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# The Expanding Role of MRI in Prostate Cancer

**OBJECTIVE.** The purpose of this article is to review the many evolving facets of MRI in the evaluation of prostate cancer. We will discuss the roles of multiparametric MRI, including diffusion-weighted MRI, dynamic contrast-enhanced MRI, and MR spectroscopy, as adjuncts to morphologic T2-weighted imaging in detection, staging, treatment planning, and surveillance of prostate cancer.

**CONCLUSION.** Radiologists need to understand the advantages, limitations, and potential pitfalls of the different sequences to provide optimal assessment of prostate cancer.

rostate cancer is the most commonly diagnosed cancer in males and the second cause of cancer related death in men. Detection and clinical staging of prostate cancer currently includes a prostate-specific-antigen (PSA) test, a digital rectal examination, and a transrectal ultrasound (TRUS)-guided prostate

biopsy. The TNM stage is obtained using these variables and treatment of prostate cancer is based on clinical stage and is patient specific. The first part of this article outlines how prostate MRI increases the accuracy of tu-

prostate MRI increases the accuracy of tumor detection, localization and staging and thus facilitates guidance of patient specific treatment. We also discuss the role of MRI in guiding repeat prostate biopsy for patients with previous negative TRUS biopsy, the use of MRI as a baseline test for patients with suspected prostate cancer before TRUS biopsy and the emerging potential role of MRI to replace TRUS biopsy in patients on active surveillance. The second part of this paper reviews prostate MRI technique, morphologic T2-weighted imaging and multiparametric MRI, including diffusion weighted MRI (DWI), dynamic contrast-enhanced MRI (DCE-MRI), and MR spectroscopy (MRS).

## The Role of MRI in Prostate Cancer

Role of MRI in Guiding Prostate Biopsy

Prostate cancer diagnosis is primarily based on prostate-specific antigen (PSA) screening and transrectal ultrasound (TRUS)-guided prostate biopsy. However, PSA has low specificity (36%) because benign conditions can cause elevated PSA. Thus, increased PSA is not equivalent with a tumor, and normal PSA does not exclude a tumor [1, 2]. Because routine TRUS biopsy is systemic, nontargeted, and directed toward the peripheral gland, some tumors can be missed, particularly those in the anterior prostate. TRUS biopsy has a negative predictive value (NPV) of 70–80%; thus, up to 20–30% of patents with a negative biopsy may still have prostate cancer [3].

Patients with a suspected false-negative biopsy are a diagnostic challenge because there is a progressively lower diagnostic yield from subsequent repeat prostate biopsies [4]. Second, third, and fourth repeat biopsies are reported to detect cancer in only 25-27%, 5-24%, and 4-21% of cases, respectively [4, 5]. The reasons for this are multifactorial. PSA-based screening has led to stage migration at the time of prostate cancer detection, with an increasing number of low-risk low-volume tumors detected. The volume of gland extracted in core biopsy specimens is approximately 1% of the prostate gland [5]. Finally, because prostate cancer is multifocal in 85% of cases, TRUS biopsy may underestimate the extent and grade of cancer, which can result in Gleason upgrading after prostatectomy [5]. It is well documented that approximately 30% of men who undergo radical prostatectomy for low-grade disease are upgraded on final pathology [6].

Therefore, there is a need for an alternative acceptable test for patients with elevated or rising PSA but negative initial biopsy. Multiple studies have now shown that multiparametric MRI can help to identify tumors missed on biopsy, thus increasing biopsy yields with fewer core samples [2, 3, 7]. Many of these tumors are deep in the prostate further from the rectal wall than typically reached with a standard TRUS biopsy approach (Fig. 1).

A recent study evaluating MRI in patients with elevated PSA and no previous biopsy found a higher cancer detection rate (30% vs 10%) and higher positive core biopsy rate (10.0% vs 2.5%) in the MRI group compared with the non-MRI group [8]. Another study evaluating patients with persistently elevated PSA and two or more negative TRUS biopsies who subsequently underwent MRI-guided repeat biopsy found a tumor rate of 59% (40/68 cases), and of the 40 patients with identified tumors, 37 (93%) were considered highly likely to harbor clinically significant disease [2]. A further study evaluating the role of MRI in assessing anterior prostate tumors found that MRI had a positive predictive value (PPV) for anterior tumors of 87% (27/31 patients) [7]. These studies highlight the role of MRI in detecting clinically significant tumor foci and guiding repeat prostate biopsy after an initial negative TRUS biopsy for patients with a high clinical suspicion of harboring prostate cancer.

