

## The predictive role of MRI cognitive biopsy for gleason score on radical prostatectomy material

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### Abstract

Enhancements in the concordance between prostate biopsy results and radical prostatectomy (RP) specimens are expected to improve both oncological and functional outcomes for patients. This study aimed to assess the level of agreement in Gleason scores between biopsy specimens and RP materials in individuals who underwent magnetic resonance imaging (MRI) cognitive + systematic biopsy or only systematic biopsy. 73 patients who underwent RP between November 2015 and November 2017 were included in the study. Four patients who received chemotherapy before RP were excluded from the study. While MRI cognitive+systematic biopsy was performed in 38 patients, only systematic biopsy was performed in 31 patients. In the last stage, histopathological results of MRI cognitive + systematic biopsy, only systematic biopsy and RP specimens were compared retrospectively. When compared according to RP results, Gleason score was decreased in 5 (13.2%) of 38 patients who underwent MRI cognitive + systematic biopsy, did not change in 22 patients (57.9%) and was increased in 11 (28.9%) patients. Of the 31 patients who underwent only systematic biopsy, Gleason score decreased in 2 patients (6.5%), remained unchanged in 10 patients (32.3%), and increased in 19 patients (61.3%). Statistically significant difference was found between those who underwent MRI cognitive+systematic biopsy and those who only underwent systematic biopsy in terms Gleason score concordance according to the RP result ( $p=0.026$ ). Gleason grade of tumors after RP can be more accurately predicted with MRI cognitive + systematic biopsy. Thus, surgical success may increase (necessity of lymph node dissection, etc.). For this reason, we think that MRI cognitive + systematic biopsy should be performed in patients with suspected PCa.

**Keywords:** prostate cancer, prostate biopsy, MRI cognitive biopsy, radical prostatectomy

### 1. Introduction

Prostate cancer (PCa) is the second most common malignancy diagnosed in men in the world (1). For many years, trans-rectal ultrasonography (TRUS) guided prostate biopsies (TRUSG-Bx) have been used most frequently as a diagnostic tool in patients with suspected PCa. However, the diagnostic efficiency of systematic 10-12 core biopsy, currently accepted as the standard in primary care, is limited in diagnosing PCa. Despite the developments in biopsy technique over time, it is possible to miss a tumor that is present in 20-25% of patients or to define clinically important prostate cancers as low risk due to insufficient sampling. Reasons such as difficult-to-diagnose cases and false negativity have brought along alternative diagnostic methods with the developing technology.

Recent developments in the field of multiparametric magnetic resonance imaging (mpMRI) have provided the opportunity to evaluate the detailed structure of the prostate

and subsequent research has shown that the accuracy of diagnosis and staging of prostate cancer can be improved (2, 3). After adapting the valuable information obtained by mpMRI to prostate biopsy, the usage method to enhance the quality of prostate biopsy has also been developed. Today, MR-targeted biopsies are applied in three ways in the clinic: 1. MR cognitive biopsy (correlation of the lesion detected with mpMRI with TRUSG and biopsy from that area). 2. MRI/TRUSG fusion biopsy 3. Direct MRI-guided (in-bore) biopsy. Studies have demonstrated that all of these biopsy methods produce comparable outcomes in identifying clinically significant prostate cancer (4, 5). Concomitant standard biopsies are nevertheless advised because of the potential of overlooking specific areas of interest and the possibility of large false-negative outcomes with mpMRI (6). Combining routine biopsy and MR-targeted biopsies provides convincing proof for improved identification of clinically

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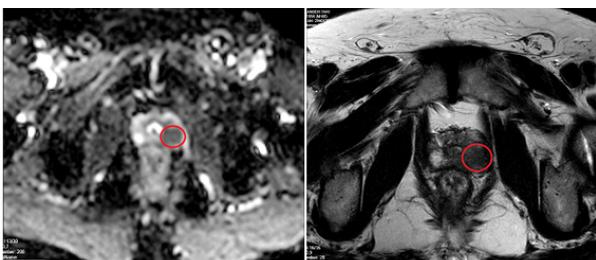
significant PCa (7-10).

