NICE National Institute for Health and Care Excellence

Transperineal biopsy in people with suspected prostate cancer

Diagnostics Assessment Report (DAR) – Comments

Stakeholder	Comment no.	Page no.	Section no.	Comment	EAG Response
JEB Technologies Ltd	1	37	1.2.2	Camprobe description states that Camprobe does not have a needle guide. We agree that Camprobe does not employ the use of a "fixed to the ultrasound probe" guidance system but, the cannula does act a needle guide for the biopsy needle. Therefore can this statement be modified to recognise this point?	Thank you, comment noted
JEB Technologies Ltd	2	160	Table 63	Please explain why the nurse, Urologist and place of biopsy costs are higher than a number the other devices?	These costs are adjusted for the duration of procedure, as explained in Appendix 12 of the DAR (page 329). The differences in costs between LATP methods do not change the cost-effectiveness results. For example, with a procedure duration of 17.51 minutes for all LATP methods and 14.73 min for LA-TRUS (durations reported by Guo et al. 2015, n=339),[1] the ICER of the revised EAG base case (reported in section 3 of the Addendum) falls from £15,669 per QALY to £14,646 per QALY for LATP-any compared with LATRUS and from £743 per QALY to £509 per QALY for LATP-freehand compared with LATRUS.
JEB Technologies Ltd	3	5		Limitations – This is not the biggest issue but is it best to just state the facts of the limitations, and not to state what evidence is or is not available within this sub-section?	Our point here is that the key limitation is that there is uncertainty due to the lack of evidence for freehand devices other than PrecisionPoint™.
Royal Surrey NHS Foundation Trust	4	5	Conclusions	General: We commend Dr. Shepherd and his team for the diagnostic assessment report and economic model and agree with the conclusions reached in the abstract on page 5. However, we would like to draw attention to some points that we believe deserve further consideration. These concern the evaluation of the six free hand devices for perineal access that have been described in the assessment. There is comparative evidence for the PrecisionPoint™ Transperineal Access	We agree that comparative evidence for the freehand devices other than PrecisionPoint™ is lacking. This is highlighted in the Limitations section of the Abstract and at various points through the DAR. We also present a cost-effectiveness scenario using costs for PrecisionPoint™ only, to align with the clinical effectiveness evidence (DAR Table 87, page 209).

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				System including a randomised trial but limited evidence or none for the other freehand devices. Therefore, it is assumed that all the devices have same efficacy and safety profile as the Precision Point device which may or may not be the case. These assumptions impact on both the diagnostic assessment and the economic model.	
Royal Surrey NHS Foundation Trust	5	Various		Evidence base: As the authors note, the evidence for the 6 free hand devices is sparse. Even so we feel that the use of conference abstracts as references is unacceptable as they are not peer reviewed and do not provide the level of evidence required for this type of evaluation. Some examples follow.	Evidence for diagnostic assessments can be sparse, in which case abstracts may still be an important source of information. Abstract presented at national or international conferences usually undergo review by a the conference scientific committee, thus, scientific credibility is required. We therefore included relevant abstracts published in the last 4 years only (2018- 2021) if they contained sufficient details to allow appraisal of the methodology and assessment of results, as specified in the protocol for the DAR.
Royal Surrey NHS Foundation Trust	6	58 and 232	Table 3 Reference list	Conference Abstracts: Ref 26 Lam et al. and Ref 31 Hung et al. do not indicate what transperineal access device has been used for the transperineal route yet are ascribed to the Precision Point device in table 3 page 58 of the assessment. Ref 32 Kum et al is described as conference abstract when in fact a peer reviewed observational study with the same title was published in 2019. (Kum F et al, PMID: 30431694). Ref 44 Yamamoto does not identify the transperineal access device employed although it is ascribed to the UA1232	We confirmed by email correspondence with Lam (lead author on Lam et al. 2021 and co-author on Hung et al. 2020)[2 3] that both of these abstracts do relate to LATP with the PrecisionPoint™ device. The Kum peer reviewed publication [4] and the Kum conference abstract[5] report the same study. Some data are exclusively reported by the abstract by and likewise the peer reviewed publication, therefore we extracted data from both publications for this study. Where we reference the Kum study in our report we should have cited both publications but, due to an oversight, we only cite the conference abstract. Apologies for the confusion.

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Royal Surrey NHS Foundation Trust	7	Various pages		Stakeholders are being asked to give an opinion on a document containing redacted information noted as Academic in Confidence (AIC). What does this mean and how should it be evaluated? Will the final document also be redacted?	The NICE Diagnostics Assessment Programme manual does allow for submission of confidential information.[6] Any such information is redacted in the DAR released to stakeholders and from documents published on the NICE website, unless the confidential status of the information changes during the course of the evaluation.
Royal Surrey NHS Foundation Trust	8			Lopez et al. (PMID 33448607), describe the "real world" experience of LATP in 1218 patients in 9 UK and 2 international hospitals and should be added to the references.	Lopez et al. (2021)[7] is single arm prospective cohort study and was identified in our searches. It did not meet the inclusion criteria for the review because it did not compare LATP to any alternative method. However, we included it in a 'reserve' list of LATP freehand device single-arm studies. If comparative evidence for a LATP freehand device was lacking we would draw on single arm studies as an alternative. This was not necessary for Lopez et al because we identified comparative evidence for PrecisionPoint.™ However, we agree that this paper does provide useful background information on use of LATP with PrecisionPoint™ in clinical practice.
BXTAccelyon Limited	9	5	Limitations	"*There is limited evidence for efficacy in detecting clinically significant cancer detection rates.*" We note and acknowledge that evidence is not abundant hence this comment but believe there is data that has suggested a higher detection rate for transperineal biopsies for clinically significant and anterior prostate cancers . We refer you to these studies: 1) Pietro Pepe 1, Antonio Garufi et al.Transperineal Versus Transrectal MRI/TRUS Fusion Targeted Biopsy: Detection Rate of Clinically Significant Prostate Cancer Clin Genitourin Cancer. 2017 Feb;15(1):e33-e36.	1) We identified the study by Pepe et al (2017) [8] in our searches but excluded it as a single arm (non-comparative) study. 2) Ber et al. (2020) is a study in which biopsies were performed using computer fusion software. Cognitive fusion biopsies were eligible for inclusion in our review, however software-based fusion biopsies were not. Thus, Ber would not meet our inclusion criteria on this basis. 3) We screened the reference lists of relevant systematic reviews identified by the database searches, to identify any additionally relevant primary studies we had not already found. Rai et al. (2021) [9] was one of the systematic reviews we identified and whose reference list we screened for

