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Comparison of Prostate Imaging Reporting and Data System (PI-RADS) version 1 and version 2 and combination with apparent diffusion coefficient as a predictor of biopsy outcome

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Abstract

PURPOSE: The main aim of the study was to compare the diagnostic performance of Prostate Imaging Reporting and Data System (PI-RADS) versions 1 and 2 for detection of prostate carcinoma (PCa) and clinically significant prostate carcinoma (CSPCa). The second aim was to evaluate the potential benefit of adding the apparent diffusion coefficient (ADC) and prostate specific antigen (PSA) density to the standard evaluation protocol.

METHODS: A total of 167 consecutive patients with elevated PSA underwent magnetic resonance imaging. The images were evaluated prospectively using both versions of the PI-RADS and the results compared with 12-core template biopsy and magnetic resonance/transrectal ultrasound fusion biopsy. Receiver-operating characteristic (ROC) curves were compared for each scoring system using DeLong's test. The area under the curve (AUC) was calculated for ADC and PSA density for lesions scored 4.

RESULTS: PI-RADS V2 had high discriminative ability for PCa prediction with an AUC of 0.824 (95% CI 0.763 to 0.885), compared to an AUC of 0.724 (95% CI 0.654 to 0.794) for PI-RADS V1 (p = 0.0335). ADC demonstrated a higher discriminative ability with an AUC of 0.702 (95% CI 0.548 to 0.856) in CSPCa prediction. Using the obtained ADC threshold of 828x10^-6 mm^2/s improved specificity to 86.73% with a sensitivity of 60.38%.

CONCLUSION: PI-RADS version 2 exhibited significantly higher discriminative ability for PCa and CSPCa detection compared to PI-RADS version 1. Using the ADC can improve the tumor predictability of PI-RADS version 2 in lesions scored 4.

O R I G I N A L A R T I C L E

Abbreaviations:

PI-RADS	- Prostate Imaging Reporting and Data System
V1, V2	- version 1, version 2
PCa	- prostate carcinoma
CSPCa	- clinically significant prostate carcinoma
ADC	- apparent diffusion coefficient
PSA	- prostate specific antigen
ROC	- receiver-operating characteristic
AUC	- area under the curve
Mp-MRI	- multiparametric magnetic resonance imaging
T2WI	- T2-weighted imaging
DCE	- dynamic contrast-enhanced imaging
MRS	- magnetic resonance spectroscopy
ESUR	- European Society of Urogenital Radiology
BHP	- benign prostate hyperplasia
MR/TRUS	- magnetic resonance/transrectal ultrasound
T1WI	- T1-weighted imaging
NPV	- negative predictive value
PPV	- positive predictive value

INTRODUCTION

Multiparametric magnetic resonance imaging (mp-MRI) has become a standard technique for detecting prostate carcinoma and local cancer staging (Turkbey *et al.* 2011; Abd-Alazeez *et al.* 2014; Margolis, 2014). Mp-MRI combines morphologic T2-weighted imaging (T2WI) with at least two functional techniques, such as diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC), dynamic contrast-enhanced imaging (DCE), and magnetic resonance spectroscopy (MRS).

In 2012, the European Society of Urogenital Radiology (ESUR) published guidelines for structured magnetic resonance imaging (MRI) reporting of suspicious lesions, the Prostate Imaging Reporting and Data System (PI-RADS), defining acquisition protocols for both 1.5T and 3T MRI scanners and score criteria using a 5-point scale based on T2WI, DWI, DCE, and MRS (Barentsz *et al.* 2012). For routine clinical work, the total PI-RADS score is recommended, defined as the sum of the score of each used technique (Röthke *et al.* 2013).

In 2015, the first standard PI-RADS system (PI-RADS V1) was modified. The new PI-RADS, version 2 (PI-RADS V2), was developed in conjunction with the American College of Radiology and ESUR (Weinreb *et al.* 2015). The new scoring system was simplified for easier clinical use. Though DWI become decisive for evaluating lesions in peripheral zone, T2WI become the most important sequence in transition zone. DCE plays only a secondary role for lesions in peripheral zone, and MRS is not even a recommended sequence in the standard prostate mp-MRI protocol (Barentsz *et al.* 2016; Weinreb *et al.* 2016).

DWI is a routine technique that reflects the microscopic random motion of water molecules within a tissue. The motion can be quantified by the ADC (Le Bihan *et al.* 1986). Calculated map images display the ADC values of each voxel in an image calculated based on two or more b-values and a monoexponential model of signal decay with increasing b-value (Weinreb *et al.* 2016). ADC values inversely correlate with histological grade and are useful in differentiating between benign and malignant tissue (Verma *et al.* 2011; Hambrock *et al.* 2011).

Prostate specific antigen (PSA) is a serine protease produced by epithelial prostatic cells with the function of liquefying seminal coagulum (Pérez-Ibave *et al.* 2018). PSA is used as a biomarker in the diagnosis and screening of prostate cancer. Isolated PSA has not demonstrated a sufficient sensitivity and specificity to be useful in routine examination of the prostate (Benson *et al.* 1992). However, PSA density can be useful for distinguishing benign prostate hyperplasia (BHP) and prostate cancer (PCa). PSA density is calculated as a ratio of the absolute PSA and the prostate volume (Benson *et al.* 1992) and has been described as a useful factor for suggesting clinically significant prostate cancer and the aggressiveness of prostate cancer (Corcoran *et al.* 2011).

We hypothesized that the diagnostic performance of PI-RADS V2 for the detection of both clinically significant prostate cancer (CSPCa) and PCa would be better than the older classification system, PI-RADS V1. Therefore, the aim of our study was to compare the diagnostic performance of PI-RADS versions 1 and 2 in the detection of PCa and CSPCa. The second aim was to evaluate the benefit of the ADC and PSA density when these parameters were added to the standard evaluation.

