NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

MRI fusion biopsy in people with suspected prostate cancer

Final scope

May 2022

1 Introduction

Following discussions during the ongoing diagnostics assessment for transperineal biopsy in people with suspected prostate cancer, stakeholders identified MRI fusion biopsy as an area that would benefit from NICE guidance. The topic selection oversight panel selected and routed MRI fusion biopsy for guidance development by the Diagnostics Assessment Programme on the basis of a topic briefing.

The final scope was informed by discussions at the scoping workshop on the 7 April 2022 and the assessment subgroup meeting held on 21 April 2022. A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided to NICE by manufacturers and experts, and information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technologies

Prostate biopsies can be targeted or systematic or a combination of both. A targeted approach takes only a small number of tissue samples or cores, for people who have a suspicious lesion identified by an MRI scan. A systematic biopsy approach is taken where clinical suspicion is high but not reflected in the MRI, and for this multiple samples are taken from different regions of the left and right side of the prostate. A combined targeted and systematic biopsy approach can be taken if lesions are equivocal, and clinical suspicion is high.

Targeting of the prostate biopsy (transrectal or transperineal) is informed by a multi-parametric MRI (mpMRI) or biparametric MRI (bpMRI) obtained prior to the procedure. The image is used to guide the biopsy to areas of interest within the prostate. This is usually done using visual estimation (cognitive fusion) to associate the MR image with the live transrectal ultrasound (TRUS) used during the biopsy procedure. Because of the differences in positioning when a person has an MRI versus when they have an ultrasound, the prostate shape differs on MR and ultrasound images. This deformation of the prostate image can make targeting the lesion more difficult. Where a lesion has been identified by MRI, technologies are available to fuse the MR image onto the live ultrasound (MRI fusion) to aid biopsy targeting. MRI fusion systems are indicated for targeted biopsies of suspicious lesions. They would not be used for solely systematic biopsies.

Before the MRI fusion procedure, the prostate is contoured (outlined to define the shape of the prostate) on the MR images, and lesions or other suspicious areas are also marked on the image. MRI fusion software combines the MRI image to match the shape of the prostate in the live ultrasound. The technologies can be used for transrectal or transperineal biopsies. A 3D image of the prostate generated by the fusion software helps the clinician visualize the position of the biopsy cores. A report including information about any regions of interest and biopsy positions can be generated. Some MRI fusion systems are currently used in NHS practice.

Clinical experts explained that 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 following the biopsy. More accurate targeting of suspicious prostate lesions could increase prostate cancer detection rates (missing fewer cases) particularly for people with small lesions, and could reduce the number of repeat biopsies needed, leading to improved outcomes for people with prostate cancer.

The technology could benefit people who have had a negative biopsy previously, for example people having a follow-up appointment.

The technology is contraindicated for people who can’t have an MRI scan, or do not have a suspicious lesion on their MR image.

2.2 Product properties

MRI fusion software may be compatible with any ultrasound device, or the software may require proprietary hardware such as specified ultrasound probes or workstations. Software packages may also differ in their compatibility with fixed (using a probe holder for steadying) or freehand

(without additional supports) ultrasound probes. Some systems also offer additional features such as a stabilising arm or robotic arm to help with the biopsy procedure. The software can be ‘elastic’, which reflects deformation of the prostate as the probe moves through the rectum, or ‘rigid’, where some rotational adjustments are made to the overlaid MRI and ultrasound images (Bass et al., 2021). The systems also track patient movement in real-time, so that adjustments can be made during the biopsy.

The technologies suggested for the assessment are systems that include MRI fusion software that overlay the diagnostic MR image with the real-time TRUS image, to assist targeting of prostate biopsies. The essential criteria identified for technologies to be included in the final scope are listed below:

- intended for use in people with suspected prostate cancer
- available in the UK
- holds a CE-mark
- is compatible with MRI scanners of 1.5 Tesla field strength or above

The identified technologies are summarised in table 1.

2.2.1 Artemis (InnoMedicus Artemis)

The Artemis fusion biopsy system includes a semi-robotic mechanical arm and a mobile workstation. The system uses the ProFuse radiology software for preparation of MRI data for fusion and for reporting findings on the ARTEMIS biopsy system. The system uses both elastic and rigid estimation to account for prostate deformation, and supports both transrectal and transperineal biopsies. The mechanical arm is used to track the prostate in real-time and guide the biopsy needle accordingly.

No information on its compatibility with Picture Archiving and Communication Systems (PACS), image measurement capabilities and ability to produce archivable cartograms has been received from the company.

