Reviewer's report

Title: Quantification of Bone Marrow Lesion Volume and Volume Change Using Semi-automated Segmentation: Data from the Osteoarthritis Initiative

Version: 3 Date: 6 November 2012

Reviewer: Daichi Hayashi

Reviewer's report:

Major Compulsory Revisions:

1. In the Background section, authors cited a study by Tanamas et al (ref 2, Rheumatology Oxford 2010), but this study has a significant shortcoming in the methodology regarding BML assessment using MRI. Basically, the authors used T1-weighted fat-suppressed 3D gradient echo-type sequence, which is known to be inadequate. Correct pulse sequences should always be used for reliable BML assessment on MRI. Thus, the reference 2 should be deleted. Instead, authors can cite a much more important publication describing the relationship between BML and pain in OA and their fluctuation: Zhang Y et al. Arthritis Rheum 2011;63:691-9.

2. The same methodological flaw is evident in reference 5 (Raynauld JP et al. ARD 2008). This citation should also be deleted from the manuscript. The authors of the submitted manuscript did use the correct pulse sequence for the present study, so it is surprising to see that they are citing two studies that have significant methodological flaws.

3. In Discussion, page 12, second paragraph, authors cite reference 5 again to support their discussion. However, as I noted earlier, this reference should not be cited because it will not support the authors’ claim in a scientifically meaningful manner. Please cite alternative publication instead of ref. 5.

Minor Essential Revisions:

Abstract:

4. In the Methods section, please state what statistical method was used to derived z and p values described in the Results section. Was p<0.05 considered statistically significant?

5. Please concisely state in the Methods section how the proposed ‘new’ segmentation method is different from pre-existing one.

6. In the results section, please state how many BMLs were identified/involved in each study.

Background:

7. While the reference 7 (Peterfy CG, et al. OAC 2004) does indeed mention the appropriate choice of pulse sequences for semiquantitative assessment of various OA features, it is not specific to bone marrow lesions. Perhaps it would
be better that the citation of ref 7 (page 3, last line) be replaced by a more specifically BML-oriented imaging paper, such as: Xu L, et al. Semin Arthritis Rheum 2012;42:105-18.

Methods:

8. In page 8, the first paragraph of "Study 1" section, authors state: "We selected 80 right knees with ..........and had acceptable quality fixed-flexion knee radiograph and MR imaging sequences (identified as read project 4 in kmri_qcart_ecksteinXX [version 0.4 and 3.3])." This last part, "identified as read project 4 in kmri_qcart_ecksteinXX" does not mean anything to readers who are unfamiliar with specific terminology used by Dr. Eckstein's research group. Please cite appropriate reference(s) so that it can be understood by general readers who are (mostly) not an expert of quantitative cartilage morphometry.

9. Please explain why authors selected to use BLOKS as the semiquantitative scoring method of their choice. Why not other scoring systems that are available in the literature?

10. The selection criteria/exclusion criteria should be concisely presented in a flow-chart, which would greatly help readers of this paper. Please use a flow chart to explain how the authors narrowed down their sample from a vast collection of OAI database.

Results:

11. I suggest authors include a table which summarizes the results of pertinent statistical analyses. It is easier to see them in a table, rather than reading through the text only.

Conclusion:

12. Authors state that "this new method will enable researchers to assess larger MR data sets in a time efficient and cost effective manner." However, authors did not present any data regarding the cost in this paper. Thus, this statement is not supported by the evidence and should be modified accordingly.

Figures:

13. Figure 1: Each figure parts should be cropped so that the region of interest can be magnified. Authors should crop the upper and lower parts (proximal femur and distal tibia), as well as left and right margins of the images (black space and fat in front of patella, and fat behind the posterior compartment).

14. Figure 2: Within this figure, authors wrote "Distribution of v00vol by tib". This is a specific terminology for their analysis, and is not universally understood by general readers. Please replace this notion by a more generally understandable term.

Level of interest: An article whose findings are important to those with closely related research interests
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 I have no competing interests.