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Review

Perspectives on technology – prostate cancer: is local anaesthetic transperineal prostate biopsy really better than transrectal biopsy?

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For many years, transrectal ultrasound-guided (TRUS) prostate biopsies have been performed to establish a histological diagnosis of prostate cancer. This has been the recommended standard of care procedure, but has always carried risks, in particular the risk of post-procedural sepsis, and the associated antibiotic burden and risk of development of antibiotic resistance. Transperineal (TP) prostate biopsies performed under local anaesthetic (LA) have been proposed as a possible solution to these issues, with potentially lower infectious complications, and avoidance of need for antibiotic prophylaxis. The European Association of Urology produced guidance in 2023 with 'weak' recommendations in favour of LATP biopsy as a new standard of care, citing its safety profile. Both the National Institute for Health and Care Excellence in the UK, and the American Urological Association in the United States, have concluded for now that the body of evidence is inadequate and not offered a similar recommendation. We discuss the available evidence, pros and cons of each technique, and the status of current trials in the field. We believe that clinical equipoise remains necessary, given the disparity in national and international guidelines highlighting the need for large randomised controlled trials to answer the question: is LATP biopsy really better than TRUS biopsy?

Keywords

cancer detection, complications, infections, prostate, transperineal biopsy, transrectal biopsy

Introduction

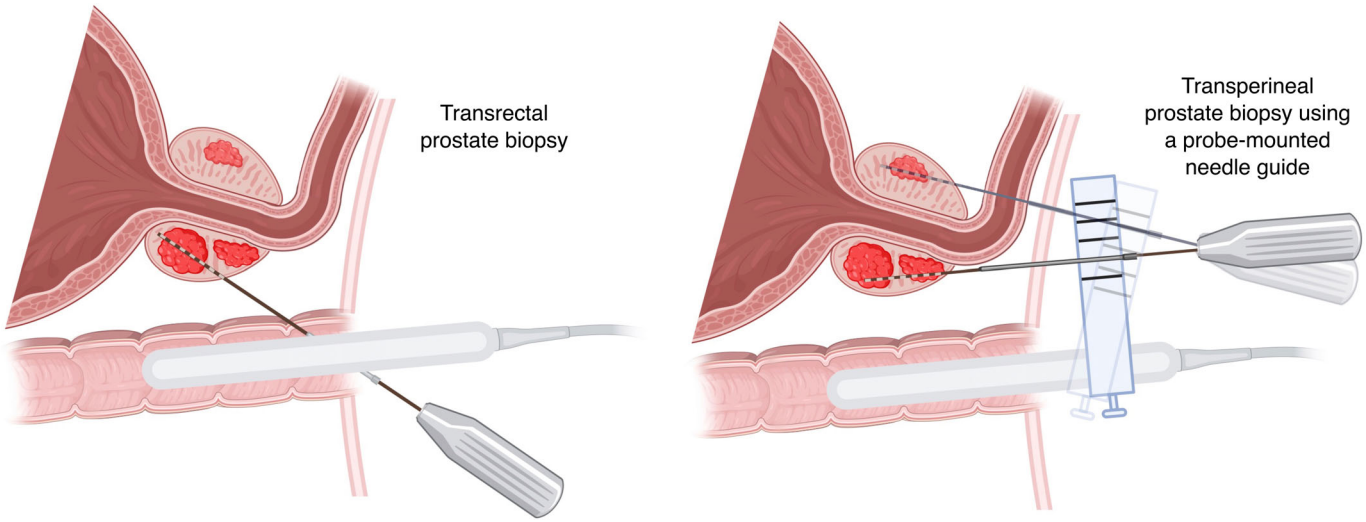
Diagnostic pathways for suspected localised prostate cancer have changed significantly over the last 10 years, with a key change being the introduction of pre-biopsy multiparametric magnetic resonance imaging (MRI). Nevertheless, prostate biopsy remains a mainstay in the diagnosis of prostate cancer, and the histological findings are a key requirement to inform decisions regarding clinical management of this malignancy.

Approximately 52 000 new diagnoses of prostate cancer are made each year in the UK [1], although the most recent National Prostate Cancer Audit highlighted fewer diagnosed cases during the COVID-19 pandemic [2]. Given the significant number of men diagnosed with prostate cancer annually, and the 73 000 annual biopsy procedures required to deliver this number of new diagnoses [3], any improvement in biopsy technique could have a large impact, whether this affects patient experience, procedural risk, diagnostic accuracy, or financial costs.

The traditional method of prostate biopsy for the last few decades of clinical practice has been a transrectal ultrasound (TRUS)-guided prostate biopsy. This technique involves the biopsy needle passing through the rectal wall to access the prostate (Fig. 1). Whilst a substantial proportion of the prostate cancer diagnostic and staging evidence base was established with TRUS biopsy, the technique has potential flaws. There is concern regarding infective and sepsis complications from the procedure, with associated concerns regarding appropriate prophylactic antibiotic resistance and stewardship. Furthermore, there have been concerns about the ability of TRUS biopsy to adequately biopsy anterior and apical prostate lesions. The transperineal (TP) approach to prostate biopsy is a potential alternative, however this has historically required a general anaesthetic (GA). TP biopsy avoids the need for the biopsy needle to traverse the rectal mucosa, and this may potentially reduce infection and sepsis complication rates for the prostate biopsy procedure. However, the need for a GA, with the attendant need for operating theatre time, and associated cost and impracticalities, has precluded the adoption of GATP biopsy on a large scale.

With the development of TP prostate biopsy techniques under local anaesthetic (LA), the 'TREXIT' initiative in

Fig. 1 The TRUS and LATP biopsy procedures. TRUS biopsy involves needle passage through the rectal wall, and may have difficulty accessing apical or anterior lesions, which may be more accessible via LATP biopsy. However, current evidence is weak and does not favour either technique. Figure created with Biorender.com.



