



Beyond transrectal ultrasound-guided prostate biopsies: available techniques and approaches

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Abstract

Objectives Recent advances have led to the use of magnetic resonance imaging (MRI) alone or with fusion to transrectal ultrasound (TRUS) images for guiding biopsy of the prostate. Our group sought to develop consensus recommendations regarding MRI-guided prostate biopsy based on currently available literature and expert opinion.

Methods The published literature on the subject of MRI-guided prostate biopsy was reviewed using standard search terms and synthesized and analyzed by four different subgroups from among the authors. The literature was grouped into four categories—MRI-guided biopsy platforms, robotic MRI–TRUS fusion biopsy, template mapping biopsy and transrectal MRI–TRUS fusion biopsy. Consensus recommendations were developed using the Oxford Center for Evidence Based Medicine criteria.

Results There is limited high level evidence available on the subject of MRI-guided prostate biopsy. MRI guidance with or without TRUS fusion can lead to fewer unnecessary biopsies, help identify high-risk (Gleason $\geq 3 + 4$) cancers that might have been missed on standard TRUS biopsy and identify cancers in the anterior prostate. There is no apparent significant difference between MRI biopsy platforms. Template mapping biopsy is perhaps the most accurate method of assessing volume and grade of tumor but is accompanied by higher incidence of side effects compared to TRUS biopsy.

Conclusions Magnetic resonance imaging-guided biopsies are feasible and better than traditional ultrasound-guided biopsies for detecting high-risk prostate cancer and anterior lesions. Judicious use of MRI-guided biopsy could enhance diagnosis of clinically significant prostate cancer while limiting diagnosis of insignificant cancer.

Keywords Prostate cancer · MRI biopsy · Template biopsy · MRI fusion

Introduction

The role of prostate biopsies has changed, evolving from pure cancer detection to assisting in clinical patient management. As we move more toward strategies such as active

surveillance and focal therapy, the ability to accurately define the location and extent of cancer prior to treatment has become more important. This may be achieved by template-based three-dimensional (3D) cancer mapping, but also to an increasing extent, through magnetic resonance

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image-guided biopsy targeting. This review will discuss commonly used novel techniques for prostate biopsy that may provide benefit over traditional biopsy approaches and highlight the consensus recommendations of the ICUD panel on this topic.

Methodology

The consensus statements in this review were derived from an analysis of the literature consistent with a modified version of the Oxford Centre for Evidence-Based Medicine (June 5th 2001, <http://www.cebm.net>). Briefly, this process involves identification of a specific question, identification and analysis of the relevant literature, synthesis of the evidence, considered judgement of the evidence and generation of a final grade for the recommendation.

Results

Cognitive fusion

Cognitive fusion involves obtaining a diagnostic multiparametric MRI and then using the information gained from the MRI to inform the selection of biopsy cores during a transrectal ultrasound (TRUS)-guided biopsy. Thus, the “fusion” of MRI data onto the ultrasound image is performed in the mind of the operator. Appropriate selection of the area for biopsy can be facilitated by partitioning the prostate into multiple sectors (sextants or octants) and documenting the location of the MRI-suspicious regions according to this map. Cognitive fusion has the advantage of being less expensive and readily available to most practices. A disadvantage is that the approach is extremely user dependent, and accurate targeting of the MRI-suspicious areas cannot be verified. This limitation may be lessened by oversampling of the suspicious region. In addition, sometimes a corresponding abnormality seen on MRI can be detected on ultrasound once particular attention is paid to the area.

Comparative studies of cognitive fusion biopsy against a standard TRUS biopsy show targeting lesions increases the rate of cancer detection, as well as more accurately represents the disease burden and Gleason grade [1–3]. Transperineal cognitive fusion biopsy was shown to detect equal rates of clinically significant prostate cancer with fewer cores sampled when compared to a systematic template-guided transperineal biopsy [4]. A study by Puech et al. [5] reported that while targeted biopsies revealed more cancer than systematic biopsies in men with a suspicion of prostate cancer, there was no significant difference in the cancer yield between men undergoing cognitive fusion or MRI/US fusion biopsies. Thus, overall, cognitive fusion may be beneficial

in increasing cancer detection rates when MRI-suspicious lesions are present compared to systematic TRUS biopsy. However, the ultimate success of this approach will be variable and likely dependent upon the experience and skill of the operator, the size of the prostate, the size and location of the suspicious area as well as the biopsy strategy utilized. Direct MRI or MRI/US fusion guidance systems address some of these limitations, likely providing more consistent results as discussed below.

MRI-compatible prostate biopsy platforms

There are two direct MRI-guided systems commercially available; the DynaCad/DynaTrim system from Invivo (Gainesville, FL, USA) and an MR-compatible robotic system from Soteria Medical (Arnhem, The Netherlands). Near-in-bore MRI-guided biopsies are conducted in two phases; the first phase is the diagnostic multiparametric MRI from which suspicious lesions are identified. Additional T2 and diffusion-weighted images performed at the time of the biopsy with the needle guide in the rectum are utilized to plan delivery of the biopsy needle to the appropriate location [6].