2.2.2 BioJet (Healthcare Supply Solutions Ltd)

The BioJet MR Fusion system comprises MRI fusion software, a mobile workstation, and is compatible with third party ultrasounds. The system uses elastic estimations to account for prostate deformation and supports both transrectal and transperineal biopsies. The system supports both stabilised and freehand biopsy approaches. For stabilised biopsies patient movement is tracked through the stepper, whereas freehand biopsies done without the stepper need more manual input from the user.

The software enables image measurements and a report with detailed information is generated, graphically showing the sampled areas with exact locations. BioJet can be connected to a local PACS.

2.2.3 BiopSee (Medcom)

The BiopSee consists of the BiopSee software and the MedSta cart (workstation) and is compatible with third party ultrasounds. The system uses both elastic and rigid estimation to account for prostate deformation, and supports both transrectal and transperineal biopsies. The system 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 which is 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.

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.

2.2.4 bkFusion (BK Medical UK Ltd and MIM Software Inc)

BK Medical UK Ltd offers 3 versions of bkFusion software: one for transrectal, one for freehand transperineal and one for stabilised transperineal biopsies. The software can be integrated into either the bk3000 or bk5000 ultrasounds. The bkFusion system uses rigid estimation to account for prostate deformation. Predictive Fusion software reorientates the MRI image before the biopsy. The transrectal and freehand transperineal fusion systems use a magnetic field generator and sensor to track the probe position. The stabilised transperineal fusion system uses a stepper to track the probe position.

Image measurements such as prostate volume are possible. A detailed report of the biopsy can be saved locally, or transferred to a PACS.

2.2.5 Fusion Bx 2.0 (Focal Healthcare)

The Fusion Bx 2.0 is a biopsy device comprising a counterbalanced, semi-robotic arm that is mounted to a mobile cart. The Fusion Bx 2.0 uses Fusion MR software which is compatible with third party ultrasounds. The system uses both elastic and rigid estimation to account for prostate deformation, and supports both transrectal and transperineal biopsies. The counter-balanced semi-robotic arm can be used as a stepper for stabilised biopsies, or can

allow complete freedom of movement for use during a freehand biopsy. All patient movements are tracked with sensors inside the semi-robotic arm.

The software allows image measurements such as prostate volume and distances can 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 PACS using a wired Ethernet or WiFi connection.

2.2.6 ExactVu (ExactImaging)

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

The software provides image measurements such as prostate volume and lesion size. Information on the orientation of all images and video frames are 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.

2.2.7 iSR'obot Mona Lisa (Biobot iSR'obot)

The iSR'obot Mona Lisa is a robotic transperineal prostate biopsy system with MRI-ultrasound fusion capability. The system uses UroFusion software to highlight regions of interest on MR images and fuses the MRI model with the ultrasound model. The 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.

Reports are generated with 3D images and precise coordinates are recorded of each biopsy sample. No information on the tracking of patient movement, whether freehand biopsies can be done, PACS compatibility and image measurement capabilities of this system has been received from the company.

2.2.8 KOELIS Trinity (KOELIS and Kebomed)

The KOELIS Trinity is a mobile ultrasound system with mapping fusion software. It comprises PROMAP 3D-Prostate Suite software and the TRINITY ultrasound system (workstation, RECFIRE ultrasound probes, guides specific

to transperineal or transrectal biopsies, and a Steady Pro probe holder). The system uses both elastic and rigid estimation to account for prostate deformation, and supports both transrectal and transperineal biopsies. It enables both stabilised and freehand probe biopsies. The Organ Based Tracking Fusion software identifies and compensates for patient movements and prostate deformations to record each core location.

The PROMAP software produces a 3D map of the prostate recording the position of MRI lesion targets and location of biopsy samples. The KOELIS Trinity provides image measurements such as prostate volume, exact measurements of the regions of interest and other quantitative measurements of the image. Data can be transferred to a PACS.

2.2.9 UroNav Fusion Biopsy System (Phillips)

The UroNav Fusion Biopsy System comprises an electromagnetic tracking system, a mobile workstation and DynaCAD Prostate fusion software. The system is compatible with third party ultrasounds. It supports both transperineal and transrectal biopsies, with stabilised or freehand approaches. The system can be used with the UroNav mobile stepper system and the two navigation sensors to track patient movement.

The UroNav Fusion Biopsy system provides the core location data, images and videos. No information on image estimation methods for prostate deformation, patient movement tracking feasibility for freehand biopsies, PACS compatibility and image measurement capabilities of this system has been received from the company.

