Reviewer's report

Title: Radiofrequency Ablation of Liver Lesions: Quantitative Assessment of Treatment Completeness through CT Image Processing.

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Reviewer: Christof M Sommer

Reviewer's report:

The submitted manuscript documents an experimental work designed to evaluate the RFA completeness of focal liver lesions applying numerical quantification after CT image registration and segmentation before and after treatment.

The study addresses an issue that is clinically very relevant. Overall readability and logical progression in the text are good.

My major points of criticism (from a radiological/oncological point of view) are:

1. basis of CT image processing are very thick slices (5mm), which are not used any more in our clinical routine. Although those images reduce image noise compared to thinner slices, partial volume effects are significant. Especially for the study described herein, with results in the sub dimensions of 1 mm (such as T.F.M.), this might be a major limitation. Moreover, important details of the CT scan (such as pitch, kVp and mAs) and of the image reconstruction (such as increment, kernel, window/level) are not given. The contrast protocol is old fashioned (no bolus triggering, instead fixed acquisition of the different CT phases). Additionally, it is not clear, which CT phases were analyzed (for HCC, the arterial phase might be optimal, for metastasis the venous phase).

2. the RFA technique is insufficient: antique needle designs and a weak generator (with a maximum power of only 50W) were used. Consequently, the relatively short ablation cycles (between 12-20min) in your relatively big liver lesions seem to be rather short.

3. the oncological success of your ablations is frustrating. Only 2/8 ablations had no residual tumor, and not a single one showed the intended safety margin of 1 cm. The reasons for this have to be evaluated in detail. Who selected the RFA cases analyzed in this study? Was it a negative selection of cases, and especially problematic RFA cases were included to emphasize the need and benefit of a complex registration/segmentation approach? What was the experience of the RFA operators? How many RFA cases are performed per year in your center? From a clinical point of view, it would be also very interesting to follow up the cases with incomplete tumor necrosis. Is it possible with your approach to predict the location of residual tumor/recurrence applying the given numeric quantifications? This would be a real benefit of your study with lasting clinical relevance. You should consider this in your revision.
4. please include the detailed times necessary to realize the different steps for CT image processing (such as pre-processing, clustering, etc.).

5. specific techniques (such Fuzzy-C-means approach, non-linear B-splines-based algorithm, Live-Wire algorithm, etc.) have to be explained in such a manner, that also non-familiar experts have the chance to understand the procedure and to follow the central theme.

6. P5, second paragraph: Once the ...
What are the different intensity patterns for necrosis and lesion – are they identical for HCC/metastasis in all cases? From my experience, it is sometimes extremely difficult to characterize a focal change in liver density as post-RFA lesion or as a tumor (not to mention as a HCC or as a metastasis). This point should be explained and discussed more detailed, inclusive of additional references.

7. the importance of the inter-barycentric distance:
How was the barycenter defined (or calculated)? It is quite obvious, that an inter-barycentric distance with the same magnitude order of the target lesion indicates insufficient positioning of the RFA lesion. However, can the authors give numerical data (e.g. an equation) for adequate and non-adequate inter-barycentric distances with respect to oncological success?

My minor points of criticism (from a radiological/oncological point of view) are:

1. P2, first paragraph: Image guided ...
Please point also out, that RFA is a curative alternative to surgery in circumscribed tumors <3cm.

2. P2, fifth paragraph: After validation ...
Point out the selection criteria (and expertise) for the RFA cases included in this study.

3. P2, sixth paragraph: The method ...
Please indicate also max. lesion diameters, not only volumes.

4. P3, fifth paragraph: For HCC ...
"11.5mm balloon" is unclear for me (please indicate diameter and length).

5. P4, first paragraph: image noise ...
What is a 5 x 5 median filter – please explain.

6. please use the same nomenclature throughout the entire manuscript: e.g. post-RFA necrosis and original liver lesion! (to minimize confusion).

7. P5, second paragraph: Liver clustering ...
Only one radiologist was involved? I would recommend to involve three
radiologists and compare also their results!

8. P7, second paragraph: necrosis: ...
   “classify them iteratively“ – unclear for me, please explain more detailed.

9. P8, third paragraph: The effect...
   I wished you had treated more healthy liver tissue in your patients. Then
   probably, also the tumors might have been destroyed completely! From the
   oncological point of view, in case of doubt, we should sacrifice healthy liver tissue
   to cover the tumor completely.

10. Results paragraph:
   Please include also the detailed CT image processing times.

11. P11, fourth paragraph: The inter-barycentric ...
   Who defined the critical range of 60-120 degrees for O.I.? Please explain the
   rational, or give a reference instead. We know RFA or microwave systems, which
   ablate in other configurations (non-elliptical). Please comment on this.

12. P15, first paragraph: Table 2 ...
   “Lesion volume range of 1.5-9.5cm3“ – I cannot reproduce those numbers in
   Table 2?? Please explain.

13. Table 2:
   Annotation: “post-RFA lesion – some people might misunderstand this measure
   as the volume of the necrosis, and not as the residual tumor volume.

14. P 17, second paragraph: There were ...
   “the short interaction time“ – you should not discuss an issue, which was not
   evaluated or indicated in the “results” or “materials and methods” section.

15. P 17, fourth paragraph: There are ...
   Which are “the vital anatomical structures“ in the context of malignant liver
   lesions? – I would be as aggressive as possible to destroy the tumor completely!
   You have also to decide prior to intervention, if you perform a curative or
   palliative RFA! Please clarify and discuss.

16. P 17, last paragraph: Besides, there ...
   The last sentence on the page is very interesting (“Thus, in this RFA ...“). Please
   indicate some references, and also in this context, the question of local
   recurrence or residual tumor is very interesting. Please implement the follow-up
   findings in your work.

In summary, the paper describes an interesting experiment based on an
important hypothesis. Language style is good. Presentation is good. The findings
are interesting and have potential clinical relevance.

From a radiological/oncological point of view, the study has some major
limitations (especially CT technique and reconstruction technique (which is the entire basis for image processing with registration and segmentation), RFA technique and the very bad oncological success rate). Therefore, it is unacceptable for me to recommend “manuscript acceptance”, also because people might get a completely wrong impression of the power of RFA in this manuscript/as presented in this manuscript.