NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Transperineal biopsy in people with suspected prostate cancer

Final scope

June 2021

1 Introduction

Following routine surveillance of NICE's recently updated guideline for diagnosis and management of prostate cancer (NG131), stakeholders identified transperineal prostate biopsy as an area that would benefit from NICE guidance. The topic selection oversight panel selected and routed transperineal prostate 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 held on 28 April 2021 and the assessment subgroup meeting held on 13 May 2021. 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 technology 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 technology

Prostate biopsies can be targeted, when MRI is used to identify lesions from which a small number of tissue samples or cores are taken. They can also be systematic, where multiple samples are taken from different regions of the left and right side of the prostate. 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. However, this can result in some people getting serious infections, requiring hospital admission and antibiotics. TRUS biopsies are usually done under local anaesthetic. In transperineal biopsy the biopsy needle enters the body

through the perineum, the skin area between the anus and the scrotum. This can greatly reduce the risk of biopsy related sepsis compared with a TRUS biopsy and therefore may reduce the need for preventative antibiotics.

Additionally, transperineal biopsy may provide easier access to the anterior region (in the front) and apex (lowest part) of the prostate. These are areas that may be difficult to reach by TRUS biopsy. This could lead to improved cancer detection rates compared with TRUS biopsies.

Traditionally, transperineal biopsies were performed under general anaesthetic using a template or grid and a stepping device. This template or grid based biopsy approach requires the needle to pass through the perineum multiple times as the needle is passed through different holes in the grid to access different regions of the prostate. The grid is mounted on the stepping device which is also used to hold and position the ultrasound probe. An alternative approach is to perform a local anaesthetic transperineal (LATP) prostate biopsy during an outpatient appointment. This could reduce the need for theatre time for biopsy procedures and therefore reduce waiting times. LATP biopsies can be done using: a grid and stepping device; a freehand transperineal biopsy device; or a double freehand approach.

LATP biopsy using a grid and stepping device requires multiple biopsy needle entry points through the perineum. Therefore, this approach may require more local anaesthetic compared with using a freehand transperineal biopsy device or a double freehand approach.

Freehand transperineal devices are used without a stepping device. Instead, 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. 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. This coupling of the biopsy needle and the ultrasound probe helps to keep them in phase during the procedure. The use of an access or coaxial needle means that a limited number of punctures of the skin are needed.

The double freehand approach is when a positioning guide is not used to attach the access or coaxial needle to the ultrasound probe. Instead the needle and probe need to be kept in phase manually. This technique is technically more challenging and therefore may take longer to train people to use.

Until recently the majority of all prostate biopsies in the NHS used the TRUS method. However, clinical experts explained that there has been a trend

towards transperineal biopsy over the last 2 years. This has in part been driven by the requirement for LATP prostate biopsy during the COVID-19 pandemic, such that in 2020 more than 65% of all prostate biopsies in the NHS were transperineal biopsies.

2.2 Product properties

2.2.1 PrecisionPoint (BXTAccelyon)

The PrecisionPoint transperineal access system is a single use device that enables freehand LATP prostate biopsies in an outpatient setting. It uses the Perineologic 15 gauge, 7 centimetre access needle that is securely attached onto the transrectal ultrasound probe via the PrecisionPoint needle guide. The guide comprises of a clip and moving carriage with 5 vertical holes in it giving a fixed alignment of the access needle with the ultrasound probe.

The device can be used to perform targeted or systematic biopsies, with no limitation on the size of the prostate or the number of biopsies. The integral access needle is aligned with the ultrasound probe, and so when the needle is inserted into the perineum it can be seen on the ultrasound image. This helps the clinician target the areas of the prostate with lesions or locate different regions of the prostate during a systematic biopsy.

The access needle typically requires only 2 entry points: one on the left and one on the right side of the anal verge. The biopsy needle can then be guided and directed to the relevant regions. The company state that the device is compatible with any biplane TRUS or transperineal probe from any ultrasound manufacturer.

