With an estimated annual incidence of 230,000 cases in 2004, prostate cancer is the most common noncutaneous cancer in men in the United States [1]. Despite an impressive scope of research efforts, difficult challenges persist in various aspects of prostate cancer care, including diagnosis, prognostication, and treatment.

First and foremost is a pressing need to appropriately tailor therapeutic interventions to the spatial extent and biologic aggressiveness of disease for individual patients. Individualized therapy for localized disease could significantly reduce the treatment-related morbidity incurred by this population of patients but requires the development of better measures to delineate and characterize disease. At present, these measures are limited to nonspecific prostate-specific antigen (PSA) serum levels [2], histopathologic estimates of tumor burden, and Gleason grading, which is subject to random biopsy sampling error [3–5] and insensitive digital rectal examinations that are poorly reproducible among observers [6].

The authors believe that in the near future, imaging will bridge the gap between characterization of disease and individualized therapy. An ability to visualize the complete extent and biologic profile of prostate cancer with regard to prostatic anatomy may counter biopsy sampling error, enable appropriate patient selection for local therapy, guide local therapy to the disease rather than to the entire prostate gland, and provide a noninvasive means of monitoring progression or response to therapy.

Here, the authors review the studies that are currently investigating the potential role of MR imaging in guiding needle-based prostate interventions. This review omits studies that use MR images for guidance of external beam radiotherapy [7] and, instead, focuses primarily on interventional procedures that are conducted in the MR imaging scanner room. The article starts with a brief overview of the role of diagnostic MR imaging in prostate cancer.

**MR imaging for prostate cancer**

It is unfortunate that there is no single imaging method that embodies all of the optimal characteristics for the integration of diagnostic and interventional procedures for prostate cancer. CT permits accurate spatial visualization of interventional devices (Fig. 1A) but does not provide real-time feedback or adequate soft tissue delineation. Transrectal ultrasound (TRUS) is the current “gold standard” for guiding prostate interventions due to its ease of use and real-time image feedback. Soft tissue delineation is better with TRUS than with CT, but most tumors are not visible under ultrasound, and biologic profiling is currently limited [8]. In addition, accurate visualization of interventional needles remains challenging (see Fig. 1B). The interventional
needles and the prostate anatomy are clearly visible in MR images (see Fig. 1C). From this perspective, MR imaging is well suited for guidance of interventional procedures. The principal limitations to its routine use include a lack of real-time feedback and a complex and technically challenging environment.

A number of anatomic structures can be clearly delineated on MR imaging, including the distal prostatic urethra (up to the point of insertion in the central gland), the central zone, the peripheral zone, the prostatic capsule, the levator ani, and the rectal mucosa [9]. On contrast-enhanced MR images, the neurovascular bundles can also be identified (Fig. 2) [10]. Diagnostic MR imaging, however, has the potential to provide more than high image resolution of the prostate anatomy. Endorectal coil MR imaging of the prostate gland has demonstrated value for staging and prognostication in patients with localized disease [11–16]. When T2-weighted anatomic images, which are sensitive but not specific for malignancy, are combined with biologic imaging techniques such as MR spectroscopic imaging [17–20] and dynamic contrast-enhanced (DCE) MR imaging [8], MR imaging may be able to accurately identify predominant subsites of tumor burden.

DCE MR imaging is a promising tool for visualizing the vascular physiology of solid tumors. With the advent of modern multislice imaging techniques and data analysis tools, imaging the entire prostate gland with high spatial and temporal resolution using DCE MR imaging is
feasible. In a recent study [8], the sensitivity and specificity of DCE MR imaging for localizing malignancy in the peripheral zone were estimated to be 87% and 74%, respectively, based on a subjective coregistration to TRUS-guided biopsies. This level of accuracy is not maintained in the central gland (sensitivity 96%, specificity 46%) because coexisting benign prostatic hyperplasia is also characterized by high vascularity.

Kurhanewicz and colleagues [17] proposed a three-dimensional MR spectroscopic imaging technique for the detection of prostate cancer. This promising method compares the ratios of choline and creatine to citrate peak levels as a marker of malignancy in the peripheral zone. One of the main limitations of this MR spectroscopic imaging technique is the relatively long data acquisition time and the low signal-to-noise ratio inherent to spectroscopy. The use of large voxels in the imaging protocol partially solves this problem but introduces partial volume effects whereby small lesions may become invisible.