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				2) Ber, Y., Segal, N., Tamir, S. et al. A noninferiority within-person study comparing the accuracy of transperineal to transrectal MRI–US fusion biopsy for prostate-cancer detection. Prostate Cancer Prostatic Dis 23, 449–456 (2020). https://doi.org/10.1038/s41391-020-0205-7A noninferiority within-person study comparing the accuracy of transperineal to transrectal MRI–US fusion biopsy for prostate-cancer detection 3) Rai BP, Mayerhofer C, Somani BK, Kallidonis P, Nagele U, Tokas T. Magnetic Resonance Imaging/Ultrasound Fusion-guided Transperineal Versus Magnetic Resonance Imaging/Ultrasound Fusion-guided Transrectal Prostate Biopsy-A Systematic Review. Eur Urol Oncol. 2021 Jan 18:S2588-9311(21)00002-X. doi: 10.1016/j.euo.2020.12.012. Epub ahead of print. PMID: 33478936.	potentially relevant primary studies. However, we did not include Rai et al or any of the other systematic reviews in our review.
BXTAccelyon Limited	10	5	Limitations	*"There is comparative evidence for the PrecisionPoint™ Transperineal Access System but limited or no evidence for the other freehand devices"* We note and appreciate that this has been acknowledged by the report authors. We will refer to this in later comments.	No response required.
BXTAccelyon Limited	11	5	Conclusions	*"Transperineal prostate biopsy under local anaesthetic is equally efficient at detecting prostate cancer as transrectal ultrasound-guided prostate biopsy under local anaesthetic but it may be better with a freehand device. LATP is associated with urinary retention type complications whereas LATRUS has a higher infection*	No response required.

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				rate. For people at high risk of prostate cancer, LATP biopsy with a freehand device appears to meet conventional levels of cost effectiveness." We note and agree with this conclusion of the report	
BXTAccelyon Limited	12	6/7	Background	*"Various freehand devices to assist with LATP prostate biopsy are being introduced to the market. The six specific freehand devices specified in the NICE scope for this review are: Cambridge Prostate Biopsy Device (CamPROBE) (JEB Technologies Ltd, Suffolk, UK); EZU-PA3U; PrecisionPoint™ Transperineal Access System (BXTAccelyon Ltd, Burnham UK); SureFire Guide (LeapMed, Jiangsu, China); Trinity® Perine Grid (KOELIS®, New Jersey, USA); UA1232 puncture attachment (BK Medical, Massachusetts, USA).* The devices differ in a number of respects: 1. Registration status (some do not have CE mark); 2. The method of use of the devices. [We note that in sections of the report it is assumed a number of the devices are used with an access needle. Please could the authors clarify what the assumption is based upon? If there is no evidence or data for that assumption and devices have not been tested for use with an access needle we would respectfully ask that guidance is included to that effect and that there is no endorsement of this within the report?] 3. Only PrecisionPoint has been used in any meaningful form of comparative study (other than potentially a single-arm study for one or two of the other devices).	At this point in the Summary we are simply listing the interventions as in the NICE scope. We do not state here or elsewhere that the devices are 'similar' with regard to the characteristics listed in this comment – this is a misquotation of our report.

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				Therefore, in our view it is unreasonable and inappropriate to classify all these devices as being 'similar'. Each should be categorised according to the criteria listed above and with clear guidance on their recommended use.	
BXTAccelyon Limited	13	10	Results	*"The study suggests that LATP using the CamPROBE freehand device is more cost-effective than LATRUS, assuming a zero rate of infection for LATP and equal diagnostic accuracy for LATP using CamPROBE and LATRUS. There is, however, a high degree of uncertainty in the study"* We agree that the economic analysis of CamPROBE may have a high risk of uncertainty. The product is not CE marked, has had limited evaluation and any claims made on behalf of the device such as equal efficacy to TRUS are simply assumptions rather than evidenced on data. We believe that the data put forward in support of CamPROBE is highly speculative.	As stated in this quote, we agree that there is a high degree of uncertainty over the cost-effectiveness estimates for LATP with the CamPROBE device from the study by Wilson and colleagues.[10]
BXTAccelyon Limited	14	28	GLOSSARY	*"For the purpose of this assessment report, 'LATP-freehand' refers to local anaesthetic transperineal prostate biopsy done using one of the six freehand devices within the NICE scope. This is a sub-category of the LATP-any grouping of biopsy methods."* We do not believe it is reasonable to group all the LATP-freehand devices together. Their mechanism of use is widely different. For example, the CamPROBE requires independent movement of probe and device and, accordingly, it cannot be assumed that results will be similar in terms of cancer detection rates and complications. Other devices require multiple punctures of the perineum for prostate tissue sampling hence, again, detection rates, tolerability and complication rates cannot be assumed to be similar given this very	We appreciate that there are differences in the mechanisms of action between the included transperineal freehand devices, and that these differences may or may not translate to differences in detection rates, complications and numbers of repeat biopsies. In the absence of evidence directly comparing one or more freehand devices it is uncertain whether they are similar or different in these effects. We have followed the NICE scope for this assessment which groups all available freehand devices as a single intervention. As it turns out, all of the available comparative evidence for freehand devices on PrecisionPoint™; thus 'LATP freehand' can be considered as *de facto* 'LATP PrecisionPoint™'

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				different sampling method. Therefore, they should be separated into their relevant categories.	With respect to the economic evaluation, given the lack of comparative evidence on cancer detection rates for the devices other than PrecisionPoint™, we have no choice but to generalise this evidence across the other included devices. We do note in the DAR that this is subject to a high degree of uncertainty.
BXTAccelyon Limited	15	36	1.2.2	*"As an alternative to double freehand approach, the access needle can also be inserted through a positioning guide which is attached to the ultrasound probe. When the access needle and the ultrasound probe are physically coupled together the device may be referred to as a freehand transperineal biopsy device and the user can more easily track the location of the biopsy needle in relation to the ultrasound probe. The access needle is typically inserted only twice, once to the left of the anal verge and once to the right of the anal verge. This limited number of access points means the procedure can be routinely completed using local anaesthetic during an outpatient appointment. The NICE scope for this assessment identified six proprietary freehand devices which are available for use in clinical practice in the UK."* We do not accept that all the devices fall into the definitions in this section: 1. CamPROBE is a double Freehand coaxial device. It is NOT available for clinical use and does not have regulatory approval or CE marking for routine clinical use. 2. The single column grids, attachments and guide devices (other than PrecisionPoint) that are attached to the ultrasound probe are designed for prostate sampling directly with a biopsy needle and it is unclear from where the assumption originates that an access needle is used with these devices	1. See our response to comment 17 re: CamPROBE and CE marking. as a 'double Freehand coaxial device'? See also the response to comment 26 below regarding assumptions about the cost of coaxial needles in the economic analysis. 2. Comments noted

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BXTAccelyon Limited	16	37	1.2.2	***UA1232 puncture attachment (BK Medical, Massachusetts, USA)*** *"The coaxial/access needle can be inserted at different heights using the vertical guide channels and then localisation to the left and right is achieved by rotating the ultrasound probe (and so the attachment). If necessary, the position of the coaxial/access needle in the vertical guide can be changed (requiring an additional skin puncture) to access anterior, middle and posterior regions of the prostate. The 14-gauge needle is used for access and a separate biopsy needle is inserted through this to obtain the biopsy samples."* It is assumed that UA1232 puncture attachment (BK Medical, Massachusetts, USA) is used with an access needle. Please could the authors clarify what the assumption is based upon? We would ask if there is no evidence for that assumption then guidance is included to that effect and hence that there is no endorsement of this use of the puncture attachment?	See comment 15 above regarding assumption about use of access/coaxial needles.
BXTAccelyon Limited	17	37	1.2.2	*"The CamPROBE device is currently for research use only whilst an application for CE marking is under consideration. Full availability is anticipated in early 2022."* CamPROBE is not a Freehand device since the probe and coaxial needle are not connected and require independent hand movement. Results cannot be attributed to CamPROBE that result from a single Freehand device. We draw your attention to the fact that it was also confirmed by NICE in the scoping discussions that products <u>without a CE mark</u> would not be included in the final assessment report.	See comment 15 above regarding CamPROBE as a 'double freehand device' The NICE Diagnostic Assessment Programme manual states that for technologies that require CE marking, NICE will not make public any draft guidance for public consultation or publish recommendations before the technology is CE marked.[6] We understand that the granting of CE marking of CamPROBE is imminent. However, if CE marking is not granted by the time this assessment concludes then it will not be included in the final NICE guidance.