2019–2020 presented LATP biopsy as an alternative to TRUS biopsy [4]. LATP biopsy has subsequently been adopted in several centres in the UK, USA, Australia and elsewhere, and observational cohort data suggests a potential reduction in infective and sepsis complications for LATP biopsy when compared with rates quoted for TRUS biopsy. Based on this observational evidence, LATP biopsy has recently been recommended in national and international guidelines. In 2023 the European Association of Urology (EAU) guidelines recommended LATP biopsy as the preferred method of prostate biopsy over TRUS biopsy [5], based on the reported diagnostic equivalence and reduced complications, albeit in the absence of robust large-scale randomised controlled trial (RCT) evidence. However, the National Institute for Health and Care Excellence (NICE) guidance in the UK continues to recommend both techniques [6], a more conservative stance predicated on the lack of high-quality evidence definitively demonstrating that either procedure is superior. NICE, and many clinical guidelines committees elsewhere, await the results of the large RCTs currently in progress; indeed, NICE currently recommends UK centres to actively support the UK-based TRANSrectal biopsy versus Local Anaesthetic Transperineal biopsy in Evaluation of men with potential clinically significant prostate cancer (TRANSLATE) trial (NCT05179694) with current recruitment.

In this narrative review, we present the key arguments in favour of each technique and discuss why policymakers and clinical guidelines committees ought to await Level 1 evidence before deciding whether to transition all prostate diagnostic services to LATP biopsy.

Table 1 Summary recommendations from the EAU [5], AUA [10] and NICE [7].

Guideline	Recommendation	Strength/Grade
EAU	Perform prostate biopsy using the TP approach due to the lower risk of infectious complications	Strong/1a
AUA	Clinicians may use either a TR or TP biopsy route when performing a biopsy	Conditional/C
NICE	The evidence suggests no significant difference in cancer detection rates between LATP biopsy and LA-TRUS biopsy, but it suggests lower rates of infection and sepsis after LATP biopsies. Centres are encouraged to take part in research and data collection, including the RCT of transrectal biopsy compared to LATP biopsy (the TRANSLATE trial) to help refine clinical practice	–

Guidelines

To our knowledge there are three separate guidelines panels that have issued statements on TP prostate biopsy (Table 1). The EAU guidelines have been the first to recommend TP biopsy over TRUS biopsy, citing comparable cancer detection rates and a reduced infection risk [5]. However, these guidelines do not mention LATP biopsy specifically, nor do they address freehand techniques. In the UK, NICE reported diagnostic guidance (DG54) on TP biopsy in June 2023, and concluded that available non-randomised studies describe comparable cancer detection rates between LATP and TRUS biopsy, with fewer infectious

complications following LATP biopsy [7]. The studies were found to have a high risk of bias and methodological heterogeneity, and therefore a key recommendation of NICE DG54 was for UK centres to support the ongoing TRANSLATE RCT, which we discuss further below.

European Urology recently published letters from Mian [8] and Kaplan-Marans et al. [9] outlining the need for further evidence before adopting the EAU guideline position [8,9]. In these letters, the authors highlight the disparity between the AUA guidance and the EAU guidance and discuss the EAU guidelines' strong recommendation in favour of TP prostate biopsy. The AUA has interpreted the currently available evidence, and has arrived at the same conclusion as NICE, citing only Grade C level evidence to favour LATP biopsy [10].

Evidence

Most evidence cited in the EAU guidelines arises from the grid-based biopsy method performed under a GA or regional anaesthetic. It is inappropriate to extrapolate the findings from these studies to the LATP biopsy procedure given that these are different biopsy techniques. GATP biopsy often involves acquisition of a greater number of biopsy cores and is performed in an operating theatre environment under GA/regional anaesthetic, with an inevitable impact on patient tolerability and acceptability of the procedure, combined with differing costs and training requirements.

The EAU guidelines cite one RCT (NCT04108871) [11,12] comparing LATP to TRUS biopsy, with cancer detection as a primary endpoint. Secondary endpoints assessed patient tolerability and infection rates. The findings of this RCT were published as a meeting abstract in *BJUI* following the Hong Kong Urological Association Annual Scientific Meeting in October 2021. This study was also presented at the AUA Annual Congress in 2022, and the definitive results await publication. The study was stopped at interim analysis of results, after randomisation of 266 patients, as the trial steering committee felt it would be unethical to continue the study. A reported 8.3% of patients developed sepsis after TRUS biopsy, compared with zero patients in the LATP biopsy group. Analysis of the primary outcome revealed no evidence for a difference in detection of clinically significant prostate cancer between the two techniques (16.4% vs 14.4% for LATP and TRUS biopsy, respectively, $P = 0.74$). Notably, patients in this trial did not undergo pre-biopsy MRI as this was an exclusion criterion for recruitment to the study.

Following the publication of both EAU and AUA guidelines the Prostate Biopsy, Transrectal vs Transperineal: Efficacy and Complications (ProBE-PC) trial (NCT04081636) from Albany Medical College, New York presented primary outcome results at the AUA Annual Congress in 2023 [13]. This study randomised 718 patients to TRUS or LATP biopsy, with the primary outcome being the rate of development of post-biopsy infection complications, which were observed to be 2.6% and 2.7%, respectively. The rate of overnight admission post-procedure was 0.55% for TRUS biopsy and 0.27% for LATP biopsy. This RCT is now published, including the secondary outcomes of the study, with no evidence of a difference for urinary retention, bleeding, or re-attendance [14].