In addition to the techniques of T2-weighted MR imaging, DCE MR imaging, and MR spectroscopic imaging, there are a number of complementary techniques under investigation to improve the diagnostic accuracy of MR imaging. For example, tissue hypoxia, a known biomarker associated with prostate cancer, can be interrogated using blood oxygen level–dependent imaging techniques [21,22]. Diffusion maps of the prostate gland can also be generated with MR imaging, thus providing noninvasive information related to interstitial fluid pressure changes in normal and malignant prostate tissue [23,24].

**Needle core biopsy**

Currently, prostate biopsy is conducted under TRUS guidance. Although a positive biopsy result is a clear indication of cancer, a negative biopsy result is often indefinite and problematic because it is known that the sextant biopsy procedure has a relatively low sensitivity and high sampling error [25]. To address this problem, an 8- to 10-biopsy regimen, depending on prostate size, has been proposed [26], with sensitivity increasing up to 80%. Repeat sextant biopsy is another approach, which further increases the sensitivity of this approach [27]. Image-guided biopsy may be the best approach to this problem, but ultrasound can be blind to 40% of lesions, which are isoechoic [28].

MR-guided biopsy may have an immediate impact by improving the sensitivity of needle core biopsies to detect prostate cancer, specifically for those 20% of patients who have false-negative biopsy results from sampling error when performed under TRUS guidance [29]. By combining tissue biopsy with MR imaging (ie, to directly biopsy tissue regions with a suspicious MR imaging appearance), the high sensitivity of MR imaging [30] may be obtained while gaining the specificity of tissue biopsy.

In addition, MR imaging guidance of needle biopsies is a critical step in the histopathologic validation of emerging MR imaging techniques for prostate cancer delineation and characterization. These new imaging techniques must be validated against gold standard measures to establish their accuracy, and in this case, the gold
standard is prostate biopsy and histopathology. Notable intraprostatic [31] and intratumoral [32] biologic heterogeneity mandates millimeter colocalization accuracy between tissue samples and their corresponding image pixels. When prostate MR imaging and tissue acquisition procedures are performed in different settings and at different times, however, spatial coregistration is fraught with error.

Stereotactic needle placement under MR imaging guidance enables two critical steps in the coregistration of tissue and MR imaging data. First, it directly guides biopsies to sites of suspected tumor on MR imaging, and second, it permits volumetric verification and documentation of the actual biopsy location with regard to MR imaging data.

Investigators at Harvard University were the first to report MR-guided prostate biopsies, which were performed in patients with suspicion of prostate cancer who were not candidates for the standard TRUS-guided technique because of a previous proctocolectomy [33,34]. Using an open-configuration 0.5-T MR imaging scanner and a pelvic coil, transperineal needle core biopsies were performed with patients in the dorsal lithotomy position. Sites deemed suspicious for cancer on previously acquired diagnostic MR imaging were subjectively correlated to corresponding sites on the interventional MR imaging images and specifically targeted through a stereotactically registered perineal template (Fig. 3). A nonconventional transgluteal approach has also been reported using an open low-field MR

Fig. 3. Images obtained during MR-guided diagnosis and treatment of prostate cancer in a 62-year-old man. (A) Coronal view of the prostate gland and bladder. The tip of the biopsy needle has been placed through the perineum and into the lesion, located in the right midportion of the gland. The template was used for accurate placement of the needle. (B) Axial view of the prostate gland with the tip of the biopsy needle in the right midportion of the gland. (C) Real-time intraoperative catheter placement in the sagittal plane during MR-guided prostate brachytherapy. The black spots are previously deposited radioactive sources posterior to the needle. (From D’Amico AV, Cormack RA, Tempany CM. MRI-guided diagnosis and treatment of prostate cancer. N Engl J Med 2001;344(10):776; with permission.)
imaging scanner in patients with uncertain or suspicious prostate lesions on diagnostic MR imaging [35]. Diagnostic images were similarly subjectively correlated to interventional MR images to define biopsy target sites. Using T1-weighted sequences, 25 biopsy procedures were performed successfully with MR guidance in all cases without any side effects or complications. Alternatively, diagnostic MR images have been rigidly coregistered to interventional ultrasound images for guidance [36].

