MRI fusion biopsy in people with suspected prostate cancer

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Exact Imaging	1	40, 42, 55, 268, 348	Title of section 2.3.6 Table 2 Section 4.3 Table 60 (several times) Table 100	**Exact Imaging company name incorrectly spaced** Currently "ExactImaging" (no space) should be "Exact Imaging" (with space)	Noted. This will be rectified in the published report where Exact Imaging is mentioned. Given the nature of the request, which does not impact on decision-making, and to limit the amount of additional documentation for the Diagnostic Assessment Committee (DAC), we will not add this change to the Erratum document.
Exact Imaging	2	42, 268	Table 2 Table 60 (several times)	**Inconsistent spelling of "FusionVu" throughout the document** Term sometimes has an incorrect space "Fusion Vu" where it should be one name as above, with capitalization also as above.	As above, this will be rectified in the published report in sections referring to FusionVu.
Exact Imaging	3	40	Section 2.3.6	**Micro-ultrasound potential benefits not included** The Micro-Ultrasound basis of the ExactVu/FusionVu system is not mentioned in the report but is a significant and critical factor in the underlying mechanism of the FusionVu Software Fusion feature. The definition of Micro-Ultrasound (ultrasound at >20MHz) should be included in section 2.3.6, and reference provided to the data indicating that Micro-Ultrasound may provide additional benefits to usability and cancer detection rate, details of which are beyond the scope of the report.	The fact that ExactVu/FusionVu integrates micro-ultrasound is already mentioned in section 2.3.6 (Description of FusionVu) and in section 6.3.7.1 (Biopsy procedure costs). A definition of Micro-Ultrasound was added to section 2.3.6. As micro-ultrasound is beyond the scope of the report, we do no think there is a need to provide additional references on its potential benefits.
Exact Imaging	4	95, 205	Sections 4.6, 7.3	**FusionVu excluded from meta-analysis due to lack of data comparing to cognitive fusion, which does not make sense on ExactVu due to micro-ultrasound imaging** The report specifically excludes FusionVu from the meta-analysis citing no data comparing it to cognitive fusion. We don't dispute this, but suggest that the comparison is	Micro-ultrasound, or the evidence comparing its performance against mpMRI, are beyond the scope of this assessment. The meta-analyses included both direct and indirect evidence, although none of the studies of FusionVu met the criteria for inclusion in the meta-analyses, and several studies of FusionVu failed to meet more than one inclusion criterion in the review (e.g. Claros et al. 2020). Table 59

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				irrelevant because micro-ultrasound itself has been demonstrated to perform equivalently to mpMRI (see Hofbauer et al. 2021, Weimer et al. 2020, Sountoulides et al. 2021, You et al. 2021, etc.). We request that the cited reason for exclusion in the report be updated to clarify that FusionVu is not compared to cognitive fusion because cognitive fusion on the ExactVu device is not comparable to cognitive fusion with traditional TRUS.	provides at least one reason for the exclusion of studies screened at full text stage (including several FusionVu publications), as per standard reporting practice. Therefore, we do not think there is a need to update Table 59 or to provide further reasons for exclusion.
Exact Imaging	5	86	Section 4.4.3.3	**Comparison between fusion systems ignores study comparing FusionVu to Artemis** Section 4.4.3.3 is missing the data published on the ExactVu system compared to the Artemis system (Claros et al. 2018). This paper has similar population and sample size to the ones listed in Table 15 and should be included and discussed.	We assume the company are referring to Claros et al (2020), which was included in their submission. This was screened as per our selection criteria, and excluded at full text stage. In addition to the lack of relevant comparator, the study retrospectively compared two separate cohorts that received either fusion biopsy or micro-ultrasound. It is listed in Table of excluded studies (Table 59).
Exact Imaging	6	348	Table 100	**The number of uses of the FusionVu biopsy guide is not included in Table 100** The box of guides quoted includes 24 parts for the £1,333 cost (i.e. individual cost is £1,333/24 = £55.54) so either the "Number of uses" column should list 24 here or the cost should be updated to the unit cost.	We have corrected Table 100 with this information. This change does not affect the biopsy costs presented in the main report and applied in the cost-effectiveness analysis.
Prostate Cancer UK	7	202	7.1	*Additional meta-analyses of cancer detection rates suggest that, compared with cognitive fusion biopsy, software fusion may identify more prostate cancer (any grade) (OR 1.30; 95% CrI 1.06, 1.61) and more non-clinically significant cancer (ISUP 1) (OR 1.98; 95% CrI 1.28, 3.06). Adding systematic biopsy to cognitive or software fusion may increase the detection of all prostate cancer and of clinically significant cancer, and from this evidence there is no suggestion that software fusion with concomitant systematic biopsy is superior to cognitive fusion with systematic biopsy.*	Thank you for raising this important point. Since submitting our report, we have sent an Addendum to the report to NICE which provides further clarity. The results of the synthesis models require careful interpretation as they refer to different comparisons between different cancer grades. The odds ratio (OR) of 1.30 quoted here is comparing detection of any cancer, i.e., all ISUP 1 to 5 combined, and not only the detection of non-clinically significant cancer. The OR of 1.98 refers to odds of ISUP 1 with software fusion vs. odds of no cancer with cognitive fusion. The increase in the ORs for detection of any cancer is largely driven by the increase in

