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Comparison of multiparametric prostate MR imaging and Ga-68 PSMA PET-CT imaging in prostate cancer staging

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Ethics Committee Approval
The study was approved by the Health Sciences University Gulhane Scientific Research Ethics Committee on February 25, 2020 with the decision number 2020-87.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Staging in prostate cancer is essential for determining the right treatment approach and its execution. This study assessed the staging effectiveness of multiparametric prostate magnetic resonance imaging (MpMRI) compared to prostate-specific membrane antigen (PSMA) positron emission tomography – computed tomography (PET-CT) and examined the preoperative information that they provide.
Methods: We collected data from patients diagnosed with prostate cancer who visited our clinic between June 2020 and November 2022. The results from MpMRI performed prior to biopsy were compared to those from PSMA PET-CT conducted after diagnosis, alongside the outcomes of pathological evaluations.
Results: There was no significant correlation between MpMRI and PSMA PET-CT findings and the final pathology results regarding extraprostatic extension. However, both imaging techniques showed a significant correlation with the final pathology in evaluating pelvic lymph-node metastasis and seminal vesicle invasion. In terms of lesion localization, no significant correlation was found between the final site of the pathological lesion and MpMRI, while a significant correlation was noted with PSMA PET-CT. Patients with positive surgical margins had significantly elevated serum PSA levels, size of the index lesion identified in MpMRI, and maximum standardized uptake values (SUV max) of PSMA.
Conclusion: Although both imaging methods offer important staging insights, further research is needed to clarify their respective limitations and benefits. In the future, these techniques may have additional roles in predicting surgical margin positivity before surgery.

Keywords: MRI, prostate cancer, PSMA, staging, surgical margin

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Introduction

A diagnosis of prostate cancer is confirmed by histopathological examination, which typically is performed after clinical suspicion arises based on the findings of a digital rectal examination and elevated serum levels of prostate-specific antigen (PSA). Imaging modalities alone are currently insufficient for definitive diagnosis, and confirmation requires biopsy and histology [1]. However, imaging plays a crucial role in guiding biopsies and staging the disease prior to treatment [2].

A wide range of imaging techniques are employed for staging purposes in prostate cancer. These include bone scintigraphy, multiparametric prostate magnetic resonance imaging (MpMRI), Ga-68 prostate-specific membrane antigen positron emission tomography/computed tomography (Ga-68 PSMA PET-CT), conventional CT, fluoride PET, and choline PET [3]. Among these, MpMRI and Ga-68 PSMA PET-CT have gained prominence due to their high-resolution anatomical and molecular imaging capabilities, respectively. The aim of this study was to evaluate the staging performance of MpMRI and Ga-68 PSMA PET-CT in assessing lymph-node involvement, tumor localization, extraprostatic extension, and seminal vesicle invasion. Additionally, the study compared the preoperative information that each modality provides to assess their potential clinical utility.

Materials and methods

Approval was obtained from the Ethics Committee of Health Sciences University Gülhane (February 25, 2020, decision number 2020/87). The study included patients diagnosed with prostate cancer at our urology clinic between June 2020 and November 2022. The inclusion criteria consisted of elevated PSA levels, suspicious findings from digital rectal examinations, and a confirmed histopathological diagnosis of prostate cancer. All patients underwent radical prostatectomy.

MpMRI was performed before the biopsy for staging, and Ga-68 PSMA PET-CT was conducted after the diagnosis. We recorded demographic information, serum levels of PSA, and biopsy results. Additionally, we compared data on lesion localization, extraprostatic spread, lymph node metastasis, and seminal vesicle invasion from imaging with the final pathology findings.

Imaging protocols

MpMRI was carried out on a 3-Tesla MRI machine with intravenous gadolinium contrast. The reporting followed the PIRADS v2.1 scoring system. Key parameters were documented, such as extraprostatic spread, seminal vesicle invasion, bladder neck invasion, lymph node involvement, and lesion size and location. Ga-68 PSMA PET-CT imaging took place 55–60 minutes after intravenous administration of 0.06 mCi/kg Ga-68 radiopharmaceutical. The scans covered the area from the vertex down to the mid-thigh.

Pathological examination

Radical prostatectomy specimens were analyzed for ISUP grade, tumor percentage, extraprostatic spread, lesion size and location, seminal vesicle invasion, lymph-node metastasis, and findings related to surgical margins.

Statistical analysis

Descriptive statistics were computed, and the distribution of variables was evaluated using the Kolmogorov–Smirnov test. An independent-sample *t*-test, Mann–Whitney U test, chi-squared test, and Fisher's exact test were applied as needed. Correlation analyses were conducted using the kappa test. All statistical analyses were performed using SPSS 28.0.

