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OPEN PEER REVIEW

Comparison of Phase-Sensitive Inversion Recovery and Conventional Magnetic Resonance Imaging for Detection of Cortical Plaques in MS Patients

Hassan Hashemi, Maryam Mohammadzadeh, Mohammad hossein Dianat, Amir Reza Azimi, Hamed Naghibi, Madjid Shakiba, Kavous Firouznia

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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Contents

1 **Original submission** Referee 1, Editor-in-Chief 2
2 **Revision 1** Referee 2, Referee 1, Associate Editor, Editor-in-Chief 3
Authors' reply to reviewers 4
Reviewer and editor comments 7

1 Original submission

2 comments · 23 Dec 2020 – 6 Mar 2021

Referee 1 Reviewer

MINOR REVISION 23 Dec 2020

In general, it can be said that this study was properly designed and implemented; it is also well written but requires only minor editing, as detailed below:
1. The study is cross-sectional, which should be stated in the abstract and in the methods section of the full text.
2. The calendar period of the study should be stated in the methods section.
3. The demographic characteristics of the patients should be added at the beginning of the results section in both the abstract and the full text.
4. In the results section, when a variable is compared between several groups (methods), in addition to the significance level, the value for each group must also be expressed in parentheses.
5. In the sample section of the full-text methods, the patient sampling method must also be added.
6. This sentence in the methods section, "The mean age was 31 (range: 18-48 year) and the median EDSS was 3.5 (range: 1- 6.5)." is part of the results and should be moved to the next section.
7. In the statistical analysis section, it was stated that the Bonferroni correction method was used for the post hoc test; the significance level must be added for both the Friedman and Cochran Q tests.
8. In the statistical analysis section, only within-reader agreement was calculated, but it is better to calculate the agreement between the methods as well.
9. The order of figures is incorrect in the manuscript.

Editor-in-Chief

MAJOR REVISION 6 Mar 2021

Dear authors,
Your article needs Major revision.
Regards

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewers' Comments:

Reviewer 1:
In general, it can be said that this study was properly designed and implemented; also it well written but requires only minor editing, which were stated below:
1. The type of study is a cross-sectional that should be added in the the abstract and full text method.

Response: Thank you for your valuable comments. The corrections have been done in paper. (line number 34,101)
2. The study calendar time should be stated in the method section.

Response: Thank you for your valuable comments. The corrections have been done in paper. (line number 34,101)
3. Demographic characteristics of patients should be added in the initial section of the results in abstract and full-text.

Response: Thank you for your valuable comments. Patient's features are summarized in **Table 1**.The corrections have been done in paper. (line number 160,161)
4. In the results section, when a variable is compared between several groups (methods), in addition to the level of significance, the value of each group must also be expressed in the parenthesis.

Response: Thank you for your valuable comments. The corrections have been done in paper. (line number 165,166,168)
5. In the full-text method, the sample section, the patient sampling method must also be added.

Response: Thank you for your valuable comments. The corrections have been done in paper. (line number 101-107)
6. This sentence in method "The mean age was 31 (range: 18-48 year) and the median EDSS was 3.5 (range: 1- 6.5)." is part of results and should be moved to the next part.

Response: Thank you for your valuable comments. The corrections have been done in paper. (line number 160,161)
7. In the statistical analysis section, it was said that Bonferroni correction method was used for the post-hoc test, which it is necessary to add a significant level value for both Friedman and Cochran Q tests.

Response- Thank you for your valuable question. When we implemented a Friedman or Cochran test for whole comparison between three groups together, naturally the P-value significance was considered at the level of 0.05 [for comparison of T2, FLAIR and PSIR together]. Then if we had to compare each pair groups together [for example PSIR vs. FLAIR], then we should consider Bonferroni correction. For bonferroni correction, regarding we had 3 pairwise comparisons [T2 vs. FLAIR, T2 vs. PSIR and FLAIR vs. PSIR], then we correct the P-value for significance at the level of 0.017 (equal to 0.05/3). The related corrections and explanations have been added to statistical analysis section of paper.

(line number 136-138)

8. In the statistical analysis section, only the agreement within the reader was calculated, but it is better to calculate the agreement between the methods as well.

