The Importance of Preoperative Prostate Multiparametric MRI: Accuracy and Correlation with the Pathological Findings

T. Telecan[1,2], I. Andraș[1,2], P. A. Kadula[2], A. Posea[1], E. D. Căta[1,2], Ș. A. Medan[2], L. Giurgiu[2], A. I. Tișe[2], M. Platon[3,4], C. Bungărdean[5], I. Coman[1,2], D. V. Stanca[1,2], N. Crișan[1,2]

[1] *„Iuliu Hatieganu" University of Medicine and Pharmacy, Department of Urology, Cluj-Napoca, Romania*
[2] *Clinical Municipal Hospital, Cluj-Napoca, Romania*
[3] *„Iuliu Hatieganu" University of Medicine and Pharmacy, Department of Radiology and Medical Imaging, Cluj-Napoca, Romania*
[4] *„Octavian Fodor" Gastroenterology and Hepatology Institute, Department of Radiology and Medical Imaging, Cluj-Napoca, Romania*
[5] *Clinical Municipal Hospital, Department of Pathology, Cluj-Napoca, Romania*

Abstract

Introduction and Objectives. Prostate cancer is staged based upon digital rectal examination findings, with average accuracy. As such, special magnetic resonance imaging (MRI) protocols have been implemented and particularized for identifying prostate cancer (PCa), reaching a concordance of 87% between preoperatory prediction and pathological staging. The aim was to determine the accuracy of mpMRI in terms of staging, as well as serving as a preoperative planning tool, by analyzing all cases who underwent mpMRI prior to radical prostatectomy in our department, in the past 5 years.

Materials and Methods. A total number of 177 patients were included, from 2017 to 2022. All patients had preoperative mpMRI that certified a lesion with a PIRADS score ≥ 3 and had performed systematic or targeted prostate biopsy confirming the malignancy. 2D/3D laparoscopic radical prostatectomy was performed in all cases.

Results. The preoperative mpMRI staged 91.08% of the patients with prostate-confined disease, whereas 8.97% were suspected of harboring extracapsular extension or seminal vesicle invasion. Comparing the mpMRI prediction to the final pathological staging, we observed a 75% concordance rate. Upstaging from cT2 at MRI to pT3 on RP specimen was observed in 21.15% of the patients. The presence of a PIRADS 5 lesion has an OR of 1.33 for upstaging ($p = 0.48$) and OR 2.93 for positive surgical margins ($p = 0.05$). The upstaged patients had a significantly higher average PSA value (12.46 versus 8.26, $p = 0.001$).

Conclusions. mpMRI performed before radical prostatectomy has a high local staging accuracy and allows for a tailored surgical planning. The presence of a PIRADS 5 lesion and a PSA value greater than 10 ng/ml were associated with a higher risk of upstaging at final pathology.

Key-words: multiparametric magnetic resonance imaging, prostate cancer, radical prostatectomy

Correspondence to: Dr. Andras Iulia M.D.
Department of Urology, Clinical Municipal Hospital
11 Tabacarilor St., Cluj Napoca, code 400139, Cluj county, Romania
Tel: +40735406258
e-mail: dr.iuliaandras@gmail.com

Introduction and objectives

Prostate cancer (PCa) is the most frequent urological malignancy encountered in male population, as 1 in 12 patients will receive this diagnosis by the age of 70 [1]. In terms of PCa detection, special magnetic resonance imaging (MRI) protocols have been implemented and particularized for enhancing the identification and characterization of suspect PCa areas. Called multiparametric MRI (mpMRI), the scan provides anatomical acquisitions such as T2 weighed images (T2WI), sequences that use the signal produced by the diffusion of water molecules between cells (diffusion weighed images or DWI and apparent diffusion coefficient map or ADC), as well as dynamic contrast-enhanced images (DCE) [2]. Based upon the combined features on each acquisition, Turkbey et al. [3] developed the Prostate Imaging-Reporting and Data System (PIRADS), a probability score ranging from 1 (most likely benign) to 5 (most likely malignant). Of diagnostic importance are nodules graded 3 to 5, which must further undergo prostate biopsy.

