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Role of multi-parametric (mp) MRI in prostate cancer

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Abstract

Multi-parametric magnetic resonance imaging is increasingly being recommended as standard imaging modality for prostate cancer diagnosis and staging. It comprises structural T2 and T1 sequences supplemented by functional imaging techniques, i.e. diffusion-weighted, dynamic contrast enhanced and spectroscopic imaging. Pre-biopsy multi-parametric magnetic resonance imaging is recommended for both detection and staging as it avoids biopsy artefact, and when normal, has a negative predictive value of 95% for significant cancer. Magnetic resonance imaging-guided prostate biopsy targets only area(s) considered to be suspicious for prostate cancer, hence resulting in improved accuracy. Dynamic contrast enhancing helps in the detection of cancer and for the assessment of extra-capsular extension, distal urethral sphincter and seminal vesicles involvement. The role of multi-parametric magnetic resonance imaging in follow-up of patients on active surveillance is also increasingly recognised. Its role is now further expanded to facilitate targeted therapies. This review focuses on the evolving role of multi-parametric magnetic resonance imaging in diagnosis and management of prostate cancer.

Keywords: Magnetic resonance imaging, Prostate, Cancer, Multi-parametric.

Introduction

Prostate cancer is one of the most common cancers and leading causes of death in industrialised nations.[1,2] The classical diagnostic tools for detecting prostate cancer are prostate specific antigen (PSA), digital rectal examination (DRE) and trans-rectal ultrasound (TRUS)-guided biopsy. Imaging has a pivotal part in prostate cancer treatment selection and planning.[3] In the recent years, magnetic resonance imaging (MRI) has taken up a greater role in the diagnostic algorithm of prostate cancer.

MRI equipment and technical considerations

Compared with the conventional MRI using phased- array

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coil, combining the endo-rectal coil provides state-of-the-art imaging for staging prostate cancer with excellent signal quality and improved spatial resolution.[3,4] Higher magnetic fields at 3-Tesla provides a twofold increase in signal-to-noise ratio (SNR), shorter overall scan time and increase in spatial, temporal and spectroscopic resolution with better structural and functional detail compared to low field strength (e.g. 1.5 T) MRI.[5]

Multi-parametric (mp) MRI

Multi-parametric MRI (mp-MRI) includes combination of high-resolution T2-weighted images assessing the anatomy and at least two functional MRI techniques, i.e. diffusion weighted imaging (DWI) and magnetic

Table: Different components of multi-parametric (mp) MRI.

Modality	Principle	Clinical utility
T 2 weighted images	Fast spin echo sequence with long repetition time and long echo time	Primary sequence of visualization of structures in and out of the gland. Best depiction of prostate zonal anatomy (Detection, localization and staging of prostate cancer). Cancer is low in signal. Sensitive but not specific for prostate cancer.
Diffusion weighted images	Brownian motion of water molecules in tissues	Detection of prostate cancer foci Rapid cell turnover with reduced extracellular space Low signal intensity on ADC (apparent diffusion coefficient) maps. Discriminatory power to distinguish b/w high vs. low Gleason grade disease Adds specificity and lesion characterization.
Dynamic Contrast enhanced	Micro-vascular properties of tumour angiogenesis	Uses T1W sequences Differentiates carcinomatous foci from BPH nodules. Expressed by enhancement pattern i.e. early enhancement and early washout Adds sensitivity for cancer detection
MR spectroscopy	Biochemical and metabolic status of tissues Cell membrane turnover	Detect malignancy in peripheral zone. Increased choline/ citrate ratio Adds specificity and lesion characterization.

