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1.5-TESLA MULTIPARAMETRIC-MAGNETIC RESONANCE IMAGING FOR THE DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER

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Abstract

Background and aim. *Multiparametric-magnetic resonance imaging (mp-MRI) is the main imaging modality used for prostate cancer detection. The aim of this study is to evaluate the diagnostic performance of mp-MRI at 1.5-Tesla (1.5-T) for the detection of clinically significant prostate cancer.*

Methods. *In this ethical board approved prospective study, 39 patients with suspected prostate cancer were included. Patients with a history of positive prostate biopsy and patients treated for prostate cancer were excluded. All patients were examined at 1.5-T MRI, before standard transrectal ultrasonography–guided biopsy.*

Results. *The overall sensitivity, specificity, positive predictive value and negative predictive value for mp-MRI were 100%, 73.68%, 80% and 100%, respectively.*

Conclusion. *Our results showed that 1.5 T mp-MRI has a high sensitivity for detection of clinically significant prostate cancer and high negative predictive value in order to rule out significant disease.*

Keywords*:* Prostate cancer, Multiparametric-MRI, Cancer imaging,•1.5-T MRI

BACKGROUND AND AIMS

In the last three decades, Magnetic Resonance Imaging (MRI) has been used for noninvasive assessment of the prostate and surrounding structures. Initially, prostate MRI was only based on morphologic assessment, using T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI) sequences. Its role was primarily for loco-regional staging of the prostate cancer as it provided limited capability to distinguish between benign pathological tissue and clinically insignificant tumors from significant prostate cancer [1]. To increase the diagnostic accuracy, anatomic T2WI and functional MRI sequences - such as dynamic contrast enhanced MRI (DCE-MRI), diffusion-weighted imaging (DWI) with its derivate apparent-diffusion coefficient (ADC) map and hydrogen 1 MR spectroscopic imaging (MRSI) - were combined in an integrated multiparametric MRI (mp-MRI) examination [2].

The technological advances, combined with a growing interpreter experience, have substantially improved

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the detection of clinically significant prostate cancer, which is critical for reducing mortality, and increased confidence in ruling out benign diseases and dormant malignancies, in order to reduce unnecessary biopsies and treatment [1].

In 2012 the European Society of Urogenital Radiology (ESUR) working group developed the guidelines for mp-MRI of the prostate. The acquisition protocols were then proposed, in order to provide the Prostate Imaging Reporting and Data System (PI-RADS), which relays the probability of cancer risk and its aggression [3].

The PI-RADS scoring system was then validated by several research groups [4].

Recently, the PI-RADS version 2 was developed, including the following changes: (a) the concept of a dominant sequence depending on the location of the lesion; (b) the statement that DCE-MRI should be scored positive if early focal enhancement is present and negative, if not or if diffuse enhancement is noticed, instead of using the curve-type analysis described in PI-RADS version 1; (c) for positive DCE-MRI results, the PI-RADS score should be increased by one point, if it makes a clinically relevant difference; (d) finally, an overall PIRADS score, on a scale of 1–5 is assigned, according to the revised rules from PI-RADS version 2 [1,4].

In the second version of PI-RADS, clinically significant cancer is defined on pathology as Gleason score ≥7 (including 3+4 with prominent Gleason 4 component), and/or volume ≥0.5 cc, and/or extraprostatic extension. This definition is intended to standardize reporting of mp-MRI and correlation with pathology for clinical and research applications [1].

The aim of this study is to evaluate the diagnostic performance of mp-MRI at 1.5-Tesla (1.5-T), for the detection of clinically significant prostate cancer.

METHODS

Patients

A total of 90 patients with clinically suspected prostate cancer were examined by mp-MRI, between October 2013 and February 2016, in a prospective single-center study.

We included in this study patients with clinically significant prostate cancer proved on biopsy or prostatectomy.

The patients with a history of positive prostate biopsy and the patients who were treated for prostate cancer were excluded.

Finally, 39 patients - mean age 68.02 years (ranging from 51 to 78 years) were included in this study.

This prospective study was approved by the local ethics committee. Written informed consent was obtained from all the patients included in the study, in order to use their laboratory, imaging and histopathologic data.

The patients were informed about the study protocol and signed their informed consent. The study was carried out in agreement with The Code of Ethics of the World Medical Association (Helsinki Declaration) for experiments involving human subjects.

Multiparametric-MRI protocol

All patients were examined by using a 1.5-Tesla equipment (Magnetom Avanto, Siemens Healthcare, Erlangen, Germany).

The same mp-MRI protocol was used for all patients: axial T2WI, sagittal T2WI, coronal T2WI, axial DWI with ADC map, axial T2 fat-sat, coronal T1WI and axial DCE-MRI (Table I).

For DCE-MRI a bolus injection of 0.1 mmol/kg body weight of gadolinium-based contrast agent followed by a saline flush of 20 ml was given.

