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A decade in image-guided prostate biopsy

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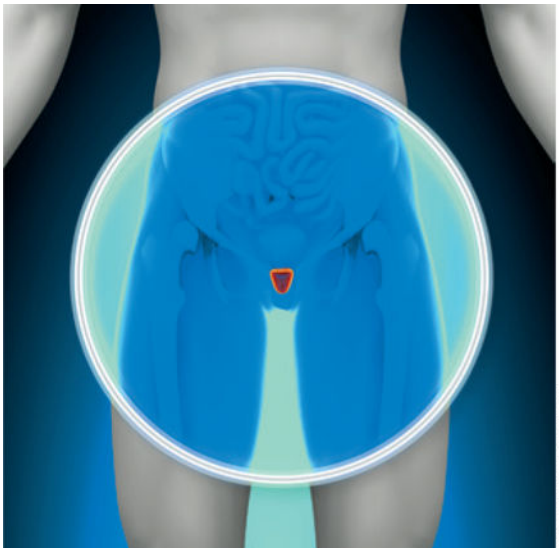
Abstract

The prostate is still largely assessed by random biopsy, but developments in prostate MRI and fusion with transrectal ultrasonography (TRUS) have made targeted biopsy of the prostate a reality. MRI/TRUS techniques promise to address the issues of overdiagnosis and underdiagnosis in prostate cancer.

Graphical Abstract



Unlike biopsies of the breast, thyroid and colon, which are guided into lesions of radiological concern, the prostate is still largely assessed by random biopsy. Transrectal ultrasonography (TRUS)has proven to be rather poor at detecting prostate cancers, so biopsies undertaken using this method are essentially blind. In the meantime, multiple technical improvements have occurred in prostate MRI, which has emerged as the imaging technique of choice for prostate cancer. Specifically, multiparametric MRI (mpMRI) offers high sensitivity through a combination of high-resolution anatomical T2-weighted (T2W) MRI and functional pulse sequences, such as diffusion-weighted MRI (dwMRI), dynamic-

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Competing interests

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contrast-enhanced MRI (DCE MRI) and MR spectroscopy imaging (MRSI). Dramatic technological improvements in dwMRI have meant that, over the past decade, this technique has been more heavily relied upon than the others

The wider availability of high field strength, 3T magnets and new coil designs have substantially improved mpMRI techniques. These methods have proven to be the most accurate yet for identifying localized prostate cancer. However, if mpMRI simply detected lesions but did not enable biopsy of those lesions, it would not be clinically relevant. Thus, from the beginning, attempts were made to biopsy lesions within the MR scanner. Initial efforts focused on in-bore MRI guided biopsies; the main advantage of this approach is that it enables precise lesion sampling. For instance, Hoeks *et al.*[1] performed in-bore MRI guided biopsies in 265 patients with elevated PSA and previous negative TRUS-guided biopsies. Prostate cancer was detected in 41% of patients and the majority of the detected cancers (87%) were clinically significant. Roethke *et al.*[2] investigated the tumour detection rate of in-bore MRI-guided biopsy technique in 100 patients with previous negative TRUSguided biopsy with a tumour detection rate of 52.0%; 80.8% of the detected prostate tumours were clinically significant. However, in-bore MRI-guided biopsies have considerable limitations, such as discomfort related to patient position, increased costs related to long procedure duration and the requirement for special nonmagnetic equipment. Another problem is that there is insufficient MR capacity and expertise to handle the number of patients requiring guided biopsy. This approach has not proved popular with urologists either, as the biopsy is performed in the radiology department and interferes with normal workflow. For these reasons, attempts have been made to perform the biopsy outside the MRI suite while retaining the information afforded by MRI.

The first attempt to transfer MRI information to TRUS-guided biopsy was ‘cognitive fusion’. In cognitive fusion guidance (CFG), the operator first determines the location of the MRI-positive lesions and then guides the needle to that location under real-time TRUS using a ‘best guess’ approach. The main advantage of this technique is that it does not need additional equipment; however, this method depends strongly on the experience and training of the operator and, therefore, results in inconsistent outcomes. The transverse plane on MRI and the transverse plane on an axial TRUS are often different, and excellent hand– eye coordination is required to account for this discrepancy. Also, CFG does not enable documentation of biopsy locations for repeat biopsies and active surveillance. Nevertheless, the impact of the CFG technique has been positive, Haffner *et al.*[3] reported that CFG-targeted biopsies had a sensitivity and specificity of 95% and 100%, respectively, compared with sensitivity and specificity values for extended systematic biopsies of 95% and 83%, respectively. CFG biopsies also detected 16% more highgrade tumours and produced longer mean cancer core lengths (5.56 mm compared with 4.70 mm [$P = 0.002$]) than extended systematic biopsies. However, whether this method can be effective on a broad scale remains to be proven.