To circumvent the need for and the error associated with deformable or rigid registration of previously acquired diagnostic MR images, transperineal biopsies have been performed under direct MR imaging guidance in a cylindric 1.5-T scanner [37]. To address the challenge of accessing the perineum under the geometric constraint of a 60-cm diameter bore, patients were positioned in the left lateral decubitus position (Fig. 4). Biopsies were again performed through a stereotactically registered perineal template that in this case was affixed perpendicularly to a rigid endorectal coil, thereby increasing signal-to-noise ratio and image quality. The mean biopsy-needle targeting accuracy of the stereotactic system was 2.1 mm.

Finally, two competing devices for transrectal prostate biopsy in a cylindric 1.5-T scanner have recently been developed [38,39] and clinically tested in patients with prostate cancer [39,40]. The main advantage of the transrectal approach is a shorter needle path length, which translates to less tissue trauma and patient discomfort. For access, patients are positioned prone on the MR imaging table.

The first MR-guided transrectal biopsy system was developed at Charité, Humboldt-Universität zu Berlin in cooperation with MRI Devices/Daum (Schwerin, Germany). This device is made of polyoxymethylene and consists of a base plate, an adjustable arm, and a needle guide filled with contrast material gel that can be visualized on MR imaging. After the patient is positioned, the needle guide is inserted into the rectum and connected to the arm of the biopsy device (Fig. 5). The arm enables the needle guide to be rotated, translated...
forward and backward, and adjusted in height. In addition, the insertion angle can be changed by rotating the needle guide about a point inside the rectum.

In the initial study, biopsies were obtained from suspicious areas of the prostate (Fig. 6) in 12 patients by means of an MR imaging–compatible automatic \( n = 5 \) or semiautomatic \( n = 7 \) 16-gauge core needle biopsy device (Double-Shoot Biopsy Gun or Semi-Automatic Biopsy Gun; MRI Devices/Daum). The authors reported that of the 16 biopsy specimens from areas that were highly suspicious for prostate cancer at prebiopsy MR imaging, 8 were positive and 8 were negative. Of the 24 biopsy specimens from moderately suspicious areas, 4 showed prostate cancer and 20 showed no prostate cancer. Of the 57 specimens from nonsuspicious areas, 2 showed prostate cancer and 55 did not.

It is important to note that the investigators did not use DCE MR imaging or MR spectroscopic imaging to identify the suspected tumor.

Fig. 6. (A) Axial T2-weighted diagnostic MR image of the prostate showing suspicious lesions (arrows). (B) Sagittal interventional image of the endorectal biopsy procedure. The arrow shows the location of the biopsy device. (From Beyersdorff D, Winkel A, Hamm B, et al. MR imaging-guided prostate biopsy with a closed MR unit at 1.5 T: initial results. Radiology 2005;234(2):579; with permission.)
locations; however, they demonstrated a very strong correlation between MR imaging findings and biopsy results. These results are very encouraging for the future widespread use of MR-guided biopsy procedures.

The other transrectal biopsy device, the “access to prostate tissue under MR imaging guidance” (APT MR imaging) system (Fig. 7) [38,40], consists of a 23-mm diameter hollow endorectal sheath, placed at the beginning of the procedure, that remains immobile throughout the intervention. The sheath includes an integrated 20-mm diameter single-turn imaging coil surrounding an anterior window that allows for needle access to the prostate. An 18-mm diameter cylindric needle guide fits inside the stationary rectal sheath and contains three MR tracking microcoils (allowing for device registration). Needle channels at 20° and 30° of angulation permit transrectal needle access to the prostate gland. The cylindric needle guide is mounted on a positioning stage containing the mechanism that converts the rotation of two flexible control rods—each extending to the edge of the scanner bore—into the rotation and translation of the needle guide. Finally, the positioning stage is attached to an immobilization arm mounted on a linear rail.

