Prostate cancer is the most common cancer in men, with a one in eight lifetime risk and 46,690 new cases diagnosed in the UK in 2014.\textsuperscript{1} Between 1979 and 2011 the incidence of prostate cancer in the UK has increased by 155%. The introduction of PSA testing and systematic transrectal ultrasound (TRUS) biopsies is responsible for a significant proportion of these new diagnoses.\textsuperscript{2} Over the same period survival rates for prostate cancer have dramatically improved, with a 10-year survival rate of 25% in 1981 compared with 84% in 2011.\textsuperscript{3} While this is partly explained by improvements made in treatment protocols, the introduction of PSA testing and TRUS-guided biopsy has seen a significant shift in the disease stage at diagnosis with a large proportion of men diagnosed with early stage disease or clinically insignificant prostate cancer. Conversely, clinically significant prostate cancer (csPCa),\textsuperscript{4,6} remains prevalent and is the second most common cause of male cancer deaths in the UK and Ireland.

Current methods for the investigation of prostate cancer with PSA testing and non-targeted TRUS biopsy have a low sensitivity and specificity for the diagnosis of csPCa.\textsuperscript{7} Multiparametric prostate MRI (mpMRI) prior to prostate biopsy and subsequent image-guided targeted biopsy of suspicious prostate lesions are becoming standard practice. The combination of pre-biopsy mpMRI and image-guided targeted biopsy have been shown to significantly improve the sensitivity for detection of clinically significant prostate cancers.\textsuperscript{8} A number of approaches to MRI-guided prostate biopsy have been reported including ultrasound-guided fusion biopsy (transrectal or transperineal) and in-bore MRI-guided biopsy. This article will review the different approaches and highlight the advantages and challenges with each method.

**Introduction**

**MRI guided prostate biopsy: The future for prostate cancer diagnosis?**

**Ultrasound-guided MRI fusion biopsy**

Ultrasound fusion biopsy can be performed by a transrectal approach or transperineal approach and with either cognitive or software-based fusion.

**TRUS cognitive fusion biopsy**

In this technique, the pre-biopsy MRI is reviewed and a target lesion is identified. TRUS biopsies are targeted to this site ‘cognitively’ fusing the real-time ultrasound images with the MR images which can be viewed on a separate monitor at the time of the procedure if desired. There is no formal fusion of MR and US images, instead relying on the operator’s ability to correlate MR and US anatomy to target the biopsy. The technique requires an experienced operator familiar with the prostate imaging planes on US and MRI in order to accurately target the tumour. Disadvantages include reduced accuracy for the detection of small tumours and an inability to formally track biopsy sites. This technique has been shown to be beneficial in the detection of PCa in men with a previous negative TRUS biopsy but persistent high clinical suspicion of prostate cancer.\textsuperscript{9} A study evaluating MRI-directed cognitive fusion biopsy of anterior gland lesions in patients with negative TRUS biopsy demonstrated accurate sampling of lesions with 90% positivity rate of PI-RADS category 5 lesions.\textsuperscript{10}

**TRUS software-based fusion biopsy**

The concept of image fusion is already well established for many imaging modalities and enables real-time US images to be fused with MR images. This allows for direct targeting of tumours identified on MRI.

There are multiple fusion platforms available. A pre-procedure MRI is uploaded onto the software package for image co-registration (figure 1). The suspicious lesions are labelled on the MRI and this is then co-registered with the transrectal ultrasound (figures 2 and 3). The biopsy platforms available differ in terms of their image co-registration technique, mechanical versus manual controlledarm and patient movement compensation.\textsuperscript{11}

The ability to target biopsies relies heavily on the accuracy of MRI and US image co-registration. Registration can be rigid or elastic. Rigid registration utilises rotation or magnification of the MRI and US 3D constructs to achieve alignment. Owing to changes in patient position and motion as well as deformation pressure of the TRUS probe, the 3D shape of the prostate will vary between the mpMRI and TRUS resulting in a degree of mis-registration with a rigid approach. Elastic registration allows for real-time deformation of the pre-procedure MRI to try to compensate for changes in prostate shape and position at time of 3D TRUS imaging and is the preferred co-registration technique.

MRI-TRUS software fusion significantly increases the accuracy of biopsy compared to systematic TRUS biopsy. The technique is dependent on accurate interpretation of mpMRI and requires specialised equipment and software as well as formal training, however, it utilises the same principles of standard TRUS biopsy and similarly can be performed in an outpatient setting. Compared to cognitive fusion the use of software fusion automates the complex process of superimposing MRI and US and allows for exact localisation of biopsy sites, enabling repeat targeted biopsies of specified locations.
The risk of sepsis associated with TRUS biopsy is not substantially reduced with either fusion approach as standard systematic cores are usually taken in addition to the fusion cores.