The success of CFG prompted interest in new technologies, such as MRI/TRUS fusion, to help guide biopsies based on MRI findings. MRI/TRUS fusion is a collection of technologies that operate under the same principle. First the MRI image is obtained, the prostate is segmented from the remainder of the pelvis and the lesions are identified. Next

the patient is seen in the ultrasonography suite, where a 3D image is obtained, to which the segmented prostate MRI is electronically fused. The TRUS and the MRI are combined so that as the TRUS probe is moved or rotated the corresponding MRI moves and rotates in the same way, which allows the operator to use an MRI obtained at a different time during the TRUS-guided biopsy. MRI/TRUSfusion-guided biopsy is rapidly developing and several commercial instruments are already available

In the original implementation, MRI and TRUS images were linked together using passive electromagnetic tracking sensors that transmit the position of the TRUS probe, allowing the operator to see both MR and TRUS images moving in real-time. Initial results reported by Pinto *et al.*[4] demonstrated that more cancers per core were detected than standard 12-core TRUS-guided biopsy alone. Rastinehad *et al.*[5] reported an overall cancer detection rate of 62.9%, and 14.3% of cancers were only detected using MRI/TRUS-fusion biopsy. Also, approximately 23% of cancers deemed clinically insignificant by 12-core biopsy were found to be clinically significant by MRI/TRUS-fusion biopsy

Replacing the freehand electromagnetic trackers with a mechanical arm that holds the TRUS probe in place is another approach. Once the MRI and TRUS images are fused, the needle and probe positions are tracked by angle-sensing encoders embedded in the joints of the mechanical arm. Using this device, Wysock *et al.*[6] prospectively compared targeted biopsy outcomes between mechanical arm MRI/TRUS-fusion biopsies and CGB. Mechanical arm MRI/TRUS fusion resulted in a 32.0% detection rate compared with 20.3% for CGB for clinically significant cancers, and similar results were observed by Sonn *et al.*[7]

Combining MRI and TRUS images using spatial features alone, without GPS or mechanical arm tracking, enables the TRUS probe to be used freehand. Rud *et al.*[8] evaluated accuracy of this method and reported a 52% tumour detection rate. Delongchamps *et al.*[9] compared the detection rate of CGB with this form of MRI/TRUS biopsy guidance and found the latter to significantly improve detection rates over that of systematic 12-core TRUS-guided biopsy. Targeted biopsies decreased the number of cores needed and the detection of microscopic cancer, and increased the detection of highgrade cancer. However, the accuracy of this method has been questioned.

Transperineal biopsies, which are more common in Europe, can also be guided by MRI using a platform that includes a TRUS probe mounted on a stepper fixed to the operating table. The probe movements are tracked by two encoders and the biopsy needles are placed through a grid mounted to the mechanical stepper, similar to a brachytherapy seed placement setup. Kuru *et al.*[10] evaluated this platform in 347 patients, demonstrating that 58% had prostate cancer and 73.5% of biopsy-proven prostate cancer was clinically significant. The tumour detection rate was 82.6% and 72% of tumours were Gleason score ≥7. Overall, the use of targeted cores detected significantly more cancer than systematic biopsies (30% compared with 8.2%). Thus, the concept of MRI/TRUS fusion has taken hold and multiple companies have jumped into the market to address the need for equipment. No direct comparison of different MRI/TRUS methods exists, but it is clear that all of the methods are superior to the current standard of care. This technology is likely to continue to evolve and replace traditional blind biopsies. However, whilst MRI-guided biopsies are unquestionably

superior to unguided biopsies, they raise concerns over cost, as the MRI and MRI/ TRUS-fusion instruments are expensive. Some costs can be reduced by eliminating the endorectal coil and it is also unclear whether contrast enhancement will be needed in the future. Eliminating these should reduce the cost of MRI/TRUS-fusion techniques. As the technology evolves, market forces should reduce the cost of fusion equipment further, and better clinical guidelines for the selection of candidates for biopsy will emerge, reducing the number of patients requiring this technology.

Over the past decade there has been a distinct change in philosophy regarding the nature of prostate cancer. Previously, prostate cancer was thought to be a multifocal disease that required random sampling to fully identify the extent of disease. However, experience has shown that many cancers are incidental and random biopsies can miss significant disease. Thus, the concept that there are dominant, clinically significant cancers and multiple inconsequential tumours, and that treatment should be determined by the former, is being increasingly accepted. The 12-core random TRUS-guided biopsy is still the standard of care, but there is growing awareness of its limitations and the value of image-guided biopsy. Serum PSA screening significantly increased prostate cancer diagnosis rates; however, it brought challenges of overdiagnosis without addressing the persistent problem of underdiagnosis. Developments in mpMRI have been rapid and impressive over the past 10 years and have enabled better detection and staging of prostate cancer. Using mpMRI in biopsy guidance for prostate cancer diagnosis has the potential to reduce both overdiagnosis and underdiagnosis. As genomic assessment of prostate cancer becomes more important, there will be a premium on obtaining better samples and longer cores of cancer, which can only be provided with imaging guidance. Nonetheless, the ultimate acceptance of MRI/ TRUS-fusion biopsy awaits the results of large-scale multicentre, randomized studies, which are needed to convince clinics to pay for this new technology.

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