MRI: Magnetic resonance imaging
T1W: T1-weighted
BPH: Benign prostatic hyperplasia.

resonance spectroscopic imaging (MRSI), adding specificity and lesion characterisation.[6] Perfusion-based dynamic contrast-enhanced MRI (DCE-MRI) has high sensitivity in cancer detection[6] (Table). De Rooij M. et al. in a meta-analysis found mp-MRI to have high specificity, negative predictive value (NPV) and sensitivity for detecting prostate cancer.[7]

Morphological / Anatomical information

The detection of prostate cancer depends upon the type of image sequence used. Higher resolution T2-weighted (T2W) MRI imaging offers best information about prostatic capsule and zonal anatomy, hence used for detection, localisation and staging of prostate cancer[7] (Figure-1).
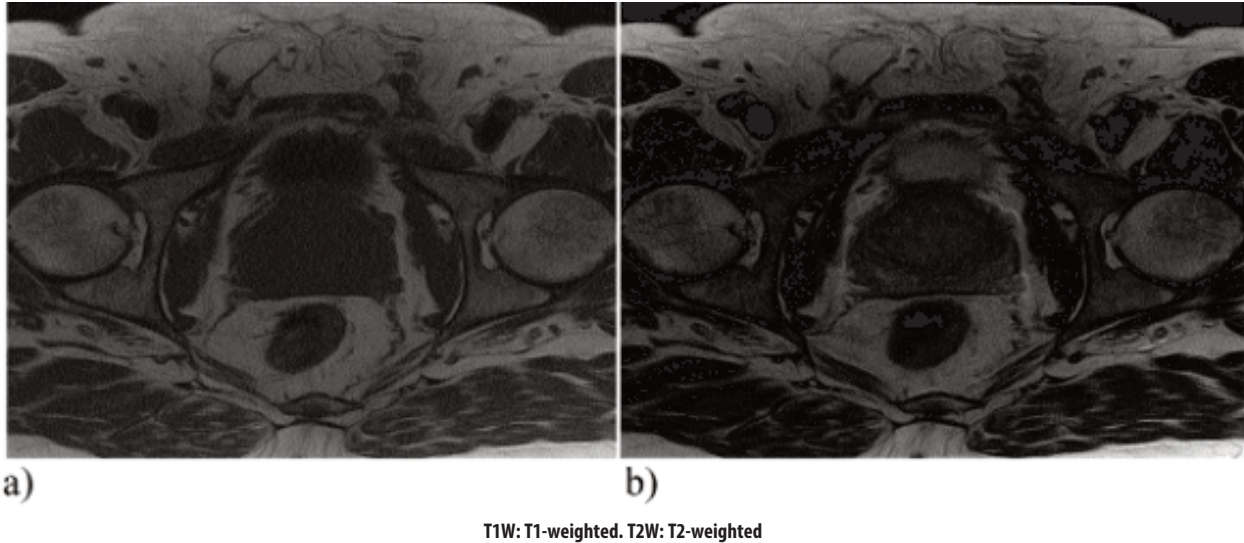

