Author’s response to reviews

Title: Electrical Conductivity-based Contrast Imaging for Characterizing Prostatic Tissues: In Vivo Animal Feasibility Study

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Details of Revision

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Authors: Yong Soo Cho, Young Hoe Hur, Hyun Ju Seon, Jin Woong Kim

Dear Dr. Tillie Cryer,

Thank you for the opportunity to revise this paper. We deeply appreciate to the reviewers for their valuable comments to improve the paper. In the revised paper, we have addressed each comments and marked changes in red color.

Yours sincerely,

Hyung Joong Kim, Ph.D.
Corresponding Author

To First Reviewer (Dr. Robert Lenkinski)

This an interesting manuscript describing a sophisticated technical approach to creating tissue contrast
in the prostate based on differences in electrical conductivity. The results acquired on 5 beagles show contrast between the peripheral zone and the central zone of the prostate. The results are interesting but it is unclear how this information will impact clinical decision making in clinical MRI of the prostate. The acquisition time employed is quite long (40 minutes) and since the beagles had no pathologies it is difficult to assess how useful these methods will be in visualizing and/or characterizing prostate cancer. In addition it is unclear whether the spatial resolution is sufficient to detect small cancers. These initial results are sufficiently encouraging to form the basis for planning a study to study prostate cancer with pathological confirmation in an appropriate large animal model. In its current form this manuscript is not suitable for publication in BMC Urology but should be published in a more technical journal.

> Thank you for your valuable comments to improve our paper. I completely agree with your comments. Electrical conductivity is an inherent material property which its contrast originates from the concentration and mobility of ions inside and outside the cells. Over last 15 years, MR-based electrical conductivity imaging method have been developed technically, and now finding the clinical applications is a critical point (refs. 12,13,18, Lee et al. PLoS ONE. 2018;13(5):e0197063, Sajib et al. Sci. Rep. 2018;8:290, Choi et al. Int. Neurourol. J 2017;21(1):S32-38). This study focused on evaluating the application of the conductivity imaging method to the male pelvis region to provide different tissue contrast information comparing to the conventional imaging method and quantitatively analyzing the tissue contrast based on the absolute conductivity value.

As you point out, there are some limitations to this study. We can provide solutions to your concerns through recent technical advances as well as clinical usefulness. First, we have reduced the acquisition time to less than 4 minutes by applying the latest MRI technology, such as images acquisition with multi-band. I think we can use these techniques to get a high-resolution electrical conductivity image with a pixel size of less than 1.0 mm. Second, we have developed a new conductivity tensor imaging method that improves the current conductivity imaging method for the detailed information on tissue conditions (ref. 25). Third, as an example of the usefulness of clinical applications, we have published a paper which provides high sensitivity to tissue response after radiation therapy (ref. 26).

We added several sentence for the limitations of this study in the Discussion section. We also added two references for the above mentioned. To support and probe the results of this study, we have a plan for detailed study on the information of tissue conditions from both the animal disease model and patients with prostatic diseases.

To Second Reviewer (Dr. Robert Bok)

This manuscript reports an interesting new imaging technique for the prostate, utilizing ion-based conductivity measurements, in the context of MRI. Various other MRI techniques are currently employed to help render anatomical and functional information about the prostate gland and its diseases, but this methodology is rather unique. The canine prostate model is appropriate for these preliminary investigations. Unfortunately, it is unclear how and to what degree this technique might compliment those other methods, but the authors appropriately temper their conclusions in this regard and focus on simply reporting the basics of the technology and initial findings.

> Thank you for your valuable comments to improve our paper. We added several sentence for the limitations of this study in the Discussion section. We also added two references (25, 26) to support the potential of electrical conductivity imaging for clinical usefulness as well as technical advances.

There were a number of places in the manuscript where the English wording could be improved:
I am sorry for the numerous errors in English wording. In the revised paper, we tried our best to improve English through the paper as much as possible by proof reading and by having a professional editing service from Edanz.

1. Abstract, 2nd sentence of Background — The phrase "evaluated tissue contrast both the conductivity distribution and anatomical significance" does not make much sense. It is unclear what authors are trying to convey here and needs rephrasing.

> I am sorry for the wrong expression of this. We improved the sentence for the better understanding. “evaluated tissue contrast in terms of both the conductivity distribution and anatomical significance”

2. P. 4, Lines 28-30 — the points being communicated in this sentence are not clear. Even if this sentence is just a summary of points made in the preceding paragraph, the sentence needs to be re-worded and made more clear.

> I am sorry for the unclear expression of this. We improved the sentence as your suggestion. “image-based qualitative and quantitative information on prostatic tissues can provide a prior knowledge of the zonal information associated with prostatic diseases.”

3. P.5, Line 6 — "A new imaging techniques…” should be changed to "New imaging techniques…”

> Thank you for pointing out this. We made correction as your suggestion.

4. P.5, line 27-28 — "high-resolved" should be "high-resolution"

> We made correction as your suggestion.

5. P. 10, Lines 8-11 — This first sentence of the Discussion needs re-wording, perhaps something along the lines of "Differences exist in the tissue composition of the various prostate zones, such as gland (acini) density per zone, and the incidence of prostatic diseases are know to have zonal predilections".

> Thank you for pointing out this. We made correction as your suggestion.

6. P.12 Lines 47-50 — This last sentence of the Conclusion should also be re-worded, something akin to "Future studies are focused on the verification and evaluation of conductivity differences between normal, healthy men and patients with prostatic disease.

> Thank you very much for pointing out this. We made correction as your suggestion.