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BXTAccelyon Limited	18	55	RESULTS OF CLINICAL AND DIAGNOSTIC ASSESSMENTS 4.1 Quantity and validity of research available	*"Even so, we did not identify any evidence for SureFire, the Trinity® Perine Grid (for which all the studies we found used software based fusion techniques outside the scope of this review) or EZU-PA3U." (Page 77)* *"Comparative studies were identified for one of the six freehand biopsy devices within the scope of this review (PrecisionPoint™). We therefore modified our inclusion criteria to include single-arm (i.e. non comparative) studies for the remaining five freehand devices, when reported. We considered that these studies may be informative to the committee's consideration when the only alternative would be no evidence at all for these devices."* It is difficult to see what justification there is for devices to be included in the assessment that have no supporting evidence. For the Health Technology Assessment any reference to these devices is therefore made on a basis of 100% assumption with respect to safety, effectiveness and usability of the device without any evidence to support this. We believe that such an approach challenges the credibility of the assessment. Please may we ask that it is made clear that the devices listed are those that have been seen and that the report does not endorse any of the devices that have not been proven independently or have any supporting evidence.	The DAR does not endorse interventions or specify minimum levels of evidence for recommendations; these are issues for the NICE Diagnostic Assessment Committee to discuss. Assessment of the efficacy, safety, and usability of devices by single arm studies is empirical evidence, not "assumption" as claimed. Single arm studies cannot, however, inform decisions about relative efficacy, safety, usability, but we do not make such claims. In fact, we focus on describing the characteristics of these studies but do not report their results.
BXTAccelyon Limited	19	79	Summary	*"The evidence available for LATP-freehand devices specified in the NICE scope, other than the PrecisionPoint™ device, is limited to single arm studies: CamPROBE42 with a small population; and UA1232 with limited information from three conference abstracts.43-45 There is no evidence for the other devices in the NICE scope. Details of study*	No response required. This is an issue for committee discussion.

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				characteristics and participant characteristics are limited." The evidence for CamPROBE was a single arm non-comparative study of 40 patients. The UA1232 data is all from a single UK centre and only presented as conference abstracts. It is difficult to accept that these meet with a minimum threshold of evidence to support these devices in terms of safety, efficacy and inclusion.	
BXTAccelyon Limited	20	114	5.1.3	*"We identified one economic evaluation for inclusion within the scope of this assessment: Wilson et al. 2021.58 Wilson and colleagues reported the cost-effectiveness of LATP (with the CamPROBE transperineal prostate biopsy device) versus LATRUS for use in the diagnosis of prostate cancer in men with suspected localised prostate cancer from the perspective of the UK NHS"* There are significant and, in our judgement, unmerited assumptions in this study on detection rate and infection rate on a device that has only been evaluated in 40 patients. The authors of the DAR report note there is a high degree of uncertainty in the study and we would agree.	We note the high degree of uncertainty over the results of the cost-effectiveness evaluation of CamPROBE by Wilson and colleagues[10] at the end of DAR section 5.1.3 (page 116).
BXTAccelyon Limited	21	126	5.3	*"This study assumed that LATP and GATP have the same rate of achieving a successful biopsy (with no need to repeat the procedure) and fewer complications than LATRUS biopsies. The majority of clinical experts providing feedback to the EAG reported that they would expect better diagnostic performance for transperineal biopsies compared with LATRUS. This suggests that the assumption of equal diagnostic performance may not be realistic."*	The YHEC report did state that LATP "*achieves the same outcomes as GA TP biopsies, without the infective complications associated with TRUS biopsies*." And that "*LA TP and GA TP biopsies have the same rate of achieving a successful biopsy (with no need to repeat the procedure) and fewer complications than TRUS biopsies*." (YHEC page 5) However, in practice, the analysis includes fewer cases of 'detection failure' for TRUS (12.5 repeat MRIs per 250 cases) than for GATP (37.5 repeat biopsies per 250

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				This is an incorrect interpretation of the YHEC study content. The study states that the Freehand LATP biopsy with PrecisionPoint is equivalent to GATP detection rates but higher than TRUS. The rates of biopsy detection failure are similar for LATP and GATP but lower than for TRUS. There is therefore a clear acknowledgment in the YHEC study that there is better diagnostic performance for transperineal biopsies compared with LATRUS.	cases), and no repeat MRI/biopsies for LATP (see YHEC Table 2.2, reproduced in DAR Table 47). The rationale for these differences is unclear.
BXTAccelyon Limited	22	149	5.7.2	"*The NMA value for 'LATP-freehand' is based on a single RCT (Lam et al. 2021), which used the PrecisionPoint™ device.26 It is not clear whether this is representative of the list of freehand devices included in the scope. Given the lack of evidence for other devices we model LATP-freehand for decision question 2 as a single intervention but test the impact of using different prices in scenario analysis."* Since all the Freehand LATP devices have a very different mode of action then the assumption that cancer detection rates and complication rates are all the same as PrecisionPoint is completely unjustified. This undermines the cost modelling as presented other than for PrecisionPoint Freehand TP biopsies.	We appreciate these limitations in the evidence base, hence our comment in the cited quote. Nevertheless, there is an expectation from NICE that all interventions and comparators specified in the scope should be evaluated in the DAR, with appropriate discussion and exploration of uncertainties for consideration by the committee.[6] So where necessary, we extrapolate evidence from PrecisionPoint™ to the other freehand devices. But we note that this extrapolation is associated with uncertainty, and present a scenario using the estimated costs of PrecisionPoint™ alone to align with the source of clinical evidence (see DAR Table 87 and Addendum Table 48).
BXTAccelyon Limited	23	151	5.7.4	*"This comprises comparative rates of admission within 30 days of a transperineal or transrectal biopsy (anaesthesia type not reported) based on an analysis of data from the National Prostate Cancer Audit (NPCA) linked to HES by Berry and colleagues.82 The audit data included all people newly diagnosed with prostate cancer between 1 April 2014 and 31 March 2017 identified from the English cancer registry (n=118,526)"* In this time period (ie 1 April 2014 to 31 March 2017) the transperineal biopsies were <u>all</u> GATP biopsies as	We accept this point and have conducted additional analysis excluding data on overnight stays from the Berry et al. paper (see DAR Addendum).[11] This has the effect of reducing the ICERs for LATP in both decision question 1 and 2 (Addendum Tables 7 and 8). We also include this change in the revised EAG base case reported in section 3 of the Addendum.

