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Multiparametric MRI in prostate cancer management

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Abstract

Prostate cancer is the second most common cancer in men worldwide. The clinical behaviour of prostate cancer ranges from low-grade indolent tumours that never develop into clinically significant disease to aggressive, invasive tumours that may progress rapidly to metastatic disease and death. Therefore, there is an urgent clinical need to detect high-grade cancers and to differentiate them from the indolent, slow-growing tumours. Conventional methods of cancer detection—such as levels of prostate-specific antigen (PSA) in serum, digital rectal examination, and random biopsies—are limited in their sensitivity, specificity, or both. The combination of conventional anatomical MRI and functional magnet resonance sequences—known as multiparametric MRI (mp-MRI)—is emerging as an accurate tool for identifying clinically relevant tumours owing to its ability to localize them. In this Review, we discuss the value of mp-MRI in localized and metastatic prostate cancer, highlighting its role in the detection, staging, and treatment planning of prostate cancer.

Introduction

Prostate cancer is the second most common cancer in men worldwide, and in the USA alone it has been estimated that 239,000 cases and 29,700 deaths have ocurred in 2013.[1,2] The clinical behaviour of prostate cancer ranges from low-grade indolent tumours that never develop into clinically significant disease to aggressive, invasive tumours that may rapidly progress into metastatic disease and, ultimately, death. Largely as a result of increased prostate-specific antigen (PSA) screening since the 1980s, prostate cancer incidence has risen, and more men are diagnosed with early-stage disease.[3] However, most of these prostate cancers grow slowly and 10–20 years can go by between diagnosis and death. Therefore, health issues related to prostate cancer treatment—such as cardiovascular disease or hypertension—must be considered when deciding treatment. Currently, about one in six men are diagnosed with prostate cancer in their lifetime, but only one in 33 will die of it.[4] The prevalence of ‘silent’ disease is enormous; an autopsy study of 1,056 men who died from causes other than prostate cancer detected undiagnosed and asymptomatic prostate

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Author contributions

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Competing interests

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cancer in 68–77% of men aged 60–79, which suggests that many prostate tumours grow so slowly that patients often die from other causes before the prostate cancer ever becomes clinically apparent.[5] Another autopsy study of 212 men aged 30–98 revealed an age-dependent increase in prostate cancer incidence, with 55% of tumours found in men aged >70 years.[6]

Because as many as 60% of cancers are low volume and low grade (Gleason score 3 + 3), PSA screening has been criticized as it can lead to the overdiagnosis of these low-grade prostate tumours that have little potential for causing death.[7] It has been suggested that tumours smaller than 0.5 cm in diameter are not clinically significant once the long doubling time of prostate cancer is considered (>24 months in 79% of patients).[8,9] In light of these statistics, it is easy to overlook the fact that many men continue to die of prostate cancer. Those men presenting with advanced-stage disease often progress to metastatic disease and ultimately to castration-resistant prostate cancer, which is incurable. Therefore, there is an urgent clinical need to detect high-grade cancers and to differentiate them from those that are indolent, slow-growing tumours. Conventional methods of cancer detection, such as serum PSA, digital rectal examination, and random biopsies are limited in their sensitivity, specificity, or both. However, MRI is a promising method of localizing prostate tumours and determining their size, aggressiveness and invasiveness, thereby predicting their future biological behaviour.[10] The combination of conventional anatomical and functional MRI is known as multiparametric MRI (mp-MRI). This method is emerging as an accurate tool for identifying clinically relevant tumours owing to its ability to establish their precise location and the additional information provided by functional MRI sequences, such as diffusion-weighted (DW) MRI, dynamic contrast-enhanced (DCE) MRI, and MR spectroscopy (MRS), which significantly improve the ability of mp-MRI to predict the behaviour of tumours. Herein, we review the value of mp-MRI in localized and metastatic prostate cancer and will highlight its role in the detection, staging, and treatment planning of prostate cancer.

Multiparametric MRI

Mp-MRI is an accurate and noninvasive imaging method that is increasingly being used in the management of patients with prostate cancer. In addition to conventional anatomical MRI provided by T_2-weighted (T2W)–MRI, mp-MRI uses additional parameters such as DW–MRI, DCE–MRI, and MRS, that significantly improve the ability of mp-MRI to predict behaviour of tumours. T2W–MRI provides superior soft-tissue resolution compared with other imaging techniques—such as CT—allowing detection and biopsy guidance as well as staging of prostate cancer.[11,12] Mp-MRI has also been used to detect residual or recurrent disease after local treatment, such as surgery or radiation.[13] A consensus publication by Dickinson *et al.*[14] suggested that the MRI data should include T_1-weighted (T1W)–MRI, T2W–MRI, DW–MRI, and DCE–MRI at a minimum, with optimal data sets also including MRS. In the following sections, these four components of mp-MRI will be discussed in detail.