While mpMRI is being employed as the gold standard technique for identifying suspect malignant areas and guiding targeted sampling, PCa staging is performed based on digital rectal examination findings. The percentage of upstaged patients at the final pathological report, compared to the initial clinical assessment, is nearly 40% [4]. Furthermore, anterior lesions, counting as 30% of all PCa, cannot be properly staged by DRE [5]. On the other hand, the accuracy of mpMRI for staging PCa reaches 87% in experienced centers [6], as such inclusion in future clinical guidelines is predictable.

The aim of the current paper is to determine the accuracy of mpMRI in terms of staging localized and locally-advanced disease, as well as serving as a preoperative planning tool, by analyzing all cases who underwent mpMRI prior to radical prostatectomy in our department, in the past 5 years.

Materials and methods

The present protocol was approved by the local Ethics Committee and was conducted according to the Declaration of Helsinki regarding human studies.

We included 177 consecutive cases who underwent radical prostatectomy in our department between 2017 and 2022. All patients had preoperative mpMRI that certified a lesion with a PIRADS score ≥ 3 and had performed systematic or targeted prostate biopsy confirming the malignancy. csPCa was defined as prostate adenocarcinoma with Gleason Grade (GG) ≥ 2.

All patients underwent 2D / 3D laparoscopic radical prostatectomy, with the patient positioned in dorsal decubitus, using a properitoneal approach. Firstly, the endopelvic fasciae were opened, until the levator anni muscles were reached. After dissecting the pubo-prostatic ligaments, a hemostatic suture was placed at the level of the dorsal venous complex. Next, the bladder neck was incised and separated from the base of the prostate, at a safe distance from the ureteral orifices. The dissection was continued by isolating the seminal vesicles and vas deferens, then the Denonvillier's rectoprostatic fascia was divided. Uni- or bilateral nerve-sparing procedure was performed according to the nodule's location based on preoperative mpMRI, the preoperative IIEF-5 score and the patient's preference. Lastly, the apex of the prostate was freed from the membranous urethra and the surgical specimen was removed. The indication for bilateral pelvic lymph node dissection was established based on Memorial Sloan Kettering Cancer Center (MSKCC) nomograms, the cut-off value being of 5%. We performed the urethro-vesical anastomosis, starting with the posterior aspect and advancing at the front, using barbed-wire suture.

All surgical specimens were analyzed by 2 senior pathologists, with over 15 years of experience in the field of prostate cancer and urological malignancies (Figure 1).

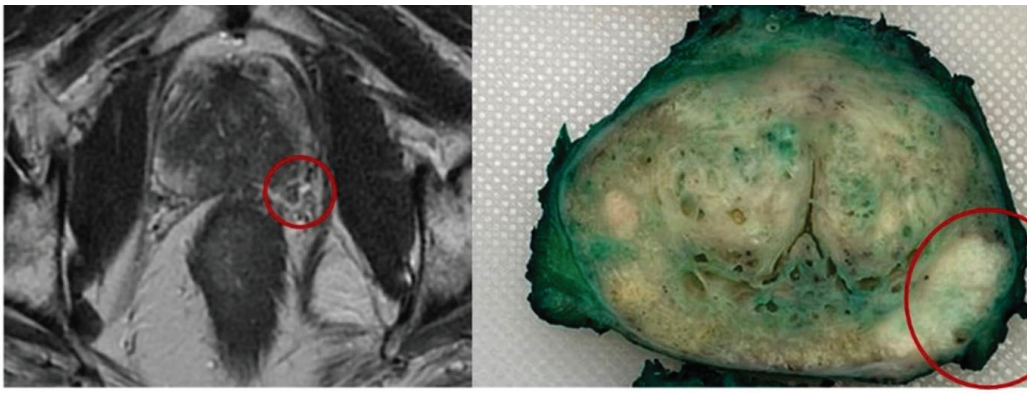


Figure 1. (Left) T2WI axial image of the prostate, showing signs of extracapsular effraction. (Right) Axial section of the inked radical prostatectomy specimen, confirming the extracapsular extension described preoperatively on mpMRI images.

