

Response to Reviewers

Dear Editor and reviewers,

Thank you for your letter and comments concerning our manuscript entitled "*Treatment of knee osteoarthritis with microfragmented adipose tissue plus arthroscopic surgery: A randomized, active-control, single-blind, multicenter clinical trial*" (Manuscript NO.: 88696). We appreciate your precious time in reviewing our paper and providing valuable comments. Your helpful and insightful words led to possible improvements in the current version. The authors have carefully considered the statements and tried our best to address every one of them. We hope the manuscript, after careful revisions, meets your high standards. The authors welcome further constructive comments, if any.

Below we provide the point-by-point responses. All modifications in the manuscript have been highlighted **with yellow color**.

Best regards,

Peijian Tong, M.D., Ph.D.

Institute of Orthopaedics and Traumatology, the First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou 310053, China

Tel:86-13906503677

E-mail: tongpeijian@163.com

Response to Rviewer 1

[Summary Comment]:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Well conducted study well written large number.

Response: Thank you very much. We have read your comments carefully and tried our best to address them one by one, especially in terms of providing recent references. Besides, we have found native English speakers to help us edit the whole manuscript and we will pay attention to improving English writing in the future. We provide the English Language Certificate issued by Charlesworth, which is a professional English language editing company. We hope that the manuscript has been improved after this revision.

[Comment 1] The methodology for both study groups - control and study - control had 3 injections of HA after 1 scopy debridement, and study group had 1 procedure for scopy debridement and mfat harvested form the abdomen The limitations regarding the possible effects of the differences in intervention and 3 injections at monthly intervals should be mentioned clearly in the limitations.

Response: Thank you very much for pointing this out. We agree with you that the differences in intervention might play a role in the results. We added this as a limitation in the discussion section:

“Moreover, the differences in the intervention in the control and study groups may have influenced the results.” [Pg18, Ln475-476]

[Comment 2] Kindly update the references. Micro-fragmented adipose tissue (mFAT) associated with arthroscopic debridement provides functional improvement in knee osteoarthritis: a randomized controlled trial. Ulivi M, Meroni V, Viganò M, Colombini A, Lombardo MDM, Rossi N, Orlandini L, Messina C, Sconfienza LM, Peretti GM, Mangiavini L, de Girolamo L. Knee Surg Sports Traumatol Arthrosc. 2023 Aug;31(8):3079-3090. doi: 10.1007/s00167-022-07101-4. Epub 2022 Aug 30. PMID: 36040510 Platelet-Rich Plasma Versus Microfragmented Adipose Tissue for Knee Osteoarthritis: A Randomized Controlled Trial. Baria M, Pedroza A, Kaeding C, Durgam S, Duerr R, Flanigan D, Borchers J, Magnussen R. Orthop J Sports Med. 2022 Sep 16;10(9):23259671221120678. doi: 10.1177/23259671221120678. eCollection 2022 Sep. PMID: 36147791 The discussion could be modified to highlight the same. The limitations have to be clearly mentioned and the recent references need to be discussed.

Response: Thank you very much for your friendly reminder. We updated the references accordingly and provided a discussion [Pg14, Ln359-362 and Pg15, Ln379-385]. Please refer to the revised manuscript.

Response to Rviewer 2

[Summary Comment]:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Dear Author(s), I appreciate your efforts in writing this paper; nonetheless, I would like you to make the following minor adjustments to improve the quality of your post:

Response: Thank you for your comments. We have gone through your comments carefully and tried our best to address them one by one. We hope the manuscript has been improved accordingly.

[Comment 1] Changing the title of the paper to reflect the present study's objectives.

Response: Thank you very much for your friendly reminder. We revised the title as follows:

“Mid-term outcomes of microfragmented adipose tissue plus arthroscopic surgery for knee osteoarthritis: A randomized, active-control, multicenter clinical trial”.

[Comment 2] The results portion of the study abstract must give a quick overview of the present research's most important findings.

Response: Thank you very much for pointing this out. We revised the results portion of the study abstract to make the research's most important findings clearer [Pg5, Ln99-109]. Please refer to the revised manuscript.

[Comment 3] It is not advisable to begin the Materials and Methods section with the phrase "Study design and participants (Table 1)," which refers to Table 1. As a result, the line beginning "This was a prospective, randomized, controlled, single, etc." must appear before the table.

Response: Thank you very much for the reminder. We have made revisions accordingly.

[Comment 4] Is there a valid justification for utilizing the statistical method given in the Statistical Analysis section to examine the research data? Please include an explanation that supports what the authors have claimed in this section.