Because MRI is the most accurate imaging modality for localization of prostate cancer,



**Fig. 1**—61-year-old man with elevated prostate-specific antigen level of 14.2 ng/mL, negative digital rectal examination, and two previous negative transrectal ultrasound biopsies.

**A**, Axial T2-weighted MR image with endorectal coil shows subtle low-signal-intensity area in anterior central gland on right (*circle*), but it is difficult to confirm tumor on this image alone with certainty.

**B**, Lesion also shows low signal intensity consistent with restricted diffusion on apparent diffusion coefficient (ADC) map (*arrow*), indicative of tumor. ADC map gives high confidence in diagnosing tumor in anterior zone over T2-weighted image alone. This patient went on to undergo repeat biopsy targeting anterior gland revealing Gleason 3 + 4 tumor.

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MRI-guided prostate biopsy offers the possibility of more precise targeting [5]. MRIguided prostate biopsy encompasses either fusion technology between ultrasound and MRI or using MRI alone. In fusion ultrasound-MRI prostate biopsy, previously performed prostate MR images are fused to the ultrasound images at the time of biopsy to guide the operator to the target. In MRI-guided prostate biopsy, MRI is used at the time of biopsy. A combination of ultrasound-guided and MRI-guided prostate biopsy has been shown to be superior to standard TRUS biopsy in prostate cancer detection [9, 10].



Fig. 2—Extracapsular tumor extension in three different patients on T2-weighted MRI.

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**A**, Axial T2-weighted MR image with endorectal coil in 71-year-old man on active surveillance for Gleason 7 prostate cancer. Prostate-specific antigen (PSA) level was stable at only 5 ng/mL but digital rectal examination revealed new palpable lesion. Patient refused repeat biopsy and underwent MRI, which shows large right peripheral zone tumor (*white arrows*) seen as low signal intensity on T2-weighted image. Tumor is causing bulging and irregularity of capsule (*black arrow*), which indicates penetration consistent with stage T3a disease.

**B**, Axial T2-weighted MR image in 51-year-old man with PSA level of 9.9 ng/mL shows low-signal-intensity tumor in left medial peripheral zone (*dashed arrow*) with obvious extracapsular extension and obliteration of left rectoprostatic angle (*solid arrow*) in comparison with normal right rectoprostatic angle, consistent with T3a tumor.

**C**, Axial T2-weighted MR image with endorectal coil in 72-year-old man with PSA level of 17 ng/mL who was clinically stage T1c (tumor identified on needle biopsy) shows low signal intensity consistent with tumor in left peripheral zone (*white arrows*). There is extraprostatic extension with tumor involving left rectoprostatic angle and associated extension into neurovascular bundle on left side (*solid black arrow*). Compare this with normal right side with intact capsule and intact neurovascular bundle (*dashed black arrow*). Before MRI, neurovascular preservation was planned; however, MRI accurately staged this patient, showing neurovascular bundle invasion consistent with extracapsular T3a tumor.

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Fig. 3—69-year-old man with prostate cancer. A and B, Sagittal (A) and coronal (B) T2-weighted MR images of pelvis without endorectal coil show gross extraprostatic extension of cancer. Tumor occupies entire prostate gland (P) and breaches capsule extending outside prostate with obvious invasion of bladder (*arrow*, A) and seminal vesicles (*arrow*, B) consistent with T4 cancer.

There is also increasing interest in using MRI before performing a biopsy in patients with elevated PSA. Potentially, the use of MRI before biopsy in men with elevated PSA levels could identify patients who require a biopsy because of a significant cancer identified on MRI or those who only require observation and thus can avoid a biopsy. This may be of particular potential benefit in patients with only mildly elevated PSA, which can be due to a cause other than prostate cancer, such as benign prostatic hyperplasia (BPH) and chronic prostatitis. Multiparametric MRI before biopsy in men with suspected prostate cancer is currently being performed in a few centers. Further investigation is required to determine the accuracy of MRI in this setting, establish how it changes patient outcomes, and determine the potential cost benefit of such an approach. Furthermore, evidence is still required to justify the role of MRI as a replacement for TRUS biopsy. The NPV of MRI in the screening population is still unknown.