Response- Thank you for your valuable question. As it was noted in the objective part of paper, the main goal of paper was assessment of the point that which sequence is better regarding detection of MS plaques. So our goal was not assessment of agreement between different sequences and so, we compared different sequences based on this goal and the details have been mentioned in the tables and result section. As we aimed to determine which sequesnce is better, we did not implement agreement analysis.

9. The order of figures is incorrect in the manuscript.

Response: Thank you for your valuable comments. The corrections have been done in paper

Reviewer 2:

The article needs more precise grammatical editing. Subnumbering of figure 1 is incomplete.

Response: Thank you for your valuable comments. The corrections have been done in paper

Reviewer 3:

This article was written in proper way but unfortunately, regarding the goal of the study and conclusion, there are numerous published articles about identification of cortical lesions in MS with PSIR, so this article does not include any new information. Moreover, regarding methods, all the previous studies emphasized on 3 Tesla machines (and sensitivity encoding compatible head coil) and have been performed with those machines, not 1.5 ones. There are also some publications against using 1.5 tesla machines for PSIR(Phase sensitive reconstruction of T1-weighted inversion recovery in the evaluation of the cervical cord lesions in Multiple Sclerosis; is it similarly eligible in 1.5 T magnet fields?Multiple Sclerosis and Related Disorders (IF 2.889) Pub Date : 2018-04-22 , A Shayganfar,..).

Response: Thank you for your valuable comments. According to the existing guidelines, 3Tesla devices are more powerful than 1.5 Tesla devices in detecting the MS lesions and their resolution is higher. Considering that according to the existing guidelines, the use of the 3Tesla device in showing both the number of lesions and increase resolution is higher than 1.5 Tesla and this limitation is not only related to the show of lesions in PSIR sequence, Rather, this issue has been observed in these sequences FLAIR (T2 hyperintensity lesions), MPRAGE (T1 hypointensity) and T1 post contrast (gadolinium enhancing lesions). Use high-field MR imaging improves MS characterization, increasing lesion load quantification in all standard protocols for MS evaluation. (Filippi, Massimo, et al. "MRI criteria for the diagnosis of multiple sclerosis: MAGNIMS consensus guidelines." *The Lancet Neurology* 15.3 (2016): 292-303. and Sinnecker, Tim, et al. "Multiple sclerosis lesions and irreversible brain tissue damage: a comparative ultrahigh-field strength magnetic resonance imaging study." *Archives of Neurology* 69.6 (2012): 739-745.)

The most important point in the PSIR sequence is the correct phase-sensitive reconstruction and the correct choice of inversion time, which play a key role in creating the desired contrast between anatomy and pathology tissue, which can ultimately be very effective in increasing the diagnostic power of the sequence. The consensus recommendation is that it is mandatory

to perform multiple sclerosis imaging at least in 1.5T MR unit and other researches have used special sequences in 1.5 T MRI machine to evaluated cortex lesions, so it is not totally wrong when we use 1.5T device for detecting cortical MS lesions. (Geisseler, Olivia, et al. "The relevance of cortical lesions in patients with multiple sclerosis." *BMC neurology* 16.1 (2016): 1-8.)

Using 1.5 Tesla device seems to be a limitation of the study, however, as we noted earlier, when we realize our main goal of the study, this limitation is less important; because we wanted to “compare” three sequences and in this situation, all there sequences are in the same device limitation and results of their comparison could be similar to the circumstances when we use a 3 tesla device. If we want to determine the exact number of the plaques in a sequence in a device, of course using 3Tesla could be better, but when we want “to compare” sequences to show which one is better, this limitation will be less important. As we showed in the result section, the comparisons showed PSIR is better than two other sequences in our condition [1.5 T]; so we can say probably it will be better in 3T so.

2 Revision 1

4 comments · 8 May 2021 – 14 Jun 2021

Referee 2 Reviewer — ACCEPT 8 May 2021

Accept

Referee 1 Reviewer — ACCEPT 12 May 2021

Thanks to the dear authors for addressing the comments in the manuscript. It is now acceptable from a methodological point of view.

Associate Editor — ACCEPT 22 May 2021

Dear authors,
Thank you for considering and addressing our reviewers' points.
Your manuscript is now acceptable for publication in IJR.
Best regards,

Editor-in-Chief — ACCEPT 14 Jun 2021

Dear authors,
Your article is acceptable for publication in IJR.
Regards