Peer Review File

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Reviewer A

You reported a clinically interesting aspect of daily urological practice. However, there is always a difficulty finding the adequate definition of a learning curve as there is no ideal reference. You set the experienced urologist as reference which might be a good option. However, I have a few points which minimize the impact of your study. Please find attached my comments, thoughts and questions:

• Page 5 line 86: I would rather call it "MRI fusion biopsy" instead of "MRI-transrectal ultrasound fusion" as it can be both transrectal and perineal

We thank the reviewer for the comment. We have modified our text as advised (See pages 5-6, lines 86-117).

• Page 5 line 90 ff: shorter duration of the procedure, increased patient compliance - compared to which reference?

We thank the reviewer for the comments. According to previous reports, MRI-US fusion biopsy has a shorter duration as compared to in-bore biopsy (Arsov et al, 2016). Furthermore, if only targeted cores are harvested, less pain has been reported by patients undergoing fusion biopsy when compared with systematic (Eineluoto et al, 2018) or in-bore sampling (Arsov et al, 2016). We added the supplementary information in the text (See page 5, lines 93-94).

• Were the external MRI reports reviewed by the experienced radiologists from your institution? Have you checked the quality of the MRI based on the criteria of PI-QUAL? Can you provide this information? This would have been interested as you also mentioned the unknown quality of external MRI in your discussion…

We thank the reviewer for his/hers comments. Indeed, the quality of the MRI scan and MRI reporting can represent causes of bias. Unfortunately, there was no possibility to review all the external MRI reports by the radiologists in our institution, but we found no difference in the diagnosis rate of prostate cancer between in-house and external MRI. Furthermore, the PI-QUAL criteria (Giganti et al, 2020) have been developed in order to assess the quality of the MRI scans, which is important when aiming to compare results between different centers. However, the PI-QUAL criteria have been published on 30th July 2020, whereas our study took place between October 2017-March 2020. A retrospective assessment of the MRI scans was precluded taking into consideration that 67.75% of them were performed in various external centers and we do not have current access to the images. We added this information in the limitations section of our study. (See page 15, lines 331-338).

• How did you bring the two different PI-RADS Versions (V1 and V2) in line together? PI-RADS V1 was a different scale with numbers ranging from 0 – 15; wheres PI-RADS V2.1 ranges from 0 – 5 ?

We thank the reviewer for the comments. Indeed, PI-RADS V1 (Barentsz et al, 2012) consists in scoring each sequence on a five-point scale. However, additionally to this scale, each lesion is given an overall score to predict its chance of being a clinically significant disease. Although no specific criteria on how to establish the overall score of a lesion have been recommended, the final scoring of the lesion was generally performed from 1 (very low risk of clinically significant disease) to 5 (very high risk of clinically significant disease), at radiologists' discretion. For PI-RADS V2 (Weinreb et al, 2015), recommendations on how to establish the final score of the lesion were detailed and were performed as such in our study. We employed the same indication for prostate biopsy – the presence of at least one lesion with PI-RADS score of 3, irrespective of the version. We added this information in materials and methods. (See page 7, line 158)

Reviewer B

The authors are to be commended on this well-conceived and well-written study on two urologists' MRI-TRUS fusion prostate biopsy experience within a multidisciplinary team.
All sections are logically written, with discussion and conclusions appropriately representing the results found.
The results show a curve for the continual learning loop indicating that experience influences detection of significant cancer.
I agree with the authors that this paper should provide a useful template for learning MRI-US fusion prostate biopsy.

The only minor changes I would recommend are:
1. The MRI reading is the key to the outcome. This, however, is not mentioned in the text. Radiologists learning curve as part of a purposeful learning/feedback has been published before (Gaziev). It would be better to indicate the radiologists' experience in the material and methods, and their effect on the learning curve should be discussed in the limitations.

We thank the reviewer for the comments. Indeed, radiologists experience and learning curve in reading mpMRI is a determining factor for biopsy outcomes. In material and methods we detailed the experience of the radiologists in our center (see page 7, lines 149-150). However, data regarding the experience of the radiologists who read external MRIs are not available. We completed the limitations section according to your recommendations (see page 15, line 333)

2. You may consider discussing the outcomes of a recently published paper (PMID: 33340435) with your findings.

We thank the reviewer for the suggestion of this very interesting paper that shows the

importance of a multidisciplinary team effort when starting an MRI-US fusion biopsy program. We added the supplementary information in the discussions section. (see page 15, lines 339-346)

3.Finally, the paper claims a clean-cut analysis however, there are too many external variables that affect the outcome. These external variables and other parameters need to be stated as limitations of the study**.**

We thank the reviewer for this comment. We agree that there are many factors that could potentially bias the outcome of the MRI-US fusion biopsy. We added this information in the limitations section. (See page 15, lines 331-338)

Reviewer C

The authors compared the learning curves in a total of 400 MRI-US fusion biopsies between an experienced urologist and a trainee using prostate cancer detection rates. Although the detection rate of all prostate cancers increased in both, the detection rate of clinically significant cancers also improved only in an experienced urologist.

This is a clinical study with a much smaller number of cases than similar papers that preceded it. In addition, there is little scientific knowledge to be newly added. Even if one experienced urologist and one trainee are compared, it may be difficult to draw a conclusion due to the bias of personal ability. Although it may be useful as a material in the hospital, there is no need to make it a peer-reviewed treatise.

We thank the reviewer for his/her input. Indeed, reports assessing the learning curve of fusion biopsy on a higher number of patients have been published before. However, we consider that a cohort of 400 patients is not negligible, taking into consideration that previous studies show a plateau was reached in the learning curve after about 100 cases. Furthermore, the ideal assessment of the learning curve of this procedure is yet to be determined since it is at the border of more specialties. It requires knowledge of MRI, mastering the fusion ultrasound, together with the capacity to perform invasive procedures. The radiologists are well trained in reading the MRI scans, but in general they do not have experience in performing prostate biopsies. On the other hand, for urologists, prostate biopsy is a common procedure, but they do not have experience in reading the scans. Standardization of the learning curve assessment and the curriculum necessary to perform fusion biopsies aims to improve the outcomes of this procedure. We detailed the limitations of our study (See page 15, lines 331-338)