**Transperineal template prostate biopsy**

In transperineal (TP) template prostate biopsy, biopsy needles are introduced through a template grid placed over the perineal skin and multiple cores are taken from the prostate under ultrasound guidance. A biplane transrectal ultrasound probe is used to enable accurate needle placement. TP biopsy is generally performed under general anaesthesia and allows an operator to take multiple cores (between 24-60). Since it is performed through the perineal skin, the risk of sepsis is lower than TRUS biopsy and it allows better access to the anterior gland. There is, however, an increased rate of urinary retention compared with TRUS biopsy.12

The template grid enables systematic mapping of the gland which gives accurate information about the location and grade of tumour. In addition to more systematic sampling, TP biopsy allows better access to the anterior gland compared to TRUS biopsy. Cancer detection rates are improved with an associated upgrading in Gleason scores when compared to TRUS biopsy.13 There is a theoretical risk of increased diagnosis of clinically insignificant prostate cancer, however, this has yet to be adequately delineated.

Fusion template biopsy was performed in the same was as TRUS biopsy fusion biopsy (either cognitively or software-based) to a pre-biopsy MRI.

**In-bore MRI biopsy**

In-bore MRI guided biopsy allows for real-time prostate biopsies via a transrectal or transperineal approach and is highly accurate at targeting abnormalities identified on MRI. Patients undergo a pre-procedure mpMRI and appropriate biopsy targets are selected. The procedure is typically performed under general anaesthesia or conscious sedation. A planning MRI is performed immediately prior to the procedure to allow for target localisation, typically including multiplanar T2 and DWI. A number of software packages are available to assist in biopsy planning and performance, eg DynaTrim system (Invivo, Gainesville, FL). After each biopsy sample, the patient is rescanned to confirm needle localisation. Generally only a small number of targeted cores are taken and systematic sampling is not performed. A transperineal approach can also be performed, with benefits including a reduced rate of urosepsis, improved access to the anterior gland and an ability to perform prostate biopsies in patients with difficult or impossible rectal access.14

Cancer detection rates vary depending on the patient cohort, with detection rates of up to 59%.15 More importantly, the majority of cancers identified are clinically significant, with a systematic review demonstrating csPCa in 81-93% of patients.16 In one study Gleason scores were upgraded in 36.7% of patients with a previous diagnosis of prostate cancer.15

Advantages of this method include the reduced number of cores taken, exact localisation of the biopsy and reduced detection of clinically insignificant prostate cancer compared to TRUS biopsy.17 Disadvantages include the need for specific MR compatible biopsy equipment, a long procedure time utilising finite MRI resources and the use of general anaesthesia/sedation for a transperineal approach. Furthermore, as concurrent systematic biopsies are not performed only MRI detected lesions are sampled, with the diagnostic utility of this technique limited by the sensitivity of MRI for the detection of csPCa. As a result this technique is currently only performed in a limited number of academic centres.

**Discussion**

A number of studies have been undertaken to compare the different image-guided biopsy techniques. A recent meta-analysis18 assessed the cancer detection rates of different MR-guided targeted biopsy techniques compared to systematic TRUS biopsies. Eleven studies with 2,602 patients were included. No significant difference was identified for overall cancer detection rates, however MRI-US fusion targeted biopsies tended to give a higher detection rate for csPCa.19 A similar meta-analysis20 demonstrated no significant difference in total prostate cancer detection rates between combined image-guided biopsy techniques and systematic TRUS biopsy, with a sensitivity of 81% and 83% respectively. However, image-guided targeted biopsies detected significantly more csPCa, with a relative sensitivity of 1.16 (95%CI 1.02-1.32). Importantly, systematic TRUS biopsy was noted to detect twice as many clinically insignificant prostate cancers compared to image-guided biopsy with an increased risk of overtreatment. No significant difference was noted in the sensitivities of in-bore MRI-guided biopsy and MRI-US fusion biopsy, however, cognitive fusion biopsy was noted to be significantly less sensitive than in-bore MRI biopsy.

**Which test to choose?**

A consensus statement published by the American Urology Association and Society of Abdominal Radiology acknowledged the role of image-guided biopsy in patients with a negative TRUS biopsy and persistent clinical suspicion of prostate cancer.21 As availability of mpMRI and image-guided biopsy technology improves, the technique used will likely be tailored to the characteristics of the MRI detected lesion. For example, an in-bore or fusion system may be chosen for small or difficult to access lesions where as cognitive fusion may be used for larger lesions or in settings where a skilled operator does not have access to software based fusion. The choice of technique is also operator dependent; in the United States most biopsies are performed in an office setting where fusion TRUS biopsy maybe the most appropriate test. However, operators with easy access to theatre may use template biopsy as their chosen biopsy method. The use of software fusion may be more appropriate for urologists who are less familiar with interpreting mpMRI, whereas cognitive fusion may work equally well for radio-logists who have a better understanding of the different imaging modalities.

**References**

   statistics-by-cancer-type/prostate-cancer
   statistics-by-cancer-type/prostate-cancer/survival

**Figure 1**
(A) T2W MRI pre-biopsy shows a PIRADS category 4 lesion in the right peripheral zone. In (B) the lesion shows diffusion restriction on the ADC map.

**Figure 2**
Localisation of suspicious MRI lesion prior to image fusion.

**Figure 3**
MRI and US images are coregistered and biopsy of the lesion is performed.