MRI and Histopathology Analysis

The examinations were read by a radiologist with 3 years of experience in prostate-MRI. The images were analyzed using the Syngo VB17 software with the commercially available applications (Siemens Medical Solutions, Erlangen, Germany) and OsiriX viewer.

The radiologist knew only the patient PSA history.

Suspected lesions were noticed in MRI reports and were categorized according to the PI-RADS 2 lexicon [1]; a PIRADS score was assigned for all MR abnormalities.

For 17 patients examined between October 2013 and December 2014, the version 1 PI-RADS score [3] was initially used. Once the PI-RADS version 2 scoring system was available, a revised PI-RADS score was reported for these patients without modifying the initial MRI report. The transition from PI-RADS version 1 to PI-RADS version 2 was made in order to use the same scoring system for all of the patients examined in the study.

The MR findings were reported as "positive" if PIRADS 3, PIRADS 4 or PIRADS 5 lesions were present and "negative" if only PIRADS 1 or PIRADS 2 findings were identified.

A standardized multiparametric-MRI reporting scheme - modified after Rothke et al. [5] - was used additionally to the MRI report (Figure 1).

All 39 patients underwent a standard 12 core transrectal ultrasonography (TRUS)–guided biopsy; additional targeted cores were picked up in 7 patients, from MR suspected lesions.

During the study period, 4 of 39 patients with prostate cancer underwent radical prostatectomy.

Tissue samples have been fixed in 10% buffered formalin and then processed routinely. All the specimens were included in paraffin and sectioned at 5µm. The slides were stained using hematoxilin-eosin, following the manufacturers specifications.

Difficult or equivocal cases on hematoxilin-eosin were assessed by immunohistochemistry. Antibodies used were p63 (Clone 7JUL, Novocastra), High Molecular Weight Cytokeratin (clone 34betaE12, Novocastra) and also Alpha-methylacyl-CoA Racemase (AMACR, P504S,

clone EPMU1, Novocastra).

Antigen retrieval was performed with a pressure cooker and HIER method. The detection system used was Novolink Polymer Detection Kit, from Novocastra.

A pathologist with 8 years of experience in prostate pathology examined the slides, using an Olympus BX43 microscope.

The clinically significant cancer was defined, according to PI-RADS version 2 system [1], as Gleason score ≥7, and/or volume ≥0.5 cc, and/or extraprostatic extension.

When prostatectomy was not performed and only biopsy result was available, we defined a clinically significant prostate cancer core as Gleason score ≥7, and/or having a cancer length greater than 5 mm.

The standard of reference was settled by the results of systematic TRUS-guided biopsy: a patient was considered "true positive" if biopsy specimens showed pathologically positive results and "true negative" if biopsy result was negative.

The radiological reports were then compared with the histopathologic data.

Statistical analyses

SPSS 16.0 for Windows and MedCalc 10.3.0.0 software programs were used for data analysis. Numerical variables were descriptive presented. For testing normality distribution of the numerical variables we used the Kolmogorov-Smirnov test. For comparison of numerical variables, the student test, Mann-Whitney and Kruskal-Wallis (depending on its distribution) were used. Comparison of qualitative variables was performed using chi square test. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. A $p<0.05$ was considered statistically significant.

RESULTS

The mean age of the examined patients was 68.02±6.38 years, ranging between 51 and 78 years. 10.3% of patients were between 50-59 years, 43.6% ranged from 60 to 69 years and 46.2% were older than 70 – table II.

The mean PSA taken from blood samples was 22.69±39.34 ng/ml, with a median PSA of 12.95 ng/ml.

Patients were categorized based on PSA value as follows: patients with PSA < 10 ng/ml – 38.5% (15), patients with PSA ranging from 10 to 20 ng/ml – 28.2% (11) and with PSA >20 ng/ml – 33.3% (13).

There was no statistically significant difference between patients age in the PSA intervals.

In our series, 8 patients (20.5%) had prior negative biopsies and 31 patients (79.5%) had no previous biopsies; we found no statistically significant difference regarding the PSA values between these two groups – table III.

25 patients had MR abnormalities, which were stratified according to the PI-RADS 2 lexicon: focal abnormalities (1), lesions (3), masses (4), nodules (5), diffuse (4), multifocal (4), regional abnormalities (4).

PIRADS 5 was the dominant score (35.9 %) in our MRI reports (Figure 2).

