Title: Local Anaesthetic Transperineal Prostate (LATP) biopsy using a probe-mounted transperineal access system: A multi-centre prospective outcome analysis

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Abstract:

Objectives:

To assess the feasibility of local anaesthetic transperineal (LATP) technique using a single-freehand transperineal access device, and report initial prostate cancer (PCa) detection, infection rates and tolerability.

Patients and methods:

Observational study of a multicentre prospective cohort, including all consecutive cases. LATP was performed in three settings: 1) first biopsy in suspected PCa, 2) confirmatory biopsies for active surveillance and 3) repeat biopsy in suspected PCa. All patients received pre-procedure antibiotics according to local hospital guidelines. Local anaesthesia was achieved by perineal skin infiltration and periprostatic nerve block without sedation. Ginsburg protocol principles were followed for systematic biopsies including cognitive MRI targeted biopsies when needed using the Precision Point™ transperineal access device. Procedure related complications and oncological outcomes were prospectively and consecutively collected. A validated questionnaire was used in a subset of centres to collect data on patient reported outcomes (PROMs).

Results

Some 1218 patients underwent LATP biopsies at ten centres: 55%, 24% and 21% for each of the three settings respectively. Any-grade PCa was diagnosed in 816 patients (67%), of

which 634 (52% of total) had clinically significant disease. Two cases of sepsis were documented (0.16%) and urinary retention was observed in 19 patients (1.6%). PROMs were distributed to 419 patients with a 56% response rate (n=234). In these men, pain during the biopsy was described as either “not at all” or “a little” painful by 64% of patients. Haematuria was the most common reported symptom (77%). When exploring attitude to re-biopsy, 48% said it would be “not a problem” and in contrast 8.1% would consider it a “major problem”. Most of the patients (81%) described the biopsy as a “minor or moderate procedure tolerable under local anaesthesia”, while 5.6% perceived it as a “major procedure that requires general anaesthesia”.

Conclusion

Our data suggest that LATP biopsy using a transperineal access system mounted to the ultrasound probe achieves excellent PCa detection with very-low sepsis rate and is safe and well tolerated. We believe a randomized controlled trial comparing LATP with TRUS to investigate the relative trade-offs between each biopsy technique would be helpful.

Patient summary:

In this international multicentre collaboration, we report the initial experience after the introduction of local anaesthetic transperineal (LATP) prostate biopsy. We found that this approach is safe and well tolerated by patients, with very low risk of infection and excellent prostate cancer detection rates.

1. Introduction

Prostate biopsy has evolved significantly during the past century as a procedure used to diagnose prostate cancer (PCa). It was first described in 1926 with an open perineal approach, evolving towards less invasive procedures (1). With the development of ultrasound (US) during the 1980s, transrectal ultrasound prostate biopsy (TRUS) became the standard. However, the emergence of antibiotic resistance has led to an increase of infectious complications after TRUS, leading the urological community to rethink the optimal way to perform a diagnostic prostate biopsy (2).

The idea to use the transperineal (TP) route was revived in the 1990s (1). Modern TP biopsy was implemented to perform mapping or template biopsies, in which an extensive sampling of the prostate was undertaken using a brachytherapy stepper, performing needle punctures in the perineum for each core taken. This makes it a painful and more complex procedure, requiring general or spinal anaesthesia in an operating theatre setting, leading to an important rise in costs and limiting availability (3). Among the advantages associated with this approach are a lower rate of infection and sepsis, and better sampling performance on the anterior and apical regions (4).

Given the sepsis rates associated with TRUS, and problems with rising antibiotic resistance rates, some groups have implemented local anaesthesia transperineal approaches (LATP) that can be performed in an outpatient setting, making it more accessible and less expensive. In light of this, current NICE and EAU guidelines no longer distinguish between TP (non-mapping) and TRUS biopsy, considering both a valid alternative in the first-biopsy setting (5)(6).

In this international collaborative study, we assessed the feasibility of a LATP single-freehand technique using a TP access device (the Precision Point^{TM}) and report initial cancer detection, infection rates and tolerability in ten centres using the device for the first time.

2. Methods

2.1. Study design

Observational, multicentre prospective cohort.

