Reviewer's report

Title: Chitosan in viscosupplementation: in vivo effect on rabbit subchondral bone

Version: 0 Date: 18 Apr 2017

Reviewer: Teja Guda

Reviewer's report:

The authors conducted an interesting study to develop and evaluate the subchondral bone loss associated with ACL transection by viscosupplementation using either HA or the HA+Cs. The study is well characterized and the details allow easy future reproduction. Some concerns were noted in review:

Major concerns:

1. Why were non-parametric tests (Kruskal-Wallis and the MWW rank test) used instead of parametric tests? What was the power of the tests? Was this because of the data not being normally distributed, or because of the groups having non-uniform standard deviations.

2. Why were only 4 non-operated knees (per group) used as contralateral controls? The normalization of the treated groups to the contralateral groups would enable the inter-animal variation to be removed and hence increase the power as well as potentially enable the use of parametric tests. Was the contralateral group data normally distributed - more crucially, was there ANY statistical significance between the HA-group contralateral samples compared to the Hybrid group contralateral samples? More crucially, how were the 4 samples per group chosen (or 2 samples excluded)? I would recommend including all 6 animals in each group.

3. The progression of OA is relative and the validity of the rabbit model in terms of cartilage and subchondral healing in the rabbit has been debated widely in literature. While the results of this study are interesting, a major drawback is that only one time point is used. How are the authors confident that this is a progressive deterioration?
Minor concerns:

1. Acronyms "DMOAD" and "SYSADOA" are introduced in the introduction, but never used in the manuscript. Introducing the terminology is necessary; the acronyms themselves are unnecessary and should be removed from the introduction.

2. The introduction should end with a one sentence purpose - such as what would be indicated if the hypothesis did proved true ("indicating that the supplementation showed OA progression in the preclinical model", etc)

3. The sentence "In order to go one step further in the evaluation of the effect of Cs on subchondral bone, the impact of bone microarchitectural parameters on the mechanical compliance will be evaluated as well as the relationship of this last on the cartilage integrity." is not appropriate for the conclusion - maybe better at the end of the discussion section.

4. Please edit language for sentence phrasing to facilitate easier readability.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics
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Needs some language corrections before being published

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