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Review

S-PI-RADS and PI-RRADS for Biparametric MRI in the Detection of Prostate Cancer and Post-treatment Local Recurrence

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Abstract. *The application of biparametric magnetic resonance imaging (bpMRI) [T2-weighted (T2W) and diffusion weighted imaging (DWI)/apparent diffusion coefficient (ADC)] using dedicated structured methods, such as Simplified Prostate Imaging Reporting and Data System (S-PI-RADS) for the detection, categorization, and management of prostate cancer (PCa) is reported. Also, Prostate Imaging Reporting for Local Recurrence and Data System (PI-RRADS) for the detection and assessment of the probability of local recurrence after radiotherapy (RT) or radical prostatectomy (RP) in patients with biochemical recurrence (BCR) is proposed. Both S-PI-RADS and PI-RRADS assign to DWI/ADC a main role for the above purpose. S-PI-RADS identifies four categories and, on the basis of the qualitative and quantitative analysis of the restricted diffusion on ADC map and lesion volume, distinguishes two categories of lesions: category 3 (moderately homogeneous hypointense on ADC map) and category 4 (markedly homogeneous or inhomogeneous hypointense on ADC map). In category 3, two subcategories (3a: volume <0.5 cm^3 and 3b: volume ≥0.5 cm^3) suggesting clinical management. PI-RRADS distinguishes four assessment categories and suggests the stratification of the probability (ranging from very low for category 1 to very high for category 4) of local disease recurrence. In clinical practice, S-PI-RADS and PI-RRADS, based on bpMRI represent a potential valid approach that may facilitates the detection and management of PCa and for detecting local recurrence after treatment improving communication with other professionals.*

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Numerous single-center and meta-analysis studies have found that overall prostate cancer (PCa) detection rates using biparametric magnetic resonance imaging (bpMRI) are equivalent to those of multiparameter MRI (mpMRI), with a comparable efficacy in guiding targeted biopsy (1-5). A narrative review from Prostate Imaging Reporting and Data System (PI-RADS) Committee, considering the high performance of bpMRI

Table I. *Prostate biparametric magnetic resonance imaging protocol: sequence parameters at 3T.*

Sequences/ Plane	Magnet strength	TR/TE (ms)	Slice thickness (mm)	Gap	B-values (s/mm^2)	NEX	FOV (mm)	Matrix
DWI/Axial	3T	3690/67	2	0	0-1500	3	Large	124×100
T2W/TSE Triplanar	3T	8380-12752/90-90	2	0	-	2	180×180	188×166
T1W-THRIVE/Axial	3T	3.0/1.5	1.5	-	-	1	370×300	252×198

ADC maps were generated from DWI images with b-values of 0, 500, 1000, and 1500 s/mm^2. DWI: Diffusion-weighted imaging; T2W: T2-weighted; T1W: T1- weighted; TSE: turbo spin-echo; THRIVE: T1 high resolution isotropic volume excitation; TR: repetition time; TE: echo time; FOV: field of view; NEX: number of excitations.

in detecting PCa, the short acquisition time, the reduced costs and the elimination of gadolinium-related risks, indicates it as a potential alternative to mpMRI, for meeting the increasing demand for MRI in the PCa diagnostic workup (6, 7).

Similarly to the diagnosis of PCa, bpMRI has a high performance in detecting local recurrences after treatment. After radiotherapy (RT), recurrence can occur at the primary tumor site or at a different site and can be detected as a focal high signal on DWI at high b-values, or focal moderate or marked low signal on apparent diffusion coefficient (ADC) maps. After completing RT, diffusion weighted imaging (DWI)/ADC can be immediately used as an alternative to dynamic contrast-enhanced (DCE). The latter, indeed, cannot be used earlier than three months because the prostate tissue develops an inflammatory reaction, which results in perfusion and blood volume increase (8). In addition, T2-weighted (T2W) and DWI achieve the highest diagnostic precision and inter-reader agreement in the detection of PCa after RT (9).