Patients with low-grade prostate cancer may be put on active surveillance, in which the patient is monitored with the intention to intervene if the disease progresses. Active surveillance includes PSA, DRE, and TRUS biopsy. There is an emerging potential role for MRI in these patients. Numerous studies have reported that between 19% and 34% of patients with low-grade disease on initial biopsy have Gleason upgrading on repeat random extended biopsy, suggesting undersampling by the initial biopsy [11–16]. Therefore, these patients may be put on active surveillance and thus be denied appropriate treatment of an occult higher Gleason grade tumor. MRI has a role in ensuring that the most aggressive tumor is sampled in these patients to help guide further treatment. Recent studies have shown that both attenuation diffusion coefficient (ADC) and MRS are correlated with Gleason grade. Thus, there is a potential role for MRI not only in localizing tumor but also in identifying the areas of more aggressive cancer that could be targeted by TRUS- or MRI-guided biopsy [1, 17–20].

# Role of MRI in Local Staging of Biopsy-Proven Prostate Cancers

Partin tables are validated predictive tools that combine information from the DRE, serum PSA, and Gleason score to predict the stage of cancer. They predict the risk of extracapsular extension (ECE) but do not provide information regarding localization or extent of ECE, which is of benefit to optimize further treatment. Prostate MRI has been shown to add value in all risk groups in the prediction of ECE; the greatest incremental value of MRI to the Partin tables has been found in high-risk patients [21]. Equally, MRI has been shown to improve other risk stratification tools and nomograms, such as the Kattan nomograms and the D'Amico classification.

For potential surgical candidates, regional imaging is crucial for surgical planning [22]. It is important to differentiate between stage T2 (disease confined to the prostate, for which curative therapy can be considered) and stage T3 (ECE). MRI can evaluate for ECE (stage T3); involvement of the



**Fig. 4**—Recurrent disease in 73-year-old man after prostatectomy with elevating prostate-specific antigen level. Sagittal gadolinium-enhanced T1-weighted MR image of pelvis without endorectal coil shows recurrent enhancing tumor mass (T) measuring 5.7 × 1.8 × 3.9 cm within prostatectomy bed at urethral anastomosis, invading base of bladder (B) anteriorly and remnant seminal vesicles posteriorly (*arrow*).

neurovascular bundle (NVB); seminal vesicle invasion (SVI) (stage T3); and invasion of adjacent structures, such as the bladder or rectum (stage T4), the presence of which may prevent curative surgery (Figs. 2 and 3). Recent studies have found high sensitivity and specificity for preoperative MRI in evaluating for ECE (0.78 and 0.96) and SVI (0.88 and 0.98), respectively [23, 24]. Therefore, MRI offers the most accurate imaging assessment of local prostate cancer and regional metastatic spread. In addition, the presence of advanced local disease at diagnosis determined by MRI has a worse prognosis with a higher risk of developing relapse and metastases after treatment [3, 25].

Pretreatment knowledge of lymph node metastases (LNM) is important for appropriate treatment planning. PSA screening has resulted in stage migration with more patients presenting with earlier-stage disease. The incidence of LNM at the time of diagnosis is low at approximately 5%, but prognosis is worse because of a higher probability of progression to distal metastatic disease after treatment [26]. For node-negative versus node-positive disease at the time of diagnosis, the risk of metastatic disease at 10 years is 31% versus 83%, [26]. MRI has high specificity but low sensitivity for the detection of LNM [26]. Using nodal size criteria alone is limited because 70% of metastatic lymph nodes in prostate cancer are small (< 8 mm) [1]. CT also

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Fig. 5-66-year-old man with normal prostate gland as seen on T2-weighted MRI. Axial T2-weighted MR image obtained with endorectal coil to increase spatial resolution is best sequence to depict prostate zonal anatomy. Central gland (C) is low signal intensity on T2-weighted imaging and thus masks tumor, which is also low signal intensity. Twenty-five percent of prostate tumors occur in central gland; 75% of tumors arise in peripheral zone (P) of prostate and are seen as low signal intensity in comparison with normal high signal intensity of peripheral zone. Neurovascular bundles are positioned at 5- and 7-o'clock positions, just outside pseudocapsule (solid arrows). Pseudocapsule is seen as thin surrounding low-signal-intensity band (dashed arrow). Anterior fibromuscular stroma (FS) has low signal intensity. Rectum (R) is closely applied to prostate, separated by thin low-signal-intensity Denonvilliers fascia. Rectum is distended with endorectal coil

has low sensitivity in the evaluation of LNM [17]. Use of ultrasmall paramagnetic iron oxide particles with MRI has been found to enable detection of nearly 100% of pathologically involved lymph nodes [5].

#### Role of Prostate MRI in Treatment Planning

Treatment of prostate cancer is patient specific and is based on clinical stage, Gleason score, and PSA levels, which stratify patients into low-, intermediate-, and high-risk groups. TNM stage is most optimally determined by MRI, which can therefore help correctly stratify patients into the best therapy option [5].