Anatomical MRI: T1W and T2W

Anatomical MRI of the prostate consists of T1W and T2W–MRI sequences. The guidelines composed by the European Society of Urogenital Radiology (ESUR) state that T2 sequences should include the prostate, seminal vesicles, and external sphincter with ≤3 mm section thickness and in-plane resolution of 0.7 mm or better.[15] T1W images are used mainly for the identification of post-biopsy haemorrhage, as haemorrhage can interfere with the diagnostic value of mp-MRI. On T1W images, biopsy-related haemorrhage demonstrates high signal intensity relative to normal prostate tissue.[16] Haemorrhage may result in artefacts making the interpretation of the MRI challenging and ultimately leading to inaccurate results on T2W–MRI and dynamic DCE–MRI. Therefore, haemorrhage identification by T1W images is critical to confirm the accuracy of image interpretation. In one study the accuracy of T2W–MRI decreased from 83% if performed less than 3 weeks after biopsy to 46% if performed more than 3 weeks after biopsy, which allows time for haemorrhage to resolve.[17] T2W images of capsular irregularity, thickening, and retraction due to injury after biopsy can be similar to extracapsular extension, which will lead to over-staging.[18] For these reasons, a delay of at least 6–10 weeks after biopsy is recommended before obtaining MRI of the prostate to allow residual h aemorrhage to resolve before imaging studies.[18–20]

T2W–MRI allows anatomical visualization of the transitional and peripheral zones, where 30% and 70% of tumours are located, respectively.[21] On T2W images, the normal peripheral zone demonstrates uniform high signal intensity due to the water content of glandular structures in the peripheral zone. Tumours are typically low in signal intensity compared with the glandular peripheral zone (Figure 1). Low signal intensity (hypo-intensity) in the peripheral zone, however, is not a specific finding for prostate cancer in itself and its differential diagnosis includes haemorrhage, prostatitis, benign prostatic hyperplasia (BPH).[22] Although tumour detection is more difficult in the transitional zone of the prostate—due to the coexistence of BPH and the heterogeneous nodularity—tumours in this area can be discerned as lenticular or irregular regions of homogenous hypo-intensity with ill-defined margins in comparison to well circumscribed nodules with distinct rims found in BPH.[23]

T2W–MRI is the most useful MRI sequence in determining whether tumours are confined to the prostate or extending beyond the capsule. The presence of extra-capsular extension (ECE) has implications for risk stratification of patients with prostate cancer because ECE automatically increases the radiological stage to T3a and could change the treatment plan and prognosis.[24] On T2W–MRI, ECE appears as a direct extension of the tumour into the surrounding periprostatic fat, or it can be identified as an asymmetric tumour capsular bulge, capsular abutment, obliteration of the rectoprostatic angle, broad capsular base or asymmetric neurovascular bundles.[15,25–28] Seminal vesicle invasion (SVI) upstages the patient to clinical stage T3b, and is associated with an increased risk of lymph-node metastasis.[29] On T2W–MRI, SVI appears as focal low signal intensity lesions within the seminal vesicles (Figure 2).[30]

When used alone, the accuracy of T2W–MRI for the detection of prostate cancer imaging is highly variable, with reported sensitivities ranging from 51% to 91%, and specificities of 27–91%.[31–35] The sensitivity ranges for local prostate cancer staging and detecting ECE are

14.4–100%, and the specificity ranges from 67% to 100%.[27,36–47] These results are highly dependent on field strength, technique, verification standards, and patient selection. When using MRI with strength of 3 Teslas (3T), lesions as small as 3 mm in diameter can generally be detected with high sensitivity. Sensitivities do not reach 100% due to the microscopic nature of some tumours that are not visible on MRI, whereas specificities do not reach 100% because other conditions—such as BPH, post-biopsy haemorrhage, and prostatitis—also display low signal intensity on T2W–MRI, similar to prostate tumours.[39] Therefore, although anatomic MRI is a useful modality in prostate cancer imaging, it achieves optimal accuracy when combined with other functional sequences in mp-MRI.