After radical prostatectomy (RP), the local tumor recurrence may specifically be detected in the prostatectomy bed as an area of restricted diffusion on DWI/ADC, unlike fibrosis, granulation tissue retained seminal vesicles, and residual glandular tissue which show no restriction diffusion on DWI/ADC. Despite the aforementioned potential in diagnosis and post-treatment of PCa, the lack of a dedicated reporting system for bpMRI does not allow its wide adoption in clinical practice. Undoubtedly, in the diagnosis of PCa, a dedicated bpMRI system cannot derive from PI-RADS v2.1, which considers the T2W and DWI as the dominant sequences for the transition zone (TZ) and peripheral zone (PZ), respectively. In PI-RADS v2.1, the DCE plays a secondary role in determining the PI-RADS 2.1 lesion category, by updating lesions from overall assessment category 3 to 4 in PZ based on positive DCE results. In addition, PI-RADS v2.1 does not define the management of score 3 or "equivocal" lesions and does not take into account quantitative measurements in order to increase the reproducibility of PI-RADS scores.

To strengthen the adoption of bpMRI in clinical practice and to facilitate the detection and localization of PCa and local recurrence after RT and RP, we propose dedicated reporting systems, S-PI-RADS and PI-RRADS, respectively, both based on bpMRI. For each system a quantitative analysis of the signal intensity (SI) of lesions based on a grayscale ADC map is suggested.

Biparametric Prostate MRI Protocol in Diagnosis and Post-treatment of Prostate Cancer

Prostate biparametric MRI at 3T without endorectal coil (ERC) and with a phased array body coil for the detection of PCa and the local recurrence of PCa workup includes: axial, sagittal, and coronal T2W, axial DWI using b-values of 0, 500, 1000 and 1500 s/mm^2 and ADC map calculation, axial pelvic T1W fat-suppression, and T2-weighted SPIR MRI. MRI scanner at 1.5T with updated/optimal protocols would also produce good quality diagnostic images.

The prostate bpMRI protocol at 3T without ERC for diagnosis of PCa and detection of local recurrence after RT and RP is shown in Table I.

Steps for Biparametric MR Images Reading and Interpretation

To simplify and facilitate the use of S-PI-RADS and PI-RRADS, we recommend utilizing a 3-step approach which includes: 1) lesion detection and categorization, 2) prostate volume measurement and 3) lesion localization.

1) Lesion detection and categorization. In the detection of PCa, preliminary the axial T1-weighted fat-suppression images were analyzed to exclude hemorrhage post-biopsy foci. Next, four images (axial DWI with high b-value image, ADC map, sagittal and axial T2W images) are displayed on one or two 21.3-inch standard radiology high resolution 2 megapixel monitors and a contrast ratio of 1400:1. DWI at high b-values at 1500 s/mm^2 (or inverted) and corresponding ADC maps were analyzed: a) for the detection PCa [both in peripheral zone and transition zone (TZ)] and for its categorization, and b) for detection and assessment of the