Table I. Mp-MRI acquisition protocol.

	sagittal T2WI	axial T2WI	coronal T2WI	axial DWI	axial T2 fat-sat	coronal T1WI	axial DCE
Sequence	TSE	TSE	TSE	EPI DWI	TSE	TSE	2D FLASH
TR (ms)	4100	4490	3000	6500	12770	706	4.9
TE (ms)	92	92	92	98	75	12	2.4
FOV (mm^2)	240	230	200	360	350	400	410
Voxel size (mm^3)	1.0x0.7x3.0	1.1x0.8x3.0	0.9x0.6x3.0	2.0x1.9x3.0	1.7x1.4x3.0	2.1x1.6x3.5	1.9x1.3x2.5
Matrix	224x320	224x320	224x320	143x192	157x256	174x256	143x320
B-values	-	-	-	50, 500, 800, 1000, 1200	-	-	-
Number of measurements	1	1	1	1	1	1	16
Slice thickness	3mm	3mm	3mm	3mm	3mm	3.5mm	2.5mm

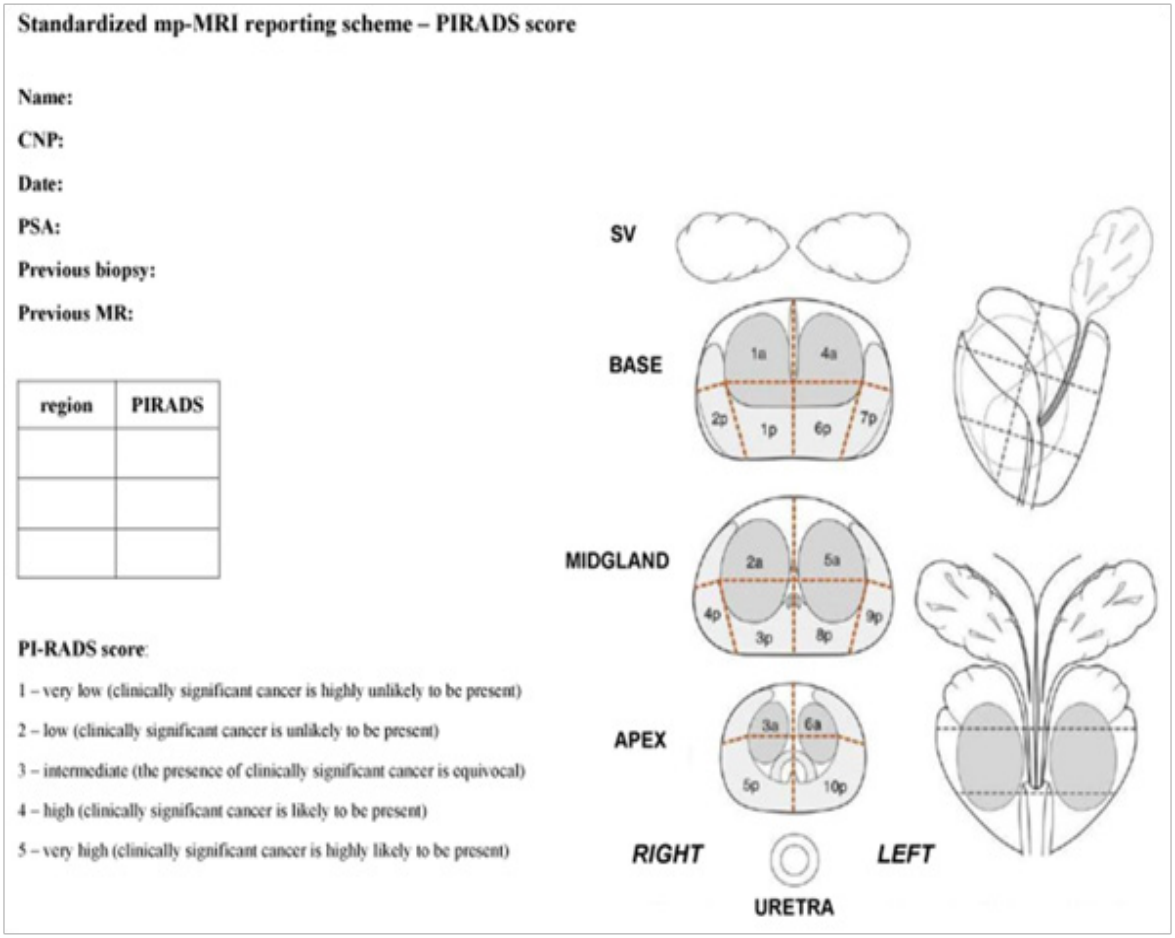


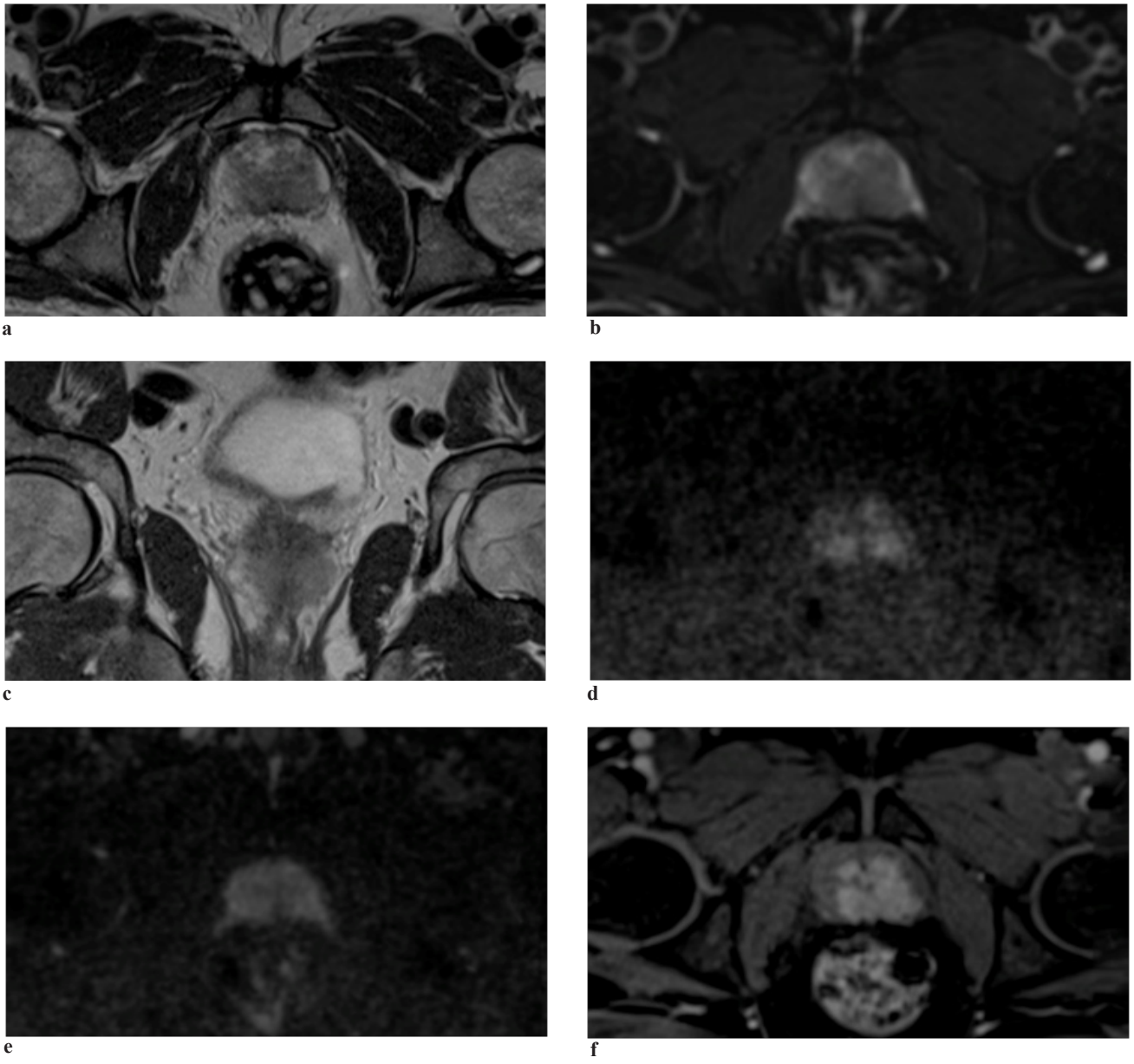
Figure 1: Standardized mp-MRI reporting scheme.

Table II. Patients age characteristics.

			PSA INTERVAL			TOTAL
			< 10	10-20	> 20	
AGE INTERVAL	50-59	NR (%)	1 (6.7%)	0 (0.0%)	3 (23.0%)	4 (10.2)
	60-69	NR (%)	9 (60.0%)	4 (36.4%)	4 (30.8%)	17 (43.6%)
	70-79	NR (%)	5 (33.3 %)	7 (63.6%)	6 (46.2%)	18 (46.2%)
TOTAL		NR (%)	15 (100%)	11(100%)	13 (100%)	39 (100%)

Table III. Patients with prior negative biopsies.

			PSA INTERVAL			TOTAL
			< 10	10-20	>20	
PRIOR BIOPSY	NEGATIVE	NR (%)	3 (20%)	3 (27.3%)	2 (15.4%)	8 (20.5%)
	NO	NR (%)	12 (80%)	8 (72.7%)	11 (84.6%)	31 (79.5%)



a. Axial T2WI TSE high-resolution, **b**. Axial T2WI fat-sat TSE and **c**. Coronal T2WI TSE high-resolution showing a hypointense mass, in the peripheral zone of the prostate, with extracapsular extension and seminal vesicle invasion. **d**. Axial DWI image and e. ADC map demonstrates restricted diffusion. f. DCE-MRI showing enhancement of the prostatic mass. According to the PIRADS v2 scoring system, the score for T2, DWI and DCE is respectively: 5, 5 and +; the overall score is 5, which means clinically significant cancer is highly likely to be present. TRUS-guided biopsy following mp-MRI was positive for prostate cancer with a Gleason score of 7 (3+4).