2.2.2 UA1232 puncture attachment (BK medical)

The UA1232 metal puncture attachment is designed for transperineal puncture and biopsy. It consists of a needle guide and a mounting ring with a lock screw. The needle guide comprises 9 parallel guide channels, spaced 5 millimetres apart, each with an internal diameter of 2.1 millimetres, suitable for a 14-gauge needle. All parts of the puncture attachment can be sterilised by autoclave or disinfected by immersion in a suitable solution. The device is indicated for use with BK Medical ultrasound probes.

2.2.3 CamPROBE (Cambridge Prostate Cancer)

The CamPROBE is a cannulated transperineal access system designed specifically for prostate biopsies. The device consists of an access needle or cannular which houses an integrated needle. This needle can be attached to

a standard syringe, allowing the device to be inserted and local anaesthetic to be injected at the same time under ultrasound guidance. This removes the need for separate punctures, nerve blocks or sedation. Once the cannular is in position, the integrated needle is removed and standard 18-gauge core-needle biopsies can be taken through the retained cannula. CamPROBE is a disposable, single use device that provides a transperineal biopsy route with only 2 puncture sites. The CamPROBE device does not attach to the ultrasound probe, therefore it requires a double freehand technique to manually keep the needle in phase with the ultrasound probe.

2.2.4 Trinity perine (Koelis)

The Koelis trinity perine is a needle guide grid that attaches to an ultrasound probe for freehand transperineal biopsies under local anaesthetic. It consists of a vertical needle guide with 20 different height settings at 3 millimetre intervals, and an ultrasound probe clamp.

2.2.5 SureFire Guide (LeapMed)

The SureFire device is a disposable transperineal biopsy needle guide. It is designed to be used freehand without the need for stepper or stabilising devices. It consists of a vertical needle guide with separate puncture channels at each of 9 different height settings, and an ultrasound probe clamp. The vertical needle guide can be rotated to reach different areas of the left and right side of the prostate, using the different height puncture channels.

2.2.6 Puncture guide fixture EZU-PA3U (Hitachi Medical Systems)

The Hitachi EZU-PA3 is a reusable dedicated transperineal biopsy device. It can be attached to either the Hitachi CC41R bi-plane transducer, or the C41L47RP bi-plane transducer for both systematic and targeted freehand prostate biopsies. The needle holder can be positioned on the vertical plane by sliding up or down before securing in the required position. The needle holder is compatible with either 14-gauge or 18-gauge needles. Needle targeting in the transverse plane is achieved by rotating the probe left or right until the needle trajectory is aligned with the lesion or area of interest.

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. 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.

The current standard of care for prostate biopsy is mpMRI influenced TRUS biopsy under local anaesthetic or mpMRI influenced local anaesthetic transperineal (LATP) biopsy. Both approaches are done in an outpatient setting. Some experts commented that although there is a trend towards LATP biopsies, TRUS biopsies might still be useful in specific clinical scenarios, for example, posterior prostate lesions might be easier to reach via the transrectal route. However, due to the risk of severe infection, some centres no longer offer TRUS biopsies. During the COVID-19 pandemic, the British association of urological surgeons section of oncology issued a COVID-19 strategy for the interim management of prostate cancer. This recommended that TRUS biopsies should be avoided if possible. The 2021 update of the European Association of Urology guidelines on prostate cancer recommends that prostate biopsies should be done using a transperineal approach due to the lower risk of infectious complications.

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 pacemaker fitted), might have a systematic biopsy but this decision would be influenced by the PSA density. The European Association of Urology guidelines 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 NICE guideline on prostate cancer: diagnosis and management recommends that a mapping transperineal template biopsy should not be offered as part of an initial assessment unless part of a clinical trial. This is because it is too resource intensive to be used as an initial assessment as it requires general anaesthetic and extensive histological analysis. However, clinical experts explained that this approach can be useful in repeat biopsies when someone has had an mpMRI and biopsy with no identification of clinically significant cancer, but their PSA density is raised and clinical suspicion remains high. A mapping biopsy may also be used following previous brachytherapy (see section 3.2.7) or radiotherapy, when the person is eligible for salvage treatment (for example, focal radiotherapy or ablation). In this scenario it is important to know the precise location and extent of the cancer, to limit the focal or targeted therapy to that area.

