RadioGraphics

Imaging-guided Prostate Biopsy: Conventional and Emerging Techniques[1]

TEACHING POINTS
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Transrectal ultrasonography (US)–guided biopsy is the standard approach for histopathologic diagnosis of prostate cancer. However, this technique has multiple limitations owing to the operator's inability in most cases to directly visualize and target prostate lesions. Magnetic resonance (MR) imaging of the prostate overcomes many of these limitations by directly depicting areas of abnormality and allowing targeted biopsies. Accuracy in the detection of prostate cancer is improved by the combined use of standard T2-weighted MR imaging and advanced MR imaging techniques such as diffusion-weighted imaging, dynamic contrast-enhanced imaging, and MR spectroscopy. Suspicious-appearing regions of the prostate seen on MR images can be targeted at real-time transrectal US–guided biopsy to improve the diagnostic yield. MR imaging also can be performed for real-time guidance of transrectal prostate biopsy. Studies among patients who underwent at least one transrectal US–guided biopsy with a negative result before undergoing an MR imaging–guided biopsy showed improved detection rates with MR imaging–guided biopsy in comparison with the detection rates achieved with a repeat transrectal US–guided biopsy; however, MR imaging–guided biopsy is a more time-consuming procedure. A technique known as fused MR imaging– and transrectal US–guided biopsy, which relies on the coregistration of previously acquired MR images with real-time transrectal US images acquired during the procedure, shows promise but is limited by deformation of the prostate; this limitation is the subject of ongoing investigation. Another technique that is currently under investigation, MR imaging–guided prostate biopsy with robotic assistance, may one day help improve the accuracy of biopsy needle placement.

Abbreviation: PSA = prostate-specific antigen

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Introduction

Prostate cancer is the most common nonskin cancer and the second most common cause of cancer-related death among men in the United States; in 2010, prostate cancer accounted for 28% of new cancer diagnoses and 11% of cancer-related deaths in this population (1). Before the widespread use of serum measurements of prostate-specific antigen (PSA) for cancer screening, prostate cancers were often diagnosed at an advanced, incurable stage. Now, an estimated 92% of new cases are clinically localized at diagnosis, and the 5-year relative survival rate approaches 100% (1).

Prostate cancer screening consists of *(a)* the measurement of PSA concentration in serum and *(b)* a digital rectal examination. The various conflicting guidelines and recommendations regarding prostate cancer screening reflect the controversies surrounding the potential benefits and limitations of PSA testing (2). For example, the American Cancer Society recommends that PSA screening be offered to men aged 50 years or older who have an average prostate cancer risk and an estimated life expectancy of at least 10 years. Patients with an elevated PSA level or with abnormal findings at digital rectal examination are candidates for further diagnostic evaluation with a transrectal ultrasonography (US)–guided prostate biopsy. Some groups, including the American Urologic Association, have recommended that a baseline PSA serum measurement be obtained in men between the ages of 40 and 50 years, whereas others remain unconvinced of a need for, or benefit from, a routine PSA measurement (2).

Approximately 90% of patients with a diagnosis of localized prostate cancer that is categorized as "favorable risk" (low risk) on the basis of clinical stage, serum PSA level, and Gleason tumor grade elect to undergo definitive treatment, which generally consists of surgery, radiation therapy, or both; the other 10% choose to undergo active surveillance (3). *Active surveillance* refers to close monitoring by means of serial PSA measurements, digital rectal examinations, and periodic biopsies, with appropriate treatment provided to patients who show evidence of disease progression. The exact definition of *favorable risk* has varied among studies but generally includes some combination of a Gleason score of 6 or less, no evidence of Gleason pattern 4 or 5, a serum PSA concentration of 10 ng/mL or less, a PSA density of less than 0.2 ng/mL per cubic centimeter, a local tumor stage of T2 or lower, no more than three positive core-needle biopsy specimens, and no core in which cancer constitutes 50% or more of the specimen (4–6). Recently published data suggest that active surveillance in appropriately selected patients is a safe and durable strategy, with low risks for metastasis and death (1%–2%) at 10 years after diagnosis (4,5). A restaging biopsy of the prostate appears to improve the selection of patients for active surveillance by excluding up to 30% of those with a higher volume of involved prostate or more advanced disease demonstrated by a Gleason pattern of 4 or 5, more than three positive core samples, or a single core sample with cancer involving 50% or more of the specimen (6). Accurate disease characterization at diagnosis is paramount for the success of any active surveillance program. Moreover, promising new focal treatment modalities (eg, high-intensity focused ultrasound ablation, cryotherapy, and laser ablation) require accurate detection, localization, and sampling of regions of aggressive prostate cancer.

At the crossroads of controversies about PSA screening and treatment methods lies the challenge of accurately detecting, localizing, and characterizing prostate cancer. The best predictor of tumor aggressiveness is the Gleason score, which can be obtained only with histopathologic analysis of biopsy samples (7). Thus, prostate biopsy, usually performed with a core needle inserted transrectally with real-time US guidance, remains an essential component of the diagnostic work-up. However, over the past decade, magnetic resonance (MR) imaging has become more useful for the work-up and follow-up of prostate cancer, with the addition of new techniques (eg, diffusion-weighted MR imaging, dynamic contrast-enhanced MR imaging, and MR spectroscopy) and technologic advances (eg, improvement in coil design and 3-T imaging systems). Although preliminary study data suggest that MR imaging can be used to assess the biologic aggressiveness of a tumor (8–10), current MR-based methods are insufficiently accurate to replace biopsy and histologic analysis for this purpose. A more reasonable near-term objective for MR imaging may be improved tumor visualization that allows targeted imaging-guided biopsies and interventions.

Teaching Point

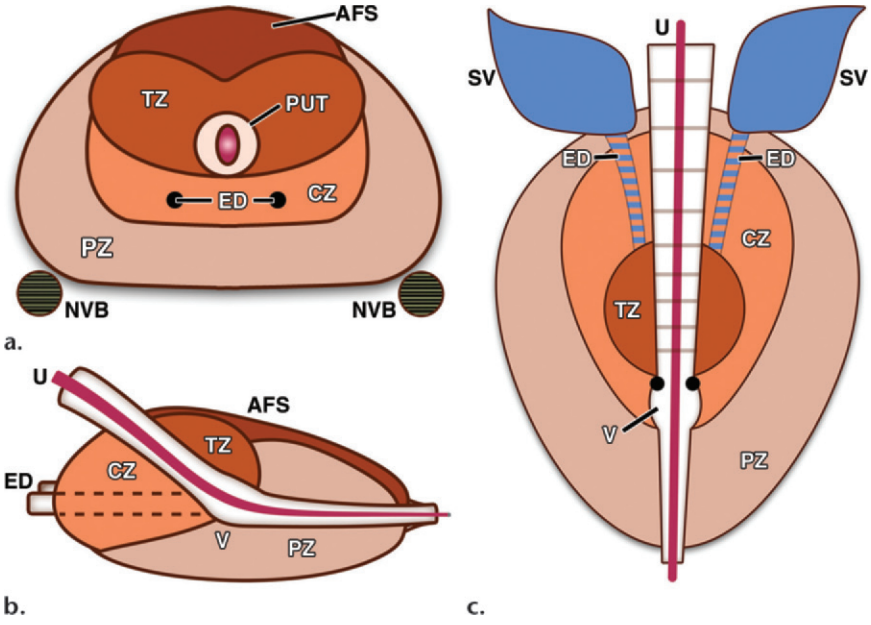


Figure 1. Diagrams show the zonal anatomy of the prostate in the axial **(a)**, sagittal **(b)**, and coronal **(c)** planes. *AFS* = anterior fibromuscular stroma, *CZ* = central zone, *ED* = ejaculatory ducts, *NVB* = neurovascular bundle, *PUT* = periurethral tissue, *PZ* = peripheral zone, *SV* = seminal vesicle, *TZ* = transition zone, *U* = urethra, *V* = verumontanum.

In this article, the current paradigm for the diagnosis of prostate cancer with transrectal US–guided biopsy is discussed, and its limitations are highlighted. New biopsy techniques that are based on tumor visualization with MR imaging—specifically, MR imaging–directed transrectal US biopsy, MR imaging–guided biopsy, fused MR imaging– and transrectal US–guided biopsy, and MR imaging–guided robotically assisted biopsy—are described in detail.

Prostate Anatomy

The prostate gland is divided into three major zones: peripheral, transition, and central zones. Figure 1 illustrates the relationship of these zones in the axial, sagittal, and coronal planes. The peripheral zone envelops the posterior, lateral, and apical portions of the prostate and shows high signal intensity on T2-weighted MR images. It constitutes 70% of the glandular tissue. The central zone is located superiorly, just posterior to the proximal urethra, and constitutes 20% of the glandular tissue. Just anterior and lateral to the proximal urethra is the transition zone, which constitutes 5% of the glandular tissue. The central zone and transition zone are referred to together as the "central gland" because they are inseparable on MR images. These zones have lower signal intensity than the peripheral zone on T2-weighted images and show less contrast enhancement. The prostate is also divided into three regions along its long axis: the base, middle, and apex.

