Reviewer's report

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

Version: 1 Date: 17 Jun 2017

Reviewer: Stephan Zeiter

Reviewer's report:

Thank you for the revised manuscript.

Most of the concerns raised by the reviewers were addressed. Especially the inclusion of the saline only group strengthens the paper.

The only point which is not yet solved is the contralateral controls. In their answer the authors first basically rise the valid concerns that the outcome/ changes observed in the contralateral group is also dependent on the efficacy of the treatment applied. Wouldn’t with this rationale the "right" comparison be the one to the knee of an unoperated animal (same age/ weight/ gender)?

On the other hand the authors "solve" the raised issue themselves by stating that there was no difference between the contralateral knees among the groups suggesting that all knee were analysed. Based on these results they decided to randomly choose legs from all groups to avoid group’s size discrepancies. In the reviewer’s opinion this is appropriate if the "random" group is not different to the contralateral legs of each group since by random selection a bias could have been introduced. Further, these information on the analysis of the contralateral knee among groups and the rationale to choose a random selection out of them has to be added to the manuscript prior to publication.

The reference to the histological analysis/ images should be added to the manuscript.

While reading the revised manuscript another discussion point raised: it is recommended to give the Ostenil for three to five weeks so that it has its appropriate effect. One rationale of the Hybrid HA is to avoid this repeated injections. Therefore, the authors investigate the effect of a single administration of both HA and HA Hybrid in this study and demonstrate that the subchondral bone changes are more pronounced in the HA Hybrid group. The question is now what would be the effect of repeated injections of HA (as recommended) on the subchondral bone? Would the changes in the subchondral bone be more pronounced and similar to HA Hybrid - this may be an interesting point which might be considered for the discussion.
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?
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Yes

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I am able to assess the statistics

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