Most recently the PReclude Infection EVEnts With No Prophylaxis Transperineal Biopsy (PREVENT)/ Patient-Centered Outcome Research Institute (PCORI) RCT (NCT04843566) reported data for 658 participants randomised to receive either TRUS or LATP biopsy [15]. The primary outcome was development of an infectious complication, with no infections in the LATP biopsy arm and four in the TRUS biopsy arm. There was no evidence for a difference in infection outcomes, although this may be a matter of statistical power (the *P* value was 0.059) and the authors highlighted the benefits of antibiotics stewardship combined with zero infections in the LATP biopsy arm. Additionally, there was no difference in cancer detection or urinary retention; however, more participants felt LATP biopsy was painful.

Kanagarajah et al. [16] performed a systematic review of LATP prostate biopsy outcomes in 2022. A total of 35 studies were included in this review, including RCTs and prospective and retrospective cohort studies. There is a marked variation in biopsy technique, devices, biopsy pattern, and number of acquired biopsy cores. The overall quality of available data was described as being poor, prompting the authors to call for higher quality evidence. One RCT comparing LATP to TRUS biopsy was included in the review [17]. In the Shanghai based study by Guo et al. (NCT01849835), 339 patients were randomised 1:1 to either TRUS or LATP biopsy. The LATP biopsy was found to be equivalent to TRUS biopsy in terms of prostate cancer detection (35.3% vs 31.9%, $P = 0.556$), and had significantly fewer post-procedure fever complications (2% vs 7%, $P = 0.099$), and fewer episodes of mild rectal bleeding (0% vs 8.7%, $P = 0.001$). Mild pain reported at the time of procedure was greater in the LATP biopsy group (35.3% LATP vs 13.0% TRUS biopsy, $P < 0.001$). Readers should note that the authors considered that the limited number of acquired biopsy cores (eight and 12 cores if prostate volume <50 or >50 mL, respectively) may have affected the results, recommending the conduct of further studies. In addition, the patients in this study did not undergo preoperative MRI, which potentially affected the cancer detection rate.

Current Trials

There are five relevant RCTs which are either very recently published, in progress or due imminent publication: the

Table 2 Current RCTs comparing LATP and TRUS biopsy outcomes.

Study name	Participants	Primary outcome	Secondary outcomes	Trial stage
ProBE-PC CI – Mian	718 Biopsy naïve and previous negative biopsy	Infectious complications	Urinary retention, need for clinical review	Published *J Urol* February 2024 [14]
PREVENT CI – Hu	658 Biopsy naïve	Infectious complications	Cancer detection, urinary retention, haematuria, pain	In press, *Eur Urol* January 2024 [15]
TRANSLATE CI – Bryant, Lamb	1042 Biopsy naïve	Clinically significant prostate cancer detection	Infectious complications, tolerability, cost effectiveness, clinically insignificant cancer detection	Recruitment complete
PREVENT2 CI – Hu	1300 (680 AS, 620 previous negative biopsy)	Infectious complications	Cancer detection, urinary retention, haematuria, pain	Recruiting
PERFECT CI – Ploussard	270 Biopsy naïve and PI-RADS 4/5	Clinically significant prostate cancer	High-grade and clinically insignificant cancer detection, adverse events	In press, *Eur Urol Oncol* April 2024 [23]

AS, active surveillance; CI, Chief Investigator.

ProBE-PC, PREVENT, PREVENT2 (previously PCORI) (NCT04815876) and TRANSLATE trials (summarised in Table 2).

The TRANSLATE RCT is currently recruiting at 10 centres in England, Scotland, and Wales in the UK, commencing in December 2021 [18]. This study aims to recruit 1042 biopsy-naïve men following pre-biopsy MRI, who have an indication for biopsy during urgent assessment for possible prostate cancer. The trial is randomising men on a 1:1 basis to either TRUS or LATP biopsy, with the latter using either the PrecisionPoint or BK TP access systems. The TRANSLATE trial's primary outcome is the detection rate of clinically significant prostate cancer between the two techniques, this being defined as Gleason Grade Group ≥2 disease. Secondary outcomes include a robust assessment of infection and other complication rates, quality of life assessments, patient tolerability and patient-reported outcomes, detection of clinically insignificant prostate cancer, and cost-effectiveness.

The ProBE-PC trial reported its primary outcome of infection rates at the AUA 2023 Annual Congress and has recently published its main results as discussed above [14]. In this RCT, participants undergoing TRUS biopsy received protocolised antibiotics, whereas participants in the LATP biopsy arm did not receive antibiotics or took a risk-assessed approach. The TRUS biopsy patients did not have pre-biopsy rectal cultures. Pre-biopsy MRI of the prostate was not mandatory within the inclusion criteria in this study; however, cancer detection was not a measured outcome.

A large RCT from Weill Cornell Medical Center, New York is recruiting 1700 patients to compare LATP to TRUS biopsy [19]. Working with PCORI, the study protocol combines two separately registered trials, PREVENT and PREVENT2 [20,21]. PREVENT, discussed above, assessed 658 biopsy-naïve participants randomised to receive TRUS or LATP biopsy. A second trial, PREVENT2, addresses the remaining 1300 patients in the protocol who have all had previous prostate biopsies. These recruited participants will be randomised to TRUS or LATP biopsy, and the research team seek to enrol 680 participants currently on active surveillance for low-risk low-volume prostate cancer, and 620 participants with a prior negative prostate biopsy. The primary outcome for both trials is an assessment of any possible difference between LATP and TRUS biopsy in the infection adverse events, evaluating both frequency and severity of this complication. For these two trials the TRUS biopsy participants receive antibiotic prophylaxis according to sensitivities on a pre-procedure rectal swab; the LATP biopsy participants will receive no antibiotic prophylaxis. Cancer detection is a secondary outcome that is subdivided into over-detection of low-grade cancer, and detection of non-low-grade cancer. Secondary outcomes include other adverse events such as haematuria and urinary retention, along with pain, anxiety, and discomfort. These studies seek to offer data in the various patient groups undergoing the same procedures.

