NICE National Institute for Health and Care Excellence

NICE guidance

# MRI fusion biopsy systems for diagnosing prostate cancer

Diagnostics guidance
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www.nice.org.uk/guidance/dg53

# Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

# Contents

# 1 Recommendations

1.1 There is not enough evidence to recommend routine adoption of MRI fusion biopsy systems for diagnosing prostate cancer. Centres already using MRI fusion biopsy systems to diagnose prostate cancer may continue to do so but are encouraged to collect data or do further research.

1.2 Further data collection and research is recommended (see the section on further research) to:

- assess the performance of MRI fusion biopsy systems compared with cognitive fusion biopsies to detect different grades of prostate cancer
- assess the impact of using the technology on the rate at which biopsies can be done, and on service capacity to do biopsies.

**Why the committee made these recommendations**

Biopsies for suspected prostate cancer are done using previously taken MRI images and live ultrasound imaging to help the operator guide the biopsy needle (cognitive fusion). In MRI fusion biopsy systems, software overlays the MRI image onto the live ultrasound image (MRI fusion). This could mean fewer cases of prostate cancer are missed and could reduce the number of repeat biopsies.

The clinical evidence is limited because none of the studies are from the UK and none are of high quality. It suggests MRI fusion biopsy systems may detect more higher-grade cancers than with cognitive fusion biopsy, but this is unclear because few higher-grade cancers were detected overall. There is not much evidence comparing the different software fusion technologies with each other. And the technologies differ in their features, so it is not clear if any are better than the others.

The cost-effectiveness estimates depend on how well MRI fusion biopsy systems detect higher-grade cancers compared with cognitive fusion. The estimates suggest that MRI fusion biopsy systems could be cost effective compared with cognitive fusion, but because the clinical evidence is uncertain, the cost-effectiveness estimates are very uncertain.

MRI fusion biopsy systems show promise for better detection of prostate cancer and could help to standardise biopsy quality across the NHS, but more evidence is needed.

# 2 The diagnostic tests

## Clinical need and practice

### Prostate cancer

2.1 The NICE guideline on prostate cancer recommends that a multiparametric MRI test should be offered to people with suspected clinically localised prostate cancer. People with a significant lesion should be offered a multiparametric MRI-influenced prostate biopsy. Based on prostate-specific antigen test results, Gleason score determined by histological analysis of the biopsy, and clinical stage based on the multiparametric MRI scan, people are assigned to risk categories. This informs treatment options (such as active surveillance, radical prostatectomy and radiotherapy).

### Current care

2.2 Targeted biopsies, which take only a small number of tissue samples or cores, are done for suspicious lesions identified by MRI. A systematic biopsy approach, in which multiple samples are taken from different regions of the left and right side of the prostate, can be done alongside a targeted biopsy. This can be done if radiologists are unsure if the lesion is malignant and clinical suspicion of cancer is high. Clinical experts explained that the biopsy approach depends on the information from the multiparametric MRI and individual clinician preference. They commented that practice in the NHS varies.

2.3 Targeted biopsies are usually done using cognitive fusion, in which the previously captured MRI image is visually compared with the live transrectal ultrasound image to guide the biopsy needle. Because of the differences in positioning when a person has an MRI scan compared with when they have an ultrasound scan, the prostate shape differs on MRI and ultrasound images. This can make targeting the lesion difficult.

## Potential value of technologies

2.4 In MRI fusion biopsy systems, the MRI image is fused onto the live ultrasound image to aid biopsy targeting. MRI fusion biopsy systems are indicated for targeted biopsies of suspicious lesions when a small number of tissue samples or cores are taken. The clinical experts commented that, as with cognitive fusion biopsies, systematic biopsies may be done alongside targeted biopsies done using MRI fusion.

