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Review Article

State-of-the-art Prostate Imaging

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ABSTRACT

Prostate cancer is one of the most common cancers in men. In addition to methods such as prostate-specific antigen test, digital rectal examination, and transrectal ultrasonography, magnetic resonance imaging has an important role for accurate and reproducible diagnosis. However, guidance in targeted biopsies and recent use in determining localization for treatment increase its importance. Due to technical difficulties, patient tolerance, and differences in interpretation, the prostate imaging reporting and data system recommends preparations for the patient and magnetic resonance imaging techniques. However, techniques continue to be developed to improve the diagnosis rate and image quality. In our article, patient preparation before imaging and techniques were tried to be discussed in detail. In addition, current approaches in biparametric magnetic resonance imaging and radiomics and new techniques such as T1 and T2 mapping will be mentioned.

Keywords: Magnetic resonance imaging, multiparametric magnetic resonance imaging, prostate cancer

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Prostate cancer is the second most common cancer in men and accounts for 15% of all cancers.[1] In Western countries, prostate cancer is the most common cancer in men.[1] The most important risk factor for prostate cancer is age. Most patients are individuals over the age of 65. Prostate-specific antigen (PSA) test, although not specific, allows early diagnosis of prostate cancer. In this way, an increasing proportion of patients can be diagnosed at an early stage.[2] Nevertheless, PSA can be elevated in many benign conditions (e.g., benign prostatic hyperplasia). However, in recent studies, it has been shown that PSA screening studies do not contribute to survival and even lead to overdiagnosis and overtreatment.[3] Digital rectal examination, on the other hand, can detect tumors over 0.2 mL, and its sensitivity is very low.

Recently, prostate cancer is accepted as a multifocal disease, in which a dominant focus and other focus coexist when detected. From a clinical point of view, clinically insignificant (Gleason ≤6) or clinically significant (Gleason ≥7) cancers should be distinguished.

Multiparametric prostate magnetic resonance imaging (MpMRI) has been developing and becoming more important in the diagnosis and treatment of prostate cancer in recent years. In the past, it was performed with abdominal imaging for staging purposes and to detect extraprostatic extension. The use of morphological and functional sequences provided a more effective diagnosis. MpMRI has begun to play a role in the degree of aggressiveness of prostate cancer, thus in the diagnosis of clinically significant and clinically insignificant prostate cancer. Recent data suggest that targeted biopsies combined with MpMRI detect more clinically significant cancers and less clinically insignificant cancers than standard biopsies.[4] However, because of the high false-negative rate of targeted biopsies, it is still stated that they should be performed together with standard biopsies.[5]

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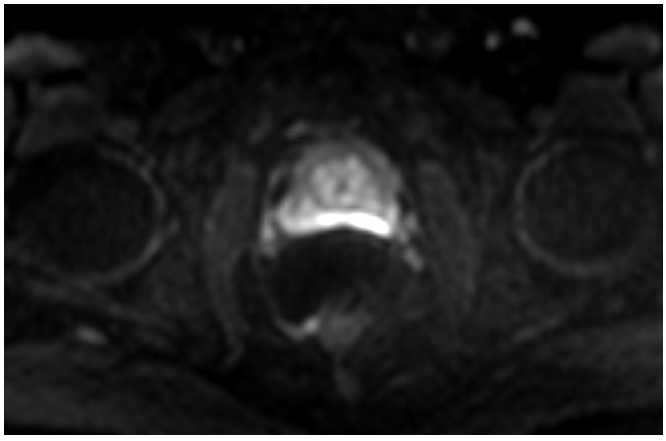

Figure 1. In the diffusion magnetic resonance imaging image obtained with the B1400, diffusion restrictions in the posterior peripheral zone of the prostate caused by gas in the rectum are observed.

The Prostate Imaging Reporting and Data System (PI-RADS)

PI-RADS version 1 was published in 2012 by the European Society of Urogenital Radiology to standardize prostate MR reports due to rapid advances in prostate MR.[6] PI-RADS v1 contained limitations with improvements in MpMRI, and PI-RADS version 2.0 was published in 2016.[7] In 2019, the PI-RADS committee published PI-RADS v2.1 because PI-RADS v2.0 contains some inconsistencies in the studies carried out since its publication and it needs to be developed.[8]

Patient Preparation

In PI-RADS v2.1, emptying the rectum before extraction is the only recommendation in patient preparation (Fig. 1). Apart from this, the use of enemas and antispasmodic agents is optional.

