

4 September 2015

To: The Editor,
World Journal of Gastrointestinal Pharmacology and Therapeutics

Re: **Response to Reviewers' Comments on Manuscript No: 21266**

Dear Sir,

Thank you for considering our manuscript entitled "**Clinical applications, limitations and future role of transient elastography in the management of liver disease**" (Manuscript No: 21266) for publication in your journal.

We have revised our manuscript according to the comments by the peer reviewers and the editor and would like to provide a point-by-point reply to the comments and suggestions made.

Response to comments by Reviewer 00159278

1. We have replaced "*Fibroscan®*" with "*transient elastography*" in the key words.
2. As per the reviewers suggestion, we have modified the statement that "*TE works by measuring shear wave velocity through the liver that is propagated by an ultrasonic transducer probe*" in the Introduction section on page 4. We have described that "*TE works by measuring shear wave speed through the liver*" and have removed the misleading statement that "shear waves are propagated by the transducer probe."
3. In response to the reviewer's suggestion to discuss technique quality parameters in greater detail, we have included a new section "2.7 Reliability Criteria" under section 2 - Limitations of TE on page 10. Reference to the new quality criteria from Boursier et al is made here and the corresponding reference has been added to the list of references^[44].
4. On page 12, we have edited the sentence "*The main role of TE in CHB is to differentiate individuals with inactive CHB from those with active disease*" to "*The main role of TE in CHB is to differentiate patients with significant fibrosis from those with inactive disease without fibrosis*" in response to the reviewer's point that TE can only assess fibrosis and not activity of CHB.
5. On page 23, we have added more information on ARFI as per the reviewer's suggestion.

6. We have improved the quality of English used in the article. However, we feel that the term “transaminitis” is acceptable as it is an accepted term in PubMed.

Response to comments by Reviewer 02441106

7. As mentioned in #1 above, we have replaced the term “Fibroscan” with “transient elastography” in the key words.
8. In the Introduction (page 4, line 5), we feel that the term “*for prognostication of liver disease.....*” is grammatically appropriate and should not be replaced with “*for prognostic of liver disease.....*”. Hence we have not made any change to this sentence.
9. As per the reviewer’s comment, we have deleted the typographical error “*with patients*” on page 6.
10. In keeping with the reviewer’s suggestion, we have added the reference by Sporea et al^[36] on page 8.

Response to comments by Reviewer 0266794

11. We have standardized the spelling to “*esophageal*” rather than “*oesophageal*” in the manuscript.
12. As mentioned in point #2 above, we have deleted the misleading statement regarding shear waves being propagated by the transducer on Page 4.
13. On page 4, line 17, we have replaced the term “*shear wave velocity*” with “*shear wave speed*” as suggested by the reviewer.
14. We agree with the reviewer’s comment that the abstract can be improved. We have thus modified the abstract to include our conclusions with regards to the clinical role of TE (Page 2).
15. We agree with the reviewer’s suggestion that “*advice to perform TE measurements on the right side of the liver should be mentioned*”. Accordingly on Page 4, Line 18, we have stated that the probe should be placed over the right lobe of the liver. We have also included a reference to the WFUMB guidelines as suggested by the reviewer.
16. In accordance with the reviewer’s suggestion, we have added a reference by Barr RG et al^[95] on Page 15 to highlight the role of TE to exclude significant fibrosis.

17. We agree with the reviewer's comment that the abbreviation "TE-CAP" may cause confusion to readers. We have thus avoided using "TE-CAP" and replaced this abbreviation with the term "*the combination of TE and CAP*" on Page 19.
18. As mentioned in point #13, we have replaced the term "*shear wave velocity*" with "*shear wave speed*" on page 4, line 17.
19. Under "2. Limitations of TE" on page 5, we have incorporated the reviewer's suggestion to replace the term "*propagated*" with "*proposed*" on Page 5, Line 3.
20. In the same paragraph on Page 5, we have replaced "*false positive interpretation*" to "*falsely high estimates*", as per the reviewer's suggestion.
21. On page 9, line 19, we have corrected "*measures the stiffness*"
22. On page 10, we have changed "*result in a higher degree of false-positive tests*" to "*result in more false-positive tests*".
23. On page 10, line 15, we have changed "*endoscopy*" to "*endoscopic*".
24. On page 14, last paragraph – we have changed "*liver processes as in AIH*" to "*liver processes in AIH*"
25. On page 15, line 9, we have changed "*to diagnosis*" to "*to diagnose*"
26. On page 17, we have edited "*one big area of focus*" to "*one area of interest*".

Response to Editor's suggestions

27. On the Title Page, we have added the city and postal code of Duke-NUS Graduate Medical School.
28. We have completed the Copyright Assignment Form which has been signed by all authors.
29. We have provided a summary for the core tip (Page 2).
30. We have provided a Audio Core Tip as requested.
31. We have added the PubMed citation numbers and DOI citations as requested.

We trust that you will find these amendments satisfactory. We look forward to the publication of our review article in your esteemed journal.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Jason' with a stylized flourish underneath.

Dr. Jason Chang Pik Eu
Corresponding author