2.2. Study cohort

Ten international centres were invited to participate in this collaborative study: Churchill Hospital (CH), Oxford, UK; Lister Hospital (LH), Stevenage, UK; Guys Hospital (GH), London, UK; Norfolk and Norwich University Hospital (NNUH), UK; Southmeads Hospital, Bristol, UK (BH); Queen Alexandra Hospital (QAH), Portsmouth, UK; Kent and Canterbury Hospital (KCH), UK; Salisbury District Hospital (SH), Salisbury, UK; Auckland City Hospital, New Zealand (NZ); Hong Kong University Medicine (HK).

In all centres except one (GH), TRUS remained the standard approach in the primary prostate cancer diagnostic pathway, while TP was performed under general anaesthesia in selected cases. In these nine units, LATP was generally offered for patients requiring a second biopsy due to discordance between TRUS results and clinically expected results, and when confirmatory biopsies for active surveillance were planned. In some centres LATP was offered upfront in cases where an anterior or apical lesion was identified on pre-biopsy MRI, and in patients assessed as high risk for sepsis or general anaesthetic complication.

We have intentionally included all consecutive LATP cases in all centres, with no exclusions. In consequence, patients with a reduced number of cores due to clinical needs or tolerance were also considered.

Data on patient characteristics, oncological outcomes and complications were collected prospectively and consecutively using an electronic proforma, which was returned by participating centres. Clinically significant PCa (csPCa) was defined as Gleason Grade Group (GGG) $\geq$2 disease.

2.3. Patient reported outcomes (PROMs)

In five centres, at the end of the procedure, each participant received a previously validated patient reported outcomes measures questionnaire (PROMs), which they were asked to complete two weeks after the procedure and return at their next appointment (7).

2.4. LATP technique

The PrecisionPoint™ TP access system was used by all centres. This consist of a carriage and a clamp that can attach to any transrectal ultrasound probe, providing support for a thick needle (15 G) that is used as a sheath to access the perineum. This permits a single-freehand TP biopsy.

After informed consent, patients received prophylactic antibiotics according to local practice (**Table 1**). The patient was then placed in the lithotomy position, the scrotum was elevated away from the perineum using the gown and tape, and the skin prepped with an iodine-based sanitizer. Local anaesthesia was achieved using a maximal dose of lidocaine 200mg without adrenaline in two steps. Firstly, the perineal skin on both sides of the raphe was infiltrated, including the anal verge to minimize discomfort with the probe which is then inserted with the TP access system attached. Secondly, under US guidance and using a spinal needle, the deep connective tissue was infiltrated and a periprostatic nerve block achieved. A 14G needle was then engaged into the perineal skin and a free hand TP biopsy performed using a 18G disposable biopsy gun. In patients with larger prostates, the height of the 14G needle was adjusted to ensure proper reach of anterior and posterior sectors (8). Biopsies were carried out following the principles of the Ginsburg protocol adapting to clinical needs. The number of biopsies where reduced in patients with a clinical diagnosis of PCa in whom histological confirmation was needed for commencement of systemic therapy. MRI targeted biopsies where added when appropriate (9) (*video reference – file supplied, awaiting update on acceptance* https://www.youtube.com/watch?v=q-lYzpuV6tk*).*

2.5. Statistical analysis

Continuous variables were expressed as median, reporting interquartile range (IQR). Categorical variables were expressed as absolute numbers and percentages.

3. Results

Some 1218 patients underwent LATP biopsy within ten participating centres. Eight of these centres were in England, one in Hong Kong and one in New Zealand. All biopsies were performed between April 2018 and March 2020.

Indications for biopsy were classified in three groups: suspected PCa in biopsy naïve patients (n= 674, 55%), active surveillance confirmatory or follow-up biopsies (n= 287, 24%) and re-biopsy due to previous negative biopsies with persistent suspicion of csPCa (n=257, 21%). Patient age was 68 (62 – 73) years (median, IQR) and median PSA was 7.6 mg/ml (IQR 5.4 – 11.7 mg/ml). Digital rectal examination was abnormal in 355 patients (35%) (**Table 1**).

The majority of patients on active surveillance had previously diagnosed GGG 1 PCa (n=213, 74%), while a smaller proportion had low-volume GGG 2 (n=74, 26%). Of the re-biopsy group 46 (18%) had either ASAP or high-grade PIN on previous biopsy.