Only rarely will a patient with clinically low-risk disease be found to have advanced disease on MRI [5]. Therefore, for patients with low-risk disease clinically, MRI can confirm early-stage tumor, thus correctly stratifying patients into active surveillance while ensuring the few patients with more aggressive disease are not being denied further appropriate treatment. As previously discussed, multiparametric MRI correlates with Gleason grade. Therefore, if required, multiparametric MRI can help guide repeat biopsy in these patients for more accurate tumor grading. Multiparametric MRI can stratify intermediate risk patients into high- and low-risk groups on the basis of the presence or absence of ECE to influence further treatment.

Treatment options are surgical and nonsurgical. For surgical candidates, because only carcinomas confined within the prostate gland are potentially curable by radical prostatectomy (RP), findings of ECE and SVI on preoperative MRI may preclude curative surgery (Figs. 2 and 3). Involvement of the NVB will preclude NVB sparing surgery (Fig. 2C). It is important for the patient to be counseled in this regard preoperatively because of the implications for the recovery of urinary and sexual function. Conversely, in patients who may otherwise have undergone radical surgery with excision of the NVB, MRI can accurately show lack of invasion of the NVB, thus enabling the patient to undergo NVB-sparing surgery [27]. Hricak et al. [28] found that MRI significantly improved the surgeon's decision to preserve or resect the NVB during RP [28]. A recent study also found that preoperative prostate MRI changed the decision to use a nerve-sparing technique during roboticassisted laparoscopic prostatectomy in 27% (28/104) of patients in the series [29].

Nonsurgical treatment options include radiation therapy (brachytherapy, external-beam radiation therapy [EBRT]), hormone therapy, and minimally invasive ablative therapies that use physical energy to cause tumor destruction, which include cryotherapy, high-intensity focused ultrasound (HIFU), vasculartargeted photodynamic therapy, and thermal laser ablation.

With the improvement of curative therapies, exact localization of prostate cancer has become increasingly important. MRI is invaluable in assisting EBRT planning for locally advanced disease to determine tumor location, volume, and extent. Knowledge of the exact tumor location within the prostate can help direct maximal therapy to the largest focus of tumor while minimizing surrounding radiation-induced tissue damage [30].

MRI helps select patients for brachytherapy, where disease must be confined within the pseudocapsule (T1–2N0M0). MRI aids in the placement of brachytherapy seeds to target the tumor site within the prostate for more focal therapy while avoiding periprostatic toxicity to the rectum and urethra [31].

MRI can aid to guide focal therapy including minimally invasive ablative therapies. Traditionally, cryotherapy and HIFU have been used to achieve whole-gland ablation. The role of MRI for these patients is similar to the role of MRI before radical prostatectomy, in which MRI is used to assess local staging, including ECE and NVB invasion. More recently, focal ablative therapy, which targets only the tumor within the prostate gland and not the entire gland, has been achieved. These techniques can be performed in an operating the-





Fig. 6—Postbiopsy fibrosis and hemorrhage in two different patients.

**A**, Axial T2-weighted MR image of prostate with endorectal coil in 72-year-old man with history of prostate biopsy shows large low-signal-intensity area in left peripheral zone, which has appearance of tumor with extracapsular extension (*arrow*). However, this was large area of fibrosis and granulomatous inflammation that mimics tumor on T2-weighted image. Patient actually had cancer on right that was not visible on T2-weighted image to T2-weighted imaging alone and need for other techniques to supplement T2-weighted imaging to ensure correct interpretation of findings.

**B**, Axial T1-weighted MR image in 79-year-old man at midprostatic level shows high-signal-intensity area in left peripheral zone (*arrow*), consistent with postbiopsy hemorrhage. If pseudocapsule or seminal vesicles have been biopsied to prove extracapsular spread, this reduces staging accuracy. Often signal characteristics may help because methemoglobin within hemorrhage is high signal intensity on T1-weighted imaging, unlike tumor. Alternatively, MRI can be repeated to allow biopsy changes to resolve.

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ater or under real-time MRI guidance with an ablation margin of 1 mm, thereby allowing highly targeted therapy and minimizing periprostatic injury [31]. MRI has a potential role in these patients in tumor localization for targeted treatment, thus enabling imaging-guided prostate-sparing therapy.

Patients with locally advanced disease at diagnosis as characterized by MRI may require more aggressive treatment, such as whole-pel-



vis and prostatic radiation, adjuvant radiotherapy after surgery, or long-term androgen deprivation therapy [25]. The extent of LNM depicted by MRI can also define the radiation field more optimally.