We found a statistically significant difference regarding the distribution of PIRADS score between the PSA groups (p=0.011) – table IV.

All 39 patients underwent the standard transrectal ultrasonography (TRUS)–guided biopsy; 7 patients had additional targeted cores on MR suspected lesions. 20 patients had positive biopsies and Gleason 7 was the dominant score (35.9 %) – table V.

There was no statistically significant difference regarding the Gleason score distribution between the PSA groups.

We found a statistically significant difference between the MRI reports in the PSA groups (p=0.016) – table VI.

The PSA groups differed significantly regarding the biopsy results (p=0.003) – table VII.

Sensitivity, specificity, positive predictive value and negative predictive value were calculated among the whole group (Table VIII).

Table IV. PIRADS score distribution.

		PSA INTERVAL			TOTAL
		< 10	10-20	> 20	
PIRADS 1	NR (%)	2 (13.3%)	0 (0.0%)	0 (0.0%)	2 (5.1%)
PIRADS 2	NR (%)	7 (46.6%)	4 (36.3%)	1 (7.7%)	12 (30.8%)
PIRADS 3	NR (%)	1 (6.7%)	2 (18.2%)	0 (0.0%)	3 (7.7%)
PIRADS 4	NR (%)	4 (26.7%)	2 (18.2%)	2 (15.4%)	8 (20.5%)
PIRADS 5	NR (%)	1 (6.7%)	3 (27.3%)	10 (76.9%)	14 (35.9%)
TOTAL	NR (%)	15 (100%)	11 (100%)	13 (100%)	39 (100%)

Table V. Gleason score distribution.

		PSA INTERVAL			TOTAL
		< 10	10-20	> 20	
PIRADS 6	NR (%)	1 (33.3 %)	1 (16.7 %)	1 (9.1%)	3 (15.0%)
PIRADS 7	NR (%)	1 (33.3 %)	3 (50.0%)	6 (54.5%)	10 (50.0%)
PIRADS 8	NR (%)	1 (33.3 %)	1 (16.7%)	1 (9.1%)	3 (15.0%)
PIRADS 9	NR (%)	0 (0.0%)	1 (16.7%)	2 (18.2%)	3 (15.0%)
PIRADS 10	NR (%)	0 (0.0%)	0 (0.0%)	1 (9.1%)	1 (5.0%)
TOTAL	NR (%)	3 (100%)	6 (100%)	11 (100%)	20 (100%)

Table VI. Relation between MRI reports and PSA values.

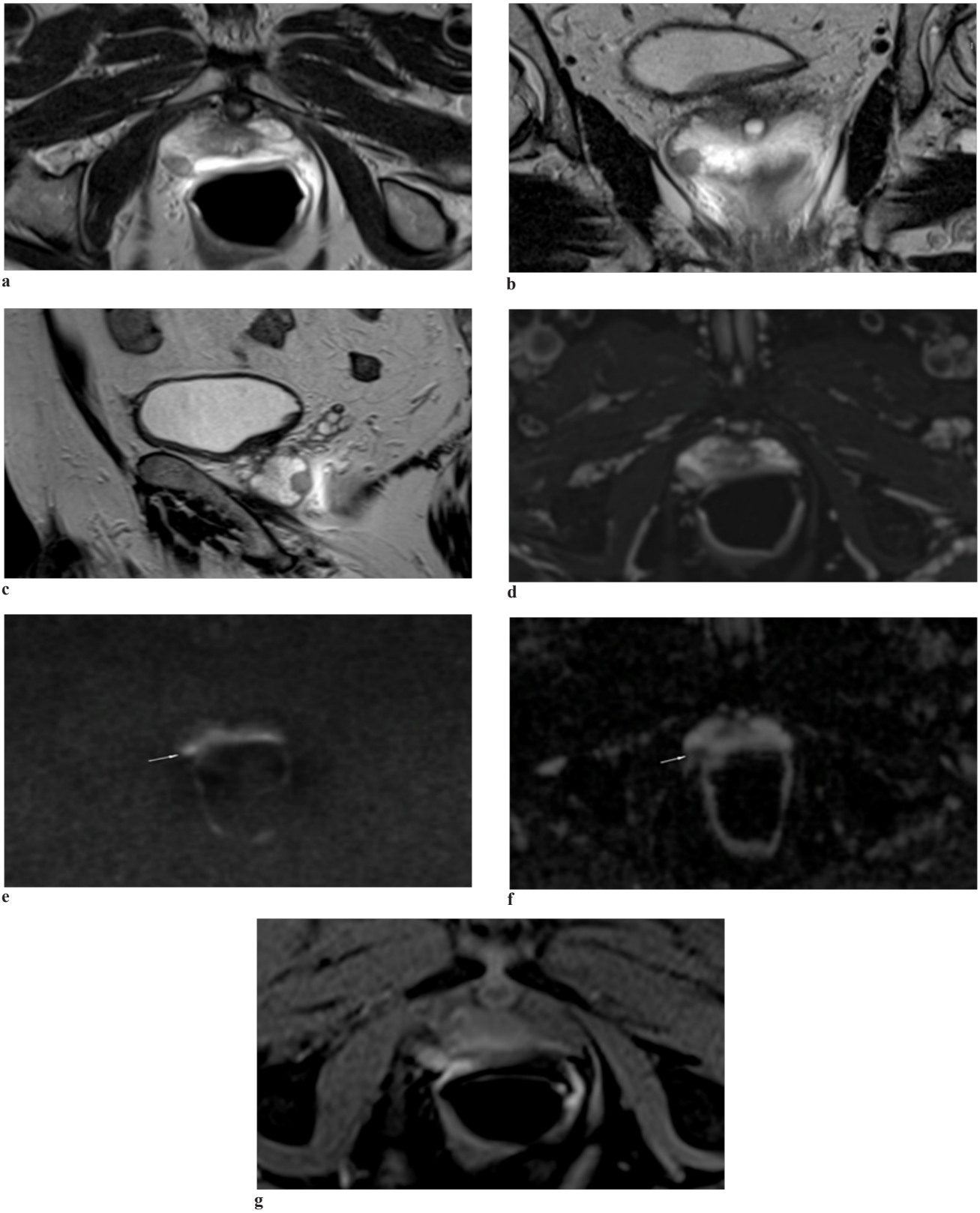
			PSA INTERVAL			TOTAL
			< 10	10-20	> 20	
MRI	NEGATIVE	NR (%)	9 (60.0%)	4 (36.4%)	1 (7.7%)	14 (35.9%)
	POSITIVE	NR (%)	6 (40.0%)	7 (63.6%)	12 (92.3%)	25 (64.1%)
TOTAL		NR (%)	15 (100%)	11 (100%)	13 (100%)	39 (100%)