METHODS

Patient selection

In this prospective study, a total of 167 consecutive patients with elevated PSA underwent mp-MRI before biopsy between February 2015 and July 2016. We enrolled patients with elevated PSA with or without previous negative biopsy. Exclusion criteria included contraindicated MRI, inability to have an endorectal coil placed, and contraindicated gadolinium-based contrast agents. The mean patient age was 62.92 ± 7.0 years [range 45 – 80 years, median 63 (58 – 68) years]. The mean PSA level was 8.82 ± 7.9 ng/ml [range 0.53 – 72.50 ng/ml, median 6.87 (4.69 – 9.95) ng/ml], and the mean PSA density 0.16 ± 0.2 ng/ml/ml [range 0.01 – 1.20 ng/ml/ml, median 0.12 (0.07 – 0.18) ng/ml/ml]. Each patient underwent magnetic resonance/transrectal ultrasound (MR/TRUS) for suspicious lesions and standard 12-core biopsy (template biopsy). The interval between mp-MRI and biopsy was 1 – 4 weeks.

The study was approved by the hospital ethics committee. Informed consent for the study, including MRI examination and prostate biopsy, was obtained from all patients.

MRI technique

The mp-MRI examinations were performed on a 1.5T MR scanner (Signa HDxT GE; General Electric, Mil-

Tab. 1. Technical parameters of used sequences

Sequence	Plane	TR/TE (ms)	Slice (mm)	Gap (mm)	Matrix (mm)	FOV (mm)	b-value (s/mm²)
T2 tse	ax	3000/120	3	0	384x288	170	N/A
	cor	3000/120	3	0.3	252x224	170	N/A
	sag	3000/120	3	0	284x288	170	N/A
T1 tse	ax	560/11.5	5	0.5	352x256	280	N/A
DWI	ax	6000/93.6	4	0	128x128	160	0, 1500
T1 gre 3D (lava)	ax	4.4/2.1	4	0	320x192	310	N/A
T2 3D (cube)	ax	2000/92.7	2	0	256x256	270	N/A

TSE – turbo spin echo; DWI – diffusion weighted imaging; GRE – gradient echo; TR – time to repeat; TE – time to echo; FOV – field of view; N/A – not applicable

waukee, USA) with endorectal coil (Medrad, Pittsburgh, USA) and 8-channel body array coil (General Electric, Milwaukee, USA). Patients were asked to empty their rectum before the examination by using glycerin suppositories the morning before the examination. All patients were examined using the standard protocol, which included multiplanar T2WI sequences (in axial, coronal, and sagittal planes) and axial DWI of the prostate with b values of 0 and 1500 s/mm^2 using the endorectal coil. ADC maps were reconstructed for qualitative and quantitative assessment of DWI using standard GE software, the AW 4.5 Workstation (General Electric, Milwaukee, USA). T1-weighted imaging (T1WI) in the axial plane covering the whole pelvis were performed with a body array coil for evaluation of pelvic lymphadenopathy. DCE images were obtained using a fast three-dimensional T1W spoiled gradient echo in the same plane as the T2WI; the 3D volume covered the entire prostate. DCE images were acquired before, during, and after fast injection of a bolus of paramagnetic contrast medium, gadobutrol, at a dose 0.1 mmol/kg with a flow of 2.0 ml/s, followed by a 20 ml saline flush with a power injector (Medrad, Pittsburgh, USA). The images were acquired every 13 s for 4 min 30 s. Perfusion curves were generated using the commercial software on the GE AW 4.5 Workstation and evaluated using the PI-RADS V1 classification. The parameters of the sequences are provided in Table 1.

MRI evaluation

All MRI were evaluated prospectively by consensus by two radiologists with 4 and 10 years of experience with prostate MRI. MRI examinations were reported according to the PI-RADS V1 and PI-RADS V2 (Figure 1). In PI-RADS V1, each T2WI, DWI, and DCE sequence was scored separately on a 5-point scale (Barentsz *et al.* 2012). To obtain the overall PI-RADS score, we used Röthke's algorithm using a sum of scores of sequences (Röthke *et al.* 2013). To report the localization of lesions, the standardized MRI reporting scheme presented by Dickinson with 27 areas within the prostate was used (Dickinson *et al.* 2011). The lesion with the highest PI-RADS score was reported as a target lesion. Next, we evaluated the lesions according to PI-RADS V2, which is based on the dominant sequences. The transition and peripheral zones were evaluated separately according to PI-RADS V2 guidelines (Barentsz *et al.* 2016). For the peripheral zone, the dominant sequence is DWI, whereas the dominant sequence for the transition zone is T2WI. A 5-point assessment scale was used. The lesion with the highest score was reported as a target lesion in the same reporting scheme with 27 regions (Dickinson *et al.* 2011). Both PI-RADS versions used the same 5-point assessment scale (Table 2).

ADCs were measured in each voxel of the target lesion with the highest PI-RADS score. The lowest ADC value in the lesion was used for statistical analysis.

Tab. 2. The 5-point assessment scale used for the final score is similar for both Prostate Imaging Reporting and Data System classifications (Röthke et al. 2013, Barentsz et al. 2016)

PI-RADS	Definition for PI-RADS V1	Definition for PI-RADS V2
1	Most probably benign	Very low - CSPCa is highly unlikely to be present
2	Probably benign	Low - CSPCa is unlikely to be present
3	Indeterminate	Intermediate - the presence of CSPCa is equivocal
4	Probably malignant	High - CSPCa is likely to be present
5	Highly suspicious of malignancy	Very high - CSPCa is highly likely to be present

CSPCa – clinically significant prostate cancer; PI-RADS – Prostate Imaging Reporting and Data System; V1 – version 1; V2 – version 2