Diffusion-weighted MRI

DW–MRI quantifies the Brownian motion of free water protons within a tissue by applying a series of magnetic gradients, known as ‘b’ values.[48] For prostate cancer, b values between 0 and 800 sec/mm^2 are commonly used during DW–MRI scans. Because molecular diffusion is inversely proportional to tissue cellularity and cell membrane integrity, water diffusion measurements provide key information about tissue architecture in benign and malignant tissues.[49] Normal, well-structured glandular prostate tissue allows free diffusion of water molecules and, therefore, displays a low intensity on high b-value DW–MRI.[50] Malignant tissue has abundant stroma with diminished extracellular space and is more densely packed than normal tissue, resulting in restricted free water motion within the tumour, therefore, reducing the diffusion of water and resulting in high intensity foci on high b-value DW–MRI.[50] Often, DW–MRI is displayed as the apparent diffusion coefficient (ADC) map. ADC represents a quantitative assessment of water diffusion; lower values are associated with a higher rate of malignancy. Prostate cancer, therefore, is identified as a low signal region on ADC maps against a background of normal tissue with higher signal intensity (Figure 1).[51] DW–MRI is a rapidly evolving technique and recent studies have demonstrated that ‘ultrahigh’ b values of 1,000 to 2,000 sec/mm^2 further increase the specificity of prostate cancer detection.[52–55] Particularly within the transitional zone, ultrahigh b values help differentiate benign conditions such as BPH from cancer.[56]

DW–MRI is an important component of prostate mp-MRI protocols and improves diagnostic accuracy, planning of targeted biopsies, and staging.[34,57–64] A meta-analysis of ten studies that included data from 586 patients with suspected prostate cancer, showed a DW–MRI sensitivity of 76% and a specificity of 86%.[65] Notably, in six studies that analysed data from 260 men with pathologically confirmed prostate cancer, the sensitivity of DW–MRI was 88% with a specificity of 84%, and this specificity was higher in patients with both suspected and confirmed cancer, suggesting that DW–MRI is useful to confirm prostate cancer for high-risk patients.[65]

DW–MRI is considered a quantitative technique because ADC values can be calculated from conventional DW–MRI. The addition of DW–MRI to T2W–MRI significantly improves the accuracy of prostate tumour volume measurements when compared with T2W–MRI alone, and it has been suggested that DW–MRI in combination with other components of mp-MRI —such as T2W–MRI and DCE–MRI—most accurately predicts prostate tumour volume in lesions larger than 0.5 cm.[66] In addition to diagnostic utility, ADC values may be useful in

predicting tumour aggressiveness as ADC values have been correlated with Gleason scores.[67–69] Jung *et al.*[68] demonstrated that use of DW–MRI, in combination with T2W–MRI, improved prostate cancer detection in the transitional zone, and also confirmed that tumour ADC values inversely correlated with Gleason scores in 156 patients scanned at 1.5T. A recent study of 20 patients by Turkbey *et al.*[70] showed that T2W–MRI and DW–MRI obtained at 3T with the use of combined endorectal coil and 16-channel surface coil had a higher sensitivity of 76% for detecting prostate lesions than without an endorectal coil, which had a sensitivity of 45%; however, it is unclear whether this has an impact on patient outcomes. There are some limitations to the use of DW–MRI. Because it is highly sensitive to increased motion artefacts, DW–MRI is not always diagnostic. Moreover, DW–MRI is less useful in staging because of the lower resolution and greater image distortion than traditional T2W–MRI, making accurate assessment of ECE difficult with this image sequence. However, the role of DW–MRI in this regard is evolving, and with the use of high b values in conjunction with 3T MRI it is possible to achieve better signal-to-noise ratios sufficient to visualize the prostate capsule. Soylu *et al.*[71] examined 131 men aged 43–75 with a known diagnosis of prostate cancer and found that the use of DW–MRI in conjunction with T2W–MRI improved the specificity from 93.1% to 96.6% and the positive predictive value from 93.6% to 98.3% from both experienced and relatively inexperienced radiologists. The noninvasive use of DW–MRI to predict tumour behaviour and its spread is highly promising and needs further investigation.