The urethra and periurethral tissue are located anteriorly in the prostate gland and are best seen in the inferior region (ie, the apex) of the prostate, appearing as a ring of low signal intensity on T2-weighted images. The periurethral glandular tissue represents less than 1% of the prostate gland. The ejaculatory ducts, which arise where the seminal vesicles join the vasa deferentia (ducta deferentia), traverse the central zone and open into the urethra at the level of the verumontanum (seminal colliculus). In the most anterior part of the prostate, there is a region of nonglandular tissue known as the anterior fibromuscular stroma, which has low signal intensity on T2-weighted images. The prostate capsule, an outer band of fibromuscular tissue, appears as a thin layer of low-signal-intensity tissue surrounding the prostate on T2-weighted images. The capsule is most apparent posteriorly and posterolaterally because it contrasts with the higher, more uniform signal intensity of the peripheral zone of the gland.

Prostate cancer arises in glandular tissue, with approximately 70% of lesions occurring in the peripheral zone, 25% in the transition zone, and 5% in the central zone (11–13).

Current Diagnostic Paradigm and Its Limitations

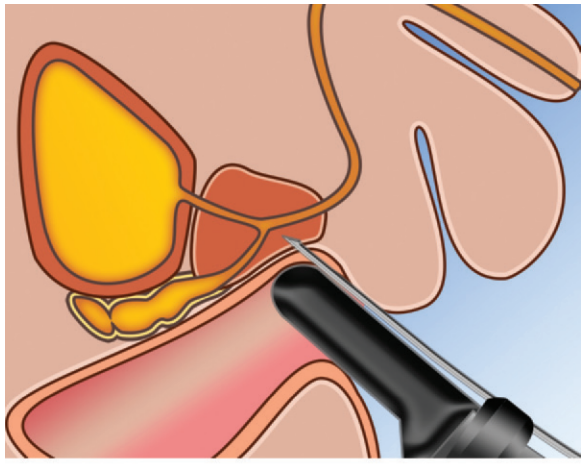
Transrectal US–guided Biopsy

The diagnosis of prostate cancer is dependent on histologic analysis of biopsy specimens. Transrectal US–guided biopsy is considered the standard approach for prostate biopsy and is most commonly offered as an outpatient procedure performed by urologists. During the procedure, which is relatively short (5–10 minutes), a US transducer is inserted into the patient's rectum, a US survey of the prostate is performed, and the prostate volume is estimated. The procedure is performed after a local anesthetic is injected via the rectum through the capsule or a regional block is administered around both neurovascular bundles. A core biopsy needle is deployed to obtain specimens from anatomically distinct areas of the prostate (from the left and right lobes and at the levels of the apex, middle, and base) (Fig 2).

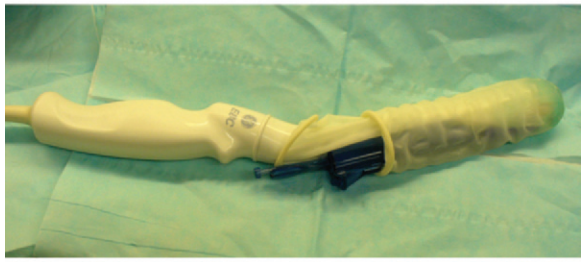
Unlike imaging-guided biopsy procedures performed in many other organs, transrectal US–guided prostate biopsy is not a targeted biopsy procedure, because most prostate tumors are not visualized on images or are indistinguishable from normal prostatic tissue and benign prostatic hyperplasia. Transrectal US is useful only to localize the prostate, not suspected lesions within it. However, areas of the prostate in which tumors are most frequently found can be sampled in a systematic fashion on the basis of zonal anatomy at transrectal US–guided biopsy. The classic prostate sampling technique was the sextant protocol described by Hodge et al, in which six samples were obtained, three in the left lobe and three in the right lobe, in equally spaced regions along a parasagittal line drawn halfway between the lateral border and the midline, from the base through the middle to the apex of the gland (Fig 3a) (14). In the 1990s, this technique was modified to improve the diagnostic yield. In the modified sextant technique, the needle is directed more laterally at the level of the middle prostate to allow sampling of the more peripheral zone, where the diagnostic yield is higher (Fig 3b) (15). Extended biopsies in which eight, 10, or 12 specimens are obtained have resulted in improved

Teaching Point

Figure 2. **(a)** Schematic of transrectal US–guided biopsy shows the transducer positioned within the rectum, against the prostate, and the needle with its tip in the prostate gland. **(b)** Photograph shows a US transducer with a needle guide mounted on its upper half in preparation for transrectal US–guided prostate biopsy.



a.

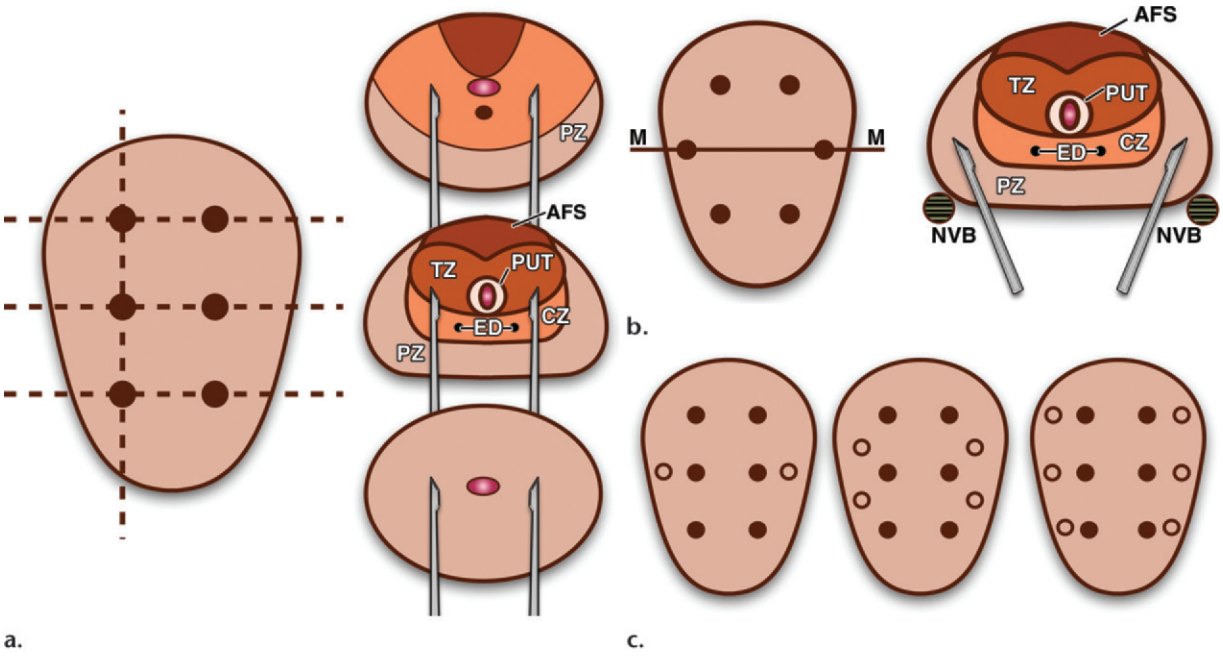


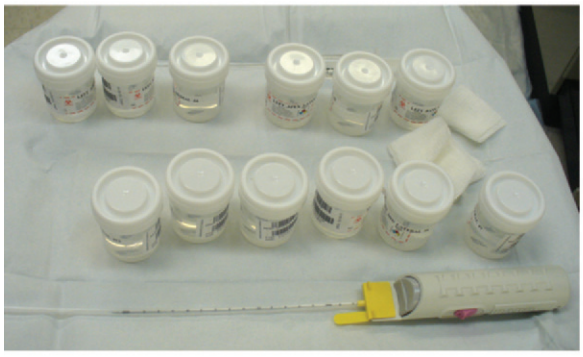
b.

detection of prostate cancers (Fig 3c) (15–17). Although some authors advocate sampling in the transition zone as well as the peripheral zone (16), others have concluded that transition zone sampling is of limited benefit (15,18,19). In our practice, at least 12 samples are obtained at all three levels in the peripheral zone. However, no standardized guidelines exist regarding which biopsy technique should be used (15).