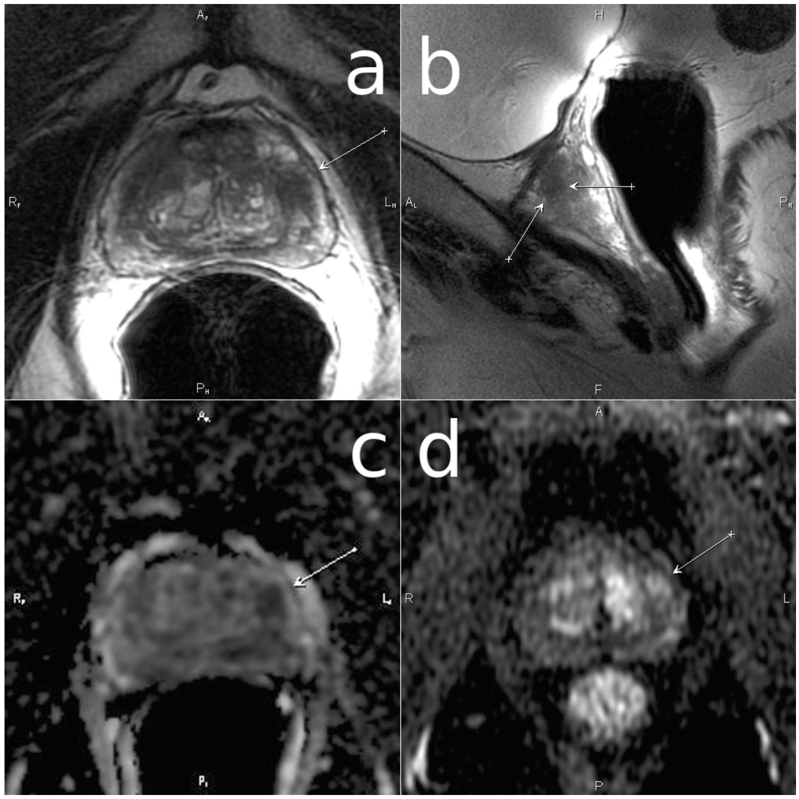

Fig. 1. Mp-MRI performed in a 68-year-old patient with elevated prostate specific antigen. A focal hypointense area in the peripheral zone of the left prostate lobe was present on T2-weighted images in axial (A) and sagittal (B) planes; corresponding diffusion-weighted axial images (C) demonstrated focal restriction of diffusion; dynamic contrast enhancement (D) showed early focal enhancement. The lesion was scored differently in both classifications, score 4 in PI-RADS V1 and score 5 in PI-RADS V2. Clinically significant prostate cancer was confirmed histologically.
PI-RADS V1 and V2 - Prostate Imaging Reporting and Data System version 1 and 2; Mp-MRI – multiparametric magnetic resonance imaging

Prostate biopsy technique

Within 4 weeks after MRI, all patients underwent prostate biopsy, which consisted of targeting MR/TRUS fusion biopsy to obtain one to four samples from the suspected lesion and a subsequent systematic template biopsy (12-core biopsy). The biopsy was performed by two experienced urologists using an ultrasound system (Toshiba Applio 500 with fusion unit SmartFusion). Tumors were identified on 2D T2WI and ADC maps, and then on 3D T2WI, which were used for MR/TRUS fusion guided biopsy. All cores were separately labeled according to their location and the biopsy scheme. Pathological biopsy evaluations were performed by an experienced pathologist blinded to MRI results. The tumor detection rate and overall sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) were calculated according to the results of the MR/TRUS fusion biopsy combined with 12-core template biopsy.

According to Epstein criteria, clinically insignificant prostate cancer is defined as the presence of cancer with Gleason score 6, less than three positive biopsy cores, and < 50% prostate cancer in a biopsy core (Epstein *et al.* 1994). This definition was used for the CSPCa, which was defined as a cancer with Gleason score > 6, more than two positive biopsy cores, and > 50% prostate cancer in one biopsy core.

Statistical analysis

Statistical analysis was performed to assess the relationship between PI-RADS V1 and PI-RADS V2 scores and the histopathological results of 12-core template biopsy, MR/TRUS fusion biopsy, and both biopsies together. For each PI-RADS score, we calculated the cancer detection rates for tumor and clinically significant carcinoma. NPV, PPV, sensitivity, and specificity were calculated for each score for both reporting systems. Receiver-operating characteristic (ROC) curves were compared for each PI-RADS using DeLong's test. Areas under the curve (AUCs) obtained in the ROC analysis for ADC and PSA density were calculated together for all scores and separately for scores of 3 and 4. A Spearman rank-order correlation test was utilized to evaluate the association between Gleason score and overall PI-RADS V1 and PI-RADS V2 scores between ADC and Gleason scores. Analyses were performed using R