After the use of hyoscine butylbromide, an antispasmodic agent, improvement was observed in T2-weighted (T2W) images in studies published by Ullrich et al.[9] and Slough et al.[10] but no improvement was observed in the study published by Roethke et al.[11] There was no improvement in diffusion-weighted imaging (DWI).[9-11]

Coskun et al.[12] reported in their study that the use of enemas did not reduce artifacts in DWI. However, Plodeck et al.[13] showed that the use of enemas resulted in an improvement in DWI artifacts. Coskun et al.[12] worked at a b value of 1500 s/mm^2 in the DWI, and Plodeck et al.[13] worked at 1000 s/mm^2. 3 Tesla MR was used in both studies, and the number of patients was similar in both studies (Coskun et al.: 117 patients, Plodeck et al.: 114 patients). Lim et al.[14] found no significant difference in artifacts in T2W images of enema use in their study.

Optimal Time

A period of 6–8 weeks is recommended for magnetic resonance imaging after biopsy.[15,16] However, in some publications, it is stated that even after 6 weeks, the absorption of hemorrhage is insufficient.[17,18] (Fig. 2). Choi et al.[19] showed

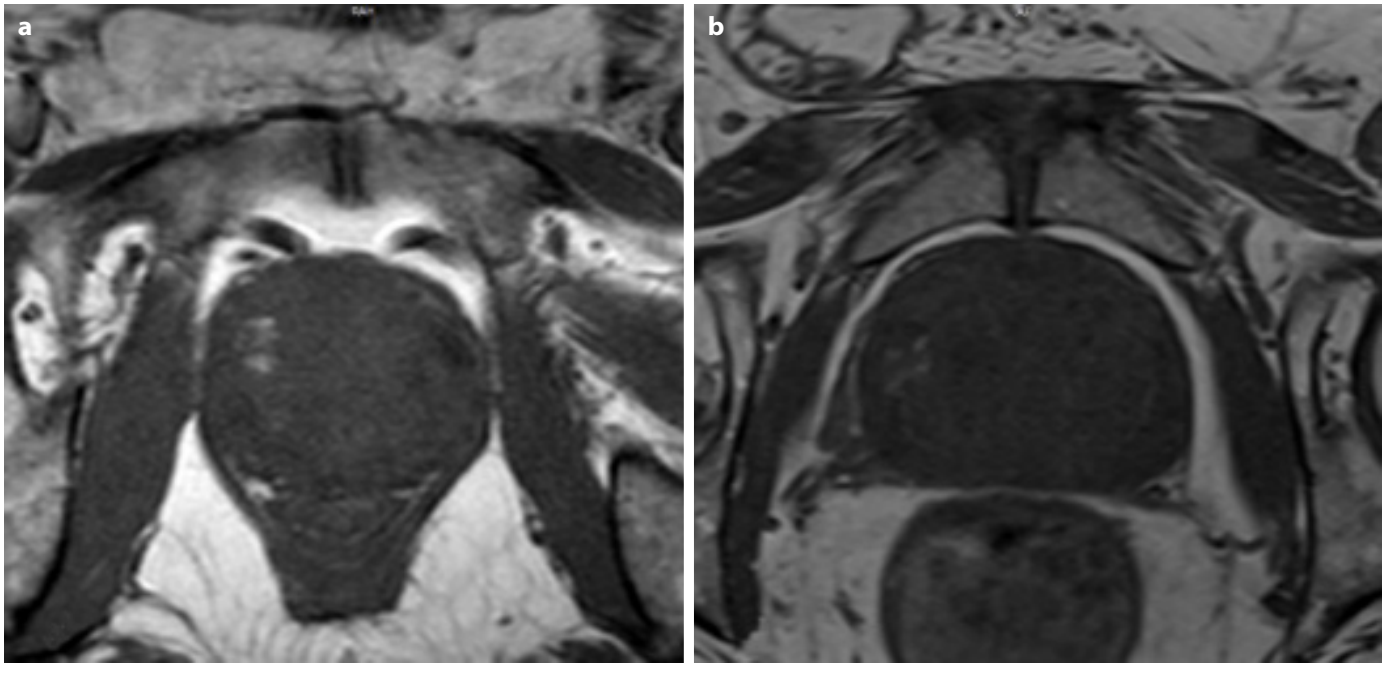

Figure 2. Post-biopsy magnetic resonance imaging (MRI) **(a)** and 6 months later MRI **(b)** of the same patient are shown. In these two T1W images, the MR obtained 6 months after the biopsy **(b)** shows that although the bleeding area is partially resolved, slight signal intensity changes persist in the lateral and posterior regions.

that staging in magnetic resonance imaging was not associated with the post-biopsy interval. It is also thought that the amount of bleeding is not related to the interval.[17,19] There is no consensus on this matter.