Magnetic resonance spectroscopic imaging

Proton magnetic resonance spectroscopic imaging (MRSI) has been used for several decades and represents a functional method that assesses the biochemical characteristics of prostate lesions, specifically the intracellular concentrations of choline and citrate. Normally, the prostate is a highly efficient producer of citrate whereas its production of choline is much less robust. Owing to the increased cell membrane turnover of rapidly dividing cancer cells, tumours display increased choline levels and higher choline-to-citrate ratios, whereas benign tissue normally expresses high citrate and low choline levels, resulting in a low choline-to-citrate ratio.[72] MRSI takes advantage of the different intracellular metabolic profiles of cancer cells versus normal cells; the areas under metabolite peaks represent metabolite concentrations that can quickly be analysed by comparing the height of the choline peak to the height of the citrate peak; the more negative the slope of the line connecting the choline peak to the citrate peak, the more suspicious the lesion is for cancer (Figure 1). Unfortunately, benign prostate hyperplasia can also demonstrate an increased choline-to-citrate ratio. However, because MRSI is carried out after T2W anatomic MR imaging, overlaying the spectral data with anatomic images can help differentiate tumours from normal tissue.

One useful application of MRSI is in the detection of cancer in patients with rising PSA levels and prior negative biopsy. Ganie *et al.*[73] performed MRSI in 87 patients with PSA >5 ng/ml and prior transrectal ultrasound (TRUS)-guided biopsy, and found that the addition of MRSI to conventional endorectal coil MRI improved detection of cancerous lesions, with a sensitivity of 87.3% and a specificity of 81.3%. A study by Kobus *et al.*[74] examined the use of MRSI alone versus MRSI plus DW–MRI at 3T in 54 patients with biopsy-proven cancer

before undergoing prostatectomy. They found a significant correla tion between aggressiveness and choline-to-citrate ratio in both the peripheral zone and transitional zone, however, further validation is needed.[71] In addition, other metabolic resonances are of interest, particularly polyamines such as spermine. Similar to citrate, polyamine levels are drastically decreased in prostate cancer cells.[74] Jung *et al.*[75] developed a 5-point standardized scoring system for the analysis of spectral data, in which a score of 1 is probably benign and a score of 5 is probably malignant.[75] This scoring system demonstrates an accuracy of 74.2–85.0% and excellent interobserver agreement.[75]

Limitations of MRSI include the longer acquisition times and the increased technical skill required compared with other mp-MRI techniques. Proper magnetic resonance shimming (that is, a device used to adjust the homogeneity of a magnetic field) is critical, and experienced readers are necessary to correctly interpret partial volume effects. Furthermore, MRSI demands increased time for post-processing the data, which requires trained employees and decreases clinical output. For these reasons, most users have decided that MRSI does not have a favourable cost-benefit ratio and other mp-MRI sequences such as T2W–MRI, DW–MRI, and DCE–MRI are more commonly used instead. Finally, because MRSI is not actually an anatomic pulse sequence, it has a limited role in determining anatomic location of a tumour or extension beyond the prostate.

Dynamic contrast-enhanced MRI

DCE–MRI evaluates the vascularity of tumours through the use of fast T1W–MRI scanning sequences before, during, and after the rapid administration of gadolinium-based MRI contrast agents, such as gadolinium chelates.[76] DCE–MRI provides an assessment of perfusion and vascular permeability throughout the prostate and specifically within a potential tumour.[77] Owing to neoangiogenesis, tumours have more permeable, heterogeneous, and disorganized vessels than normal tissue, causing prostate cancers to typically exhibit early and rapid enhancement as well as early washout, which are associated with tumour aggressiveness.[78]

The ESUR guidelines recommend a bolus injection at 3 ml/sec with a standard dose of contrast agent and suggest a minimum slice thickness of 4 mm of the MR image.[15] The easiest and most common method of evaluating DCE–MRI images is to qualitatively detect focal early enhancement with early washout as compared to normal prostate tissue (Figure 1). After a rapid rise in signal following contrast media injection, the lesion can have one of three enhancement patterns: progressively enhancing (type 1), plateauing (type 2), and washing out (type 3) (Figure 3). Type 1 curves are characteristic of benign tissue, although low-grade malignancies can also enhance in this manner. Type 2 curves demonstrate an increase in contrast followed by a plateau, and are suspicious for cancer—but not definitive—as many benign lesions exhibit this type of enhancement. Type 3 curves demonstrate rapid early enhancement as well as fast washout and are characteristic of tumours. Of the curve types, type 3 curves are most commonly associated with tumours, although heterogeneous mixtures of all three curves are often found within a single cancerous lesion (Figure 3).[79] The gadolinium concentration over time can also be used to measure the area under the plasma concentration time curve (AUC), the time to peak enhancement, and the initial slope.