As part of their diagnostic work-up, 1020 patients (84%) had a pre-biopsy multi-parametric MRI (mpMRI) prior to LATP biopsy, reporting a target in 752 (74%) of cases. The PIRADS scoring system was available for 867 (85%) of reported mpMRIs, with PIRADS 4 or 5 lesions reported in 467 (46%) of cases. PCa detection was greater among higher PIRADS scores, being 86% (82% csPCa) for PIRADS 5 lesions, 72% (56% csPCa) for PIRADS 4 and 62% (39% csPCa) for PIRADS 3 (**Table 2**). The median prostate volume was 46 cc (IQR 33 – 65 cc). Anterior lesions were reported on mpMRI in 203 patients (20%), and 168 (83%) of these cases were found to contain any-grade PCa, whilst csPCa was found in 138 cases (70%).

The median number of cores taken was 24 (range 1 – 47). Any-grade PCa was detected in 816 patients (67%), while csPCa was diagnosed in 634 (52%) **(Table 1)**. Detection rates of any-grade in biopsy naive, active surveillance and re-biopsy groups were 72%, 73%, and 46%, and csPCa in 83%, 70% and 68% respectively (**Supplemental table 1**).

Amongst patients on active surveillance, any-grade PCa was found in 210 patients (73%). Upgrading was observed in 105 cases (67%) of GGG 1 patients, with 82 (78%) upgraded to

GGG 2 and 23 (22%) to higher groups. In GGG 2 patients, upgrading was observed in 14 cases (26%) (increased proportion of Gleason pattern 4 or higher GGG).

Two cases of sepsis were documented in the entire series (0.16%). One was an immunocompromised patient with a pre-existing low-grade urinary infection and the second a patient with previous negative urine culture. Both patients were admitted for intravenous antibiotics with good response. One patient presented un-complicated epididymo-orchitis and was managed with oral antibiotics. Some patients experienced self-limiting vaso-vagal symptoms during the procedure not requiring further management. Acute urinary retention was observed in 20 patients (1.6%).

PROMs questionnaires were used in five of the ten participating centres during their initial experience (CH, LH, NNUH, BH, and HK). These were distributed to 419 patients with a 56% response rate (n=234). Haematuria was the most commonly reported symptom (77%, n=181), followed by haemoejaculate (50%, n=116) and pain (37%, n=87). Pain after the procedure was considered a moderate problem by 18 patients (7.7%) while two (0.85%) described it as a severe problem. The symptom of “feeling feverish” was reported in 11 cases (4.7%) (Table 3). A health professional was contacted by 23 patients (9.8%) due to problems related to the biopsy and 10 (4.3%) were prescribed antibiotics, although only three of these individuals (1.3%) reported a fever.

Regarding patient perception of pain during the biopsy, 148 men (64%) described the procedure as either “not at all” or “a little” painful, while 33 (14%) found it “very painful”. Furthermore, only 16 men (6.8%) found it “very embarrassing”. When exploring their attitude to re-biopsy, 111 (48%) said it would be “not a problem”, and in contrast 45 (19%) considered it would be a “moderate” and 19 (8.1%) a “major” problem. When asked about how they would describe the biopsy, 186 men (81%) said that it was a minor or moderate procedure tolerable under local anaesthesia, while 13 (5.6%) perceived it as a major procedure that requires a general anaesthetic.

4. Discussion

We report here our unabridged initial data from ten units establishing LATP biopsy programmes using a TP access system. For each unit these data include the very first biopsies performed through to the reported censoring date. We therefore believe this is a genuine reflection of what units can expect if they adopt such a programme.

The use of a TP access system is less cumbersome, flexible and painful than the brachytherapy grid (10). These can be either probe-mounted, such as the Precision Point used in this series, BK 1342/1232, Leapmed or Koelis devices, which allow a single-freehand technique where only the hand carrying the ultrasound can move freely; or non-fixed, such as a coaxial needle or the CamPROBE, which are used in a double-freehand manner where both the ultrasound and biopsy carrying hands are required to move independently(11). Although we have not been able to undertake a detailed learning curve analysis with the available data, we believe that the single-freehand technique is easier for less experienced operators facilitating the transition from TRUS. Although similar results can be achieved using a double-freehand technique, it is more difficult and can take several years (12).

We now discuss our findings across three key outcomes: any-grade csPCa detection, complication rate focussing on sepsis, and patient-reported tolerability.

4.1. Cancer detection

TP biopsy PCa detection rates reported in the literature vary widely across settings, being higher in patients known to have cancer. For primary biopsies any-grade PCa detection rates range from 18-76%, in re-biopsy for previous negative biopsy 14-68%, and in active surveillance from 48-80% (4,13–15). This variability is partly explained by the different pre-test probability among biopsied populations. Our results are similar to those described in other publications.