Ejaculation causes the collapse of seminal vesicles, also, it can cause difficulties in their evaluation.[20] Furthermore, the T2 signal in the peripheral zone decreases after ejaculation.[21] Some centers recommend 3 days of sexual abstinence, but there is no recommendation in PI-RADS v2.1 due to insufficient evidence.

Technical Specifications

According to PI-RADS v2.1, prostate MRI should be performed at a minimum of 1.5 Tesla.[22] Signal-to-noise ratio (SNR) is higher at 3 Tesla (T) MRI. Furthermore, 3T MRI proves better temporal and spatial resolution. However, 1.5 T continues to be a preferable option in examinations that may have susceptibility artifacts (e.g., hip prosthesis).

Endorectal Coil (ERC)

The purpose of the use of an ERC is to increase SNR. The use of ERC is usually required on older, 1.5 Tesla MRIs.[22] In addition, it has been shown in recent studies that ERC increases SNR in DWI, especially in the peripheral zone, and better reflects anatomical details in T2-weighted imaging in 3T MRIs. In patients using ERC, the diagnosis rate of smaller and less aggressive lesions increased and the rate of missed lesions decreased.[23] Dhatt et al.[24] showed that the use of ERC in Gleason 4+3 and higher lesions did not cause a significant difference in the diagnosis rate, but the diagnosis rate was higher in the case of ERC use in Gleason 3+4 lesions. Tirumani et al.[25] did not find any significant difference in the diagnosis rates of ERC use in the extraprostatic spread and seminal vesicle invasion in their study.

There is no standard recommendation in PI-RADS v2.1 about the use of ERC. The use of ERC varies from center to center depending on the features of the center's MR device, usability, time, and patient preference.

Treatment in Prostate Cancer with Magnetic Resonance Imaging

Recently, the opportunity to treat with magnetic resonance imaging has emerged with the wide-ranging magnetic resonance imaging technology.[26] In our institute, wide-bore MRI studies are supported with scholarship support (Fig. 3).

T2-Weighted Imaging

T2W imaging (T2W) is the major pulse sequence in prostate MR examination. It should be done with Rapid Imaging with Refocused Echoes technique, turbo spin echo (TSE), and fast spin echo are other types of this technique. In these techniques, the long echo train causes blur artifacts (Fig. 4).

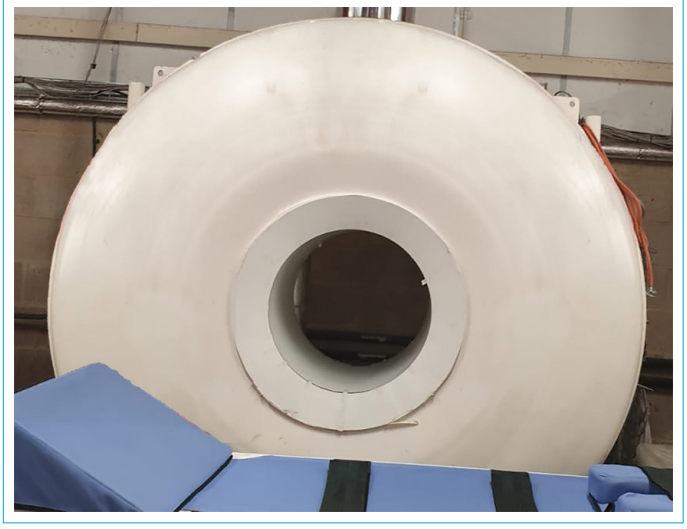

Figure 3. Wide-bore magnetic resonance imaging technology at our institute.

According to PI-RADS v2.1, at least two sections should be examined, one of which is in the axial plane. The axial plane can be taken according to the straight axial or long axis of the prostate gland (Fig. 5). The examination of the long axis of the prostate gland is considered to be better, but the straight axial plane is more applicable for technologists.[27,28]

The isotropic 3D sequence can be made in addition to the 2D images. The major advantages of 3D imaging are the lower partial volume effect and higher resolution. The 3D examination is thought to be useful in identifying the extraprostatic extension and the capsule of BPH nodules. However, it is more sensitive to motion artifacts. However, when acquiring 3D images, TR time can be shortened to reduce shooting time; however, this may influence T1 weight (Fig. 6).

Diffusion-Weighted Imaging (DWI)

DWI has gained even more importance with the popularization of biparametric MR. Spin echo planar imaging (EPI) technique is recommended in PI-RADS v2.1. The plan should be similar to T2-weighted imaging. This technique has a high SNR ratio and is less susceptible to motion artifacts due to its rapidity. However, it is more sensitive to susceptibility artifacts. Another technique, single-shot TSE, is less sensitive to susceptibility artifacts in DWI imaging, although signal loss and artifacts are its major handicaps.