Table 1 Summary of technologies

MRI Fusion system	Manufacturer	Hardware system	Fixation for biopsies	Elastic or rigid estimation
ARTEMIS Fusion Biopsy System	InnoMedicus Artemis	ARTEMIS	Stabilised, Freehand unknown, Semi-robotic arm	Both
BioJet	Healthcare Supply Solutions Ltd	Third party ultrasounds	Stabilised, Freehand (without tracking movement)	Both
BiopSee	Medcom	MedSta or third party ultrasounds	Stabilised, Freehand	Both
bkFusion	BK Medical UK Ltd and MIM Software Inc	BK3000 or BK5000	Stabilised, Freehand	Rigid
Fusion Bx 2.0	Focal Healthcare	Third party ultrasounds	Stabilised, Freehand, Robotic arm	Both
FusionVu	Exact Imaging	ExactVu	Stabilised, Freehand	Rigid
iSR'obot™ Mona Lisa	Biobot iSR'obot	iSR'obot™ Mona Lisa	Stabilised, Freehand unknown, Robotic arm	Elastic
KOELIS Trinity	KOELIS and Kebomed	TRINITY ultrasound system	Stabilised, Freehand	Both
UroNav Fusion Biopsy System	Phillips	Third party ultrasounds	Stabilised, Freehand	Unknown

3 Target conditions

3.1 Prostate cancer

The prostate is a small gland which sits underneath the bladder and surrounds the urethra in men. Its main function is the production of seminal fluid, a component of semen. Prostate cancer is a malignant tumour of the prostate and is the most commonly diagnosed cancer in men the UK (Cancer Research UK). In 2018, more than 49,000 new prostate cancer diagnoses were made in England (PHE Cancer registration statistics 2018) and about 1 in 8 men get prostate cancer at some point in their life. Prostate cancer accounts for around 13% of all cancer deaths in men in the UK, with around 11,900 deaths in the UK each year (Cancer Research UK). It mainly affects people over 50 years old and the risk of developing prostate cancer increases with age. The risk is higher for people of African family background and people with a family history of prostate cancer. Some prostate cancer can be slow growing and therefore does not cause any problems or affect a person's life expectancy. In this situation people may not require any treatment. However, some prostate cancer can grow more quickly and is more likely to spread. This may require treatment to prevent it spreading and causing further problems. When diagnosed at the earliest stage, most people with prostate cancer survive 5 years or more.

Localised prostate cancer is confined to the prostate and is usually asymptomatic. Locally advanced prostate cancer is also frequently asymptomatic. Locally advanced means that the cancer has breached the capsule that surrounds the prostate and may or may not have invaded the seminal vesicles (tubes that carry semen) and/or other nearby organs. It also includes any prostate cancer that has spread to nearby lymph nodes. The NICE guideline on prostate cancer: diagnosis and management includes high-risk localised prostate cancer in its definition of locally advanced prostate cancer (see section 3.2.4).

Prostate cancer might be suspected in people with any of the following symptoms that are unexplained:

- Lower back, or bone pain
- Lethargy
- Erectile dysfunction
- Haematuria
- Weight loss
- Lower urinary tract symptoms, such as frequency, urgency, hesitancy, terminal dribbling and/or overactive bladder.

Treatment for prostate cancer may include radiotherapy, chemotherapy, surgery or a combination of these.

3.2 Diagnostic and care pathway

3.2.1 Recognition and referral

NICE's guideline on suspected cancer: recognition and referral includes the following advice on assessing people presenting to primary care with certain clinical signs and symptoms that may be indicative of prostate cancer:

- Consider a prostate-specific antigen test and digital rectal examination to assess for prostate cancer in men with:
  - any lower urinary tract symptoms, such as nocturia, urinary frequency, hesitancy, urgency or retention or
  - erectile dysfunction or
  - visible haematuria.

- Refer men using a suspected cancer pathway referral (for an appointment within 2 weeks) for prostate cancer if their:
  - prostate-specific antigen (PSA) levels are above the age-specific reference range or
  - prostate feels malignant on digital rectal examination.

The 2018 NHS England handbook on implementing a timed prostate cancer diagnostic pathway outlines 3 timed pathways: 28 days, 21 days and 14 days. The 28-day pathway is a straight to test pathway using multiparametric magnetic resonance imaging (mpMRI). The 21-day pathway is recommended for people in whom an immediate mpMRI is not required or is contraindicated. The 14-day pathway incorporates a one-stop diagnostics clinic including mpMRI before biopsy and targeted biopsy with or without systematic biopsies.

3.2.2 Multiparametric magnetic resonance imaging (mpMRI) and biopsy

The NICE guideline on prostate cancer: diagnosis and management recommends that following the referral to secondary care, a multiparametric magnetic resonance imaging (mpMRI) test should be offered to people with suspected clinically localised prostate cancer. Clinical experts highlighted that biparametric MRI (bpMRI) was sometimes used in current practice where mpMRI is not available. The results of this MRI should be reported using a 5-point Likert scale. Some centres report the results of the mpMRI using the 5-point prostate imaging – reporting and data system (PI-RADS) v2.1 scale. People with a Likert score of 3 or more should be offered a mpMRI-influenced prostate biopsy.

