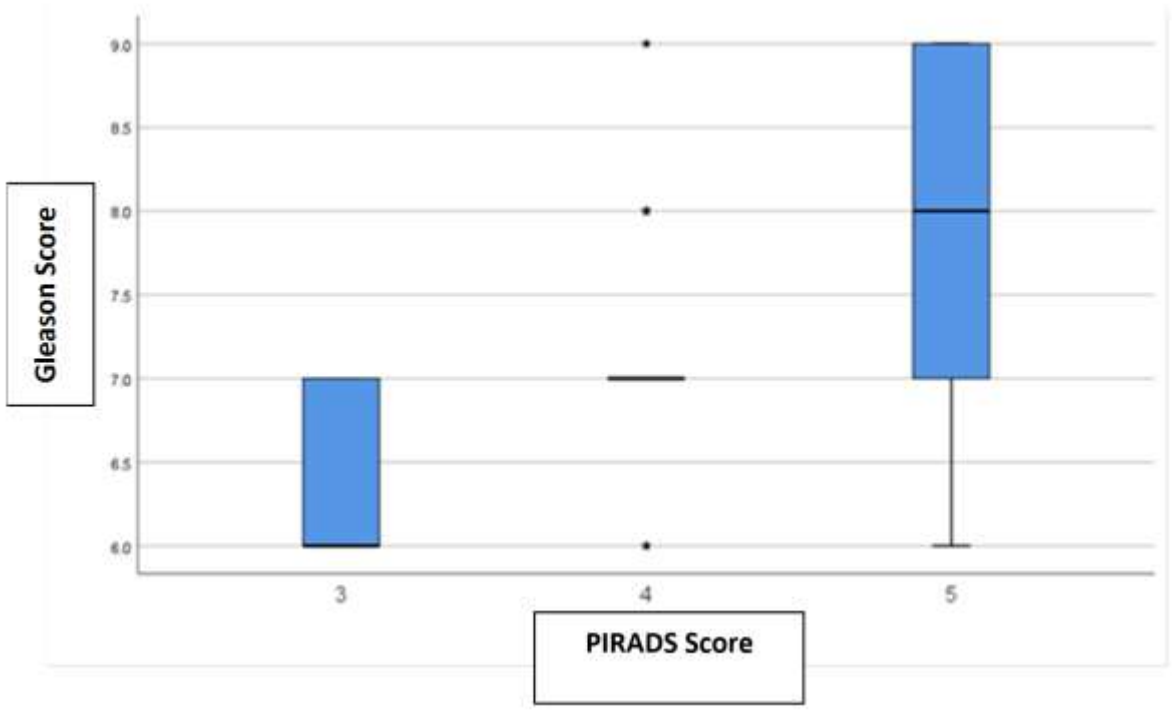


Figure 2: Distribution of Gleason scores according to PIRADS scores of lesions

**Table 1. Clinical, mpMRI and Histopathological Data of the Patients**

| Variables (n = 93) | Number (%) |
|---|---|
| **Seminal Vesicle Invasion (Pathology)** | |
| **Positive** | 14 (15.1%) |
| **Negative** | 79 (84.9%) |
| **Seminal Vesicle Invasion (MpMRI)** | |
| **Positive** | 15 (16.1%) |
| **Negative** | 78 (83.9%) |
| **Capsule Invasion (Pathology)** | |
| **Positive** | 20 (21.5%) |
| **Negative** | 73 (78.5%) |
| **Capsule Invasion (MpMRI)** | |
| **Positive** | 52 (55.9%) |
| **Negative** | 41 (44.1%) |
| **Lymph Node Involvement (Pathology)** | |
| **Positive** | 8 (8.6%) |
| **Negative** | 85 (91.4%) |
| **Lymph Node Involvement (MpMRI)** | |
| **Positive** | 7 (7.5%) |
| **Negative** | 86 (92.5%) |
| **Neurovascular Bundle Invasion (MpMRI)** | |

| | |
|---|---|
| **Positive** | 46 (49.5%) |
| **Negative** | 47 (50.5%) |
| **Extraprostatic Extension (Pathology)** | |
| **Positive** | 40 (43%) |
| **Negative** | 53 (57%) |
| **Peripheral Surgical Margin (Pathology)** | |
| **Positive** | 20 (21.5%) |
| **Negative** | 73 (78.5%) |
| **Operation Type** | |
| **RRP** | 43 (46.2%) |
| **RALRP** | 50 (53.8%) |
| **Gleason Score** | **n = 248** |
| **(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%) |
| **Grade Group (ISUP 2014)** | **n = 248** |
| **1** | 22 (8.4%) |
| **2** | 95 (36.4%) |
| **3** | 66 (25.3%) |
| **4** | 33 (12.6%) |
| **5** | 32 (12.3%) |
| **PIRADS Score** | **n = 161** |
| **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 spesific antigen; ISUP, International society of urological pathology.

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

| Variables[a] | 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 |

[a] Variables were compared by Mc Nemar test