T1W: T1-weighted. T2W: T2-weighted

Figure-1: Normal Prostate; a) T1W image-prostate gland is iso-intense to the surrounding muscles. b) T2W image- Prostate gland is slightly hyper-intense to the surrounding muscles especially the peripheral zone.
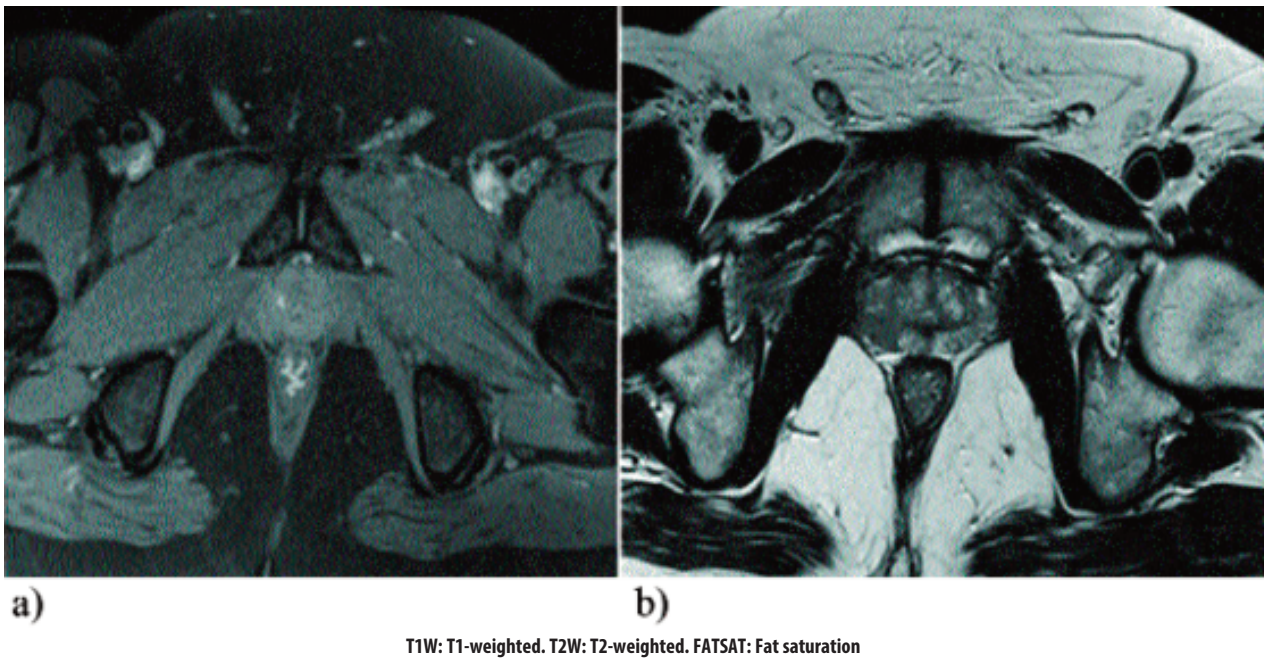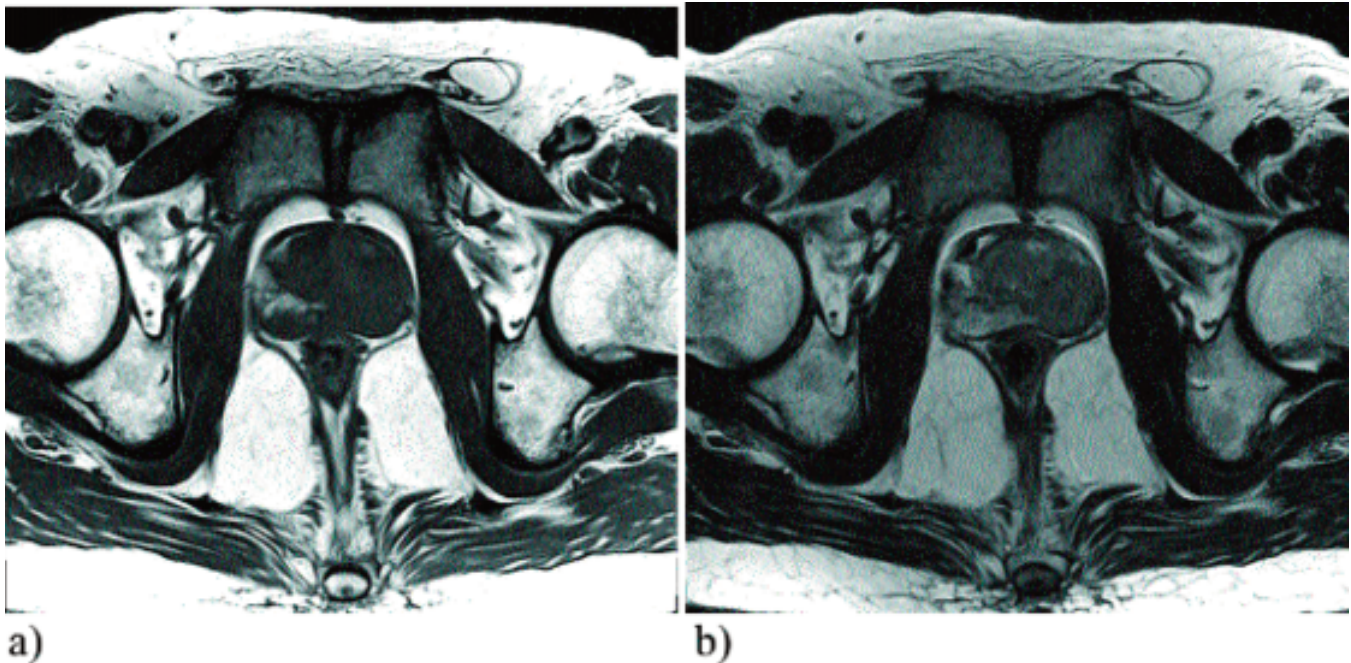