People with a Likert score of 1 or 2 might not have a prostate biopsy and experts noted around 40% of this group of people are discharged based on their prebiopsy mpMRI scan. This is decided after discussing the risks and benefits with the person and reaching a shared decision. The 2018 NHS England handbook on implementing a timed prostate cancer diagnostic pathway recommends that people with the following may be discharged from the pathway:

- a Likert or PI-RADS of 1 or 2
- a Likert or PI-RADS of 3 with PSA density less than 0.15 (or 0.12 in some centres) nanograms of PSA per ml of serum per ml of prostate volume.

Clinical experts explained that an MRI that does not show any suspicious lesions does not rule out the presence of clinically significant cancer. If a person decides to have a biopsy, then a systematic biopsy should be offered. However, clinical experts explained that there is regional variation in this practice with some centres preferring not to do systematic biopsies if there is no indication from the mpMRI. The decision might be influenced by risk factors such as PSA density, family history and ethnicity.

If the clinical suspicion of prostate cancer is high, because of a high PSA value and evidence of bone metastases (identified by a positive isotope bone scan or sclerotic metastases on plain radiographs), a prostate biopsy should not be offered for histological confirmation unless this is needed as part of a clinical trial.

There are 2 routes for taking targeted and systematic prostate biopsies: transrectal and transperineal. Both routes use a transrectal ultrasound probe inserted into the anus to image the prostate. In a transrectal ultrasound (TRUS) prostate biopsy, samples of prostate tissue are collected using a biopsy needle inserted through the rectal wall via the anus. The ongoing diagnostics assessment for transperineal biopsy in people with suspected prostate cancer recommends local anaesthetic transperineal (LATP) biopsy using freehand needle positioning devices as an option for diagnosing prostate cancer.

The standard of care also includes both targeted and systematic biopsies. Clinical experts explained that the biopsy approach is dependent on the information from the mpMRI and individual clinician preference. For example, if the mpMRI is highly abnormal with clear lesions, then 1 or 2 biopsy cores might be taken from the index lesion. Some clinicians might also decide to take additional cores from the site around the target lesion to increase the target area and ensure smaller lesions are not missed. Sometimes, a

systematic biopsy will be done in addition to the targeted biopsy. This might involve a number of cores being taken from the peripheral region, or it might involve a sectoral approach based on the Ginsburg biopsy protocol. This involves taking multiple samples from the left and right side of the prostate, covering the back, front and mid sections. A systematic biopsy might also be done if the mpMRI does not show any lesions or if the lesions are equivocal, but the clinical suspicion is high. People in whom mpMRI is contraindicated (for example, people who have a non MRI-compatible pacemaker fitted), might have a systematic biopsy but this decision would be influenced by the PSA density. The European Association of Urology guideline on prostate cancer recommends a combined targeted and systematic biopsy in people with a PI-RADS score of 3 or more who have not had a biopsy before. The guideline also states that where MRI has shown a suspicious lesion MR-targeted biopsy can be obtained through cognitive guidance, ultrasound/MR fusion software or direct in-bore guidance.

3.2.3 Follow-up after negative mpMRI or biopsy

The urological cancer multidisciplinary team should review the risk factors of all people who have had a negative first prostate biopsy. It should be discussed with the person that there is still a risk that prostate cancer is present and the risk is slightly higher if any of the following risk factors are present:

- the biopsy showed high-grade prostatic intra-epithelial neoplasia
- biopsy showed atypical small acinar proliferation
- abnormal digital rectal examination

The NICE guideline on prostate cancer: diagnosis and management recommends that if the biopsy is negative in people with a Likert score of 3 or more then the possibility of significant disease should be discussed, and the prostate biopsy might be repeated. Clinical experts explained that under these circumstances, it might be preferable to do a mapping template biopsy, where a sample is taken at 5mm intervals, under general anaesthetic. The 2018 NHS England handbook on implementing a timed prostate cancer diagnostic pathway recommends that repeat biopsy, surveillance or discharge should be considered depending on mpMRI and histology findings. It also suggests that biopsies from people with a Likert score of 4 or 5, with no atrophy or inflammation might be a false negative result and so a repeat biopsy or surveillance should be considered. The European Association of Urology (EAU) guidelines on prostate cancer recommends that people with a PI-RADS score of 3 or more who have had a previous negative biopsy should be offered a targeted biopsy only.