It is noteworthy that we diagnosed a high proportion of csPCa compared to historic transrectal biopsy series. Although there is some debate over the definition of csPCa (16,17), using the definition of any Gleason Pattern 4 we found overall 51% csPCa in this mixed cohort including many repeats after previous negative biopsies. This high rate of detection of csPCa could be explained by the use of mpMRI to select patients in over 84% of cases. Pre-biopsy prostate mpMRI has become the gold-standard of care in the prostate cancer diagnostic pathway at a large number of institutions worldwide. This has modified our biopsy populations, enriching cohorts with patients more likely to have clinically significant disease and avoiding detection in men with low grade PCa. This shift alters the composition of contemporary cohorts, introducing an important distinction when comparing PCa detection rates with historical cohorts which relied on TRUS-guided biopsy without MRI.

As the role of mpMRI evolves in the PCa diagnostic pathway (5,6), approaches to prostate biopsy cannot be assessed in isolation, particularly with respect to diagnostic rates. Inevitably, factors modifying mpMRI accuracy such as the expertise of reporting radiologists and use of a standardized reporting system, can modify the reported biopsy outcomes. In this cohort, pre-biopsy mpMRI was employed in all except one unit (HK). A mixture of 1.5T and 3T MRI magnets were used and the PI-RADSv2 protocol was used for reporting. We anticipate, therefore, a degree of uniformity in lesion targeting but acknowledge the risk of potential variation across units.

Interestingly, the detection rate of clinically significant prostate cancer was higher for PIRADS 1 when compared to PIRADS 2, finding that was similar across groups. This rises a concern on the accuracy of the interpretation of MRI, however it could be related to variability as only 42 patients (3%) were categorized as PIRADS 1. On the other hand, it is possible that the practitioner is inclined to undertake a more comprehensive systematic biopsy in case of a negative MRI.

The ability to better sample the anterior and apical prostate might improve the performance of LATP regarding PCa detection compared to TRUS. In our series, an

important number of patients had anterior lesions detected on mpMRI, of which 83% resulted in the detection of any-grade PCa, with this being csPCa in the majority of cases.

4.2. Complications

The fear of sepsis has been present since the early development of prostate biopsy when the TP approach was preferred over the transrectal to avoid faecal contamination (1). This common sense observation has been a key driver to rethink how prostate biopsies ought to be performed, developing solutions to address the shortcomings of the TP route such that it could potentially replace TRUS as the gold standard approach if high quality evidence for this shift was available (18).

Previous TP series show that sepsis rate is extremely low, regardless of the use or omission of prophylactic antibiotics (2,15,19–22). Consistent with this, we had two cases of sepsis representing a 0.16% sepsis rate. When considering the subset of patients who responded to the PROMs questionnaire, a further ten patients were treated by their general practitioners for symptoms consistent with urinary tract infections (4.3%) of whom three (1.3%) reported fever. Thus, the infection rate with LATP is lower than that reported in TRUS biopsy series (23), although to date no randomised clinical trial directly comparing these biopsy techniques has been performed.

Urinary retention is commonly considered to be a risk after TP biopsy, with rates reported to be as high as 10% (24). Some groups have proposed that this may be because the template approach used in TP biopsies involves multiple punctures of the perineum, which potentially causes more inflammation and bruising around the membranous urethra (25). However, an alternative explanation is that the urinary retention rate in older TP series may be related to the use of general anaesthetic rather than to the approach itself. This phenomenon is well-recognised in orthopaedic surgery and may be relevant regarding TP biopsy under general anaesthesia (26). This can be confirmed when analysing LATP series, which report urinary retention rates of around 2%, which are similar to TRUS (15,23), and consistent with the rate of 1.6% in the series presented herein.

4.3. **Patient reported outcomes (PROMs)**

Although PROMs has been assessed before for TP biopsies (12,27), this is to our knowledge the first experience using a validated questionnaire in the LATP setting. The response rate to the PROMs questionnaire was lower than expected across centres, mainly because this was a paper questionnaire given to each patient at the end of the procedure with collection dependent upon patients voluntarily returning questionnaires. Nonetheless, the 56% response rate achieved in the five centres where the PROMs is close to the 60% response rate generally considered to be optimal in survey data (28,29). As with most PROMs, patients without any complication are less likely to return their questionnaires, potentially introducing a bias towards unfavourable results. This is diluted with higher response rates (9).