The Gleason score remains a highly valuable prognostic marker and is crucial in identifying the optimal treatment option. The Gleason score is crucial in assessing the necessity of lymph node dissection and preserving postoperative potency in PCa surgeries (11). It also influences concordance with the nerve-sparing procedure. Enhancements in the concordance between prostate biopsy results and radical prostatectomy (RP) specimens are expected to improve both oncological and functional outcomes for patients. This study aimed to assess the level of agreement in Gleason scores between biopsy specimens and RP materials in individuals who underwent MR cognitive + systematic biopsy or only systematic biopsy.

**2. Material and Method**

A total of 296 patients who presented with abnormal serum prostate-specific antigen (PSA) levels and/or positive examination findings in favor of PCa were subjected to prostate biopsy at our clinic between November 2015 and November 2017, with the guidance of TRUSG. All patients with suspected PCa and no contraindications for MRI underwent mpMRI prior to biopsy.

In Bauer et al.'s study, a biopsy scheme involving 10 cores (sextant + 4 focal peripheral) was used in all patients. In addition to this, a minimum of 2 and a maximum of 4 biopsy samples (MR cognitive biopsy) were taken from suspicious areas identified in mpMRI. This was done in a total of 199 patients, alongside the systematic 10 core biopsy scheme. Please refer to Fig. 1. and Fig. 2. for visual representation. A total of 73 individuals diagnosed with localized or locally progressed prostate cancer by biopsy had RP and were included in the study. Chemotherapy was applied to 4 (5.5%) of 73 patients who underwent RP before surgery. These patients were excluded from further analysis. In the last stage, histopathological results of MR cognitive + systematic biopsy specimens, only systematic biopsy specimens and RP specimens were compared retrospectively.



**Fig.1.** mpMRI image of PIRADS score V lesion

MpMRI was performed in Ondokuz Mayıs University Medical Faculty Hospital, Department of Radiology, using a Philips Ingenia MRI device with 3 Tesla field strength. After MRI, images were recorded in the PACS (Picture Archiving Communication Systems) system and evaluated by a radiologist experienced in abdominal imaging. The sequence and parameters used in MpMRI were optimized in accordance with the Prostate Imaging Reporting and Data System 2nd

edition (PI-RADS v2) manual. BK Medical Pro Focus 2202 model ultrasonography device was used in the biopsy procedure, and a 12 MHz bi-planar probe was used as the rectal probe. The materials' histopathological examination was performed at our hospital's pathology department.



**Fig. 2.** TRUSG image of PIRADS score V lesion

Research data were evaluated through “SPSS (Statistical Package for Social Sciences) for Windows 22.0 (SPSS Inc, Chicago, IL)”. Descriptive statistics were presented as median (minimum-maximum), frequency distribution, and percentage. Pearson chi-square test was used to evaluate categorical variables.

The study commenced after obtaining approval from our Clinical Research Ethics Council. The date of the ethics committee's decision is November 30, 2017, and the reference number for the committee's decision is 2017/405.

**3. Results**

Chemotherapy was applied prior to RP in 4 (5.5%) of 73 patients who underwent RP. These patients were excluded from further analysis. Some descriptive and clinical features of the patients who underwent RP are shown in Table 1.

**Table 1.** General characteristics and histopathological examination results of patients undergoing RP

	(n= 69)
<b>Age (years), median (min-max)</b>	65 (47-78)
<b>Serum PSA (ng/ml), median (min-max)</b>	7 (2.8-119.0)
<b>Prostate Volume (cc), median (min-max)</b>	42 (18-124)
<b>Tumor Volume (cc), median (min-max)</b>	2.9 (0.2-38.2)
<b>PIRADS, n (%)</b>	
II	1 (1.4)
III	9 (13.0)
IV	36 (52.2)
V	23 (33.3)
<b>TRUSG-Bx Pathology Gleason Score, n (%)</b>	
6	28 (40.6)
7a	25 (36.2)
7b	12 (17.4)
8	3 (4.3)
9	1 (1.4)
<b>RP Pathology Gleason Score, n (%)</b>	
6	7 (10.1)
7a	41 (59.4)
7b	19 (27.5)
8	1 (1.4)
9	1 (1.4)
<b>According to Epstein Criteria, n (%)</b>	
Clinically significant	58 (84.1)
Clinically insignificant	11 (15.9)

n: Number of patients; %: Percentage

The distribution of RP pathology Gleason scores according to TRUSG-Bx pathology Gleason score in patients who underwent MR cognitive + systematic biopsy, and only systematic biopsy are presented in Table 2.