Transrectal US–guided biopsy also plays a role in the detection of locally recurrent prostate cancers after radical prostatectomy and radiation therapy, although that role is not completely defined. In patients who have undergone a radical prostatectomy, transrectal US–guided biopsy of the prostatic fossa appears to be an accurate method for detecting cancer recurrence, with detection rates around 50%, albeit after repeat biopsies in many cases (20–22). The accuracy of

Figure 3. **(a)** Coronal (left) and axial (right) schematics show the positions of the needle and the locations that are sampled in the prostate with the standard sextant biopsy technique. **(b)** Coronal (left) and axial (right) schematics of the modified sextant biopsy technique show more lateral positions of the needle at the middle level *(M)* of the prostate with this technique than with the standard technique. **(c)** Coronal schematics show the additional prostate locations (open circles) that may be sampled in an extended systematic biopsy, for a total of eight, 10, or 12 specimens. Filled circles indicate the six locations of sampling in a standard sextant biopsy. **(d)** Photograph shows a spring-loaded 18-gauge biopsy needle and 12 specimen cups laid out in preparation for an extended systematic biopsy. *AFS* = anterior fibromuscular stroma, *CZ* = central zone, *ED* = ejaculatory ducts, *NVB* = neurovascular bundle, *PUT* = periurethral tissue, *PZ* = peripheral zone, *TZ* = transition zone.





biopsy for the detection of recurrence is highly correlated with serum PSA levels, being lower at lower PSA levels (20).

Minor complications of transrectal US–guided biopsy, such as limited hematuria and hemospermia, are frequent and can persist as long as 1 week after the biopsy (23). About 65%–90% of patients experience mild to marked discomfort during the biopsy, but pain due to the procedure is substantially reduced by local anesthesia (24). Reported infection rates are variable but low with the use of prophylactic antibiotics. Pooled data indicate that septicemia requiring hospitalization occurred in 4% of patients or fewer (24).

Because of the inherent limitations of transrectal US for visualizing and targeting malignant lesions, various modifications of the US-guided biopsy technique have been investigated. Early studies in which color and power Doppler flow imaging were used to improve lesion visualization yielded mixed results. Recently, the use of microbubble-based US contrast agents has shown promise for improving lesion visualization and directing biopsy: Mitterberger et al reported a sensitivity of 81% for cancer detection at US-guided targeted biopsy performed with a microbubble-based contrast material (25). Mitterberger et al and Frauscher et al reported

doubling of the rate of positive core specimens with microbubble-based contrast material–enhanced targeted biopsy, in comparison with the rate with systematic biopsy (25,26). A study performed by Aigner et al showed a twofold increase in the prostate cancer detection rate and a fivefold increase in the rate of positive core specimens with the use of a modified systematic biopsy technique in patients with prostate abnormalities seen at microbubble-based contrast-enhanced transrectal US (27).

Preliminary results from investigational studies of sonoelastography, which depicts abnormally firm areas of the prostate, also are promising. The sensitivity of sonoelastography for the detection of prostate cancer has ranged from 75.4% to 91.7% in various studies (28–31). Comparing sonoelastography-guided biopsies with US-guided standard systematic biopsies, Kapoor et al showed a 1.8-fold increase in the rate of positive cores (31), whereas Aigner et al reported a 4.7-fold increase (32). None of these modifications of the standard systematic biopsy technique has yet demonstrated sufficient sensitivity to justify its substitution for the standard technique (33).

Prostate Biopsy after Anorectal Surgery

Certain situations require a different approach for prostate biopsy. In patients who have undergone a complete proctocolectomy and diverting ileostomy, various alternative approaches have been used. Cantwell et al reported the use of a transgluteal computed tomography (CT)–guided biopsy technique in 22 patients (34). An average of 10 cores (range, 4–12) were obtained with systematic sampling of the peripheral zone. Biopsy specimens from 11 of the 22 patients were positive for prostate cancer.

Transperineal biopsy is another approach that has been used in this patient group. In a study by Shinohara et al, 28 patients with a history of abdominoperineal resection underwent transperineal biopsy with the use of transperineal US for guidance (35). Although biopsy specimens from 23 of the patients were positive for prostate cancer, the authors found that transperineal US provided poorer image quality than transrectal US (35). Seaman et al reported the results of transperineal biopsy performed with transurethral US for guidance in seven patients (36). Prostate cancer was found in three patients in that study. The use of MR imaging–guided transperineal biopsy of the prostate in one patient who had previously undergone a proctocolectomy for ulcerative colitis was reported by D'Amico et al (37).

For patients with an ileoanal pouch, two additional options have been considered: transpouch biopsy, a procedure similar to the standard transrectal US–guided biopsy; and transperineal biopsy with transpouch US performed for guidance. The use of a transpouch biopsy technique has not yet been reported in the literature; this technique may be disfavored because of potential effects on pouch function or the possibility of fistula formation (38). The use of a transperineal approach with a brachytherapy template to guide biopsy needle placement during general anesthesia of the patient has been reported. Although there are few reports of the use of this technique in patients with an ileoanal pouch (38,39), numerous studies have shown it to be effective and safe in patients who have not undergone an anorectal surgical procedure (40,41).

Limitations of the Current Prostate Biopsy Paradigm

The presence of most prostate cancers is signaled by an elevated serum PSA level and is further investigated with transrectal US–guided biopsy performed by using an extended technique with at least 12 samples obtained in the peripheral zone. Several factors limit the effectiveness of this diagnostic paradigm: First, the serum PSA level has a low specificity for the detection of prostate cancer and frequently leads to unnecessary biopsy. Many benign conditions affecting the prostate (eg, benign prostatic hyperplasia, acute or chronic prostatitis) cause the PSA value to rise. In addition, the accepted threshold value defining an abnormal serum PSA level (4 ng/mL) has a major limitation: Clinically significant prostate disease may be present even in patients with a lower PSA value. In the Prostate Cancer Prevention Trial, among 2950 men with a serum PSA level of 4 ng/mL or less, prostate cancer was diagnosed in 449 (15%), and 67 of the 449 men (15%) had a cancer with a Gleason score of 7 or higher (42).

Second, transrectal US does not usually allow the direct visualization and targeting of abnormal regions of the prostate for biopsy, although in rare cases a prostate lesion may be directly depicted. As a result, transrectal US–guided biopsy has a low sensitivity (range, 39%–52%), although its specificity is approximately 80% (43). Because of high false-negative rates, repeat biopsies are often necessary. The cancer detection rate falls from 22%–38% at the initial biopsy (11,13,44) to 10%–17% at the second biopsy (43,45) and 5%–15% at the third biopsy (15,43,45). The clinical challenges of appropriate follow-up and repeated biopsies contribute to increased anxiety and morbidity among patients. To improve the yield of repeat biopsies, some have advocated the use of a saturation biopsy

technique in which 20–50 samples are obtained with either a transrectal or transperineal approach; however, the resultant increased detection rate of 18%–34% may not justify the increased pain and complications experienced by patients who undergo such biopsies (45).

Third, transrectal US–guided biopsy supplies unreliable information about the volume, extent, and aggressiveness of prostate cancers and may lead to overestimation or underestimation of the Gleason score (46). According to Chun et al, upgrading of the Gleason score as a result of findings in the prostatectomy specimen occurs in 25%–42% of cases, and downgrading occurs in 14% (47). Inaccuracies in the Gleason score at transrectal US–guided biopsy result from sampling errors and the inability to spatially localize the clinically most significant lesions at transrectal US.

Last, regions such as the anterior part of the prostate are undersampled at transrectal US–guided biopsy, although increasing evidence indicates that these areas may harbor clinically significant tumors (48). Among patients who underwent an MR imaging–guided biopsy after a negative result of transrectal US–guided biopsy, tumors were found in the anterior part of the prostate in 47%–57% (13,45). Similarly, among patients with prostate cancer detected at extensive transperineal US–guided biopsy after one or more negative transrectal US–guided biopsies, cancer was found in the anterior region in 46%–60% (40,41). In a series of 547 prostatectomy specimens, tumors were found in the anterior part of the prostate in 21% (49).

Uses of MR Imaging for Prostate Biopsy

The limitations of transrectal US–guided prostate biopsy underscore the need for an imaging modality that is capable of detecting and localizing regions with an appearance suggestive of prostate cancer, thus allowing targeted sampling. Over the past 2 decades, MR imaging technology has evolved to the point where it can now directly depict prostate cancers. The development of endorectal coils has further improved prostate tumor visualization on MR images. A T2-weighted sequence is generally used for the pretreatment evaluation of prostate cancer. Although its sensitivity is limited and variable (ranging from 60% to 96%) (43,50), T2-weighted MR imaging enables a major improvement in tumor detection over that obtainable with transrectal US, which has a reported sensitivity of 33% (51). Advanced MR-based techniques such as MR spectroscopy, dynamic contrast-enhanced MR imaging, and diffusion-weighted MR imaging, which have even higher sensitivity for the detection of prostate cancers, are often used in combination with standard T2-weighted imaging (52).