## Role of Prostate MRI in Posttreatment Surveillance

Prostate cancer recurrence after treatment is diagnosed by an elevation in serum PSA,



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**Fig. 7**—65-year-old man with prostate-specific antigen value of 10 ng/mL, negative digital rectal examination, and biopsy-proven low-grade Gleason 6 cancer for which he was under active surveillance. **A** and **B**, Axial T2-weighted MR image (**A**) and axial diffusion-weighted imaging apparent diffusion coefficient (ADC) map (**B**) obtained with endorectal coil show central gland is heterogeneous due to benign prostatic hyperplasia. There is focus of low signal intensity in anterior right transition zone (*arrow*, **A**), although it is difficult to be certain whether this represents tumor on T2-weighted image alone. This area corresponds with low signal intensity on ADC map, consistent with restricted diffusion, which indicates focal tumor.

known as biochemical relapse. Biochemical relapse after RP, defined as PSA level greater than 0.4 ng/mL, can occur in up to 40% of patients [19, 32] (Fig. 4). After RP, it is difficult to detect tumor recurrence on TRUS because both the tumor and scar tissue are hypoechoic and biopsy may often be negative. Because of the challenge of diagnosing locally recurrent tumor, suspected local relapse is often treated with local radiation without a confirmed diagnosis. A number of studies have shown the benefit of MRI encompassing DCE-MRI in detecting tumor recurrence post RP [32–37].

Up to 30% of patients after radiation therapy can relapse, defined as PSA rise of 2.0 ng/L above nadir or three consecutive increases in PSA level after a nadir has been reached [38]. For local recurrence after radiotherapy, salvage prostatectomy caries a high complication rate. Imaging-guided minimally invasive therapy may improve outcome while limiting complications but requires accurate localization of the tumor. Prostate MRI is indicated for repeat staging in patients with suspected

Fig. 8-74-year-old man with elevated prostate-specific antigen level of 17 ng/mL, negative digital rectal examination, and two previous negative biopsies. A-D, Axial T2-weighted (A), diffusion-weighted MRI (B), apparent diffusion coefficient (ADC) map (C), and dynamic contrast-enhanced (DCE-MRI) images (D) with endorectal coil. MRI was performed to assess for possible tumor missed on biopsy. On T2-weighted image (A) there is enlargement of central gland due to benign prostatic hypertrophy and peripheral zone is compressed. There is subtle small 8 × 5 mm lowsignal-intensity lesion in right medial peripheral zone (arrow, A) that is difficult to diagnose. Restricted diffusion has low signal intensity on ADC map (arrow, B) and high signal intensity on diffusion-weighted image (arrow, C). Strong early enhancement on DCE-MRI after IV gadolinium contrast administration corresponding to area of restricted diffusion (arrow, D) confirms that this represents focus of tumor. Repeat targeted biopsy confirmed Gleason 6 tumor.

recurrent or persistent tumor after radiotherapy and to guide further therapy. Because both the background prostate gland and tumor are fibrotic and have low signal intensity after radiotherapy, recurrent tumor is difficult to identify on T2-weighted imaging alone. The addition of further multiparametric MRI sequences will increase the detection rate of recurrent cancers [38-40]. One study found that combined T2-weighted imaging and diffusion-weighted MRI (DWI) had 93.8% sensitivity and 75% specificity for identifying recurrent prostate tumors larger than 0.4 cm<sup>2</sup> and would be a useful investigation in the workup for salvage procedures [38].

MRI can also be performed to assess response to ablative therapies, including HIFU, vascular-targeted photodynamic therapy, and cryoablation. MRI findings of successful treatment over time include necrosis, fibrosis, low T2 signal intensity, loss of anatomic definition, and reduced prostate volume [31].

## **Prostate MRI Technique**

Prostate MRI is performed using either 1.5-T or 3-T magnetic field strengths, typically with the combined use of endorectal and pelvic phased-array coils to maximize the signal-to-noise ratio. A bowel relaxant will also optimize the study by reducing artifact from bowel motion. Multiparametric MRI is the current reference standard because no single MRI sequence is entirely sufficient to characterize prostate cancer. The optimal combination and interpretation

approach of anatomic and functional MR sequences still needs to be established. However, the more functional sequences that are combined, the better the accuracy appears to be. Recently, Turkbey et al. [41] reported that a four-sequence multiparametric MRI (T2-weighted imaging, DWI, DCE-MRI, and MRS) had sensitivity of 86% and specificity of nearly 100% in a prospective trial of 45 patients. A number of studies that evaluated the use of a four-sequence multiparametric MRI approach in the diagnosis of localized prostate cancer reported sensitivity, specificity, accuracy, PPV, and NPV for the detection of prostate cancer of 69-95%, 63-96%, 68-92%, 75-86%, and 80-95%, respectively [30, 42].