All patients reported some symptoms after the procedure, as is to be expected. Haematuria, haemoejaculate and pain, were the most common symptoms, which rarely presented as a moderate or major problem.

Haematuria and haemoejaculate present very frequently after biopsy, however, rarely require intervention. Most patients found these symptoms problematic. We believe that anticipation through thorough counselling before the procedure would help men to cope with these symptoms, making them less important and distressful.

A considerable number of patients perceived the biopsy as moderate (22%) or very painful (14%); however, most men (81%) considered LATP to be a procedure tolerable under local anaesthesia. Moreover, three quarters of men reflected that having another LATP biopsy would be “no” or only a “minor” problem. Most of these findings are very similar to TRUS results, making LATP as tolerable and acceptable as TRUS (7). Our impression is that discomfort in prostate biopsy is related to those characteristics common to TRUS and LATP, such as the transrectal probe, anaesthesia administration and anxiety, rather than to the route used (30,31).

We did not record the number of men in whom the procedure was discontinued for pain related reasons. However, in most cases, at least one biopsy core was obtained before abandoning the procedure, some of which were diagnostic not requiring further biopsies.

Successful pain control is essential for patient experience and acceptance of any local anaesthetic procedure. Although there is relatively little evidence regarding the best approach for administering anaesthesia, the prostatic apex block seems to be most widely used (32). Other factors such as environment (clinic versus operating theatre), operator experience and patient education can all help to ease anxiety and pain.

4.4. Limitations

This data reflects the experience of ten units introducing LATP biopsies, each one of them following their prostate cancer pathway using their own resources; creating a heterogenic cohort informative of diverse clinical scenarios and practices. Patient selection for LATP can vary across centres, as well as radiologist experience interpreting prostate MRI.

The observational nature of this study and the heterogeneity of its population do not allow drawing robust conclusions; however, its results are useful to inform about real world practice and provide part of the evidence needed to design future clinical trials comparing it to the current gold standard.

To date no randomized controlled trial comparing LATP with TRUS has been published providing the robust evidence needed to potentially shift towards LATP being the new gold standard for all PCa diagnostics in resource-limited healthcare systems.

5. Conclusion

Our data suggest that LATP biopsy using a TP access system is feasible, safe and well tolerated. Some centres have successfully trained and equipped units to undertake these biopsies in outpatient clinics in place of TRUS biopsy.

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Conflicts of Interest

This was a collaborative investigator-led project. AL is supported by a Clinician Scientist Cancer Research UK award, FCH, AL and RB have been partly supported by the Oxford NIHR Biomedical Research Centre Surgical Innovation and Evaluation Theme. RP is supported as a Fellow on the NHS Innovation Accelerator; received honoraria from BXT Accelyon for teaching and training on prostate biopsies, BK Ultrasound, 3D Biopsy; and has a professional services agreement with HCA International. There are no conflicts of interest for any of the other authors

References:

1. Pandian SK, Hammadeh M, Challacombe B, Popert R, Madaan S. History of prostate

biopsy. Urol News. 2018;22(2).

2. Grummet JP, Weerakoon M, Huang S, Lawrentschuk N, Frydenberg M, Moon DA, et al. Sepsis and “superbugs”: Should we favour the transperineal over the transrectal approach for prostate biopsy? BJU Int. 2014;114(3):384–8.
3. Altok M, Kim B, Patel BB, Shih Y-CT, Ward JF, McRae SE, et al. Cost and efficacy comparison of five prostate biopsy modalities: a platform for integrating cost into novel-platform comparative research. Prostate Cancer Prostatic Dis [Internet]. 2018 Nov 9;21(4):524–32. Available from: http://www.nature.com/articles/s41391-018-0056-7
4. Ong WL, Weerakoon M, Huang S, Paul E, Lawrentschuk N, Frydenberg M, et al. Transperineal biopsy prostate cancer detection in first biopsy and repeat biopsy after negative transrectal ultrasound-guided biopsy: The Victorian Transperineal Biopsy Collaboration experience. BJU Int. 2015;116(4):568–76.
5. EAU-ESUR-ESTRO-SIOG Guidelines on Prostate Cancer. 2019.
6. National Institute for Health and Care Excellence (NICE). Prostate cancer: diagnosis and management (NG131) [Internet]. 2019 [cited 2019 Dec 3]. Available from: https://www.nice.org.uk/guidance/ng131/resources/prostate-cancer-diagnosis-and-management-pdf-66141714312133
7. Rosario DJ, Lane JA, Metcalfe C, Donovan JL, Doble A, Goodwin L, et al. Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study. BMJ [Internet]. 2012 Jan 9;344(jan09 1):d7894–d7894. Available from: http://www.bmj.com/cgi/doi/10.1136/bmj.d7894
8. Campbell A, Omer AE, Popert R, Lamb A. Local anaesthetic transperineal prostate (LATP) biopsy using the precision point access system: A step-by-step video. Eur Urol Suppl [Internet]. 2019 Mar;18(1):e2290. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1569905619316707
9. Kuru TH, Wadhwa K, Chang RTM, Echeverria LMC, Roethke M, Polson A, 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.
10. Novella G, Ficarra V, Galfano A, Ballario R, Novara G, Cavalleri S, et al. Pain assessment after original transperineal prostate biopsy using a coaxial needle.