The distribution of the change in the Gleason score between the patients who underwent MR cognitive + systematic biopsy and those who only underwent systematic biopsy is shown in Table-3. The Gleason score reduced in 13.2% of the 38 patients

who received MRI cognitive + systematic biopsy, remained unchanged in 57.9% and increased in 28.9%. Of the 31 patients who underwent only systematic biopsy, Gleason score decreased in 2 patients (6.5%), remained unchanged in 10 patients (32.3%), and increased in 19 patients (61.3%). A statistically significant difference was found between those who underwent MRI cognitive + systematic biopsy and those who only underwent systematic biopsy in terms of Gleason score concordance according to the RP result (p=0.026).

**Table 2.** Distribution of RP pathology Gleason scores according to TRUSG-Bx pathology Gleason score in patients with MR cognitive + systematic biopsy and only systematic biopsy

	Radical Prostatectomy Pathology Gleason Score					Total n (%*)
	6 n (%)	7a n (%)	7b n (%)	8 n (%)	9 n (%)	
<b>TRUSG-Bx Pathology Gleason Score</b>						
<b>MRI Cognitive + Systematic Biopsy (n=38)</b>	6	2 (25.0)	5 (62.5)	1 (12.5)	0	8 (21.1)
	7a	1 (5.9)	12 (70.6)	4 (23.5)	0	17 (44.7)
	7b	0	1 (10.0)	8 (80.0)	0	10 (26.3)
	8	0	1 (33.3)	2 (66.7)	0	3 (7.9)
	9	0	0	0	0	0
	Total	3 (7.9)	19 (50.0)	15 (39.5)	0	1 (2.6)
<b>TRUSG-Bx Pathology Gleason Score</b>						
<b>Only Systematic Biopsy (n=31)</b>	6	4 (20.0)	16 (80.0)	0	0	20 (64.5)
	7a	0	5 (62.5)	2 (25.0)	1 (12.5)	8 (25.8)
	7b	0	1 (50.0)	1 (50.0)	0	2 (6.5)
	8	0	0	0	0	0
	9	0	0	1 (100)	0	1 (3.2)
	Total	4 (12.9)	22 (71.0)	4 (12.9)	1 (3.2)	0

n: Number of patients; %: Row Percentage; \*%: Column percentage

**Table 3.** The change in the Gleason score between the patients, to whom RP was applied, who underwent MRI cognitive + systematic biopsy and those who only underwent systematic biopsy

Change in Gleason Score	MRI Cognitive + Systematic Biopsy (n=38)	Only Systematic Biopsy (n=31)	p
	n (%)	n (%)	
Decreased	5 (13.2)	2 (6.5)	<b>0.026</b>
Not change	22 (57.9)	10 (32.3)	
Increased	11 (28.9)	19 (61.3)	

n: Number of patients; %: Column percentage

**4. Discussion**

In our study, we found a significant difference when we compared MR cognitive + systematic biopsy and only systematic biopsy in terms of concordance in RP histopathology results (57.9% 32.3%). In this study, we found that systematic biopsy combined with MR cognitive biopsy outperformed systematic biopsy alone in the investigation of patients with clinically suspected PCa.

Literature indicates that mpMRI is superior to standard TRUSG-guided standard 12-core biopsy in detecting clinically significant PCa. The PRECISION study demonstrated that incorporating an MRI prior to biopsy increased the ability to

detect clinically significant prostate cancer in a smaller number of patients, regardless of whether an MRI-targeted biopsy was performed or not (12). Numerous studies have demonstrated that MRI-targeted biopsy exhibits a higher rate of detecting clinically relevant PCa and is more compatible with histopathology results from RP compared to standard biopsy (13-15). The current EAU guideline recommends mpMRI before biopsy in men with suspected PCa due to elevated PSA and abnormal digital rectal examination findings (6). The results of the present study confirmed the diagnostic effectiveness of MRI before biopsy in patients with clinically suspected PCa. Diamond et al. proposed a comparable

agreement in RP histology between standard biopsy and MRI-targeted biopsy, ranging from 49.4% to 51.2% (16). Diamond et al. conducted a comprehensive retrospective analysis involving 443 individuals with favorable MRI results and MRI fusion biopsy. The study aimed to examine the histology of prostate tissue obtained using MRI fusion biopsy, standard biopsy, and a combination of MRI fusion and standard biopsy. Concordance between standard biopsy, MRI fusion biopsy, and MRI fusion + standard biopsy was 49.4%, 51.2%, and 63.2%, respectively, according to ISUP grade. This article has also shown that when standard biopsy is performed with fusion biopsy, it significantly improves histological concordance with RP (16).