Table 1: Demographic data, clinical and pathological characteristics of patients

		Min-Max			Median	Mean±SD/n-%		
Age		46.0	-	75.0	65.0	63.9	±	6.6
Operation								
Robotic						37		68.5%
Open						16		29.6%
Laparoscopy						1		1.9%
PSA (ng/mL)		2.1	-	89.5	12.1	18.5	±	16.4
Prostate Volume (cc)		13.0	-	108.0	35.0	41.6	±	21.5
Biopsy ISUP Grade	**I**					7		13.0%
	II					21		38.9%
	III					10		18.5%
	IV					11		20.4%
	V					5		9.3%
Biopsy Tumor Side								
Left						15		27.8%
Right						8		14.8%
Bilateral						31		57.4%
Final Pathology ISUP Grade	**I**					4		7.4%
	II					18		33.3%
	III					10		18.5%
	IV					14		25.9%
	V					8		14.8%
Final Pathology Tumor Side								
Left						10		18.5%
Right						6		11.1%
Bilateral						38		70.4%
Final Pathology Tumor Percentage		1.3	-	85.0	20.0	24.6	±	18.6
Final Pathology Extra Prostatic Extension	Yes					27		50.0%
	No					27		50.0%
Final Pathology Seminal Vesicle Invasion								
Yes						12		22.2%
No						42		77.8%
Final Pathology Right Pelvic Lymph Node Metastasis	Yes					4		7.4%
	No					50		92.6%
Final Pathology Left Pelvic Lymph Node Metastasis	Yes					1		1.9%
	No					53		98.1%

Min: Minimum, Max: Maximum, SD: Standard Deviation

Results

A total of 54 patients in the study, and the mean age was 63.9 ± 6.6 years. The average preoperative PSA level was 18.5 ± 16.4 ng/mL. The majority of patients underwent robotic radical prostatectomy (68.5%), followed by an open procedure (29.6%). Demographic, clinical, and pathological characteristics are detailed in Table 1.

The mean index lesion size in MpMRI was 15.5 ± 10.1 mm. PIRADS 4 and 5 lesions comprised the majority (83.3%), and lesions were most commonly bilateral (27.8%). MRI indicated extraprostatic spread in 14.8%, seminal vesicle invasion in 11%, and perivesical/perirectal invasion in 13% of the participants. PET-CT revealed similar findings, with extraprostatic spread in 18.5%, seminal vesicle invasion in 9.3%, and perivesical/perirectal invasion in 11.1% of the participants. Lymph-node involvement was observed on the right (16.7%) and left (14.8%). The mean maximum standardized uptake value (SUV max) in Ga-68 PSMA PET-CT was 10.9 ± 9.4. The PSMA uptake was bilateral in 40.7% and absent in 13% of patients.

Correlation analyses

Extraprostatic spread: No significant correlation was found between the final pathology and MpMRI (κ=0.074, *P*=0.444) or PSMA PET-CT (κ=–0.074, *P*=0.484).

Seminal vesicle invasion: MpMRI (κ=0.348, *P*=0.005) and PSMA PET-CT (κ=0.391, *P*=0.001) both showed significant correlation with pathology (Table 2).

Table 2: Seminal vesicle invasion kappa analysis

		Final Pathology Seminal Vesicle Invasion		Sensitivity	Positive Prediction	Specificity	Negative Prediction	Kappa	*P*-value
		(+)	(-)						
MRI Seminal Vesicle Invasion	(+)	**4**	2	33.3%	66.7%	95.2%	83.3%	0.348	***0.005***
	(-)	8	**40**						
PSMA Seminal Vesicle Invasion	(+)	**4**	1	33.3%	80.0%	97.6%	83.7%	0.391	***0.001***
	(-)	8	**41**						

Lymph node metastasis:

- **Right pelvic nodes:** There was significant correlation for MpMRI (κ=0.460, *P*=0.001) and PSMA PET-CT (κ=0.400, *P*=0.001).
- **Left pelvic nodes:** There was strong correlation for MpMRI (κ=0.658, *P*<0.001) and PSMA PET-CT (κ=0.196, *P*=0.016).

Lesion localization: There was no significant correlation for MpMRI (κ=0.137, *P*=0.056), but PSMA PET-CT showed significant concordance (κ=0.163, *P*=0.040) (Table 3).

