Reviewer's report

Title: Improving the prediction of the trabecular bone microarchitectural parameters using dental cone-beam computed tomography

Version: 1 Date: 30 Aug 2018

Reviewer: Ruben Pauwels

Reviewer's report:

I strongly suggest that the authors provide a point-by-point response to the reviewers' comments, and clearly highlight the changes made to the manuscript in accordance with these comments.

As such a response was not available at this stage, the following comments are the result of an independent assessment (i.e. not a follow-up of any comments that may have been made previously).

GENERAL COMMENTS
- The topic is of interest, as the processing of images for microstructure analysis is essential (esp. in noisy, unsharp CBCT images) and often overlooked
- The sample size is relatively large compared with similar studies, resulting in high statistical power
- Only a single CBCT unit and exposure setting was used, but this is a common limitation.

SPECIFIC COMMENTS
- A single ball still allows for multiple degrees of freedom. For marker-based registration, at least 3 balls would be needed. For automatic registration, a marker would not be needed
- Please mention the exposure time that was used
- The scan conditions were far from realistic. Not only is the SNR at the detector much higher for such a small bone sample than an actual patient, the scan was quasi scatter-free and without beam hardening or motion. For every factor except the last one, the set-up can be adjusting by placing the sample in a head-equivalent phantom or container. The statement in discussion that "Some studies have indicated no significant differences between dental CBCT imaging settings with water and the settings without water [24]." is not entirely valid, because the study (not studies) in question notices a large difference in SNR between protocols, and rather considerable effects of water on BS and connectivity. Finally, the study does not mention the size of the water container.
- The registration of the images should be explained in detail. ImageJ does not have a built-in automatic registration tool. Was a third-party plugin used? Was manual setup or adjustment needed? Which registration metric was used (e.g. mutual information)? Etc
- It is somewhat unclear why a ROI was used rather than the entire sample. The latter option would avoid the need for registration altogether because the measured parameters should be independent from the sample orientation
- Sharpening and despecking/denoising are general terms. Please mention exactly the types of
convolutions or other processing steps applied in Group 2
- Please add more details regarding the radius/area used for local thresholding in Group 3
- There are 15-20 types of automatic thresholding, which was used for each group?
- The rationale and clinical applicability of Group 4 is somewhat questionable. The BMD scale is not intended to differentiate air as being BMD<0. Furthermore, the use of an appropriate thresholding method would imply that the specific removal of air voxels is unnecessary. From the figure, it is clear that this method results in approx. half of the histogram to be cut off, and the threshold to be slightly above this cut-off point. Would a global thresholding with the same cut-off value not yield the exact same result? Would an erosion (or multiple erosion steps) yield the same or a similar result without the need for a BMD phantom (which cannot be routinely used in clinical CBCT due to the small FOV)? Perhaps Group 5 can be added by including a few erosion steps (determined empirically) after binarisation
- Only a few structural parameters were used. In literature, others such as BS/TV, fractal dimension, and connectivity density are often reported as well
- It is not entirely reasonable to compare microCT and CBCT values directly; due to the large difference in resolution, one can not expect a 1:1 agreement between structural parameter values. I suggest to report the values as such (without t-test) and focus on correlation as your main outcome
- Table 3 seems to omit several studies; furthermore, the purpose of this table within the scope of this study is somewhat unclear. I suggest removing it or making it a supplementary file

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Unable to assess

**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 am able to assess the statistics
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Please indicate the quality of language in the manuscript:

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