Progress in Imaging Diagnosis and Image-guided Puncture Biopsy of Prostate Cancer

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Abstract: The current standard technique for diagnosing prostate cancer (PCa) in men at risk relies on a transrectal ultrasound (TRUS)-guided needle biopsy due to its real-time nature and simplicity to obtain systematic histological specimens of the prostate. Also several magnetic resonance imaging (MRI)-based techniques have been employed due to their high detection rate of clinically significant PCa (csPCa). MRI-TRUS fusion imaging contains both the information of MRI and TRUS images for prostate biopsies. This technique combines the strengths of these two techniques, including the superior sensitivity of MRI for targeting cancerous lesions the real time and practicality of TRUS. This review briefly introduces the development of TRUS-guided biopsy, MRI-guided biopsy and MRI-TRUS fusion imaging techniques for prostate cancer.

Key words: Ultrasound; Image-guided biopsy; Magnetic Resonance Imaging; Prostate cancer

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Prostate cancer (PCa) is the second most common cancer and the second most common cause of cancer-related deaths among males globally after lung cancer [1]. It is an epitheliogenic malignant tumor in the prostate and shows no obvious symptoms at the early stage, which contributes to a high risk of death among the patients. Accumulating evidence suggests that the incidence of PCa has been increasing continuously over the past 20 years, which may be attributable to several factors including accelerated aging, ethnicity, hormone abuse, and poor dietary patterns [2]. Furthermore, the introduction of prostate-specific antigen (PSA) screening has contributed to this increase [3]. For many years, the screening of prostate cancer has mainly been via PSA and digital rectal examination. However, a study found that the level of serum PSA was easily affected by pre-rectal digital examination, indwelling catheterization, and drugs such as finasteride for the treatment of benign prostatic hyperplasia, so the specificity is relatively low. Although digital rectal examination is simple and noninvasive, it relies on the experience of doctors and is more suitable for examining larger tumors or tumors close to the posterior capsule of the prostate [4]. Imaging examination can be helpful for diagnosing PCa and for detecting cancerous lesions of the prostate before biopsy. According to the most recent European guidelines, transrectal ultrasound (TRUS)-guided systemic biopsy is currently the standard method of diagnosing PCa [5]. Targeted biopsy has been used for studying different imaging modalities or new techniques for diagnosing PCa with limited biopsy number and to reduce complications. This review article discusses the progress in imaging diagnosis and image-guided puncture biopsy of PCa.

The Status of TRUS-guided Biopsy

The current standard technique for diagnosing PCa in men at risk relies on a TRUS-guided needle biopsy to obtain systematic histological specimens of the
prostate. In 1989, Hodge et al. introduced the use of TRUS to guide sextant biopsy of the prostate gland; TRUS involves sampling of the parasagittal apex, midzone, and base of the right and left sides of the prostate gland [6]. As is shown in Figure 1, the standard sextant biopsy test applies a random placement of 6-12 needles, one to two for each sextant, to sample the prostate that is blind to the accurate location of cancer. The advantage of guided biopsies for such lesions has been demonstrated in several studies [7]. However, the sensitivity and specificity of TRUS for detecting PCa are limited, ranging between 40% and 50% [8], which makes US-guided targeted puncture impossible. Some prostate lesions are visible on TRUS and can be targeted by experienced ultrasonographers or urologists [9], but the detection rate of clinically significant PCa (defined as at least one core with a Gleason score of 3+4 or 6 with a maximum cancer core length longer than 4 mm) with TRUS is relatively low (Fig. 2) [10]. Some PCa lesions show hyperechogenic or sometimes isoechogetic characteristics leading to sensitivity and specificity of about 18–96% and 46–91%, respectively [11]. Some studies demonstrated that only 17%–57% of ultrasound-evident lesions are malignant. Benign entities, such as prostatitis, infarction, atrophy, and benign prostatic hypertrophy, may all demonstrate hypoechoic features on TRUS.