The DynaTrim is a piece of hardware that facilitates the physical targeting of the biopsy needle to the correct location within the prostate. It consists of a disposable endorectal needle guide, a padded plastic baseplate and clampstand which contains the needle guide control apparatus allowing adjustments to be made in three dimensions. Additionally needed are fully MRI-compatible 18 GA spring-loaded biopsy devices.

The Soteria transrectal robotic device is designed to interact with the patient within any standard clinical closed-bore MR system. The entire device is constructed of MR-compatible materials and consists of the robot itself and a controller unit located outside the MR cage of Faraday. Compressed air for the pneumatic motors is delivered via plastic tubes to the robot. The robotic system is fitted with five computer-controlled degrees of freedom for delivering an interventional procedure.

Results using the near-in-bore approach in patients who have had at least one previous negative TRUS biopsy provided some of the best early data demonstrating the utility of MRI-guided targeting approaches for prostate cancer. Roethke et al. [7] reported results in a cohort of 100 patients undergoing MR-guided biopsy for a history of negative TRUS biopsy but persistent concern for cancer, with a clinically significant cancer detection rate of 80.8% (42/52) while Hoeks et al. [8] reported a cancer detection rate of 41% (108/265) in men with at least one previous negative TRUS biopsy, with approximately 90% being clinically significant cancers. Subsequently, Pokorny et al. [9] reported

detecting prostate cancer in 126/223 (56%) men, 47 (37%) of which were low risk, who had not had a previous biopsy.

In addition to transrectal biopsy approaches, Susil et al. [10] reported a system allowing for MRI-guided transperineal prostate biopsies to be performed. This system consists of a lockable positioning arm, (Siemens Medical Systems, Erlangen, Germany), an endorectal coil (USA Instruments, Aurora, OH, USA), and an MRI-compatible custom-built transperineal template. Custom software was developed to allow the tracking of the biopsy needles on the prostate images. In addition, Tokuda et al. [11] have also developed an in-bore MRI-guided transperineal system for prostate biopsy. This system allows for the patient to be placed in stirrups in a low-lithotomy position inside the MRI bore. Open source software (“3D Slicer; <http://www.slicer.org>”) was used to register the images to the transperineal template. MR-compatible needles are inserted by hand, though a motorized needle guide template is under development. [12].

Limited data exists for biopsy results using MR-guided transperineal biopsy platforms. However, Penzkofer et al. [13] reported on a mixed cohort of 87 men who underwent

MR-guided transperineal prostate biopsy for several different indications. The overall cancer detection rate was 57% (51/90). Gleason pattern of 4 or higher was diagnosed in 25/32 (78%) of men with no prior biopsy and the active surveillance groups combined. In addition, Menard et al. [14] published on the use of MR-guided transperineal prostate biopsy to improve determination of tumor boundaries to aid in the targeting of lesions for salvage focal therapy.

Magnetic resonance imaging-ultrasound fusion-guided prostate biopsy

The integration of mpMRI information with transrectal ultrasound has occurred primarily through ‘cognitive’ fusion (see above) or software-based registration platforms via either a transrectal or transperineal approach. These MpMRI–TRUS “fusion platforms,” facilitate guidance of the biopsy needle to the target, and archive the three-dimensional location of the biopsy. The process includes prostate segmentation, image registration, and biopsy tracking (Fig. 1). Software-based platforms share some steps in