MR imaging is used with increasing frequency in the work-up of patients with prostate cancer, mainly to detect extracapsular, seminal vesicular, neurovascular bundle, and local lymph node involvement for preoperative staging. MR imaging is also being investigated and used for detection and localization of prostate cancer in patients in whom the presence of prostate cancer is suspected despite a negative result at transrectal US–guided biopsy. Localization allows targeted biopsies and appropriate focal treatment of prostate lesions. However, current practice guidelines outline only a narrow diagnostic role for MR imaging in targeting prostate lesions for biopsy: According to the most recent guidelines of the European Association of Urology, MR imaging may be used to investigate the possibility of an anteriorly located prostate cancer if clinical suspicion persists despite negative results at transrectal US–guided biopsies; the area that has an abnormal appearance at diagnostic MR imaging then can be sampled at transrectal US– or MR imaging–guided biopsy (53). In U.S. and Canadian guidelines, by contrast, no role at all is outlined for MR imaging in the guidance and targeting of prostate biopsies (54,55). This omission reflects the lack of widely accepted definitions of roles both for MR imaging and for targeted biopsy in the diagnosis and management of cancers that are confined to the prostate. Multicenter trials and a consensus statement are needed before algorithms incorporating targeted biopsy techniques may achieve wide acceptance.

In the remainder of the article, various biopsy techniques that rely on tumor localization at MR imaging are described. Literature that describes the feasibility of these techniques and their potential for use in improving diagnostic accuracy and guiding management of prostate cancer is reviewed.

MR Imaging–directed Prostate Biopsy

Teaching Point

In an MR imaging–directed prostate biopsy, suspicious-appearing areas of the prostate that are depicted on diagnostic MR images are targeted for biopsy by using real-time transrectal US for guidance. Often, additional cores are obtained beyond the standard number obtained in a systematic biopsy. Targeted sampling of prostate lesions that are detected and localized at MR imaging can be expected to yield better results than systematic biopsies of the prostate (Fig 4).

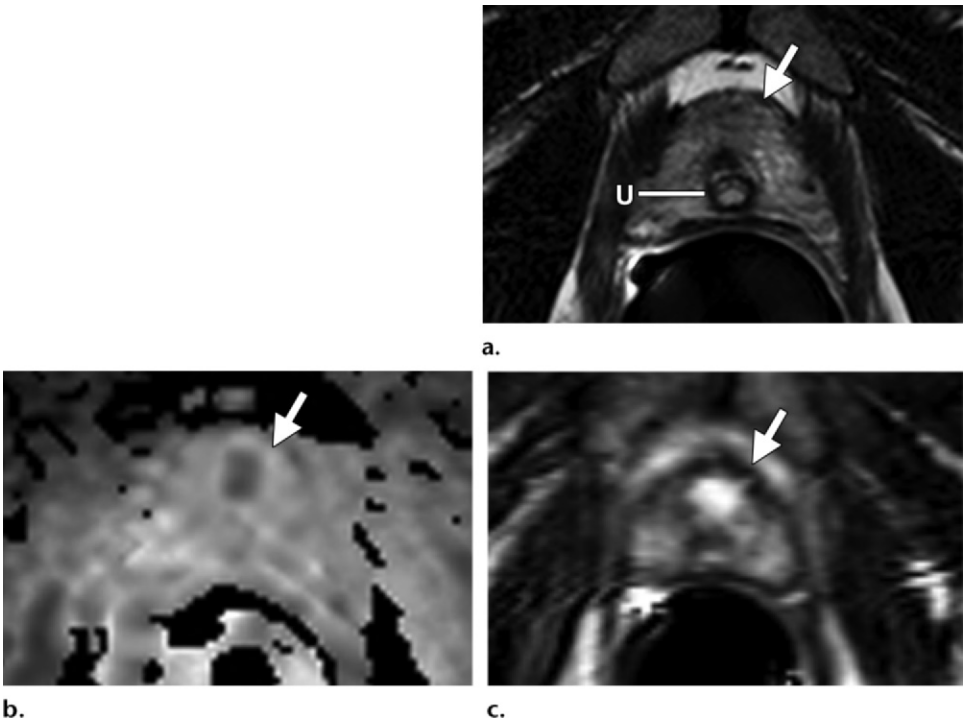


Figure 4. Prostate cancer detected at multiparametric MR imaging in a 52-year-old man with normal findings at digital rectal examination and negative results at both initial transrectal US–guided biopsy (performed 2 years earlier, when his PSA level was 4 ng/mL) and repeat biopsy (performed 1 year earlier, when his PSA level was 5 ng/mL). MR imaging was performed when the patient's PSA level reached 11 ng/mL. **(a)** Axial T2-weighted MR image shows an ill-defined region of low signal intensity (arrow) anterior to the urethra *(U)*, in the apex of the prostate, a region not sampled at systematic biopsy. This region is indistinct because of the normally heterogeneous appearance of the central gland. **(b)** Apparent diffusion coefficient map shows restricted diffusion in the same region (arrow). **(c)** Axial dynamic contrast-enhanced MR image shows early enhancement of the lesion (arrow); early washout also was seen (not shown). An MR imaging–directed transrectal US–guided biopsy was performed that included sampling of the anterior apical region in addition to the standard 12 regions sampled in an extended systematic biopsy. Only the sample from the region that appeared abnormal at MR imaging was positive for prostate cancer (Gleason score, 4 + 5). The patient underwent a radical prostatectomy, and the presence of cancer (Gleason score, 9; stage T3a) in the anterior apical region was confirmed.

In a review article by Lawrentschuk and Fleshner, six studies were identified in which MR imaging was performed before repeat biopsy. In five of these studies, lesions identified at MR imaging were targeted for sampling along with the standard six to 12 regions of the prostate sampled in a standard systematic biopsy. In 63 (32%) of the 197 patients who underwent repeat transrectal US–guided biopsy with this method, prostate cancer was identified. Of those 63 patients, 34 (54%) had prostate cancer that was detected only in MR imaging–targeted biopsy cores (56). In another study, by Kumar et al, voxels suggestive of prostate cancer were identified at MR spectroscopy in 44 of 83 patients with clinical evidence of prostate cancer. All patients underwent a systematic sextant biopsy; in addition, patients with suggestive findings at MR spectroscopy underwent transrectal US–guided biopsy in the region corresponding to the abnormal voxels. In 11 of the 44 patients (25%), the presence of prostate cancer was confirmed at biopsy, whereas none of the 39 patients with a negative result at MR spectroscopy had prostate cancer (57). In another group of 120 patients evaluated at the same institution, the prostate cancer detection rate at MR imaging–directed transrectal US–guided biopsy (25%) was superior to that at transrectal US–guided biopsy without MR imag-

ing guidance (9%) (57). By contrast, a study by Lattouf et al showed no significant increase in the diagnostic yield with repeat transrectal US–guided biopsy performed with targeting of lesions seen on diagnostic MR images (58).

MR imaging also can be used to select targets for transrectal US–guided biopsy when local recurrence of prostate cancer is suspected after radical prostatectomy or radiation therapy. T2-weighted MR imaging and standard contrast-enhanced MR imaging or dynamic contrast-enhanced MR imaging may depict different sites of local recurrence after prostatectomy (20). In a study by Casciani et al, an accuracy of 94% was found for the detection of locally recurrent prostate cancers at transrectal US–guided biopsy in patients with prostate masses seen at MR imaging (21).