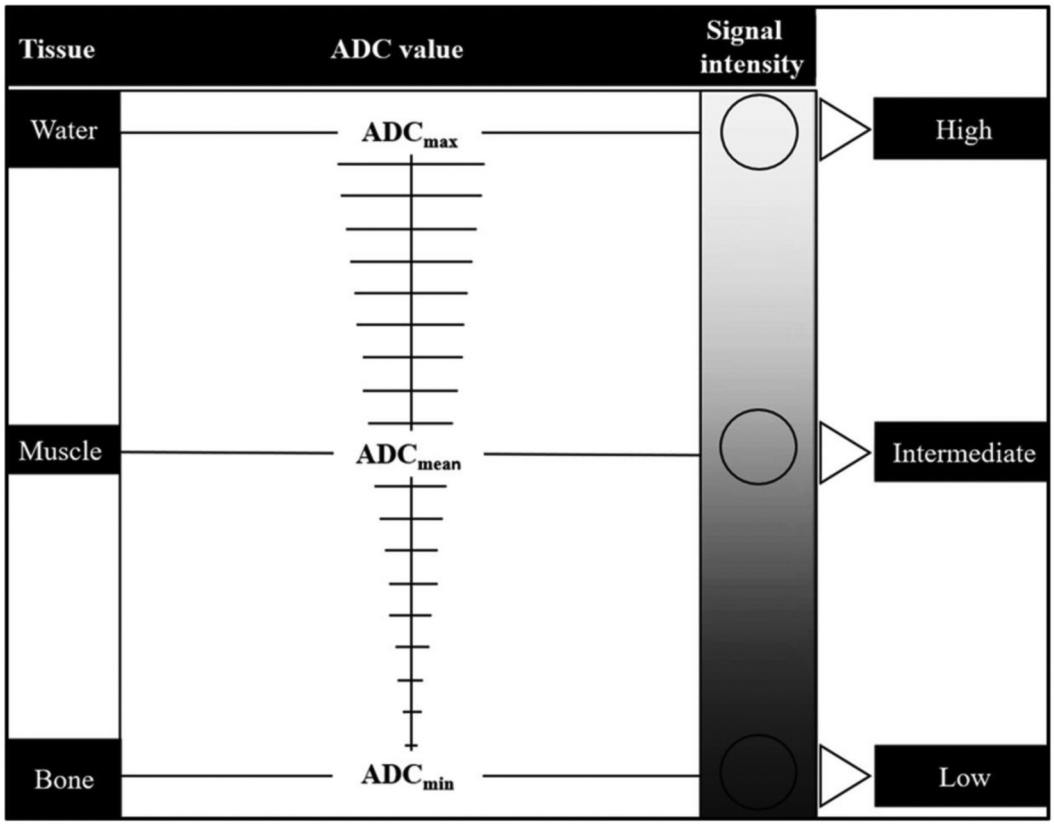

Figure 1. *Grayscale ADC map for quantitative analysis of the signal intensity (SI) of suspicious areas in S-PI-RADS and PI-RRADS. The apparent diffusion coefficient (ADC) scale measures the SI values of normal tissue and cell density of prostate cancer that increase with a decrease in ADC values. Three sub-parameters are identified: ADC minimum or ADC_{min}, ADC mean, and ADC maximum or ADC_{max}. ADC_{max} value is the water or urine (white) with high signal intensity value and is obtained from average of three circular regions-of-interest (ROIs) placed within the bladder; ADC_{max} value varies on the same MRI scanner and between different MRI scanners [for example on our 3T MRI unit (Achieva, Philips Medical Systems, Healthcare, Eindhoven, the Netherlands)] equipped with a phased array body coil, the ADC_{max} value on the ADC map generated using b-values of 0, 500, 1000 and 1500 s/mm^2 can reach an average value of 4000]. ADC_{min} value is the bone (black) equal to 0 and is obtained from a circular ROI placed within the femur head; ADC_{min} value does not vary on the same MRI scanner nor between different MRI scanners. ADCmean is obtained from the formula: $ADC_{mean}=(ADC_{max} + ADC_{min})/2$. On grayscale ADC map, measurable and homogeneous areas with ADC values ≥ ADCmean can be considered as moderately hypointense SI areas on ADC map, while those with ADC values < ADCmean are considered as markedly hypointense SI areas on the ADC map.*

probability of local recurrence in the irradiated prostate gland (PZ and TZ) and at level of the prostatectomy bed after RT and RP, respectively.

In patients suspicious of PCa, the lesion appears hyperintense on DWI at high b-values and moderate homogeneous or marked homogeneous or inhomogeneous hypointense on ADC maps. The lesions are categorized on ADC map as moderate homogeneous hypointensity (S-PI-RADS category 3) and marked homogeneous or inhomogeneous hypointensity (S-PI-RADS category 4). Moderately homogenous hypointense lesions on the ADC map are classified as S-PI-RADS category 3. These lesions were discriminated based on volume, calculated on DWI at high b-values with the ellipse formula (V=L×H×W×0.52) and in agreement with Epstein criteria (10), using a cut-off value of 0.5 cm^3, in the S-PI-RADS category 3a [volume <0.5 cm^3 (no biopsy)], and category S-PI-RADS 3b [volume ≥0.5 cm^3 (targeted biopsy)]. Otherwise, targeted biopsy is indicated for all S-PI-RADS category 4. In a prostate with multiple lesions that show different restriction of diffusion, the "index lesion" should be considered the largest with marked restriction of diffusion or the smallest with marked restriction of diffusion compared to others that may be even larger but with moderate diffusion restriction.