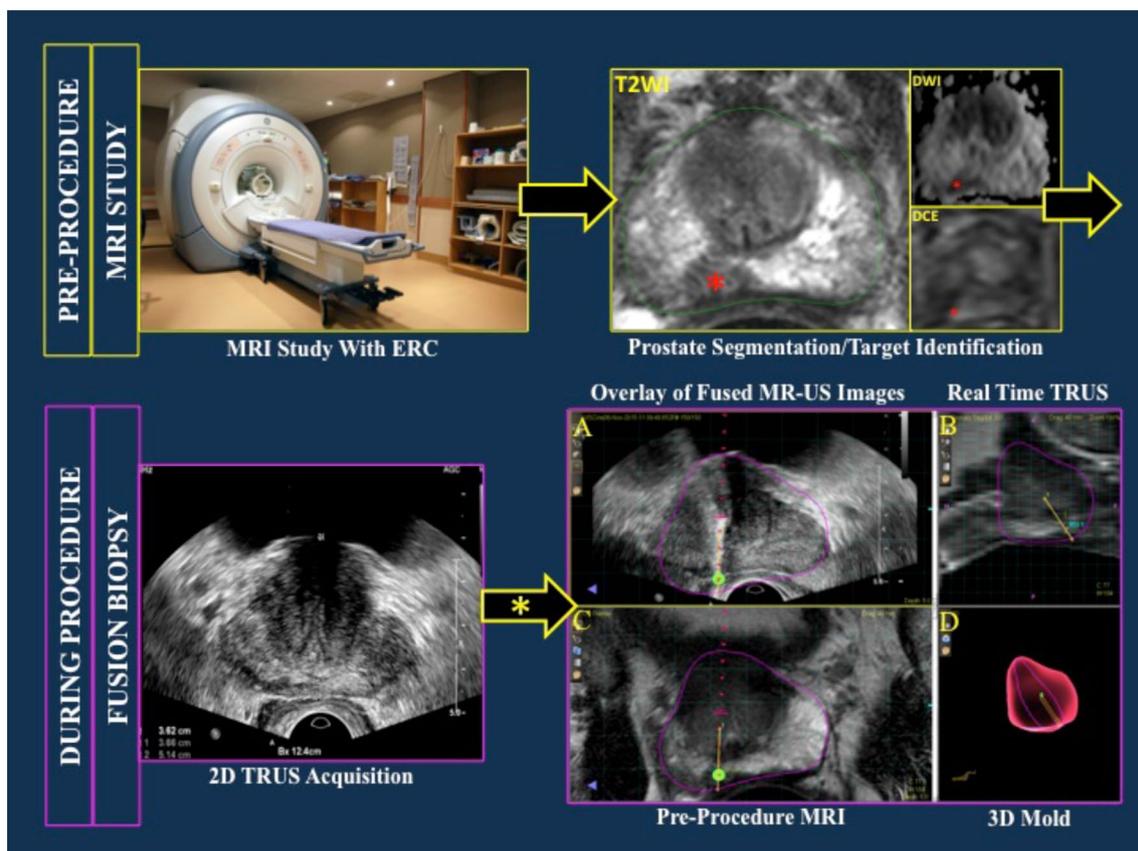


Fig. 1 Work flow for MRI/US fusion prostate biopsy. Multiparametric MRI images are acquired. T2-weighted imaging (T2W), diffusion-weighted imaging (DWI) and dynamic contrast-enhanced sequences are performed. The prostate and lesions identified on MRI are seg-

mented. During the procedure, a 2D TRUS sweep of the prostate is performed, shown in the lower left. The images are semi-automatically registered. The image co-display can be side by side or superimposed

workflow, but can differ in image registration, tracking, and hardware. Individual platforms will be discussed below in the image-tracking section as this is where the biggest differences between platforms exist.

MRI segmentation

Initial multiparametric MRI is performed with or without an endorectal coil at 1.5 or 3 T. The inclusion of the coil improves signal-to-noise ratio and can be especially useful in providing detailed imaging for staging purposes. Segmentation refers to the process by which the T2W MRI image is used to define the outline of the prostate and identify biopsy targets with subsequent transfer of the images to the biopsy workstation. While minor differences exist between platforms in how this is done, the differences are small and the process is fairly consistent.

MRI–US registration

After the processed MRI is imported to the workstation, a 2D TRUS ‘sweep’ of the prostate is completed to create a reconstructed 3D TRUS prostate volume. Semi-automated US segmentation of the prostate margins/contour is performed. Registration is the alignment of the MRI prostate volume with the TRUS volume. Either rigid or elastic registration may be used to ‘fuse’ the MR and US images. Rigid registration permits rotational and translational manipulation of each image set. Registration errors may occur when the MRI and US prostate shape differ, due to organ or patient movement, or organ deformation from the endorectal coil. Elastic registration allows for correction of deformation, warping and changes in scale. Currently, most platforms are capable of both rigid and elastic registration, allowing the operator to select the registration algorithm that produces an optimal alignment.

Biopsy tracking

Fusion platforms allow the ability to track and record the position of the biopsy needle in 3D space. This allows the user to understand on TRUS, the corresponding location on MRI and to guide the needle toward the target. Tracking is accomplished with three methods: (1) electromagnetic tracking, (2) position-encoded joints within smart robotic arms, and (3) image-based tracking. The biggest differences between the commercially available platforms are in the biopsy-tracking technology.

Electromagnetic tracking

Passive electromagnetic tracking is used by a number of commercially available platforms (UroNav, In Vivo;

Virtual Navigator, Esaote; and Real-Time Virtual Sonography, Hitachi). This tracking method uses a magnetic field generator (attached to the table) and sensor (attached to the TRUS probe). The sensor 3D location is tracked within the magnetic field. Electromagnetic tracking maintains a free-hand approach, offering a shallow learning curve since most urologists are familiar with operating a TRUS probe [15]. Once the needle biopsy is taken, mapping is used to archive the location of the biopsy. After recent technical improvements, tracking error within the UroNav system has been reported to be under 3 mm [16]. Siddiqui et al. demonstrated that fusion biopsy with the UroNav platform outperformed systematic biopsy in detecting high-risk prostate cancer [17]. Comparison of cancer detection rates revealed that fusion biopsy diagnosed 30% more high-risk- and 17% fewer low-risk prostate cancers than systematic biopsy suggesting an advantage to this approach.

Like the UroNav platform, the Virtual Navigator and Real-Time Virtual Sonography utilize a freehand TRUS technique with an external electromagnetic field generator for tracking [15]. The Real-Time Virtual Sonography platform may be used in transrectal as well as transperineal biopsies. Although the data on these two platforms are limited, both have shown higher cancer detection rates compared to a standard TRUS biopsy [18, 19].

