Reviewer’s report

Title: Three-dimensional greyscale transrectal ultrasound-guidance and biopsy core preembedding for detection of prostate cancer: Dutch clinical cohort study

Version: 0 Date: 21 Dec 2018

Reviewer: Howard L. Parnes

Reviewer's report:

Summary: This is a well-done retrospective comparison of prostate cancer detection rates using 2D (2007-2013) versus 3D (2013-2016) TRUS biopsy. The main finding is that the 3D platform (which also includes a preembedding method that the authors acknowledge may have augmented the effect of the 3D imaging) results in significantly higher detection rates of prostate cancer, both overall and "significant."

Comments:

Abstract (line 53): Suggest revising to, "3D GS TRUS-guidance with biopsy core preembedding appears to improve PCa and clinically significant PCa detection compared to 2D TRUS-guidance."

Background (line 61): With regard to the statement that early detection reduces PC mortality, I would reference the ERSPC trial. I believe the most recent update of this trial is Schroder, et al., Lancet, 2014 Dec 6;384(2027-35).

Background (line 62): I would like to suggest a primary reference (Schroder, Hugosson, Carlsson, et al. European Urology 62 (2012) 745-752) instead of the European association of urology recommendations provided in reference #2 to support the statement that early detection reduces the risk of advanced or metastatic disease.

Results: It would be worthwhile to repeat the fact that the 3D TRUS biopsies were performed from 2013-2016, whereas the 2D TRUS biopsies were performed from 2007-2013. (This is explicitly stated only in the Methods section.)

Discussion: The authors acknowledge but downplay the possibility of residual confounding with regard to the fact that the 3D approach was undertaken by more experience operators. Please revise the statement, "...we believe that confounding by experience level in our model was accurately measured and corrected for in multivariate analysis..." All you should say about this is that you attempted to correct for this important imbalance but that there could still residual confounding.

I would like to know more about how 2D and 3D TRUS biopsy compare with regard to the detection of favorable and unfavorable intermediate-risk and high-risk disease. The authors chose, instead, to only look at overall PC and "significant" PC, defined as GS > 6 or > 2 cores of GS 6. Using > 2 cores of GS
6 is not an optimal way to select patients for treatment vs surveillance in the era of multi-parametric MRI. The more important question is which patients with favorable-risk intermediate prostate cancer should be offered the surveillance option.

Lines 249 to 254: I do not understand what the authors mean by "…from 42 to 64 percent for PSA levels > 10 ng/ml."

Conclusion: (Line 279) I think it would be more in keeping with the level of evidence that this study provides to say the current study "suggests" rather than "demonstrates" an added value of 3D TRUS-guidance….

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