



Hospital for Joint Diseases
Orthopaedic Surgery

12/03/2016

Dear Editors of *the World Journal of Orthopedics*,

Thank you for your consideration of the manuscript entitled "T1ρ/T2 mapping and histopathology of degenerative cartilage in advanced knee osteoarthritis." We are gratified that the reviewers are interested in our work. We have incorporated the excellent suggestions into the new version of the manuscript, and it has greatly improved as a result.

With this resubmission you will find point-by-point responses to the reviewers' comments with page and line numbers for reference.

Again, we greatly appreciate your consideration of our manuscript for publication in the *World Journal of Orthopedics*, and we welcome any further suggestions.

I - In-Text Responses:

Title Page: Thank you, postal codes have been added.

Lines 30: The grant acceptance form and documentation have now been uploaded.

Line 44: The IRB form has also been uploaded.

Line 52: Regarding biomedical statistics, a line was added to line 261 of the manuscript, stating “Statistical review of the study was performed by a researcher with training in biomedical statistics,” to clarify how our methods were accomplished.

Line 53: We apologize if there is any confusion in this circumstance, and very much respect this section of the research process, however there are no additional data available. All raw data has been included in the tables provides.

Line 125: Thank you for this reminder, an audio recording of the core tip has been provided.

Line 179: Brackets have been added to in-text references according to the World Journal format.

Line 445: We appreciate this request, the comments section of the manuscript including background, research frontiers, etc. has been incorporated into the text.

Line 460: Thank you again for this reminder, the references have now been amended to be more in line with the World Journal format.

II - Comments Section (From Reviewers):

1. The authors are required to describe the difference between T2 and T1ρ mapping.

We apologize for any confusion in this regard but would like to direct the reviewer to the methods section of our text. Specifically T2 and T1ρ are mapping sequences that analyze different relaxation times following specific MRI pulse sequences. We have gone into great detail in the methods describing the specific sequences. Please see below: T2 mapping: 2D turbo spin-echo; TR/TE = 2700/13, 26, 39, 52, 65, 78, 91 milliseconds, NEX = 1 and total acquisition time = 13 minutes 26 seconds. T1ρ: 3D FS PROSET (Principle of Selective Excitation Technique); TR/TE = 6.4/3.4 milliseconds, flip angle = 10°, echo train length = 64, NEX = 1, spin-lock frequency = 575 Hertz, time of spin-lock (TSL), 20, 40, 60, and 80 milliseconds, and acquisition time = 4 minutes 9 seconds × 4.

2. Could the authors add immunohistochemical study with type II collagen?

This is an excellent suggestion and would add greatly to the manuscript. However, TII stains were not initially collected and while stained samples are retained, virgin samples are not available to re-analysis at this time. We believe however that analyzing the type II collagen could provide valuable information to future works that build off of our findings here.

III - With Regards to specific requirements, please see that each of the files below has been included unless otherwise noted:

1 30613-Revised manuscript

2 30613-Answering reviewers

3 30613-Copyright assignment

4 30613-Scientific research process

5 30613-Audio core tip

6 30613-Institutional review board statement

7 30613-Informed consent statement

8 30613-Biostatistics statement

9 30613-Conflict-of-interest statement

10 30613-Data sharing statement

11 30613-Google Scholar

12 30613-Grant application form(s)

13 30613-Language certificate – *All writing of the manuscript was completed by a native English speaker (RS, BSK)*