

Accepted Manuscript

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PII: S1053-8119(17)30885-6

DOI: [10.1016/j.neuroimage.2017.10.051](https://doi.org/10.1016/j.neuroimage.2017.10.051)

Reference: YNIMG 14429

To appear in: *NeuroImage*

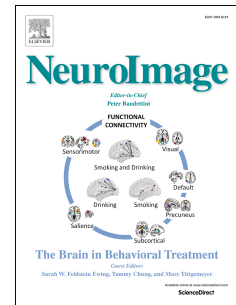
Received Date: 31 July 2017

Revised Date: 11 October 2017

Accepted Date: 25 October 2017

Please cite this article as: Dhital, B., Kellner, E., Kiselev, V.G., Reisert, M., The absence of restricted water pool in brain white matter, *NeuroImage* (2017), doi: 10.1016/j.neuroimage.2017.10.051.

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The Absence of Restricted Water Pool in Brain White Matter

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Abstract

Understanding diffusion-weighted MR signal in brain white matter (WM) has been a long-sought-after goal. Modern research pursues this goal by focusing on the biological compartments that contributes essentially to the signal. In this study, we experimentally address the apparent presence of a compartment in which water motion is restricted in all spatial directions. Using isotropic diffusion encoding, we establish an upper bound on the fraction of such a compartment, which is shown to be about 2% of the unweighted signal for moderate diffusion times. This helps to eliminate such a compartment that have been assumed in literature on biophysical modeling. **We also used the diffusion decay curve obtained from the isotropic encoding to establish a lower limit on the traces of either of intra- or extra-axonal compartment as a function of their relative water fraction.**

HIGHLIGHTS

- Isotropic diffusion measurement shows an absence of still water compartment in brain white matter.
- The lower limit on the trace of intra- and extra-axonal compartment was estimated.
- Orientation dispersion of axons and glial processes have to be accounted to fit isotropic measurement.

Keywords: Brain white matter, Diffusion MRI, Isotropic diffusion weighting, Restricted water, Micro-structure imaging

Introduction

Water diffusion in brain tissue can be investigated using diffusion-weighted magnetic resonance (DW-MR) technique, providing unique insights into cellular level micro-structure. The myriad diffusion barriers, all present in a single voxel, influence the DW-MR signal, allowing sensitivity to microscopic changes in tissue milieu. This has indeed aided detection of various tissue anomalies (Moseley et al., 1990; Benveniste et al., 1992; Werring et al., 1999; Kono et al., 2001; Maier et al., 2010).

Due to axonal morphology, the most striking micro-structural feature in WM is its anisotropy. This anisotropy is duly reflected in DW measurements, largely attributed to the axonal membrane with additional contribution from myelin

walls (Beaulieu and Allen, 1994; Beaulieu, 2002). Anisotropy has been exploited in diffusion tensor imaging (Basser et al., 1994) and fiber tracking (Basser et al., 2000; Tuch, 2004; Tournier et al., 2004; Wedeen et al., 2008; Reisert et al., 2011). While the anisotropy gives away some information about gross tissue architecture, more subtle DW-MR signal properties presumably contain further information on different compartments, their structure and possible pathologies. Though substantial efforts have applied towards detecting WM pathologies, they still depend on insufficient understanding of the micro-structural content of the DW-MR signal (Moritani et al., 2009).

Further progress in this direction demands a better understanding of the complex relation between the tissue structure and the DW-MR signal. The novelty and the difficulty of this problem is rooted in the different ways tissue micro-structure

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