MR Imaging–guided Prostate Biopsy

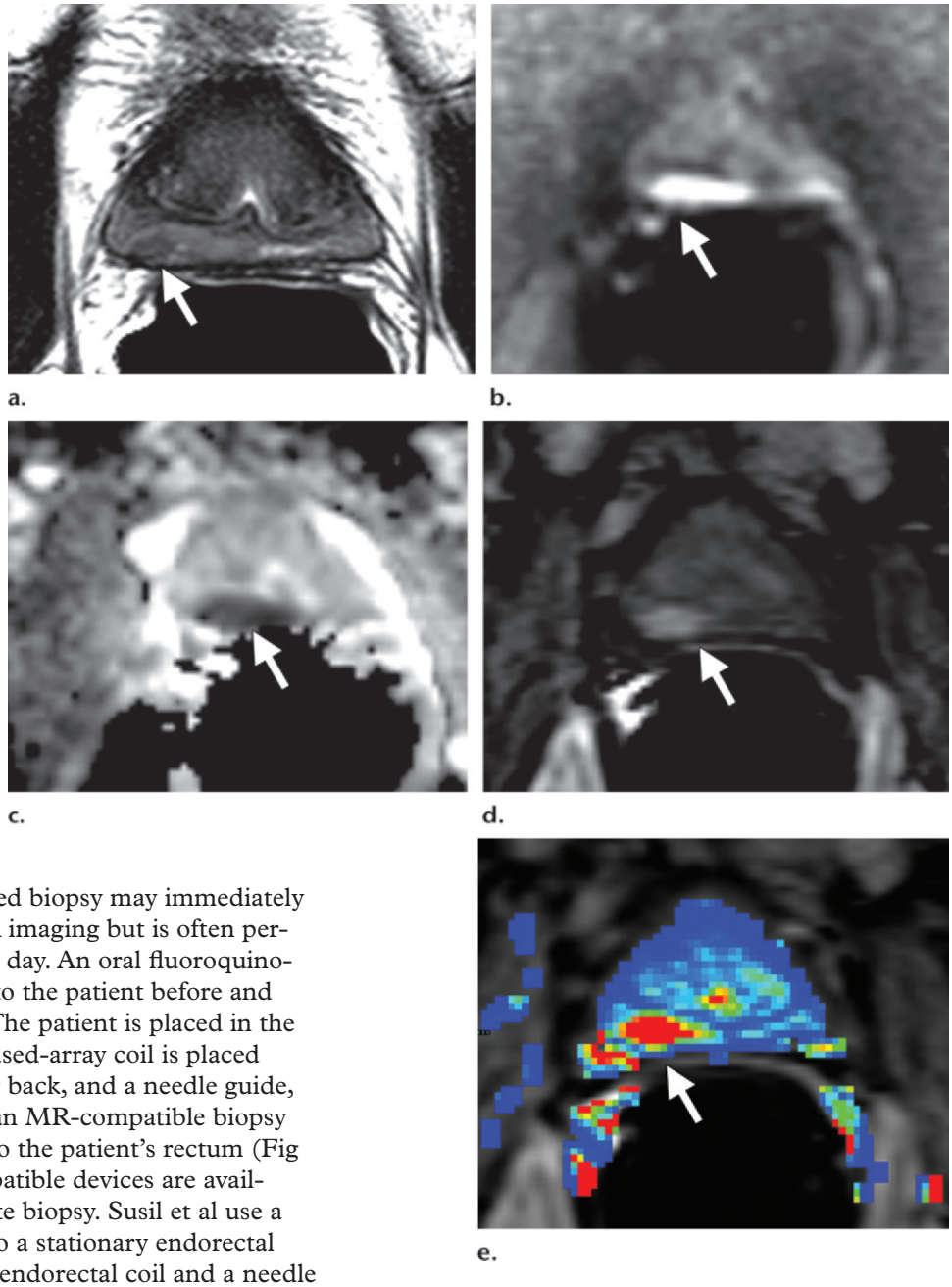
The capability of MR imaging for depicting abnormal areas of the prostate also allows targeted sampling of prostate lesions with the use of real-time MR imaging for guidance. MR imaging–guided prostate biopsy is feasible because of dramatic increases in the speed of MR imaging over the past 2 decades as well as the development of MR-compatible implements (eg, biopsy needles and deployment mechanisms) and advanced visualization tools that help guide and verify needle placement in the lesion.

MR imaging–guided prostate biopsies have been performed in low-field-strength open systems (23,37,59) and in the more widely available closed-bore MR systems with field strengths of 1.5 T (13,44,60–62) and 3 T (11,45,46,63). The low-field-strength open MR imaging system allows easy access to the patient; however, closed-bore systems offer a much higher signal-to-noise ratio, allowing clearer depiction of prostate lesions. In studies in which open MR imaging systems were used, a transperineal (37,59) or transgluteal (23) approach was used for prostate biopsy. In two cases described by Hata et al, a transperineal approach was used because the patient had undergone a rectal surgical procedure that precluded transrectal US–guided biopsy (59). Zangos et al elected to use a transgluteal approach, suggesting that it allows better access to the apex (23). However, a transrectal approach, which is considered less invasive, has been used with a closed-bore MR imaging system in most recent studies (11,13,44–46,51,60,62,63).

Before the biopsy, diagnostic MR imaging is performed for procedural planning. Traditionally, T2-weighted imaging with an endorectal coil is performed to depict regions of the prostate that have an abnormal appearance. However, T2-weighted imaging has limited sensitivity for the detection of prostate cancer; advanced techniques such as dynamic contrast-enhanced MR imaging, MR spectroscopy, and diffusion-weighted MR imaging have higher sensitivity and better detection rates (43). Hambrock et al used a combination of T2-weighted imaging, diffusion-weighted imaging, and dynamic contrast-enhanced imaging to identify suspicious regions to be targeted for biopsy (45). In a study by Franiel et al, MR spectroscopy was added to this combination to identify regions for targeted sampling at MR imaging–guided biopsy. All areas that had a suspicious or indeterminate appearance on T2-weighted MR images also appeared abnormal on images obtained with at least one advanced MR technique, but the combination of three advanced techniques allowed the identification of a larger number of abnormal regions than the combination of any two. The use of a combination of two advanced techniques would have reasonably reduced the number of areas targeted for biopsy, but about 6% of lesions would then have been missed. The most effective two-technique combinations were *(a)* diffusion-weighted imaging and contrast-enhanced imaging and *(b)* diffusion-weighted imaging and MR spectroscopy (13). In a study by Riches et al, the locations of histologically confirmed cancers in prostatectomy specimens correlated with the regions of abnormality seen at MR imaging. When receiver operating characteristic curves were calculated for various combinations of advanced MR-based techniques, the results showed that the combined use of two advanced techniques was significantly more accurate than the use of a single advanced technique for the detection of prostate cancer and that the addition of a third advanced technique did not lead to further improvement in either sensitivity or specificity (52). Thus, it is recommended that diagnostic MR imaging examinations that are performed to detect and localize abnormal prostate regions for targeted biopsy include a combination of T2-weighted imaging and two advanced imaging techniques. In our practice, a combination of T2-weighted imaging, contrast-enhanced imaging, and diffusion-weighted imaging is used (Fig 5).