Mechanical position encoders

Fusion platforms including Artemis, (Eigen, Grass Valley, CA, USA); BiopSee, (Pi Medical, Greece); and BioJet, (BK Ultrasound, Peabody, Massachusetts; DK Technologies, Barum Germany) utilize smart robotic arms with position-encoded joints as a tracking approach. The operator guides the robotic arm while the angle sensors within the arm relay the position of the probe and needle to the platform computer [20]. Though this approach may be unfamiliar to most urologists, adding to the learning curve, the steady arm of the robotic fixture diminishes mechanical error introduced by the user. The Artemis platform uses independent Eigen ProFuse software to build a 3D prostate model and identify biopsy targets using the prebiopsy MRI. This MRI data is semi-automatically aligned with the TRUS images obtained from the initial “sweep”. Navigation capabilities aid in guiding the operator to the targets and the system records the location of the biopsy site. With this, the operator can return to the site of biopsy with 2–3 mm of accuracy. A recent analysis of combined MR–US fusion/systematic versus MR–US fusion alone versus systematic biopsy alone revealed an improvement in the diagnosis of Gleason ≥ 7 prostate cancer with a combined approach (35.0 vs. 27.8 vs 24.1%, $p < 0.01$) [21].

The BioXbot robot is a transperineal biopsy system which implements a robotic arm to guide needle biopsies

[22, 23]. The system houses a movable platform with six degrees of rotational freedom. This system is distinct from the Artemis system in that it utilizes a motorized automated mechanism for needle alignment within the 3D model. The urologist selects biopsy targets on the image and the 3D prostate model, and the system simulates the needle trajectory through the targets. Once approved by the urologist, the robotic platform then aligns the biopsy needle guide to target each selected biopsy location, with reported targeting accuracy within 2 mm [23]. All needle trajectories within each side of the prostate pass through a single puncture in the perineal skin on that side, which serves as a pivot point.

Limited clinical outcomes data using the BioXbot system are available. A small pilot study of 20 patients demonstrated the safety and feasibility of the device for image-guided transperineal prostate biopsy using visual targeting in patients with at least one previous negative biopsy. A mean of 28.5 biopsies were obtained per patient [23]. With the recent implementation of a fusion platform, the system may provide the first opportunity for fusion biopsies using a robotic transperineal approach.

The BiopSee platform contains a TRUS probe on a mechanical stepper fixed to the operating table and sampling is conducted via transperineal approach. The depth and rotational position of the probe is tracked with embedded encoders within the mechanical arm of the stepper. Kuru et al. demonstrated the platform's superior ability to detect clinically significant prostate cancer in patients with MRI targets when compared to a systematic biopsy (38 vs 12%), in men without an MRI target using the BiopSee platform [24].

The BioJet platform uses a TRUS probe attached to a mechanical arm containing angle-sensing encoders. Unlike the BiopSee platform, the BioJet platform is capable of both transrectal and transperineal biopsies. Rigid registration is employed, however, elastic registration has now been piloted [25].

Image-based tracking

Unlike the other platforms, the Urostation (Koelis, France) uses an image-based registration to track the position of the needle. Image-based software registration employs the TRUS images alone. A 3D panoramic volume is generated with the TRUS and registered with the prebiopsy MRI with target information. As each biopsy is obtained, the operator acquires a 3D-TRUS image by holding the probe in place for 3 s. This image is registered to the reference panoramic TRUS volume allowing acquisition of the 3D prostate volume data with digitalized location of each biopsy-trajectory at every fire of the biopsy needle. Position tracking without additional hardware and the ability to use a freehand TRUS probe are both advantages to this approach. Baco et al.

demonstrated fusion-targeted biopsies using the system can reliably predict the location and primary Gleason pattern of an index tumor with 90% or greater accuracy [26].

Robotic in-bore MRI-guided biopsy

In addition to MRI ultrasound fusion platforms guided by TRUS, robotic systems have been introduced to facilitate true in-bore MRI-guided prostate biopsy [27–29]. Using MRI-compatible components, these systems incorporate automated needle insertion, allowing for truly real-time MRI visualization [30, 31] and precise needle localization, within 2–5 mm [29, 32]. Most trials investigating in-bore MRI-guided prostate biopsy in humans have used transrectal or transgluteal needle insertion approaches. Recently, Tilak et al. employed a transperineal approach among 99 men undergoing in-bore biopsy, and compared targeting accuracy between robotic and manual targeting templates [33]. The robotic template-improved needle accuracy as compared to the manual template, yielding mean accuracies of 2.4 vs 3.7 mm, respectively. Several efforts are underway to commercialize applications for in-gantry robots capable of conducting targeted transperineal biopsy.

Template mapping biopsies (TMB): an accurate method of risk stratification for prostate cancer

Transperineal template mapping biopsy (TMB) was developed to provide more accurate risk assessment and localisation of prostate cancer compared to TRUS biopsies [34]. TMB is based on the transperineal approach and allows access to all areas of the prostate including the apex and anterior aspects, provides excellent disease localisation and avoids the risk of infection associated with the transrectal route. The potential disadvantages include the use of a general anaesthetic, or sedo-analgesia, along with an increase in the risk of urinary retention compared to a standard TRUS approach.