People who have a raised PSA, an mpMRI Likert score of 1 or 2 and have not had a biopsy should be offered repeat PSA testing at 3 and 6 months. People who have a raised PSA, an mpMRI Likert score of 1 or 2 (or a contraindication to mpMRI), and negative biopsy, should also have repeat PSA testing at 3 to 6 months. In both groups, prostate biopsy should then be offered if there is a strong suspicion of prostate cancer as determined by PSA density and PSA velocity, taking into account the person's life expectancy and comorbidities. If the level of suspicion is low then the person should be discharged to primary care with PSA follow-up at 6 months and then every year (for people who have not had a prostate biopsy) or every 2 years (for people who have had a negative biopsy). The European Association of Urology guidelines on prostate cancer recommends that for people who have had a previous negative biopsy, mpMRI should be done before biopsy. It also recommends a systematic biopsy for people with a PI-RADS score of 1 or 2 and a previous negative biopsy when the clinical suspicion of prostate cancer is high. This should be based on a shared decision.

3.2.4 Staging

The NICE guideline on prostate cancer: diagnosis and management recommends that a Cambridge Prognostic Group (CPG) risk category: low (CPG 1), favourable intermediate (CPG 2), unfavourable intermediate (CPG 3), high risk (CPG 4) or very high risk(CPG 5), should be assigned to all people with newly diagnosed localised or locally advanced prostate cancer. The CPG categories are described in table 2. They are based on the PSA result, Gleason score determined by histological analysis of the biopsy and clinical stage based on the mpMRI scan. The clinical staging of prostate cancer uses the tumour (T), node (N), metastasis (M) system. People with high risk histologically proven prostate cancer are automatically offered additional imaging tests following the biopsy results.

Histologically proven prostate cancer can be monitored either by active surveillance or watchful waiting. Active surveillance involves monitoring with a view to the person having radical treatment if the cancer progresses. In watchful waiting the monitoring is done with a palliative intent where any treatment offered is aimed at controlling rather than trying to cure the prostate cancer.

Table 2 Risk stratification for people with localised or locally advanced prostate cancer

Cambridge Prognostic Group	Criteria
1	Gleason score 6 (grade group 1) **and** prostate-specific antigen (PSA) less than 10 microgram/litre **and** Stages T1–T2
2	Gleason score 3 + 4 = 7 (grade group 2) **or** PSA 10 microgram/litre to 20 microgram/litre **and** Stages T1–T2
3	Gleason score 3 + 4 = 7 (grade group 2) and PSA 10 microgram/litre to 20 microgram/litre **and** Stages T1–T2 **or** Gleason 4 + 3 = 7 (grade group 3) **and** Stages T1–T2
4	One of: Gleason score 8 (grade group 4), PSA more than 20 microgram/litre, Stage T3
5	Two or more of: Gleason score 8 (grade group 4), PSA more than 20 microgram/litre, Stage T3 or Gleason score 9 to 10 (grade group 5) **or** Stage T4

3.2.5 Localised and locally advanced prostate cancer treatment

The NICE guideline on prostate cancer: diagnosis and management recommends that for people with CPG 1, 2 and 3 localised prostate cancer, the benefits and harms of the treatment options should be discussed in terms of their effect on survival, disease progression and development of distant metastases. Potential treatment related side effects should also be considered including their effect on urinary function, erectile dysfunction and bowel function. People can live with low-risk cancer for a number of years without progression. Due to the lasting negative effects of radiotherapy or prostatectomy (partial or complete removal of the prostate), people might prefer active surveillance.

People with CPG 1 localised prostate cancer should be offered active surveillance, and radical prostatectomy or radical radiotherapy can be considered if active surveillance is not suitable or acceptable to the person. A choice between active surveillance, radical prostatectomy or radical radiotherapy should be offered to people with CPG 2 localised prostate cancer if radical treatment is suitable. People with CPG 3 localised prostate cancer should be offered radical prostatectomy or radical radiotherapy, and active surveillance can be considered for people who choose not to have immediate radical treatment. Radical prostatectomy or radical radiotherapy should be offered to people with CPG 4 and 5 localised and locally advanced prostate cancer, when it is likely the person's cancer can be controlled in the

long term. Active surveillance should not be offered to people with CPG 4 and 5 localised and locally advanced prostate cancer.

The NICE guideline on prostate cancer: diagnosis and management recommends that people having active surveillance who have not had an mpMRI previously should be offered mpMRI. If the mpMRI results do not agree with the biopsy findings, then a new MRI-influenced biopsy should be offered. Clinical experts explained that some centres may choose to do another biopsy every 2 years or so, however this would be guided by the mpMRI and if it looked the same then a biopsy it would not be done.

Radical treatment following a diagnosis of prostate cancer

The NICE guideline on prostate cancer: diagnosis and management recommends that the following radical external beam radiotherapy options should be offered for localised prostate cancer:

- hypofractionated radiotherapy (60 Gy in 20 fractions) using image-guided intensity modulated radiation therapy, unless contraindicated or
- conventional radiotherapy (74 Gy in 37 fractions) to people who cannot have hypofractionated radiotherapy.