"Reduced field-of-view"-DWI is a recent new technique

Figure 4. Blur artifact caused by the long echo train is visible on T2 Imaging **(a)**. Better image was obtained when the imaging was adjusted with the appropriate parameters **(b)**.

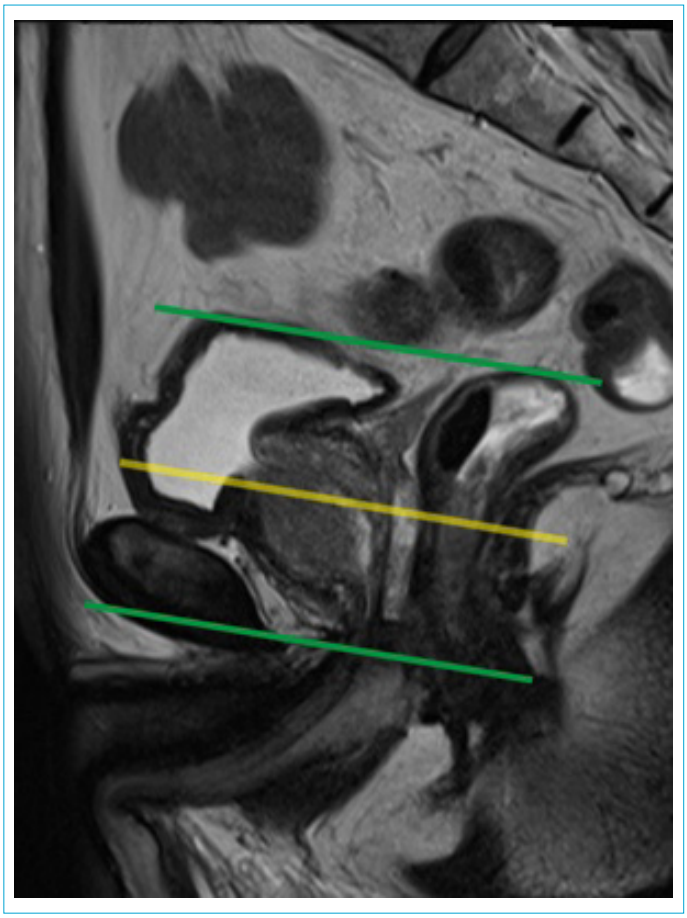

Figure 5. In the sagittal T2 image, the orientation of the axial image is seen based on the prostate long axis. It should be scanned starting from the superior seminal vesicle. The green lines represent the scan ranges. The yellow line is the reference line.

(Fig. 7). In recent studies, it has been shown that the technique provides an increase in image quality in anatomical distortion and susceptibility artifact compared to standard single-shot EPI (ssEPI).[28] Two recent articles have reported that there is no significant difference from the standard DWI technique in detecting prostate cancer.[29,30]

Another disadvantage of the ssEPI DWI is the blurring artifact, which becomes more apparent as the magnetic field strength increases.[31] It is thought that this effect is mostly due to T2* attenuation. Although blurring artifacts can be reduced with a parallel imaging technique, it remains one of the major problems of the ssEPI DWI sequence. Multishot EPI sequence shortens the shot length as it fills the k-space with multiple excitations, thus reducing blurring artifacts but being relatively sensitive to motion artifacts due to phase difference.[32]

In prostate MRI, 1500–2000 s/mm^2 is generally used as a high b value in daily practice. Insufficient suppression is observed at low b values, and a decrease in anatomical resolution is observed at high b values (such as 3000–5000 s/mm^2). Rosenkratz et al.[33] reported 1500–2500 s/mm^2 as the optimal value for the detection of prostate cancer in their study on computer-assisted b values. Similarly, Vural et al.[34] reported that in the detection of prostate cancer in computer-assisted b values, 2000 s/mm^2 and 3000 s/mm^2 were similar and superior to 1500 s/mm^2 in both. However, Zhang et al.[35] reported that the 3000 s/mm^2 images they obtained natively, provided higher AUCs than 1000 s/mm^2 and 2000 s/mm^2 in the detection of prostate cancer. Pro-