Approaches to transperineal template mapping biopsy

There is considerable variation between clinicians in the detail of the practice of TMB. When reviewing different protocols it is important to keep two key points in mind:

- The diagnostic performance for detection of any cancer, and estimation of maximum size and grade is related to the sampling density (cores per ml of prostate).
- The accuracy of assigning a positive biopsy to a given location in the prostate will depend on the number of discrete areas that the gland is divided into for the purposes of identifying the biopsy specimens.

The 5 mm mapping approach

One approach to TMB described by Barzell and Melamed reported dividing the prostate into 26 separate zones each sampled separately [35]. The prostate is divided cranio-caudally into apical and basal portions and sampled every 5 mm. A 5 mm sampling density provides similar diagnostic performance for the detection of any cancer, however, the cores are obtained. The localization accuracy is inversely related to the number of zones into which the biopsy specimens are separated. The need for localization will be dependent on the therapeutic options available—if whole gland treatment is the only available option then localization may inform nerve sparing or resection margins at radical prostatectomy, whereas a focal ablation approach based on a suspicious MRI lesion rather than a hemi or quadrant ablation would require a more precise zonal localization strategy for biopsies.

Sector-based sampling

Many of the publications on TMB describe a more limited number of biopsies per gland which is sometimes termed ‘saturation biopsies’. Saturation biopsies tend to employ a set number of biopsies in pre-specified regions of the prostate. For example, Symons et al. [36] employed a 22 sample protocol from 14 zones in the prostate irrespective of prostate volume, whilst Gershman et al. [37] concentrated their biopsies on the anterior aspect of the prostate in a cohort of men who had not shown any cancer on a previous standard transrectal biopsy.

One of the less-intensive sampling methods that is being used at Guy’s Hospital in the UK is the template sectoral approach described by Vyas et al. [38]. This approach preferentially, but not exclusively, targets the peripheral zone by dividing the gland into anterior, mid and posterior segments targeting additional basal sectors in glands above 50 cc. The rationale is to reduce biopsies of the transition zone in an attempt to minimize bleeding and urinary retention. Others consider that, as around a quarter of prostate cancer at radical prostatectomy is found in the anterior gland [39–43] and there is a relatively low incidence of side effects with either approach [44], a more intense sampling of the transition zone is justified.

Complications and side effects of TMB

When comparing the side effects of TMB, the most notable difference to TRUS biopsy is the incidence of urinary retention which varies from 4 to 11% [44–46], compared to 0.2–2.6% for a standard transrectal approach [47]. An advantage is the lower risk of hospital admission for sepsis which is usually < 1% for a transperineal approach [44]

compared with up to 3% for a transrectal approach [47]. Some authors have reported a few men with transient difficulties with erectile function after an intensive transperineal biopsy sampling, but this is not rigorously reported [44]. Additionally, the morbidity of general anesthetic is a very small added risk, and TMB can be performed in a limited manner under local and periprostatic anesthesia [34].

The diagnostic performance of TMB in the recent literature

When considering the diagnostic performance of any prostate biopsy approach, it is important to consider both the helpful diagnosis of clinically significant disease and the unwanted diagnosis of clinically insignificant disease. Whilst TMB can significantly increase the diagnosis of clinically significant disease compared to a standard transrectal biopsy, it will also increase the diagnosis of clinically insignificant disease. When detection of any cancer is reported as the primary outcome, detection rates of 56–73% have been shown [36, 48].

The diagnostic performance of TMB is demonstrated best on direct comparison with standard transrectal biopsy. Several authors have demonstrated this value in cohorts of patients who have had previous negative TRUSBx with continued suspicion of prostate cancer, reporting detection rates in the order of 60% [36, 48, 49]. A significant proportion of these lesions were located anteriorly and in areas commonly under-sampled by standard transrectal biopsy [50].

Interpreting the results of TMB

It is important to be careful that the increase in the detection of any cancer by an intensive sampling strategy used in TMB does not over-estimate the risk of the disease in a given individual and prompt unnecessary treatment. To assess risk in an intensive sampling approach to the prostate, we cannot apply the same absolute measurements of numbers of cores involved as those approaches that are based on 10–12 core transrectal biopsies. Ahmed et al. at UCL have developed a classification system [49] which attempts to address this, and is useful for both an intensive general sampling strategy and an MRI-directed approach. Ahmed used 3D computer models of 107 whole mount radical prostatectomy specimens to perform 500 TMB simulations per prostate to evaluate the maximum and total cancer core lengths on TMB that are associated with pathological volumes of 0.2 cc and 0.5 cc at radical prostatectomy. They concluded that a maximum cancer core length ≥ 6 mm on a biopsy core represents a lesion with a volume of ≥ 0.5 cc. A cancer core length involvement ≥ 4 mm represents a cancer volume of ≥ 0.2 cc. These findings when considered with the Gleason score detected are the basis of the UCL (University College