Response: Thank you for your comments. The statistical method used in this study is well-known and was commonly adopted in many other RCTs. We provided the following citations to support justification of statistical method.

Elenes EY, Hunter SA. Soft-tissue allografts terminally sterilized with an electron beam are biomechanically equivalent to aseptic, nonsterilized tendons. *J Bone Joint Surg Am.* 2014;96(16):1321-1326. doi:10.2106/JBJS.L.00841

Leder BZ, Tsai JN, Uihlein AV, et al. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): extension of a randomised controlled trial. *Lancet.* 2015;386(9999):1147-1155. doi:10.1016/S0140-6736(15)61120-5

In addition, we provided a biostatistics statement in 88696-Biostatistics Review Certificate.

[Comment 5] What are the author(s)' and the scientific community's perspectives on the current study's future directions? A supporting text must be added to this query in the last paragraph of the discussion section that presents the strengths and shortcomings of the current study.

Response: Thank you very much for your friendly reminder. We revised the sentence as follows:

“Long-term studies on the potential dose-dependent effect, including more districts, should be conducted in the future.” [Pg18, Ln479-480]

[Comment 6] Rewrite the conclusion section to clarify if the present research topic has been solved or whether the current study has met its objectives.

Response: Thank you very much for your friendly reminder. We revised the conclusion section as follows:

“In conclusion, our study demonstrates that MFAT injection combined with arthroscopic surgery is a safe and effective approach for improving function and alleviating pain in patients with KOA. MFAT therapy produced longer-lasting, statistically significant durations of efficacy at 12 and 24 months in comparison to those of the control (HA) group. Based on these results, MFAT injection combined with arthroscopic surgery may be considered a potential therapeutic option for KOA.” [Pg18-19, Ln483-489]

[Comment 7] Some references are quite old and must be replaced by new references from 2023 and five years before, as well as outdated references that no longer aid the study cause.

Response: Thank you very much for your friendly reminder. We updated the references accordingly and provided a discussion [Pg14, Ln359-362 and Pg15, Ln379-385]. Please refer to the revised manuscript.

Response to Science editor:

[Summary Comment]:

1 Conflict of interest statement: Academic Editor has no conflict of interest. 2 Manuscript's theme: The topic is within the scope of the journal. 3 Academic misconduct: No academic misconduct was found.

Response: Thank you very much.

[Comment 1] The randomized Controlled Trial aims to assess the efficacy and safety of microfragmented adipose tissue combined with arthroscopic surgery in patients with knee osteoarthritis. This article has creativity and innovation. The discussion should be improved.

Response: Thank you very much for pointing this out. We did our best to improve the discussion [Pg13-18, Ln344-480]. Please refer to the revised manuscript.

[Comment 2] The reference list should be updated with the latest studies.

Response: Thank you very much for your friendly reminder. We updated the references accordingly and provided a discussion [Pg14, Ln359-362 and Pg15, Ln379-385]. Please refer to the revised manuscript.

[Comment 3] Please add PMID and DOI numbers to your references. They are available at: <http://doi.crossref.org/simpleTextQuery>. If there are no PMID or DOI numbers, please provide the website.

Response: Thanks for your nice reminder. We revised the references accordingly.

[Comment 4] The labeling of P value in the figures does not meet the requirements of WJG, please don't include any *, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as aP <0.05, bP <0.01 (P > 0.05 usually does not need to be denoted). If there are other series of P values, cP <0.05 and dP <0.01 are used, and a third series of P values is expressed as eP <0.05 and fP <0.01.

Response: Thank you very much for your friendly reminder. We have made revisions accordingly.

[Comment 5] 5 Language evaluation: Grade A. 6 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thank you very much for your previous comments that helped us improve this manuscript. We have found native English speakers to help us edit the whole manuscript and we will pay attention to improving English writing in the future. We provide the English Language Certificate issued by Charlesworth, which is a professional English language editing company.

Response to Company editor-in-chief:

[Summary Comment]:

I have reviewed the Peer-Review Report and the full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Stem Cells, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response: Thank you very much. We hope that the manuscript has been improved towards WJSC standards after this revision.

[Comment 1] The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, the author(s) must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

Response: Thank you for your comments. We have found native English speakers to help us edit the whole manuscript and we will pay attention to improving English writing in the future. We provide the English Language Certificate issued by Charlesworth, which is a professional English language editing company.

[Comment 2] Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thank you very much for your friendly reminder. We updated the references accordingly and provided a discussion [Pg14, Ln359-362 and Pg15, Ln379-385]. Please refer to the revised manuscript.

[Comment 3] Uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2023.

Response: Thanks for the comment. We have made revisions accordingly. Please refer to the PPT we uploaded.