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 that 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 (for example, PSA density greater than 0.15 nanograms of PSA per ml of serum per ml of prostate volume or PSA velocity greater than 0.75 nanograms per ml per year, or strong family history), 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). A PSA level for primary care should be set, at which to re-refer based on PSA density (0.15 nanograms per ml per ml) or velocity (0.75 nanograms per ml per year). 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 risk category (low, intermediate or high) should be assigned to all newly diagnosed localised prostate cancer. This is 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. There is regional variation in terms of what further imaging may be available but generally includes radioisotope bone scans and cross-sectional CT scans. Some centres might also offer whole body MRI, prostate specific membrane antigen PET scans and choline PET scans. Clinical experts explained that there is

also some variation in clinical practice in terms of which risk groups receive further imaging. As intermediate risk is considered to be a spectrum, some centres might offer radioisotope bone scans to all people in this risk group while some centres might offer it to people with intermediate to high-risk criteria.

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. NICE's guideline on prostate cancer: diagnosis and management recommends that for people with histologically proven prostate cancer for whom MRI is contraindicated, CT should be considered if knowledge of the tumour or node stage could affect management. Isotope bone scans should be offered when hormonal therapy is being deferred as part of watchful waiting to asymptomatic people who are at high risk of developing bone complications. Isotope bone scans should not be routinely offered to people with low-risk localised prostate cancer.

3.2.5 Localised prostate cancer treatment

The NICE guideline on prostate cancer: diagnosis and management recommends that for people with low-risk localised prostate cancer for whom radical treatment is suitable, the following treatment options should be offered:

- active surveillance
- radical prostatectomy
- radical radiotherapy

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, people might prefer active surveillance.

3.2.6 Active surveillance

Active surveillance should be offered to people with low risk localised prostate cancer and considered for people with intermediate-risk localised prostate cancer who choose not to have immediate radical treatment. Active

surveillance should not be offered to people with high-risk localised 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 would not be done. Table 1 outlines a protocol that should be considered for people who have chosen active surveillance.

Table 1 Protocol for active surveillance

Timing	**Tests[a]**
Year 1 of active surveillance	Every 3 to 4 months: measure prostate-specific antigen (PSA)[b] Throughout active surveillance: monitor PSA kinetics[c] At 12 months: digital rectal examination (DRE)[d] At 12 to 18 months: multiparametric MRI
Year 2 and every year thereafter until active surveillance ends	Every 6 months: measure PSA[b] Throughout active surveillance: monitor PSA kinetics[c] Every 12 months: DRE[d]
[a] If there is concern about clinical or PSA changes at any time during active surveillance, reassess with multiparametric MRI and/or re-biopsy. [b] Could be carried out in primary care if there are agreed shared-care protocols and recall systems. [c] Could include PSA density and velocity. [d] Should be performed by a healthcare professional with expertise and confidence in performing DRE. In a large UK trial that informed this protocol, DREs were carried out by a urologist or a nurse specialist.	
Abbreviations: DRE, digital rectal examination	

Radical treatment should be offered to people with localised prostate cancer who are on active surveillance and showing evidence of disease progression.

People with localised prostate cancer who have chosen watchful waiting and who have evidence of significant disease progression (that is, rapidly rising PSA level or bone pain) should have their situation reviewed by a member of the urological cancer multidisciplinary team.

3.2.7 Radical treatment following a diagnosis of prostate cancer

For people with intermediate-risk or high-risk localised prostate cancer radical prostatectomy or radical radiotherapy should be offered when it is likely the person's cancer can be controlled in the long term.

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.

For people with intermediate- and high-risk localised prostate cancer who have chosen radical radiotherapy, this should be offered in combination with androgen deprivation therapy. Androgen deprivation therapy should be offered for 6 months before, during or after radical external beam radiotherapy. For people with high-risk localised prostate cancer, the continuation of androgen deprivation therapy should be considered for up to 3 years.

Brachytherapy in combination with external beam radiotherapy should also be considered. Brachytherapy alone should not be offered to people with high-risk localised 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.

3.2.8 Locally advanced prostate cancer

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

In TRUS biopsies, the needle passes through the rectum and there is a risk of severe infection including sepsis. Treatment of these infections can be challenging and clinical experts indicated that as many as 1-3% of patients may develop a serious infection after TRUS biopsy.