Table VII. Relation between biopsy results and PSA values.

			PSA INTERVAL			TOTAL
			< 10	10-20	> 20	
BIOPSY	NEGATIVE	NR (%)	12 (80%)	5 (45.5%)	2 (15.4%)	19 (48.7%)
	POSITIVE	NR (%)	3 (20.0%)	6 (54.5%)	11 (84.6%)	20 (51.3%)
TOTAL		NR (%)	15 (100%)	11 (100%)	13 (100%)	39 (100%)

Table VIII. Overall Sensitivity (Se), Specificity (Sp), Positive predictive value (PPV) and Negative predictive value (NPV) for mp-MRI in prostate cancer detection.

		Confidence interval 95%
Sensitivity	100.00%	83.01% to 100.00%
Specificity	73.68%	48.80% to 90.75%
Positive Predictive Value	80.00%	59.29% to 93.09%
Negative Predictive Value	100.00%	76.66% to 100.00%



a. Axial T2WI TSE high-resolution, **b**. Coronal T2WI TSE high-resolution, **c**. Sagital T2WI TSE high-resolution and **d**. Axial T2WI fat-sat TSE showing a moderate hypointense right peripheral zone circumscribed nodule, <1.5 cm, with capsular contact. **e**. Axial DWI image and **f**. ADC map showing focal hyperintense signal on high b-value (b - 1200) and markedly hypointense on ADC. **g**. DCE-MRI demonstrates focal enhancement of the nodule. According to the PIRADS v2 scoring system, the score for T2, DWI and DCE is respectively: 4, 4 and +; the overall score is 4, which means clinically significant cancer is likely to be present. Biopsy following mp-MRI was positive for prostate cancer in the right gland with a Gleason score of 8 (4+4).

DISCUSSION

The highest incidence of prostate cancer was for males between 70-79 years (46.2%). The result is consistent with data provided by the Cancer Report in North-Western Region of Romania [6].

In our study, the MRI reports were positive for 25 (64.1%) of 39 patients, of which 12 patients had high PSA levels (≥20 ng/ml) – table VI. We found a statistically significant difference between the MRI reports and the PSA groups (p=0.016).

PIRADS 1 and PIRADS 2 lesions were found more frequently in patients with PSA value <10 ng/ml (9 of 15 patients). In the group with PSA≥20 ng/ml, PIRADS 4 and PIRADS 5 lesions were predominant (12 of 13 patients). A statistically significant difference regarding the distribution of PIRADS score between PSA groups was found (p=0.011).

Shakir et al. [7] demonstrated that the benefit of MRI and targeted biopsy increases with the increasing level of PSA [7,8].

Recent studies that included patients with PSA levels >10 ng/ml, reported the sensitivity, specificity, accuracy, PPV and NPV for the detection of prostate cancer using combined MRI, between 69-95%, 63-96%, 68-92%, 75-86% and 80-95%, respectively [9-14].

