Author’s response to reviews

Title: Clinical evaluation of prostate cancer gene 3 score in diagnosis among Chinese men with prostate cancer and benign prostatic hyperplasia

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Author’s response to reviews:

Oct 12, 2015
Dr. Homayoun Zargar, MD
Editor-in-Chief
BMC Urology
Washington University
RE: Ms. Ref. No.: BURO-D-15-00013

Clinical evaluation of prostate cancer gene 3 score in diagnosis among Chinese men with prostate cancer and benign prostatic hyperplasia

Dear Dr. Homayoun Zargar,

Attached please find the revised manuscript entitled “Clinical evaluation of prostate cancer gene 3 score in diagnosis among Chinese men with prostate cancer and benign prostatic hyperplasia” for your review. To avoid over statement of our conclusion, the conclusions have been revised and are based on the study methods and results. All the statements about prediction value of PCA3 assay on biopsy decisions have been deleted and the limitation of our study was referred in the conclusion section. In addition, we have carefully considered and responded to all other comments from the reviewers and editors. All changes have been detailed in the point-to-point responses to reviewers listed on the following pages. My coauthors and I would like to thank the reviewers for their expert opinions. We believe that this manuscript has been improved by this revision. Thank you very much for agreeing to review our revised manuscript.
Sincerely,

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Response to Reviewer Comments:

BURO-D-15-00013

Clinical evaluation of prostate cancer gene 3 score in diagnosis among Chinese men with prostate cancer and benign prostatic hyperplasia

Jin Huang; Kathleen H. Reilly; Hui-Zhen Zhang; Haibo Wang

BMC Urology

Dear Mr Wang,

Your manuscript "Clinical evaluation of prostate cancer gene 3 score in diagnosis among Chinese men with prostate cancer and benign prostatic hyperplasia" (BURO-D-15-00013R1) has been assessed by our reviewers. Based on these reports, and my own assessment as Editor, I am pleased to inform you that it is potentially acceptable for publication in BMC Urology, once you have carried out some essential revisions suggested by our reviewers.

Their reports, together with any other comments, are below. Please also take a moment to check our website at

http://buro.edmgr.com/l.asp?i=2971&l=YYKXL2MW for any additional comments that were saved as attachments. Please note that as BMC Urology has a policy of open peer review, you will be able to see the names of the reviewers.

Once you have made the necessary corrections, please submit a revised manuscript online at:

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If you have forgotten your username or password please use the "Send Username/Password" link to get your login information. For security reasons, your password will be reset.

Please include a cover letter with a point-by-point response to the comments, describing any additional experiments that were carried out and including a detailed rebuttal of any criticisms or requested revisions that you disagreed with. Please also ensure that all changes to the manuscript are indicated in the text by highlighting or using track changes.

Please also ensure that your revised manuscript conforms to the journal style, which can be found at the Instructions for Authors on the journal homepage.

A decision will be made once we have received your revised manuscript, which we expect by 09 Nov 2015.

We look forward to receiving your revised manuscript and please do not hesitate to contact us if you have any questions.

Best wishes,

Homayoun Zargar

BMC Urology

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Reviewer reports:

Reviewer #1: All my concerns with the study have been appropriate addressed by the authors. The paper is now suitable for publication and adds to the growing body of literature regarding novel use of biomarkers in prostate cancer diagnosis and prognosis.

Reviewer #2: The authors have made several substantive changes to this retrospective analysis correlating PCA3 scores to prostate biopsy results that address a number of the issues discussed in the previous review. However, there remain several issues to address:

- In Abstract conclusion, the wording of this sentence seems to overstate the findings of this study, as this is limited to a select population of Chinese men and given that results are based on tissue, the connection to how this will help predict biopsy outcomes is not terribly clear. The authors should be cautious not to overstate their conclusions.
All the statements about prediction value of PCA3 assay on biopsy decisions have been revised according to reviewer’s suggestions. And to base on study methods and results and to display the limitation of our study, the conclusion in Abstract has been revised as following:

“Increased PCA3 in biopsy tissue correlated with prostate cancer and the PCA3 assay may improve the diagnosis efficacy as the PCA3 score being independent of PSA level. The diagnostic significance of urinary PCA3 testing should be explored in future study to determine the prediction value in guiding biopsy decision as the clinical relevance of current study was limited for PCA3 testing based on biopsy tissue in a limited number of Chinese men.”

- In abstract and methods, the wording has been simplified some which improves the readability. However, the authors declare that the formalin-fixed, paraffin-embedded tissue blocks were collected before biopsy. Where did these tissue blocks come from, if not from a biopsy? Further clarity in this methodological explanation is necessary to allow the reader to appropriately interpret the utility of these findings.

It is our mistake and we are sorry for that. Formalin-fixed, paraffin-embedded tissue blocks were collected after biopsy. And the description in abstract has been revised as follows:

“Formalin-fixed, paraffin-embedded tissue blocks were used to test PCA3 and prostate-specific antigen (PSA) mRNA.”

- While the discussion better places the results of this study into context with some updated language in the revision, the several of the conclusions drawn do not appear to be supported by the data. For example:

- "The study evaluated the PCA3 assay as an additional tool in guiding biopsy decisions in Chinese men." and "This study showed that the PCA3 assay could provide improtant information for Chinese men who would consider prostate biopsy" How is this so when the marker for PCA3 used in this study was obtained after men had already received a biopsy?

We agree with reviewer’s suggestions as the specimens were collected after biopsy.

“- "The study evaluated the PCA3 assay as an additional tool in guiding biopsy decisions in Chinese men."” has been revised as following:

“The study evaluated the PCA3 assay as an additional tool in facilitating diagnosis of prostate cancer in Chinese men.”

"This study showed that the PCA3 assay could provide improtant information for Chinese men who would consider prostate biopsy" has been revised as following:
“This study showed that increased PCA3 in biopsy tissue correlated with prostate cancer and that the PCA3 assay could aid in diagnosis of prostate cancer in a limited number of Chinese men.”

- Furthermore, the authors refer to PSA and PCA3 values throughout the paper as it pertains to the mRNA derived from their tissue blocks, rather than the more commonly used serum or urine values used in clinical literature. This creates relative confusion as to how the conclusions are applied.

- In short, several of the conclusions should be simplified and focused as hypothesis generating. From this data, it appears that one could conclude that increased PCA3 in biopsy tissue may correlate with cancer, but conclusions beyond this are difficult to draw, given that, as the authors state, "clinical relevance was limited" by the use of tissue blocks rather than urine PCA3 measures. Further discussion of this limitation and examining of the clinical context of this study is warranted.

The conclusion in our manuscript has been re-organized as following:

“This study showed that increased PCA3 in biopsy tissue correlated with prostate cancer and that the PCA3 assay could aid in diagnosis of prostate cancer in a limited number of Chinese men. The probability of a positive biopsy increased with increasing PCA3 score. In this population, the PCA3 score had a comparable diagnostic accuracy with PSA as there was no significant difference in ROC AUC between PCA3 score and PSA. Most importantly, the PCA3 assay confirmed its independent diagnosis value and may improve the diagnosis efficacy as the PCA3 score being independent of PSA level. However, the clinical relevance was limited as PCA3 testing was based on biopsy tissue. To help determine the prediction value in guiding biopsy decision, the diagnostic significance of urinary PCA3 testing should be explored in future study.”

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Editorial Requests

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Please note that all submissions to BMC Urology must comply with our editorial policies. Please read the following information and revise your manuscript as necessary. If your manuscript does not adhere to our editorial requirements this will cause a delay whilst the issue is addressed. Failure to adhere to our policies may result in rejection of your manuscript.

Ethics:

If your study involves humans, human data or animals, then your article should contain an ethics statement which includes the name of the committee that approved your study.

If ethics was not required for your study, then this should be clearly stated and a rationale provided.
An ethics statement was written in the original draft, including the name of the committee that approved your study.

Consent:

If your article is a prospective study involving human participants then your article should include a statement detailing consent for participation.

If individual clinical data is presented in your article, then you must clarify whether consent for publication of these data was obtained.

Informed consent was received from subjects and this had been stated in our manuscript.

Availability of supporting data:

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Authors Contributions:

Your 'Authors Contributions' section must detail the individual contribution for each individual author listed on your manuscript.

Author Contributions had been described in our manuscript.

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