Reviewer’s report

Title: Radiomic features from MRI distinguish myxomas from myxofibrosarcomas

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Reviewer: I-M. Noebauer-Huhmann

Reviewer’s report:

In this single-center, retrospective case-control study, radiomic parameters and conventional MR imaging features of 27 patients with myxofibrosarcomas are compared with those of 29 patients with myxomas.

The topic is clinically important, as myxofibrosarcomas are often considerably heterogeneous, and biopsy specimen may not contain the most representative areas. The study is very interesting, as the use of radiomic parameters is evolving, may revolutionize MR interpretation, and has hardly been investigated in soft tissue tumors so far.

Specific comments:

1) The title is adequate.

2) Abstract:

- The text is clear.

- I very much agree to the first parts of the conclusion. The last part ("Radiomic texture features best differentiate myxofibrosarcomas from myxomas using T1-weighted sequences...") does not completely follow from what has been tested; T2w sequences and T1w sequences post contrast agent administration or others could not be investigated in comparison to T1w sequences.

3) Keywords:

Keywords should be added.

4) Approval:

Institutional review board approval and HIPAA compliance: approved/compliant.

5) Introduction:

- In the very nice article of Kaya et al. Skeletal Radiol. 2008; 37(12):1085-90, dealing with the growth pattern of myxofibrosarcoma, MFS is described as "hypointense", but in fact is almost isointense to skeletal muscle in their fig 1 (in their figure 3, the legend might be slightly mixed); so the reference is correct. Otherwise, you could use the reference of Petscavage-Thomas RadioGraphics 2014; 34:964-980 (wonderful article, however a review).

- Page 11, line 220: do you mean fluid sensitive fat saturated sequences? If so, please replace "T2/STIR" by "T2w FS/STIR"; otherwise, differentiation of muscle with fatty atrophy may be an issue.

6) Materials and Methods:

- The total number of patients is impressive for this entity.

- As the authors mention correctly in the discussion, the main limitation of the study is the non-uniform pre-treatment MRI technique, with inconsistent use of T2w sequences. Also, the T1w contrast may vary with different field strength and sequence parameters. Please mention that the T1 contrast was comparable, or could be used, as the contrast vs. muscle was similar (I personally have got no experience with a field strength of 0.6T) if applicable.

- Histopathology: one of the criteria for the grading of MFS is the presence of necrosis. MFS Grade 1 and Grade 3 differ significantly (please also see discussion).

- Radiomics:

The radiomics approach of the paper is sound. The authors extracted radiomics features, and used a random forest classifier to classify tumors. They evaluated if this classification is better than more simple features such as volume, and use cross validation to separate training and test sets.

One comment regarding the feature importance: this is an interesting result of the paper. A possible added value would be to repeat this feature selection with random sub-samples of the data set to test up to which top ranked feature it is stable.

7) Results:

- It would be important to discriminate between solid tissue and necrosis. Were there differences in Normalized T1-weighted signal intensity between G1, G2, and G3? Presumably, the number of patients in each group would be too small for statistics, but it may be interesting to visualize
this result. This is also interesting for subtle differences in homogeneity measurements and the normalized T1-weighted signal intensity. Please comment.

- If you combined the information of volume measurement and T1w signal intensity, and calculated the AUC, would the results using radiomics features still be better than the combination of conventional parameters?

8) Discussion:

- The study is very interesting, and the results are novel.

It would have been interesting to correlate the T1 signal of different intralesional areas with the final histology within this area. The hypothesis of protein content and hemorrhage is interesting but a bit speculative; necrotic areas may have variable content. Please comment.

- In the discrimination of MFS and Myxoma by MRI, the AUC comparison of conventional MR features (please also see section "results") and radiomics it would have been desirable to include several crucial conventional MR parameters: T2w signal (without FS) and T1w post contrast series would have been helpful.

The study very nicely shows, however, that even in cases of incomplete or inconsistent preoperative MRI examinations, radiomics can help to predict whether a lesion is more likely to be myxoma or MFS (irrespective of the grade).

- Page 15, Line 314: the references of Kaya, of Murphey and of Abdelwahab do not really report the capability of T1w sequence to differentiate between benign and malignant myxoid tumors. Please replace by another reference.

- Page 15, Line 318: core biopsies should be image-guided, and MR sequences seem helpful for intralesional targeting also of MFS (we have seen that targeting is very accurate, and that inclusion of necrotic tissue in one of the samples may even add to the correct grade specifically in MFS (Eur Radiol 2015; 25:2041-204)).

- Page 16, Line 323: The sentence "We have shown that MRI image-derived radiomic features can quite accurately differentiate two extremely rare tumor types (myxomas and myxofibrosarcomas) which are challenging for pathologists and radiologists" represents the conclusion and could be moved there.

However, the present study represents an excellent radiomics feasibility study. An issue is the comparison of a selection of conventional MR parameters with radiomics. The conclusion could focus on the strength of the study, which is the novel method; radiomics may also be used to better use discriminatory information out of suboptimal MRI (e.g. from teleradiology…).
There are two studies on radiomics in soft tissue sarcoma which could be discussed: (1) Corino J Magn Reson Imaging 2018;47:829-840, and (2) Crombé J Magn Reson Imaging 2018.

9) References:

Some of the references mentioned above could be added. Otherwise, the references are adequate.

11) The text of the article is clear.

12) The nomenclature is correct.

13) Tables:

The tables are adequate

14) Figures/figure legends:

Fig.1 is very impressive and informative. Please submit it in higher resolution.

Fig. 2 please see above

Fig. 3 please see above.

**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.

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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