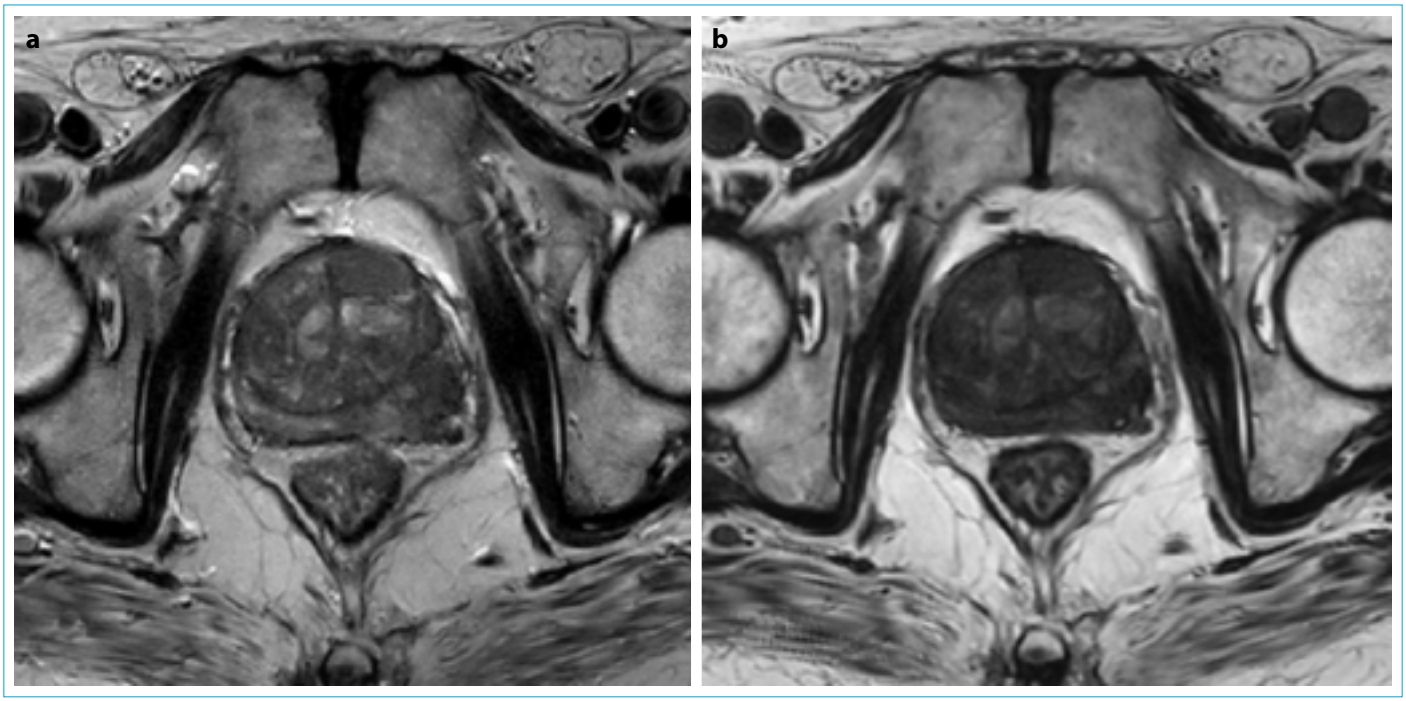

Figure 6. 2D T2-weighted image **(a)** and 3D isotropic T2-weighted image **(b)** of the lesion with extraprostatic extension in the left peripheral zone. While T2 images are obtained in 3D images, an increase in T1 weight can be observed. (The case was obtained from Medmar Imaging Center with permission).

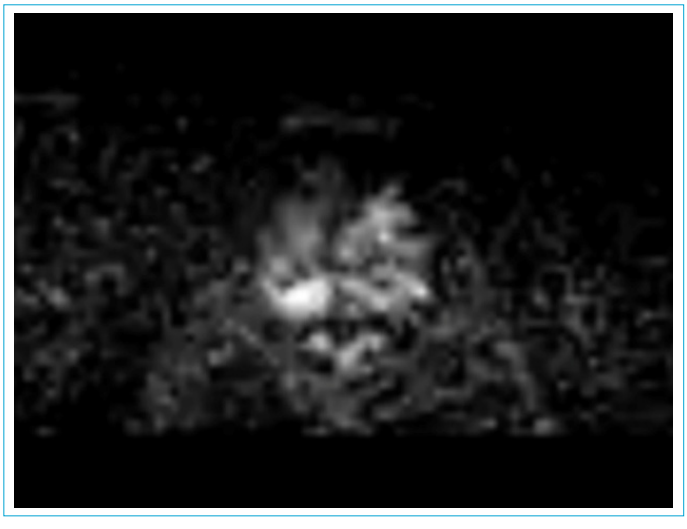

Figure 7. Peripheral zone tumor is seen in the reduced field of view image. (The case was obtained from Medmar Imaging Center with permission).

spective and multicenter studies are needed to prove the diagnostic performance of high B values.

