**Reviewer’s report**

**Title:** A prospective study of magnetic resonance imaging and ultrasonography (MRI/US)-fusion targeted biopsy and concurrent systematic transperineal biopsy with the average of 18-cores to detect clinically significant prostate cancer

**Version:** 0  **Date:** 24 Apr 2017

**Reviewer:** Daniel Jason Margolis

**Reviewer’s report:**

One of the main aspects that sets this investigation apart from prior MRI-ultrasound fusion biopsy papers is the transperineal, rather than transrectal, approach. This should be stressed in the abstract and, I would suggest, the title. It should also be addressed in the Introduction, and again in the first paragraph of the Discussion.

Some aspects of language render the meaning unclear. E.g., the last paragraph in the introduction, "Image guided biopsy methods were classified as cognitive targeting without any technological guidance, targeting in the MRI gantry and real-time MRI/US fusion guided biopsies." Does this mean that the investigators considered these, or are they being listed as potential methods of image fusion targeted biopsy? Also, in the Discussion, the 3rd sentence states, "Regrettably, such trend resulted in a substantial number of indolent PC." I think the authors mean it resulted in the detection of indolent cancers.

The first paragraph in the Methods states this was prospective. How does this differ from clinical practice at this hospital?

It is unclear from table 1 what the temporal resolution of dynamic contrast-enhanced (DCE) imaging was. Although DCE does not add much to suspicion assessment, it may add to detection.

Please define explicitly the CSPC criteria used; the "insignificant" criteria are unclear. Must all of these be true for the cancer to be considered insignificant? Since the number of cores is a "per-subject" rather than a "per-core" parameter, how did this relate to targeted vs. systematic biopsies? When the authors mention "Gleason score was under 3+3," does this mean that any GS 3+3 was significant? Did PSA density overrule GS?

In the results, a further description of demographics is needed to define the population. How many patients had never had a prior biopsy? How many had a prior negative biopsy? How many were on active surveillance (prior positive biopsy for clinically insignificant disease)? Please consider using the START criteria (Moore et al, Eur Urol 2013; 64(4):544-552) to define the biopsy cores.

How many subjects did, and how many did not, have targets on MRI? Were only subjects with targets included? In other words, we do not know how many subjects without targets would have
been found to have any or significant cancer by 18-core transperineal systematic biopsy, correct? Can we determine the performance of a "negative" MRI with no targets to exclude significant cancer?

Assuming all subjects had targets by MRI, is there any means to determine whether positive systematic biopsies occurred in the region of MRI-based targets? In other words, is it possible to infer whether the insensitivity of TB is based on MRI not finding targets, or the image-fusion targeted biopsy system missing them?

In the 3rd paragraph of the Discussion, the authors state "The upgraded rates by TB over SB were reported as 22%(43/198) (3). We performed extended systematic biopsies and the rate of upgrading by TB was lower (9.0%, 16/177)" but I cannot determine in which case there was upgrading by TB over SB, and which was upgrading by SB over TB.

Do the authors have any explanation why so few subjects had insignificant cancer? Could it be due to the definition? Many subjects had 3+3 cancer, so significance must have included size or number of positive biopsies. It may be that the definition of <3 positive cores does not apply to 18 vs. 12 or fewer cores.

Are the methods appropriate and well described? If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls? If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown? If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review? If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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