Reviewer's report

Title: Repeatability and reproducibility of cerebral 23Na imaging in healthy subjects

Version: 0 Date: 23 Oct 2018

Reviewer: Yongxian Qian

Reviewer's report:

General Comments:

It's known that sodium MRI on the brain is repeatable and reproducible. But this is not well known among clinicians who are interested in sodium MRI, due to poor documentation in literature. It is difficult for a clinician to find meaningful references and get confidence to practice sodium MRI in clinical research. This manuscript is filling the gap just in time. In general, the work is presented well, such as a right pulse sequence for imaging, a reasonable pool of study subjects, a proper analysis of data, and a nice organization of the manuscript. However, this reviewer has a major concern on the confusion of definition between repeatability (repeated by the same experimental setup) and reproducibility (repeated by different experimental setups) shown in this work. The repeated sodium MRI scans at one visit should be used for repeatability study while those at different visits for reproducibility study. Both scans should not be mixed together in the data analysis. The authors should report either repeatability or reproducibility, or both, in the result section, based on their specific design of the experiments. In addition, some minor concerns/comments are listed below.

Specific Comments:

1. Page 4, Abstract/Results, "Moderate to good correlation was found between the readers". There was no definition in the Method about the comparison between readers. Please clarify who are the readers and how to compare between their readings.

2. Page 4, line 36, "low in-vivo sodium concentrations" should not be classified as technical challenges. It should be the low SNR (due to low sodium concentration) as a technical challenge.

3. Page 5, line 58, "8f, 4m" was confusing to readers. It should read as "8 females, 4 males".

4. Page 6, lines 1-7, in the sentences with "the first day of scanning, …, the second day of scanning". It's better to say "the first visit, …, the second visit".
5. Page 6, lines 1-7. Please describe the setup of two scans on the same day at the 1st or 2nd visit, such as the time gap, repositioning of the subject, and/or repositioning of the isocenter. This is an important part for the design of your study on reproducibility (by different experimental setups) or repeatability (by the same experimental setup).

6. Page 6, line 14, the scan scheduled at the same time of the day. It's better to explain why you need to scan subject at the same time of the day.

7. Page 6, lines 48-53. These sentences should be moved to the description of experiment (Page 6, lines 1-7).

8. Page 6, Lines 48-53. The two consecutive Na scans without repositioning of the subject in between should work for the repeatability study, not for the reproducibility study.

9. Page 7, Table 1, TE. Please define TE (from the center or the end of RF pulse?).

10. Page 8, line 34, quantification of Na concentration. It's better to describe the math and procedures for the calibration and quantification of Na concentration, not just referring to Ref. 2.

11. In the results section, to improve readership of this work, you should add a table and summarize your findings about the repeatability and/or reproducibility of your quantified sodium MRI.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes
**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**

If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**

Please complete a declaration of competing interests, considering the following questions:

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