Reviewer's report

**Title:** Automatic Segmentation of Meningioma from Non-Contrasted Brain MRI Integrating Fuzzy Clustering and Region Growing

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**Reviewer:** Kyrre Emblem

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Summary: In this study, the authors use an automatic fuzzy c-mean clustering technique for Meningioma segmentation from anatomical MR images and compare the method to manual and semi-automatic readings. In 29 patients, the results show diagnostic accuracy values in the range of 70-90%.

The paper addresses an issue of obvious clinical and methodological interest, i.e. reducing the user-dependence of tumor identification and delineation. However, while the authors should be acknowledged for using elegant tools for assessment of tumor regions, the manuscript in its current form has several methodological shortcomings as well as limitations in terms of structure and language. The main critique is related to reproducibility. As discussed below, based on limited descriptions, it is very hard for readers to reproduce or adapt the proposed technique.

Major Compulsory Revisions:

1. The first paragraph in the Introduction section can be removed. A more to-the-point focus on the current status of MR brain tumor segmentation and available manual and automatic methods may be in order. Is the proposed method a novel approach? Are there other techniques that may provide similar results? Other examples of fuzzy clustering in medical brain tumor imaging?

2. The manual reference method is not well described. How was the manual tumor reading performed? By whom? Using what criteria?

3. The authors state that T1-w post Gd images were used for the reference method, but not for the segmentation method. What was the rationale behind this? For comparison, shouldn’t the same images be used for both techniques? Contrast enhanced Meningiomas typically have a ‘dural tail’ – how was this accounted for in the reference and segmentation methods?

4. The MR imaging sequence parameters (TR, TE, matrix size, etc), magnetic field strenght, coil system and MR vendor need to be listed.

5. If edema is a problem for the segmentation routine, what about including FLAIR images? Or diffusion? Also, because of the extensive contrast uptake usually seen in Meningiomas, will including DSC or DCE imaging help? This needs to be discussed.
6. The Materials & Methods section consists of a large theory section on FCM. For better reading, background information that is not specific for this manuscript may be referred to only, or used in an appendix. The literature on FCM clustering (or similar methods) on brain tumors is extensive. The authors should focus on the parts of the proposed segmentation routine that is new compared to previous work.

7. The pre-processing paragraph is not well described and difficult to reproduce. How was the coregistration procedure performed? Using what algorithm? What about the reslicing routine? (Interpolation, etc). Were the patient scan orientations geometrically aligned before imaging? What about image intensity normalization?

8. The authors say that the method provide high diagnostic accuracy values as long as the 5 patients in which the method failed are excluded. The rationale behind this exclusion is not well understood, nor the criteria for the exclusion. Any method will obtain high accuracy if the cases that fail are removed. The authors say that the patients that fail usually had ‘significant edema tissue’. What is the limit for significant edema tissue? Was there a test for this? For a reader trying to adapt this method, it will be very hard to know when the method is expected to fail.

9. The authors show values of ‘percent match’ and ‘correspondence ratio’. As long as values of true/false positives/negatives are derived, why not include values of sensitivity and specificity? And maybe more important, assess the reproducibility (test-retest) of the manual and automatic method? In general, in terms of reproducibility (and speed), an automatic method should be superior to a manual method.

10. A symmetry measure was used to locate the tumor. How is this dependant on tumor size and whether or not the tumor is shifted towards one of the hemispheres? As the authors briefly point out in the Background section, there are issues related to this approach. How many tumors were in the midline?

11. The semi-supervised procedure is not well described. Based on the results, it looks like this was performed late in the automatic tumor segmentation routine. Is this a critical step for the analysis?

12. The concept of ‘logistic calculation’ needs to be described.

13. Morphological image processing section; erosion and deilation operations were used to clean the binary image. What if the tumor is not homogenous and a ‘solid’ object because of calcifications etc?

14. Table 3; three patients/values seem to be different between the semi-supervised and the automatic method. What happened here? Who are the 5 patients that did not obtain a satisfactory result?

15. The authors state that the semi-supervised method was significantly better
than the automatic method. Using what test? P-value?

16. The manuscript is sometimes difficult to read and lacks consistency. The Background section has sentences that belong in Materials & Methods (‘In order to effectively eliminate the fragment...’) The Result section has text (statistics) describing how the study was performed which should be in the Materials & Methods section. Also, results are discussed in the Results section instead of in the Discussion section.

17. The Discussion section is short and only a single reference is included related to the choice of cluster number. First, the Discussion section should state the main findings of this study. What makes this method stand out compared to other methods reported in the literature? The results should be compared with previous work, and the accuracy of the method (and the reference method) should be discussed in detail. Also, the clinical usefulness of the proposed method should be discussed.

18. There are language issues throughout the text. A colleague with English as their native language should read the manuscript to ensure that the words used both accurately and clearly convey the intended meaning.

Minor Essential Revisions:
1. Histologically, there are many Meningioma sub-types. Did any patients undergo surgery prior to MR imaging? If so, what were the results and why were they included?

2. Information on patient age and gender should be included.

3. Did the authors perform any skull-stripping prior to tumor segmentation? If not, could this aid the routine?

4. The computational language used and the time to perform the end-to-end analysis should be clearly stated in the beginning or end of the M&M section.

5. Symmetrical histogram analysis section: removing pixel grayscale values below 50% seems a bit arbitrary. What about Otsu’s method or similar?

6. Statistics; were the TN, TP, FP and FN values based on pixel-by-pixel analysis?

7. References: some of the reference titles are not in bold.

8. The word ‘Hitogram’ in Figure 6 is misspelled

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests