Reviewer’s report

Title: Topical Zoledronic Acid decreases Micromotion induced Bone Resorption in a Sheep Arthroplasty Model

Version: 1 Date: 25 Aug 2017

Reviewer: Bettina Willie

Reviewer's report:

The authors aim at investigating in a sheep model whether local treatment with zolendronate would reduce the bone resorption and fibrous tissue formation around implants subjected to micromotion.

The strengths of the study are 1) the experimental model is well established and is clinically relevant, 2) the sample size of 10 sheep and paired design using an internal contralateral control removes biological individual differences. The weaknesses are related to the lack of more in-depth characterization and study of the underlying molecular mechanisms. For example, the inclusion of microCT analysis to quantify periprosthetic bone, backscattered electron imaging analysis to quantify the bone apposition & periprosthetic bone, and fluorochrome labeling/histomorphometric analysis to examine mineral apposition rates would have enhanced the characterization. Although the focus of the study is on resorption, examining formation would have provided additional insights into how bone remodeling dynamics are affected by treatment and micromotion. However, despite these weaknesses this study provides novel data in a large animal model that will inform the readership regarding the use of local bisphosphonates to improve implant stability.

Minor comments:

Abstract

Page 2, Line 7: Add here "and fibrous tissue" to the aim so it is consistent throughout the manuscript.

Background

Page 3, Line 9: Please reference here and mention in Discussion the recent work by Dr. Fahlgren that is addressing the molecular mechanism(s).


Methods:

Page 7 line 2: Why were log-transformations performed to make data normally distributed? Why not analyze data using non-parametric analyses?

Results:

Page 7, Line 13: -Typo "thick fibrous membrane"

Discussion:

Page 9, Line 19: Awkward sentence please rework.

Page 10, line 2 Typo "too strong stimulus"


**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 recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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