The TransPERineal Fusion Biopsy Versus transrectal (PERFECT) study (NCT05069584) is a RCT comparing TRUS vs TP biopsy, when performing MRI-targeted fusion biopsies, with a primary outcome of detection of clinically significant prostate cancer [22]. Prostate Imaging-Reporting and Data System (PI-RADS) 4 or 5 lesions are required for targeting, and systematic biopsies are also performed. Secondary outcomes include detection of high-grade prostate cancer and clinically insignificant prostate cancer, and adverse events. This study was published during proof-review of this article [23].

Available TP Biopsy Systems

In a previous review, we explored the various procedural techniques for TP biopsy [24]. There are two approaches,

namely the freehand technique, and the stepper technique using a grid. The stepper with grid technique is an adaptation of a standard mapping TP biopsy or GATP. Published studies focus on freehand techniques, as these involve fewer perineal punctures, and are felt to be better tolerated by the patient. The recently published NICE DG54 guidance lists the currently evaluated systems as PrecisionPoint (BXTAccelyon Ltd, Burnham, Slough, UK), EZU-PA3U (FUJIFILM, Kanagawa, Japan), SureFire (Delta Surgical Ltd, Newcastle Under Lyme, Staffordshire, UK), Trinity Perine Grid (Koelis/Kebomed, Auburndale, MA, USA), UA1232 (BK Medical. Burlington, MA, USA), and CAMbridge PROstate Cancer Biopsy devicE (CamPROBE; JEB Technologies Ltd, Mildenhall, Bury Saint Edmunds, UK) [7]. The NICE committee felt that the CamPROBE technique differed significantly (as it uses a double freehand technique) such that it ought to be considered separately, and at present lacks sufficient comparative data to be recommended for routine clinical use.

PrecisionPoint, EZU-PA3U, Trinity Perine Grid and UA1232 are all freehand needle positioning devices that keep the biopsy needle in line with the probe and a coaxial needle. The coaxial needle reduces the typically required number of TP skin punctures to four or less. NICE considered these to all be sufficiently similar devices that they could be recommended for use, based on the available evidence from studies using the PrecisionPoint device.

Cancer Detection

We observed significant heterogeneity of study populations in our previous review, including biopsy-naïve individuals, patients on active surveillance for low-risk low-volume prostate cancer, and a combination of both sets of patients. We have also observed differences in sampling techniques, with varying strategies and numbers of acquired biopsy cores [24]. These observations highlight the need for robust large-scale RCTs directly comparing TRUS with LATP prostate biopsy, with a standardised approach to these procedures.

Kanagarajah et al. [16] distinguished those studies with and without pre-biopsy MRI. Overall, the detection rate of clinically significant prostate cancer using LATP biopsy in their systematic review was 37%, but this improved with the use of pre-biopsy MRI to 47% (95% CI 0.20–0.75) compared to 23% (95% CI 0.18–0.29) without pre-biopsy MRI. The methodological heterogeneity of the studies is clear with cancer detection rates ranging from 48.8% to 84% in studies solely analysing the use of the PrecisionPoint device. Zattoni et al. [25] demonstrated a greater detection rate of clinically significant prostate cancer in the TP group following the use of pre-biopsy MRI, although this study combines cohorts of LATP and TP prostate biopsies under GA or regional anaesthetic.

Whilst the PROstate MRI Imaging Study (PROMIS) trial assessed MRI prostate sensitivity, it also compared TRUS biopsy to TP biopsy as its 'gold standard' test [26]. The TP biopsies were performed under GA or spinal anaesthesia, and these results are therefore not comparable to LATP biopsy in the clinic. This study provides a reference for the detection rate of clinically significant prostate cancer using TRUS biopsy without pre-biopsy MRI as being 19%. Importantly, the PROMIS trial did not include targeted biopsies, and defined clinically significant prostate cancer as International Society of Urological Pathology (ISUP) ≥3 disease.

In 2023, two meta-analyses by Wu et al. [27] and Uleri et al. [28] were published comparing TRUS and LATP biopsy techniques for MRI-targeted lesions. Both reviews included non-randomised heterogenous data, frequently GATP rather than LATP biopsy, and thus should be interpreted with caution. They both found TP biopsy to have a higher cancer detection rate for anterior lesions. Wu et al. [27] concluded that MRI-guided TP biopsies detected more clinically significant prostate cancer than TRUS biopsy, whereas Uleri et al. [28] found no difference between the techniques.

We collated the largest prospective observational cohort series of 1218 patients undergoing LATP biopsy published in this journal, reporting a detection rate of clinically significant prostate cancer of 52%, with 67% having any-grade disease [29]. This study comprised both biopsy naïve, active surveillance, and repeat-biopsy patients, introducing heterogeneity into the figures. However, the LATP biopsy technique was standardised in this study, with all 10 centres using the PrecisionPoint device and performing sampling according to the Ginsburg protocol [30]. Furthermore, 84% of biopsied individuals had pre-biopsy MRI. Interestingly, this multicentre cohort reported the presence of anterior prostate lesions on MRI in 20% of patients, with clinically significant prostate cancer being detected at LATP biopsy in 70% of patients with such radiological lesions. This represents an important subgroup of patients who may potentially be under-sampled by TRUS biopsy, and who may potentially avoid the need for subsequent repeat biopsy if they undergo an initial LATP biopsy, rather than receive an initial false negative TRUS biopsy.