The statistical analysis was carried out using the EpiInfoTM platform (Center for Disease Control and Prevention, Atlanta, Georgia, USA).

Results

The study cohort comprised of 177 patients. All demographic data are summarized in Table 1. The median age was 65 years (IQR 62 – 68) and median PSA was 9 ng/ml (IQR 6.155 – 13.49). The PIRADS score was 3 in 15.74% of cases, 4 in 50% and 5 in 34.25%, with the median of the maximum diameter of the index lesion being 13.5 mm (IQR 9 – 19). csPCa was found in 71.17% of biopsies. The preoperative mpMRI staged 91.08% of the patients with prostate-confined disease, whereas 8.97% were suspected of harboring extracapsular extension or seminal vesicle invasion.

Table 1. Demographic data of the study population

Variables	Value	
Age (years) Median (IQR)	65 (62 – 68)	
PSA (ng/ml) Median (IQR)	9 (6.155 – 13.49)	
Prostate volume (cmc) Median (IQR)	43 (36.265 – 54.3)	
Index lesion maximum diameter (mm) Median (IQR)	13.5 (9 – 19)	
PIRADS score (%)		
	3:	15.74
	4:	50
	5:	34.25
Biopsy GG (%)		
	1:	28.81
	2:	51.41
	3:	16.38
	4:	2.82
	5:	0.56
Risk groups – EAU (%)		
	Low-risk:	16.38
	Intermediate-risk:	57.06
	High-risk:	26.55
MRI staging (%)		
	T2a:	37.28
	T2b:	25
	T2c:	28.2
	T3a:	7.05
	T3b:	1.92

All patients underwent laparoscopic radical prostatectomy. Median operative time was 180 minutes (IQR 144.25 – 225) starting from the induction of anesthesia. Nerve-sparing procedures were performed at least unilaterally in 47.44% of cases, while lymph nodes dissection was performed in 54.22% of interventions. Mean hospitalization after surgery was 4 days (IQR 3.5 – 6). The urethro-vesical catheter was removed after a median time of 10 days (IQR 7 – 14.5), after performing a control cystography. 11.29% of patients required prolonged catheterization (up to 21 days) due to suspected perianastomotic extravasation. Postoperative complications at 30 days were present in 6.21% of cases (n = 11). According to Clavien-Dindo classification, 7 patients were staged as grade I: transitory tachycardia (n = 1), fever (n = 1), pulmonary atelectasis managed by breathing exercises (n = 1), acute urinary retention after catheter removal (n = 2), Retzius space hematoma (n = 1) and prolonged lymphorrhea (n = 1); 2 patients had grade II complications: urosepsis, managed by antibiotherapy (n = 1) and chest pain, managed by administering nitroglycerin sublingually (n = 1); finally, 2 patients had IIIb complications, consisting in prevesical fluid collection due to urinary catheter obstruction, managed by surgical drainage (n = 2).

The pathological report of radical prostatectomy specimens revealed csPCa in 87.55% of cases, 31.07% associating secondary lesions such as high-grade prostatic intraepithelial neoplasia (HGPIN) (Table 2). In 71.73% of cases PCa was organ confined, whereas in 28.27% of cases the disease was locally-advanced.