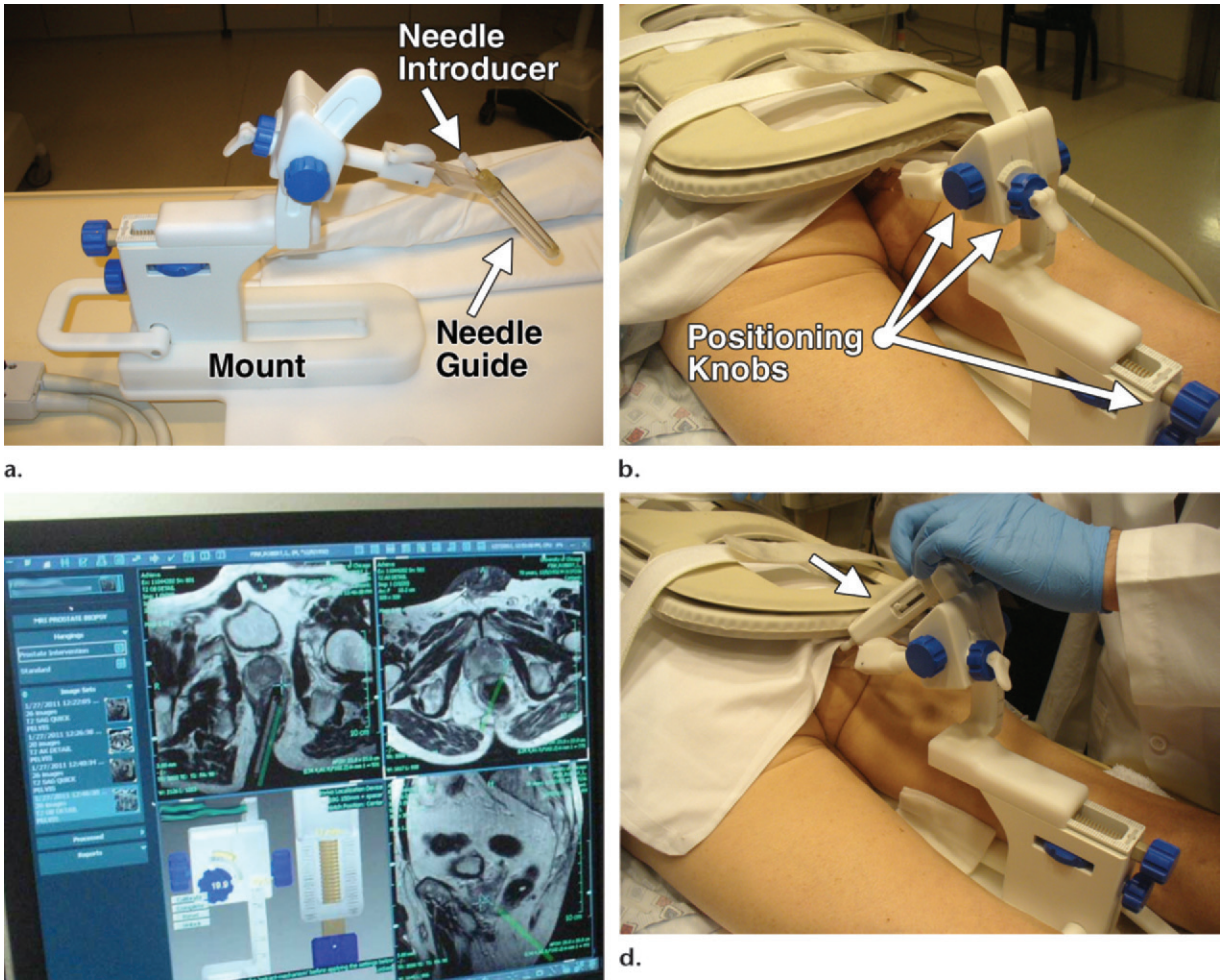
Teaching Point

Figure 5. Recurrent prostate cancer in a 58-year-old man with an elevated serum PSA level 2 years after completion of radiation therapy for stage II adenocarcinoma of the prostate. **(a)** Axial T2-weighted MR image shows a focus of hypointense signal toward the right side of the peripheral zone, at the level of the middle gland (arrow). **(b, c)** Axial diffusion-weighted MR image **(b)** and apparent diffusion coefficient map **(c)** show a corresponding region (arrow) with hyperintense signal in **b** and a dark appearance in **c**. **(d, e)** Axial dynamic contrast-enhanced MR images without **(d)** and with **(e)** a color-coded overlay show intense early enhancement of the lesion (arrow).



MR imaging–guided biopsy may immediately follow diagnostic MR imaging but is often performed on a different day. An oral fluoroquinolone is administered to the patient before and after the procedure. The patient is placed in the prone position. A phased-array coil is placed on the patient's lower back, and a needle guide, which is attached to an MR-compatible biopsy device, is inserted into the patient's rectum (Fig 6). Various MR-compatible devices are available for use in prostate biopsy. Susil et al use a device that attaches to a stationary endorectal sheath containing an endorectal coil and a needle guide that can be rotated and translated (62). A multiplanar sequence (typically, a T2-weighted fast spin-echo sequence) is applied for the localization of regions of interest. In most cases, the region of interest has low signal intensity on T2-weighted localization images and can be identified and targeted for biopsy on that basis;

Figure 6. **(a)** Photograph shows an MR-compatible prostate biopsy device with a needle guide attached (DynaTRIM; Invivo, Gainesville, Fla). **(b)** Photograph shows the device after insertion of the needle guide into the patient's rectum. **(c)** Photograph shows the display at an independent workstation running advanced visualization and interventional planning software (DynaCAD; Invivo) that calculates the appropriate adjustments in needle guide position in three dimensions on the basis of the localization image dataset. **(d)** Photograph obtained with the needle guide in the appropriate position for biopsy shows the insertion of an 18-gauge MR-compatible biopsy needle (arrow).



however, in some cases the anatomic location of a target must be identified by visually matching the T2-weighted localization image to the prebiopsy diagnostic MR image. The needle guide, which is filled with a gadolinium-based contrast material, is then directed toward the lesion by adjusting the angle of the biopsy device, and additional images are acquired between adjustments to verify the position of the needle guide. An advanced visualization and interventional planning software program assists with needle placement by providing adjustment parameters for the needle guide. The MR imaging sequences that have been used to verify the needle guide position include T2-weighted fast spin-echo, gradient-echo (eg, balanced fast field echo, FIESTA [fast imaging employing steady-state acquisition], and true FISP [true fast imaging with steady-state precession]), and single-shot fast spin-echo sequences applied in a sagittal or axial plane parallel to the needle guide (13,44–46). After each tissue sample is obtained, additional images are acquired with the

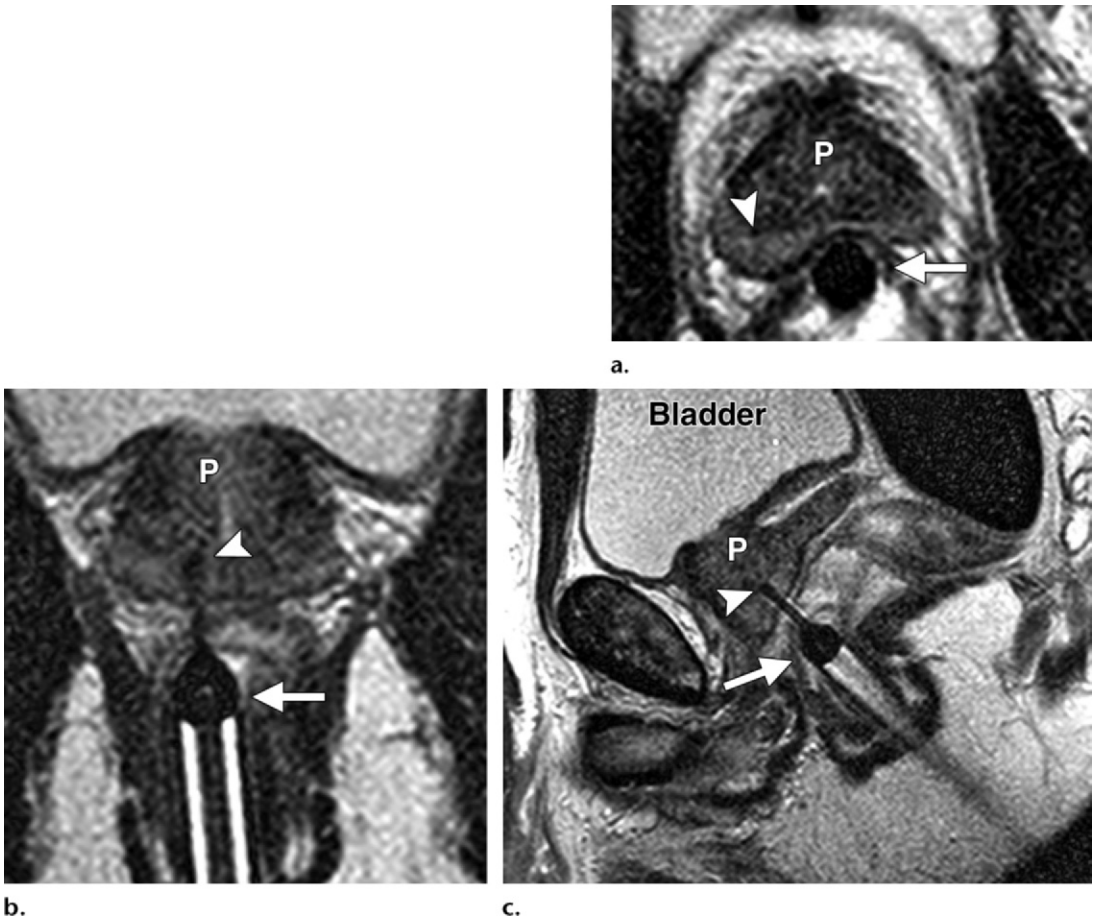


Figure 7. MR imaging–guided prostate biopsy (same patient as in Fig 5). **(a)** Axial T2-weighted MR image obtained after insertion of the needle guide in the rectum shows the location of the prostate lesion (arrowhead). The position of the needle guide (arrow) was subsequently adjusted with guidance from advanced visualization and interventional planning software and was verified on a second T2-weighted MR image (not shown). An 18-gauge MR-compatible biopsy needle was then inserted through the guide, and tissue samples were obtained. *P* = prostate. **(b, c)** Oblique axial **(b)** and sagittal **(c)** T2-weighted MR images obtained along the axis of the needle guide (arrow) for confirmation of accurate targeting after tissue sampling show the needle tip (arrowhead) within the lesion. Pathologic analysis of the biopsy specimens yielded adenocarcinoma. *P* = prostate.

biopsy needle left in place to allow verification of its position within the targeted region (Fig 7). Table 1 provides a step-by-step description of the protocol used for MR imaging–guided prostate biopsies performed at our institution.