Sepsis and Antibiotics

The rate of sepsis from TRUS biopsy has been variably reported as being between 0.53% and 3.6% [31]. Large scale studies include that by Tamhankar et al. [32] in 2020, and their analysis of UK Hospital Episode Statistics (HES) data, which demonstrate sepsis rates of 0.53% after TRUS biopsy vs

0.31% after TP biopsy. It is again noteworthy that the TP cohort in this report predominantly comprised GATP biopsy procedures. Rosario et al. [33] reported that TRUS biopsy resulted in a 1.3% overall acute hospital admission rate, with 17.5% of these reporting fever, and 5% classifying this as a moderate or severe problem. The National Prostate Cancer Audit reported a sepsis rate of 1.4%, reduced to 1% in the TP group [34]. On systematic review, Pradere et al. [35] found a significantly reduced sepsis rate when performing TP prostate biopsies vs TRUS biopsy, risk ratio 0.55 (95% CI 0.33–0.92). In comparison, the LATP biopsy sepsis rate was found to be 0.16% in the Lopez et al. [29] report. Jacewicz et al. [36] performed a RCT of antibiotic prophylaxis vs no prophylaxis when performing LATP biopsy. A total of 555 patients were equally split across the two arms of the study, with zero sepsis cases in either study arm, suggesting the potential to avoid routine antibiotic prophylaxis, thus improving antibiotic stewardship.

Acute Urinary Retention

The risk of acute urinary retention was reported to be between 0.2% and 1.7% following TRUS biopsy in a systematic review by Loeb et al. [37]. Of the TP studies included in this review, the rate of acute urinary retention ranged from 1.6% to 8.8%, although these were following GATP biopsies. Kanagarajah et al. [16] reported a 2% risk of acute urinary retention following LATP biopsy in their systematic review, whilst Lopez et al. [29] found the rate to be 1.6%.

Bleeding and Erectile Dysfunction

Transient haematuria is commonly reported following both TRUS and LATP biopsy, but rarely results in the requirement for emergency admission. The risk of haematuria requiring bladder irrigation following TRUS biopsy is reported as being 0.4% [38]. Berquin et al. [39] reported significantly more patients with haematuria at 24 h post-procedure in LATP compared to TRUS biopsy (61.2% vs 36.1%), although there was no significant difference by 48 h. They also reported initial rectal bleeding post-TRUS biopsy to be more common than post-LATP biopsy. Erectile function post-biopsy has been measured using the International Index of Erectile Function (IIEF) questionnaire in several studies. The IIEF results have been reported to not be significantly altered vs baseline following either LATP biopsy [40] or TRUS biopsy [37]. Baseline IIEF was found to be unchanged at 40 days following LATP biopsy in a further study [41]. However, there is anecdotal evidence that LATP biopsy may be more likely to cause erectile dysfunction compared to TRUS biopsy, and it will be interesting to see the definitive results of the currently recruiting RCTs regarding post-biopsy erectile dysfunction rates.

Procedure Tolerability

Several studies include patient-reported outcome measures (PROMs) following prostate biopsy, focussing primarily on pain, tolerability, and embarrassment. Berquin et al. [39] found LATP biopsy to be more painful during the procedure, but no difference in postoperative pain. Lopez et al. [29] reported that 14% of men described the LATP biopsy as 'very painful', 6.8% 'very embarrassing', and 5.6% felt the procedure should have required a GA. Procedure abandonment was reported to be 0.37% in the Kanagarajah et al. [16] systematic review. Using the same PROMs as the multicentre Lopez et al. [29] cohort, Rosario et al. [33] found 19.6% of patients undergoing TRUS biopsy would consider further biopsy a 'major or moderate issue'. They found evidence for a correlation between negative PROMs and those who reported they would not wish to undergo the procedure again.

Cost effectiveness The NICE summarise existing cost-effectiveness data within their DG54 recommendations. They found that greater adverse events from TRUS biopsy in previous studies may lead to increased overall costs of an otherwise less expensive diagnostic procedure [7]. Despite this, TRUS biopsy remains the most cost-effective biopsy procedure based on their assessment of the currently available research data. Cost effectiveness was calculated as the incremental cost-effectiveness ratio (ICER), and NICE specifies an upper limit of between £20 000–£30 000 per quality-adjusted life year (QALY) to assess value.

The LATP biopsy was most cost effective when performed on high-risk men based on the findings of pre-biopsy MRI (PI-RADS ≥3), with an ICER of £8447/QALY. This increases to £18 196 when performing LATP biopsy on men with MRI findings graded PI-RADS 1 and 2. It should be noted repeat biopsy groups further increased the ICER to >£30 000/QALY. The cost effectiveness of LATP biopsy as a more expensive procedure is derived from its greater diagnostic yield, reducing the need for further procedures for repeat sampling.

These costs were established through a micro-costing analysis included in the NICE evidence overview of TP biopsy, which forms the basis of the current NICE DG54 recommendations. Micro-costing included device, consumables, clinical room, and pathology costs, in addition to staff, training, and consultation costs. The cost of complications from each procedure was calculated separately. All LATP biopsy techniques are more expensive than TRUS biopsy, with LATP biopsy performed using the PrecisionPoint device representing a 69% cost increase in this analysis (Table 3). This is a marked additional cost for LATP biopsy, but this might be recouped through improved accuracy of cancer detection at initial biopsy, thus reducing the need for repeat

Table 3 The NICE calculated cost per procedure according to technique and device [7].

Biopsy technique	Device	Cost per procedure, £ [7]
LA TRUS	–	345.59
LATP	PrecisionPoint	583.72
	EZU-PA3U	414.60
	UA1232	410.25
	Trinity Perine	405.72
	CamPROBE	475.10
GATP	–	919.75

sampling, coupled with the possibility of reduced costs incurred from acute adverse events requiring emergency hospital admission following LATP compared with TRUS biopsy.