Another method of analysing DCE–MRI is to use pharmacokinetic parameters K^{trans} (transfer of gadolinium contrast from the vasculature to the tumour, representing forward vascular perfusion and permeability) and K_{ep} (reverse transfer of contrast agent from the extra cellular space back to the plasma, representing backward leakage) to quantify tumour enhancement.[80,81] DCE–MRI has higher sensitivity than T2W–MRI alone, with an overall sensitivity of 73% and specificity of 81%,[82,83] and its diagnostic capabilities are even more improved in lesions of >0.5 cm, with a sensitivity of 90% and a specificity of 88%.[82,84] This high sensitivity of DCE–MRI makes it a useful functional imaging modality in the detection of tumours as well as the assessment of treatment response.

A recent study of 45 patients with prostate cancer examined the ability of DCE–MRI at 3T to predict prostate cancer aggressiveness when compared with the gold-standard prostatectomy pathology results.[85] They found that both quantitative (K^{trans} and K_{ep}) and semi-quantitative (wash-in and wash-out) DCE parameters were helpful in assessing prostate cancer aggressiveness in the peripheral zone.[85] Another study by Li *et al.*[86] found that the combination of diffusion tensor imaging with DCE–MRI improved the diagnostic performance of detecting prostate cancer in the peripheral zone compared with either technique alone.

Limitations in the interpretation of DCE–MRI data include overlap in enhancement properties between benign and malignant regions in the transitional zone, as benign prostatic hyperplasia and other benign inflammatory conditions within the transitional zone also exhibit substantial hypervascularity.[87,88] DCE–MRI is typically of lower spatial resolution than other sequences, especially when DCE–MRI is performed rapidly in a short period of time and for pharmacokinetic analysis. In such cases, DCE–MRI should be combined with T2W–MRI to provide anatomic information for local staging of a tumour.

Detection of prostate cancer

The traditional method of prostate cancer detection includes serum PSA measurements, routine digital rectal examinations, and a systematic TRUS-guided biopsy, which provides 12 random cores of tissue from the posterior part of the gland. However, the 12–14 core TRUS-guided biopsy has only a cancer detection rate of 27–44% and leads to overdiagnosis of clinically insignificant tumours while missing or under sampling clinically relevant tumours, particularly in the anterior area of the prostate gland.[89–91] The anterior prostate gland accounts for up to 20% of the largest tumours in patients with suspected prostate cancer, and is a difficult area to biopsy using the traditional 12-core random TRUS-guided technique currently used by most urologists because the needle has to travel further to the anterior part of the gland.[92] Adding mp-MRI to this traditional biopsy strategy or using mp-MRI as a substitute for a biopsy in selected patients with low-risk lesions detected on mp-MRI can improve prostate cancer detection (Figure 4).[57,93–95] Performing mp-MRI before biopsy is based on the principle of guiding biopsies according to lesions identified on imaging, rather than systematically sampling the posterior region of the prostate. TRUS–MRI fusion biopsy can be used to direct biopsy needles into abnormal regions of the prostate, similar to virtually all other cancer biopsies.[93] Targeting biopsies to a suspicious lesion identified by mp-MRI may detect high-grade tumours in an equivalent or higher

percentage of patients than random biopsies while using fewer biopsy cores with fewer complications and lower diagnosis rates of insignificant tumours.[96] A study of 555 patients with suspicion of prostate cancer demonstrated that targeted biopsies as determined by pre-biopsy mp-MRI had increased detection accuracy of significant prostate cancer than extended systematic biopsies.[97] In another study, 1,448 patients suspected of having prostate cancer underwent targeted and systematic biopsies; the cancer detection rate was higher in the targeted biopsy group with a positive predictive value for mp-MRI of 70.1–90.1%.[98] A study of 582 patients by Siddiqui *et al.*[99] showed that targeted biopsy detected 67% more Gleason ≥4 + 3 tumours than 12-core biopsy alone and missed 36% of Gleason ≤3 + 4 tumours, thus minimizing the detection of lower grade disease. It should be noted that the economic implications of performing a pre-biopsy mp-MRI are not trivial, with an estimated $2,000–3,000 charge in the USA, although real costs are considerably lower.[100]

