Dear Editor,

Thanks very much for the precious suggestions for my manuscript. Here, I have some responses to your comments.

Reviewer 1

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Manuscript ID: 75350 Manuscript Title: How to Select The Quantitative Magnetic Resonance Technique for subjects With Fatty Liver: A Systematic Review This systematic review is interesting and has applicability in medicine. Therefore, to contribute to its improvement, some suggestions are proposed: 1. There are some problems with the structure and formatting of the manuscript, please see the "Guidelines for Manuscript Preparation and Submission: Systematic Reviews": • According to the rules of the Journal the manuscript must be prepared using the Book Antigua font. The topics METHODS, RESULTS and CONCLUSION present number of words discrepant from the Journal rules. • The authors' ORCID should be provided. • The coretip is present in "Manuscript information" but not in the text of the manuscript. • There is no request for abbreviations in the manuscript structure. • Correct the double "T" in "Ttwo-point Dixon imaging" keyword. • The word "Figure" should not be abbreviated (e.g. Figure 1 and not Fig. 1), see RESULTS. • Subtopics should not be numbered. • Figure 2 has low quality and Tables 1-3 are formatted outside Journal rules. Tables 1-3 could not be carefully analyzed because they are too large and unconfigured. 2. During the analyses data about the country where the study was performed were collected. Why were these data collected and what would be relevant to the study?

Comment 1: There are some problems with the structure and formatting of the manuscript, please see the "Guidelines for Manuscript Preparation and Submission: Systematic Reviews": • According to the rules of the Journal the manuscript must be prepared using the Book Antigua font. The topics METHODS, RESULTS and CONCLUSION present number of words discrepant from the Journal rules. • The authors' ORCID should be provided. • The coretip is present in "Manuscript information" but not in the text of the manuscript. • There is no request for abbreviations in the manuscript structure. • Correct the double "T" in "Ttwo-point Dixon imaging" keyword. • The word "Figure" should not be abbreviated (e.g. Figure 1 and not Fig. 1), see RESULTS. • Subtopics should not be numbered. • Figure 2 has low quality and Tables 1-3 are formatted outside Journal rules. Tables 1-3 could not be carefully analyzed because they are too large and unconfigured.

Replay: Thank the reviewer for great suggestions. We have corrected according to the "Guidelines for Manuscript Preparation and Submission: Systematic Reviews".

Changes in text: see revised manuscript.

Comment 2: During the analyses data about the country where the study was performed were collected. Why were these data collected and what would be relevant to the study?

Replay: Thank the reviewer for great suggestions. We deleted the "country" from the data.

Changes in text: *Data extraction*

The following data were extracted: first author, publication year, study design, number of patients, mean age, studied etiology, data about MR techniques such as field strength and scan sequences, comparison, interval between MR methods and comparison, and study's outcomes. Tables 1-3 have been corrected.

Reviewer 2

Scientific Quality: Grade C (Good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: Authors should point out the following points: Hepatologists need those studies to be conducted with longer follow up and thus evaluating the costs in case of repeated exams and at different stages of a patient's journey – for example in primary care, secondary care, and tertiary care. Furthermore, it is necessary to put these techniques in correct settings , i. e., epidemiological studies or in the field of research. Finally, the rationale to use these expensive and "requiring high expertise" tools is mainly based on assessing the efficacy of therapy, more than ascertain the presence of NAFLD, at the light that there are many drugs on the pipeline, as evident in.....Insights into the molecular targets and emerging pharmacotherapeutic interventions for nonalcoholic fatty liver disease, Metabolism,Volume   126,2022,154925,ISSN 0026-0495,https://doi.org/10.1016/j.metabol.2021.154925.

Comment 1: Authors should point out the following points: Hepatologists need those studies to be conducted with longer follow up and thus evaluating the costs in case of repeated exams and at different stages of a patient's journey – for example in primary care, secondary care, and tertiary care.

Replay: Thank the reviewer for great suggestions. We added the content in "Discussion".

Changes in text: How to select these techniques in daily practice? For epidemiological studies, MR and CT is unsuitable to because of the expensive

and time-consuming of MR and the radiation damage from CT, while ultrasound is preferred. For clinical study, especially following up or assessing the efficacy of therapy, two-point Dixon and multiple-point Dixon imaging are preferred because of their subjective and robust characteristic. However, in primary or secondary care where there is no MR machine, CT can be selected for short following up. MRS id the most accurate noninvasive technique and can be considered as good standard in the research studies although its accuracy depends on high expertise and the result is difficult to explain. For stratification and therapeutic management of patients with NAFLD, multiparametric MRI protocol including MR elastography and T1-T2 mapping may be useful.

Comment 2: it is necessary to put these techniques in correct settings , i. e., epidemiological studies or in the field of research.
Replay: Thank the reviewer for great suggestions. We added the content in "Discussion".
Changes in text: see "changes in text" in Comment 1.