Four MR-guided prostate biopsy procedures have been reported to date with the APT MR imaging system for the histomolecular validation of DCE MR imaging [41]. Biopsy locations were selected throughout the peripheral zone of the prostate using T2-weighted fast spin-echo images and DCE MR images. Subsequently, after inserting the biopsy needle but before collecting the tissue core biopsy, T1-weighted fast spin-echo images were acquired to confirm biopsy needle placement accuracy. Fifteen tissue biopsies were collected; the mean biopsy needle placement accuracy was 1.8 mm (maximum error, 4.0 mm) [41]. All biopsy cores were suitable for histologic evaluation and for genomic and proteomic microarray profiling. These data demonstrate the feasibility and value of stereotactic biopsies under MR imaging guidance and verification to provide a platform for rigorous histopathologic and biologic validation of MR imaging techniques (Fig. 8).

The APT MR imaging system has also been adapted to a 3-T MR imaging scanner and tested in six patients to date [41]. Because higher field strength translates to higher MR signal, the authors expect an improvement in the resolution of diagnostic images.

In summary, five different techniques of MR-guided prostate biopsy have been reported in the clinical literature. Given the need and rationale for needle guidance to be based on diagnostic-quality MR images, the authors favor a stereotactic approach without real-time image guidance within a diagnostic scanner. One of the limitations to a broader application of the latter cylindric scanner techniques relates to the instability and discomfort associated with the left lateral decubitus and prone positions. Although spatially accurate and robust, stereotactic guidance systems mandate an immobile prostate gland. A number of studies have shown that prostate motion is greatly reduced when patients are positioned supine, stemming from greater patient comfort and reduced respiratory motion [42–44]. Supine immobilization and perineal access in the cylindric

Fig. 7. The APT MR imaging system developed at the Johns Hopkins University. A stationary sheet minimizes the motion of the prostate during rotation and translation of the needle guide. The position of the needle guide is determined by active tracking coils.
scanner is only be possible with custom-designed interventional MR imaging tables, which is the subject of ongoing work. Finally, larger studies are required to confirm the clinical value and role of MR-guided biopsy in patients with prostate cancer.

**Brachytherapy**

**Permanent implant**

For patients with localized prostate cancer at low risk for extraprostatic extension, permanent-seed brachytherapy is an accepted and effective
minimally invasive treatment strategy. Radioactive seeds are conventionally placed and left throughout the prostate gland under ultrasound guidance using a transperineal template. One important performance measure of the procedure is the proportion of the prostate gland receiving the minimum desired dose. Treatment-related toxicity is associated with radiation dose delivered to the surrounding normal organs, including the urethra, bladder wall, rectal wall, penile bulb, and neurovascular bundles.

In an effort to avoid toxicity with permanent-seed brachytherapy, investigators at Harvard University translated the conventional transperineal ultrasound technique to an open MR imaging scanner architecture [45]. Even at low field strength, the peripheral zone of the prostate gland (where most cancers are known to reside) could be distinguished from the central gland, thus permitting partial prostatic irradiation whereby permanent seeds were placed in the peripheral zone only, thereby reducing the radiation dose to the urethra and bladder wall (Fig. 9). Five-year results confirmed the equivalence of this approach to radical prostatectomy in biochemical disease-free survival [46].

Ultrasound or low-field interventional MR images, however, cannot accurately identify prostatic subsites of tumor burden that may benefit from targeted radiation dose escalation. For this reason, a number of investigators have attempted to coregister previously acquired diagnostic MR images to interventional images using techniques ranging from subjective interpretation to finite element–based deformable registration [47–52]. Permanent-seed brachytherapy performed directly in a high-field diagnostic scanner would circumvent this step and potentially reduce the error introduced by coregistration. This methodology is currently being investigated in the Netherlands, where the technical feasibility of a novel single-needle technique has been proposed [53].

**Temporary implant**

Patients with intermediate- or high-risk prostate cancer have a higher intraprostatic burden of disease. A number of prospective randomized studies have confirmed that such patients may benefit from escalation of radiation dose [54–56]. By virtue of the “inverse square” law, brachytherapy “radiation boosts” result in a much steeper dose gradient and, hence, can achieve better sparing of adjacent normal structures compared with external beam radiotherapy. Such a highly desirable quality can paradoxically lead to important errors; therefore, the technique demands a high level of accuracy and precision and mandates optimal image guidance.

