Author’s response to reviews

Title: Mild (not severe) disc degeneration is implicated in the progression of bilateral L5 spondylolysis to spondylolisthesis

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08 March 2018

Assistant Professor Kang Li
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Dear Dr. Li:

On behalf of all my co-authors, I would like to submit the revised version of our manuscript entitled “Mild (not severe) disc degeneration is implicated in the progression of bilateral L5 spondylolysis to spondylolisthesis” that we hope you will consider for publication in the BMC Musculoskeletal Disorders.
Below, please find our point-wise response to the issues raised by the reviewers on our last submission.

I can confirm that: there are no potential competing interests related to this work, all the co-authors have read and approved this version of the manuscript, the manuscript has not been published or submitted for publication elsewhere.

We would like to sincerely thank you and the two reviewers for their prompt and constructive feedback on this manuscript. We look forward to hearing from you soon.

Sincerely yours,

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Response to the Reviewer's comments on “Mild (not severe) disc degeneration is implicated in the progression of bilateral L5 spondylolysis to spondylolisthesis”

Xiaoju Zhang: Reviewer 1
This is an interesting computational simulation study to investigate the causation of Spondylolytic (or lytic) spondylolisthesis with disc degeneration. In general, the findings of the study bear clinical interests. The experiment of this study is well designed, and the methods are clearly described.

Response: We would like to thank the reviewer for their encouraging feedback on our manuscript.

1. However, the results can be presented with more details. Since five different spondylolytic models were constructed, it would be more informative if the results are reported for all models, instead of only reporting M-DEG LYRIC model for several cases, such as Range of Motion (RoM) and Interpedicular Kinematics.

Response: We believe that reporting the data for range of motion (RoM) and interpedicular kinematics (IPT) in the text would be redundant in this case, given that data are already available (and easily distinguishable) in Figure 2 (RoM) and Figure 3 (IPT) already.

2. Line 180 to 181. "(Fx: 7.2˚ to 12.4˚; Ex: 7.0˚ to 9.5˚)." The two numbers reported for Fx/Ex are ambiguous. Do they mean changed "from 7.2 to 12.4" or the change values are in the range of "minimum 7.2 to maximum 12.4"? For both cases, is statistical summary available, as the results shown in Table 2?

Line 190. Same as above.

Response: We would like to clarify that the reported numbers “(Fx: 7.2˚ to 12.4˚; Ex: 7.0˚ to 9.5˚)” refer to the change between the intact and mildly degenerate states in both cases the reviewer has referred to, as has been stated in the text prior. We have removed any ambiguity from the reported numbers with specific changes in lines 179, 188 and 189. Since there was only one FE model assembled to represent each degenerative condition of the L5-S1 disc, no statistical analysis could be performed on the kinematics results (n=1).
3. Line 209-212. May report standard deviation with the average numbers.

Response: Standard deviations have now been included with the average normal (lines 199-202) and shear stress (lines 208-211) data.

4. Fig 2, 3, 5, 7. The bars might need to have standard errors.

Response: Since there was one FE model assembled to represent each degenerative condition of the L5-S1 disc, only one data point for the average value for each model could be extracted. Therefore, the standard error was same as the standard deviation (n=1).

Svante Berg: Reviewer 2

A well performed and ambitious study that I think is well worth getting published. I think what is shown in this study is how disc degeneration, especially mild, can add mechanical weakening of a segment, thus no longer resisting the forces that are directed into slipping. I do have some concerns on the conclusions, especially as written in the abstract. This study clarifies the possible mechanism of how a segment with lysis develop to a slipped stage. However, it does not answer the question on whether lysis in itself induce the disc degeneration. The findings in ref 11 does just report a higher frequency of disc degeneration in patients with lysis. Maybe the same defects, genetically or of other origins induce both? Probable, but not shown. More than half of adult patients searching care with symptomatic spondylolisthesis also have some disc degeneration in adjacent segment. In section 2 of the discussion part, it is written that bony defect caused the disc degeneration. I my mind this is not proven in this study or referred articles. I would propose some alterations in the conclusions and discussion parts, this study give valuable results in its own, why speculations is not necessary.

Response: We would like to thank the reviewer for their inputs and review of the manuscript. We accept that there was some ambiguity in the Discussion and Conclusion sections regarding the natural history of isthmic spondylolisthesis. The results of this study do not provide any insights
into the natural history of isthmic spondylolisthesis. The main objective of this study was to examine the cause-and-effect relationship between different grades of disc degeneration and the progression of a L5-lytic defect to spondylolisthesis. We have now clearly stated that these results only suggest one of the many plausible restabilisation mechanism (disc height collapse) available to the L5-S1 segment in order to mitigate segmental instability due to a bilateral L5 lytic defect (lines 51,52,302,303).