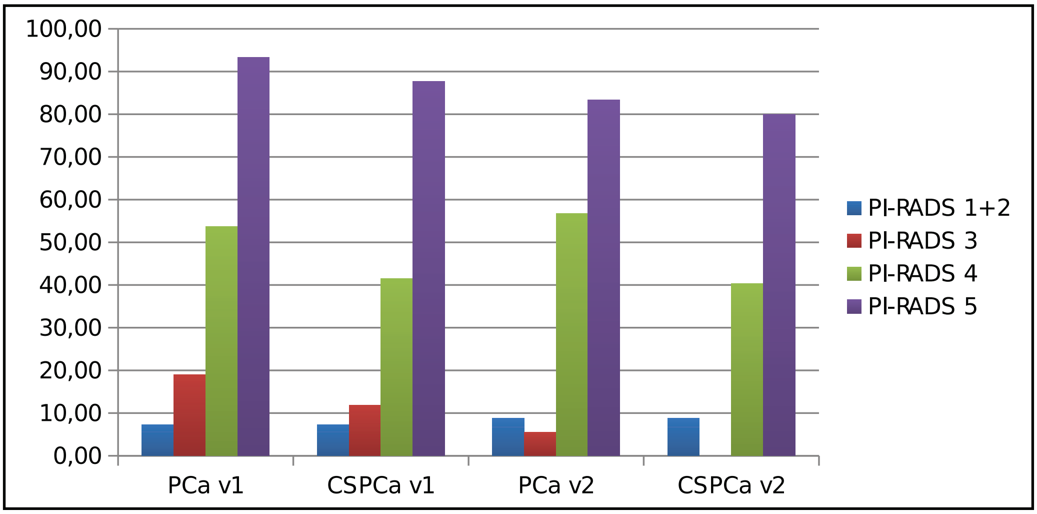

Fig. 2. Prostate cancer and clinically significant prostate cancer detection rates in Prostate Imaging Reporting and Data System versions 1 and 2
PI-RADS – Prostate Imaging Reporting and Data System; PCa V1 – prostate cancer evaluated in PI-RADS version 1; CSPCa V1 – clinically significant prostate cancer evaluated in PI-RADS version 1; PCa V2 – prostate cancer evaluated in PI-RADS version 2; CSPCa V2 – clinically significant prostate cancer evaluated in PI-RADS version 2

statistical package, version 3.4.2 (R Core Team, 2017). *P*-value < 0.05 was considered as significant.

RESULTS

Results of biopsy

Among a total 167 patients who underwent MR/TRUS fusion biopsy combined with 12-core template biopsy, PCa was histologically proven in 65 (38.92%) and CSPCa histologically detected in 52 (31.13%). The cancer detection rate was 34.73% (58/167) for PCa and 26.95% (45/167) for CSPCa diagnosed by MR/TRUS fusion biopsy, and 26.95% (45/167) for PCa and 23.35% (39/167) for CSPCa diagnosed by 12-core template biopsy. The cancer detection rates are given in Figure 2.

Results of MRI evaluation

Using PI-RADS V1, a total of 103 patients were scored as category 4 or 5 with high suspicion of cancer. Among these patients, PCa was histologically proven in 58 (56%) and CSPCa in 47 (46%). Using PI-RADS V2, 97 patients were scored as category 4 or 5, with PCa histologically confirmed in 63 (65%) and CSPCa in 51 (53%).

PI-RADS V2 demonstrated high discriminative ability in prostate cancer detection (prediction) with an AUC of 0.824 (95% CI 0.763 to 0.885), which was significantly higher (p = 0.0335) than the AUC of PI-RADS V1 0.724 (95% CI 0.654 to 0.794) in the ROC analysis (Figure 3). Similar results were obtained for CSPCa, with an AUC of 0.819 (95% CI 0.754 to 0.886) with PI-RADS V2.

Results of the ROC analysis for PCa and CSPCa prediction when the reference standard was 12-core template biopsy, MR/TRUS fusion biopsy, and both biopsies together are given in Table 3.

Details on the sensitivity, specificity, NPV, and PPV are given in Table 4.

The NPV for a score of 1 and 2 (considered probably benign) was high for both scoring systems. An overall assessment score of 5 (higher suspicion of malignancy) had a high specificity and PPV for the presence of prostate carcinoma for both PI-RADS V1 and V2. Comparing both scoring systems revealed a high NPV for both

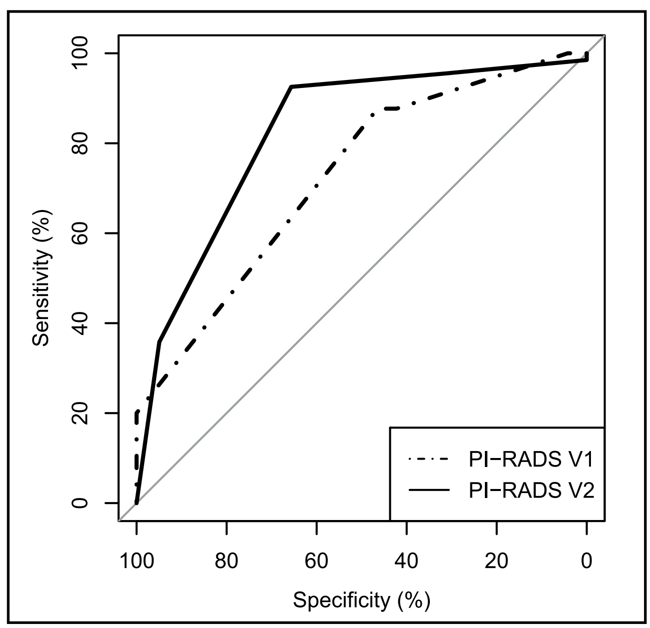

Fig. 3. Receiver-operating characteristic curve demonstrates that Prostate Imaging Reporting and Data System version 2 has better discriminative ability for prostate cancer detection than version 1
The gray line is the reference line. PI-RADS V1 – Prostate Imaging Reporting and Data System version 1; PI-RADS V2 – Prostate Imaging Reporting and Data System version 2

Tab. 3. Areas under the curve of the receiver-operating characteristic analysis for prostate cancer and clinically significant prostate cancer when the histopathological results were compared to 12-core template biopsy, magnetic resonance/transrectal ultrasound fusion biopsy, and both biopsies together

PCa	MR/TRUS fusion biopsy	12-core template biopsy	MR/TRUS fusion biopsy and 12-core biopsy
AUC for PI-RADS V1 (95% CI)	0.722 (0.649 – 0.795)	0.721 (0.649 – 0.792)	0.724 (0.654 - 0.794)
AUC for PI-RADS V2 (95% CI)	0.831 (0.774 – 0.887)	0.793 (0.727 – 0.859)	0.824 (0.763 - 0.885)
p- value	*0.0109*	*0.2121*	*0.0335*
CSPCA			
AUC for PI-RADS V1 (95% CI)	0.721 (0.646 – 0.796)	0.705 (0.627 – 0.784)	0.725 (0.654 – 0.797)
AUC for PI-RADS V2 (95% CI)	0.832 (0.776 – 0.888)	0.777 (0.704 – 0.852)	0.820 (0.754 – 0.885)
p- value	*0.0128*	*0.1130*	*0.0150*

AUC – area under the curve; PCa – prostate cancer; CSPCa – clinically significant prostate cancer; PI-RADS – Prostate Imaging Reporting and Data System; V1 – version 1; V2 – version 2; CI – contingent interval

scoring systems, though PI-RADS V2 had better NPV for CSPCa detection with a score of 5. PI-RADS V1 had a better PPV for CSPCa detection for each score (Figure 4). Nevertheless, in ROC analysis, for both PCa and CSPCa, prediction was better using PI-RADS V2 than PI-RADS V1 ($p = 0.0335$ and $p = 0.0150$).