After RP, the PCa recurrence appears as lobulated, curvilinear, or semi-circumferential, nodular-like, or plaque-like soft tissue thickening hyperintense on DWI at high b-values and moderately homogeneous or markedly

Table II. *Simplified PI-RADS with biparametric magnetic resonance imaging.*

Simplified PI-RADS				
Category	ADC/DWI	T2WI	Lesion volume*	Management
1	No abnormality	Homogeneous intermediate signal intensity (normal)	-	Follow-up by PSA
2	No restriction of diffusion	Focal rounded, lenticular or irregular mild/moderate or marked hypointensity	-	Follow-up by PSA and bpMRI eventually within 2 years
3				
3a	Focal rounded, lenticular, or irregular moderate homogeneous hypointensity on ADC map and hyperintensity on high b-value DWI	Focal rounded, lenticular, or irregular homogeneous or inhomogenous mild/moderate hypointensity	<0.5 cm^3	Follow-up by PSA and repeat bpMRI within 1 year**
3b	Focal rounded, lenticular, or irregular moderate homogeneous hypointensity on ADC map and hyperintensity on high b-value DWI	Focal rounded, lenticular, or irregular homogeneous or inhomogenous mild/ moderate hypointensity	≥0.5 cm^3	Targeted biopsy
4***	Focal rounded, lenticular, or irregular marked homogeneous or inhomogeneous hypointensity on ADC map and hyperintensity on high b-value DWI	Focal rounded, lenticular, or irregular homogeneous or inhomogenous marked hypointensity	Any	Targeted biopsy

*Lesion volume is calculated by ellipsoidal formula; **Age assessment and clinical information are needed; ***Category 4 includes lesions with both intraprostatic and extraprostatic extension. ADC: Apparent diffusion coefficient; DWI: diffusion weighted imaging; T2WI: T2-weighted imaging.

homogeneous or inhomogeneous hypointense on ADC maps. DWI/ADC after RP allows detection of lesions suspected of local recurrence ≥5 mm (11).

After RT, the signal pattern of recurrence on DWI/ADC is similar to that of in situ primary PCa (12, 13); it appears as mass-like, focal rounded, lenticular or irregular.

After RT and RP, local recurrence appears as a lesion with SI moderately or markedly hypointense on ADC and classified as category 3 and 4, respectively.

In addition to qualitative analysis of lesions, for accurate PCa risk stratification by S-PI-RADS and categorization of 3 and 4 probability of local recurrence in PI-RRADS, and to improve inter-reader agreement, we proposed quantitative analysis of the SI of lesions using a grayscale ADC map.

We suggest the adoption of ADC quantitative analysis for measurable lesions. In particular, in S-PI-RADS, for differentiating lesions with volume <0.5 cm^3 (S-PI-RADS category 3a *vs.* 4) and to indicate the follow-up for the subcategory 3a, while, in the PI-RRADS to distinguish probability categories (PI-RRADS category 3 vs. 4) and to monitor the treatment response. The grayscale ADC map for quantitative analysis of the SI of lesions in S-PI-RADS and PI-RRADS is reported in Figure 1.

2) Prostate volume measurement. In the detection of primary PCa and/or local recurrence after RT, the prostate volume is calculated on axial and sagittal T2W imaging using the ellipsoidal formula (V=L×H×W×0.52).

3) Lesion localization. In the detection of PCa and after RT, T2W imaging is able to localize the lesion detected on DWI/ADC and in the assessment of the prostate capsule involvement. In these patients, T2W imaging confirms the lesion detected on DWI/ADC: on T2W imaging PCa appears as a hypointense focus, and recurrence appears after RT local as a mass-like or focal moderate hypointensity compared to the irradiated prostatic tissue, in the site of the lesion detected on DWI/ADC. For lesion localization both in the detection of PCa and after RT, a prostate 41-sectors map is used (14).

Table III. PI-RRADS with biparametric magnetic resonance imaging.