People with CPG 2, 3, 4 and 5 localised or locally advanced prostate cancer should be offered a combination of radical radiotherapy and androgen deprivation (an antihormone therapy), rather than radical radiotherapy or androgen deprivation therapy alone. People with prostate cancer in these groups should be offered androgen deprivation therapy for 6 months before, during or after radical external beam radiotherapy. People with CPG 4 and 5 prostate cancer should consider continuing androgen deprivation therapy for up to 3 years.

Brachytherapy in combination with external beam radiotherapy should also be considered for people with CPG 2, 3, 4 and 5 localised or locally advanced prostate cancer. Brachytherapy alone should not be offered to people with CPG 2, 3, 4 and 5 localised or locally advanced prostate cancer.

The option of docetaxel chemotherapy should be discussed with people who have newly diagnosed non-metastatic prostate cancer, are starting long term androgen deprivation therapy, have no significant co-morbidities and have high-risk disease.

The NICE guideline on prostate cancer: diagnosis and management recommends that pelvic radiotherapy should be considered for people with locally advanced prostate cancer who have a higher than 15% risk of pelvic

lymph node involvement and who are to receive neoadjuvant hormonal therapy and radical radiotherapy.

3.3 Patient issues and preferences

Clinical experts explained that there is a risk of over sampling during a prostate biopsy, leading to increased urinary retention and risk of infection. They highlighted that MRI fusion biopsies could reduce the number of samples taken, potentially reducing pain and risk of sepsis associated with the procedure.

People may experience anxiety before and during the biopsy procedure. The technology could reduce the number of repeat biopsies, avoiding unnecessary travel and anxiety for the person. People may also experience pain, loss of dignity and embarrassment during the biopsy. Clinical experts commented that the technology could add up to 10 minutes to the biopsy procedure, due to the time needed fuse the images. This could prolong anxiety, loss of dignity and embarrassment during the biopsy.

4 Comparator

The comparator for the assessment is targeted transperineal or transrectal prostate biopsy using cognitive fusion biopsy (use of an MRI image to visually estimate the location of interest) with or without systematic biopsy, under local or general anaesthesia. Clinical experts highlighted that the expertise of the person performing the biopsy may affect the accuracy and procedure time of cognitive fusion.

5 Scope of the assessment

Table 3 Scope of the assessment

Decision question	Do MRI fusion biopsy systems offer a clinically and cost-effective use of NHS resources in people with suspected prostate cancer?
Populations	People with suspected prostate cancer who have had an MRI scan that indicates a significant lesion (Likert or PI-RADS score of 3 or more). Where data permits, the following subgroups may be considered: • People with anterior lesions • People with posterior lesions

	• People who have had a previous negative prostate biopsy and are referred for a repeat biopsy within 12 months
Interventions	Targeted transperineal or transrectal prostate biopsy using MRI Fusion software with or without systematic biopsy, under local or general anaesthesia: • Artemis (InnoMedicus Artemis) • Biojet (Healthcare Supply Solutions) • BiopSee (Medcom) • bkFusion (BK Medical UK Ltd and MIM Software Inc) • Fusion Bx (Focal Healthcare) • FusionVu (Exact Imaging) • iSR'obot Mona Lisa (Biobot Surgical) • KOELIS Trinity (KOELIS and Kebomed) • Philips UroNav (Phillips)
Comparator	Targeted transperineal or transrectal prostate biopsy using cognitive fusion with or without systematic biopsy, under local or general anaesthesia.
Healthcare setting	Secondary care
Outcomes	Intermediate measures for consideration may include: • Measures of diagnostic accuracy • Cancer detection rates • Clinically significant cancer detection rates • Clinically insignificant cancer detection rates • Cancer detection rates in Cambridge Prognostic groups 1 to 5 • Biopsy sample suitability/quality • Number of biopsy samples taken • Procedure completion rates • Software failure rate • Time to diagnosis • Length of hospital stay (emergency department and inpatient stay) • Time taken for MR image preparation • Time taken for biopsy procedure • Number of repeat biopsies within 12 months
	Clinical outcomes for consideration may include: • Hospitalisation events after biopsy