Urology [Internet]. 2003 Oct;62(4):689–92. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0090429503004837

11. Omer A, Lamb AD. Optimizing prostate biopsy techniques. Curr Opin Urol [Internet]. 2019 Nov;29(6):578–86. Available from: http://insights.ovid.com/crossref?an=00042307-201911000-00004
12. Marra G, Marquis A, Tappero S, D'Agate D, Oderda M, Calleris G, et al. Transperineal Free-hand mpMRI Fusion-targeted Biopsies Under Local Anesthesia: Technique and Feasibility From a Single-center Prospective Study. Urology [Internet]. 2020;140:122–31. Available from: https://doi.org/10.1016/j.urology.2019.11.078
13. Ganesan V, Dai C, Nyame YA, Greene DJ, Almassi N, Hettel D, et al. Prognostic Significance of a Negative Confirmatory Biopsy on Reclassification Among Men on Active Surveillance. Urology [Internet]. 2017;107:184–9. Available from: http://dx.doi.org/10.1016/j.urology.2017.06.014
14. Pepe P, Cimino S, Garufi A, Priolo G, Russo GI, Giardina R, et al. Confirmatory biopsy of men under active surveillance: extended versus saturation versus multiparametric magnetic resonance imaging/transrectal ultrasound fusion prostate biopsy. Scand J Urol [Internet]. 2017 Jul 4;51(4):260–3. Available from: https://www.tandfonline.com/doi/full/10.1080/21681805.2017.1313310
15. Marra G, Zhuang J, Beltrami M, Calleris G, Zhao X, Marquis A, 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 [Internet]. 2020 Aug 2; Available from: http://doi.wiley.com/10.1111/bju.15121
16. Ahmed HU, El-Shater Bosaily A, Brown LC, Gabe R, Kaplan R, Parmar MK, et al. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. Lancet. 2017;
17. Sathianathen N, Omer A, Harriss E, Davies L 3, Kasivisvanathan V, Punwani S, et al. Negative predictive value of multi-parametric MRI in detection of clinically significant prostate cancer in the PI-RADS era: a systematic review and meta-analysis. Eur Urol. 2020;in press.
18. Grummet J, Gorin MA, Popert R, O'Brien T, Lamb AD, Hadaschik B, et al. "TREXIT 2020": why the time to abandon transrectal prostate biopsy starts now. Prostate Cancer Prostatic Dis [Internet]. 2020 Jan 13; Available from:

