Author’s response to reviews

Title: Automatic volumetry on MR brain images can support diagnostic decision making

Authors:

   Rolf A Heckemann (soundray@imperial.ac.uk)
   Alexander Hammers (alexander.hammers@imperial.ac.uk)
   Daniel Rueckert (d.rueckert@imperial.ac.uk)
   Richard I Aviv (richard.aviv@sunnybrook.ca)
   Christopher J Harvey (charvey_99@yahoo.co.uk)
   Joseph V Hajnal (jo.hajnal@imperial.ac.uk)

Version: 2 Date: 29 April 2008

Author’s response to reviews: see over
Dear Madam or Sir

Thank you for considering our manuscript “Automatic volumetry on MR brain images can support diagnostic decision making” for publication in BMC Medical Imaging. We have considered the editorial requests and reviewers’ comments and made changes as described below.

With best regards

Rolf Heckemann (on behalf of all authors)

Reviewer #1, Tom den Heijer

We thank the reviewer for his assessment and insightful comments.

I have the following comments:
1) How severely demented were the AD patients (i.e. what was their CDR or MMSE?)

For the data set used in this pilot study, we had no detailed clinical information beyond the diagnostic classification as probable or possible AD (Methods – Study data). In ongoing work, we aim to correlate diagnostic results with disease stage and severity.

2) Was there a difference in diagnostic accuracy between the neuroradiologist and general radiologist?

The neuroradiologist made correct initial diagnoses without the colour overlay in a larger number of cases than the general radiologist. He was also somewhat more effective in the way he made use of the colour overlay. Our case numbers are, however, too small to attribute any significance to this trend. Due to this lack of statistical significance, and because the objective of the work was to assess the impact of the decision support method, rather than comparing individual diagnostic performance, we chose not to comment on these results in the paper.

3) Were the readers blinded on how many subjects had dementia and how many not in their total of 14 scan readings?

No, the readers were aware that seven of the 14 cases presented would be AD patients. We agree with the reviewer on the importance of this point and have corrected the oversight of not having mentioned this in Methods – Visual review.

4) What were the initial confidence scores and the confidence score after the overlay method? Can the authors put this in a table according to reader and subject?

We have added a table following this suggestion.

5) It would be nice if intrareader consistency measures on the confidence score are available. Also, it might be nice to see confidence scores on overlain scans and normal scans independently (ie not scored directly one after the other)

Given the pilot nature and small case number of this study, we posed the hypothesis fairly narrowly and designed the experiment to answer the question of usefulness of the colour overlay in a per-case fashion. By comparing diagnostic confidence in each case prior to and after the intervention (supplying the colour overlay), we ascertained that the additional information contained in the overlay was indeed beneficial to the decision process. Investigating a broader hypothesis as the
reviewer suggests will require larger numbers of subjects and, crucially, reviewers. The results presented here have encouraged us to design a more extensive study, where we will assess the direct impact of the overlay on diagnostic accuracy.

6) In the figure of the AD patient (d) the left hippocampus is red indicating a relatively large volume, which is counter to expected. Was the absolute volume of this hippocampus indeed larger than the other 16 subjects?

The large size of the hippocampus in this case was due to a mislabelling of a neighbouring region (the temporal horn of the lateral ventricle, not seen in the section shown) as part of the hippocampus. The reviewers observed this mislabelling and discounted the resulting overestimation as an artefact. Please see also our comment on Reviewer #2.

**Reviewer #2, Ricardo Insausti**

The manuscript aims at examining the usefulness of a colour overlay presenting the size rank in the segmentation used, as complement of pattern recognition and visual judgement of the pathological state of individual cases so it can help in decision making. The usefulness of elaborating raw data is particularly highlighted in this manuscript. The methodology is sound, although not devoid of limitations, and the results are self-explanatory.

We are grateful to the reviewer for this favourable assessment. Although we are aware of the methodological limitations of the study, we feel we have discussed these and appropriately considered them in our conclusions.

However, one might think that the cases presented in figure 1 allow more interpretations than that provided in the figure legend. In row b, authors should comment on color overlay showing a blue hue (decreased volume) over the entorhinal cortex on the left hand side of the axial section, and in the medial thalamus (mediodorsal nucleus perhaps) in the coronal section. Likewise, it would be very interesting the comment on, the red hue that seems to be coincident with the hippocampus on the left hand side in row d, the AD case; the asymmetry is even more accentuated in the coronal section of the AD case.

While we agree that the colour overlays present plenty of information that may be of interest beyond the classification that we asked of the readers, we are wary of the temptation to speculate about their diagnostic significance, as this would distract from the study objective, which was to investigate the usefulness of the colour overlay for the purposefully narrow decision AD versus non-AD. As the results of this work have encouraged a larger-scale investigation based on a more accurate segmentation procedure, there will be opportunities to examine pathological appearances in observation studies and to assess their diagnostic potential. Please also note our response to Reviewer #1.

The journal details in reference 10 should be completed to volume 33, and pages, 115-126.

We thank the reviewer for pointing out this omission, which we have corrected.

**Editorial comments**

We have provided additional information on the ethics and consent framework of this research in Section Methods – Study data. We have added a declaration of no competing interests.