Table 2. Summary of the pathological reports

Area of PCa per RP specimen (%) Median (IQR)	20 (12 – 38)	
Radical prostatectomy GG (%)		
	1:	12.42
	2:	67.45
	3:	15.38
	4:	1.77
	5:	2.95

HGPIN (%)	31.07	
Pathological staging (%)		
	pT2a:	1.12
	pT2b:	5.64
	pT2c:	64.97
	pT3a:	16.38
	pT3b:	11.86
	pN0:	97.74
	pN1:	2.25
Positive surgical margins (%)		
	Overall:	15.81
	pT2:	14.17
	pT3	20

Comparing the mpMRI prediction to the final pathological staging, we observed a 75% concordance rate. Upstaging from cT2 at MRI to pT3 on RP specimen was observed in 21.15% of the patients, while 3.84% were downstaged. Out of the upstaged cases, 54.54% presented extracapsular extension, while the rest of 45.45% had seminal vesicle involvement. Two thirds of the upstaged cases were diagnosed by performing systematic prostate biopsy and 53.84% of cases had a PIRADS 5 nodule described at mpMRI. 21.21% of the upstaged cases had positive surgical margins (Table 3). The presence of a PIRADS 5 lesion has an OR of 1.33 for upstaging (p=0.48) and OR 2.93 for positive surgical margins (p=0.05).

Regarding functional outcomes at 6 months, the continence rate, defined as 0 – 1 pads/day, was achieved in 89.88% of patients, 15% of them requiring anticholinergic medication. The erectile function was regained in 32.69% of patients that underwent uni- or bilateral nerve-sparing procedure. Median PSA at the given timeframe was 0.03 (IQR 0.004 – 0.0475). 22.47% of patients required adjuvant therapy: 50% of them received hormonal therapy, 30% radiation therapy alone, while 20% benefited from combined multimodal treatment.

Discussions

The current study shows that mpMRI is an accurate method for preoperative staging of PCa, thus creating the premise of a personalized treatment, within the oncological safety requirements. The imagistic prediction matched the pathological staging in 3 quarters of the selected cases, reiterating the reliability of this method. Moreover, by grading each lesion according to the PIRADS classification, upstaging and positive surgical margins can be predicted in high-risk patients with scores of 4 and 5.

We aimed to reinforce the importance of preoperative imagistic assessment of PCa and the correlation between the staging predicted by the mpMRI and the final histopathological report. According to the current international practices, prostate cancer is staged based on clinical findings at digital rectal examination. However, it is considered that the accuracy of staging and thus of predicting PCa nodules is under 60% [7].

Table 3. Upstaging rates and patients' characteristics

Variables	Concordant cT – pT cases (n = 136)	Upstaged cases (n = 41)	Statistical significance (p)
PSA (ng/ml) Median (IQR)	8.24 (6.01 – 12.295)	12.46 (7.9 – 20.25)	0.001
Type of biopsy (%)			
Systematic:	54.41	65.85	0.195
FUSION:	45.58	34.14	0.195
Nodule diameter (mm) Median (IQR)	13 (9 – 18)	14 (11 – 21)	0.247
PIRADS Score (%)			
3:	16.47	15.38	0.868
4:	54.11	30.76	0.008
5:	29.41	53.84	0.004
Positive surgical margins (%)	14.7	21.21	0.322

EAU, NCCN and AUA guidelines advise the use of mpMRI in low-risk patients that are fit for active surveillance programs, as well as high-risk cases with localized disease (cT2 associated with PSA over 20 ng/ml or Gleason Grade of 4 – 5 at biopsy) or locally-advanced malignancy (cT3 – cT4 or documented lymph node involvement) [8]. The reported average accuracy of mpMRI tumoral staging reported in literature ranges between 66.1% and 79.4%, being consistent with our findings (75% concordance between mpMRI stage prediction and pathological assessment).

Regarding the preoperative prediction of capsular effraction, mpMRI has shown high specificity, up to 91%, but low to moderate sensitivity, reaching only 57%. It is due to certain radiologic signs that hint the extraprostatic invasion, which are directly linked to image resolution and the radiologist's experience. Therefore, capsular irregularity, spiculation or retraction, obliteration of the recto-prostatic angle, neurovascular bundles asymmetry or a nodule that comes into contact with the prostatic capsule on a distance greater than 10 mm depend of the mpMRI magnetic field power. A 3T MRI scanner can improve the sensitivity up to 68%, due to better image resolution in comparison with 1.5T [9]. Seminal vesicle invasion can be depicted as an enlarged vesicle with a low signal intraluminal mass, or as an obliteration of the angle formed by the base of the prostate and the vesicle. mpMRI sensitivity and specificity reaches similar values to those of extraprostatic extension, 58% and 96%, respectively. When compared to 3T scanners, the sensitivity can increase up to 75.9% [10].

