NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

DIAGNOSTICS ASSESSMENT PROGRAMME

Diagnostics consultation document

MRI fusion biopsy systems for diagnosing prostate cancer

The National Institute for Health and Care Excellence (NICE) is producing guidance on using MRI fusion biopsy systems in the NHS in England. The diagnostics advisory committee has considered the evidence and the views of clinical and patient experts.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from registered stakeholders, healthcare professionals and the public. This document should be read along with the evidence (the diagnostics assessment report and the diagnostics assessment report addendum).

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound, and a suitable basis for guidance to the NHS?

Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the recommendations may need changing to meet these aims. In particular, please tell us if the recommendations:

- could have a different effect on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology

- could have any adverse effect on people with a particular disability or disabilities.

Please provide any relevant information or data you have about such effects and how they could be avoided or reduced.

Note that this document is not NICE's final guidance on MRI fusion biopsy systems. The recommendations in section 1 may change after consultation.

After consultation, the committee will meet again to consider the evidence, this document and comments from the consultation. After considering the comments, the committee will prepare its final recommendations, which will be the basis for NICE's guidance on the use of the technology in the NHS in England.

For further details, see the diagnostics assessment programme manual.

Key dates:

Closing date for comments: 31 January 2023

Second diagnostics advisory committee meeting: 16 February 2023

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 (see section 4).

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). MRI fusion software overlays the MRI image onto the live ultrasound. 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 software fusion biopsy systems may detect more higher-grade cancers than cognitive fusion biopsy, but this is unclear because few higher-grade tumours 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 fusion software detects higher-grade cancers compared with cognitive fusion. The estimates suggest that fusion

biopsy systems could be cost effective compared with cognitive fusion, but because the clinical evidence is uncertain, the cost-effectiveness estimates are uncertain too.

MRI fusion software shows 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 cancer and clinical suspicion 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, the MRI image is fused onto the live ultrasound image to aid biopsy targeting. MRI fusion 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 prostate deformation, 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 prostate deformation 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 prostate deformation, 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 prostate deformation. 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, excluding the ultrasound costs).

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 prostate deformation, 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 prostate deformation.

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 prostate deformation, and supports transrectal and transperineal biopsies. It supports stabilised and freehand probe biopsies. The software identifies and compensates for patient movements and prostate deformations 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 can be used with a mobile stepper system and 2 navigation sensors to track patient movement.

2.24 The UroNav system provides core location data, images and videos. No information was received from the company on image estimation methods for prostate deformation, patient movement tracking feasibility for freehand biopsies, PACS compatibility, image measurement capabilities 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. 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 software 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 biopsies 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 software fusion technologies for its base-case analysis. The results suggested that software fusion, compared with cognitive fusion, may detect more International Society of Urological Pathology (ISUP) grade 2 or higher prostate cancer. But whether software 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 software fusion devices.

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 technology to show the performance of others. There was limited data directly comparing the different technologies, and evidence levels varied across the different software 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 software systems which may influence outcomes. Only 2 software fusion technologies 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 no 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 software fusion technologies were superior to others.

Potential impact on waiting times of adopting MRI fusion biopsy

3.5 The committee considered that adopting MRI fusion software 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 fusion software highlighted that more preparatory time is needed per biopsy with fusion software than with cognitive fusion, although this does decrease with greater 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 software 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 software 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 software 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 software 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 software and fusion biopsy).

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 software fusion biopsy (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 (ISUP2 or higher). When targeted fusion was combined with systematic biopsy, there were more cost savings and health benefits in the long-term model for software 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 software 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 software 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 software fusion is at detecting higher-grade cancers means that the cost effectiveness of these technologies, while potentially favourable, is also 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 software fusion biopsy compared with transrectal cognitive fusion or transperineal software fusion.

3.9 The clinical experts suggested that using MRI fusion biopsy 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 shows promise, but better quality evidence is needed

3.10 The committee recognised that MRI fusion software shows 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 the potential impact of adopting software fusion technology on how many biopsy procedures can be done per day, and consequently on waiting times for this procedure (see section 3.5). Further data on this would help reduce concerns about the impact of adopting software fusion technologies.

Research considerations

An ongoing study may fill some evidence gaps

3.11 The ongoing IP7-PACIFIC trial (NCT05574647, accessed 14 November 2022) is likely to provide further, potentially high quality, data on software fusion biopsy 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 participants will provide data on software fusion performance (the study is 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). Given the uncertainty about the generalisability of data generated using 1 software fusion technology to others (see section 3.4), it would be beneficial if data was reported separately for each fusion software. The committee concluded that this will be a useful trial for reducing uncertainty about software 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 where possible.

4 Recommendations for further research

4.1 Further research is recommended to determine the impact of MRI software fusion biopsy 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 software fusion technologies 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 Review

NICE will regularly monitor its published technology guidance to check for any new evidence or information that could affect the recommendations. Guidance will not have a fixed review date.

Brian Shine

Chair, diagnostics advisory committee

December 2022

7 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

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Urology oncology advanced nurse, NHS Ayrshire & Arran

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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

ISBN: