Author's response to reviews

Title: Is there a role for anterior zone sampling as part of saturation trans-rectal ultrasound guided prostate biopsy?

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Author's response to reviews: see over
Re: Manuscript entitled “Is there a role for anterior zone sampling as part of saturation trans–rectal ultrasound guided prostate biopsy?”

Dear Editor

We would like to thank Drs. Sexton and Golijanin for reviewing our manuscript, their insightful comments and suggestions. We have addressed their comments and revised our manuscript (changes are now marked in red) as ordered below.

Dr. Sexton’s comments:

Dr. Sexton comment #1 asked us to better clarify the rational of including patients on active surveillance (AS) in our study. We apologize if that was not clear and hope that our comments and revisions better clarify it:

a. “Justify the inclusion of low risk prostate cancer patients in this study”:
We would like to thank Dr. Sexton for asking us to clarify this and apologize that it was not clear in the original submission.
Our clinical practice is to perform saturation biopsy as the first surveillance biopsy for all patients who are enrolled to AS program with an attempt to improve risk stratification (as suggested for example by Abouassaly R et al Urology. 2008) since PC is often multi-focal. Because the AZ has not been sampled at the time of the diagnostic biopsy in any of the patients enrolled to active surveillance we include the AZ as part of the surveillance biopsy template. We hypothesize that in a patient who was discovered with PC elsewhere, AZ sampling will be more likely to be positive (field effects) and since this zone cannot be assessed by DRE and to the best of our knowledge literature describing its involvement in low risk PC patients (AS population) is lacking we feel that our data is very novel and valuable. We now included this explanation in the discussion section.

b. “Wouldn’t the risk of sampling the anterior zone (added discomfort, complication etc.) overweight the benefits?”
We perform the biopsy samples with local peri-prostatic anesthetic. We first sample the peripheral zone and only then the anterior zone. None of our patients experience additional discomfort specifically when the AZ was targeted. We report no significant additional complications for the procedure. Jones S et al (J Urol 2002) reported the safety tolerability of performing saturation biopsies in an office setting. Although we did not assess pain with a visual analog scale as Jones et al reported our technique was similar.
We do however question in our conclusion the need for AZ sampling for patients not on AS (group 1) based on our results that report low yield of significant cancer detection in the AZ.

c. “Please justify the number of biopsies for AS patients especially if not on a prospective study”

We apologize again that this point was not clear in the original submission. Our clinical practice is to perform saturation biopsy as the first surveillance biopsy post diagnosis and enrollment into active surveillance for all patients who did not have saturation biopsy as part of their diagnostic biopsy. Our saturation biopsy is of 20 cores (16 from the peripheral zone including the “far lateral aspects of the gland and the apex, and 4 from the TZ). The same number of cores was used in similar patient population by others (e.g. Abouassaly R et al Urology. 2008). To sample the AZ adequately we added 6 cores. This was implemented in 2008 when data about potentially aggressive anterior zone tumors began to surface. We revised the methods section to include a more clear explanation of this template which is also demonstrated in Figure 1. Both the median and mean number of cores was 26, only 18 patients experienced more than 26 cores, and only 2 > 30. The few patients who received more cores had larger TRUS volumes.

d. “Why did you believe the active surveillance group would benefit from AZ biopsies over their counterparts (group 1) based on their already established low risk characteristics? Were the patients on AS originally diagnosed at the author’s facility”?

Please refer to our comment above. Also, all AS patients were diagnosed within McMaster University hospitals.

e. “Explain whether this study was performed in a prospective fashion. Were the patients accrued to this study prospectively or was this a retrospective review of institutional practice pattern and thus review of existing data”?

We apologize for not having this information clear. This study was a retrospective review of institutional practice pattern. We added the information now to the method and discussion sections.

f. We revised Table 2 according to Dr. Sexton’s suggestions. We also changed “TRUS volume” to prostate volume”

g. “The authors should address the probability of sampling error for AZ biopsies in patients with larger volume gland”.

We thank Dr. Sexton for this suggestion which is indeed very important. We discussed this now in the second paragraph of the discussion section.

h. “The authors do not discuss the results very well for the group of AS patients who were taken off the AS setting following the biopsy. Namely, what % of patients had higher volume tumors or what % had higher-grade tumors that led to their change from AS to apparently active treatment”.

We thank Dr. Sexton for pointing out these deficiencies and accordingly add this information in the discussion section.
i. “Although the authors suggest that the saturation technique is reasonable in AS patients, they should consider as a limitation that prostate cancer risk categories are largely based on standard biopsy techniques and not on saturation biopsies. Thus, although a larger volume of tumor might be identified based on the authors’ technique, it might not necessarily translate into different risk given the different diagnostic techniques.”

We thank Dr. Sexton for this insightful comment and added it to our discussion section.

j. ”Methods section, first and second paragraphs. Define what local “freezing” means. Do the authors mean local “anesthesia”? Freezing should be changed to anesthesia?”

We apologize for this error and changed the wording from local freezing to local anesthesia.

Dr. Golijanin’s comments:

We would like to thank Dr. Golijanin for his interest in our manuscript and his helpful suggestions for further analysis. Particularly, Dr Golijanin wondered whether we could clarify/examine:

1. The race of our patient population given recent reports of AZ tumors in African American populations

Dr. Golijanin raises an interesting point. Unfortunately most of our patients were Caucasian and we did not have any Afro-Canadian patients in our series. There were a small number of Asian patients but not enough to make for a separate statistical analysis.

2. “Is there a potential correlation between PSA velocity and AZ tumors?”

Most patients in group 1 were referred to us so we did not have enough data over time to correlate an adequate PSA velocity and only very few had free/total PSA ratios. As well in group 2 free/total PSA ratios were not commonly calculated.

3. “How did the total number of biopsy cores affect decision making?”

The number of positive cores affected 8/49 patients in the AS group leading to the decision to pursue treatment and abort their active surveillance protocols. Only in 3 patients from group-1 did the number of positive cores play a role in the clinical decision.

4. “It would be worthwhile to find even more precise marker that could predict negative and/or insignificant biopsies. 6% of AZ only significant biopsies is a significant percentage knowing that increased number of prostate cancer patients are included in AS today.”

We completely agree with Dr. Golijanin that 6% of AZ only significant biopsies is a significant percentage and verify that it will be echoed in our discussion and conclusions.

5. “Correlation to RRP”.

All final pathology reports were reviewed to ensure they were in line with the biopsy results (tumor grade etc). Unfortunately it is not a standard protocol to report AZ involvement on the final pathological report at our institution so we don’t have that specific data available to us. Given that there were only 2 patients in group 1 and 3 patients in group 2 that underwent treatment based on the upstaging in the AZ of the biopsy, and that the focus of the study was on biopsy results and not long-term outcomes or survival we felt the lack of final RRP specimen correlation was minor and would not affect the message of our paper.

We would like to thank again Drs. Sexton and Golijanin for their time and helpful comments which we feel improved our manuscript. We hope you will find our manuscript interesting and suitable for publication.
Sincerely,

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