In our series of patients, TRUS-guided biopsies were positive in 20 patients (51.3%) of which 11 had a PSA ≥ 20 ng/ml. 19 patients (48.7%) had negative biopsies, 12 of them having low PSA levels (< 10 ng/ml). We found a statistically significant difference between the biopsy results and the PSA groups (p=0.003).

Our overall sensitivity and specificity for mp-MRI detection of clinically significant prostate cancer detection were 100% and 73.68%, respectively.

Tanimoto et al. [15] evaluated the clinical value of DWI and DCE-MRI in combination with T2WI for the detection of prostate cancer, in a series of 83 consecutive male patients, taking as reference the systematic biopsy results. They reported a sensitivity of 95%, a specificity of 74% and an accuracy of 86% [15].

In a retrospective study of 2011, Tamada et al. [16] reported a sensitivity of 83% and a specificity of 80% for combined MRI techniques (T2WI, DCE-MRI and DWI) in prostate cancer detection, on a per-patient basis. Their study evaluated a series of 50 patients and reference test was the12 cores TRUS-guided systematic biopsy. The accuracy, PPV and NPV reported were 82%, 91% and 67%, respectively [16].

Futterer et al. [17] found great variations in the detection of clinically significant prostate cancer in a systematic review of the literature from 2015. 12 studies (1981 patients) were included in this meta-analysis of which 5 were prospective studies. Six studies were performed at 3-T scanner, two studies used a 1.5-T unit, and four studies alternately used 1.5- and 3-Tesla equipments. The selected studies performed prostate MRI with at least two functional techniques (DW-MRI, DCE-MRI or MRSI) in addition to anatomical T2WI. Sensitivity ranged from 58 to 96%, specificity from 23 to 87% and accuracy from 44 to 87%. The NPV and PPV for the detection of clinically significant disease ranged from 63 to 98% and from 34 to 68%, respectively. The authors have concluded that mp-MRI is able to detect significant prostate cancer in biopsy-naïve males and men with prior negative biopsies. The high NPV of mp-MRI is important to the clinician because mp-MRI could be used to rule out significant disease [17].

In our study, the positive predictive value and the negative predictive value were 80% and 100%, respectively.

Eight of 39 patients had prior negative biopsies. In 4 patients the MRI report was positive and in 3 cases the prostate cancer was confirmed by TRUS-guided biopsy (two patients had Gleason 7 and one had Gleason 6).

Abd-Alazeez et al. [18] assessed the performance of multiparametric MRI in patients with prior negative TRUS-guided biopsy and showed that mp-MRI had good performance for detecting and ruling out clinically significant prostate cancer, with a Se of 90% and a NPV of 95%. They concluded that mp-MRI can be used as a triage test in the population with persistently elevated PSA levels following a negative biopsy and thereby identify patients who can avoid unnecessary prostate biopsy [8,18].

A published study in 2014 by Itatani et al. [19] reported a clinical NPV for mp-MRI of 89.6% for clinically significant prostate cancer, over a longitudinal follow-up period of 5 years. Therefore, the authors concluded that mp-MRI can to rule out clinically significant prostate cancer before biopsy [8,19]

Some potentially influential factors need to be discussed.

A limit of our study is the lack of accurate correlation between the MR localization of suspicious lesions and the TRUS-guided biopsy. Using the MR-in bore biopsy or the MRI-ultrasound fusion techniques could exceed this limit. Some recent studies have shown that the detection of more clinically significant cancers in the MRI-guided biopsy compared with systematic biopsy, improve the biopsy performance and the diagnostic benefits [17,20-23].

The positive MRI was reported per patient and not per lesion and this might potentially influenced our data.

Another limit of this study was that we used only one reader for mp-MRI examinations. Therefore, studies on larger groups of patients, with multiple readers are needed to confirm our data.

CONCLUSION

Our results show that 1.5 T mp-MRI has a high sensitivity for the detection of clinically significant prostate cancer and high negative predictive value in order to rule out significant disease.

References

1.Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS Prostate Imaging – Reporting and Data System: 2015, Version 2. Eur Urol. 2016;69(1):16-40.

2.Hoeks CM, Barentsz JO, Hambrock T, Yakar D, Somford DM, Heijmink SW, et al. Prostate cancer: multiparametric MR imaging for detection, localization, and staging. Radiology. 2011;261(1):46-66.

3.Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villeirs G, et al. ESUR prostate MR guidelines 2012. Eur Radiol. 2012;22(4):746–757.

4.Muller BG, Shih JH, Sankineni S, Marko J, Rais-Bahrami S, George AK, et al. Prostate Cancer: Interobserver Agreement and Accuracy with the Revised Prostate Imaging Reporting and Data System at Multiparametric MR Imaging. Radiology. 2015;277(3):741–750.

5.Rothke M, Blondin D, Schlemmer HP, Franiel T. PI-RADS classification: structured reporting for MRI of the prostate. Rofo. 2013;185(3):253–261.