PI-RRADS					
Category	DWI/ADC		T2WI		Probability
	RT	RP	RT	RP	
1	No abnormality	No abnormality	Homogeneous intermediate signal intensity (normal)	No abnormality	Very low
2	No restricted diffusion	No restricted diffusion	Focal or diffuse moderate hypointensity or nodule	Diffuse thickening or nodule at vesicourethral anastomosis or nodule or mass in the prostatectomy bed	Low
3	Mass-like, focal rounded, lenticular, or irregular hyperintensity on DWI at high b-values and moderate homogeneous hypointensity on ADC map	Lobulated, curvilinear, or semi-circumferential mass, nodular or plaque-like or irregular hyperintensity on DWI at high b-values and moderate homogeneous hypointensity on ADC map	Moderate hypointensity compared to the irradiated prostatic tissue in the corresponding site of DWIADC	Intermediate signal intensity or slightly hyperintensity compared to pelvic muscle in the corresponding site of DWI/ADC	High
4	Mass-like, focal rounded, lenticular, or irregular hyperintensity DWI at high b-values and marked homogeneous or inhomogeneous hypointensity on ADC map	Lobulated, curvilinear, or semi-circumferential mass, nodular or plaque-like or irregular hyperintensity on DWI at high b-values and marked homogeneous or inhomogeneous hypointensity on ADC map	Moderate hypointensity compared to the irradiated prostatic tissue in the corresponding site of DWIADC	Intermediate signal intensity or slightly hyperintensity compared to pelvic muscle in the corresponding site of DWI/ADC	Very high

In patients with biochemical recurrence (BCR) after RT or RT, when whole body imaging (*e.g.*, PET/CT with prostate specific membrane antigen positron emission tomography) excluded distant metastasis, PI-RRADS bpMRI assessment criteria, in addition to the Gleason score of the previous biopsy or prostatectomy, according to ISUP and EAU-ESTRO-SOG guidelines (19, 20) allow a valid assessment of local recurrence after RT or RP. ADC: Apparent diffusion coefficient; DWI: diffusion weighted imaging; T2WI: T2-weighted imaging.

On T2W the local recurrence after RP appears as a mass-like or focal lesion slightly hyperintense to the pelvic muscle in the site of the lesion detected on DWI/ADC and that occurs anywhere in the prostatectomy bed, but most commonly at the vesico-urethral anastomosis, the retro-vesical space, the bladder neck, near the seminal vesicles bed, or adjacent to the vas deferens (15, 16). Local recurrence after RP can be located exactly on T2W, using as landmarks, the vesico-urethral clock on the axial T2W and the distance of the lesion from the lower margin of the pubic symphysis on the sagittal T2W images.

S-PI-RADS and PI-RRADS Categories bpMRI-based

S-PI-RADS and PI-RRADS provide minimum acceptable technical standards for MR image acquisition and suggest a dedicated structured method for bpMRI reporting.

S-PI-RADS assesses four categories and indicates the management for each of them. Lesions with extra-prostatic extension (EPE) and/or invasion of the seminal vesicle are included in category 4 in addition to intraglandular lesions (17, 18).

S-PI-RADS categories based bpMRI are reported in Table II.

PI-RRADS allows the detection of local recurrence after RP or RT in men with suspected BCR. Relapse after local therapy is defined by a rising PSA level >0.2 ng/ml following RP and >2 ng/ml above the nadir after RT (19, 20).

PI-RRADS includes four categories of bpMRI assessment of the likelihood of recurrence at the prostatectomy site after RP and in the prostate gland after RT. PI-RRADS assessment criteria, similarly to those of S-PI-RADS, are based firstly on DWI/ADC for lesion detection, size, and shape and then on anatomical T2W imaging for the lesion location in the prostatic bed after RP or intra-glandular site or extra-glandular extension after RT. PI-RRADS assessment categories and probability of recurrence are summarized in Table III.

In the initial diagnostic approach for PCa workup, and in post-treatment, T2W spectral presaturation with inversion recovery sequence of the the entire pelvis, in addition to DWI, is useful in the detection of lymph nodes and bone metastases, and other findings.

Conclusion

In our experience, S-PI-RADS and PI-RRADS based on bpMRI can facilitate multidisciplinary cooperation and improve the detection and potential diagnosis of PCa and local prostate recurrence after RT and RP. Both systems will continue to develop and further studies are needed to validate them in clinical practice.

Conflicts of Interest

All Authors declare no conflicts of interest in relation to this study.

Authors' Contributions

Conception and study design: MS, EM, GBS, FMM, FT, PS, ADB, supervision MS, EM, ADB; literature review: EB, AMC, ADM, writing: MS, EM, EB, AMC; critical review: MS, EM, FT, ADA, ADB. All Authors approved the final version of the manuscript.

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