Peer Review File

Article Information:

Comment: The manuscript is a review for topic of using DKI and conventional DWI in PCa.

The manuscript is a s of now quite hard to read due to presentation with short one-sentence paragraphs. There is omission of various timely topics for DWI in PCa, and I would recommend for the authors to revise and submit systematic review instead to have better coverage of the literature and in this way increase contribution and importance of the manuscript.

Reply: Dear reviewer, thanks for your comment. We understand the intent of the reviewer, however our main purpose was to provide a narrative review on the argument, which implies a different structure and analysis

Changes in the text: NA

Comment: Abbreviation DKI here can be easily confused with kurtosis model in multi-shell variant of DTI model, also called DKI in brain imaging, but having larger amount of diffusion direction to make tensor calculation possible and feasible. Please clarify the separation to the reader, e g I would recommend talking about "DWI kurtosis" model to highlight the difference

Reply: Dear reviewer, thanks for your comment. We understand the intent of the reviewer, however we preferred to mention DKI in accordance with the works cited within the paper

Changes in the text: NA

Comment: The manuscript contains number of orphan sentences, making it very hard for the reader to follow. Please revise the whole manuscript for combined paragraphs with clear message in each

Reply: Dear reviewer, thanks for your comment. An extensive revision of the manuscript has been performed

Changes in the text: NA

Comment: Please add following timely points to the review: Discussion of imaging time and hardware requirements for kurtosis model. Discussion of reproducibility of DWI in PCa. Discuss more on how radiomics and artificial intelligence relates to DWI in PCa.

Reply:

Comment: As other general notion, I suggest giving attention to which manner the validation of the results were made in each citation, e g with biopsy, whole gland histology, as these affect to the accuracy of the results

Reply: Dear Reviewer, thanks for your comment. A table including different studies was enclosed in the paper

Changes in the text: A summary of the mentioned studies published focusing on DKI in prostate analysis is shown in Table 1

Comment: 4 DKI and PCa:

- "Given these premises, DKI did not show a clear added value compared with standard DW imaging for clinical PCa, therefore remaining debatable whether it should be incorporated into routine clinical imaging, also considering the complexity of the analysis." Please elaborate of why complexity of analysis would be problem here. Please consider adding instead requirement for longer scanning time due to minimum of 3 b-values instead of two, etc.

Reply: dear reviewer, thank for your comment. The paragraph was corrected as suggested

Changes in the text: also considering the longer scan time given the need to acquire at least three b-values

Comment: "Kapp is a phenomenological parameter with some similarity with ADC, which also has only indirect biophysical correlate." wouldn't the authors refer to Dapp i e diffusion rather than Kurtosity (deviation from exponential decay) here?

Reply: dear reviewer, we corrected the sentence in an attempt to better explain the concept

Changes in the text: Kapp is a phenomenological parameter with no biophysical correlate, as known also for ADC.

Comment: Please add clear justification into the introduction of why bi-exponential model, stretched exponential model and gamma model, all used with context of PCa classification, have been omitted. Alternatively please include then to the review

Reply: dear reviewer, main purpose of this review was to compare DKI and DWI, beyond all other mathematical model currently appliable for high b-value. However, we mentioned a recent paper which compare all main model

Changes in the text: However, up to date, all models for high b-factor diffusion- weighted images in prostate cancer, including the biexponential, kurtosis, stretched exponential, and gamma distribution models achieve similar AUCs for discrimination of normal and cancer tissue

Comment: "Besides, high attention is recently poses on deep learning and radiomics, with recent development in artificial intelligence that has promoted radiomics studies in various district and pathologies, including prostate cancer (17, 18, 57-67)." please revise the sentence for grammar

Reply: dear reviewer, thank for your comment. Conclusion were corrected as suggested

Changes in the text: Besides, high attention is recently poses on deep learning and radiomics application in various district and pathologies, including prostate cancer

Comment: Conclusion:

- "DWI and its associated ADC map remain, at present, the gold standard in the approach to the prostate cancer." while gland histology would suit better as a gold standard, while ADC can be considered rather a state-of-the-art or most conventionally used method. Please consider correcting.
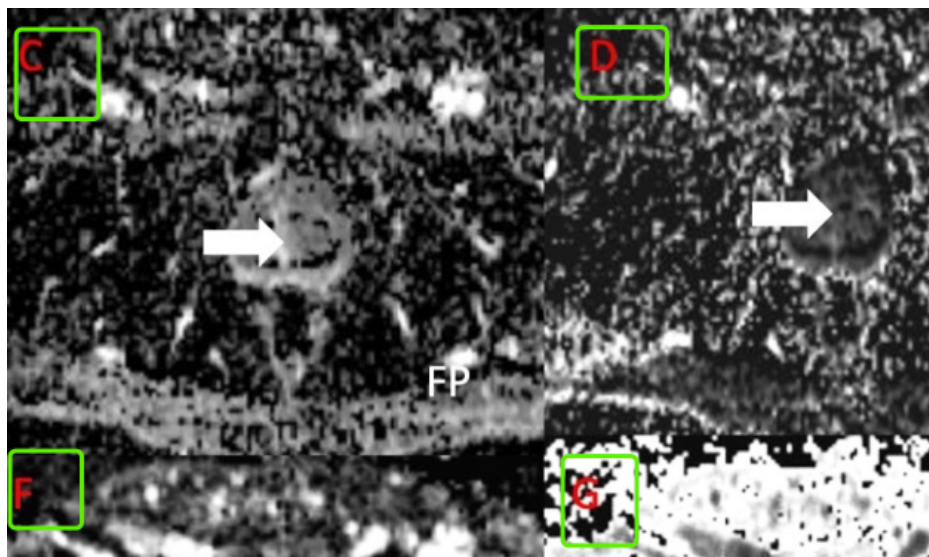
Reply: dear reviewer, thank for your comment. Conclusion were corrected as suggested

Changes in the text: DWI and its associated ADC map remain, at present, the most reliable imaging approach to the prostate cancer.

Comment: Figures
- Please indicate the meanings of arrowheads and arrows in the figure legends.
- Why there are A, B, C, D, F, G parts in your Figures 2-3, not A, B, C, D, E, F?

- Please check through your table to ensure all the abbreviations have been defined in their footnotes. For example, please provide the full name of ADC in the legend of Table 1.

Reply: All the abbreviations and figure letters were checked and corrected. And explanation has been added.