Table 1 Consensus statements for MRI-guided biopsy

Consensus statement	LOE	SOR
MRI-guided biopsy can lead to fewer biopsies	3	B
MRI-guided biopsy can detect tumors missed on systematic TRUS biopsy	3	B
MRI-guided biopsy can detect anterior tumors	3	B
There are no significant differences in detection rates between different platforms for MRI-guided biopsy	3	B
Robotic prostate biopsy is a feasible technique	3	C
TMB is the most accurate method of mapping extent and grade of cancer	4	C
5 mm TMB can provide very good spatial information on location and extent of cancer in a given prostate	3	B
TMB carries higher risk of side effects than transrectal biopsy	3	B
MRI–TRUS-guided fusion-targeted biopsy can lead to increased detection of high-risk prostate cancer	2	B
MRI–TRUS-guided fusion biopsy can lead to decreased detection of low-risk prostate cancer	2	B
MRI–TRUS-guided fusion biopsy can detect anterior tumors	3	B

LOE level of evidence, *SOR* strength of recommendation, *TMB* template mapping biopsy, *MRI* magnetic resonance imaging, *TRUS* transrectal ultrasound

London) risk stratification, with 3 mm Gleason 3 + 3 or less being low risk, any secondary Gleason pattern 4 or 4 mm disease intermediate risk and 6 mm of any grade of disease, or any primary pattern 4 being highest risk. These parameters need to be correlated with long-term outcomes to assess their true utility.

TMB as a reference standard

Template mapping biopsies is currently considered an accurate reference standard ideal for research use. It has been employed in both large-scale therapeutic and diagnostic trials and research [51–53]. Its particular advantages include:

- Apart from radical prostatectomy (RP), TMB is the most accurate method for mapping the grade and extent of disease in a given prostate. Yet unlike RP, TMB can be employed prior to and/or after treatment, which is particularly useful in assessing focal therapy modalities.
- Most men recommended a prostate biopsy can undergo a TMB procedure allowing assessment of a large spectrum of cases ranging from large volume high-risk disease to benign prostates. This eliminates the significant bias towards high-risk disease when RP is used as a reference standard.
- 5 mm TMB biopsies provide excellent spatial information on the location and extent of a given lesion in the prostate. If categorized accurately with detailed coordinate documentation, they can register a 3D representation of a histological lesion

Template-guided prostate mapping biopsies are the most intensive method of diagnosing and characterizing prostate cancer short of radical prostatectomy specimens. They are not susceptible to the systematic errors of standard

transrectal biopsy and can detect disease not well detected by standard transrectal biopsy with an acceptable side-effect profile.

Conclusion

Both TMB- and MRI-targeted biopsies seem to improve the assessment of prostate cancer location and extent which is critical for strategies such as focal therapy and active surveillance to be fully realized. TMB serves as an excellent reference standard for research studies. With further validation from larger prospective studies, MRI-targeted biopsy is likely to emerge as the preferred approach for performing prostate biopsy due to the higher likelihood of identifying clinically significant cancer. Based on the extensive review of the current literature, a series of consensus recommendations are outlined in Table 1.

MR-guided biopsy represents the first large-scale interventional application to take advantage of mpMRI for prostate cancer. This approach may require fewer biopsies to gain similar if not better information regarding the presence of clinically significant disease. In addition, it is apparent that an advantage of MR-guided biopsies is in the detection of anterior tumors which may not be sampled routinely on TRUS-guided biopsies [13, 54, 55]. However, it is also apparent that MRI-guided biopsies are not perfect. A recent study utilizing a fusion platform demonstrated that 16% of patients without MR lesions harbored clinically significant prostate cancer on systematic biopsy which also identified 15 additional patients with high-risk disease (Gleason \geq 8) missed with MR–US fusion alone [21]. Nonetheless, despite current limitations, regardless of platform used, it is apparent that MR-guided biopsy will see an expanded set of indications in the future.

