Reviewer’s report

Title: MRI texture analysis in differentiating luminal A and luminal B breast cancer molecular subtypes - a feasibility study

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Reviewer: Pål Erik Goa

Reviewer's report:

There is an increasing number of studies on the use of texture analysis in cancer imaging. This current study is looking specifically into the potential of using texture features from pre-contrast T1-weighted MRI to differentiate between luminal A and luminal B molecular subtypes of breast cancer. The results are interesting and adding to the growing evidence that quantitative texture analysis of MRI data provides information that can be useful in the management of breast cancer. However, before publication there are a number of issues that should be addressed, as detailed below.

Major comments:

1. The focus of the paper is unclear in terms of the data analysed. On one hand the authors state that they focus on pre-contrast T1-weighted MRI images, on the other hand they also include post-contrast images in the analysis for comparison, but without providing the reader sufficient information in order to assess these results properly. Either the post-contrast results must be removed completely, which I think would reduce the interest of the paper, or this part should be included, compared and discussed properly.

2. The whole manuscript seems to have been prepared somewhat in haste. For example there are a number of inaccuracies and ambiguities in the text (some detailed out below). Please revise the manuscript carefully.

3. The discussion should be revised. Please remove the parts that simply repeat or re-iterate statements from the results section. I miss a comparison of the types of texture features that have shown to be significant in different existing studies. Also, the importance of using pre-contrast as opposed to post-contrast images should be even more clearly stated and discussed. Is it even relevant to compare texture features from those two different sets of images, especially if subtraction images are being used for the post-contrast? Finally, there is no discussion on the statistical significance and effect of multiple comparisons.
4. In an explorative study like this, it would be natural to include also the T2-weighted images for texture analysis. It would be very interesting to see whether T2-weighted images contain the same or different texture information than the T1-weighted images.

Detailed comments:

1. Definition of luminal B. In the abstract it is stated that for luminal B the HER2 status can be both positive or negative, while in section 2.1 (p 5 lines 45-47) it says only HER2 negative.

2. It is not clear how the 27 patients were chosen among the 50 original ones. Were all the 23 excluded patients excluded due to the stated reasons (lesion size or MRI artefacts), or did you also exclude some patients based on subtype (not luminal-like for example). Please clarify the text. in section 2.1. Please state clearly the exclusion criteria and number of patients excluded for the different reasons.

3. In the abstract it is stated that the T1-weighted images are fat-suppressed, while in figure 1 it is clear that no fat-suppression has been applied. Please correct the abstract and section 2.3, p7 lines 5-7.

4. Important information about the MRI acquisition protocol is missing in section 2.3. Please add information about flip angle, slice thickness, number of slices, volume repetition time. Also, since the ROI size is fixed to a circle of radius 5 image voxels, the voxel dimension in the images should be stated clearly.

5. It is not stated whether raw or subtracted post-contrast images are used (p 7 .lines 32), also not whether all time points are used or not.

6. Is grey level normalization performed using the whole image as input to determine sigma and rho, or only the voxels within the ROI?

7. Please remove Figure 1 legend on page 8.

8. "not strongly correlated" on p 9 line 20 is not a clear statement. Please state your threshold used for definition of "strong correlation" and provide the measured correlation values.

9. Please consider last sentence in section 2.5

10. Table 2. Please remove abbreviations in the table and write terms fully out. There seems to be no good reason for using abbreviations.

11. p 10, lines 33 and p 11 lines 26. Again correlation results are referred to without any data given to assist the reader. Please add the actual correlation values in the text or in a new table.
12. Figure legend on p 10 is misnumbered (only two figures in the paper) and should be removed from the body text.

13. Statistical significant threshold is stated differently (0.05 in the text (p 9 line 29), 0.005 in the tables).

14. P 11 lines 48. "The theory is ...". Please revise and provide references.

15. P 13 lines 50-51. The statement in the first sentence must be explained. Do you draw this conclusion from your own study? How? Please clarify.

16. Please add a few example ROI from different lesions together with the texture feature scores for each of them to exemplify for the reader the link between visual appearance and texture feature scores. There is a lot of effort in the paper to describe in words this link, but some example of low and high scores would be helpful.

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

No

**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.

No

**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 recommend additional statistical review

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