	• Rates of biopsy related complications, including infection, sepsis, haematuria, urinary retention, erectile dysfunction and bowel function • Survival • Progression free survival • Adverse events from treatment
	Patient and carer-reported outcomes for consideration may include: • Health-related quality of life • Patient reported outcome measures such as tolerability, embarrassment and loss of dignity
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Costs of MRI fusion software and any proprietary hardware (including the workstation, ultrasound systems, probe holders, replacement parts, consumables such as guides, and maintenance) • Cost of staff time (including MR image interpretation time and biopsy procedure time) and any associated training • Medical costs arising from the biopsy such as anaesthetic, sedation, hospital stays • Costs related to using intervention (including any time analysing and storing data) • Costs of histopathology biopsy analysis • Cost of treatment of cancer (including costs of any adverse events) • Costs relating to follow-up • Costs of subsequent biopsies • Costs arising from watchful waiting • Costs arising from active surveillance
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

6 Other issues for consideration

6.1.1 Other MRI guided biopsy methods

Another MRI-guided biopsy method is ‘in-bore’ biopsy or ‘in-gantry’ biopsy. This technique involves performing the prostate biopsy in the MRI scanner, using the MR images taken immediately after each needle placement to guide the biopsy. MRI fusion software that integrates AI-driven diagnosis of prostate cancer is also available. In-bore biopsy systems and AI-driven software are outside the scope of this assessment.

6.1.2 Number of biopsy cores

It is uncertain what the optimum number of cores needed is to detect clinically significant cancer in patients with a definable lesion on MRI (Devetzis et al., 2021). There is particular uncertainty around whether there is a need for systematic biopsy in the face of equivocal MRI findings to prevent missing clinically significant cancer.

6.1.3 Overdiagnosis and overtreatment

Some clinical experts highlighted concerns around detection of clinically insignificant prostate cancer leading to overdiagnosis and potentially overtreatment. One clinical expert highlighted that this issue was not specific to this technology, and is instead a consideration for all targeted biopsy approaches including both cognitive and MRI fusion techniques.

6.1.4 Software updates

MRI fusion software may have periodic updates and upgraded versions with new functionality becoming available. These updates may impact the device’s accuracy in guiding biopsies. Evidence based on earlier versions of the software may not accurately reflect the effectiveness of the current versions.

6.1.5 Increased procedure time

The technology leads to an increase in procedure time. This could extend biopsy waiting lists.

6.1.6 IT and administration

MRI Fusion software can be challenging to integrate with Picture Archiving and Communication System (PACS) where MRI scan images are reviewed and reported. This may also increase review time.

6.1.7 Ongoing studies

The PACIFIC trial aims to evaluate the role of biparametric MRI and image-fusion targeted biopsies for the detection of prostate cancer. [redacted] The trial will evaluate the NHS healthcare burdens of these technologies compared to visual-registration (cognitive fusion) targeting, in terms of adverse events, proportion of patients biopsied and proportion of patients diagnosed with clinically significant and insignificant cancers that do not require treatment. [redacted]

7 Potential 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.

- All people with cancer are covered under the disability provision of the Equality Act (2010) from the point of diagnosis.
- Radical treatment for prostate cancer can affect fertility.
- Prostate cancer is more common in older people, people of African family background and people with a family history of prostate cancer.
- People with learning disabilities are often disproportionally impacted by cancer.
- Trans women should have access to prostate biopsy if needed.
- Enlarged prostate is most common in older people and prevalence may vary by ethnic background.
- Some people are at a greater risk of complications during general anaesthetic. This might include people with diabetes, older people, people who are overweight, people with heart disease and people with high blood pressure.
- The technology is contraindicated for people who cannot have an MRI, for example, people with implanted non MRI-compatible pacemakers, intracranial aneurysm clips and cochlear implants.
- The technology may not be suitable for people who have a proctectomy (removal of the rectum). This may be more prevalent in people who have inflammatory bowel diseases, such as ulcerative colitis.

8 Potential implementation issues

MRI fusion biopsy is currently in routine use in a few NHS hospitals.

8.1.1 Increased procedure time

Clinical experts estimated that the technology doubles the time it takes to prepare the MRI images before the biopsy (taking an additional 5 minutes). They commented that the biopsy procedure is also prolonged by up to 10 minutes, due to the time it takes to fuse the MR and ultrasound images. The increased procedure time could reduce the number of biopsies performed in a day, leading to additional clinics being needed. Experts suggested that use of the technology could lead to one less patient biopsy per day. They also noted that consequences of an increased procedure time might be mitigated by a reduction in repeat biopsies.

8.1.2 Training

Clinical experts highlighted the current need for more radiologists and expressed concerns that training could take staff away from current practice.

8.1.3 Procurement

The cost of procurement of MRI fusion systems may be quite high for some hospitals. However, one company stated that rental, finance and lease options are available. Currently, the additional time taken for an MRI fusion biopsy is not reimbursed, cognitive fusion biopsies are charged under the same cost code as an MRI fusion biopsy.

8.1.4 IT Issues

Some experts highlighted that integration of the software into their PACS has not been easy. They experienced frequent interruptions with their local IT networks which prevents the download of MRI images into the MRI Fusion systems, where they've had to revert to cognitive fusion.