High dose rate temporary implants offer several advantages over permanent-seed implants. Dosimetric calculations are performed immediately following the catheter placement procedure, which permits the treatment plan to be based on the actual geometry of the implant relative to the anatomy. The treatment is immediately delivered with an afterloading technique, and problems with organ motion, setup error, and postimplant edema are circumvented. A single high-intensity $^{192}$Ir source can be placed at any position for any length of time within each needle. These two variables (dwell position and dwell time) can be optimized using computer programs designed to achieve dose distribution that conforms to the target volume, while limiting dose to normal structures at risk of radiation injury.

Investigators at the University of California–San Francisco have manually aligned previous diagnostic MR imaging/MR spectroscopic imaging datasets to “treatment planning” CT or MR images acquired after brachytherapy catheters were inserted into the prostate gland under ultrasound guidance [57]. Based on the diagnostic images, subprostatic sites suspicious for tumor burden that were specifically targeted for further dose escalation were defined. It was found that the dose could be safely escalated to these sites without overdosing the urethra or the rectum.

To circumvent the error associated with coregistration of previously acquired diagnostic images, a technique for transperineal placement of brachytherapy catheters in a 1.5-T scanner was developed [37]. This technique is identical to the biopsy technique described previously, whereby patients are placed under general anesthesia in the left lateral decubitus position on the MR imaging table. This approach permits diagnostic images to be acquired first, followed immediately by the placement of brachytherapy catheters throughout the prostate gland. After the catheters are in place, a final diagnostic-quality T2-weighted image set can be acquired and directly used to plan and optimize radiation delivery [58]. The authors have used this approach to demonstrate a unique ability to limit radiation dose to the neurovascular bundle—a structure critical to sexual function—which is immediately adjacent to the prostate gland and best visualized on MR imaging [10].
This procedure may also offer a therapeutic advantage for those patients who have extracapsular extension of disease visualized on MR images, whereby extracapsular disease may be included in the radiation target volume (Fig. 10).

**Thermal therapy**

The role of thermal therapies for patients with prostate cancer remains investigational at this time. Beyond anatomic guidance, there is a strong rationale for integrating thermal treatment, specifically heat therapy, in the MR imaging environment where temperature can be monitored noninvasively during the procedure [59]. This treatment has been demonstrated by Chen and colleagues [60], whereby patients who had locally recurrent prostate carcinoma received percutaneous interstitial microwave thermoablation continually guided with MR imaging. Four MR imaging–compatible microwave applicators were placed in the four quadrants of the prostate gland under ultrasound guidance. Patients were transferred to MR imaging, where treatment was delivered while phase images were obtained with a rapid gradient-echo technique to derive tissue temperature change on the basis of proton-resonance frequency shift (Fig. 11).

Prostate treatments with high-intensity focused ultrasound under MR imaging guidance with a transurethral [61,62] or transrectal [63] approach have been reported in the literature only at the preclinical stage to date.

**Summary**

MR imaging is currently the most effective diagnostic imaging tool for visualizing the anatomy and pathology of the prostate gland. Currently, the practicality and cost effectiveness of transrectal ultrasound dominates image guidance for needle-based prostate interventions. Challenges to the integration of diagnostic and interventional MR imaging have included the lack of real-time feedback, the complexity of the imaging technique, and limited access to the perineum within the geometric constraints of the MR imaging scanner.
Two basic strategies have been explored and clinically demonstrated in the literature: (1) coregistration of previously acquired diagnostic MR imaging to interventional TRUS or open scanner MR images, and (2) stereotactic needle interventions within conventional diagnostic scanners using careful patient positioning or the aid of simple manipulators.

Currently, researchers are developing techniques that render MR imaging the method of choice for the direct guidance of many procedures. This article focuses on needle-based interventions for prostate cancer, including biopsy, brachytherapy, and thermal therapy. With rapid progress in biologic imaging of the prostate gland, the authors believe that MR imaging guidance will play an increasing role in the diagnosis and treatment of prostate cancer.

References