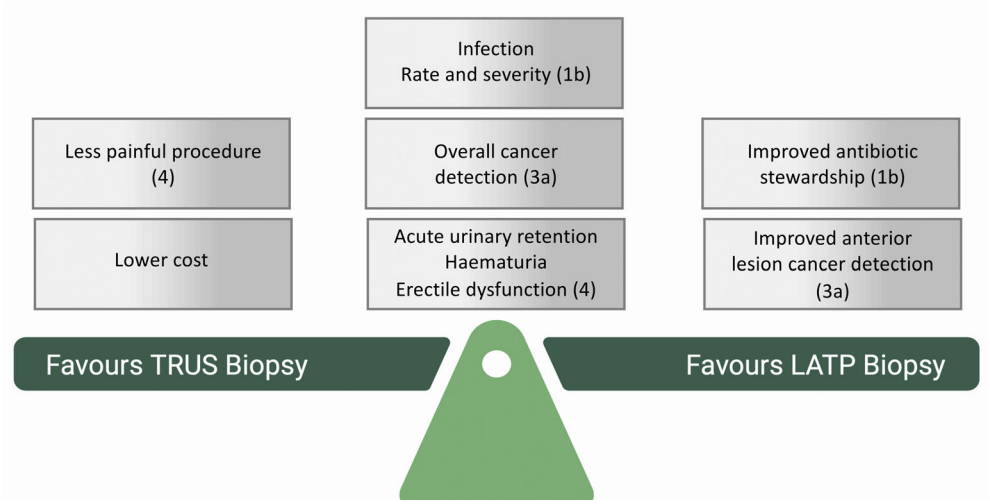
The TRANSLATE trial in the UK seeks to provide robust health economics data for TRUS and LATP prostate biopsy, and NICE recommended UK centres to support its recruitment. TRANSLATE is using a patient-reported questionnaire at multiple time-points after biopsy to collate data regarding procedural complications, follow-up consultations (including within primary care), acute hospitalisations, and any treatments. The cost of the biopsy procedure is captured through a combination of standardised national unit costs and reporting of both procedure time and equipment usage, including reusable and disposable items. Through the robust assessment of the cost of both the biopsy procedure and any additional care requirements, a thorough cost analysis should be reached.

Conclusion – Equipoise

We have discussed the current guidelines regarding prostate biopsy technique in the initial assessment and diagnosis of possible prostate cancer, and have outlined their differences, coupled with the current evidence base (Fig. 2). Whilst observational cohort evidence suggests that LATP biopsy may demonstrate improvements in terms of cancer detection through improved anterior zone sampling, and reduced infective complications, conflicting results continue to emerge as to the overall extent of the improvement, and whether observed differences might be driven by enthusiasm for LATP over TRUS biopsy. Only the results of robust RCTs will deliver definitive evidence in this space.

In 1987 Freedman [42] wrote in the *New England Journal of Medicine* that 'clinical equipoise' requires the expert medical community to retain uncertainty about a proposed treatment when there is no definitive evidence supporting a single best approach. We believe that the answer to our title question is: 'we do not yet know'; and we therefore believe that we remain in a state of equipoise. This stance has implications for our member organisations, which seem to have arrived at conflicting viewpoints. It also has implications for the individual practitioner trying to consider how best to counsel their patient regarding methods of prostate biopsy, whilst the results of the ongoing RCTs are awaited. Whether you feel there is sufficient evidence for LATP biopsy or not, there remains uncertainty amongst the global urological community, and therefore we should remain in equipoise. The urological community eagerly awaits the RCTs currently in progress, which we anticipate will provide definitive evidence regarding the question as to whether LATP biopsy is superior to TRUS biopsy as the primary method of sampling for prostate cancer diagnostics. Only then will we know whether to recommend universal adoption of LATP biopsy with abandonment of TRUS biopsy, or whether a more subtle paradigm will be required.

Fig. 2 Summary of key issues in prostate biopsy technique which may favour either biopsy modality, along with current levels of evidence. (Level 1b = RCT; Level 3a = case-series; Level 4 = expert opinion). Figure created with Biorender.com.



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Disclosure of Interests

Richard J. Bryant and Alastair D. Lamb received support from BXT Accelyon to attend LATP biopsy training provided by Guys' Hospital, London, UK. Alastair D. Lamb is a co-author of a paper campaigning to move away from TRUS biopsy [4]. Richard J. Bryant and Alastair D. Lamb are co-Chief Investigators of the TRANSLATE clinical trial in the UK.

Key References

- European Association of Urology Guidelines on Prostate Cancer – DIAGNOSTIC EVALUATION – Uroweb. Available from: https://uroweb.org/guidelines/prostate-cancer/chapter/diagnostic-evaluation.
- NICE DG54 Transperineal biopsy for diagnosing prostate cancer Available from: https://www.nice.org.uk/guidance/dg54/chapter/1-Recommendations.
- Mian BM, Feustel PJ, Aziz A, Kaufman RP, Bernstein A, Avulova S, et al. Complications Following Transrectal and Transperineal Prostate Biopsy: Results of the ProBE-PC Randomised Clinical Trial. J Urol. 2024 Feb;211 (2):205–13.
- Hu JC, Assel M, Allaf ME, Ehdaie B, Vickers AJ, Cohen AJ, et al. Transperineal Versus Transrectal Magnetic Resonance Imaging–targeted and Systematic Prostate Biopsy to Prevent Infectious Complications: The PREVENT Randomised Trial. Eur Urol 2024 Jan 11 Available from: https://www.europeanurology.com/article/S0302-2838(23)03342-0/fulltext#.
- Bryant RJ, Yamamoto H, Eddy B, Kommu S, Narahari K, Omer A, et al. Protocol for the TRANSLATE prospective, multicentre, randomised clinical trial of prostate biopsy technique. BJU Int. 2023;131 (6):694–704.