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				Freehand LATP biopsies were not available until January 2018. Any data from this study should therefore reflect that the data represents GATP transperineal biopsy outcomes and complications and not LATP.	
BXTAccelyon Limited	24	160	Table 63 Micro-costing analysis: cost components and total cost of biopsy methods	The table is based on a number of assumptions that are incorrect and unsupported by evidence. The devices all have different methods of operation: 1. The training requirements are vastly different; for example, the 'double freehand approach' (CamPROBE) is recognised as being difficult to teach and may not be possible for junior and ancillary staff to learn quickly. The learning curve is long and requires considerably more training, time and investment and should be reflected in the costing data. 2. The multiple use of reusable guides does not have any evidence to support the figures. The costs of reprocessing (autoclaving, time and resources) appear very low for reusable devices. The reusable guides require multiple punctures of the perineum for sampling and therefore detection rates and complication rates are unproven. As they are intended to be used with multiple punctures of the perineum, it is unlikely that they can be outpatient procedures tolerated under local anaesthetic. 3. The table as presented is misleading since it represents all devices as effectively having the same safety, effectiveness and learning curve and gives an unfounded basis of relative costs of the respective devices. It is our firm view that the table should be divided into groups of devices that reflect their mode of operation and with strong guidance that the data in the table	We understand that there are uncertainties over a number of data sources and assumptions in our micro-costing analysis. 1. Training costs for the CamPROBE, PrecisionPoint™, EZU-PA3U, UA1232 and Trinity® Perine devices are based on time required per operator per year, as reported by the respective companies (see Appendix 12 for further details). In the absence of other evidence for the remaining biopsy methods, we assumed 8 hours of training per operator per year. The contribution of training to the overall cost per biopsy is small (from 0.08% to 0.65% of total costs) and does not impact on cost-effectiveness results. Scenarios with the assumption of equivalent training for all biopsy methods, less training for LA-TRUS or more for double freehand devices give small reductions in the ICERs for LATP. 2. The manufacturer of Trinity® Perine device reported that their device could be reused 100 times (see DAR Appendix 12). We applied this same assumption to the other reusable devices (EZU-PA3U and UA1232). The cost of reprocessing (£5 per item) was informed by advice from a specialist committee member. 3. The micro-costing analysis only provides estimates of the cost of the biopsy procedure. Other costs related to the biopsy (rates of complications and repeat biopsies and long-term costs of cancer detection failures) are based on other model inputs and assumptions

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				requires considerable review and validation. Where data is more robust through clinical evidence and extensive use that too should be formally acknowledged.	We would appreciate further evidence on the validity of the parameters and assumptions in our micro-costing.
BXTAccelyon Limited	25	182	5.8 Model Assumptions	*"The cost of SureFire Guide is an average of the other two disposable LATP devices (CamPROBE and PrecisionPoint™)."* If the cost of the device is not known, it should not be assumed or guessed. The device should not be included in the costing table or the section should be left blank and a note made. The point has been made in our response that the device should not be included in the assessment, since there is no clinical evidence, and no available data. It is an unknown device and it has no validated use to base its inclusion in the report.	NICE received a submission from Delta Surgical after completion of the DAR. This submission includes a price for the SureFire device of £120 per biopsy, which we included in the revised EAG base case presented in the DAR Addendum of 10 Jan 2022.
BXTAccelyon Limited	26	182	5.8 Model Assumptions	*"Co-axial needle was assumed to be used for biopsies using both freehand and double freehand devices"* Please could the authors clarify what the assumption is based upon? If there is no evidence for that assumption, and devices have not been tested for use with an access needle we would respectfully ask that guidance is included to that effect and that there is no endorsement of this approach?	For the DAR economic analysis, we had included the cost of a coaxial needle (£21.40) for LATP with all 'freehand devices' listed in the NICE scope. However, we understand that a coaxial needle is only needed for transperineal biopsy with the EZU-PA3U device or double freehand approach. Removing the cost of the coaxial needle for other devices reduces the ICERs for LATP (see DAR Addendum).
BXTAccelyon Limited	27	182	5.8 Model Assumptions	*"We assumed that a whole day (8 hours) of training would be required per person for SureFire Guide, LATP using grid and stepper unit, LATP using double freehand devices and GATP. For LATRUS, we assumed that this would only require one hour of training."*	See response to comment 24 above. Note that the estimated training costs in the model are intended to reflect annual training needs for appropriately qualified professionals to conduct specific biopsy techniques. They do not include costs for general professional training required to undertake an ultrasound guided prostate biopsy, which would be

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				The training on double free hand devices is not similar to PrecisionPoint. It seems a vast underestimation to assume only 1 hour is required for TRUS training. Training on devices that puncture the perineum multiple times for sampling is not known but it is likely that, if done under local anaesthetic, then significant training is required to ensure the procedure is tolerable.	incurred for all interventions and comparators (amortized over the professional working lifetime).
BXTAccelyon Limited	28	182	5.8 Model Assumptions	*"We assumed that 1000 biopsies are carried out per year on average per hospital. This informed estimates of the cost per patient for capital equipment"* This figure is incorrect. Hospital Episodes Data would suggest the average per hospital is 300-400 procedures and so the cost per patient for the capital equipment should be corrected.	We did not identify a source for the mean number of biopsies conducted per hospital per year, so we obtained the estimate of 1,000 biopsies per hospital per year from clinical experts. We do not have access to HES data, so do not have a source for the estimate of 300-400 procedures. We note that reducing the number of biopsies to 300 per hospital per year increases the revised base case ICERs for LATP-any and LATP-freehand compared with LATRUS, but they remain below £20,000 per QALY for subgroup A and below £30k for the other subgroups.
BXTAccelyon Limited	29	215	5.10.4 Three-way sensitivity analyses	We believe that a number of the costing assumptions in Table 63 'Micro-costing Analysis' are incorrect. it is our firm position that the assumptions and data in this section require complete review and overhaul. The devices should not be compared as equivalent and the tables (Tables 89-96) and should be recalculated and re-presented according to the mode of operation of each group of devices and based on the existing evidence on costs, safety, efficacy and complication rates. As presented the tables are misleading and give the impression that all devices are similar and that the costings provide a meaningful comparative analysis which we believe is grossly misleading.	See responses above to comment numbers 24 to 28 regarding the micro-costing analysis. The 'three-way' tables in section 5.10.4 of the DAR illustrate the sensitivity of cost-effectiveness results to three key uncertainties, including the cost of LATP (represented by the range of cost estimates for different LATP approaches).
BXTAccelyon Limited	30	226	7.4 Uncertainties	*"The microcosting analysis is also associated with some uncertainty, although the majority of assumptions relate to values that cancel out across biopsy methods. There*	See responses above to comment numbers 24 to 28 regarding the micro-costing analysis.