PI-RADS v2.1 recommendation is to have a minimum b value of ≥1400 s/m^2 for DWI. However, ≤1000 s/m^2 is recommended for apparent diffusion coefficient (ADC) calculation. The reason for this is the diffusion kurtosis effect that may occur at high b values (Fig. 8). Recently, it has been investigated whether ADC histogram analyses provide a higher diagnostic rate than standard ADC. Tamada et al.[36] showed that 0–10. Percentiles achieved the best results in serial MR scans. Zhang et al.[37] demonstrated that the bi-exponential model (IVIM) provides better performance than the mono-exponential model. However, it is thought that it does not provide better performance than other studies.[38,39] There was no significant difference between the stretched exponential model and the mono-exponential model.[40] Diffusion kurtosis imaging is another model studied, and it has been found to have better diagnostic performance than the mono-exponential model in some studies, worse in some, and similar diagnostic performance in others.[40,41] In current studies, it is seen that these models are not clearly good compared to the mono-exponential model and need to be improved.

Dynamic Contrast Enhancement (DCE)

DCE-MRI is acquired by taking serial images T1W images with 2D or 3D gradient echo techniques after bolus injection of gadolinium-based contrast agents with low-molecular-weight chelation. Fat suppression techniques and subtraction images are recommended. Due to current technological developments, 3D imaging is applied more often, which increases image quality.

In prostate cancer, an increase in angiogenesis and capillary permeability is observed. As a result, early-focal enhancement and washout are seen.[42] Detailed parameters were

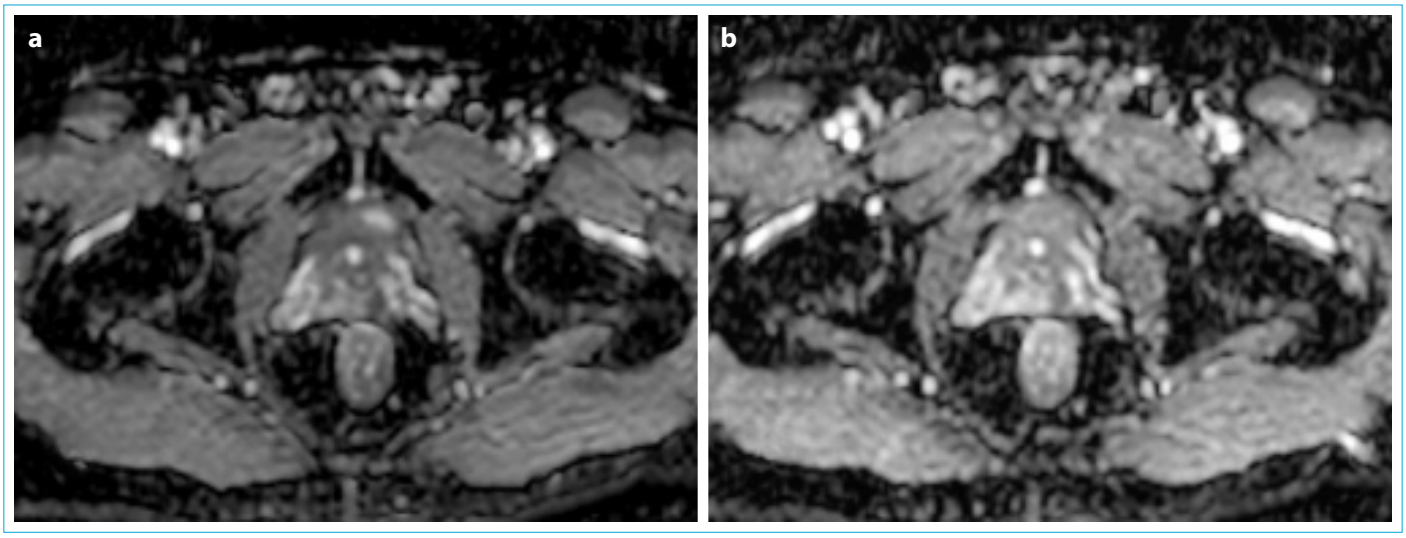

Figure 8. Images of apparent diffusion coefficient (ADC)-b800 **(a)** and ADC-b1400 **(b)** are shown. Peripheral zone tumor is more demonstrative in B800 ADC because of the diffusion kurtosis effect that occurs at high b values.

available in PI-RADS v2 because of the importance of DCE-MRI standardization. The imaging plan used for DWI should be used for DCE-MRI. Slice thickness should be 3 mm, with no gaps. The field of view should cover the prostate gland and seminal vesicle. Minimum temporal resolution should be ≤15 s for each image. For gadolinium-based contrast agents (GBCAs), a dose of 0.1 mmoL/kg and an injection rate of 2–3 cc/s are recommended. Total examination time should be at least 2 min with no gaps in between. DCE imaging can be a "safety-net" examination in DWI when adequate SNR is not obtained or contains artifacts. In PI-RADS v2.1, no changes were made in the technical recommendations, some recommendations were made for biparametric MRI (bpMRI) performed without DCE due to some limitations of DCE.