T1W: T1-weighted. T2W: T2-weighted. FATSAT: Fat saturation

Figure-2: Tumour nodule. a) FATSAT -T1W image shows an iso-intense nodule at the right lateral zone of the prostate gland which is difficult to differentiate from the normal prostate gland due to similar signal intensity, but appears as an asymmetrical bulge. b) T2W image; re-demonstration of an iso-intense nodule in the right lateral aspect of the prostate gland. This is relatively hyper-intense to the surrounding muscles but is still hypo-intense to the peripheral zone.

T1W: T1-weighted. T2W: T2-weighted

Figure-3: a) T1W image of the prostate shows a nodule occupying the left half of the prostate gland. As this is iso- intense to the prostate gland, therefore, difficult to appreciate on T1W images. A tiny hyper-instense focus at the right lateral aspect of the prostate represents hemorrhage due to recent biopsy. b) T2W image show the nodule in left lateral aspect of the prostate gland which is slightly hyper-intense to the surrounding muscles but is still hypo-intense to the normal prostate gland.
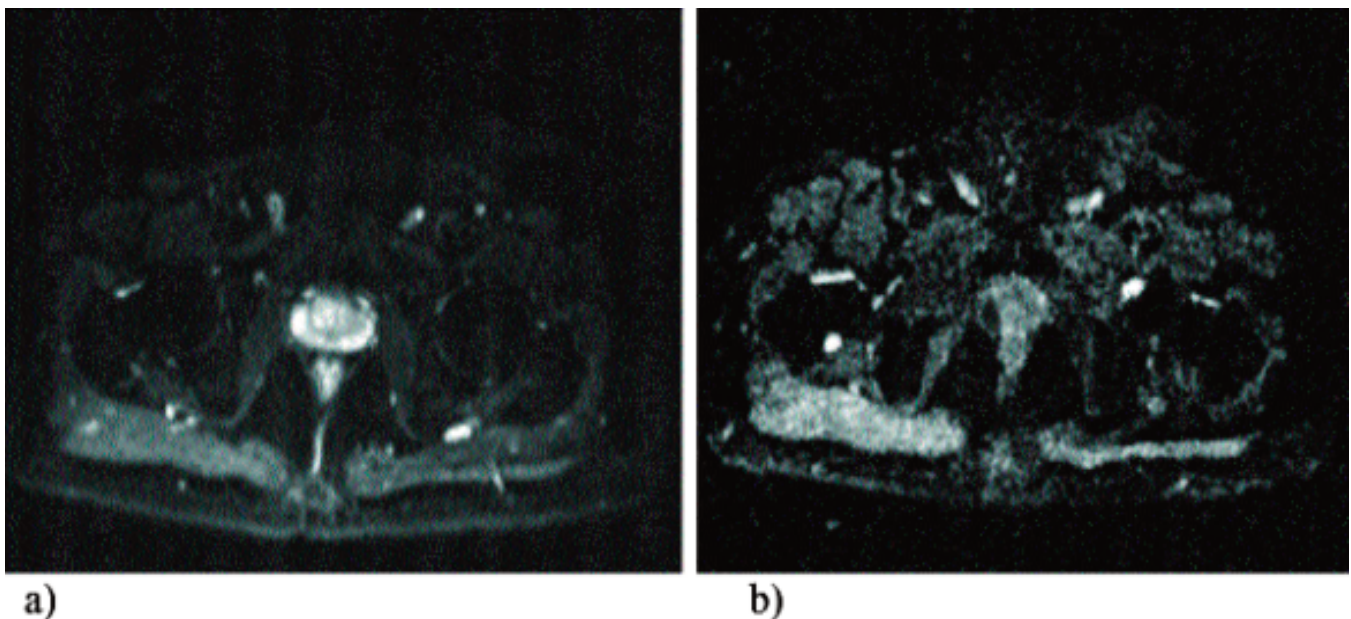
MR: Magnetic resonance.