2.5 The more samples taken during a prostate biopsy, the higher the risk of adverse events. Refined targeting of the prostate for biopsy could avoid taking unnecessary samples. This could reduce the risk of adverse events such as urinary retention, infection and sepsis after the biopsy. More accurate targeting of suspicious prostate lesions could increase prostate cancer detection rates (missing fewer cases), particularly for people with small lesions. It could also reduce the number of repeat biopsies needed by reducing the risk of missing the cancer in the first biopsy.

# The interventions

2.6 The technologies are systems that include MRI fusion software to assist targeting of prostate biopsies.

## Artemis

2.7 The Artemis fusion biopsy system (InnoMedicus Artemis) includes a semi-robotic mechanical arm and a mobile workstation. The system uses ProFuse radiology software for preparing MRI data for fusion and for reporting findings. The system uses both elastic and rigid estimation to account for changes in the shape of the prostate during the procedure, and supports transrectal and transperineal biopsies. The mechanical arm is used to track the prostate in real time and guide the biopsy needle.

2.8 It is unclear if the system is compatible with third-party ultrasound systems or picture archiving and communication systems (PACS), what its image measurement capabilities are or if it can produce archivable cartograms. No information on costings or regulatory approval has been

received from the company.

## Biojet

2.9 The Biojet MR Fusion system (Healthcare Supply Solutions) comprises MRI fusion software, a mobile workstation, and is compatible with third-party ultrasound systems. The system uses elastic estimations to account for changes in the shape of the prostate during the procedure, and supports transrectal and transperineal biopsies. It supports stabilised and freehand biopsy approaches. For stabilised biopsies, patient movement is tracked through the stepper; freehand biopsies done without the stepper need more manual input from the user.

2.10 The software enables image measurements and a report is generated, graphically showing the sampled areas with exact locations. Biojet can be connected to a local PACS. No information on costings or regulatory approval has been received from the company.

## BiopSee

2.11 The BiopSee system (Medcom) consists of BiopSee software and a MedSta cart (workstation) and is compatible with third-party ultrasound systems. The system uses elastic and rigid estimation to account for changes in the shape of the prostate during the procedure, and supports transrectal and transperineal biopsies. It can be used for stabilised and freehand biopsy approaches. A stabilising arm is available for transperineal stabilised biopsies. Patient movement is tracked through the stepper during stabilised biopsies, or through a magnetic tracker attached to the probe during freehand biopsies. The system can automatically adjust for patient movement, or the user can manually adjust the contours when a patient moves.

2.12 The BiopSee records all positions of the needle and shows the coverage of the prostate. Image measurements such as prostate and lesion volumes are also possible. The data is stored locally and can be connected to a PACS for import and export of images. The software costs £20,000 for transperineal biopsies and £15,000 for transrectal biopsies. The cart for transrectal biopsies costs £12,000, and the cart for

transperineal biopsy costs £8,000 for stabilised biopsy and £20,000 for freehand biopsy.

## bkFusion

2.13 BK Medical UK Ltd and MIM Software Inc offer 3 versions of bkFusion software: 1 for transrectal, 1 for freehand transperineal and 1 for stabilised transperineal biopsies. The software can be integrated into either the bk3000 or bk5000 ultrasound systems. The bkFusion system uses rigid estimation to account for changes in the shape of the prostate during the procedure. The stabilised transperineal fusion system uses a stepper to track the probe position.

2.14 Image measurements such as prostate volume are possible. A report of the biopsy can be saved locally, or transferred to a PACS. The software and cart cost £52,250 (provided for transperineal biopsy only).

## FusionVu (ExactVU system)

2.15 FusionVu is a software feature that enables MRI fusion biopsy as part of the ExactVu micro-ultrasound system (ExactImaging). A stabiliser arm or stepper is available for stabilised biopsies, and freehand biopsies are also possible. The system uses rigid estimation followed by real-time visualisation of the lesions using micro-ultrasound. It supports transperineal and transrectal biopsies. The system tracks and adjusts for patient movement using data from a movement sensor together with the live ultrasound images.