To increase the detection of PCa, some experts support an increase in the number of cores using the same transrectal approach (saturation biopsies). Others also support transperineal template mapping biopsy (sampling the prostate every 5 mm) [12]. The cancer detection rates have increased up to 30% due to the use of the extended 10- to 12-core biopsy protocols, which include performing the standard sextant biopsy and additional biopsies in the apical and far lateral zones. It has a more accurate attribution of cancer risk, and the likelihood of detecting insignificant cancers doesn’t increase [13]. However, Taverna et al. also reported an accuracy of 29% for 13-core TRUS-guided biopsy in a sub-cohort of 100 patients in a prospective analysis. This low detection rate has been confirmed by Mitterberger et al. in a retrospective cohort involving 1776 men [14].

There are also several targeted biopsies using new US techniques, such as sonoelastography-targeted and CEUS-targeted biopsies. These have been reported to increase the detection rates of cancer and also required just half the number of cores needed in systematic biopsy protocols [15]. Regardless, van Hove et al. reported in a systematic literature review that no definite conclusion can be reached regarding the superiority or inferiority of ultrasound-targeted biopsies compared with systematic biopsies, owing to the large number of contradictory studies [16]. In almost all studies, systematic biopsies combined with targeted biopsies had greater accuracy for detecting cancer, and sometimes were greater than systematic biopsies alone. Absolute cancer detection rates increased 2%–8% and 7%–15%, respectively, when CEUS- and ultrasound elastography-targeted biopsies were combined with systematic biopsies [17].

Figure 1  The needle deployment of systematic biopsy. (A) The coronal position with the deployment of 12 needles; (B) The cross section, the shaded part is the external gland; (C) The sagittal position. Figure C1 is the needle deployment beyond the red line of Figure B; Figure C2 is the inside deployment of the red line. The red line is the dividing line of the needle deployment.

The Value of MRI in Prostate Biopsy

Magnetic resonance imaging (MRI) of the prostate, which is the practice of combining multiple MRI parameters for the functional and anatomical assessment of the prostate, has become an increasingly utilized and accurate way for diagnosis, risk stratification, and treatment planning in PCa. There are several MRI-based techniques employed in the diagnosis of PCa [18], including T1-weighted (T1W), T2-weighted (T2W), diffusion-weighted imaging (DWI), and
dynamic contrast-enhanced (DCE) imaging, which are useful in the process of prostate biopsy [19]. Increasing numbers of hospitals conducting prostate MRI use the multiparametric prostate MRI (mpMRI) approach. The relative clinical value of mpMRI component techniques differs. T2WIs depict the best structures of the prostate, such as the zones, urethra, ejaculatory ducts, and capsule [20]. DCE imaging provide a way to evaluate tumor vascularity. A previous report showed that the detection rate of tumor vascularity by DCE is 92.9% in patients with PCa [21]. DWI uses techniques which quantify free water motion [22]. Apparent diffusion coefficient (ADC) map can be used to assess the aggressiveness of PCa, which is calculated from DWI imaging (Fig. 3). A study reported that there were significant differences in Gleason score, imaging features of cancerous lesion, and solid growth between detected and missed PCa using mpMRI ($P < 0.0001$) [23].

![Figure 2](image1.png) Transrectal ultrasound (TRUS) in a 67-year-old man with bilateral prostate cancer. Although the prostate borders are clearly visible and some intraprostatic structure is seen, no suspicious lesions were identified.