References

- Haffner J et al (2011) Role of magnetic resonance imaging before initial biopsy: comparison of magnetic resonance imaging-targeted and systematic biopsy for significant prostate cancer detection. *BJU Int* 108:E171–E178
- Park BK et al (2011) Prospective evaluation of 3-T MRI performed before initial transrectal ultrasound-guided prostate biopsy in patients with high prostate-specific antigen and no previous biopsy. *AJR Am J Roentgenol* 197:W876–W881
- Cerantola Y et al (2016) Accuracy of cognitive MRI-targeted biopsy in hitting prostate cancer-positive regions of interest. *World J Urol* 34:75–82
- Kasivisvanathan V et al (2013) Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. *J Urol* 189:860–866
- Puech P, Rouviere O, Renard-Penna R et al (2013) Prostate cancer diagnosis: multiparametric MR-targeted biopsy with cognitive and transrectal US–MR fusion guidance versus systematic biopsy—prospective multicenter study. *Radiology* 268(2):461–469
- Hambrock T, Hoeks C, Hulsbergen-van de Kaa C et al (2012) Prospective assessment of prostate cancer aggressiveness using 3-T diffusion-weighted magnetic resonance imaging-guided biopsies versus a systematic 10-core transrectal ultrasound prostate biopsy cohort. *Eur Urol* 61(1):177–184
- Roethke M, Anastasiadis AG, Lichy M et al (2012) MRI-guided prostate biopsy detects clinically significant cancer: analysis of a cohort of 100 patients after previous negative TRUS biopsy. *World J Urol* 30(2):213–218
- Hoeks CM, Schouten MG, Bomers JG et al (2012) Three-Tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. *Eur Urol* 62(5):902–909
- Pokorny MR, de Rooij M, Duncan E et al (2014) Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. *Eur Urol* 66(1):22–29
- Susil RC, Camphausen K, Choyke P et al (2004) System for prostate brachytherapy and biopsy in a standard 1.5 T MRI scanner. *Magn Reson Med* 52(3):683–687
- Tokuda J, Tuncali K, Iordachita I et al (2012) In-bore setup and software for 3T MRI-guided transperineal prostate biopsy. *Phys Med Biol* 57(18):5823–5840
- Song SE, Tokuda J, Tuncali K, Tempany CM, Zhang E, Hata N (2013) Development and preliminary evaluation of a motorized needle guide template for MRI-guided targeted prostate biopsy. *IEEE Trans Biomed Eng* 60(11):3019–3027
- Penzkofer T, Tuncali K, Fedorov A et al (2015) Transperineal in-bore 3-T MR imaging-guided prostate biopsy: a prospective clinical observational study. *Radiology* 274(1):170–180
- Menard C, Iupati D, Publicover J et al (2015) MR-guided prostate biopsy for planning of focal salvage after radiation therapy. *Radiology* 274(1):181–191
- Sonn GA, Margolis DJ, Marks LS (2014) Target detection: magnetic resonance imaging-ultrasound fusion-guided prostate biopsy. *Urol Oncol* 32:903–911
- Xu S et al (2008) Real-time MRI–TRUS fusion for guidance of targeted prostate biopsies. *Comput Aided Surg* 13:255–264
- Siddiqui MM et al (2015) Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. *JAMA* 313:390–397
- Miyagawa T et al (2010) Real-Time Virtual Sonography for navigation during targeted prostate biopsy using magnetic resonance imaging data. *Int J Urol* 17:855–860
- Delongchamps NB, Peyromaure M, Schull A, Beuvon F, Bouazza N, Flam T, Zerbib M, Muradyan N, Legman P, Cornud F (2013) Prebiopsy magnetic resonance imaging and prostate cancer detection: comparison of random and targeted biopsies. *J Urol* 189(2):493–499. <https://doi.org/10.1016/j.juro.2012.08.195> (Epub 2012 Oct 8)
- Hadaschik BA et al (2011) A novel stereotactic prostate biopsy system integrating pre-interventional magnetic resonance imaging and live ultrasound fusion. *J Urol* 186:2214–2220
- Filson CP, Natarajan S, Margolis DJ, Huang J, Lieu P, Dorey FJ, Reiter RE, Marks LS (2016) Prostate cancer detection with magnetic resonance–ultrasound fusion biopsy: the role of systematic and targeted biopsies. *Cancer* 122(6):884–892. <https://doi.org/10.1002/cncr.29874> (Epub 2016 Jan 7)
- Ho H, Yuen JSP, Cheng CWS (2011) Robotic prostate biopsy and its relevance to focal therapy of prostate cancer. *Nat Rev Urol* 8:579–585
- Ho H, Yuen JSP, Mohan P, Lim EW, Cheng CWS (2011) Robotic transperineal prostate biopsy: pilot clinical study. *Urology* 78:1203–1208
- Kuru TH et al (2013) Critical evaluation of magnetic resonance imaging targeted, transrectal ultrasound guided transperineal fusion biopsy for detection of prostate cancer. *J Urol* 190:1380–1386
- Tewes S et al (2015) Targeted MRI/TRUS fusion-guided biopsy in men with previous prostate biopsies using a novel registration software and multiparametric MRI PI-RADS scores: first results. *World J Urol* 33:1707–1714
- Baco E et al (2015) Magnetic resonance imaging–transrectal ultrasound image–fusion biopsies accurately characterize the index tumor: correlation with step-sectioned radical prostatectomy specimens in 135 patients. *Eur Urol* 67:787–794
- Futterer J, Barentsz JO (2012) MRI-guided and robotic-assisted prostate biopsy. *Curr Opin Urol* 22:316–319
- Elhawary H, Zivanovic A, Rea M et al (2006) The feasibility of MR-image guided prostate biopsy using piezoceramic motors inside or near to the magnet isocentre. *Med Image Comput Assist Interv* 9:519–526
- Schouten M, Bomers JR, Yakar D et al (2012) Evaluation of a robotic technique for transrectal MRI-guided prostate biopsies. *Eur Radiol* 22:476–483
- Elhawary H, Tse Z, Rea M et al (2010) Robotic system for transrectal biopsy of the prostate: real-time guidance under MRI. *IEEE Eng Med Biol Mag* 29:78–86
- Zangos S, Melzer A, Eichler K et al (2011) MR-compatible assistance system for biopsy in a high-field-strength system: initial results in patients with suspicious prostate lesions. *Radiology* 259:903–910
- Xu H, Lasso A, Guion P et al (2013) Accuracy analysis in MRI-guided robotic prostate biopsy. *Int J Comput Assist Radiol Surg* 8:937–944
- Tilak G, Tuncali K, Song S-E et al (2015) 3 T MR-guided in-bore transperineal prostate biopsy: a comparison of robotic and manual needle-guidance templates. *J Magn Reson Imaging* 42:63–71
- Barzell W, Whitmore W, Andriole G (2003) How to perform transperineal saturation prostate biopsy: technique addresses diagnostic, therapeutic dilemmas that arise following TRUS biopsies. *Urol Times* 31:41
- Barzell WE, Melamed MR (2007) Appropriate patient selection in the focal treatment of prostate cancer: the role of transperineal 3-dimensional pathologic mapping of the prostate—a 4-year experience. *Urology* 70:S27–S35