While reliable results for PCa detection were obtained for scores 1, 2 and 5, we received less reliable results for scores 3 and 4. To increase the low specificity obtained for scores of 3 and 4, two additional factors were tested that may help increase the specificity: PSA density and minimum ADC in the prostate. The ROC curve had an AUC of 0.567 (95% CI 0.415 to 0.719) for PSA density as a predictor of CSPCa detection. The ADC had a greater ability to discriminate, with an AUC of 0.702 (95% CI 0.548 to 0.856) for CSPCa detection, but the difference was not significant with $p = 0.241$, (Figure 5). Using the ROC analysis of ADC as a predictor of CSPCa, the ADC threshold for a specificity of 80% was calculated. For lesions scored 4 and a specificity of 80%, the ADC threshold was 828 x 10^{-6} mm^2/s for both PI-RADS V1 and V2. Because the same value was obtained for both scoring systems, this ADC was used as a threshold for all patients, which improved the overall specificity to 86.73% with a sensitivity of 60.38%. The reference standard for lesions scored 3 and 4 was MR/TRUS fusion guided biopsy histopathology results.

Tab. 4. Diagnostic performance of Prostate Imaging Reporting and Data System versions 1 and 2 for prostate cancer and clinically significant prostate cancer

	PCa				CSPCa			
Scores	Sensitivity %	Specificity %	NPV %	PPV %	Sensitivity %	Specificity %	NPV %	PPV %
PI-RADS V1								
1+2	2.94	72.34	50.75	7.14	3.70	75.93	61.19	7.14
3	11.76	68.09	51.61	21.05	9.63	69.44	60.48	13.16
4	64.71	59.57	70.00	53.66	62.96	55.56	75.00	41.46
5	20.59	100.00	63.51	100.00	24.07	99.07	72.30	92.86
PI-RADS V2								
1+2	4.48	68.69	51.52	8.82	5.66	72.57	62.12	8.82
3	2.30	65.66	50.00	5.56	0.00	68.14	59.23	0.00
4	56.72	70.71	70.71	56.72	50.94	64.60	73.74	40.30
5	35.82	94.95	68.61	82.76	43.40	94.69	78.10	79.31

NPV – negative predictive value; PPV ¬– positive predictive value; PCa – prostate cancer; CSPCa – clinically significant prostate cancer; PI-RADS – Prostate Imaging Reporting and Data System; V1 – version 1; V2 – version 2

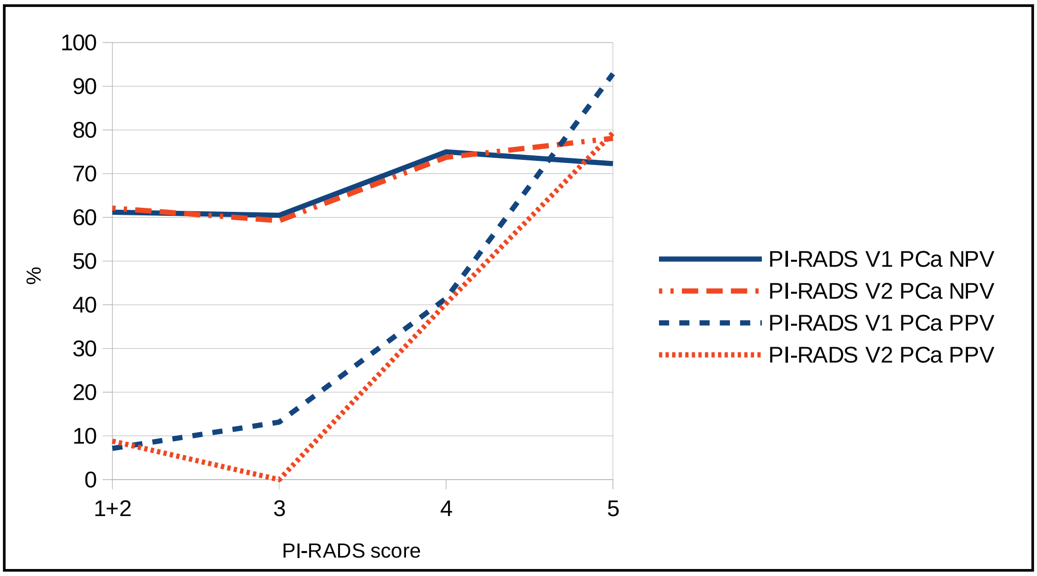

Fig. 4. Comparison of the positive predictive values and negative predictive values in Prostate Imaging Reporting and Data System versions 1 and 2
PI-RADS V1 – Prostate Imaging Reporting and Data System version 1; PI-RADS V2 – Prostate Imaging Reporting and Data System version 2; PCa – prostate cancer; PPV – positive predictive values; NPV – negative predictive values

Spearman´s rank-order correlation revealed an inverse correlation between ADC and Gleason score (Spearman´s correlation coefficient ρ = -0.254, p = 0.043).