Figure-4: a) Diffusion weighted image (DWI) show a hyper intense focus corresponding to the nodule seen in the right lateral zone of prostate gland. (1.5 Tesla MR images). b) Apparent diffusion coefficient (ADC) map show a corresponding low intensity focus in the right lateral zone of prostate gland. The hyper-intense signal on DWI and corresponding hypo-intensity on ADC map represent diffusion restriction. (1.5 Tesla MR images).

The classical MR appearance of prostate cancer is a round or ill defined, low signal intensity focus (hypo-intense) in the background of bright peripheral zone tissue. This is due to loss of normal glandular (ductal) morphology in prostate cancer[6] (Figure-2).

On T1-weighted images, the tumour is almost impossible to detect because of homogenous medium signal intensity with difficulty discerning the zonal anatomy.[4,8] This sequence, however, is useful to detect the post biopsy haemorrhage, which appears as areas of high T1 signal intensity due to paramagnetic, iron-rich, blood by products[9] within the otherwise homogeneous prostate. Blood has low signal intensity on T2-weighted images, and can either mimic cancer and/or lead to an inaccurate estimate of its volume[4] (Figure-3).

Extra capsular extension (ECE) / Seminal Vesicle (SV) involvement

The criteria for extra-capsular extension include asymmetry, bulge of prostate contour, thickening of neuro-vascular bundle(s), capsular enhancement and breach, tumour signal in peri-prostatic fat and obliteration of recto-prostatic angle.[4,10,11] On T2WI, these findings provide a specificity of more than 90%.

The SVs are seen as elongated fluid-filled structures with thin septae with low signal intensity on T1-weighted (T1W) images and high signal intensity on T2W images.[12] Combination of tumour at prostate base extending beyond the capsule and low signal intensity within SV in the background of high signal fluid on T2-weighted images are highly predictive of SV invasion.[13]

The reported sensitivity of MRI scan for the detection of extra capsular extension is 13-95% with specificity ranging from 49-97%.[14-16]

Diffusion-weighted imaging (DWI)

Diffusion-weighted MRI uses principle of Brownian motion of water molecules in tissues.[17,18] It has advantage of short acquisition time, improved specificity and no requirement for any specialised hardware.[19]

The rate of diffusion of water in soft tissues is lower than in free solution and is described by the apparent diffusion coefficient (ADC), which correlates inversely with tissue cellularity.[20] Increased cellularity and loss of ductal morphology result in restriction of water diffusion in prostate cancer with corresponding low signal intensity in ADC Values.[20]

ADC maps can be calculated on DWI thus enabling

qualitative and quantitative assessment of the aggressiveness of prostate cancer.[6] The ADC values for malignant tissue are commonly lower than those of normal gland as well as benign prostatic hyperplasia (BPH) nodules[21-23] (Figure-4).

Limitations

DWI has low spatial resolution and hence lower accuracy in the assessment of extra-capsular extension.[24] Benign conditions such as prostatitis, compact fibro muscular stroma seen in BPH[25] and organ motion[26] can also lower the ADC and hence give false positive results. Well-differentiated tumours with predominantly glandular components can lead to false negative results.[27]

Dynamic contrast-enhanced MRI (DCE)

This imaging sequence relies on tumour neo-angiogenesis.[4] Administration of gadolinium-based contrast is done for enhancing tumour vascularity.[3] Early nodular enhancement before the rest of prostate and early washout of signal intensity is characteristic of prostate cancer.[3]

The data generated by DCE MRI is assessed in 3 ways, i.e. qualitatively, semi-quantitatively and quantitatively. The former way is applied in routine clinical practice.[4,28] Intensity-time curves are generated to evaluate time to peak, maximum uptake slope, peak enhancement and washout rates. The quantitative approach uses more sophisticated pharmacokinetic parameters to describe tissue vascularisation such as mean transit time, blood flow and permeability surface area.[4,29] Jackson et al.[30] showed that the sensitivity and specificity of DCE-MRI (50% and 85%, respectively) is higher than that of T2W imaging (21% and 81%, respectively).