The European Society of Urogenital Radiology (ESUR) and the European Association of Urology (EAU) have recently published clinical guidelines for multiparametric MRI of prostate outlining both minimal and optimal requirements to allow a more consistent and standardized approach [1, 20]. Both articles recommend including T1-weighted, T2weighted, DWI, and DCE-MRI sequences, but the addition of MRS is optional [1, 20]. The ESUR guidelines also outline the prostate imaging reporting and data system (PI-RADS) structured reporting system, which includes a 5-point scale for reporting the likelihood of clinically significant prostate cancer and probability of extraprostatic disease being present [1]. The value of PI-RADS as a diagnostic tool and as a predictor of patient outcomes remains to be determined.

#### T2-Weighted Imaging

T2-weighted imaging is used to depict zonal anatomy and to detect and stage cancer [17]. T2-weighted imaging depicts the zonal anatomy with exquisite detail because of its high spatial resolution, superior contrast resolution, multiplanar capability, and large FOV [17] (Fig. 5).

The prostate gland can be divided into the peripheral and central glands (Fig. 5). The peripheral gland comprises the peripheral zone, which comprises the most glandular tissue, and 70% of prostate cancers arise here [18]. On T2-weighted imaging, because the normal peripheral zone has high signal intensity and tumor has low signal intensity, a tumor is usually easily identified (Fig. 6). However, signal intensity changes within the prostate should be interpreted with caution because other pathologic processes, including infection, postbiopsy hemorrhage, fibrosis, inflammation, chronic prostatitis, BPH, effects of hormone or radiation treatment, scars, calcifications, smooth muscle hyperplasia, and fibromuscular hyperplasia, can mimic cancer because these processes all appear as low signal intensity within the peripheral zone on T2-weighted imaging [1, 5, 18, 43] (Fig. 6). It is recommended to wait 8-12 weeks after biopsy to perform MRI to avoid misinterpretation, although methemoglobin within hemorrhage is seen as high signal intensity on T1-weighted imaging, which helps differentiate it from tumor (Fig. 6B).

Thirty percent of prostate tumors occur in the central gland, which comprises the central zone and the transition zone. It is not possible to determine on MRI whether a cen-



Fig. 9—77-year-old man with biopsy-proven Gleason 6 (3 + 3) prostate cancer, prostate-specific antigen value of 16.5 ng/mL, who underwent prostate MRI before referral to radiotherapy.

A–C, Axial T2-weighted (A), apparent diffusion coefficient (ADC) map (B), and diffusion-weighted (C) images with endorectal coil show central gland is heterogeneous. There is "smudgy" low signal intensity in right peripheral zone measuring 2.7 × 1.6 cm (*arrow*, A) that corresponds to low signal intensity on ADC map (*solid arrow*, B) and high signal intensity on diffusion-weighted image (*solid arrow*, C), indicating restricted diffusion consistent with tumor. Capsule is intact, consistent with stage T2 disease. However, on ADC map and diffusion-weighted image, there is another focus of tumor that is not visible on T2-weighted image in left anterior peripheral zone (*dashed arrow*, B and C). Downloaded from www.ajronline.org by Queen's Univ on 03/06/14 from IP address 130.15.241.167. Copyright ARRS. For personal use only; all rights reserved

tral gland tumor arises in the central zone or transition zone. MRI is limited in the detection of tumor in the central gland, which is heterogeneously low in signal intensity on T2-weighted imaging because of BPH and thus masks tumor, which is also low in signal intensity [18, 19] (Fig. 7). Although only approximately 2.5% of prostate cancers occur in the central zone, these cancers tend to be more aggressive and are more likely to cause SVI [44]. The NVB is best visualized posterior to the base. It penetrates the posterolateral capsule of the gland and is a preferential path for tumor spread (Fig. 2C).

Because of the number of entities outlined that can cause signal abnormality and a false-positive finding, T2-weighted imaging has high sensitivity but low specificity (75– 94% and 37–53%, respectively) [43, 45]. In addition, some cancers show minimally reduced T2 signal intensity, making them nearly isointense on T2-weighted imaging [19]. Increased accuracy and detection of primary and recurrent prostate cancer by T2-weighted imaging can be achieved if combined with other multiparametric MRI sequences [1, 20, 40] (Figs. 1, 7, 8, and 9).