Table 3: Tumor localization kappa compliance analysis

		Final Pathology Tumor Localization			Compliance Rate	Stats
		Left	Right	Bilateral		
MRI Lesion Localization	Left	***6***	0	12	55.3%	Kappa=0.137 *P*=0.056
	Right	0	***4***	13		
	Bilateral	3	1	***11***		
	No Lesion	1	1	2		
PSMA Involvement Side	Left	***7***	1	7	65.8%	Kappa=0.163 ***P=0.040***
	Right	0	***1***	9		
	Bilateral	3	2	***17***		
	No Involvement	0	2	5		

Surgical margins: There was no significant difference in age, surgical type, or prostate volume between groups (*P*>0.05). However, patients with positive surgical margins had:

- Higher PSA levels (*P*=0.013) (Figure 1)
- Larger index lesions in MRI (*P*=0.021) (Figure 2)
- Higher SUV max of PSMA (*P*=0.008) (Figure 3)

The distribution of PSMA involvement was not significantly different (*P*>0.05).

Figure 1: Serum PSA level averages in groups with positive and negative surgical margins

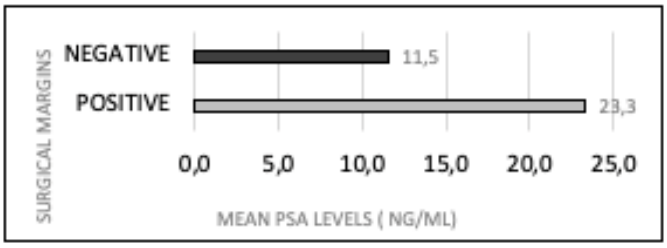


Figure 2: Mean index lesion size in MR imaging in groups with positive and negative surgical margins

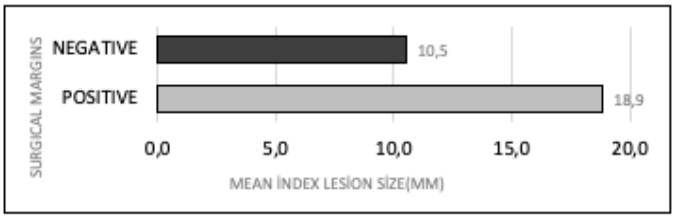
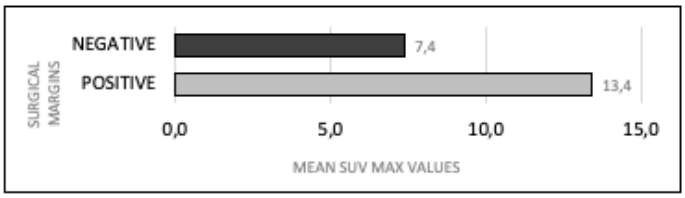


Figure 3: Mean SUV max values in groups with positive and negative surgical margins



Discussion

Accurate staging after a diagnosis of prostate cancer is vital for determining the appropriate treatment strategy. Local staging plays a key role in differentiating between localized and locally advanced disease. Recent publications highlight MpMRI as a highly recommended imaging modality for local staging. The European Association of Urology's prostate-cancer guidelines suggest that MpMRI should be conducted prior to biopsy for patients with elevated serum PSA levels [4]. Furthermore, MpMRI provides crucial anatomical information for treatment planning after diagnosis. Imaging findings such as broad tumor contact, asymmetric capsular bulging, obliteration of the rectoprostatic angle, and neurovascular bundle asymmetry are associated with extracapsular extension [5].

In a meta-analysis by de Rooij et al. [6], the sensitivity and specificity of MpMRI for detecting extracapsular extension were reported as 57% and 91%, respectively. For seminal vesicle invasion, the sensitivity was 58%, and the specificity was 96%. In our study, MpMRI demonstrated a sensitivity of 18.5% and specificity of 88.9% for extracapsular extension. However, no significant correlation with final pathology was found.

A multicenter study by Soeterik et al. [7] compared the accuracy of digital rectal examination and MRI in detecting extracapsular disease. They reported a sensitivity of 51% and specificity of 82% for MRI. The variability in MRI performance

has been attributed to differences in image-acquisition protocols and inter-reader interpretation [8]. Yılmaz et al. [9] compared Ga-68 PSMA PET-CT with MpMRI for local staging. The reported sensitivity and specificity of PSMA PET-CT for extracapsular extension were 30% and 85.7%, respectively, while for seminal vesicle invasion, they were 75% and 90%.

In our study, PSMA PET-CT showed a sensitivity of 14.8% and specificity of 77.8% for extracapsular extension, and there was no significant correlation with pathology. Although both modalities lacked statistical correlation with the final pathology, MpMRI outperformed PSMA PET-CT in sensitivity and specificity. The relatively low resolution of PET-CT may account for its reduced accuracy in evaluating extracapsular disease.