Radiologists' performance can impact lesion grading, tumor staging and subsequently, the chosen treatment. Interobserver agreement varies proportionally with the PIRADS score, being as low as 43% for nodules graded 1 and 2 and 72% for those scored as 3 to 5, with intermediate and high probability of harboring PCa [11]. In terms of extracapsular extension, the sensitivity of experts' interpretation is approximately 60%. Recent papers and state-of-the-art publications emphasize the potential of artificial intelligence-aided diagnostic tools, that can support novice radiologists and thus increasing their accuracy up to 84.62% [12], providing a reliable prediction of tumor extension and good correlation with pathological findings. The greatest risk of preoperative substaging of the disease is the higher percentage of positive surgical margins. In our study, over a fifth of the upstaged cases had positive surgical margins, therefore requiring adjuvant therapy.

Regarding the upstaging rate and the predictive factors that have the potential of foreseeing such outcomes, it has been suggested that cases with a PI-RADS score of 5 have a five-fold greater chance of upgrading and upstaging at the final pathological report, while patients with positive surgical margins at frozen section analysis of the posterolateral plane had a three-fold chance [13, 14]. On the other hand, in patients assigned a PIRADS score bellow the cut-off value of 3, mpMRI could rule-out pT3a disease with a sensitivity and negative predictive value of 99% and 98%, respectively, the authors concluding that a PIRADS score of 1 – 3 had a protective effect compared to PIRADS 4 – 5 cases [15].

The study has a few limitations. Firstly, mpMRIs were done in multiple centers, implying great variability in terms of magnetic field strength, acquisition protocols and reader experience. Secondly, the design of the study is retrospective, limiting the extracted parameters from each patient.

Conclusions

mpMRI performed before radical prostatectomy has a high local staging accuracy and allows for a tailored surgical planning. The presence of a PIRADS 5 lesion and a PSA value greater than 10 ng/ml were associated with a higher risk of upstaging at final pathology.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020 Jan;70(1):7-30. DOI: 10.3322/caac.21590.
2. Borofsky S, George AK, Gaur S, Bernardo M, Greer MD, Mertan FV, Taffel M, Moreno V, Merino MJ, Wood BJ, Pinto PA, Choyke PL, Turkbey B. What Are We Missing? False-Negative Cancers at Multiparametric MR Imaging of the Prostate. Radiology. 2018 Jan;286(1):186-195. DOI: 10.1148/radiol.2017152877.
3. Turkbey B, Rosenkrantz AB, Haider MA, Padhani AR, Villeirs G, Macura KJ, Tempany CM, Choyke PL, Cornud F, Margolis DJ, Thoeny HC, Verma S, Barentsz J, Weinreb JC. Prostate Imaging Reporting and Data System Version 2.1: 2019 Update of Prostate Imaging Reporting and Data System Version 2. Eur Urol. 2019 Sep;76(3):340-351. DOI: 10.1016/j.eururo.2019.02.033.
4. D'Elia C, Cerruto MA, Cioffi A, Novella G, Cavalleri S, Artibani W. Upgrading and upstaging in prostate cancer: From prostate biopsy to radical prostatectomy. Mol Clin Oncol. 2014 Nov;2(6):1145-1149. DOI: 10.3892/mco.2014.370.
5. Sahu M, Wijesekera N, Donohue JF. Anterior prostate cancer: Current perspectives and diagnostic dilemmas. JCU. 2017;10(1):49–55. DOI: 10.1177/2051415816655724.
6. Zhen L, Liu X, Yegang C, Yongjiao Y, Yawei X, Jiaqi K, Xianhao W, Yuxuan S, Rui H, Wei Z, Ningjing O. Accuracy of multipara-