Spearman´s rank-order correlation revealed a better positive correlation between PI-RADS V1 and Gleason score (Spearman´ s correlation coefficient ρ = 0.331, p = 0.009) than between PI-RADS V2 and Gleason score (Spearman´s correlation coefficient ρ = 0.263, p = 0.036).

DISCUSSION

The main aim of our study was to compare the diagnostic performance of PI-RADS V1 and PI-RADS V2 for the detection of PCa and CSPCa. We found that both scoring systems have high discriminative ability for predicting PCa and CSPCa, but PI-RADS V2 had significantly higher discriminative ability for both. Similar results were reported by Kasel-Siebert and Feng (Kasel-Seibert *et al.* 2016; Feng *et al.* 2016). In addition, some studies comparing PI-RADS V1 and 2 have shown that PI-RADS V2 is more effective for tumor detection in the transition zone (Feng *et al.*, 2016; Polanec *et al.* 2016). However, some studies have reported better diagnostic performance of PI-RADS V1. Visschere and Auer reported a large discriminative ability in tumor prediction in two retrospective studies (De Visschere *et al.* 2016; Auer *et al.* 2016).

Both PI-RADS V1 and V2 demonstrated a high NPV for scores of 1 and 2 for PCa and CSPCa detection and a high PPV with specificity for a score of 5 for both PCa and CSPCa detection, which is in agreement with previous studies (De Visschere *et al.* 2016; Rastinehad *et al.* 2015).

We found a better PPV for each score for CSPCa detection when PI-RADS V1 was used. In contrast, a higher NPV of CSPCa prediction was obtained when scored with the PI-RADS V2 for scores 5. One reason for this discrepancy could be in the different approaches of the two systems. In PI-RADS V1, multi-

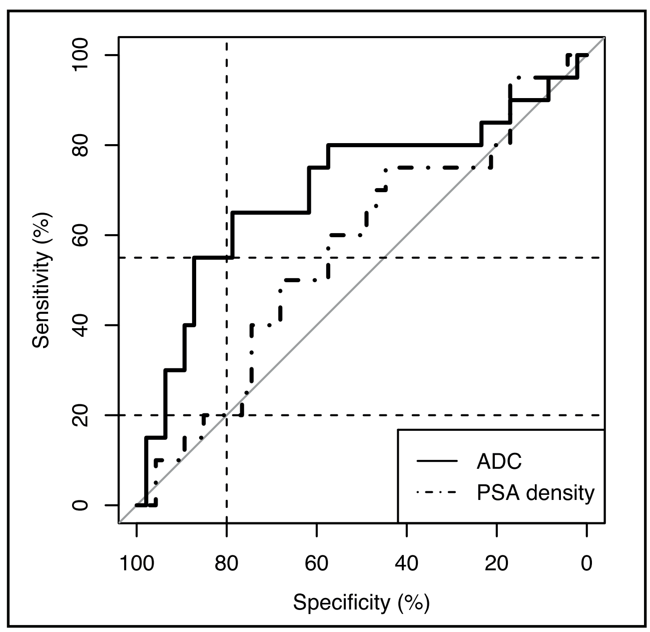

Fig. 5. Receiver-operating characteristic curve demonstrating different diagnostic performance of the apparent diffusion coefficient and prostate specific antigen density in lesions scored 4 by Prostate Imaging Reporting and Data System version 2
Dotted lines indicate the 80% specificity thresholds. The gray line is the reference line. ADC – apparent diffusion coefficient; PSA density – prostate specific antigen density

ple parameters are used together, such as T2WI, DWI, ADC maps, and DCE (sum of scores is used to prove the presence of the tumor), whereas PI-RADS V2 uses only one dominant sequence capable of excluding the presence of the tumor.

Both scoring systems had the highest PCa and CSPCa detection rates for scores of 5 (80% – 93%), whereas for scores of 3 and 4 the cancer detection rates were low. Our results are similar to those reported by Mertan and Mathur in smaller groups of patients (Mertan *et al.* 2016; Mathur *et al.* 2016).

Our data show a high false-positive rate for PCa and CSPCa of category 3 and 4 in both scoring systems. Therefore, we tested additional tumor predicting factors, such as the ADC and PSA density. The calculated ADC and PSA density were used for categories 3 and 4 in a separate, retrospective statistical evaluation. When PSA density was used as an additional factor in lesions scored 4, this parameter had a smaller effect on tumor predictability. In contrast, Jordan *et al.* demonstrated an improved performance of PI-RADS V2 when it was combined with PSA density (Jordan *et al.* 2017). One reason for our results could be the greater number of higher Gleason scores for lesions scored 4 in our study. A strong correlation exists between Gleason score and PSA density in well/intermediate-differentiated tumors; they produce high amounts of PSA per unit volume of cancer, whereas high grade tumors produce less PSA per unit volume (Corcoran *et al.* 2011). ADCs in the same settings improved the CSPCa specificity of both scoring systems in lesions scored 4. However, the difference in tumor predictability when the ADC and PSA density were used as additional parameters in lesions scored 4 was not significant. The potential benefit of incorporating ADCs in PI-RADS V2 was described recently (Jordan *et al.* 2018).

Our data demonstrated a negative correlation between the ADC and Gleason score in PCa, which is consistent with other studies reported that the ADC is a useful factor in differentiation between high risk, intermediate risk, and low risk tumors (Verma *et al.* 2011; Vargas *et al.* 2011; Dias *et al.* 2016; Kim *et al.* 2016). The decrease in ADC in high grade tumors was explained by the increased cellularity in high risk tumors (Chen *et al.* 2013; Surov *et al.* 2017). The best cutoff value for the ADC obtained in our study was 828 x 10^{-6} mm^2/s, which is similar to the cutoff reported by Kim, who found the best ADC cutoff for identifying prostate cancer to be 830 x 10^{-6} mm^2/s (Kim *et al.* 2016). Using this ADC threshold in lesions scored 4 could lead to a decreased number of false positive lesions. Our results are in line with the recommendation of PI-RADS V2 to use a threshold of 750 x 10^{-6} – 900 x 10^{-6} mm^2/s (Weinreb *et al.* 2016). Calculating the same parameters for lesions scored 3 was inconclusive due to a small number of such patients with PCa in our study.