## Dynamic Contrast-Enhanced MRI

Contrast enhancement in cancerous tissue is greater than in normal tissue because of tumor angiogenesis and increased number and permeability of vessels. DCE-MRI is a method to detect and quantify tumor angiogenesis and provides direct depiction of tumor vascularity (Figs. 8 and 10). Data reflecting tissue perfusion, microvessel permeability, and extracellular leakage space can be obtained. A rapid set of gradient-echo T1-weighted images are acquired immediately before, during, and after the administration of gadolinium contrast agent. Gadolinium shortens the T1 relaxation time of water, producing high signal intensity on T1-weighted imaging (Figs. 8 and 10). Various perfusion parameters can be used to differentiate cancerous from benign tissue, including onset time to enhancement, time to peak enhancement, peak enhancement, relative peak enhancement, and washout time. An alternative to parameter calculation is to detect cancer as areas of enhancement on early contrast-enhanced images (within the first 30-60 seconds after contrast material injection).

DCE-MRI is a fast sequence that scans the entire prostate gland in a few seconds and may obviate the use of an endorectal coil. There are varying reported ranges of sensitivity and specificity of DCE-MRI in the literature of 46-96% and 74-96%, respectively, but there is accepted improvement in the addition of DCE-MRI to T2-weighted imaging compared with T2-weighted imaging alone [19, 46]. Studies have reported sensitivity and specificity of combined T2-weighted imaging and DCE-MRI of 70-96% and 88-97%, respectively, compared with T2-weighted imaging alone, which has range of reported sensitivity and specificity of 75-94% and 37-53% [43, 45]. Because T2-weighted imaging already has high sensitivity in the detection of lesions, the addition of DCE-MRI is mainly to improve specificity. The role of DCE-MRI is not to detect further lesions that are not seen on T2-weighted imaging but to be used as an adjunct to T2-weighted imaging to determine whether a lesion seen on T2-weighted imaging is cancerous or benign [43]. Therefore, tumors can be detected with higher accuracy.

DCE-MRI also provides information regarding prognosis and response to treatment. It is a useful prognostic marker and indicator of tumor aggressiveness because the degree of angiogenesis correlates with pathologic staging of prostate cancer [43]. Tumor microvascularity may also be correlated with the risk of recurrence and simple survival outcome measurements. DCE-MRI may have a role as a biomarker in assessing the effect of antiangiogenic treatment on tumor vascularity. DCE-MRI can also be useful for determining the effectiveness of hormone deprivation therapy by showing a reduction of tumor permeability and changes of washout pattern [18].

Noise due to misregistration from motion artifact because of peristalsis can be a major source of error. It can be difficult to identify central gland tumors with DCE-MRI alone because normal central gland tissue, particularly in patients with hypervascular BPH, is more susceptible to enhancement with gadolinium, resulting in insufficient delineation of tumor against the background enhancing normal prostate tissue [18, 46]. Therefore DCE-MRI is mostly of benefit for evaluation of the peripheral zone. Inflammatory lesions, such as prostatitis, also enhance early and may be mistaken for tumor [43, 46]. Like-



Fig. 10-68-year-old man with prostate-specific antigen value of 117 ng/mL and biopsy-proven Gleason 8 tumor.

**A**, T2-weighted image with endorectal coil shows large area of low signal intensity in right peripheral zone, extending across midline to left medial peripheral zone and extending into transitional zone (*solid white arrows*). Capsular bulging is seen on right, consistent with extracapsular extension and stage T3a disease (*dashed white arrow*). Neurovascular bundle was intact (*black arrow*).

B, ADC map shows clear area of corresponding low signal intensity with restricted diffusion (arrow).

**C**, Dynamic gadolinium-enhanced MR image shows area of strong early enhancement within center of lesion, corresponding with area of restricted diffusion and confirming that this represents focus of tumor (*arrow*).

wise, repair tissue after biopsy can show angiogenesis, thus masking or mimicking tumor angiogenesis [43]. It is therefore important to interpret DCE-MRI findings in conjunction with other sequences to avoid misinterpretation. Limitations from postbiopsy hemorrhage, which manifests as high signal intensity on T1-weighted imaging (Fig. 6B) can be overcome with the help of subtraction.

