Reviewer’s report

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

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Reviewer: Diederik Somford

Reviewer's report:

Overall a very well-written paper, however it adds limited knowledge to current practice. While detecting more prostate cancer with 3D ultrasonography (US) using a preembedding technique, the modest increase of detected prostate cancer does not convincingly overcome the known limitations of grayscale ultrasound. At this point in time more sophisticated techniques are available to increase the detection rates of clinical significant prostate cancer, such as multiparametric MRI and consequent MR/TRUS-fusion. At the same time a pre-biopsy MR pathway limits the detection of clinically insignificant cancer, the described biopsy technique certainly does not seem to deliver on that. Whereas it is likely that the introduction of 3D US with preembedding of biopsy cores has led to significantly more overall prostate cancer detection, it remains uncertain whether it truly detects more significant prostate cancer as the two methods (2D US versus 3D US with preembedding) were used consecutively in time and not simultaneously. Detecting more significant prostate cancer could thus well be caused by Gleason score shift over time (as the authors correctly state in the discussion: the Gleason score was updated in 2014), making the conclusion of the paper that the new technique detects more significant prostate cancer at best indicative. Furthermore, it remains unclear whether the increased detection of (significant) prostate cancer is due to the use of 3D US or use of the preembedding method as both measures were introduced at the same time. The effect of preembedding might well have the most influence on prostate cancer detection, as the authors have shown in an earlier study that 2D US using a preembedding technique was not inferior to 3D US. This paper concludes that 3D US with preembedding is superior to 2D US, but this conclusion is of limited value as it is not certain which factor causes this observation, the use of 3D US or the preembedding technique. Unfortunately, it is unlikely that the authors' database will be able to answer this question. As the series represents an analysis of a large population using solid methods it is still worth publication, but the authors should formulate their conclusion less firm and give solid recommendations for future research on 3D US as well as preembedding of prostate biopsy cores. Furthermore the reported improved detection rates should be compared to those of multiparametric MRI and MR-targeted biopsies in the discussion as this should be considered the state of the art in the current era. It is at least surprising that MRI is mentioned in a paper on prostate cancer diagnosis merely once, only stating that it was not used for selecting patients for biopsy.

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