http://www.nature.com/articles/s41391-020-0204-8

19. Gorin MA, Meyer AR, Zimmerman M, Harb R, Joice GA, Schwen ZR, et al. Transperineal prostate biopsy with cognitive magnetic resonance imaging/biplanar ultrasound fusion: description of technique and early results. World J Urol [Internet]. 2019;(0123456789). Available from: https://doi.org/10.1007/s00345-019-02992-4
20. Stefanova V, Buckley R, Flax S, Spevack L, Hajek D, Tunis A, et al. Transperineal Prostate Biopsies Using Local Anesthesia: Experience with 1,287 Patients. Prostate Cancer Detection Rate, Complications and Patient Tolerability. J Urol [Internet]. 2019 Jun;201(6):1121–6. Available from: http://www.jurology.com/doi/10.1097/JU.0000000000000156
21. Wadhwa K, Carmona-Echeveria L, Kuru T, Gaziev G, Serrao E, Parashar D, et al. Transperineal prostate biopsies for diagnosis of prostate cancer are well tolerated: A prospective study using patient-reported outcome measures. Asian J Androl. 2017;19(1):62–6.
22. Vyas L, Acher P, Kinsella J, Challacombe B, Chang RTM, Sturch P, et al. Indications, results and safety profile of transperineal sector biopsies (TPSB) of the prostate: A single centre experience of 634 cases. BJU Int. 2014;114(1):32–7.
23. Borghesi M, Ahmed H, Nam R, Schaeffer E, Schiavina R, Taneja S, et al. Complications After Systematic , Random , and Image-guided Prostate Biopsy. Eur Urol [Internet]. 2016; Available from: http://dx.doi.org/10.1016/j.eururo.2016.08.004
24. National Institute for Health and Care Excellence (NICE). Interventional procedures programme: Interventional procedure overview of transperineal template biopsy and mapping of the prostate (IP793). 2010.
25. Kum F, Jones A, Nigam R. Factors influencing urinary retention after transperineal template biopsy of the prostate: outcomes from a regional cancer centre. World J Urol [Internet]. 2019;37(2):337–42. Available from: https://doi.org/10.1007/s00345-018-2390-8
26. Halawi MJ, Caminiti N, Cote MP, Lindsay AD, Williams VJ. The Most Significant Risk Factors for Urinary Retention in Fast-track Total Joint Arthroplasty are Iatrogenic. J Arthroplasty [Internet]. 2019 Jan;34(1):136–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0883540318307484
27. Miah S, Eldred-Evans D, Simmons LAM, Shah TT, Kanthabalan A, Arya M, et al. Patient

Reported Outcome Measures for Transperineal Template Prostate Mapping Biopsies in the PICTURE Study. J Urol [Internet]. 2018;200(6):1235–40. Available from: https://doi.org/10.1016/j.juro.2018.06.033

28. Fincham JE. Response Rates and Responsiveness for Surveys, Standards, and the Journal. Am J Pharm Educ [Internet]. 2008 Sep 1;72(2):43. Available from: http://www.ajpe.org/lookup/doi/10.5688/aj720243
29. Morton SMB, Bandara DK, Robinson EM, Carr PEA. In the 21 st Century, what is an acceptable response rate? Aust N Z J Public Health [Internet]. 2012 Apr;36(2):106–8. Available from: http://doi.wiley.com/10.1111/j.1753-6405.2012.00854.x
30. Luscombe CJ, Cooke PW. Pain during prostate biopsy. Lancet. 2004;363(9424):1840–1.
31. Marra G, Zhuang J, Marquis A, Zhao X, Calleris G, Kan Y, et al. Pain in Men Undergoing Transperineal Free-Hand mpMRI Fusion-Targeted Biopsies under Local Anesthesia: Outcomes and Predictors from a Multicenter Study of 1,008 Patients. J Urol [Internet]. 2020 Jul 6; Available from: http://www.jurology.com/doi/10.1097/JU.0000000000001234
32. McGrath S, Christidis D, Clarebrough E, Ingle R, Perera M, Bolton D, et al. Transperineal prostate biopsy – tips for analgesia. BJU Int. 2017;120(2):164–7.

Table 1. Patient characteristics, pathology outcomes and complications per centre

