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: 09 Feb 2020

Reviewer: Ali Ghasem-Zadeh

Reviewer's report:

Brunet et al. have tried to elevate one of the important technical challenges of HR-pQCT when multi-stack scanning is required to cover larger scanning ROI. In addition to stack-shift correction, image-based bone remodelling assessment have provided an excellent opportunity to illustrate the bone resorption and formation regions, however, the accuracy of resorbed or new-formed bone regions would be challenging due to fix-threshold based assessment.

The question is, if there is a fluctuation on x-ray tube or detector functioning for 1st scan and 2nd scan(for example, after 6 month) how do you rule out the effect of x-ray flux changes on images and assessment of bone resorption or formation?

Please provide some information about the accuracy this procedure, alternatively may you can use the QC1 phantom rods or cadaveric bone to see the magnitude of error for this assessment.

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.

Not relevant to this manuscript

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

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