Transperineal biopsies could lower the risk of serious infection such as sepsis, reduce antibiotic use and complication-related hospital admissions. They could also reduce pain during and after prostate biopsy compared with a template mapping transperineal biopsy as some devices require fewer punctures of the skin. Compared with TRUS biopsy, transperineal biopsy may lead to an increased risk of urinary retention.

While there is a trend towards the use of local anaesthetic transperineal prostate biopsy, there is still a proportion of people who will not be able to tolerate a prostate biopsy under local anaesthetic. Therefore, these people might be offered sedation or have a general anaesthetic transperineal biopsy. Clinical experts explained that there is a risk of over sampling the prostate during general anaesthetic, leading to increased urinary retention and risk of infection. People may also experience anxiety before and during the biopsy procedure.

4 Comparators

The comparators for the assessment are local anaesthetic transrectal ultrasound (TRUS) biopsy, local anaesthetic transperineal biopsy using a grid or template and stepping device, and general anaesthetic transperineal biopsy using a grid or template and stepping device.

TRUS biopsy is commonly used to take prostate biopsies from people with suspected prostate cancer in clinical practice in the NHS. However, a number of centres in the NHS now only offer transperineal prostate biopsies. Some of these are done using existing templates or grids and stepping devices under local anaesthetic. It is also possible to take prostate biopsies via the transperineal route using a coaxial needle without a device or needle guide. This is sometimes referred to as a ‘double freehand’ approach and is technically more difficult as both hands are required to align the needle with the probe manually. This approach is not widely used in clinical practice in the NHS.

5 Scope of the assessment

Table 2 Scope of the assessment

Decision questions	1. Do local anaesthetic transperineal (LATP) prostate biopsies in patients with suspected prostate cancer represent a clinically and cost-effective use of NHS resources? 2. Do freehand transperineal biopsy devices for LATP prostate biopsies in patients with suspected prostate

	cancer represent a clinically and cost-effective use of NHS resources?
Populations	People with suspected prostate cancer where prostate biopsy is indicated. Where data permits, the following subgroups may be considered: • People with anterior lesions • People with posterior lesions • People with apical lesions • People with basal lesions • People with a Likert or PI-RADS score of 2 or less • People with a Likert or PI-RADS score of 3, 4 or 5 • People with enlarged prostate • People who have never had a prostate biopsy • People who have had a previous negative prostate biopsy and are referred back
Interventions	1. Local anaesthetic transperineal prostate biopsy (for example, using a grid and stepping device, a coaxial needle, or a freehand transperineal biopsy device). 2. Local anaesthetic transperineal prostate biopsy done using one of the following freehand transperineal biopsy devices: • PrecisionPoint transperineal access device (BXTAccelyon) • UA1232 puncture attachment (BK Medical) • Trinity Perine Grid (Koelis) • CamPROBE • SureFire (LeapMedical) • EZU-PA3U device TBC (Hitachi Medical Systems)
Comparators	1. For local anaesthetic transperineal (LATP) prostate biopsies: • Local anaesthetic transrectal ultrasound prostate biopsy • General anaesthetic transperineal prostate biopsy using a grid and stepping device 2. For LATP prostate biopsies using a freehand transperineal biopsy device: • Local anaesthetic transrectal ultrasound prostate biopsy • Local anaesthetic transperineal prostate biopsy using a grid and stepping device

	• General anaesthetic transperineal prostate biopsy using a grid and stepping device
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 • Low, medium, high risk cancer detection rates • Biopsy sample suitability/quality • Number of biopsy samples taken • Procedure completion rates • Re-biopsy events within 6 months
	Clinical outcomes for consideration may include: • Hospitalisation events after biopsy • Rates of biopsy related complications, including infection, sepsis and haematuria. • Rates of urinary retention • Rates of erectile dysfunction • Survival • Progression free survival • Adverse events from treatment
	Patient-reported outcomes for consideration may include: • Health related quality of life • Patient reported tolerability
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Costs of biopsy devices • Cost of additional ultrasound equipment if needed for compatibility with transperineal biopsy device • Cost of template grid and stepping device for centres that do not have these available • Costs of staff and associated training • Medical costs arising from the biopsy such as anaesthetic, sedation and hospital stay • Costs of histopathology biopsy analysis • Medical costs arising from adverse events including biopsy related infection and use of antibiotics • Costs relating to the treatment of cancer