Comparing MRI cognitive biopsy and MRI/TRUS fusion biopsy, Puech et al. found no difference in cancer detection rate (17). Wysock et al. showed that the overall cancer detection rate was comparable across the described biopsy techniques (18). Nevertheless, both investigations had limitations as they did not incorporate RP samples as a standard component. These data demonstrate that the MRI cognitive biopsy technique is equivalent to other techniques in accurately predicting the histological grade of RP. MRI -targeted biopsy diagnosis fewer number of ISUP grade 1 compared to standard biopsy. In our study, only 64.5% (n:20) of the cases with systematic biopsy and 21.1% (n:8) of cases with MRI cognitive + systematic biopsy was defined as clinically insignificant PCa. Systematic biopsy diagnoses clinically insignificant prostate cancers more frequently compared to MRI cognitive + systematic biopsy.

There are also concerns about the significance of performing a standard biopsy at the same time as an MRI target biopsy, considering that the latter should accurately biopsy the main lesion and accurately predict the final histology of the prostate after RP. The utilization of standard biopsy techniques may yield a diagnosis of PCa that lacks clinical significance, hence resulting in unnecessary therapy or the implementation of expensive and intrusive active surveillance programs. Recent extensive, collaborative investigations have investigated the effectiveness of doing standard biopsies simultaneously to predict the final histology of radical prostatectomy in patients with favorable MRI results. These studies showed a notable enhancement in grading agreement after including standard biopsy. (7, 8, 16). Ploussard et al. included 478 patients who underwent RP and showed that the concordance rate between MRI-targeted biopsy pathology and RP pathology was 45.2%, while the concordance rate between MRI-targeted biopsy + systematic biopsy and RP pathology was 51.7%. They found that grade-group concordance between biopsy and final RP histology was improved by adding systematic biopsy to MRI-targeted biopsy (7). Considering these findings and our study, it is seen that the final RP histology and MRI targeted + systematic biopsy are similar. Ryan et al. performed a standard biopsy and MRI cognitive biopsy on 115 patients before RP. They evaluated the

agreement between biopsy and RP histologies. The concordance rates between standard biopsy, MRI cognitive biopsy, and MRI cognitive plus standard biopsy with RP histopathology were determined to be 28.7%, 49.6%, and 50.4%, respectively. The distinction between MRI cognitive biopsy and MRI cognitive plus standard biopsy was not statistically significant. While the rate of upgrade in the last histology of the cases (n:26) diagnosed with ISUP 1 cancer in MRI cognitive biopsy was 62.5%, they observed that the upgrade rate decreased to 37% with the addition of standard biopsy (19). In our study, the concordance between MRI cognitive + standard biopsy and systematic biopsy with RP histopathology was 57.9% and 32.3%. On the other hand, the rate of upgrade was 28.9% and 61.3%, respectively, for MRI cognitive + standard biopsy and systematic biopsy.

A few limitations should be highlighted in our study. The study was a retrospective review carried out at a single center, exclusively involving RP patients. Patients who underwent active follow-up, radiotherapy and chemotherapy were not included in the study. The number of patients included in our study was relatively limited. There was heterogeneity among the biopsy groups.

MpMRI is a valuable tool for identifying and determining the extent of tumor growth during RP procedures. Simultaneously, the Gleason score of tumors after RP can be more precisely predicted using a combination of MRI imaging and systematic biopsies. Thus, surgical success may increase (necessity of lymph node dissection, etc.). For this reason, we think that patients with suspected PCa should undergo MRI cognitive + systematic biopsy.

#### **Conflict of interest**

The authors declared no conflict of interest.

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None to declare.

#### **Authors' contributions**

Concept: S.Ö., Y.B., Design: S.Ö., Y.B., Data Collection or Processing: M.G., Analysis or Interpretation: Y.K.Y., Literature Search: Ş.S., E.Ö., Writing: S.Ö.

#### **Ethical Statement**

The study commenced after obtaining approval from our Clinical Research Ethics Council. The date of the ethics committee's decision is November 30, 2017, and the reference number for the committee's decision is 2017/405.

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