References

1 **Prostate Cancer UK [Internet]**. About prostate cancer. [cited 2023 Jun 14]. Available from: https://prostatecanceruk.org/prostate-information-and-support/risk-and-symptoms/about-prostate-cancer/

2 **National Prostate Cancer Audit [Internet]**. NPCA Annual Report. 2022 [cited 2023 Jun 14]. Available from: https://www.npca.org.uk/reports/npca-annual-report-2022/

3 **NPCA-Annual-Report-2021_Methodology-Supplement_Final_19.12.21.docx.pdf [Internet]**. [cited 2023 Oct 12]. Available from: https://www.npca.org.uk/content/uploads/2021/12/NPCA-Annual-Report-2021_Methodology-Supplement_Final_19.12.21.docx.pdf

4 **Grummet J, Gorin MA, Popert R et al.** "TREXIT 2020": why the time to abandon transrectal prostate biopsy starts now. *Prostate Cancer Prostatic Dis* 2020; 23: 62–5

5 **Uroweb – European Association of Urology [Internet]**. EAU Guidelines on Prostate Cancer - DIAGNOSTIC EVALUATION - Uroweb. [cited 2023 Jun 14]. Available from: https://uroweb.org/guidelines/prostate-cancer/chapter/diagnostic-evaluation

6 Overview | Prostate cancer: diagnosis and management | Guidance | NICE [Internet]. NICE. 2019 [cited 2023 Jun 14]. Available from: https://www.nice.org.uk/guidance/ng131

7 1 Recommendations | Transperineal biopsy for diagnosing prostate cancer | Guidance | NICE [Internet]. NICE. 2023 [cited 2023 Jun 14]. Available from: https://www.nice.org.uk/guidance/dg54/chapter/1-Recommendations

8 **Mian BM**. Prostate biopsy: hyperbole and misrepresentation versus scientific evidence and equipoise. *Eur Urol* 2023; 85: 99–100

9 **Kaplan-Marans E, Zhang TR, Hu JC**. Differing recommendations on prostate biopsy approach to minimize infections: an examination of the European Association of Urology and American Urological Association Guidelines. *Eur Urol* 2023; 84: 445–6

10 **Early Detection of Prostate Cancer: AUA/SUO Guideline**. American Urological Association [Internet]. 2023 [cited 2023 Jul 24]. Available from: https://www.auanet.org/guidelines-and-quality/guidelines/early-detection-of-prostate-cancer-guidelines#x18473

11 **Abstract – 2022 – BJU International – Wiley Online Library [Internet]**. [cited 2023 Jun 15]. Available from: https://doi.org/10.1111/bju.15675?af=R

12 **Lam DW**. Randomized-controlled Trial: Whether Transperineal Prostate Biopsy Under Local-anaesthesia Using a Transperineal-access System is Non-inferior to Standard Transrectal Biopsy to Detect Prostate Cancer in Biopsy-naïve Men [Internet]. Report No: NCT04108871. 2019 [cited 2023 Jun 13]. Available from: https://clinicaltrials.gov/ct2/show/NCT04108871

13 **Mian BM, Feustel PJ, Aziz A et al.** Lba03-03 infectious and non-infectious complications following prostate biopsy: a randomized clinical trial. *J Urol* 2023; 209(Supplement 4): e1192

14 **Mian BM, Feustel PJ, Aziz A et al.** Complications following transrectal and Transperineal prostate biopsy: results of the ProBE-PC randomized clinical trial. *J Urol* 2024; 211: 205–13

15 **Hu JC, Assel M, Allaf ME et al.** Transperineal versus transrectal magnetic resonance imaging–targeted and systematic prostate biopsy to Prevent infectious complications: the PREVENT randomized trial. *Eur Urol* 2024. Online ahead of print. Available from: https://doi.org/10.1016/j.eururo.2023.12.015

16 **Kanagarajah A, Hogan D, Yao HH, Dundee P, O'Connell HE**. A systematic review on the outcomes of local anaesthetic transperineal prostate biopsy. *BJU Int* 2023; 131: 408–23

17 **Guo LH, Wu R, Xu HX et al.** Comparison between ultrasound guided Transperineal and transrectal prostate biopsy: a prospective, randomized, and controlled trial. *Sci Rep* 2015; 5: 16089

18 **Bryant RJ, Yamamoto H, Eddy B et al.** Protocol for the TRANSLATE prospective, multicentre, randomised clinical trial of prostate biopsy technique. *BJU Int* 2023; 131: 694–704

19 **Hu J, Zhu A, Vickers A et al.** Protocol of a multicentre randomised controlled trial assessing transperineal prostate biopsy to reduce infectiouscomplications. *BMJ Open* 2023; 13: e071191

20 **Weill Medical College of Cornell University**. Randomized trial comparing Transperineal vs. Transrectal MRI-Targeted Prostate Biopsy [Internet]. Report No: NCT04815876. 2023 [cited 2023 Jul 24]. Available from: https://clinicaltrials.gov/study/NCT04815876

21 **Weill Medical College of Cornell University**. Evaluation of Transperineal Biopsy Under Local Anesthesia, a Novel Approach to Decrease Post-Biopsy Infections and Improve Cancer Detection [Internet]. Report No: NCT04843566. 2023 [cited 2023 Sep 8]. Available from: https://clinicaltrials.gov/study/NCT04843566

22 **Touzani A, Fiard G, Barret E et al.** Clinical trial protocol for PERFECT: a randomised controlled trial comparing the efficiency and tolerance of Transperineal fusion versus transrectal imaging-targeted prostate biopsies (CCAFU-PR1 study). *Eur Urol Open Sci* 2022; 45: 76–80

