

Peer Review File

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Reviewer A

The study aimed to evaluate the performance of three-dimensional (3D) magnetic resonance elastography (MRE) imaging in predicting microvascular invasion (MVI) of T1 stage renal clear cell carcinoma (ccRCC). The paper is well-written.

1. Author has mentioned “Other functional MRI techniques could be combined with MRE in order to increase the positive predictive value in the Part “discussion”, please specified which functional MRI technique could be used.

Reply: Since MRE mainly reflect the tissue stiffness, which may be influenced by cell density, perfusion et al. This may be quantified by Intravoxel incoherent motion DWI imaging and arterial spin labelling. This has been added in the Part “discussion”.

Changes in the text: Page 11, Line 325-326

2. Whether the different weight of people would influence the image quality of MRE ?

Reply: People with lower weight could receive better image quality since the unobstructed transfer to the target organ. Even so, all MRE images we achieved could be used for analysis.

Changes in the text: None.

Reviewer B

This is a prospective study to use 3D MRE to predict MVI in renal clear cell carcinoma, which has promising results. There are a few questions:

1. Authors have mentioned that CT enhancement ratio could help to predict MVI , is there other CT parameters like enhancement pattern could predict?

Reply: In previous studies, tumor size, irregular tumor margin and enhancement pattern (peritumoral or intratumoral regions) are important for the prediction of MVI, but there are no significant difference in our study.

Changes in the text: None.

2. Authors could specify more about the advantage of 3D MRE than 2D MRE.

Reply: The advantage of 3D MRE compared with 2D MRE has been specified more in the Part “discussion”.

Changes in the text: Page12, Line 364-368, Line 371-373.

Reviewer C

First of all, my major concern regarding this study is the low specificity of 3D-MRE for the diagnosis of microvascular invasion, in particular the 75% specificity of MRE stiffness. The authors also did not consider to combine MRE tumor stiffness and CT kidney tumor enhancement to improve the diagnostic accuracy.

Reply: The specificity 3D-MRE for the diagnosis of microvascular invasion is 75%, which is close to the specificity of CT tumor enhancement ratio. Due to there were no better imaging technique have been reported, 3D-MRE could be used as a non-invasive and non- radiation method to predict microvascular invasion. The combination of MRE and CT kidney tumor enhancement have been done, but the diagnostic accuracy (especially specificity) has not been significantly improved, indicated that some tumors without microvascular invasion may have high stiffness and sufficient blood supply, these two methods may not fit to combine, so the authors just describe the comparison of these two methods.

Second, in the title please directly indicate the clinical research design of this study, i.e., a diagnostic test.

Reply: This has been specified in the revision paper.

Changes in the text: Page 1, Line 3.

Third, the abstract is not standardized and needs further revisions. The background did not describe the clinical needs for new diagnostic approaches for the microvascular invasion and the limitations of available diagnostic approaches. The methods did not describe the inclusion of subjects, how the diagnosis of the microvascular invasion was made, and the statistical methods for assessing the diagnostic accuracy. In the results, please briefly summarize the clinical characteristics of the study sample. The conclusion needs comments for the clinical implications of the findings.

Reply: The abstract has been revised following each point.

Changes in the text: Page1-2, Line31-61.

Fourth, in the introduction of the main text, the authors need to indicate the clinical importance of the early diagnosis of microvascular invasion, review available approaches for the early diagnosis of microvascular invasion, have comments on the limitations and diagnostic accuracy of available approaches, explain why 3D-MRE is potentially accurate for the diagnosis of microvascular invasion, and have comments on the knowledge gap on this research focus.

Reply: The clinical importance of the early diagnosis of microvascular invasion and available approaches for the early diagnosis of microvascular invasion have been specified in the first paragraph of “Introduction”. The explanation of “why 3D-MRE is potentially accurate for the diagnosis of microvascular invasion” and comments on the knowledge gap on this research focus have been added in the second paragraph of “Introduction”.

Changes in the text: Page 4, Line 91-101; Page 4-5, Line 110-118.

Fifth, in the methodology of the main text, the authors need to correctly describe the clinical research design of this study, which is not “prospective and single-center cohort study”, as well as the sample size estimation. The current sample size estimation procedures in the statistics is wrong, which did not indicate the sample sizes needed for case and non-case groups. In statistics, the authors need to consider to combine MRE tumor stiffness and CT kidney tumor enhancement to improve the diagnostic accuracy and provide the threshold values of AUC, sensitivity, and specificity for a good diagnostic test.

Reply: The description of clinical research design of this study has been revised. The current sample size estimation has been corrected. The combination of MRE and CT kidney tumor enhancement have been done, but the diagnostic accuracy (especially specificity) has not been significantly improved, indicated that some tumors without microvascular invasion may have high stiffness and sufficient blood supply, these two methods may not fit to combine, so the authors just describe the comparison of these two methods.

Changes in the text: Page 5, Line 136. Page 7, Line 217-218.

Finally, please consider to cite the below related papers: 1. Li Y, Gao Q, Chen N, Zhang Y, Wang J, Li C, He X, Jiao Y, Zhang Z. Clinical studies of magnetic resonance elastography from 1995 to 2021: Scientometric and visualization analysis based on CiteSpace. *Quant Imaging Med Surg* 2022;12(11):5080-5100. doi: 10.21037/qims-22-207. 2. Zhang T, Li Q, Wei Y, Yao S, Yuan Y, Deng L, Wu D, Nie L, Wei X, Tang H, Song B. Preoperative evaluation of liver regeneration following hepatectomy in hepatocellular carcinoma using magnetic resonance elastography. *Quant Imaging Med Surg* 2022;12(12):5433-5451. doi: 10.21037/qims-22-306.

Reply: The two related papers has been cited (reference 27,28) in the Part “discussion”.

Changes in the text: Page 11, Line 346-347.