While comparing the PI-RADS classifications, our experience was consistent with results in the literature. We found the PI-RADS V2 classification to be easier and faster for daily radiology practice. The inter-observer agreement for malignant lesions has been reported to be better with PI-RADS V2 than PI-RADS V1, and the time needed for PI-RADS V2 scoring is significantly shorter (Tewes *et al.* 2016). Becker reported similar inter-reader agreement in PI-RADS V2 and V1 at comparable diagnostic performance (Becker *et al.* 2017). Thus, DCE in PI-RADS V2 became a second sequence in the evaluation of lesions in peripheral zone, it may lead to decreasing of the number of contrast media injections.

This study has some limitations. First, we used TRUS biopsy as the standard instead of the whole-mount pathology section. However, all MRI results were compared with both MR/TRUS fusion biopsy and systematic template biopsy to minimize the potential to miss the cancer. Another limiting factor is the small number of positive lesions scored 3 in both PI-RADS versions. Another limitation could be the use of absolute ADC values, given their high variability when acquired from different MRI scanners. Several studies have reported significant variability in ADCs described in different body tissues depending on coil system, vendors, field inhomogeneity, field strengths, and differences in the design of the DWI sequences (Sasaki *et al.* 2008; Kivrak *et al.* 2013). Finally, we did not compare the inter-reader variability of PI-RADS V1 and PI-RADS V2 in this study. All MR images were evaluated by the consensus of two experienced radiologists. However, several studies have shown very good inter-reader reliability of PI-RADS V2 (Kasel-Seibert *et al.* 2016; Tewes *et al.* 2016). An advantage of this study is the prospective design. Other advantages are the sufficient number of included patients and the use of both MR/TRUS fusion biopsy and systematic template biopsy for histological analysis.

CONCLUSION

PI-RADS V2 demonstrated significantly higher discriminative ability for PCa and CSPCa detection compared to the previous scoring system, PI-RADS V1. Detecting the minimum ADC in the lesion < 828 x 10^{-6} mm^2/s increases the probability of detecting prostate carcinoma. Using the ADC as an additional parameter in lesions scored 4 with PI-RADS V2 could improve tumor predictability.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICAL APPROVAL

The study was approved by the hospital ethics committee.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study.