	• 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

In targeted biopsies the transperineal biopsy devices can be used in conjunction with MRI information from the pre-biopsy scan. This can be as part of a fusion biopsy system, where software is used to overlay the MRI scan image onto the live ultrasound image. Alternatively, the clinician may choose to target the lesion of interest using prior information from the MRI and using that to target a specific region using the live image from the ultrasound without the MRI overlay. This latter technique can be referred to as either 'cognitive MRI-targeted biopsy' or 'cognitive fusion biopsy'. Both approaches may be broadly described as MRI-influenced biopsy. MRI fusion biopsy systems are outside the scope of this assessment.

A UK based randomised controlled trial of transrectal biopsy versus local anaesthetic transperineal biopsy evaluation (TRANSLATE) of potential clinically significant prostate cancer, is due to start in April 2021. The trial will aim to recruit 1042 men over a 15-month period from 9 NHS hospitals in the UK. Men are eligible if they have been referred for a biopsy with a new suspicion of prostate cancer based on an abnormal prostate-specific antigen (PSA) blood test or digital rectal examination of the prostate, and have already received a pre-biopsy MRI scan. The primary outcome is detection rates of clinically significant prostate cancer, defined by presence of any Gleason pattern 4 disease. Secondary outcomes will include rates of infection, health related quality of life, patient reported tolerability of the procedure, patient reported biopsy-related complications, number of subsequent prostate biopsy procedures, cost-effectiveness and histological parameters. The trial will last for 31 months and has an expected end date of October 2023.

There are also 2 randomised controlled trials due to take place in the US. The ProBE-PC trial will aim to recruit 568 men scheduled to undergo prostate biopsy for suspected prostate cancer as part of their regular medical care. Participants will include men with and without an MRI and will be randomised to receive either transrectal needle biopsy or transperineal biopsy, with each

study arm further divided into either ultrasound-guided systematic biopsy or MRI-guided targeted biopsy. The primary outomes include rate of infectious complications and rate of bleeding complications. Secondary outcomes include cancer detection rate, tolerability under local anaesthetic, patient reported urinary function measures, cost of the procedures and patient reported sexual function measures. The ProBE trial is currently recruiting and is expected to be completed in December 2022.

The transperineal vs. transrectal MRI-targeted prostate biopsy trial is a collaboration between Cornell University and the patient-centered outcomes research institute. It will aim to recruit 1302 men across multiple centres and will include men on active surveillance and men with a prior negative biopsy. Participants will be randomised to receive either transperineal MRI-targeted or transrectal MRI-targeted prostate biopsy. The primary outcome is change in infection adverse events. Secondary outcomes include change in patient-reported pain and discomfort, change in patient-reported anxiety, detection of clinically significant disease and change in adverse events. The trial is due to begin in July 2021 and has an estimated completion date of April 2025.

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.
- Transperineal prostate biopsies may be more suitable than transrectal biopsies for people with inflammatory bowel disease.
- Trans women should have access to prostate biopsy if needed.
- 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.

8 Potential implementation issues

The use of transperineal access devices may have a resource impact including the set up and ongoing costs of the single use or reusable components needed to undertake the procedure. There are also clinician concerns of prostate biopsy tolerability using local anaesthetic. With greater anterior prostate access there could be an increase in the numbers of samples taken at biopsy and sent to pathology departments. As the transperineal approach to prostate biopsy is very different to TRUS there is also a need for sufficient training, which will vary depending on previous clinical experience.

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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.

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.

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.

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.

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

DRE	Digital rectal examination
Gy	Gray
LATP	Local anaesthetic transperineal
mpMRI	Multi parametric magnetic resonance imaging
ng	nanogram
PET	Positron emission tomography
PI-RADS	Prostate imaging – reporting and data system
PSA	Prostate specific antigen
TRUS	Transrectal ultrasound