Reviewer's report

Title: A role for subchondral bone changes in the process of osteoarthritis: a micro-CT study of two canine models.

Version: 1 Date: 19 October 2007

Reviewer: David Holdsworth

Reviewer's report:

Reviewer’s report: “A role for subchondral bone changes in the process of osteoarthritis: a micro-CT study of two canine models,” Sniekers et al.

Summary:

This Research Article describes an investigation of subchondral bone changes in two canine models of OA. Micro-CT and histology are used to investigate bone architecture and cartilage histology. Significant differences are observed between the “groove” and “ACLX” models in the dog.

This paper addresses an important topic; the questions posed are novel and quite well-defined. The methods are sound, and (with a minor exception related to the details of the CT experiments) sufficient details are provided so that others could replicate the study. The discussion and conclusions are well-balanced. The title and abstract are appropriate.

The paper is very well written, with a succinct style and few errors. I am happy to recommend publication, with only a few revisions, as described below.

Major Compulsory Revisions:

1/ The only revision I would like to see is quite straightforward, related to the description of the micro-CT acquisition and analysis on pages 8 and 9. It would be helpful to have more details about the micro-CT acquisition parameters, so that this study could be replicated by others. Important parameters include the kVp, the mA, the exposure time, and the number of views. In addition, it would probably be more accurate to say that the scan was acquired “with isotropic voxel spacing of 18 µm,” rather than refer to spatial resolution (unless spatial resolution has been measured independently).

Minor Essential Revisions:

1/ Background, page 4, paragraph 3: The point about previous animal models showing either increase or decrease in subchondral bone is important. It is possible that, in some cases, the confusion may result from the time at which the bone density was measured. This was certainly the case in the rabbit ACLX model studied by Battiste et al., where the subchondral density fell to a minimum at 8 weeks post-surgery, and then rose again at 12 weeks. Is it possible for the authors to elaborate a bit on this point, with respect to previous studies? The
timing of the observation of BMD could be very important in an animal OA model.

2/ With respect to the data analysis (page 10), could the authors provide some additional clarification? Why was a non-parametric test used? Did the data fail the test for normality, or was it just because of the small sample size? Why change from one-sided test to two-sided test for cartilage and bone, respectively? Note that I am not disputing the correctness of the decisions, but it might help the reader to clarify why these choices were made.

3/ Related to the discussion, page 15, second paragraph: The finding that “Since the subchondral bone changes in the tibia cannot be caused directly by the grooves, we believe that these changes are part of the osteoarthritic process” is interesting and potentially significant. Can the authors provide any speculation about how this can come about, mechanistically? Could it be due to a change in joint loading? Changes in the local environment of the synovial fluid? If there is any likely explanation for this observation, it could be included here.

Discretionary Revisions:

1/ Abstract; page 2: Consider replacing “… and architecture of subchondral plate” with “… and architecture of the subchondral plate”

2/ page 9, third last line: change “… of which bone volume was calculated…” to “… of which bone volume fraction was calculated…”

3/ page 14, last line: add a period (full stop) to this sentence.

4/ page 16, end of first paragraph: with respect to the location of osteophytes, it may be useful to compare the findings in this paper with those of Batiste in a rabbit ACLX model, also studied with micro-CT.

5/ related to Figure 3: It is difficult to follow the anatomical orientation of the sections presented here. Perhaps some additional labels could be included, to clarify the orientation within the animal? Otherwise, an accompanying “cartoon” could be used to show the orientation of the sections.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.