2.16 The software provides image measurements such as prostate volume and lesion size. Information on the orientation of all images and video frames is recorded so that the same position can be found if a repeat biopsy is done. The system is PACS compatible, but Weasis DICOM viewer software is available where a PACS is not available. The ExactVu unit costs £124,958 (includes ultrasound components).

## Fusion Bx 2.0

2.17 The Fusion Bx 2.0 (Focal Healthcare) is a biopsy device comprising a

counterbalanced, semi-robotic arm that is mounted on a mobile cart. The system uses Fusion MR software which is compatible with third-party ultrasound systems. It uses elastic and rigid estimation to account for changes in the shape of the prostate during the procedure, and supports transrectal and transperineal biopsies. The counterbalanced semi-robotic arm can be used as a stepper for stabilised biopsies, or can allow complete freedom of movement for a freehand biopsy. All patient movements are tracked with sensors in the semi-robotic arm.

2.18 The software allows image measurements such as prostate volume and distances to be calculated. Data on the biopsied samples and the regions of interest are recorded on a 3D image of the prostate. The system can connect to a PACS using a wired ethernet or wireless connection. The software costs £24,244 (USD $30,000) and the cart costs £96,974 (USD $120,000).

## iSR'obot Mona Lisa

2.19 The iSR'obot Mona Lisa (Biobot Surgical) is a robotic transperineal prostate biopsy system with MRI-ultrasound fusion capability. The system uses UroFusion software to highlight regions of interest on MRI images and fuses the MRI model with the ultrasound model. A robotic needle guide allows automated positioning and depth control of the biopsy needle to the targeted biopsy core. The system uses elastic estimation to account for changes in the shape of the prostate during the procedure.

2.20 Reports are generated with 3D images and coordinates are recorded for each biopsy sample. No information was received from the company on the tracking of patient movement, whether freehand biopsies can be done, PACS compatibility, image measurement capabilities, costs or confirmation of regulatory approval.

## KOELIS Trinity

2.21 The KOELIS Trinity (KOELIS and Kebomed) is a mobile ultrasound system with mapping fusion software. It comprises PROMAP 3D-Prostate Suite software and the Trinity ultrasound system (workstation, ultrasound

probes, guides specific to transperineal or transrectal biopsies, and a probe holder). The system uses elastic and rigid estimation to account for changes in the shape of the prostate during the procedure, and supports transrectal and transperineal biopsies. It supports stabilised and freehand probe biopsies. The software identifies and compensates for patient movements and changes in the shape of the prostate during the procedure to record each core location.

2.22 The PROMAP software produces a 3D map of the prostate, recording the position of MRI lesion targets and the locations of biopsy samples. The KOELIS Trinity system provides image measurements such as prostate volume, measurements of the regions of interest and other quantitative measurements from the image. Data can be transferred to a PACS. The system costs £23,620, plus £39,948 for transrectal software, £41,754 for transperineal software, and £45,000 for the ultrasound components.

### UroNav

2.23 The UroNav (Phillips) comprises an electromagnetic tracking system, a mobile workstation and DynaCAD Prostate fusion software. The system is compatible with third-party ultrasound systems. It supports transperineal and transrectal biopsies, with stabilised or freehand approaches. The system uses elastic and rigid estimation methods to create 3D images to account for changes in the shape of the prostate during the procedure. The system can be used with a mobile stepper system and 2 navigation sensors to track any movement the person makes.

2.24 The UroNav system provides core location data, images and videos. It works with DynaCAD Prostate fusion software, an image analysis and reporting tool. No information was received from the company on PACS compatibility or costs.

## The comparator

2.25 The comparator for the evaluation is targeted transperineal or transrectal prostate biopsy using cognitive fusion biopsy (using an MRI image to visually estimate the location of interest) with or without systematic

biopsy, under local or general anaesthesia.

# 3 Committee discussion

The diagnostics advisory committee considered evidence on MRI fusion biopsy systems using Artemis, Biojet, BiopSee, bkFusion, Fusion Bx 2.0, FusionVu, iSR'obot Mona Lisa, KOELIS Trinity and UroNav from several sources, including a diagnostics assessment report and an overview of that report. Full details are in the project documents for this guidance.