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Appendix A Glossary of terms

Active surveillance
This is part of a 'curative' strategy and is aimed at people with localised prostate cancer for whom radical treatments are suitable, keeping them within a 'window of curability' whereby only those whose tumours are showing signs of progressing, or those with a preference for intervention are considered for radical treatment. Active surveillance may thus avoid or delay the need for radiotherapy or surgery.

Androgen deprivation
An antihormone therapy for treating prostate cancer. Lowering androgen levels or stopping them from getting into prostate cancer cells often makes prostate cancer shrink or grow more slowly for a time.

Brachytherapy
A type of internal radiotherapy. A small radioactive material called a source is put into your body, inside or close to the cancer. Or into the area where the cancer used to be before having surgery.

Cognitive fusion biopsy
The use of an mpMRI scan to overlay a mental image of where regions of interest in the prostate might be on a live-ultrasound image during the procedure.

Freehand biopsy
Freehand transperineal biopsy devices generally consist of an access or coaxial needle (that is a needle through which a biopsy needle can be passed) attached to a positioning guide that is mounted to the ultrasound probe. The ultrasound probe is held and positioned by one hand, while the other hand is used to position the biopsy needle to take samples. This enables fine manipulation of the probe and needle.

Local anaesthetic transperineal (LATP) biopsy
This is either targeted or systematic sampling of sites from the prostate using a transperineal route under local anaesthetic.

Locally advanced prostate cancer
Includes: high-risk localised prostate cancer (PSA over 20 ng/ml, or Gleason score 8 to 10, or clinical stage T2c or more); T3b and T4, N0 prostate cancer; and any T, N1 prostate cancer.

Localised prostate cancer
Cancer that has been staged as T1 or T2 (confined to the prostate gland).

Multiparametric MRI-influenced prostate biopsy
The information from the mpMRI scan taken before prostate biopsy is used to determine the best needle placement. In rare cases, the biopsy may be MRI-guided (the needle is inserted within the MRI machine). In most cases, the biopsy that follows the mpMRI will be ultrasound-guided, but the specific area(s) targeted will be predetermined by the mpMRI data.

MRI Fusion biopsy
The overlay of MRI scan images on to live ultra-sound images, to assist targeted prostate biopsies. MRI Fusion systems comprise specialist software with or without proprietary hardware.

Prostatectomy
Surgery to remove part, or all of the prostate gland. Radical prostatectomy aims at the removal of the entire prostate gland and lymph nodes. This can be performed by an open approach or by keyhole technique (laparoscopic or robotically assisted laparoscopic prostatectomy).

PSA density
The concentration of serum PSA in nanograms per ml divided by the volume of the prostate.

PSA velocity
The rate of change of PSA in nanograms per ml per year.

Radiotherapy
Radiotherapy is a treatment where radiation is used to kill cancer cells.

Stabilised biopsy
A stabilised prostate biopsy approach commonly uses a stepping device, to which the ulstrasound probe is attached to. The biopsy needle passes through template grids or guides which attach to the stepping device. Some biopsy devices have a semi-robotic arm which can act as a stepper.

Systematic biopsy
A biopsy approach where multiple samples are taken from different regions of the left and right side of the prostate.

Targeted biopsy
A biopsy approach which utilises an MRI scan to identify lesions from which a small number of tissue samples or cores are taken.

Transrectal ultrasound guided biopsy (TRUS)
This is where core biopsies of the prostate are taken via the rectum under local anaesthetic.

Template biopsy and mapping template biopsy
A template biopsy is normally performed under a general anaesthetic, and involves taking transperineal core biopsies using a grid system. This might involve taking multiple cores from multiple sites, but usually 2 to 3 cores from 8 sites. A mapping template biopsy is where 20 sites are systematically sampled, with 2 or 3 cores per site, sometimes meaning over 50 core biopsies are taken.

Watchful waiting
This is part of a strategy for 'controlling' rather than 'curing' prostate cancer and is aimed at people with localised prostate cancer who do not ever wish to have curative treatment, or it is not suitable for them. Instead, it involves the deferred use of hormone therapy. Watchful waiting avoids the use of surgery or radiation, but implies that curative treatment will not be attempted.

Appendix B Abbreviations

AI	Artificial intelligence
bpMRI	Biparametric MRI
DRE	Digital rectal examination
Gy	Gray
LATP	Local anaesthetic transperineal
mpMRI	Multiparametric magnetic resonance imaging
ng	nanogram
PET	Positron emission tomography
PI-RADS	Prostate imaging – reporting and data system
PSA	Prostate specific antigen
TRUS	Transrectal ultrasound

Appendix C References

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