Comment 3: the rationale to use these expensive and "requiring high expertise" tools is mainly based on assessing the efficacy of therapy, more than ascertain the presence of NAFLD, at the light that there are many drugs on the pipeline, as evident in.....Insights into the molecular targets and emerging pharmacotherapeutic interventions for nonalcoholic fatty liver disease, Metabolism,Volume 126,2022,154925,ISSN 0026-0495,https://doi.org/10.1016/j.metabol.2021.154925.
Replay: Thank the reviewer for great suggestions. We added the content in "Discussion".
Changes in text: see "changes in text" in Comment 1.

Reviewer 3
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors: Evaluation of the paper 75350-Manuscript

"How to Select The Quantitative Magnetic Resonance Technique for subjects With Fatty Liver: A Systematic Review". The aim of this study was to contribute to the selection of the quantitative MRI for patients with fatty liver. The authors conclude that proton density fat fraction derived from multiple-point Dixon imaging is a noninvasive method for accurate, quantitative measurement of the hepatic fat content. It can be used to diagnose the fatty liver and follow up the progression of the disease and treatment effect. Comments 1. This is a well written paper on a very interesting issue: the selection of the appropriate MRI method to diagnose and follow-up the progression of fatty liver. 2. The text, the tables, and the figure are satisfactory and informative. 3. References are up-to-date, however the following references might improve the paper: - Zheng D, Guo Z, Schroder PM, Zheng Z, Lu Y, Gu J, He X. Accuracy of MR Imaging and MR Spectroscopy for Detection and Quantification of Hepatic Steatosis in Living Liver Donors: A Meta-Analysis. Radiology. 2017 Jan;282(1):92-102. Doi: 10.1148/radiol. 2016152571. Epub 2016 Aug 1. PMID: 27479639. - Springer F, Machann J, Schwenzer NF, Ballweg V, Würslin C, Schneider JH, Fritsche A, Claussen CD, Schick F. Quantitative assessment of intrahepatic lipids using fat-selective imaging with spectral-spatial excitation and in-/opposed-phase gradient echo imaging techniques within a study population of extremely obese patients: feasibility on a short, wide-bore MR scanner. Invest Radiol. 2010 Aug;45(8):484-90. Doi: 10.1097/ RLI.0b013e3181df2afb. PMID: 20479651. 4. The results of the paper have clinical implications and are very useful for patients with fatty liver.

Comment 1: This is a well written paper on a very interesting issue: the selection of the appropriate MRI method to diagnose and follow-up the progression of fatty liver.

Replay: Thank the reviewer and we are surprised and excited by the comment.

Comment 2: The text, the tables, and the figure are satisfactory and informative.

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Comment 3: References are up-to-date, however the following references might improve the paper: - Zheng D, Guo Z, Schroder PM, Zheng Z, Lu Y, Gu J, He X. Accuracy of MR Imaging and MR Spectroscopy for Detection and Quantification of Hepatic Steatosis in Living Liver Donors: A Meta-Analysis. Radiology. 2017 Jan;282(1):92-102. Doi: 10.1148/radiol. 2016152571. Epub 2016 Aug 1. PMID: 27479639. - Springer F, Machann J, Schwenzer NF, Ballweg V, Würslin C, Schneider JH, Fritsche A, Claussen CD, Schick F. Quantitative assessment of intrahepatic lipids using fat-selective imaging with spectral-spatial excitation and in-/opposed-phase gradient echo imaging

techniques within a study population of extremely obese patients: feasibility on a short, wide-bore MR scanner. Invest Radiol. 2010 Aug;45(8):484-90. Doi: 10.1097/ RLI.0b013e3181df2afb. PMID: 20479651.

Replay: Thank the reviewer for great suggestions. We added two references.

Changes in text: Mounting evidence has shown that MR has high accuracy in quantitatively analyzing fatty liver and can be repeated with no radiation exposure[11-14]. [14. **Zheng D,** Guo Z, Schroder PM, Zheng Z, Lu Y, Gu J, He X. Accuracy of MR Imaging and MR Spectroscopy for Detection and Quantification of Hepatic Steatosis in Living Liver Donors: A Meta-Analysis. *Radiology* 2017; **282(1):** 92-102. [PMID: 27479639 Doi: 10.1148/radiol. 2016152571]

Springer[78] used additional individual time-consuming T1 and T2* measurements for correction of the measured intrahepatic lipids, but are mostly not applicable in time-restricted examination protocols. [78 **Springer F,** Machann J, Schwenzer NF, Ballweg V, Würslin C, Schneider JH, Fritsche A, Claussen CD, Schick F. Quantitative assessment of intrahepatic lipids using fat-selective imaging with spectral-spatial excitation and in-/opposed-phase gradient echo imaging techniques within a study population of extremely obese patients: feasibility on a short, wide-bore MR scanner. *Invest Radiol* 2010; **45(8):** 484-90 [PMID: 20479651 Doi: 10.1097/ RLI.0b013e3181df2afb]

Comment 4: The results of the paper have clinical implications and are very useful for patients with fatty liver.

Replay: Thank the reviewer and we are surprised and excited by the comment.

All the amends on my manuscript have been highlighted.
Your sincerely,
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