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## **Myelin Imaging Can Be Affected by a Number of Factors**

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## Myelin Imaging Can Be Affected by a Number of Factors



We read with great interest the article by Yu et al,<sup>1</sup> which investigated the utility of myelin volume fraction, axon volume fraction, and G-ratio, which is the ratio of the inner-to-outer diameter of a nerve fiber, in the evaluation of WM in patients with MS. They used macromolecular tissue volume imaging to calculate myelin volume fraction and revealed that myelin volume fraction was lower in the normal-appearing WM of patients with MS compared with the WM of healthy controls. Furthermore, they also revealed that disability, as measured by the Expanded Disability Status Scale, was significantly associated with myelin volume fraction in the normal-appearing WM of patients with MS. We believe that this study is an important step toward the introduction of myelin imaging into clinical practice.

We thank Yu et al<sup>1</sup> for referring to our article entitled, “Analysis of White Matter Damage in Patients with Multiple Sclerosis via a Novel In Vivo MR Method for Measuring Myelin, Axons, and G-Ratio.”<sup>2</sup> The myelin volume fraction used in our study was calculated from the R1 and R2 relaxation rates and proton density measured by synthetic MR imaging, by simulating a 4-compartment model: myelin volume fraction, cellular volume fraction, excess parenchymal water volume fraction, and free water volume fraction.<sup>3</sup> Myelin volume fraction in the MS lesions in our study was lower than in their study, and they discussed this discrepancy possibly being because the 4-compartment model used in our study did not incorporate the partial volume pool to account for magnetization transfer effects. Even though magnetization transfer effects may have resulted in small changes in the measured R2 estimations, myelin is estimated from combinations of the measured R1, R2, and proton density values by the model used in our study, and the effect of a potential offset in R2 is expected to be small.

Here, we should also consider the fact that magnetization transfer imaging, which detects macromolecules, is known to be sensitive to not only intact myelin but also other macromolecules, including myelin debris.<sup>4</sup> Hence, macromolecular tissue volume may also be affected by myelin debris, which may have led to the

higher myelin volume fraction in the study by Yu et al<sup>1</sup> than in our study. Because myelin debris is assumed to have much lower R2 than the tightly packed myelin, the contribution of myelin debris to the estimated myelin by synthetic MR imaging is expected to be small. Because myelin imaging can be affected by a number of factors, the interpretation of the results is not straightforward. A histologic study comparing macromolecular tissue volume and synthetic myelin imaging is awaited to further disentangle the mechanism underlying the discrepancy in the results between the study by Yu et al<sup>1</sup> and our study.

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