## Benefits of the technology for people with suspected prostate cancer

3.1 Patient experts explained that technologies that help correctly diagnose prostate cancer could reduce the number of missed cancers and repeat biopsies. Overtreatment was highlighted as a particular issue and concern for patients. During consultation on the draft guidance, a stakeholder further highlighted concerns that higher rates of overdiagnosis from using MRI fusion could lead to potentially higher levels of overtreatment. Any reduction in the number of samples taken during the biopsy could lower the likelihood of biopsy-related complications. Any reduction in the need for further biopsies would help avoid some of the stress and anxiety associated with this. The external assessment group (EAG) stated that there is no evidence of a significant difference in safety outcomes between biopsies done with MRI fusion and cognitive fusion, but that the evidence is limited by poor reporting and at high risk of confounding because of differences in biopsy routes and anaesthesia methods. The patient experts also highlighted that a shorter procedure time could help to preserve dignity and minimise stress and anxiety during the biopsy. During consultation on the EAG's report, stakeholders highlighted the importance of minimising the biopsy procedure time and pain or discomfort, particularly for biopsies under local anaesthetic. They added that stress and anxiety over the biopsy can lead to a poor experience for the person, which can deter them from having additional procedures.

# Clinical effectiveness

## Benefits of MRI fusion biopsy systems from the trials

3.2 The committee agreed that the evidence for MRI fusion technology looked promising, but that there was a lot of uncertainty around the performance of the technology when compared with cognitive fusion. The EAG's network meta-analyses used pooled data from different MRI fusion technologies for its base-case analysis. The results suggested that MRI fusion, compared with cognitive fusion, may detect more International Society of Urological Pathology (ISUP) grade 2 or higher prostate cancer. But whether MRI fusion truly detected more higher-grade cancer, and if so by how much, was very uncertain. The EAG explained that few studies in the meta-analysis included people with higher-grade cancer, and few cases were detected in these studies.

3.3 The committee discussed the limitations of the clinical evidence included in the EAG's meta-analyses. None of the studies were done in the UK. The EAG judged all studies used in the meta-analysis to be at high risk of bias, and it stated that no high-quality randomised controlled trials have been published. The meta-analyses also showed moderate heterogeneity that could not be explained by differences in individual MRI fusion biopsy systems.

## Performance differences between the different MRI fusion biopsy systems

3.4 The committee was uncertain how appropriate it was to use data generated using 1 system to show the performance of others. There was limited data directly comparing the different systems, and evidence levels varied across the different MRI fusion technologies. The EAG combined data from different technologies in its base-case analysis, based on advice from clinical experts. The committee noted that there are fundamental differences between the MRI fusion biopsy systems, which may influence outcomes. Only 2 MRI fusion systems had more than 1 study included in the meta-analysis. For 1 of these (KOELIS Trinity), all studies used a previous version of the software included in

the current device. The company commented that the KOELIS Trinity uses an updated version of the same software included in the KOELIS Urostation (which is now discontinued). The EAG did not identify any evidence for Fusion Bx 2.0 or FusionVu, and none of the identified studies for the bkFusion or ISR'obot Mona Lisa met the inclusion criteria for the meta-analysis. The EAG stated that evidence was insufficient to conclude whether any MRI fusion biopsy systems were superior to others.