36. Symons JL, Huo A, Yuen CL et al (2013) Outcomes of transperineal template-guided prostate biopsy in 409 patients. *BJU Int* 112:585–593
37. Gershan B, Zietman AL, Feldman AS, McDougal WS (2013) Transperineal template-guided prostate biopsy for patients with persistently elevated PSA and multiple prior negative biopsies. *Urol Oncol* 31:1093–1097
38. Vyas L, Acher P, Kinsella J et al (2014) Indications, results and safety profile of transperineal sector biopsies (TPSB) of the prostate: a single centre experience of 634 cases. *BJU Int* 114:32–37
39. Reissigl A, Pointner J, Strasser H, Ennemoser O, Klocker H, Bartsch G (1997) Frequency and clinical significance of transition zone cancer in prostate cancer screening. *Prostate* 30:130–135
40. Augustin H, Erbersdobler A, Graefen M et al (2003) Biochemical recurrence following radical prostatectomy: a comparison between prostate cancers located in different anatomical zones. *Prostate* 55:48–54
41. Stamey TA, Donaldson AN, Yemoto CE, McNeal JE, Sozen S, Gill H (1998) Histological and clinical findings in 896 consecutive prostates treated only with radical retropubic prostatectomy: epidemiologic significance of annual changes. *J Urol* 160:2412–2417
42. Noguchi M, Stamey TA, Neal JE, Yemoto CE (2000) An analysis of 148 consecutive transition zone cancers: clinical and histological characteristics. *J Urol* 163:1751–1755
43. McNeal JE, Redwine EA, Freiha FS, Stamey TA (1988) Zonal distribution of prostatic adenocarcinoma. Correlation with histologic pattern and direction of spread. *Am J Surg Pathol* 12:897–906
44. Losa A, Gadda GM, Lazzeri M et al (2013) Complications and quality of life after template-assisted transperineal prostate biopsy in patients eligible for focal therapy. *J Urol* 189:1291–1296
45. Merrick GS, Taubenslag W, Andreini H et al (2008) The morbidity of transperineal template-guided prostate mapping biopsy. *BJU Int* 101:1524–1529
46. Buskirk SJ, Pinkstaff DM, Petrou SP et al (2004) Acute urinary retention after transperineal template-guided prostate biopsy. *Int J Radiat Oncol Biol Phys* 59:1360–1366
47. Liss MA, Ehdaie B, Loeb S, Meng MV, Raman JD, Spears V, Stroup SP (2017) An update of the American Urological Association white paper on the prevention and treatment of the more common complications related to prostate biopsy. *J Urol* 198(2):329–334. <https://doi.org/10.1016/j.juro.2017.01.103> (Epub 2017 Mar 29)
48. Bittner N, Merrick GS, Bennett A et al (2015) Diagnostic performance of initial transperineal template-guided mapping biopsy of the prostate gland. *Am J Clin Oncol* 38:300–303
49. Ahmed HU, Hu Y, Carter T et al (2011) Characterizing clinically significant prostate cancer using template prostate mapping biopsy. *J Urol* 186:458–464
50. Mabjeesh NJ, Lidawi G, Chen J, German L, Matzkin H (2012) High detection rate of significant prostate tumours in anterior zones using transperineal ultrasound-guided template saturation biopsy. *BJU Int* 110:993–997
51. Barzell WE, Melamed MR, Cathcart P, Moore CM, Ahmed HU, Emberton M (2012) Identifying candidates for active surveillance: an evaluation of the repeat biopsy strategy for men with favorable risk prostate cancer. *J Urol* 188:762–768
52. Onik G, Miessau M, Bostwick DG (2009) Three-dimensional prostate mapping biopsy has a potentially significant impact on prostate cancer management. *J Clin Oncol* 27:4321–4326
53. Onik G, Barzell W (2008) Transperineal 3D mapping biopsy of the prostate: an essential tool in selecting patients for focal prostate cancer therapy. *Urol Oncol* 26:506–510
54. Ouzzane A, Puech P, Lemaitre L et al (2011) Combined multiparametric MRI and targeted biopsies improve anterior prostate cancer detection, staging, and grading. *Urology* 78(6):1356–1362
55. Volkin D, Turkbey B, Hoang AN et al (2014) Multiparametric magnetic resonance imaging (MRI) and subsequent MRI/ultrasound fusion-guided biopsy increase the detection of anteriorly located prostate cancers. *BJU Int* 114(6b):E43–E49