Reviewer’s report

Title: The Utility of Multi-Stack Alignment and 3D Longitudinal Image Registration to Assess Bone Remodeling in Rheumatoid Arthritis Patients from Second Generation HR-pQCT Scans

Version: 0 Date: 05 Jan 2020

Reviewer: Ko Chiba

Reviewer's report:

The authors developed a correction method for stack shift artifact and a voxel based evaluation method for bone remodeling in the imaging analysis of RA using HR-pQCT. These are very important and interesting techniques. However, there are several points that should be corrected.

(1) Success rate

The authors investigated 20 joints, but bone remodeling analysis was performed in only 9 joints (45%). This is one of the big limitations of this technique. The authors should mention it (success rate) clearly in the limitation paragraph.

Also, in lines 251-253, you state that "six joints did not meet our motion scoring criteria for quantitative assessment." What is this criteria?

(2) Reliability of bone remodeling analysis

The right image in Fig.4 shows a tendency for the upper side of the cortical bone to have a linear bone formation area; on the other hand, the lower side has a linear bone resorption area. This is a little bit strange. Were these images correctly matched?

(3) Scan length

Do three stacks of scans with 25% overlap mean that it was scanned at 25 mm? This should be clarified in the manuscript.

(4) Fig. 2 &amp; 4
Please use different colors since the combination of red and green is not recommended in scientific papers.

https://www.nature.com/articles/510340e

(5) Supplementary material
The supplementary material does not contain data for 20 joints.

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.

Unable to assess

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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Please indicate the quality of language in the manuscript:

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