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				are two main uncertainties: the cost of SureFire Guide, which we assumed was an average of the other two disposable LATP freehand devices in the absence of an official price; and the number of cores taken, which we assume to be 12 cores for every biopsy method" For the various reasons provided above, the microcosting is associated with more significant uncertainties than the two listed in this section. It would be good to see an acknowledgement that PrecisionPoint does have comparative evidence for its safety and efficacy.	The cited quote does explicitly refer to two main uncertainties relating specifically to the micro-costing. We agree that there are other uncertainties. The first paragraph in section 7.4 states that the only evidence on cancer detection for LATP-freehand is based on a single RCT which used the PrecisionPoint™ device.
BXTAccelyon Limited	31	228	*8 Conclusions*	*"Based on pooled evidence for all types of LATP biopsy (with or without a specified freehand device), it is unlikely to be a cost-effective option for any of the patient subgroups that we considered: LATP has an estimated incremental cost of over £70,000 per QALY gained compared with LATRUS biopsy."* We would challenge this statement in that pooling LATP-data detracts from the benefits of freehand LATP biopsy and further comparative evidence will we believe show the cost effectiveness of LATP biopsies va LATRUS for all patient groups with no previous biopsy irrespective of risk.	The NICE scope specifies a comparison between LATP as a general approach and transrectal biopsy (decision question 1). We therefore present results for this question, and the sentence quoted relates to this question.
BXTAccelyon Limited	32	228	8.1 Implications for service provision	*"This analysis suggests that the use of LATP freehand transperineal biopsy devices is potentially cost effective. However, this conclusion is uncertain, as it is based on limited data. The comparative cost-effectiveness of different freehand transperineal biopsy devices is unknown"* We note the conclusion of the report and support the further research priorities to gather cancer detection	No response required. This is an issue for committee discussion.

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				rates and complication rate data between different biopsy methods (freehand LATP and TRUS) to strengthen the cost effectiveness argument for LATP biopsies with freehand devices. We also support the priority to collect outcomes data for the additional patient groups identified. We also would strongly emphasise that the only meaningful comparative data currently available is for the PrecisionPoint device and that other devices should present equivalent data and clarify their Indications For Use. These devices should not be assessed as comparators for PrecisionPoint unless robust, detailed evidence on safety, efficacy and cost is presented.	
Prostate Cancer UK	33	Overall		Generally we are pleased with the evidence analysis and conclusions of the Diagnostics Assessment Report.	No response required.
Prostate Cancer UK	34	11	Recommendations	We agree that the overall volume of evidence around LATP biopsy is limited, particularly around side effects as these remain rare, thus necessitating a large cohort in any study. However, we would not see this as reason to delay adoption of the technique given the encouraging signs around cancer detection rates and the positive reports from clinicians and hospitals who have made the switch from TRUS biopsy.	No response required. This is an issue for committee discussion.
Prostate Cancer UK	35	126	5.3	We note the comment that experts would expect better diagnostic performance from LATP than TRUS biopsy. Given the observational evidence did show a statistically significant improvement in cancer detection, we would be interested to see a cost-effectiveness analysis using this rather than assuming equivalent diagnostic effectiveness. We hope that this will be possible once the TRANSLATE study has reported.	We presented scenario analyses based on observational estimates of cancer detection rates in DAR Tables 79 and 80. Additional scenarios including different sets of observational studies are reported in Tables 5 and 6 of the DAR Addendum of 10 Jan 2022. Tables 37 and 38 of this Addendum also report results for the observational scenarios applied to a revised EAG base case.

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Prostate Cancer UK	36	Overall		We have heard, anecdotally, that some of the freehand LATP techniques (particularly "double freehand") are quite hard to learn. We would be interested in NICE's view on how many cases are required to become an expert in these techniques and thus deploy them to the standard used in the studies analysed here.	No response required. This is an issue for committee discussion.
University of Cambridge	37	5	Limitations	This report should not include named devices in the summary and main outcomes. This may suggest that this device is preferred over others. The one mentioned only happens to be the longest on the market but other devices are being tested and evaluated. Suggest this is made clearly neutral especially as all devices facilitate LATP biopsies and cannot themselves claim to be better than any other	The NICE scope does specify named devices as interventions for decision question 2. We refer to the general category of 'LATP-freehand' (including LATP with any of the named devices) throughout the report in relation to our meta-analyses and cost-effectiveness analyses. However, we do think it is appropriate to note where evidence relates to only one of the named devices.
University of Cambridge	38	10	Economic data from YHEC	Is this data peer reviewed and available to be seen? A search of the YHEC website for 2020 does not show this evidence? https://yhec.co.uk/2020/?post_type=publication nor in 2019 or 2021 See also comments further below	The YHEC report was provided with the company submission from BXTAccelyon.
University of Cambridge	39	11	Second para cost of device	The figure is £584 – is this only the cost of device used? how o use this data to help clinical practice if only certain subgroups benefit? (see later) Can a cost-effective price not be defined as the range of costs may be very variable?	This is the estimated cost of the LATP biopsy procedure with the PrecisionPoint™ device. DAR Table 63 (page 160) shows cost estimates for this and other interventions and comparators. See DAR section 5.7.6 (pages 158-159) for a description of what is included in the micro-costing analysis, and DAR Appendix 12 for further details.
University of Cambridge	40	11	Conclusions	What is meant by LATP by other methods? Presume this refers to LATP using a grid stepper – if so this should be clearer?	LATP-'other' is a category we created during evidence synthesis to allow us to conduct network meta-analyses. LATP-other comprises studies of LATP grid and stepping device and studies of LATP coaxial needle (double freehand), these two categories being mutually exclusive. It is what remains of the 'LATP-any' category

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					when LATP-freehand studies are removed to form their own category.. This is explained in section 4.8.4 of the DAR but, granted, it is not explicit in the Scientific Summary.
University of Cambridge	41	10	Last para	What are the non-freehand LATP approaches mentioned here? “However, results were different for the economic analysis including LATP freehand compared with **other LATP methods**, as well as LATRUS and GATP”? There is no head to head comparison of different freehand devices or against co-axial devices for double freehand for that matter. No evidence one approach for TP is better than the other	See response to comment 40 above.
University of Cambridge	42	7	Definition of freehand devices	Freehand includes coaxial devices and those fixed to the US probe, non-freehand means using fixed devices in space and position i.e. stepper and grid. Indeed, devices that fix onto probes are also not technically freehand as they are limited to the line of the probe?	Thank you, noted
University of Cambridge	43	39	Clinically significant cancer	The only relevant one is Gleason 7 or more on a biopsy – others are not in use nor recommended by any guideline body	Thank you. Our expert clinical advisors tell us that the UCL definitions are used in research studies rather than in practice. We appreciate that the NICE guideline definition is the standard of care.
University of Cambridge	44	42	Comparators	The comparators here are LATRUS, GATP and LATP using a grid – there is no other LATP method listed here so presume this is the comparator mentioned in page 11?	That is correct. Please refer to our response to comment 40 above.
University of Cambridge	45	47	Identification of studies	How far back did the lit review go? Some studies of coaxial needles LATP v LATRUS RCT were done over 10 years ago	The systematic review literature search had no date restriction; all health and medical research databases were searched from their inception to the current day (at the time of running the searches). This is stated in Appendix 1 of the report, but we acknowledge this information is missing from section 3.1 ‘Identification of studies’ where it would be easier to find.