As the magnetic field strength increases (3 Tesla), SNR increase. There are also improvements in spatial and temporal resolution. Shooting time is shortened. Furthermore, the relaxation time of GBCA decreases. For these reasons, the contrast difference between prostate cancer and the surrounding tissue increases and the contribution of DCE-MRI to the diagnosis increases.[43] Image quality is improved using ERC, especially in the peripheral zone around the rectum wall, but ERC is not preferred in most centers for patient comfort and additional costs.[44]

DCE-MRI can be evaluated with qualitative, semi-quantitative, and quantitative methods. The qualitative method is the visual assessment of the evaluated operator. Four different types have been defined in PIRADS v1 as progressive (Type 1), plateau (Type 2), washout (Type 3), and non-diagnostic (Type 0). The semi-quantitative technique is based on mathematical computation in the signal-time

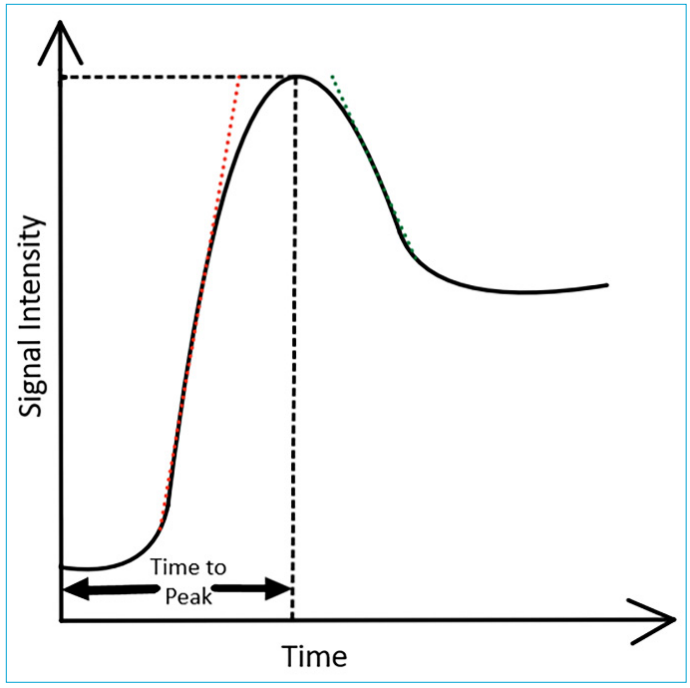

Figure 9. Graphic overview of semi-quantitative dynamic contrast enhancement-magnetic resonance imaging parameters. The red-dotted line represents the wash-in rate, and the green-dotted line represents the wash-out rate.

curve (Fig. 9). Mathematical models used to smooth the contrasting signals yield diagnostically useful kinetic parameters. This approach can be functional for heterogeneous enhancements, but frequently used compartment models may not be compatible with accurate spatial and temporal spread.[45] Quantitative analysis allows measures such as permeability and blood flow. This is one of its main advantages. The challenge of quantitative analysis is the

accurate measurement of arterial input function (AIF). The gold standard in selecting a specific AIF is serial blood collection after contrast agent injection. However, since this method is invasive, the average AIF values of the population are generally used. Cardiac output differences can create differences in AIF. AIF may vary from person to person and even between shots in the same person.[46]

bpMRI

DCE may have a limited role in prostate imaging. bpMRI provides lower cost and faster acquisition.[47] In addition, because the contrast is not used, negative side effects are avoided. For this reason, bpMRI, an MRI of the prostate without DCE, is being studied with increasing interest. In some meta-analyses, bpMRI has achieved comparable diagnostic rates compared to mpMRI.[48] Nevertheless, the number of readers may be limited in these meta-analyses. In addition, these meta-analyses did not study low-quality images, to which DCE contributed relatively. According to PI-RADS v2.1, there are three indications for DCE:

- Identification of PI-RADS 3 lesions that contain clinically significant prostate cancer
- Assist in T2 and DWI imaging with suboptimal image quality
- Assisting radiologists with less experience.
- In addition, PIRADS v2.1 suggests opting for mpMRI in certain situations:
- Patients with negative previous biopsies and suspected elevated PSA
- Rapid PSA doubling time or change in clinical status in active surveillance
- Patients with previous bpMRI imaging and clinical suspicion
- Patients receiving prostate interventions or drug-hormone therapy, who may have altered prostate anatomy
- Biopsy-naïve men with a family history, genetic predisposition, or a higher than average risk
- Conditions that may reduce DWI or T2 image quality, such as a hip implant.