# Diffusion-Weighted MRI

DWI is based on differences in diffusion of water molecules, mainly attributable to differences in cellular density. Cancerous tissue has more restricted diffusion than does normal tissue because the high cell densities inhibit the movement of water molecules. Therefore, there is restriction of diffusion and reduction of ADC values in cancer tissue. This results in cancer tissue showing higher signal intensity on DWI with a high b value, which represents the molecular diffusion of water almost exclusively, and reduced signal intensity on ADC maps (Figs. 1, 7, 8, 9, and 10).

There is a high degree of differentiation between normal and cancerous prostate tissue on DWI, enabling tumor detection [18, 47]. DWI can aid in the prediction and assessment of response to therapy [47]. As previously outlined, it is difficult to detect central gland tumors on T2-weighted imaging and DCE-MRI. DWI is superior for delineating central gland cancer by yielding sufficient contrast to distinguish cancer from normal tissue [20, 46] (Figs. 1 and 7). Studies have shown improved sensitivity and specificity of T2-weighted imaging combined with DWI (0.77 and 0.81) over T2weighted imaging alone (0.58 and 0.77) [30, 48]. In addition, DWI requires only a short acquisition time and does not require an endorectal coil. Limitations of DWI include poor spatial resolution and potential risk of image distortion related to susceptibility [18].

The ADC values of prostate cancer in both the peripheral zone and transition zone are significantly lower than those of healthy or benign tissue because of increased cellular density [46]. Therefore, ADC measurement is useful for distinguishing between malignant and benign lesions [46]. ADC values also correlate with the Gleason score of prostate cancers, therefore providing prognostic information [1, 5, 19, 20].

# MR Spectroscopy

MRS separates the total MRI signal into its different molecular components by using the

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changes in signal frequency induced by the molecular environment. Therefore, it can detect and quantify metabolites in tissues and tumors. MRS imaging of the prostate evaluates the metabolites choline, creatine, and citrate. Normal prostate tissue contains a high level of citrate and a low level of choline. In prostate cancer, the citrate level decreases and the level of choline is elevated. Therefore cancer is characterized by increased choline and creatine–tocitrate and choline-to-citrate ratios [18].

There is an association between primary tumor volume and local extent of disease, progression, and survival [17, 18, 49]. TRUS biopsy and T2-weighted imaging alone are disappointing in tumor volume estimation. MRS provides more accurate tumor volume estimation, which strongly correlates with ECE. The relative tumor volume is determined on MRS by counting the voxels containing abnormal spectra. Combined with T2-weighted imaging, MRS improves cancer detection, localization, and volume measurement in the peripheral zone and improves accuracy in determining ECE [17, 18, 49]. MRS is also more accurate for cancers in the apical portion of the prostate than TRUS biopsy [27].

The major indicator of tumor aggressiveness is the Gleason grade, which can be underestimated by TRUS biopsy [17]. MRS is potentially useful as a prognostic indicator to assess cancer aggressiveness because an increasing ratio of choline and creatine to citrate is associated with an increasing Gleason score [17, 18]. MRS also aids in monitoring treatment because a decreasing ratio is indicative of response to treatment [18]. One study found the combination of MRS and T2-weighted imaging increased sensitivity and specificity to 91% and 95% compared with T2-weighted imaging alone [18].

There are limitations of MRS. It requires a long acquisition time and does not show prostatic or periprostatic anatomy. After prostate biopsy, hemorrhage may lead to misinterpretation of metabolite ratios. Therefore, it is advised to ideally wait for 8-12 weeks after biopsy to perform MRI [18, 50]. Acute prostatitis and stromal BPH can mimic tumors, and small-volume cancers less than 0.5 cm<sup>2</sup> can be missed because a tumor can be masked by the signal from the adjacent surrounding normal tissue [50]. Surrounding lipid can contaminate MR signal, but saturation bands applied around the prostate can limit this issue. Voxels may contain nondiagnostic levels of metabolites or artifacts that obscure the metabolite frequency range, and there can be variability in results dependent on postprocessing or shimming, all of which can interfere with image interpretation [16, 18].

### Conclusion

Multiparametric MRI offers the single most accurate imaging assessment of local prostate cancer and regional metastatic spread and aids in many aspects of prostate cancer management, including initial detection, biopsy guidance, treatment planning, and follow-up and has further potential emerging roles to replace TRUS biopsy for patients undergoing active surveillance and to initially evaluate patients with suspected prostate cancer before TRUS biopsy. Multiparametric MRI is the current standard because no single MRI sequence is entirely sufficient to characterize prostate cancer. However, the optimal combination and interpretation approach of anatomic and functional MRI sequences still needs to be established. Radiologists need to understand the advantages, limitations, and potential pitfalls of the different sequences to provide optimal assessment of prostate cancer.

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