Author’s response to reviews

Title: Simulated Increased Soft Tissue Thickness Artefactually Decreases Trabecular Bone Score: A Phantom Study

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Responses to Reviewers

We are grateful to the reviewers for their constructive and relevant inputs, which, we believe, have much improved our manuscript. Our responses to the comments are presented in a point-by-point basis as shown below. The changes to the manuscript are indicated in the text by highlighting.

Reviewer #1: Review of BMSD-D-15-00346

This is an interesting paper but I have some comments and questions for the authors:

1- Abstract: consider revising the Conclusion to also mention the effect of soft tissue thickness in BMD.

Response

The abstract is revised as shown below.

However, these changes did not exceed the least significant change (LSC) derived from patients.
Conclusions Increased soft tissue thickness results in lower TBS value. Although BMD is also affected, it is unlikely to pose a clinical problem because the change is unlikely to exceed the patient-derived LSC.

2- Background: In some paragraphs the authors confuse fractures with the 'fracture risk'. I.e.: "Since BMD is not a perfect indicator of fracture,…"

Response

The background is revised as shown below.

Although BMD identifies many individuals at risk of fracture, a large degree of overlap exist in BMD values between individuals who develop fractures and those who do not [1]. Since BMD does not capture all of the aspect of fracture risk, trabecular bone score (TBS) has been proposed to improve the assessment [2].

References in this section


3- Background: The sentence "The higher the variation, the higher the TBS" should be corrected.

Response

The sentence is revised as shown below.

High variation among the pixels results in high TBS value.

4- Background: I would like the authors explain why, if TBS in negatively associated with BMI, soft tissue underestimates TBS.

Response

The background is revised as shown below.
However, subjects with high BMI are likely to have thicker soft tissue. Soft tissue could act like a blurring filter, which diminishes clarity of the DXA image. The variations among the image pixels could be more difficult to detect, resulting in underestimation of TBS.

5- Methods: The authors may explain why the array mode of the Hologic system is not considered and why GE-Lunar iDXA is considered if there isn't a control phantom for iDXA.

Response

The explanation was added as shown below.

Since the array mode took longer time (75 seconds) than the fast array mode (40 seconds), the latter was used in our routine clinical practice. However, we were interested in comparing it with the high definition mode, which was supposed to give the best image quality despite the fact that it took the longest time (145 seconds). Because we also used an iDXA system (GE/Lunar, Madison, WI) in our routine work, it was of our interest to explore the effect of soft tissue on the derived TBS. However, the Hologic phantom was also used with the iDXA system because the TBS image of the iDXA phantom did not resemble that of a human lumbar spine [14].

Reference in this section


6- Results: When the mean differences in BMD and TBS of the phantom (soft tissue 0 cm) are analyzed I would like that the authors shown a comparison between Hfa and Hhd models only.

Response

The comparison between Hfa and Hhd in terms of TBS and BMD are shown below using t-test.

TBS analysis

The Stata output of the TBS comparison between Hfa and Hhd is shown below (Please see Image 1 at the end of the cover letter).

Description of variable are as follows:

- h_tl14: Hfa TBS
- hd_tl14: Hhd TBS

Image 1 Stata output for Hfa and Hhd TBS comparison

From the Stata output (Image 1), the 2-sided t-test (in the red textbox) gives p values < 0.001, indicating statistically significant difference in mean TBS between Hfa and Hhd.

BMD analysis

The Stata output of the BMD comparison between Hfa and Hhd is shown below (Please see Image 2 at the end of the cover letter).

Description of variable are as follows:

- h_bl14: Hfa BMD
- hd_bl14: Hhd BMD

Image 2 Stata output for Hfa and Hhd BMD comparison

From the Stata output (Image 2), the 2-sided t-test (in the red textbox) gives p values < 0.001, indicating statistically significant difference in mean BMD between Hfa and Hhd.

7- Discussion: I agree that the authors provide an explanation why soft tissue is negatively associated with BMD in the Hfa and Hhd models but no in iDXA but in TBS soft tissue is negatively associated in three models.

Response

The discussion part was revised as shown below:

Our study on a phantom showed that increased soft tissue thickness significantly decreased TBS, regardless of the mode of acquisition or of the DXA system used, be it Hfa, Hhd, or iDXA. This finding suggests that some, if not all, of an apparent decrease in TBS with increasing weight is artefactual and does not reflect actual decreases in bone quality with increasing BMI. For any acquisition mode or DXA system, the DXA image became fuzzier with increased soft tissue thickness (Figure 3). The soft tissue seemed to act as noise or a blurring filter. As a result, there was less variations among the image pixels; therefore, lower TBS value. This was in keeping with a review by Bousson et al [14] that adding noise tended to lower the TBS values.

Reference

8- Discussion: In Limitations the authors explain that soft tissue could not be directly translated into the amount of weight or BMI gain. Perhaps the authors should correct the sentence "First, for a given bone quality, subjects with higher BMI are likely to have lower TBS. Secondly, TBS could appear to be decreased in subjects who gain weight during a course of follow-up"

Response

This part has been revised accordingly as shown below.

First, for a given bone quality, subjects with thicker soft tissue (as probably seen with subjects with higher BMI) are likely to have lower TBS. Secondly, TBS could appear to be decreased in subjects who gain soft tissue thickness (such as those who gain weight) during a course of follow-up. Those who develop ascites could possibly suffer the same effect.

Reviewer #3

Reviewer #3: The authors describe the results of effects of increased soft tissue in the abdominal region on the measurements of image texture parameter TBS in a simple "in vitro" experiment.

The description of the method is adequate and the results and limitations of the experiment are also well described. However, and this is not obstacle for the recommendations to be published this study, it would have been of interest that the experiment could be completed with the use of different materials that allow recognizing the impact of different fat-free mass and fat mass quantities and proportions. In this sense, the increase in fat-free mass can occur in clinical cases in which there is intra-abdominal fluid (ascites), or in cases of major abdominal fat accumulation (visceral or subcutaneous) in overweight or obese cases. So that could warn if the "noise" caused by the higher amount of soft tissue hits differently, according to the change of composition of tissues.

Response

Thank you so much for taking the trouble to review this manuscript. I am grateful for your kind comments and relevant inputs. I took the liberty of adding your comments into the manuscript as shown below.

First, for a given bone quality, subjects with thicker soft tissue (as probably seen with subjects with higher BMI) are likely to have lower TBS. Secondly, TBS could appear to be decreased in subjects who gain soft tissue thickness (such as those who gain weight) during a course of follow-up. Those who develop ascites could possibly suffer the same effect.