Reviewer’s report

Title: Brain perfusion imaging with voxel-based analysis in secondary progressive multiple sclerosis patients with a moderate to severe stage of disease: A Boon for the Workforce

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Reviewer: Yingxin Chen

Reviewer's report:

1. Introduction:

According to its clinical course, MS has three main types: relapsing remitting (RR), primary progressive (PP), and secondary progressive (SP). Please supply the reference to support for this classification. It is more popular view that four disease courses have been identified in multiple sclerosis: relapsing-remitting MS (RRMS), primary-progressive MS (PPMS), secondary-progressive MS (SPMS), and progressive-relapsing MS (PRMS). PRMS — the least common of the four disease courses (5%) — is characterized by steadily progressing disease from the beginning and occasional exacerbations along the way.

2. Imaging protocols:

Scans were performed on a dual head gamma camera (Siemens, Germany), which model? Such as Multi SPECTII, please clarify it.

SPM8, Please list more detail of SPM8, though SPM is one of common software on functional imaging.

Results were obtained using (p < .05) corrected for multiple comparisons. P<0.05

3. Visual analysis Scintigraphic results were analyzed by two experienced nuclear medicine physicians who were not aware of the medical history of the patients. Why not three experienced physician?

4. Figure1 Unit of y axis. Or Please show the percentage of each type/total patients
5. Figure 1. Brain regions with significantly reduced perfusion (statistical parametric mapping) in patients Vs. control subjects (group analysis). Figure 1 or 3? Please clarify it.

6. Figure 4. The left columns indicate transverse 99mTc-ECD SPECT images; the middle columns indicate coronal 99mTc-ECD SPECT images; and the right columns indicate sagittal 99mTc-ECD SPECT images.

According to shape of ventricle. Left would be transverse 99mTc-ECD SPECT images but double check ventral or dorsal, please clarify left or right; middle is sagittal 99mTc-ECD SPECT images; right would be coronal 99mTc-ECD SPECT images.

7. Figure 6. First brain perfusion study of MS woman patient showed moderate hypoperfusion of inferior temporal lobe on the right side. The upper rows indicate transverse 99mTc-ECD SPECT images; the middle rows indicate coronal 99mTc-ECD SPECT images; and the lower rows indicate sagittal 99mTc-ECD SPECT images. Please check the middle rows is sagittal imaging? The lower rows is coronal imaging.

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

Yes

**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

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Needs some language corrections before being published

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