Since mpMRI has improved the detection of csPCa in the prostate [24], MRI-guided biopsy methods have been used, such as MRI-TRUS fusion image-guided biopsy, in-bore MRI-targeted biopsy, and cognitive biopsy. MRI-TRUS fusion imaging provides MRI information with TRUS images, which are used in prostate biopsy. This technique combines the superior visibility of MRI for targeting suspicious lesions with TRUS for real-time guidance. In-bore MRI-targeted biopsy uses MRI in a more direct way [20]. Although some reviews showed no significant differences in accuracy of PCa detection between in-bore MRI-targeted biopsy and MRI-TRUS fusion image-guided biopsy ($P = 0.13$), in many hospitals, in-bore MRI-targeted biopsy is not acceptable due to its time limitations, high costs, and the need for general anesthesia. Cognitive biopsy has improved accuracy which is based on performer’s suspicions of the cancerous lesion on MRI with no fusion device [25]. Several studies have demonstrated that there were no significant differences between MRI-TRUS fusion image-guided biopsy and cognitive biopsy ($P = 0.11$). Haffner et al. described that the detection rate of targeted biopsy was higher compared to systematic biopsies for significant cancer detection ($P < 0.001$). In addition, Park et al. [25] reported that the accuracy of cancer detection was significantly higher in cognitive biopsies (29.5%) than in systematic biopsies (9.8%) ($P = 0.03$). They also found a significantly higher positive percent core in cognitive biopsies than in systematic biopsies ($P < 0.001$). Sometimes, tracking the accurate position of all biopsy sites is difficult, especially when the diameter of the lesion is less than 10 mm [26]. Experienced specialists in prostate biopsy usually perform cognitive fusion biopsies successfully.

![Figure 3](image2.png) Multiparametric prostate MRI [(A) axial T2-weighted; (B) sagittal T2-weighted; (C) dynamic contrast-enhanced subtraction; (D) apparent diffusion coefficient (ADC) map (b = 500 s/mm2)] of a 60-year-old man with biopsy-proven prostate cancer (Gleason 4 + 3 = 7) and rapidly rising prostate-specific antigen (PSA). MRI shows signal abnormalities in the medial part of the seminal vesicle, suggestive of seminal vesicle invasion (arrows) (Reprinted with permission from [23]).

In order to detect csPCa, mpMRI can be performed at 1.5Tesla (T) or 3.0T, using either a combination of an endorectal coil and a pelvic phased-array coil. However, a pelvic phased-array coil is now the recommended and preferred approach to all men presenting for prostate imaging. In recent years, the employment of the endorectal coil and 3.0T imaging is optional [27] which is feasible with sufficient high quality image [28]. It is not an essential requirement of mpMRI according to the recent European consensus [29]. The lesion was graded on a Likert scale according to the European Society of Urogenital Radiology prostate MRI guidelines [30], which is very similar to breast mammography reporting in which 1 refers to the lowest radiologic suspicion for cancer and 5 suggests that the radiologist is definitely
confident that a lesion is cancer. Others made use of a 3- or 4-point scale, and some reported mpMRI according to the Prostate Imaging-Reporting and Data System that contains a 5-point scale for each type of MRI sequence [31]. The guidelines are as follows: score 1 = clinically significant PCa is highly unlikely to be present; score 2 = clinically significant PCa is unlikely to be present; score 3 = clinically significant PCa is equivocal; score 4 = clinically significant PCa is likely to be present; and score 5 = clinically significant PCa is highly likely to be present. mpMRI with T2W, DWI and DCE sequences allows for high detection rate, characterization and staging of PCa. MRI-targeted biopsy is of great value in the detection and diagnosis of PCa.