In most studies, the patients who underwent MR imaging–guided biopsy had undergone at least one previous transrectal US–guided biopsy procedure with negative results, and most had undergone two or more previous biopsy procedures. The prostate cancer detection rates at MR imaging–guided biopsy in most of these studies ranged from 38% to 59% (13,23,44,45,60,61). In a study by Hambrock et al, a detection rate of 59% was obtained with MR imaging–guided biopsy in 68 patients, in comparison with rates of 22% for a second transrectal US–guided biopsy in 248 patients and 15% for a third transrectal US–guided biopsy in 65 patients, all at the same institution (45). In a subgroup analysis, the difference in detection rates was significant for all subgroups except those with the highest serum PSA levels (>20.1 ng/mL) and largest prostate volumes (>65.1 cm^3). Of the 40 patients with a positive biopsy result in that study, 37 (93%) were found to have clinically significant disease (45). The utility of MR imaging–guided biopsy with a small number of cores for detecting prostate cancer recurrence after external beam radiation therapy was demonstrated in at least one study (64). Most specimens from MR imaging–guided prostate biopsies in which no cancer was detected showed evidence of chronic prostatitis at pathologic examination; such findings

Table 1
Protocol for MR Imaging–guided Prostate Biopsy

1. Preprocedural diagnostic multiparametric MR imaging is performed with an endorectal coil to identify regions in the prostate that have an abnormal appearance (Fig 5).
2. Patient preparation is completed, and an oral antibiotic is administered prophylactically.
3. Biopsy is performed.
   (a) Patient is placed prone on the table.
   (b) Phased-array coil is placed on the patient's back.
   (c) Needle guide is attached to the MR-compatible biopsy device (Fig 6a) and inserted into the patient's rectum (Fig 6b).
   (d) Calibration (sagittal T2-weighted fast spin-echo) and localization (axial and oblique axial T2-weighted fast spin-echo) sequences are applied.
   (e) Suspected lesions are reidentified on axial T2-weighted fast spin-echo images (Fig 7a).
   (f) With use of advanced visualization and interventional planning software (Fig 6c), the appropriate position of the needle guide is calculated in three dimensions.
   (g) Needle guide is adjusted accordingly, and T2-weighted fast spin-echo imaging is repeated to verify its correct placement; additional adjustments are made as needed for optimal positioning.
   (h) Fully automated 18-gauge double-shot core-needle firing mechanism is inserted through the needle guide and triggered (Fig 6d).
   (i) T2-weighted fast spin-echo images are obtained to verify that the needle has stopped within the target (Figs 7b, 7c).
   (j) Two or more cores are obtained from each suspected lesion.
4. Postprocedural steps are completed.
   (a) Patient is helped to arise slowly from the table to minimize the risk of a fall due to vasovagal syncope.
   (b) Patient is observed for 30 minutes.
   (c) Patient is discharged with a prescription for an additional antibiotic.

are indicative of the difficulty of distinguishing benign lesions from prostate cancers even with the use of advanced MR imaging techniques (44,45,60,61,63).

MR imaging–guided prostate biopsy has a few potential disadvantages. Although the procedure in most cases can be completed in 1 to 1½ hours, it may be more time consuming; the reported duration has varied from ½ hour to 2½ hours, depending on the number of samples obtained and the experience of the operator (44,45). In one study, two suspicious regions in the base of the prostate could not be accessed with the biopsy device (61), a limitation that also has been encountered at our institution. Reported complications from MR imaging–guided biopsy are relatively few and mild; they include self-limiting hematuria, uncomplicated urinary tract infection, and minor pain (45).

Fused MR Imaging– and Transrectal US–guided Biopsy

The fusion of MR imaging and transrectal US technologies offers a promising alternative to targeted prostate biopsies. Recent advances have enabled the coregistration of previously acquired MR images and real-time transrectal US images. This fusion of the two imaging modalities has demonstrated value for improving the results of prostate biopsy by allowing the targeted sampling of lesions with an appearance suggestive of cancer.

The techniques and systems that are used for fused MR imaging– and transrectal US–guided biopsy were initially developed for use in brachytherapy (65,66). Early systems that relied on fiducial markers for image registration were limited by prostate motion, which resulted in a loss of accuracy of registration. Other techniques have since been developed to resolve this problem (67–71).

Fused MR imaging– and transrectal US–guided prostate biopsy combines the advantages of each procedure in a single technique while decreasing sampling errors, a problem endemic to transrectal US–guided biopsy. Preprocedural MR imaging data are fused with real-time transrectal US images to allow targeted sampling by directing the biopsy needle toward regions with an abnormal MR imaging appearance.

Teaching Point

Few commercial systems are available that were designed specifically for use in fused MR imaging– and transrectal US–guided prostate biopsy. A conventional US system may be used with a transrectal transducer and volume navigation software. Miniature sensor coils that are

integrated into the biopsy needle, needle guide, or US transducer perform a function similar to that of Global Positioning System chips, receiving electromagnetic signals that allow the system to determine the actual position of the device.

The diagnostic MR imaging study and the biopsy procedure are often performed on different days. The biopsy procedure is the subject of an ongoing clinical trial at our institution and is used in patients with previous negative prostate biopsy results but persistently elevated PSA levels and at least one prostate region with an abnormal appearance on diagnostic MR images. The diagnostic MR imaging examination used for this procedure at our institution, like that for other MR imaging–guided prostate biopsy procedures, is based on a combination of T2-weighted imaging, dynamic contrast-enhanced imaging, and diffusion-weighted imaging sequences. Suspected lesions are identified on T2-weighted and multiparametric MR images. The MR images that best depict the lesion are stored on a compact disc and uploaded to the US system. During the prostate biopsy, the stored MR images are electronically transferred to the workstation for volumetric reconstruction and fusion with real-time US images.

Patient preparation for the fusion biopsy procedure is similar to that for transrectal US–guided biopsies. An oral fluoroquinolone is administered to the patient before and after the procedure. The patient is placed in a left lateral decubitus position, and a transrectal US transducer equipped with a needle guide is inserted into the rectum. These steps are similar to those followed in a transrectal US–guided biopsy procedure. The US transducer that we use for fused MR imaging– and transrectal US–guided biopsy has an end-fire array and is equipped with a commercial needle guide (Civco, Kalona, Iowa) to enable spatial tracking and image coregistration.

First, an axial sweep of the entire prostate is performed. With use of positional and orientational information from the tracking sensor attached to the transducer, the initial two-dimensional US dataset is automatically reconstructed as a volumetric US image of the prostate. Coregistration of the volumetric US image with the volumetric MR image showing the region targeted for biopsy is performed electronically by the US system. Manual registration based on visual methods is performed to verify the accuracy of image fusion. For manual registration, internal markers such as the urethra and the bladder neck are identified on the transrectal US image. After manual registration, real-time transrectal US images are automatically fused with the volumetric MR image, and suspicious regions are displayed on both the initial MR image and the real-time fused image (Fig 8). A targeted transrectal US–guided biopsy of the abnormal regions seen on MR images can then be performed. Targets and biopsy sites in the three-dimensional fused image volume can be stored for future recall. The average duration of this biopsy procedure is approximately 15 minutes, although the duration varies, depending on the number of biopsy targets and the operator's experience (72).

Some prostate biopsy guidance systems rely on US image–based elastic registration. The primary limitation of this technique is deformation of the prostate, which may occur at prebiopsy MR imaging as well as at transrectal US. The prostate may undergo considerable deformation due to pressure from the transducer or patient movement during transrectal US–guided interventional procedures. Advanced registration algorithms that might compensate for transducer pressure, especially in the posterior regions of the prostate, are under investigation.

An advantage of this fusion biopsy technique is that it is not performed in the MR imaging suite and, thus, it is both less costly and less time consuming than MR imaging–guided biopsy, allowing higher patient throughput. However, the technique is still evolving, and, despite promising early results, large-scale multicenter studies are needed to assess its accuracy.

Robotically Assisted MR Imaging–guided Biopsy

Robotic technology is currently undergoing evaluation for use in guiding prostate interventions and may increase the accuracy of needle placement in the prostate gland. All robotic components are constructed of nonmagnetic and dielectric materials for MR compatibility. These components are designed to accept as input the high-resolution anatomic and functional information provided by the MR imaging system and to be fully operational in the MR imaging suite.

An early robot prototype for robot-assisted MR imaging–guided prostate interventions was constructed by Chinzei et al and used within an

