Magnetic Resonance Imaging–Based Quantitative Iron Mapping at 7-Tesla Remains to Be Elusive in Multiple Sclerosis

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We read with interest Hammond and colleagues'[1] recent article in which high-resolution and high-field 7-Tesla magnetic resonance imaging data were collected from healthy control subjects and multiple sclerosis (MS) patients. In view of the considerable interest in the role of iron in various neurodegenerative diseases, including MS, this article is timely and informative. The article used local field shift (LFS) at 7 Tesla as a quantitative marker, and showed that gray matter structures such as globus pallidus, caudate, and putamen have significantly larger LFS in MS patients compared with healthy adult control subjects ($p < 0.01$). The LFS showed a trend in the thalamus ($p = 0.06$) and no significant difference in the compact white matter of the corpus callosum ($p = 0.47$). The authors conclude, based on their results, that LFS is a sensitive marker of iron content.[1]

The LFS data presented in Table 1 of Hammond and colleagues'[1] article show that the globus pallidus and caudate have comparable LFS in both healthy control subjects and age-matched MS patients.[1] These observations appear to be inconsistent with the published trend of larger iron concentration in globus pallidus compared with caudate.[2] Previous in vivo measurements even at lower magnetic fields (eg, 1.5 and 3 Tesla) and using relaxation rates (see Haacke et al.[3] for extensive review) or magnetic field correlation methods[4] showed that globus pallidus and caudate have significantly different values as a result of larger iron content, which is consistent with postmortem histochemical measurements that show much greater iron content in globus pallidus compared with caudate.[3]

It is also interesting that the method that Hammond and colleagues[1] used did not predict the natural aging of increasing iron content even in the globus pallidus, which has the greatest iron concentration compared with any other region in the human brain.[2,3]

That the LFS using phase mapping at 7 Tesla as Hammond and colleagues[1] presented is not proportional to iron concentration is further supported by the data presented in Yao et al.[5] more recent work using both in vivo 7-Tesla magnetic resonance imaging and histochemical analyses.

Based on these observations, it appears that current iron mapping methods using phase shifts at 7 Tesla may not have the specificity or accuracy for quantifying iron content in neural tissue.

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References

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Reply

Daniel Pelletier, MD[1] and
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In response to a letter you received entitled "MRI-Based Quantitative Iron Mapping at 7T Remains to Be Elusive in Multiple Sclerosis," we would like to refer your readers to our original article published in *Annals of Neurology* in 2008.[1] Table 1 of the article clearly demonstrates that the method used to measure local field shift (LFS) at 7T does find differences in the globus pallidus and caudate gray matter regions between multiple sclerosis (MS) patients and normal age-matched healthy controls, as expected and shown in histopathological MS studies. It seems that the authors have simply misread Table 1.

Furthermore, we did not attempt in this pilot study to compare LFS between gray matter regions of MS patients, because we did not know the sensitivity of this technique against healthy controls and the appropriate sample size needed to see differences between deep gray matter regions. We would also like to warn your readers on the conclusive remarks found in the letter regarding the accuracy and specificity of LFS at 7T to iron mapping. To address these relevant questions and make appropriate conclusions would have required a different study design than our initial work, which explored sensitivity rather than specificity and accuracy. Lastly, we hope additional phase imaging studies at 7T examining histochemical–magnetic resonance imaging correlation, with in vivo longitudinal follow-ups of sufficient sample size, will help increasing our current understanding of neurodegeneration in MS.

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Reference

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