

Format for ANSWERING REVIEWERS

September 3, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12135-review.doc). Please note that the title of the manuscript misses the first 'P' in the online system. I could not modify it in the online system. The title just below this line is the correct one.

Title: Partial volume effect modeling for segmentation and tissue classification of brain magnetic resonance images: a review

Author: Jussi Tohka

Name of Journal: *World Journal of Radiology*

ESPS Manuscript NO: 12135

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewers (major changes are marked with the red color in the manuscript) as follows:

Reviewer 1 comments: The author performs a review of partial volume segmentation for brain MRI's. The author presents several real world clinical examples such as Alzheimers and Multiple Sclerosis where partial volume effects could have profound implications for clinical decisions. The manuscript is well written but could benefit from some additional clinical examples or even a case illustration.

Answer: Thanks for encouraging comments. I have added examples and an illustration to Figure 2, where now effects of the partial volume effect for hard tissue classification are demonstrated. The figure is discussed in the introduction section and in the section 5.2. I have also added a sentence explaining better the ramifications of the partial volume to the section 5.3.

Reviewer 2 comments: Paper is generally well-written and topic is important, especially for automatic processing of MRI images. It would be good to use images to show the effects of the proposed solution. This would improve readability and understanding.

Answer: Thanks for suggestion. I have included specific images and pointers/arrows to demonstrate the advantages of partial volume estimation over conventional segmentation in Figure 2.

Reviewer 3 comment 1: On the topic of partial volume effect modelling in brain MRI. The author discussed the statistically-based approaches and mainly focused on the mixel model. The author highlighted the advantage of an two-step algorithm and parameter estimation for the solution of the mixel model. The author did a great job to provide a tutorial-like overview for partial volume estimation in brain MRI. One of my major concerning is that the Markov random field (MRF) was proposed and integrated for solving the mixel model in both of direct solution and two-step algorithm. As Gonzalez-Ballester et al. [22] argued that this would introduce the typical problems of MRFs, i.e. determining the correct parameters and the weighting between the prior and the data, as well as huge computational cost. Please add information or discuss it as limitation for these problems of MRF.

Answer: Thanks for encouraging comments. I have added the discussion concerning the issue to section 3.2.2.

Reviewer 3 comment 2: The partial volume effect (PVE) was caused by the limited resolution of the imaging in brain MRI. However, a higher resolution will decrease this effect, as it better resolves the tissue. However, as a review on partial volume effect nowadays, please discuss the influence of resolution on PVE and potential effect for the parameter estimation in the investigated approach.

Answer: Thanks for the suggestion. This issue is now discussed in Section 6 (Future perspectives).

Reviewer 3 comment 3: As the authored mentioned, the partial volume estimations is very important for volume quantification and cortical thickness analysis. In the view of cortical thickness calculation, it's meaningless to state "cortical thickness measures can be shown to be improved if the partial volume effect is taken into account" only. Please elaborate it in more details.

Answer: This has been elaborated in more details in the end of Section 5.2.

Reviewer 3 comment 4: Please correct the formats references in 3rd, 17th, 20th. Please add explanations to Figure 3. Did the color-bar apply for all brains in Figure 2? If not, please correct it.

Answer: The mentioned issues have been corrected. Because the new reference numbering scheme requested by the editor Ref [3] is now [70] (in press added), ref [17] is now ref [73] (extra information removed and typesetting corrected), and ref [20] is [49]. Explanation have been added to Figure 3. Colorbar refers only to bottom row in Fig 2 which is now stated in the caption.

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3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Radiology*.

Sincerely yours,

Jussi Tohka