There is still no standardized reporting system for bpMRI, which leads to heterogeneity in meta-analyses.[49] More multicenter meta-analyses are needed for the development of bpMRI.

T1 and T2 Mapping

T1 and T2 mapping is based on the calculation of T1 and T2 relaxation times of tissues and the creation of color maps. It is obtained by collecting data at several TE times in a TR interval. The average relaxation time of voxels at different TE times is calculated mathematically. The modified Look-Locker inversion recovery (MOLLI) technique, which is an inversion recovery technique, can be used for T1 mapping, and the EPI technique, which is a spin echo technique, can be used for T2 mapping (Fig. 10).

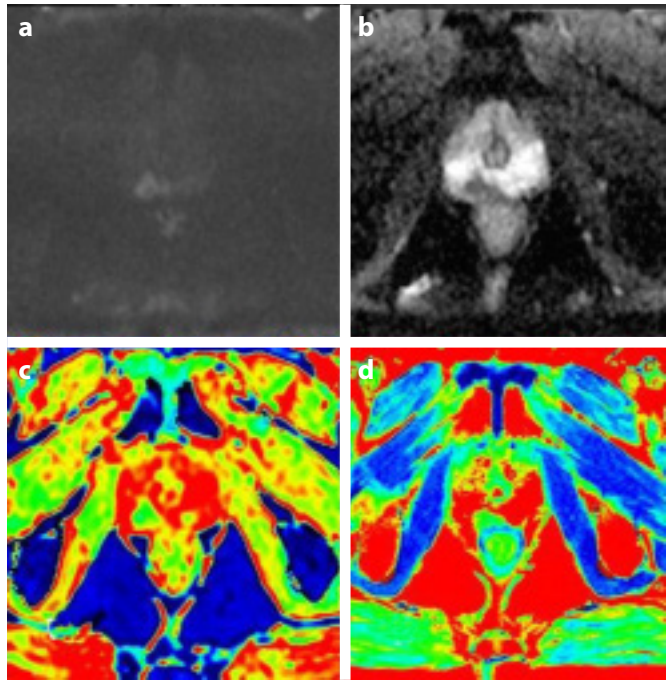

Figure 10. Diffusion-weighted ımaging **(a)** and apparent diffusion coefficient **(b)** imaging shows a tumor localized in the right peripheral zone mid-gland, posteromedial. T1 mapping **(c)** and T2 mapping **(d)** images are shown as well. The diagnosis of this patient after the biopsy was adenocarcinoma.

T1 and T2 relaxation times may vary with many parameters such as gender, age, exercise, and hemoglobin. Significant differences were observed in T1 and T2 times in some of the malignancies, and it is thought that this difference can be used especially in prostate and breast cancers.[50]

Radiomics

Radiomics is a relatively new field of medicine that is created by extracting quantitative features from images that are invisible to the naked eye and, supporting clinical decisions. Features such as size, shape, and first-order texture are obtained from computed tomography, magnetic resonance imaging, or other modalities. Numerous studies have been published in tumoral and non-tumoral diseases related to radiomics in the last decade. Some of these studies are on prognosis prediction, while others are on diagnostic and genomic prediction. Despite recent advances in MpMRI, 25% of tumors in the transition zone still cannot be diagnosed. In studies published in recent years, it has

been shown that radiomics determines prostate cancer diagnosis and location with high sensitivity and specificity.[51] In addition, in recent years, many studies have been published on the role of radiomics in determining PIRADS, Gleason score, the presence of extraprostatic extension, response to tumor therapy, and prognosis predictions. [51] There is an increasing interest in radiomics, and multicenter studies are needed for its development.

Conclusion

Prostate imaging techniques, including T2 imaging, DWI, DCE, radiomics, and T1 and T2 mapping techniques, have revolutionized the field of prostate imaging. These advanced imaging modalities offer improved accuracy, sensitivity, and specificity in detecting and characterizing prostate diseases. In addition, advancements in artificial intelligence and machine learning hold great promise in further enhancing image interpretation and quantitative analysis. Incorporating these cutting-edge techniques into clinical practice can lead to better diagnosis, risk stratification, treatment planning, and patient management. As the field of prostate imaging continues to evolve, radiologists play a pivotal role in staying updated with the latest advancements to provide the best care for their patients.

Disclosures

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