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				Prostate Cancer UK would welcome clarity on whether the addition of software fusion, and the subsequent potential for an increase in insignificant disease to be detected, would outweigh the benefits of the increase in detection of significant cancer. **We would be concerned over an increase in detection of clinically insignificant prostate cancer by this modality. We would suggest that any evaluation of a biopsy technique should focus on the detection of high grade cancers (ISUP grade 2 and above) and minimising the detection of clinically insignificant cancers. The more clinically insignificant cancers detected can lead to a higher rate of overdiagnosis and therefore potentially higher levels of overtreatment in patients with prostate cancer that would otherwise not become symptomatic in their lifetime.**	the probability of categorisation at ISUP > 1 (and more specifically by increases at ISUP 2) with software fusion. The interpretation of these results as probabilities (rather than odds ratio) is more intuitive and directly relevant to clinical practice. In summary, considering all meta-analysis results, compared with software fusion, we found that cognitive fusion shows: i) a higher probability of being classified as not having cancer, ii) similar probability of being classified as having non-clinically significant cancer (ISUP 1), and iii) lower probability of being classified at higher ISUPs, particularly ISUP 2. In the Addendum to the report to NICE, we also note that the increased correct detection at ISUP 1 with software fusion leads to net health losses in the economic analysis, so the model accounts for the potential consequences of overtreatment for these individuals. The economic analysis suggests that at the disease prevalence across ISUP grades applied, the net health losses from increased ISUP 1 detection are offset by the net health gains from increased detection at ISUP grade 2 and above. However, we also note that the value of software fusion is driven by i) comparative diagnostic accuracy derived where evidence is particularly sparse (ISUP grades above 2), and by prevalence, which is also affected by evidence sparsity.
Prostate Cancer UK	8			There was some evidence that systems with rigid registration (Biojet or Uronav) are easier and significantly faster to use than elastic registration (KOELIS Trinity), although this is informed by a single, small study and is not conclusive.	We agree with this point. This finding in part informed our recommendation for research in section 8.2, which is mentioned in the next comment.

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				For patients, one of the most important aspects when it comes to biopsy is the length of time the procedure might take, especially when concerning biopsy that is administered under a local anaesthetic where the patient will be awake and aware of what is happening. Stress and anxiety over the procedure can lead patients to have less than optimal experience and potentially not return for subsequent procedures if needed. From speaking to patients about biopsy, Prostate Cancer UK is aware that these initial observations of an "easier and faster" approach using Biojet or Uronay devices would appeal more and be favourable to patients who may undertake this procedure. We would call for more clarity surrounding this evidence with further research and data collection.	
Prostate Cancer UK	9		8.2	Qualitative evidence on the acceptability of software fusion to patients, notably where biopsy procedure time might be significantly increased, is needed. **Again as stated above, Prostate Cancer UK would stress the importance of an efficient procedural time taken especially when considering biopsy under a local anaesthetic. We would urge for the inclusion of more patient input into this diagnostics assessment to underpin any decisions made by the committee in future considerations for this procedure. We would also call for more clarification as to whether an increase in procedural time may also lead to additional discomfort or pain for the patient.**	Unfortunately, we did not identify evidence as to whether any increase in procedural time may affect patient comfort and pain for the patient, although we recognise the importance of this issue. This partly informed our recommendations for future research.