		Centre									
	Total	BH	CH	GH	HK	KCH	LH	NNUH	NZ	QAH	SH
Number of patients (n)	1218	163	227	43	48	175	171	116	24	156	95
Indication n, (%)											
Biopsy näive	674 (55%)	100 (61%)	39 (17%)	37 (86%)	48 (100%)	56 (32%)	91 (53%)	92 (78%)	24 (54%)	140 (90%)	59 (62%)
Active surveillance	287 (24%)	17 (10%)	101 (44%)	1 (2.3%)	-	73 (42%)	25 (15%)	16 (14%)	8 (33%)	11 (7.0%)	35 (37%)
Re-biopsy	257 (21%)	46 (28%)	87 (38%)	5 (12%)	-	46 (26%)	55 (32%)	9 (7.7%)	3 (13%)	5 (3.2%)	1 (1%)
Age (years) median (IQR)	68 (62 – 73)	68 (62 – 72)	66 (60 – 70	65 (60 – 69)	-	70 (63 – 73)	68 (62 – 75)	68 (63 – 72)	68 (62 – 70)	73 (66 – 77)	69 (62 – 72)
PSA (mg/ml) median (IQR)	7.6 (5.4 – 11.7)	8.2 (5.9 – 12.5)	7.2 (5.2 – 10.9)	7.9 (5.4 – 13.8)	6.5 (5.0 – 9.9)	6.9 (4.8 – 10.1)	6.8 (5.1 – 9.6)	8.7 (5.9 - 12.5)	7.5 (5.2 – 12.4)	12.8 (7.1 – 30.4)	6.6 (5.1 – 9.1)
Volume (ml) median (IQR)	46 (33 - 65)	40 (29 - 53)	48 (38 - 75)	42 (30 - 62)	-	50 (37 - 69)	52 (40 - 72)	41 (30 - 55)	-	41 (30 - 56)	-
mpMRI done, n (%)	1020 (84%)	157 (96%)	220 (97%)	41 (95%)	0 (0%)	172 (98%)	171 (100%)	96 (83%)	24 (100%)	48 (31%)	91 (96%)
PIRADS, n (%)											
1	42 (4.1%)	4 (2.5%)	19 (8.6%)	0 (0%)	-	6 (3.4%)	0 (0%)	12 (12%)	1 (4.1%)	0 (0%)	0 (0%)
2	141 (16%)	32 (21%)	12 (5.5%)	3 (7.3%)	-	58 (34%)	2 (4.5%)	16 (17%)	2 (8.2%)	5 (11%)	11 (12%)
3	217 (25%)	65 (42%)	54 (27%)	14 (34%)	-	31 (18%)	10 (23%)	13 (13%)	5 (23%)	4 (8.3%)	21 (24%)
4	287 (33%)	36 (23%)	84 (41%)	13 (32%)	-	60 (35%)	25 (56%)	17 (18%)	9 (41%)	6 (13%)	38 (43%)
5	180 (21%)	18 (12%))	34 (17%)	11 (27%)	-	17 (10%)	7 (16%)	38 (40%)	5 (23%)	32 (67%)	19 (21%)
Cancer detection	816 (67%)	100 (61%)	130 (57%)	36 (83%)	13 (27%)	106 (61%)	114 (67%)	94 (81%)	20 (83%)	127 (81%)	76 (80%)

Clinically significant cancer	634 (78%)	67 (67%)	102 (78%)	32 (89%)	9 (69%)	75 (71%)	85 (75%)	84 (89%)	15 (75%)	118 (93%)	47 (62%)
Acute urinary retention, n (%)	20 (1.6%)	0 (0%)	3 (1.3%)	0 (0%)	4 (8.3%)	0 (0%)	5 (4.2%)	5 (4.3%)	0 (0%)	1 (0.64%)	2 (2.1%)
Prophylactic antibiotics	-	Ciprofloxacin, single dose, PO	Ciprofloxacin, single dose, PO	Co-amoxiclav, single dose, PO	Ciprofloxacin, single dose, PO	not used	Co-amoxiclav, single dose, PO	Ciprofloxacin, single dose, PO	Cephalexin, single dose, PO	Ciprofloxacin, single dose, PO	Gentamicin, single dose, IM
Sepsis, n (%)	2 (0.16%)	0 (0%)	1 (0.44%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.64%)	0 (0%)

Table 2. PIRADS score and cancer detection rates

PIRADS	n	Cancer detection rate	
		Any-grade cancer	Clinically significant
1	42	52% (22)	38% (16)
2	141	43% (60)	20% (28)
3	217	62% (135)	39% (84)
4	287	72% (206)	56% (160)
5	180	86% (155)	82% (147)
Not reported / Not done	351	68% (238)	57% (199)
Overall	**1218**	**67% (816)**	**52% (634)**

Table 3. Patient reported symptoms (PROMs) - prevalence and association with moderate or severe problem after biopsy.

Symptom reported	Symptom present, n (%)	Moderate/major problem, n (%)
Fever	11 (4.7%)	6 (2.5%)
Nausea	13 (5.5 %)	3 (1.3%)
Pain	87 (37%)	19 (8.1%)
Felt unwell	21 (8.9%)	9 (3.8%)
Haematuria	282 (77%)	16 (6.8%)
Haematochezia	27 (11%)	4 (1.7 %)
Haematospermia	116 (49%)	19 (8.1%)