The Role of MRI-TRUS Fusion Imaging

Most recently, an increasing number of studies have emphasized the prostate imaging limitations and the potential opportunity for the use of TRUS. Several articles have reported that mpMRI has high sensitivity and specificity [32], and is the most promising imaging technique for depicting the anatomy of the prostate as well as detecting cancerous lesions. However, MRI imaging is expensive and it is typically time consuming. The biopsy is also conducted on different days and commonly performed using a transrectal ultrasound probe. While some studies have shown that similar detection rates of PCa with in-bore MRI-targeted biopsy and MRI-TRUS fusion imaging, in-bore intervention is expensive and time-consuming [33]. A pragmatic way to overcome the dilemma is to introduce a number of devices that fuse previously acquired MRI data to the real-time TRUS, which can exploit the strengths of both techniques [32] (Fig. 4). Making use of these complementary techniques, the deployment of needle in the prostate can be more accurate than with each method alone. MRI-transrectal ultrasound fusion imaging has increasingly been used to diagnose csPCa because of its growing accuracy and its availability. MRI-TRUS fusion imaging contains both the MRI information and TRUS images for prostate biopsies. This technique combines the strengths of the two techniques including the superior sensitivity of MRI for targeting suspicious lesions and the familiarity and practicality of TRUS. The images of the prostate for diagnostic purposes are generally obtained using a 3T or 1.5T MRI scanner [34]. The MRI images can be acquired days, weeks, or even months before the biopsy. The endorectal coil is crucial to improve the quality of MRI image and to simulate the force of the ultrasound probe through the rectal wall, but the deformation is inevitable. Cancerous lesions are generally obviously showed on the T2-weighted, diffusion-weighted or dynamic contrast-enhanced images. The MRI images would be transferred to the workstation. The patient firstly has an examination using 2D TRUS probe with tracking sensors which is placed in the rectum [35]. The examination must ensure that the series of 2D ultrasound images cover the whole volume of the prostate. The images and corresponding data from the tracking sensors will be transferred to the workstation in real time. The MRI images and the ultrasound volume which is reconstructed on the workstation according to the images and corresponding data are then spatially aligned with each other. Figure 5 shows two screen shots of fused MRI-TRUS guidance in a targeted prostate biopsy [36]. Figure 3a shows the MRI image registered to the color-coded reference ultrasound volume. The green contours are the segmentation of the prostate based on the MRI image. Figure 3b shows the live ultrasound and the corresponding MRI MPR views at the time of needle deployment. The white line is the biopsy guide line, which is dictated by the needle guide and is fixed relative to the ultrasound image. The suspicious regions were identified on the T2-weighted MRI image and transformed to the real-time ultrasound display. In the process of needle insertion, the distortion of the prostate happens frequently. There are several reasons for the inevitable prostate motion in the pelvic cavity. First, the patient would move involuntarily because of pressure or pain related to the needle insertion. Second, the ultrasound probe may move and cause the deformation of the prostate, and last, the patient’s respiratory motion can also distort the prostate [37]. At present, the devices for MRI-TRUS fusion image-guided prostate biopsy have become commercially available. In a simplified description, MRI-TRUS image fusion is a method to align a preprocedural MRI image to an intraprocedural

![Figure 4](image-url) MRI-TRUS fusion image-guided biopsy combines the strengths of these two techniques which include the superior sensitivity of MRI for targeting suspicious lesions a the familiarity and practicality of TRUS.
US image for a more accurate deployment of the needle to a US region of interest defined by mpMRI. The devices can be classified by the fusion process as either rigid or elastic [38]. The mode of acquisition of the prostate US is either automatic or manual [39], and the biopsy approach is either transrectal or transperineal. There is no adjusting for the distortion of the prostate due to the pressure of the transrectal ultrasound probe as the process of rigid image registration overlays MRI images to TRUS images [39]. Conversely, elastic fusion is expected to be more accurate than rigid image registration because it adapts to deformation.

The paper demonstrated that the median detection rate of any cancer was 43.4% (range: 14.3–59%) and 50.5% (range: 23.7–82.1%) with the use of the standard biopsy and the MRI-TRUS image fusion biopsy, respectively. The median detection of clinically significant disease was 23.6% (range: 4.8–52%) for standard biopsy and 33.3% (range: 13.2–50%) for MRI-TRUS image fusion targeted biopsy. Across all the studies, the MRI-TRUS targeted biopsy resulted in the detection of the greater numbers of clinically significant cancers compared to the standard biopsy. Some authors reported that there was more clinically insignificant disease detected in the standard biopsy than with the software-based method [40].

**Conclusion**

TRUS-guided biopsy is still the current standard method for the diagnosis of PCa, although it is limited in the accurate location of suspicious lesions. MRI is the most widespread and accurate technique to detect cancerous lesions of PCa. However, MRI-targeted biopsy is time-consuming and costly. MRI-TRUS image fusion offers the most accurate approach for diagnosing PCa and conducting image-guided prostate biopsy.

**Conflicts of Interest**

The authors have no conflict of interest to declare.

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