Prostate cancer staging

Mp-MRI can assess the risk of prostate cancer based on the appearance of the lesions. Mp-MRI is recommended before a patient is considered for active surveillance, as it allows detection of poor prognostic features—such as a large tumour volume or high-grade tumours, particularly in the anterior prostate—that would be unsuitable for active surveillance. In an effort to standardize the level of detection of suspicious lesions on mp-MRI, Dickinson *et al.*[101] reported a 5-point scale for scoring mp-MRI sequences, with a score of 1 indicating a low risk of clinically significant disease (Gleason ≥4 + 3 and/or lesions ≥0.5 cm), and a score of 5 indicating that clinically significant disease is highly likely to be present. In a study of 800 patients who underwent 3T mp-MRI of the prostate, patients with low suspicion lesions according to mp-MRI were more likely to have negative biopsies or low-grade tumours. These results suggest that the risk of clinically significant disease in patients with low-risk lesions on a pre-biopsy mp-MRI is sufficiently small to justify deferring biopsy or pursuing active surveillance if a cancer is identified after biopsy. In patients with intermediate-risk or high-risk disease, the follow-up after focal therapy should include a mp-MRI after 6 months and, again, on a yearly basis thereafter.[102]

Treatment planning

In patients with a new diagnosis of prostate cancer, the role of mp-MRI is to help to determine the best treatment option for the patient. For patients with low-risk disease (PSA<10 ng/ml with biopsy Gleason score ≤6 and clinical stage T1–T2a), treatment is with curative intent by radical prostatectomy, radiation therapy, or active surveillance.[15] In these patients, mp-MRI can be used to confirm eligibility for active surveillance when significant disease is absent, and to help with surgical and radiation treatment planning.[15] In patients with intermediate-risk disease (PSA 10–20 ng/ml, biopsy Gleason score 7, or clinical stage T2b or T2c), mp-MRI is most helpful in staging disease to detect ECE.[15] In patients with high-risk disease (PSA >20 ng/ml, biopsy Gleason score 8–10, or clinical stage >T2c), mp-MRI can be used to detect skeletal or nodal metastases, although lymph-node staging can be unreliable because 70% of metastatic lymph nodes in men with prostate cancer are <8 mm and, therefore, difficult to detect with mp-MRI.[15,103] Finally, in patients with a PSA recurrence after focal therapy mp-MRI is a useful tool to evaluate the prostatic fossa as other

techniques such as PET imaging or a TRUS-guided biopsy have a low sensitivity for recurrent disease.

Conclusions

Because prostate cancer often grows slowly with a long latency time before becoming clinically significant, there is a great need to accurately assess the size and invasiveness of detected cancers. The use of imaging to noninvasively identify prostate cancer and evaluate the extent of disease burden enables optimal treatment planning. Mp-MRI can help to differentiate clinically significant tumours from benign lesions by combining anatomical and functional imaging techniques. Mp-MRI is also clinically useful in prostate cancer staging by detecting ECE and seminal vesicle invasion. Mp-MRI is currently most widely used for tumour localization and cancer staging in patients with prostate cancer, however, it is increasingly being used in patients undergoing active surveillance as a monitoring tool as well as to monitor recurrence in patients after definitive therapy. Future development of novel imaging techniques that provide biological information about tumour behaviour may further guide diagnosis and treatment options.

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Key points

- T_2-weighed MRI allows anatomical visualization of both the transitional and peripheral zones of the prostate, where 30% and 70% of tumours are located, respectively
- A delay of at least 6–10 weeks after a biopsy procedure is recommended before obtaining MRI of the prostate to allow residual haemorrhage to resolve
- The addition of diffusion-weighted (DW) MRI significantly improves the accuracy of prostate tumour volume measurements when compared with T_2-weighted MRI alone
- There is a significant negative correlation between tumour apparent diffusion coefficient (ADC) values and Gleason scores, suggesting that ADC values are useful in predicting the aggressiveness of tumours
- Dynamic contrast-enhanced MRI provides an assessment of perfusion and vascular permeability of the tumour; semiquantitative parameters in this approach (peak enhancement and washout gradient) are associated with tumour aggressiveness
- MR spectroscopy compares the metabolic profiles of cancer cells with those of normal cells; increased levels of choline and high choline:citrate ratios can identify different types and grades of tumours

Review criteria

We searched for original articles focusing on prostate cancer in PubMed published between 1990 and 2014. The search terms we used were “multiparametric MRI” and “prostate cancer”. All papers identified were English-language full-text papers. We also searched the reference lists of identified articles for further papers.