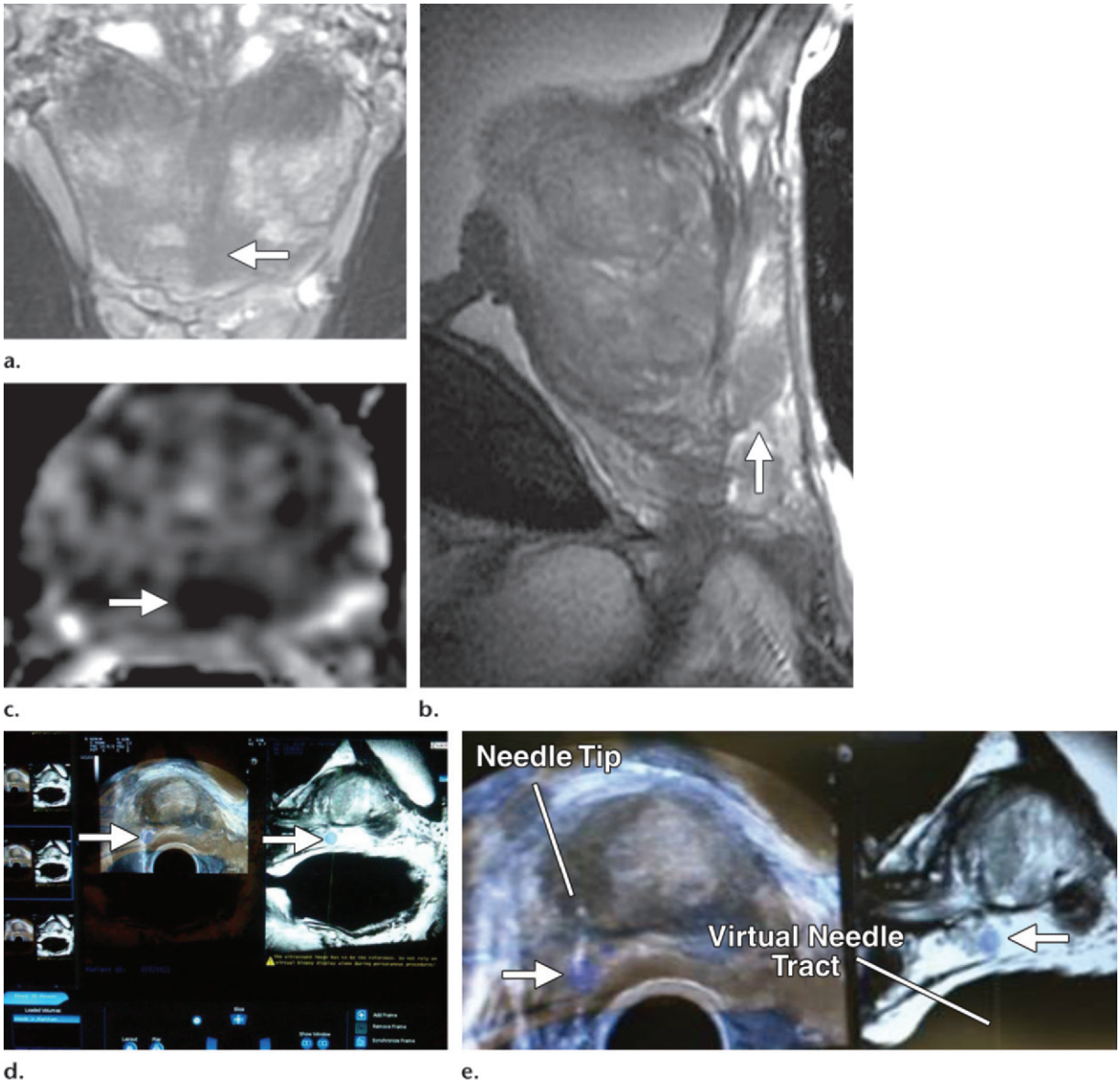


Figure 8. Fused MR imaging– and transrectal US–guided prostate biopsy in a 54-year-old man with an elevated serum PSA level and a negative result at initial transrectal US–guided biopsy. **(a, b)** Coronal **(a)** and sagittal **(b)** T2-weighted MR images show a dominant ill-defined region of low signal intensity in the left apical part of the prostate, close to the midline (arrow). **(c)** Apparent diffusion coefficient map shows a corresponding focal region of restricted diffusion (arrow). On the basis of these findings, the patient elected to undergo a fused MR imaging– and transrectal US–guided biopsy. Before the biopsy, the MR imaging dataset in the plane that best depicted the lesion was loaded onto the US system for reconstruction as a three-dimensional volumetric image. After the patient was positioned on the table and the transrectal transducer with needle guide was inserted in the rectum, an axial sweep of the prostate was performed. The resultant two-dimensional US image dataset was reconstructed as a three-dimensional US image that was then automatically coregistered with the volumetric MR image. A virtual needle tract generated by the US system on the fused US/MR image was used to manually direct the needle guide toward the target. After the needle guide position was verified, an 18-gauge needle was deployed. **(d)** Screenshot of the fusion workstation shows dynamic image navigation. Sagittal real-time US image obtained after needle deployment and fused with the MR image depicts the lesion (arrow at left), which is highlighted by a blue dot on the MR image (arrow at right). **(e)** Magnification of the same screenshot as in **d** more clearly shows the virtual needle tract on the MR image and the actual needle tip within the lesion on the fused image. Prostate cancer with a Gleason score of 7 (4 + 3) was found.

open MR imaging system to guide the placement of needles and brachytherapy seeds (73). Krieger et al developed a manually manipulated mechanical device to guide transrectal prostate biopsy (74). This device is used along with an advanced three-dimensional visualization system at the U.S. National Cancer Institute to perform MR imaging–guided prostate biopsy and brachytherapy seed placement. A retrospective evaluation of the system suggests that work is still needed to compensate for prostate displacement and improve targeting accuracy (75). In recent years, a number of other MR-compatible robotic intervention systems have been introduced (76–81). Stoianovici et al developed a fully automated robot for transperineal prostate access that is mounted alongside the patient on the MR table and operated from the control room with MR imaging feedback; the operator does not directly control the robot but defines its tasks and monitors its actions on MR images (82).

Until recently, none of these systems was commercially available. The first commercially available robotically assisted MR imaging–guided system (Innomotion; Innomedic, Herxheim, Germany) was evaluated in a cadaver study (83), in which it was used to guide prostate interventions performed with a transgluteal approach. Preliminary results show that the use of this type of system has potential for improving prostate interventions (84).

Summary

Prostate biopsy remains essential for the diagnosis of prostate cancer and individualization of management decisions. The information obtained from prostate biopsy is increasingly relevant, as active surveillance of prostate cancer becomes a more common management strategy and as numerous clinical trials of focal prostate cancer therapies are in progress. Current diagnostic and staging algorithms, which are based largely on transrectal US–guided biopsy, have substantial limitations that can lead to unnecessary biopsies, inaccurate characterization of the aggressiveness of prostate cancers, increased patient anxiety and morbidity, and increased costs. Multiparametric MR imaging is currently the optimal noninvasive modality for diagnosis of prostate cancer. The use of information obtained at MR imaging to directly target lesions for biopsy may help increase the diagnostic yield, improve the accuracy of identification and characterization of prostate cancers, and aid in the selection of patients for specific therapies. Table 2 compares the advantages and disadvantages of conventional and evolving prostate biopsy techniques.

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Table 2
Advantages and Disadvantages of Conventional and Emerging Prostate Biopsy Techniques

Technique	Advantages	Disadvantages
Systematic transrectal US–guided biopsy	Quick, office-based procedure; widely available; least costly of the four techniques described	Lesion targeting is not possible in most cases; diagnostic yield is low (22%–38% at first biopsy, 10%–17% at second biopsy, 5%–15% at third biopsy); technique is unreliable for assessing tumor volume, extent, and aggressiveness; transrectal approach leads to undersampling of some regions (eg, anterior part of the gland)
MR imaging–directed transrectal US–guided biopsy	Quick, office-based procedure; allows lesion targeting, with a better detection rate than that for systematic biopsy in small single-institution studies	More costly than systematic biopsy because of the use of MR imaging for preprocedural planning; targeted lesions are not seen during biopsy
MR imaging–guided biopsy	Allows lesion targeting, usually with visualization of target during biopsy and with ability to confirm placement of biopsy needle in the target; small number of cores; detection rate is higher (38%–59%) than that at repeat transrectal US–guided biopsy; shows potential for targeting of the most aggressive lesions to yield a more reliable Gleason score	Most costly of the four techniques because of the use of MR imaging and a higher procedural cost overall; more time consuming; availability is limited
Fusion MR imaging– and transrectal US–guided biopsy	Allows targeting of lesions; does not require use of the MR imaging suite during biopsy; shows potential for targeting of the most aggressive lesions to yield a more reliable Gleason score	More costly than systematic biopsy because of the need for preprocedural MR imaging; availability is limited; data on performance are limited

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Imaging-guided Prostate Biopsy: Conventional and Emerging Techniques

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The best predictor of tumor aggressiveness is the Gleason score, which can be obtained only with histopathologic analysis of biopsy samples (7). Thus, prostate biopsy, usually performed with a core needle inserted transrectally with real-time US guidance, remains an essential component of the diagnostic work-up.

Page 822
Transrectal US is useful only to localize the prostate, not suspected lesions within it. However, areas of the prostate in which tumors are most frequently found can be sampled in a systematic fashion on the basis of zonal anatomy at transrectal US–guided biopsy.

Page 825
In an MR imaging–directed prostate biopsy, suspicious-appearing areas of the prostate that are depicted on diagnostic MR images are targeted for biopsy by using real-time transrectal US for guidance. Often, additional cores are obtained beyond the standard number obtained in a systematic biopsy.

Page 827
Thus, it is recommended that diagnostic MR imaging examinations that are performed to detect and localize abnormal prostate regions for targeted biopsy include a combination of T2-weighted imaging and two advanced imaging techniques.

Page 831
Preprocedural MR imaging data are fused with real-time transrectal US images to allow targeted sampling by directing the biopsy needle toward regions with an abnormal MR imaging appearance.