## Potential impact on waiting times of adopting MRI fusion biopsy systems

3.5 The committee considered that adopting MRI fusion biopsy systems could prolong waiting time for prostate biopsies, and that this was not captured in the cost-effectiveness estimates. The clinical experts explained that radiologist services are at full capacity in the NHS. Clinical experts with experience using MRI fusion biopsy systems highlighted that more preparatory time is needed per biopsy with MRI fusion than with cognitive fusion, although this does decrease with more experience in using the technology. This lowers the number of biopsies that can be done in a day. In its economic model, the EAG assumed that additional procedure time for MRI fusion use would be 10 minutes in a high throughput centre (5 minutes radiologist time to import and obtain appropriate MRI sequences and 5 minutes during the biopsy), based on expert advice. It was suggested that this would be longer when the technologies were first used, because of lack of experience. The additional time was added to the cost of doing MRI fusion biopsy in the model (for example, for staff time), but the model did not include any impact of this on slowing biopsy throughput. The clinical experts commented that MRI fusion could improve patient throughput if it reduced the repeat biopsies needed (for example, if there was more confidence in a negative biopsy). The EAG commented that how much MRI fusion increases wating times would depend on whether the capacity constraint was access to the biopsy procedure or to the initial MRI (which would be the same for MRI fusion and cognitive fusion biopsy). The committee was also concerned about how adopting software fusion technology could potentially impact how many biopsy procedures can be done per day, and consequently the effect on waiting

times for this procedure.

# Cost effectiveness

## Improving detection of higher-grade prostate cancer makes the technology more cost effective in the model

3.6 The cost-effectiveness estimates for MRI fusion biopsy systems (with or without systematic biopsy), compared with cognitive fusion, were generally favourable, but uncertain. Potential adverse impacts on the capacity of services to do biopsies (see section 3.5) were not considered in the model. The EAG's analysis showed that cost effectiveness was most affected by the improved detection of localised or locally advanced higher-grade cancers (ISUP 2 or higher). When targeted fusion was combined with systematic biopsy, there were more cost savings and health benefits in the long-term model for MRI fusion than for cognitive fusion.

3.7 The EAG cautioned that the uncertainties in the clinical evidence should be considered alongside the overall cost effectiveness, because the evidence used in its network meta-analysis underpinned its economic model. The committee recalled that although the data suggested that MRI fusion may detect more higher-grade cancers, this was very uncertain (see section 3.2). It noted that a scenario analysis done by the EAG in which any benefit to detecting cancer for MRI fusion was removed from the model, the incremental cost-effectiveness ratios (ICERs) increased to over £500,000 per quality-adjusted life year (QALY) gained. The committee concluded that the uncertainty about how much better MRI fusion is at detecting higher-grade cancers means that the cost effectiveness of these technologies, while potentially favourable, is also very uncertain.

## Benefits to less experienced health professionals

3.8 The committee acknowledged that the technology could benefit less experienced healthcare professionals, and help to standardise care across different centres and improve accessibility. The clinical experts

noted that biopsies are done by various healthcare professionals including urologists, radiologists and nurse specialists. The level of experience in doing biopsies varies, and specialist centres are more likely to have professionals with more experience. They suggested that the accuracy of cognitive fusion is highly dependent on the operator. The EAG identified 1 study that reported cancer biopsy positivity rates by operator experience (Stabile et al. 2018). It reported an increase in the biopsy positivity rates in the first 60 procedures, where it plateaued, regardless of the biopsy approach. Operator experience predicted the biopsy positivity rate of targeted biopsies, particularly for transrectal MRI fusion biopsy compared with transrectal cognitive fusion or transperineal MRI biopsy fusion.

3.9 The clinical experts suggested that using MRI fusion biopsy systems could help standardise biopsy quality. They said that this could minimise geographical variation in procedure standard caused by the variation in operator expertise. Improving the ability of less experienced operators to do the procedure may allow it to be available more widely, improving accessibility.

## MRI fusion biopsy systems show promise, but better-quality evidence is needed

3.10 The committee recognised that MRI fusion biopsy systems show promise, could help improve standards across the NHS and patient access (see section 3.9), and may be cost effective. But it felt there was too much uncertainty about how much it would improve detection of prostate cancer to recommend its use for routine adoption (see sections 3.6 and 3.7). Further research is needed to reduce this uncertainty, and so also reduce the uncertainty about the cost effectiveness. The committee was also concerned about how adopting MRI fusion technology could potentially impact how many biopsy procedures can be done per day, and consequently the effect on waiting times for this procedure (see section 3.5). Further data on this would help reduce concerns about the impact of adopting MRI fusion biopsy systems.