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					The searches yielded references to publications as far back as the 1980s, though these did not meet our inclusion criteria. Of the references that did meet our inclusion criteria, the oldest dates are from 2003. We do not, therefore, consider there is a risk of any chronological publication bias.
University of Cambridge	46	79	Camprobe – indication's for biopsy **were** reported	This is an error, in this study the indications for biopsy were Cleary stated in the abstract and in the body of the text - 19/40 were first prostate biopsies and 21/40 repeat procedures. Of the first biopsies the clinically significant cancer detection rate was 47% (9/19)	Our conception of the term 'indication' appears to be more granular than the stakeholder's. In section 3.2.1 we say: *"People included in the review may have a clinical suspicion of prostate cancer (for example, raised PSA level or abnormal DRE findings), or people may have had a previous prostate biopsy that was negative for prostate cancer but have a continued clinical suspicion."* We needed to discern whether the purpose of a prostate biopsy (first or second) was to investigate *suspected* prostate cancer, or was for a different purpose (e.g. monitoring people with a confirmed prostate cancer diagnosis to assess histological changes over time). Hence, when assessing publications for inclusion screening we looked for mention of clinical signs such as raised PSA level or abnormal DRE findings as cause for clinical suspicion and hence an indication for doing a (first) biopsy. Apologies if this wasn't made clear enough.
University of Cambridge	47	Page 88 and Page 96	Non RCT comparisons of LATP versus historic LATRUS - confounding effect of biased case selection by MRI positivity	One important caveat in studies comparing LATP versus historic LATRUS detection rates is the current selection bias introduced by using MRI in modern series. As modern cohorts are selected to only biopsy MRI positive men the overall cancer biopsy rate is usually higher. In contrast comparisons to non-MRI LATRUS may seem lower as many were done before MRI was introduced.	Some of the more recently published studies included in the systematic review used pre-biopsy mpMRI to inform biopsy sampling, but this constitutes a small proportion of the whole evidence base as a whole. There are three prospective observational studies of LATP with an historical TRUS comparison group; • Bojin 2019 mpMRI was used in 93% LATP participants; and 69% LATRUS participants.

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				Thus, on page 96 it is stated that "It is only when observational evidence for LATP-freehand versus LATRUS is combined with RCT that a significant result is seem However, has this been corrected for the confounding effect of MRI case selection in use of modern LATP devices? i.e. was the LATRUS comparators also in MRI detected men or were they historical? If not then this is a significant cause for bias. It is notable that when like for like comparison is made i.e. MRI based LATRUS vs MRI based LATP series that detection rates are very similar van der Leest M, Cornel E, Israël B, et al. Head-to-head comparison of transrectal ultrasound-guided prostate biopsy versus multiparametric prostate resonance imaging with subsequent magnetic resonance- guided biopsy in biopsynaïve men with elevated prostate specific antigen: A large prospective multicenter clinical study. Eur Urol 2019; 75: 570–578. Rouvière O, Puech P, Renard-Penna R, et al. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): A prospective, multicentre, paired diagnostic study. Lancet Oncol 2019; 20: 100–109. Bryant RJ, Hobbs CP, Eyre KS, et al. Comparison of prostate biopsy with or without pre-biopsy multi-parametric MRI in prostate cancer detection: An observational cohort study. J Urol 2019; 3: 510–519. Ahdoot M, Wilbur AR, Reese SE, et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis.N Engl J Med 2020; 382: 917–928.	Both systematic and targeted sampling was used. • Chen et al 2021, 30% of LATP participants had pre biopsy MRI; a "handful of patients" in the LATRUS arm had an MRI before biopsy; sampling described as systematic. • Kum et al 2018 does not explicitly state whether mpMRI was used in LATP but it does report PIRADS scores; Sampling - systematic (52%); targeted (25%); systematic and targeted (23%). Due to lack of detail on pre-biopsy imaging in study publications, it is difficult to draw firm conclusions about the presence of confounding within these studies and its impact on biopsy outcomes. Nonetheless it appears that there were differences between LATP and historical LATRUS in the proportions of participants receiving mpMRI; mpMRI was more common with LATP. Confounding effects cannot be ruled out.

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University of Cambridge	48	127	YHEC economic model	This output is also not in the public domain as above? In the YHEC website it is not listed as a publication Table 47 does not seem to match national data reported event rates The number of hospital admissions after TRUS in national studies is 1.4% (infection and sepsis – *Berry B, Parry MG, Sujenthiran A, Nossiter J, Cowling TE, Aggarwal A, Cathcart P, Payne H, van der Meulen J, Clarke N. Comparison of complications after transrectal and transperineal prostate biopsy: a national population-based study. BJU Int. 2020 Jul;126(1):97-103. doi: 10.1111/bju.15039.)- this paper is discussed on page 151 as well* In this table 47 it is suggesting a readmission rate of 10/250? Which is 4% and very high (1.25+8.75 cases/ 250) In this table there is also the claim that LATRUS needs a repeat MRI – but what is the basis for this claim? In modern pathways all men get MRI before any biopsy and this is not repeated - if the reasons that LATRUS is less accurate then what is the evidence base? We are not aware of any such data In addition, this table is missing the reported 1.9% readmission rate for urinary retention which is inherent in TP biopsies (see above reference) – if we assume that this is also for 3 days then it is £4574.25 for GATP and LATP (£963 cost per case) This table therefore seems to use figures much higher that the national reported infection and sepsis rate, ignore the retention event costs and assume extra	See response to comment 38 above regarding the availability of the YHEC report. See also response to comment 21 above regarding the rates of complications and repeat MRI/biopsy used in the YHEC cost minimisation study. Berry and colleagues (2020) [11] reported a rate of 1.35% for admissions due to sepsis within 30 days of transrectal biopsy. This was based on analysis of Hospital Episode Statistics (HES) data only for biopsies conducted prior to a new diagnosis of prostate cancer between 2014 and 2017. Tamhankar and colleagues (2020) [12] analysed HES data for all non-elective readmissions within 28 days of a prostate biopsy. For the most recent period (2017-2019), they reported admission rates after transrectal biopsy of 1.12% for sepsis but 3.74% overall (including other infections and urinary retention). This is similar to the overall admission rate for transrectal biopsy in the YHEC analysis. It is our understanding that MRI would not usually be repeated after a negative biopsy result. We have not included repeat MRI in the EAG model.