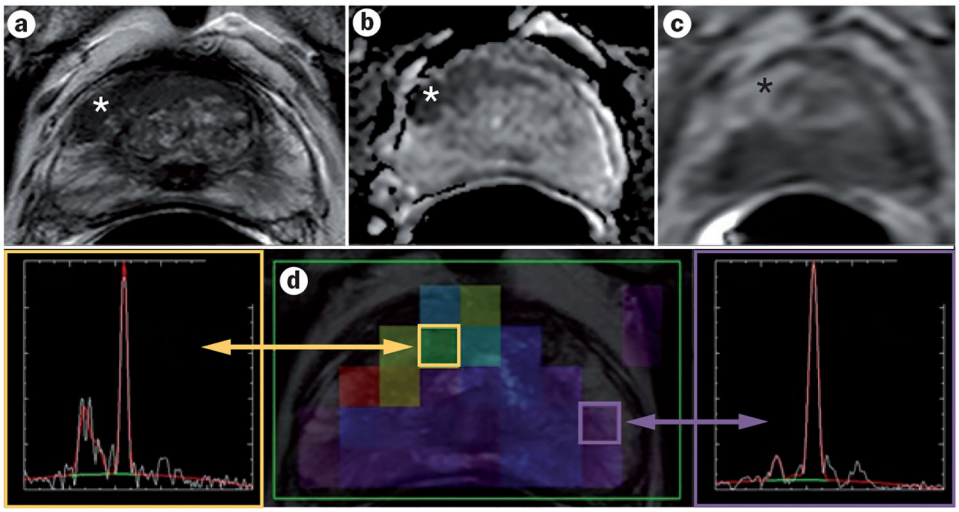

Figure 1 |.

A 61-year-old man with serum PSA of 23.85 ng/ml. **a** | Axial T2W–MRI, **b** | apparent diffusion coefficient map of diffusion-weighted MRI, and **c** | raw DCE–MRI demonstrate a 1 cm right apical mid-peripheral zone lesion (asterisk). **d** | Magnetic resonance spectroscopy shows an elevated choline-to-citrate ratio in the right mid-base anterior transitional zone compared with the normal left peripheral zone. Subsequent TRUS–MRI fusion-guided biopsy revealed a Gleason 4 + 4 tumour within that lesion. Abbreviations: DCE–MRI, dynamic contrast-enhanced MRI; PSA, prostate-specific antigen; T2W–MRI, T_2-weighted MRI; TRUS, transrectal ultrasound.

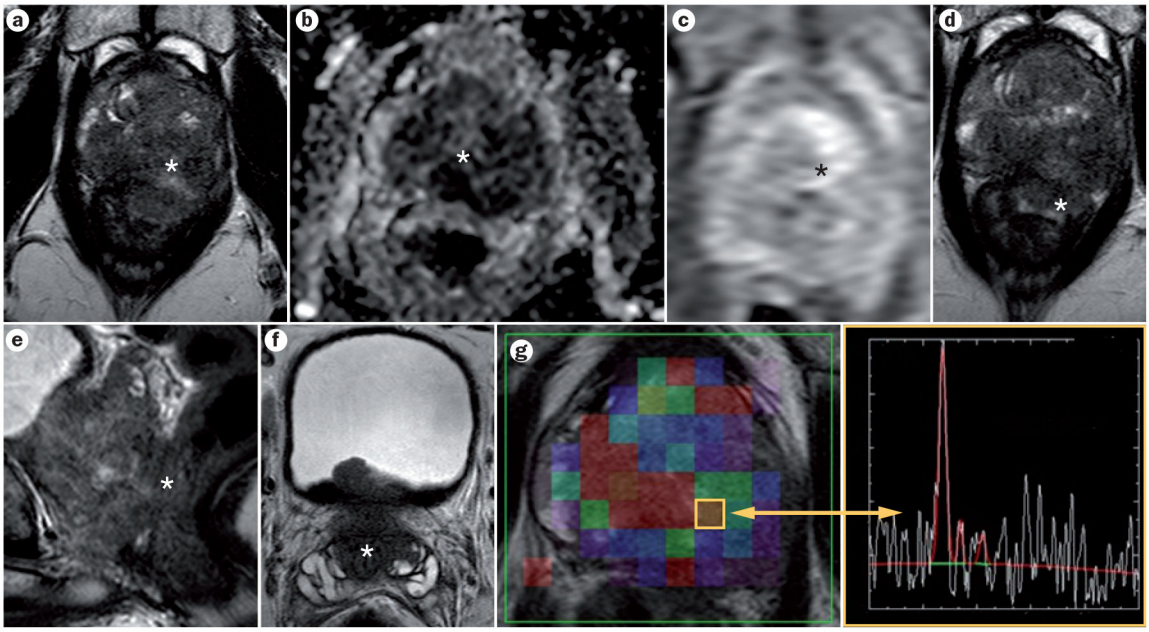

Figure 2 |.

