Reviewer's report

**Title:** Disparate voxel based morphometry (VBM) results between SPM and FSL softwares in ALS patients with dementia: Which VBM results to trust?

**Version:** 1  
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**Reviewer:** Michael Hornberger

**Reviewer's report:**

Rajagopalan and Pioro investigate the differences of neuroimaging software packages (SPM, FSL, Freesurfer) in detecting cortical volume and thickness changes in amyotrophic lateral sclerosis with frontotemporal dementia (ALS-FTD). The authors find that motor, as well as prefrontal and temporal brain regions showed widespread atrophy for ALS-FTD compared to controls for FSL and Freesurfer software packages only. By contrast, SPM revealed only a very small percentage of atrophy identified by the other packages.

Overall, this is an interesting study with potentially important implications for the imaging of ALS-FTD. Nevertheless, there are quite a few shortcomings which the authors need to address. There is also the concern that the authors used the same patient and control sample for a very similar analysis in a previous publication.

- One concern with the findings is that FSL and SPM applied very different thresholding methods (TFCE vs. voxel-wise), which could explain the results. The authors need to conduct a post-hoc analysis using voxel-wise thresholding for both packages to allow a better comparison.

- It’s not clear how cortical volume was calculated for Freesurfer and cortical thickness was calculated for FSL, SPM. Please clarify this in detail.

- Please explain the DICE similarity index in more detail for readers, as it is a critical factor in the paper. Currently there is only a study cited using this technique, which is not sufficient.

- The title should explicitly state the patients have ALS-FTD and not simply ALS with dementia. Please state this more clearly and change the title and abstract accordingly.

- There is virtually no information on the diagnosis of the patients. Were the Strong diagnostic criteria for ALS-FTD applied? Again, this is critical for the characterisation of the patients.

- Similarly, there are no demographics given for both groups. Please include this information, which will also allow to judge whether any nuisance covariates need to be employed (eg age).

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

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.