Limitations

The limiting factors in DCE-MRI are motion and biopsy artefacts. The rectal motion and patient movements may lead to noisy curves and distorted low quality images, therefore, bowel preparation with enema and anti-peristaltic agents are recommended to overcome these pitfalls.[31]

MR Spectroscopy Imaging (MRSI)

MRSI depicts the metabolic profile of the prostatic tissue.[4] Neoplastic proliferation leads to increased phospholipid cell membrane turnover with resultant difference in concentration of chemical metabolites.[3] This study enables to show lower levels of citrate (marker of benign tissue) and higher levels of choline (marker of malignant tissue) from volumes of interest

(voxels) that encompass prostate cancer.[4]

MRSI not only detects cancer but also provides information about the lesion aggressiveness (Gleason scoring).[32] This approach can be used to evaluate the "metabolic atrophy" after treatment and for the detection of recurrence after radiation therapy.[33] A sensitivity and specificity as high as 95% and 91%, respectively, has been reported for MRSI in conjunction with endo-rectal MRI.[34]

Limitations

The interpretation of MRSI is challenging. The spatial resolution is poor and therefore this study is unable to depict the peri-prostatic area and accurate staging information.[35] It needs additional software for interpreting the data adding to time and cost.[36]

MRI-guided prostate biopsy

Contrary to standard set of TRUS-guided prostate biopsies, MRI-guided prostate biopsy targets only area(s) considered to be suspicious, hence resulting in improved accuracy in prostate cancer detection and localisation, especially for the lesions that are not routinely targeted on TRUS-guided biopsies such as anterior tumours.[37,38] MRI scan also helps in localising the site of tumour recurrence after definitive treatment.[39]

Role of MRI in planning surgery and follow-up (surveillance and recurrence)

A safe and effective operation can be guided by information from MRI imaging leading to oncological clearance while preserving the peri-prostatic tissues important for recovery of urinary and sexual function.[3] MRI also helps to predict the intra-operative blood loss. A positive correlation was observed b/w prominence of apical peri-prostatic veins and associated blood loss.[40]

Moreover, mpMRI can also predict functional outcome after surgery. The length of membranous urethra on coronal endo-rectal MR image is an important predictor for urinary incontinence.[41] Patients with longer than average (14mm) membranous urethra experience more rapid return to complete continence.

MpMRI is helpful in patients with biochemical recurrence (rising PSA value) without any palpable tumour in prostatic fossa. The sensitivity and specificity of endo-rectal MRI to evaluate local recurrence (peri-anastomotic and retro-vesical region) after prostatectomy was reported to be 91% and 45%.[42]

MRI-guided focal therapies

Cryoablation and high-intensity focused ultrasound (HIFU) are the two contemporary treatment modalities used as focal therapy. MR-guided targeted focal and regional therapies are increasingly used for localised primary (native) and recurrent prostate cancer as well as for monitoring the effectiveness of these treatments.[43] Recently, pre-clinical and phase 1 trials have also reported real-time MR-guided focal laser ablation (FLA).[44]

Reporting and communication of mp-MRI data (prostate imaging reporting and data system (PI-RADS) classification)

European Society of Urogenital Radiology (ESUR) prostate MR guidelines of 2012 recommend structured reporting system for mp-MRI data, including the following set of information:[6]

A) PI-RADS score (probability of cancer risk and its aggression)

B) Location and probability of extra-prostatic disease

C) Pertinent incidental findings.

Individual lesion(s) should be given a PI-RADS score on a five-point scale from 1-5, with a score of "1" denoting that clinically significant disease was highly unlikely to be present and a score of "5" denoting that clinically significant disease was highly likely to be present.[45] Grey A.D. et al.[46] found PI-RADS system to be a very good predictor for trans-perineal prostate biopsy outcome.

Conclusion

Mp-MRI is a rapidly evolving and useful tool for the diagnosis, localisation and staging of prostate cancer and to facilitate the targeted therapies. It has the potential for reduction of unnecessary biopsies and provides a rapid and accurate diagnosis for both native and recurrent tumours. It should become an integral part of prostate cancer risk assessment.

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