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				investigations in the TRUS arm. The conclusion that the device is cost saving versus LATRUS is therefore not clear or justified at present, it is certainly cheaper than GATP as GA costs are saved	
University of Cambridge	49	160	Table 63 Device costs	Why has the Camprobe been costed as more expensive for place of biopsy urologist time and nurse time? What is the evidence for the difference across each biopsy type and device? It should be identical for usage and time and personnel for all devices -where did this source data come from? for that matter how were costs ascribed for the other devices like trinity and surefire if there is no published data? These costs appear to be very speculative as there is no head to head comparison or HE study to do a comparison? The only item that can be costed is the list device prices- the rest should be the same for all LATP devices – This table should be reviewed again and clear on source data?	See response to comment 2 above.
University of Cambridge	50	161	Risk groups	Please note that NICE guidance NG131 on risk groups is currently being reviewed and is likely to change a early as December 2021	No response required.
University of Cambridge	51	198	Probability of repeat biopsy	Please note that as above, it is the MRI use before biopsy which determines accuracy and so far no evidence that route of biopsy has an impact on likelihood. Certainly, it cannot be concluded that LATP is better than LATRUS in likelihood of needing a re-biopsy. In our experience there is no difference in LATRUS v LATP. The re-biopsy likelihood for GATP should not be applied to LATP as there is no evidence for parity - LATP take much fewer samples and is more akin to LATRUS.	Advice from other experts is also that rates of repeat biopsy are similar for LATP and LATRUS, but lower for GATP. We report additional scenario analysis with the rebiopsy rate for GATP of 5.36% reported by Jimenez and colleagues [13], and a second scenario applying this lower rate to both LATP and GATP (see section 2.4 in the DAR Addendum). The number of cores taken in the Jimenez study differed for LATRUS (12-18 cores) and GATP (30 cores). However, we understand that more cores are commonly taken in practice with transperineal biopsy

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				Thus, saying that LATP is 5.36% and LATRUS is 15.45% is not sound. Using the study by jimemez et al 2021 is flawed as the comparison here is LATRUS with only up to 18 biopsies versus GATP with 30 samples – simply by doing more biopsies you may detect more cancers. This paper should not be used to assess comparative cancer detection rates between LATP and LATRUS – furthermore no sub analysis of the MRI group is done and this is important given the conclusion of the subgroup that benefits from LATP which is a part of this report (i.e. MRI M3 and above).	(particularly under the Ginsburg protocol) than with LATRUS: see discussion in section 2.6 of the Addendum. If so, this difference in the Jimenez study may be seen as a reflection of practice rather than a source of confounding. We report additional scenario analysis with costs for different number of cores (DAR Addendum section 2.6), this does not model clinical consequences of changing the number of cores, Due to uncertainty over whether and how repeat biopsy rates and numbers of cores differ between biopsy methods, we retained our original assumptions of equal repeat biopsy rates (15.45%) and equal numbers of cores (12) for all biopsies in our revised base case (DAR Addendum section 4). Scenarios for these two sets of parameters are reported in sections 4.3 and 4.4 Addendum.
University of Cambridge	52	208	Cost of biopsy devices	Uptake and use of LATP is sensitive to cost effectiveness as well as patient safety. As we don't have good heard to head data as yet for all devices, would it not be better to have a modelling to determine the ideal cost of a device? AS an example of this LATRUS is considered in this document as 1 universal procedure but there is actually different devices to enable this - holders, needle systems reusable versus disposable etc.. Therefore, for TRUS it the route of biopsy which is being used as comparator here not the costs of different systems. Yet for the TP devices individual costs are bring compared. If it is the route of LATP being compared to LATRUS then devices should not be separated out. Instead LATP as a whole whould be considered together (perhaps excluding the LA grid approach). What about future TP devices and systems? Would it not be better to state the ideal cist bracket and tariff	It is expected that the DAR should evaluate all interventions and comparators in the NICE scope, and the scope does name specific freehand devices as interventions. We have used average costs for LATP and LATP-freehand in our base case analyses because of a lack of clinical evidence to differentiate between the named devices. The cost scenarios in DAR Tables 86 and 87 and the three-way sensitivity analysis in DAR section 5.10.4 illustrate how the cost of different devices may affect the cost-effectiveness results.

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				rather than depend on costing one versus the other? Until such time as there is comparative date? This will remove the rather unusual process of estimating a device cost for this analysis by averaging 2 other devices (e.g. on page 209).	
University of Cambridge	53	224	ICER and risk subgroup	The conclusion here states that "increasing the cost of LATP with a freehand device by assuming the cost of the most expensive device (£584), the CER remained below £20,000 per QALY for the highest-risk subgroup but not for the other subgroups" however biopsies are done for all risk subgroups in standard clinical practice - does this mean that the highest cost device should only be used for this subgroup? And we should use a cheaper for other risk groups? Or perhaps TRUS? A above trying to do this for individual devices is difficult– instead there should be a single tariff estimate for benefit across all risk group based on ICER. As the authors detail in the limitation section (page 226) these many uncertainties and gaps in the evidence suggest that there should be a general review and costing for the ideal LATP device rather than one specific to a device. Eventually LTAP should become like TRUS i.e. the costs are not much dissimilar regardless of the device and it's the route that is important rather than the device.	No response required. This is an issue for committee discussion.
University of Cambridge	54	228	Conclusion	If a study is non-significant it cannot be stated to be an improvement (Line 4).	Expressed another way, it was a 'non-significant increase'.
Delta Surgical Ltd	55	7	Background	SureFire Transperineal Needle Guide, is manufactured by Advance Medical Designs, Inc. 1241 Atlanta Industrial Drive Marietta, GA 30066 USA. Distributed and supported in the UK by Delta Surgical Ltd, Unit 10	Thank you, noted.

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				Evolution, Lymedale Business Park, Newcastle Under Lyme, ST5 9QF.	
Delta Surgical Ltd	56	37	1.2.2	SureFire Transperineal Needle Guide does not require an Introducer, although one of at least 7cm can be used. The vertical needle guide has nine equidistant guide channels at allowing vertical access to 8 cm.	Thank you, noted
Delta Surgical Ltd	57	38	1.2.2	The SureFire Transperineal Needle Guide has 2 models Commercialized and 2 models in Beta testing. The two commercialized are the SureFire 8848 which adapts to the 8648, 8848, 9048 and E14C4b BK biplane probes. Also, the SureFire Hitachi which adapts to the Hitachi Healthcare biplane probes EUP-U533, C41L47RP and UST-672. The two in Beta testing are the SureFire 8818 which adapts to the 8818, 9018, and E14C4t BK triplane probes. Finally, the SureFire Universal which will be released in Q12022. The Universal adapts to other common biplane probes available in the UK. The BK Medical and Hitachi Healthcare Surefire Transperineal Needle Guide channels correspond to puncture lines superimposed on the scan image as part of their preloaded software biopsy packages.	Thank you, noted
Delta Surgical Ltd	58	49	3.2.2	SureFire Transperineal Needle Guide (Advanced Medical Designs, Inc.)	Thank you, noted
Delta Surgical Ltd	59	77	4.6.1	The SureFire Transperineal Guide is similar to the UA1232 in the position and hole configuration of the Channel Guide. It differs in that the SureFire uses a carriage to advance and retract the channel guide. The UA1232 uses a screw clamp which must be loosened and retightened to move the channel guide. We see the Yamamoto 2019; Yamamoto 2020; and Lau 2020 studies on the UA1232 to be relevant in evaluating the SureFire with exceptions that pertain to sterility as the SureFire is disposable. A Single-Arm Safety and Efficacy study framework is being drafted Internationally	Thank you, noted

