Dear Editor and Reviewers:

Thank you very much for your hard work and consideration of our manuscript entitled "Noninvasive evaluation of liver steatosis with imaging modalities: new techniques and applications" (No: 82557). We also thank all the reviewers for their positive, encouraging and constructive comments. We have revised the manuscript in accordance with the reviewers' comments, point by point. We strive to impress the readers with comprehensive and concise information. We hope that these changes fulfill the requirements to make the manuscript acceptable for publication in *World Journal of Gastroenterology*. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

#### **Reviewer #1:**

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

**Specific Comments to Authors:** Zeng et al wrote a review article about noninvasive ultrasound-based techniques for liver steatosis evaluation. The topic is interesting and it has been analyzed in depth. Minor comments: 1) ASQ: it seems that only one study (ref 92) has been performed on humans. Is it the only one? If so, more caution for ASQ is necessary. 2) Conclusions are too vague. Please add Authors' point of view and personal opinion about possible future perspectives.

### **Response to the reviewer #1:**

- Considering the reviewer's suggestion, we have updated our literature search and found additional original studies regarding ASQ on humans. We have added results of these studies to the "Acoustic structure quantification (ASQ)" section.
- **2.** We thank the reviewer for the kind suggestion. According to the reviewer's suggestion, we have enriched the conclusion section. We added

the discussion of clinical significance of liver fat quantification and future perspectives.

## **Reviewer #2:**

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

**Specific Comments to Authors:** The present review shows the advantages and disadvantages of different imaging methods for assessing the fat content of the liver. Mainly the most different ultrasonic methods are evaluated. I don't think an MRI examination is a practical screening due to the high costs. Overall, the article shows no new insights. Especially because the available studies are not particularly meaningful due to the low number of cases.

# **Response to the reviewer #2:**

We really appreciate the reviewer's approval of our work and we thank the reviewer for the very constructive suggestion. In accordance with the reviewer's opinion, we believe that MRI examinations are not suitable for clinical utility due to limitations of high cost, low availability and timeconsuming. We have added the "speed of sound" part and "clinical significance of liver fat quantification" part to our manuscript.

## **Reviewer #3:**

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

**Specific Comments to Authors:** Summary This review article made clear and extensive demonstrations on current non-invasive liver steatosis measurement modalities. The performance, benefit and shortage of each modality were well listed in two Tables. Although a significant part of this review derived from Ref 4, we believe that this article is suitable for publication in the journal after minor

revision. Comments: 1. The mechanisms of steatosis measurement were described in the text. Very little is explored on the differences between modalities. 2. Please give illustrations to describe the mechanism of steatosis measurements and list its use in current modalities. 3. Please point out that CAP, ATI and MRI-PDFF are unable to differentiate grade 2 with grade 3 liver steatosis. 4. English needs to be improved. In the ATT section, "The results are presented in dB/cm/MHz with the liver stiffness measurement." This sentence is confusing. It will be better to separate it into two sentences. For example: The results are presented in dB/cm/MHz. The steatosis measurement is obtained together with the stiffness value.

### **Response to the reviewer #3:**

- We are grateful for the profound suggestion. We have added a section named "Mechanism of quantitative ultrasound techniques" to give full illustrations of mechanism of steatosis measurements and the differences between modalities.
- 2. We fully agree with the reviewer's suggestion. We have designed a new table (table 3) to describe the mechanism of steatosis measurements and list its use in current commercial techniques.
- 3. We have pointed out this issue in the Conclusion section.
- 4. We have polished the language by the editing service from an English language editing company to improve readability of the manuscript.

Finally, we appreciate the editors' and reviewers' kind and constructive suggestions to our manuscript and we have tried our best to improve the manuscript and made some changes in the manuscript.

Thank you for your further consideration of our manuscript. Best regards.

Qiang Lu, M.D.