6.Coza D, Suteu O, Nicula FA, Blaga L, Todescu A, Moldovan A, et al. Cancer report in north-western region of Romania 2010-2011. Cluj-Napoca: Casa Cartii de Stiinta; 2014;35-84.

7.Shakir NA, George AK, Siddiqui MM, Rothwax JT, Rais-Bahrami S, Stamatakis L, et al. Identification of threshold prostate specific antigen levels to optimize the detection of clinically significant prostate cancer by magnetic resonance imaging/ultrasound fusion guided biopsy. J Urol. 2014;192(6):1642-1648.

8.Ghai S, Haider MA. Multiparametric-MRI in diagnosis of prostate cancer. Indian J Urol. 2015;31(3):194–201.

9.Itatani R, Namimoto T, Kajihara H, Katahira K, Kitani K, Hamada Y, et al. Triage of low-risk prostate cancer patients with PSA levels 10 ng/ml or less: comparison of apparent diffusion coefficient value and transrectal ultrasound-guided target biopsy. Am J Roentgenol. 2014;202(5):1051-1057.

10.Petrillo A, Fusco R, Setola SV, Ronza FM, Granata V, Petrillo M, et al. Multiparametric MRI for prostate cancer detection: performance in patients with prostate-specific antigen values between 2.5 and 10 ng/mL. J Magn Reson Imaging. 2014;39:1206-1212.

11.Chong Y, Kim CK, Park SY, Park BK, Kwon GY, Park JJ. Value of diffusion-weighted imaging at 3 t for prediction of extracapsular extension in patients with prostate cancer: a preliminary study. Am J Roentgenol. 2014;202(4):772-777.

12.Tamada T, Sone T, Jo Y, Yamamoto A, Ito K. Diffusion-weighted MRI and its role in prostate cancer. NMR Biomed. 2014;27, 25-38.

13.Shukla-Dave A, Hricak H. Role of MRI in prostate cancer detection. NMR Biomed. 2014;27:16-24.

14.Murphy G, Haider M, Ghai S, Sreeharsha B. The expanding role of MRI in prostate cancer. Am J Roentgenol. 2013;201(6):1229-1238.

15.Tanimoto A, Nakashima J, Kohno H, Shinmoto H, Kuribayashi S. Prostate cancer screening: the clinical value of diffusion-weighted imaging and dynamic MR imaging in combination with T2-weighted imaging. J Magn Reson Imaging. 2007;25(1):146-152.

16.Tamada T, Sone T, Higashi H, Jo Y, Yamamoto A, Kanki A, Ito K. Prostate cancer detection in patients with total serum prostate-specific antigen levels of 4-10 ng/mL: diagnostic efficacy of diffusion-weighted imaging, dynamic contrast-enhanced MRI, and T2-weighted imaging. Am J Roentgenol. 2011;197(3):664-670.

17.Fütterer JJ, Briganti A, De Visschere P, Emberton M, Giannarini G, Kirkham A, et al. Can Clinically Significant Prostate Cancer Be Detected with Multiparametric Magnetic Resonance Imaging ? A Systematic Review of the Literature. Eur Urol. 2015;68(6):1045-1053.

18.Abd-Alazeez M, Ahmed HU, Arya M, Charman SC, Anastasiadis E, Freeman A, et al. The accuracy of multiparametric MRI in men with negative biopsy and elevated PSA level--can it rule out clinically significant prostate cancer? Urol Oncol. 2014;32(1):45.e17-22.

19.Itatani R, Namimoto T, Atsuji S, Katahira K, Morishita S, Kitani K, et al. Negative predictive value of multiparametric MRI for prostate cancer detection: outcome of 5-year follow-up in men with negative findings on initial MRI studies. Eur J Radiol. 2014;83(10):1740-1745.

20.Haffner J, Lemaitre L, Puech P, Haber GP, Leroy X, Jones JS, et al. Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging-targeted and systematic biopsy for significant prostate cancer detection. BJU Int. 2011;108(8 Pt 2):E171–E178.

21.Mozer P, Rouprêt M, Le Cossec C, Granger B, Comperat E, de Gorski A, et al. First round of targeted biopsies using magnetic resonance imaging/ultrasonography fusion compared with conventional transrectal ultrasonography-guided biopsies for the diagnosis of localised prostate cancer. BJU Int. 2015;115:50–57.

22.Puech P, Rouvière O, Renard-Penna R, Villers A, Devos P, Colombel M, et al. Prostate cancer diagnosis: multiparametric MR-targeted biopsy with cognitive and transrectal US-MR fusion guidance versus systematic biopsy--prospective multicenter study. Radiology. 2013;268:461–469.

23.Schoots IG, Roobol MJ, Nieboer D, Bangma CH, Steyerberg EW, Hunink MG. Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol. 2015;68(3):438-450.