# Research considerations

## An ongoing study may fill some evidence gaps

3.11 The ongoing IP7-PACIFIC trial (see trial NCT05574647 on the ClinicalTrials.gov website, accessed 14 November 2022) is likely to provide further, potentially high-quality, data on MRI fusion biopsy systems for detecting clinically significant prostate cancers, compared with cognitive fusion biopsy. The primary outcome of the trial is the proportion of clinically significant cancers (defined as ISUP 2 or above) detected in people who had a biopsy with a suspicious MRI (MRI score 3, 4 or 5 on either the Likert or Prostate Imaging-Reporting and Data System [PI-RADS] schema). The EAG commented that the study aims to recruit 3,600 people with suspected prostate cancer in the UK, but that not all of these people will provide data on MRI fusion performance (the study includes 2 linked randomised controlled trials, and is also comparing biparametric and multiparametric MRI to detect clinically significant prostate cancers). The EAG emphasised that to help inform cost-effectiveness estimates from its model, the numbers of cancer detected by ISUP grade should be reported (rather than just the number of ISUP grade 2 or higher). During consultation on the draft guidance, a stakeholder further highlighted the importance of collecting data on the effect of MRI fusion technologies on detecting clinically insignificant prostate cancer, as well as higher-grade cancers. Given the uncertainty about the generalisability of data generated using 1 MRI fusion technology to others (see section 3.4), it would be beneficial if data was reported separately for each MRI fusion biopsy system. The committee concluded that this will be a useful trial for reducing uncertainty about MRI fusion biopsy performance, but noted that the estimated study completion data is not until 2026. It stated that people should be encouraged to participate in the trial.

## Existing data and resources to collect data

3.12 The clinical experts highlighted that professional bodies such as the British Association of Urological Surgeons and the Royal College of Radiologists may have data that could contribute to a future assessment.

They also suggested that establishing further registries may help data collection. The committee suggested that centres should consider contributing to existing audit tools such as the National Prostate Cancer Audit when possible.

# 4 Recommendations for further research

4.1 Further research is recommended to determine the impact of MRI fusion biopsy systems compared with cognitive fusion biopsy on the detection of different grades of prostate cancer.

4.2 Further data collection or research is recommended on the impact of implementing MRI fusion biopsy systems on the rate at which biopsies can be done, capacity resources and waiting times for this procedure.

# 5 Implementation

NICE intends to develop tools, in association with relevant stakeholders, to help organisations put this guidance into practice.

In addition, NICE will support this guidance through a range of activities to promote the recommendations for further research. The research proposed will be considered for developing specific research study protocols as appropriate. NICE will also incorporate the research recommendations in section 4 into its guidance research recommendations database and highlight these recommendations to public research bodies.

# 6 Diagnostics advisory committee members and NICE project team

## Committee members

This topic was considered by the diagnostics advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the test to be assessed. If it is considered there is a conflict of interest, the member is excluded from participating further in that assessment.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Additional specialist committee members took part in the discussions for this topic:

### Specialist committee members

**Steve Allen**
Patient expert

**Pauline Bagnall**
Uro-oncology nurse specialist, Northumbria Healthcare NHS Foundation Trust

**Oliver Hulson**
Consultant radiologist, Leeds Teaching Hospitals NHS Trust

**Sanjeev Madan**
Consultant urological surgeon, Dartford and Gravesham NHS Trust

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**Graeme Spencer**

Patient specialist

**Lillian White**
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**Hide Yamamoto**
Consultant urologist, Maidstone and Tunbridge Wells NHS Trust

# NICE project team

Each diagnostics assessment is assigned to a team consisting of a technical analyst (who acts as the topic lead), a technical adviser and a project manager.

**Vera Unwin**
Topic lead

**Thomas Walker**
Technical adviser

**Harriet Wilson**
Project manager

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# Accreditation