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				with endpoints similar to Transperineal Studies of other commercially available devices.	
Delta Surgical Ltd	60	158	5.7.6	SureFire device costs £120	This cost was submitted after completion of the DAR. This cost causes a small reduction in the base case ICERs for LATP-any and LATP-freehand: see DAR Addendum section 2.7 and Tables 19 and 20.
Delta Surgical Ltd	61	159	6.7.6	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	62	160	Table 63	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	63	182	5.8 table 67	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	64	207	Biopsy Costs	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	65	215	5.10.4	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	66	226	7.4	SureFire device costs £120	See response to comment 60 above.
Delta Surgical Ltd	67	284	Appendix 2 PICO table	SureFire Transperineal Needle Guide is manufactured by Advance Medical Designs, Inc. 1241 Atlanta Industrial Drive Marietta, GA 30066 USA. Distributed and supported in the UK by Delta Surgical Ltd, Unit 10 Evolution, Lymedale Business Park, Newcastle Under Lyme, ST5 9QF.	Thank you, noted
Delta Surgical Ltd	68	323	Appendix 12- cost of devices	SureFire device costs £120	See response to comment 60 above.

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Economic Model – Comments

Stakeholder	Issue	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Royal Surrey NHS Foundation Trust	1	Given the information provided, health economics comparisons between the free hand devices are premature at this point. Attributing a cost to the SureFire device in the absence of information from the manufacturer is not a logical basis for evaluating its cost effectiveness, especially as there is no clinical evidence available.	The Translate study is to be welcomed as this will provide level 1 evidence that should not only validate the findings from the publications already cited but also compare the performance of the transperineal devices used in the trial.	The cost for the SureFire device (comment 60 above) gives a small reduction in the ICERs for LATP and LATP-freehand for decision question 1 and 2 respectively (DAR Addendum Table 19, 20). We have included this cost in the revised base case analyses (DAR Addendum section 3). Impact of results of the Translate study on cost-effectiveness results currently unknown.
Royal Surrey NHS Foundation Trust	2	Micro costing Training portion is undervalued given that training on a new biopsy approach and new device requires considerable time and expertise. Steps include consultant led didactic training, practise on phantoms, consultant-led on-site mentoring, training for nursing and theatre staff.	Each of these actions should be incorporated in the modelling. At present there is only such training for the Precision Point device which should be reflected in the text.	See responses to comments 24 and 27 above
Royal Surrey NHS Foundation Trust	3	Learning curve analysis between the different devices	This should be considered as some of the free hand devices are biopsy needle guides i.e., a guide through which biopsies are taken directly by the biopsy needle thereby requiring multiple punctures of the perineum. This differs from the integral access needle of the Precision Point device which involves only two perineal punctures.	Impact of 'learning curve analysis' unknown.

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Stakeholder	Issue	Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
Royal Surrey NHS Foundation Trust	4	Our overall conclusion is that the free hand devices and the health economic analysis is based on very little evidence. It should be deferred until level 1 evidence from the Translate trial becomes available.		No response required. This is an issue for committee discussion.
BXTAccelyon Limited	5	The "Microscosting-Inputs" tab is misleading. A number of entries are assumptions or no data exists to verify thev costing	Any devices where there is no evidence of use or cost are unknown should be removed from the table or table left blank	See responses above to comment numbers 24 to 28 regarding the micro-costing analysis.
BXTAccelyon Limited	6	The table of "Device costs" tab is misleading Devices are grouped together to give the impression of similar outcomes, complications and use. This is incorrect. Classification of the Devices should reflect the following: • One device is not clinically available • Several devices are reusable and method of use needs to be clarified • Several devices have no clinical data to support their use and have limited or no costing data. They should be removed or reclassified in a separate section. Only one device (PrecsionPoint) has comparative and clinical outcomes data.	The "Device-costs" table should be amended and grouped according to classification described in the "description of the problem"	See responses above to comment numbers 24 to 28 regarding the micro-costing analysis.
Delta Surgical Ltd	7	Cost of SureFire device over estimated +£15.00. actual device cost £120.00	Adjust price to £120.00	See response to comment 60 above.

1. Guo L-H, Wu R, Xu H-X, et al. Comparison between Ultrasound Guided Transperineal and Transrectal Prostate Biopsy: A Prospective, Randomized and Controlled Trial. *Scientific Reports* 2015;5(1):16089. doi: 10.1038/srep16089

2. Hung WPL, Chun S, Wong T, et al. Transrectal vs. transperineal prostate biopsy under local anaesthesia: Prospective comparative analysis of cancer detection, safety and tolerability using patient-reported outcome measures at a single centre. *European Urology Open Science* 2020;19 (Supplement 2):e2315.
3. Lam W, Wong AHG, Chun S, et al. P0999 Prostate cancer detection, tolerability and safety of transperineal prostate biopsy under local-anaesthesia versus standard transrectal biopsy in biopsy-naïve men: A pragmatic, parallel group, randomized-controlled study. *European Urology* 2021;79:S1405. doi: https://doi.org/10.1016/S0302-2838(21)01372-5
4. Kum F, Elhage O, Maliyil J, et al. Initial outcomes of local anaesthetic freehand transperineal prostate biopsies in the outpatient setting. *BJU International* 2020;125(2):244-52.
5. Kum FE, Elhage O, Maliyil J, et al. Outcomes of local anaesthetic freehand transperineal biopsies in the outpatient setting: How does this compare to conventional biopsy methods? *Journal of Endourology* 2018;32 (Supplement 2):A212.
6. National Institute for Health and Care Excellence (NICE). Diagnostics Assessment Programme manual. Manchester: National Institute for Health and Clinical Excellence 2011.
7. 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 International* 2021;128(3):311-18. doi: https://doi.org/10.1111/bju.15337
8. Pepe P, Garufi A, Priolo G, et al. Transperineal Versus Transrectal MRI/TRUS Fusion Targeted Biopsy: Detection Rate of Clinically Significant Prostate Cancer. *Clinical Genitourinary Cancer* 2017;15(1):e33-e36.
9. Rai BP, Mayerhofer C, Somani BK, et al. Magnetic Resonance Imaging/Ultrasound Fusion-guided Transperineal Versus Magnetic Resonance Imaging/Ultrasound Fusion-guided Transrectal Prostate Biopsy-A Systematic Review. *European Urology Oncology* 2021
10. Wilson ECF, Wreford A, Tamer P, et al. Economic Evaluation of Transperineal versus Transrectal Devices for Local Anaesthetic Prostate Biopsies. *PharmacoEconomics - Open* 2021 doi: 10.1007/s41669-021-00277-4
11. 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(1):97-103. doi: 10.1111/bju.15039 [published Online First: 2020/03/04]
12. Tamhankar AS, El-Taji O, Vasdev N, et al. 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(1):133-41. doi: 10.1111/bju.15062 [published Online First: 2020/04/02]
13. Marenco Jimenez JL, Claps F, Ramón-Borja JC, et al. Rebiopsy rate after transperineal or transrectal prostate biopsy. *Prostate International* 2021;9(2):78-81. doi: https://doi.org/10.1016/j.prnil.2020.10.001