metric magnetic resonance imaging for diagnosing prostate Cancer: a systematic review and meta-analysis. BMC Cancer. 2019 Dec 23;19(1):1244. DOI: 10.1186/s12885-019-6434-2.
7. Naji L, Randhawa H, Sohani Z, Dennis B, Lautenbach D, Kavanagh O, Bawor M, Banfield L, Profetto J. Digital Rectal Examination for Prostate Cancer Screening in Primary Care: A Systematic Review and Meta-Analysis. Ann Fam Med. 2018 Mar;16(2):149-154. DOI: 10.1370/afm.2205.
8. Michael J, Neuzil K, Altun E, Bjurlin MA. Current Opinion on the Use of Magnetic Resonance Imaging in Staging Prostate Cancer: A Narrative Review. Cancer Manag Res. 2022; 14:937-951. DOI: 10.2147/CMAR.S283299
9. de Rooij M, Hamoen EH, Witjes JA, Barentsz JO, Rovers MM. Accuracy of Magnetic Resonance Imaging for Local Staging of Prostate Cancer: A Diagnostic Meta-analysis. Eur Urol. 2016 Aug;70(2):233-45. DOI: 10.1016/j.eururo.2015.07.029.
10. Grivas N, Hinnen K, de Jong J, Heemsbergen W, Moonen L, Witteveen T, van der Poel H, Heijmink S. Seminal vesicle invasion on multi-parametric magnetic resonance imaging: Correlation with histopathology. Eur J Radiol. 2018 Jan;98:107-112. DOI: 10.1016/j.ejrad.2017.11.013.
11. Flood TF, Pokharel SS, Patel NU, Clark TJ. Accuracy and Interobserver Variability in Reporting of PI-RADS Version 2. J Am Coll Radiol. 2017 Sep;14(9):1202-1205. DOI: 10.1016/j.jacr.2017.04.012.
12. Hou Y, Zhang YH, Bao J, Bao ML, Yang G, Shi HB, Song Y, Zhang YD. Artificial intelligence is a promising prospect for the detection of prostate cancer extracapsular extension with mpMRI: a two-center comparative study. Eur J Nucl Med Mol Imaging. 2021 Nov;48(12):3805-3816. DOI: 10.1007/s00259-021-05381-5.
13. Bianchi R, Cozzi G, Petralia G, Alessi S, Renne G, Bottero D, Brescia A, Cioffi A, Cordima G, Ferro M, Matei DV, Mazzoleni F, Musi G, Mistretta FA, Serino A, Tringali VML, Coman I, De Cobelli O. Multiparametric magnetic resonance imaging and frozen-section analysis efficiently predict upgrading, upstaging, and extraprostatic extension in patients undergoing nerve-sparing robotic-assisted radical prostatectomy. Medicine (Baltimore). 2016 Oct;95(40):e4519. DOI: 10.1097/MD.0000000000004519.
14. de Cobelli O, Terracciano D, Tagliabue E, Raimondi S, Bottero D, Cioffi A, Jereczek-Fossa B, Petralia G, Cordima G, Almeida GL, Lucarelli G, Buonerba C, Matei DV, Renne G, Di Lorenzo G, Ferro M. Predicting Pathological Features at Radical Prostatectomy in Patients with Prostate Cancer Eligible for Active Surveillance by Multiparametric Magnetic Resonance Imaging. PLoS One. 2015 Oct 7;10(10):e0139696. DOI: 10.1371/journal.pone.0139696.
15. Alessi S, Pricolo P, Summers P, Femia M, Tagliabue E, Renne G, Bianchi R, Musi G, De Cobelli O, Jereczek-Fossa BA, Bellomi M, Petralia G. Low PI-RADS assessment category excludes extraprostatic extension (≥pT3a) of prostate cancer: a histology-validated study including 301 operated patients. Eur Radiol. 2019 Oct;29(10):5478-5487. doi: 10.1007/s00330-019-06092-0.