Seminal vesicle invasion staged as T3b is suggested in MpMRI by a low T2 signal within the seminal vesicles and in PSMA PET-CT by increased uptake at that level. In our findings, MpMRI and PSMA PET-CT both demonstrated moderate sensitivity (33.3%) and high specificity (95.2% and 97.6%, respectively), and each correlated significantly with the final pathology. Despite lower sensitivity compared to previous reports, both modalities provided valuable information that aligned with literature findings.

Lymph-node status was evaluated separately for right and left pelvic nodes. MpMRI revealed significant correlation with the final pathology for right-sided nodes with 50% sensitivity and 96% specificity. PSMA PET-CT also showed significant correlation with higher sensitivity (75%) but lower positive predictive value (PPV) (33.3%). For the left side, both modalities achieved 100% sensitivity. MpMRI had higher specificity (98.1%) compared to PSMA PET-CT (86.8%), and there was significant correlation for both.

These findings are supported by earlier studies. Budiharto et al. [10] reported a diffusion-weighted MRI sensitivity of 18.8% and specificity of 97.6%. A 2018 systematic review cited PSMA PET-CT sensitivities of up to 99% with specificities exceeding 90% [11]. Wu et al. found that PSMA PET-CT was superior to MpMRI for detecting lymph-node metastases in intermediate- and high-risk patients [12]. In our study, both methods correlated significantly with the final pathology, although MpMRI's resolution limitations in wider-field imaging may restrict its nodal staging utility. In contrast, the whole-body imaging capacity of PSMA PET-CT enhances its role in systemic staging.

Preoperative lesion localization is critical for nerve-sparing surgery. Lesions were classified as right-sided, left-sided, or bilateral. Both index and secondary lesions were included in the evaluation. MpMRI did not correlate significantly with the final pathology, while PSMA PET-CT did. In a study by Zamboglou et al. [13], PSMA PET-CT showed higher sensitivity and specificity (75% and 87%) than MpMRI (70% and 82%) in tumor-volume detection.

A significant association was observed between positive surgical margins and larger index-lesion size (mean 18.9 mm), higher PSA levels, and elevated SUV max. Tamada et al. [15] linked extracapsular extension and tumors at the base or apex with increased risk of positive margins. In our study, however, no direct correlation was found between extracapsular extension or tumor localization and margin status. Nonetheless, imaging characteristics of larger tumors may support preoperative planning decisions. Patients with extracapsular extension, seminal vesicle invasion (pT3b), ISUP grade >2, or positive surgical margins face increased risk of progression, with up to 50% risk at five years [16]. Preoperative identification of high-risk features may aid in optimizing treatment and improving outcomes.

The clinical implications of our findings are particularly relevant for surgical planning and treatment selection. Although MpMRI is limited in detecting extracapsular extension, it provides detailed anatomical guidance that is critical for nerve-sparing techniques. Ga-68 PSMA PET-CT offers broader systemic staging value, especially in identifying nodal involvement. When used together, these imaging tools can provide information for tailored surgical approaches, support decisions on wider excision or intraoperative frozen section use, and guide discussions about adjuvant therapy.

Limitations

A major limitation of our study is the absence of blinding for radiologists and surgeons. The image readers had access to clinical data, and surgeons were aware of the imaging results during surgery. This lack of blinding could have introduced interpretation and procedural bias. Radiologists may have been influenced by clinical expectations, which could have potentially affected the objectivity of the reported findings. Similarly, surgical decision-making could have been subconsciously shaped by the imaging results, particularly in margin control. This limitation may have impacted the generalizability of our findings and highlights the need for blinded assessments in future prospective trials.

Conclusion

Prostate cancer remains a major public health concern due to its high prevalence and the potential morbidity associated with its treatment. Accurate preoperative staging is critical for distinguishing between patients who require immediate intervention and those eligible for active surveillance, as well as for guiding surgical strategies. Our findings highlight the complementary strengths of MpMRI and Ga-68 PSMA PET-CT in this setting. While PSMA PET-CT demonstrated high sensitivity and specificity for lymph-node staging and seminal vesicle invasion, MpMRI provided detailed anatomical information that is valuable for lesion characterization and local staging.Importantly, we identified significant associations between positive surgical margins and factors such as index lesion size, PSA levels, and SUV max values. This suggests that these imaging parameters could support preoperative risk stratification and surgical planning. These findings are consistent with the literature and support the integration of both modalities into personalized treatment algorithms. As the clinical applications of advanced imaging continue to expand, future prospective and blinded studies are warranted to further clarify their roles and optimize their use in staging, treatment selection, and long-term outcome prediction for the management of prostate cancer.

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