REFERENCES

1 Abd-Alazeez M, Ahmed HU, Arya M, Charman SC, Anastasiadis E, Freeman A, et al (2014.) The accuracy of multiparametric MRI in men with negative biopsy and elevated PSA level – Can it rule out clinically significant prostate cancer? Urol Oncol. **32**(1): 45e17-45e.22.
2 Auer T, Edlinger M, Bektic J, Nagele U, Herrmann T, Schäfer G, et al (2016). Performance of PI-RADS version 1 versus version 2 regarding the relation with histopathological results. World J Urol. https://doi.org/10.1007/s00345-016-1920-5.
3 Barentsz JO, Richenberg J, Clements R, Choyke P, Verma S, Villiers G, et al (2012). ESUR prostate MR guidelines 2012. Eur Radiol. **22**: 746-757.
4 Barentsz JO, Weinreb JC, Verma S, Thoeny HC, Tempany MC, Shtern F, et al (2016). Synopsis of the PI-RADS v2 guidlines for multiparametric prostate magnetic resonance imaging and recommendations for use. Eur Urol. **69**: 41-49.
5 Becker AS, Cornelius A, Reiner CS, Stocker D, Ulbrich EJ, Barth BK, et al (2017). Direct comparison of PI-RADS version 2 and version 1 regarding interreader agreement and diagnostic accuracy for the detection of clinically significant prostate cancer. Eur J Radiol. **94**: 58-63.
6 Benson MC, Whang IS, Pantuck A, Ring K, Kaplan SA, Olsson CA, et al (1992). Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer. J Urol. **147**: 815-16.
7 Chen L, Liu M, Bao J, Xia Y, Zhang J, Zhang L, et al (2013). The correlation between apparent diffusion coefficient and tumor cellularity in patients: a meta-analysis. PLoS One. https://doi.org/10.1371/journal.pone.0079008.
8 Corcoran NM, Casey RG, Hong MKH, Pedersen J, Connolly S, Peters J, et al (2011). The ability of prostate-specific antigen (PSA) density to predict an upgrade in Glreason score between initial prostate biopsy and prostatectomy diminishes with increasing tumour grade due to reduced PSA secretion per unit tumour volume. BJU Int. **110**: 36-42.
9 De Visschere P, Pattyn E, Ost P, Claeys T, Lumen N, Villeirs G (2016). Comparison of the prostate imaging reporting and data system (PI-RADS) version 1 and 2 in a cohort of 245 patients with histopathological reference and long-term follow-up. J Belg Soc Radiol. **100**(1): 1-10
10 Dias JL, Pina JM, Costa NV, Carmo S, Leal C, Bilhim T, et al (2016). The utility of apparent diffusion coefficient values in the risk stratification of prostate cancer using a 1.5T magnetic resonance imaging without endorectal coil. Acta Urol Port. **33**(3): 81-86.
11 Dickinson L, Ahmed HU, Allen C, Barentsz JO, Carey B, Futterer JJ, et al (2011). Magnetic resonance imaging for the detection, localisation and characterisation of prostate cancer: recommendation from a European consensus meeting. Eur Urol. **59**: 477-494.
12 Epstein JI, Walsh PC, Carmichael M, Brendler CB (1994). Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA. **271**(5): 368-374.
13 Feng ZY, Wang L, Min XD, Wang SG, Wang GP, Cai J (2016). Prostate cancer detection with multiparametric magnetic resonance imaging: prostate imaging reporting and data system version 1 versus version 2. Chin Med J. **129**(20): 2451-2459.
14 Hambrock T, Somford DM, Huisman HJ, Oort IM, Witjes JA, Hulsbergen-van de Kaa CHA, et al (2011). Relationship between apparent diffusion coefficients at 3.0 T MR imaging and Gleason grade in peripheral zone prostate cancer. Radiol. **259**/2: 453-461.
15 Jordan EJ, Fiske Ch, Zagoria RJ, Westphalen AC (2017). Evaluating the performance of PI-RADS v2 in the non-academic setting. Abdom Radiol. https://doi.org/10.1007/s00261-017-1169-5.
16 Jordan JE, Fiske Ch, Zagoria RJ, Wetsphalen AC (2018). PI-RADS v2 and ADC values: is there room for improvement? Abdom Radiol. https://doi.org/10.1007/s00261-018-1557-5.
17 Kasel-Seibert M, Lehmann T, Aschenbach R, Guettler FV, Abubrig M, Grimm MO, et al (2016). Assessment of PI-RADS v2 for the detection of prostate cancer. Eur J Radiol. **85**: 726-731.
18 Kim TH, Kim ChK, Park BK, Jeon HG, Jeong BCh, Seo SII, et al (2016). Relationship between Gleason score and apparent diffusion coefficients of diffusion-weighted magnetic resonance imaging in prostate cancer patients. Can Urol Assoc J. **10**(11-12): E377-E382.
19 Kivrak AS, Paksoy Y, Erol C, Koplay M, Özbek S, Kara F (2013). Comparison of apparent diffusion coefficient values among different MRI platforms: a multicenter phantom study. Diagn Interv Radiol. **19**: 433-437.
20 Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M (1986). MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. Radiol. **161**: 401-407.
21 Margolis DJA (2014) Multiparametric MRI for localized prostate cancer: lesion detection and staging. BioMed Res Int. https://doi.org/10.1155/2014/684127.
22 Mathur S, O´Malley ME, Ghai S, Jhaveri K, Sreeharsha B, Margolis M, et al (2018). Correlation of 3T multiparametric prostate MRI using prostate imaging reporting and data system (PIRADS) version 2 with biopsy as reference standard. Abdom Radiol. https://doi.org/10.1007/s00261-018-1696-8.
23 Mertan FV, Greer MD, Shih JH, George AK, Kongnyuy M, Muthigi A, et al (2016). Prospective evaluation of the prostate imaging reporting and data system version 2 for prostate cancer detection. J Urol. https://doi.org/10.1016/j.juro.2016.04.057.
24 Pérez-Ibave DC, Burciaga-Flores CH, Elizondo-Riojas MA (2018). Prostate-specific antigen (PSA) as a possible biomarker in noprostatic cancer: A review. Cancer Epidemiol. **54**: 48-55.
25 Polanec S, Helbich TH, Bickel H, Pinker-Domenig K, Georg D, Shariat SF, et al (2016). Head-to.head comparison of PI-RADS v2 and PI-RADS v1. Eur J Radiol. **85**: 1125-1131.
26 R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. www.R-project.org.
27 Rastinehad AR, Waingankar N, Turkbey B, Yaskiv O, Sonstegard AM, Fakhoury M, et al (2015). Comparison of multiparametric MRI scoring systems and the impact on cancer detection in patients undergoing MR US fusion guided prostate biopsies. PLoS One. https://doi.org/10.1371/journal.pone.0143404.
28 Röthke M, Blondin D, Schlemmer HP, Franiel T (2013). PI-RADS Classification: Structured reporting for MRI of the prostate. Magnetom Flash. **4**: 30-38.
29 Sasaki M, Yamada K, Watanabe Y, Matsui M, Ida M, Fujiwarw S, et al (2008). Variability in absolute apparent diffusion coefficient values across different platforms may be substantial: a multivendor, multi-institutional comparison study. Radiol. **249**(2): 624-630.
30 Surov A, Meyer HJ, Wienke A (2017). Correlation between apparent diffusion coefficient (ADC) and cellularity is different in several tumors: a meta-analysis. Oncotarget. **8**(35): 59492-59499.

31 Tewes S, Mokov N, Hartung D, Schick V, Peters I, Schedl P, et al (2016). Standardized reporting of prostate MRI: comparison of the prostate imaging reporting and data system (PI-RADS) version 1 and version 2. PLoS One. https://doi.org/10.1371/journal.pone.0162879.
32 Turkbey B, Mani H, Shah V, Rastinehad AR, Bernardo M, Pohida T, et al (2011). Multiparametric 3T prostate MR imaging to detect cancer: histopathologic correlation using prostatectomy specimens processed in customized MRI-based molds. J Urol. **186**(5): 1818-1824.
33 Vargas HA, Akin O, Franiel T, Mazaheri Y, Zheng J, Moskowitz Ch, et al (2011). Diffusion-weighted endorectal MR imaging at 3T for prostate cancer: tumor detection and assessment of agressiveness. Radiol. **259**(3): 775-784.
34 Verma S, Rajesh A, Morales H, Lemen L, Bills G, Delworth M, et al (2011). Assessment of aggressiveness of prostate cancer: correlation of apparent diffusion coefficient with histologic grade after radical prostatectomy. Am J Roentgenol. **196**: 374-381.
35 Weinreb JC, Barentsz JO, Choyde PL, Cornud F, Haider MA, Macura KJ, et al (2015). Prostate Imaging – Reporting and Data System. Version 2. https://www.acr.org/-/media/ACR/Files/RADS/Pi-RADS/PIRADS-V2.pdf?la=en.
36 Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al (2016). PI-RADS Prostate Imaging – Reporting and Data System: 2016, version 2. Eur Urol. **69**: 16-40.