A 59-year-old man with serum PSA of 24.7 ng/ml. **a** | Axial T2W–MRI, **b** | apparent diffusion coefficient map of DW–MRI, and **c** | raw DCE–MRI demonstrate a large 5 cm lesion, which affects almost the entire prostate (asterisk). **d**,**e** | The lesion has extracapsular extension and invades the rectum (asterisk). **f** | Seminal vesicles are invaded bilaterally (asterisk). **g** | Magnetic resonance spectroscopy shows an elevated choline-to-citrate ratio (asterisk). Subsequent TRUS/MRI fusion-guided biopsy revealed a Gleason 5 + 5 tumour within the prostate. Abbreviations: DCE–MRI, dynamic contrast-enhanced MRI; DW–MRI, diffusion-weighted MRI; PSA, prostate-specific antigen; T2W–MRI, T_2-weighted MRI; TRUS, transrectal ultrasound.

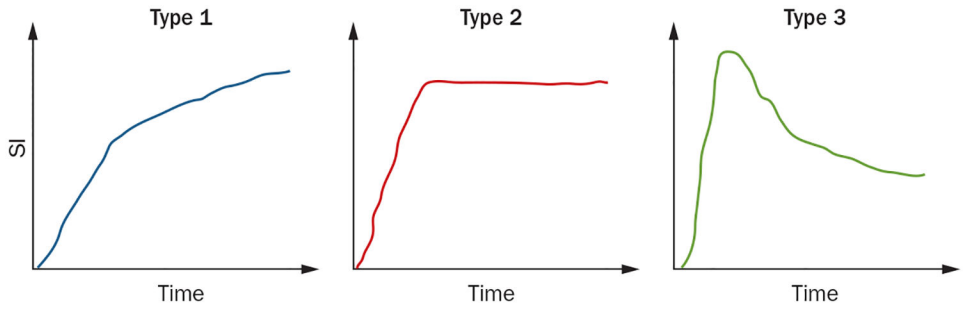

Figure 3 |.

Curve types representing enhancement patterns on DCE–MRI. Type 1 represents progressive enhancement, type 2 rapid enhancement with plateauing, and type 3 represents rapid enhancement followed by a rapid wash out of the contrast material. Abbreviations: DCE–MRI, dynamic contrast-enhanced MRI; SI, signal intensity.

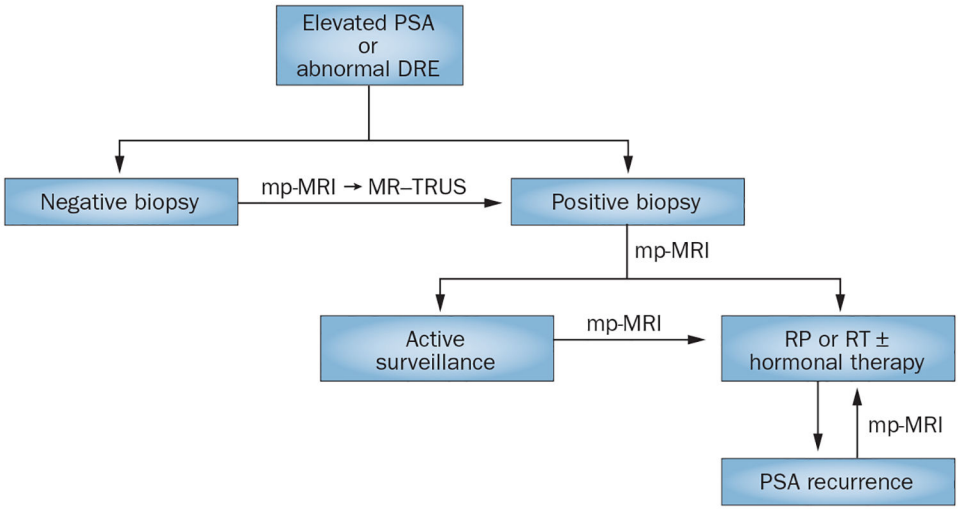

Figure 4 |.

Flowchart showing the utility of mp-MRI in various clinical scenarios of prostate cancer. MRI can be used as a cancer staging tool after a positive biopsy before definitive treatment, to identify target lesions before a targeted biopsy, as a way to monitor active surveillance patients and as a guide for patients with prior negative biopsies but rising serum PSA levels. MRI also has a role in the follow up of patients with a PSA recurrence after treatment. Abbreviations: DRE, digital-rectal examination; mp-MRI, multiparametric MRI; PSA, prostate-specific antigen; RP, radical prostatectomy; RT, radiotherapy; TRUS, transrectal ultrasound.