23 **Ploussard G**, **Barret E**, **Fiard G et al.** Transperineal versus transrectal magnetic resonance imaging–targeted biopsies for prostate cancer diagnosis: final results of the randomized PERFECT trial (CCAFU-PR1). *Eur Urol Oncol* 2024. https://doi.org/10.1016/j.euo.2024.01.019

24 **Omer A**, **Lamb AD**. Optimizing prostate biopsy techniques. *Curr Opin Urol* 2019; 29: 578–86

25 **Zattoni F**, **Marra G**, **Kasivisvanathan V et al.** The detection of prostate cancer with magnetic resonance imaging-targeted prostate biopsies is superior with the Transperineal vs the transrectal approach. A European Association of Urology-young academic urologists prostate cancer working group multi-institutional study. *J Urol* 2022; 208: 830–7

26 **Ahmed HU**, **Bosaily AES**, **Brown LC et al.** Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* 2017; 389: 815–22

27 **Wu Q**, **Tu X**, **Zhang C et al.** Transperineal magnetic resonance imaging targeted biopsy versus transrectal route in the detection of prostate cancer: a systematic review and meta-analysis. *Prostate Cancer Prostatic Dis* 2023. Online ahead of print. Available from: https://doi.org/10.1038/s41391-023-00729-4

28 **Uleri A**, **Baboudjian M**, **Tedde A et al.** Is there an impact of Transperineal versus transrectal magnetic resonance imaging–targeted biopsy in clinically significant prostate cancer detection rate? A systematic review and meta-analysis. *Eur Urol Oncol* 2023; 6: 621–8

29 **Lopez JF**, **Campbell A**, **Omer A et al.** Local anaesthetic transperineal (LATP) prostate biopsy using a probe-mounted transperineal access system: a multicentre prospective outcome analysis. *BJU Int* 2021; 128: 311–8

30 **Kuru TH**, **Wadhwa K**, **Chang RTM et al.** Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg Study Group for Enhanced Prostate Diagnostics. *BJU Int* 2013; 112(5): 568–77

31 **Batura D**, **Gopal Rao G**. The national burden of infections after prostate biopsy in England and Wales: a wake-up call for better prevention. *J Antimicrob Chemother* 2013; 68: 247–9

32 **Tamhankar AS**, **El-Taji O**, **Vasdev N**, **Foley C**, **Popert R**, **Adshead J**. The clinical and financial implications of a decade of prostate biopsies in the NHS: analysis of hospital episode statistics data 2008–2019. *BJU Int* 2020; 126: 133–41

33 **Rosario DJ**, **Lane JA**, **Metcalfe C et al.** Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. *BMJ* 2012; 344: d7894

34 **Berry B**, **Parry MG**, **Sujenthiran A et al.** Comparison of complications after transrectal and transperineal prostate biopsy: a national population-based study. *BJU Int* 2020; 126: 97–103

35 **Pradere B**, **Veeratterapillay R**, **Dimitropoulos K et al.** Nonantibiotic strategies for the prevention of infectious complications following prostate biopsy: a systematic review and meta-analysis. *J Urol* 2021; 205: 653–63. https://doi.org/10.1097/JU.0000000000001399

36 **Jacewicz M**, **Günzel K**, **Rud E et al.** Antibiotic prophylaxis versus no antibiotic prophylaxis in transperineal prostate biopsies (NORAPP): a randomised, open-label, non-inferiority trial. *Lancet Infect Dis* 2022; 22: 1465–71

37 **Loeb S**, **Vellekoop A**, **Ahmed HU et al.** Systematic review of complications of prostate biopsy. *Eur Urol* 2013; 64: 876–92

38 **Pinkhasov GI**, **Lin YK**, **Palmerola R et al.** Complications following prostate needle biopsy requiring hospital admission or emergency department visits – experience from 1000 consecutive cases. *BJU Int* 2012; 110: 369–74

39 **Berquin C**, **Perletti G**, **Develtere D et al.** Transperineal vs. transrectal prostate biopsies under local anesthesia: a prospective cohort study on patient tolerability and complication rates. *Urol Oncol Semin Orig Investig* 2023; 41: 388.e17–388.e23

40 **Merrick GS**, **Irvin S**, **Fiano R**, **Anderson R**, **Butler WM**, **Adamovich E**. Pathology and quality of life outcomes following office-based Transperineal prostate biopsy. *Urology* 2016; 94: 24–8

41 **Marra G**, **Zhuang J**, **Beltrami M et al.** Transperineal freehand multiparametric MRI fusion targeted biopsies under local anaesthesia for prostate cancer diagnosis: a multicentre prospective study of 1014 cases. *BJU Int* 2021; 127: 122–30

42 **Freedman B**. Equipoise and the ethics of clinical research. *N Engl J Med* 1987; 317: 141–5

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Abbreviations: CamPROBE, CAMbridge PROstate Cancer Biopsy device; DG, diagnostic guidance; EAU, European Association of Urology; GA, general anaesthetic; ICER, incremental cost-effectiveness ratio; IIEF, International Index of Erectile Function; LA, local anaesthetic; NICE, National Institute for Health and Care Excellence; PCORI, Patient-Centered Outcome Research Institute; PERFECT, TransPERineal Fusion Biopsy Versus transrectal (study); PI-RADS, Prostate Imaging-Reporting and Data System; PREVENT, PReclude Infection EVEnts With No Prophylaxis Transperineal Biopsy (trial); ProBE-PC, Prostate Biopsy, Transrectal vs Transperineal: Efficacy and Complications (trial); PROM, patient-reported outcome measure; QALY, quality-adjusted life year; RCT, randomised controlled trial; TP, transperineal; TRANSLATE, TRANSrectal biopsy versus Local Anaesthetic Transperineal biopsy in Evaluation of men with potential clinically significant prostate cancer (trial).