Further Evidence of an Orientation Dependence of Magnetization Transfer Parameters from Investigations in Post-Mortem Marmoset Brain

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Target audience. Researchers interested in quantitative magnetization transfer (qMT) and white matter microstructure.

Introduction. Information on myelin can be obtained indirectly from magnetization-transfer (MT) experiments [1-4]. Quantification of MT imaging is usually based on a two-pool model consisting of a free water pool "a" and a semi-solid, macromolecular pool "b". Integral part of this model is a lineshape describing the absorption probability of the semi-solid pool, which is often assumed to be super-Lorentzian (SL) [3-5]. It was recently found that T_{2b} shows an apparent dependence on Θ, the major orientation of white matter (WM) fibers with respect to B_0 [6-7]. To explain this observation, a novel lineshape function was proposed that considers lipid bilayers enveloping a cylindrical axon [7]. While this hypothesis yielded reasonable results, it is based on analyzing different voxels of human WM *in vivo*. In the current work, the hypothesis is further evaluated by examining a *post-mortem* monkey brain at different orientations with respect to B_0, a procedure that allows analyzing the same voxel as a function of Θ.

Methods. *MRI scans:* qMTI data were acquired from a *post-mortem* marmoset brain (male, 10 years, 4% PFA immersion fixation) on a 3T MedSpec 30/100 human scanner (Bruker, Ettlingen, Germany) with a custom-made transceiver Helmholtz coil [8]. The sample was placed in a spherical container and submerged in perfluoropolyether. A paraffin mold was used to restrict sample mobility within the sphere. The sample holder could be rotated horizontally with approx. 5° precision. 20 image volumes (222×286×286 µm nominal resolution) were recorded with an MT-prepared 3D FLASH sequence (TR/TE: 35 ms/6 ms; α: 20°; pulsed off-resonance saturation: 10 ms Gaussian pulse; 6 different pulse amplitudes between 942 and 6694 rad/s; 9 offset frequencies between 250 and 30000 Hz). Off-resonance frequencies and amplitudes were chosen by an optimization algorithm [10]. The measurements were repeated for 10 different azimuthal angles covering a 180° rotation in the axial plane ($\mathbf{B}_0$ orthogonal to the coronal plane). *MT Parameter Fitting:* All qMT parameters (pool size ratio M_{0b}/M_{0a}, exchange rate R and the longitudinal and transversal relaxation times of each pool) were obtained by non-linear least-squares fitting. Subsequently, the discussion is limited to T_{2b}. A super-Lorentzian absorption lineshape was assumed for fitting consistent with previous work [7,9]. *Fiber orientation:* DTI measurements could not be performed with the current hardware at the desired resolution, which prevented the direct measurement of Θ. Instead, Θ was estimated in selected regions of the corpus callosum (*cc*), where the fiber orientation follows the structural orientation (for comparison see Fig. 2a). In particular, the fibers run within a plane that is orthogonal to the medial longitudinal fissure. From the orientation of this plane and estimating the fiber pathway within this plane, Θ was calculated by coordinate transformations.

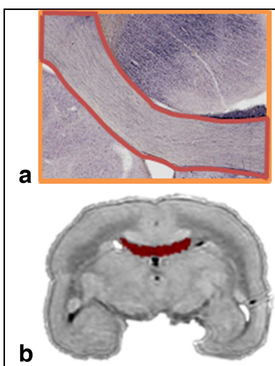

Fig. 1. Histology slice of example brain zooming in the cc (red) with clearly visible orientations of single fibers **(a)**. Coronal slice of the investigated brain with red ROI of analyzed structures**(b)**.

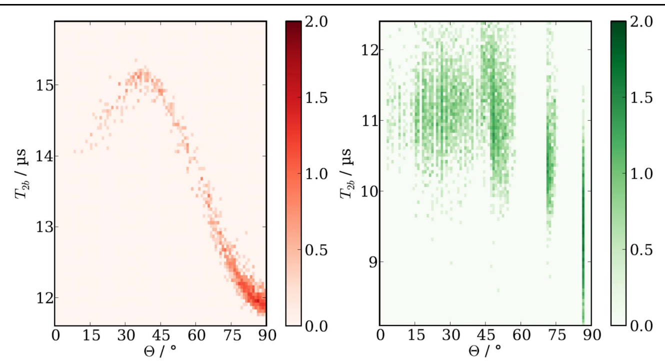

Fig. 2. 2D histograms of T_{2b} as function of the major fiber orientation relative to B_0 comparing previous *in vivo* data in humans [7] (**left**) to results obtained in *cc* in post-mortem marmoset brain (**right**; approx.. 1500 voxels) with rotation of the sample.

Results and Discussion. A clear dependence of T_{2b} on the fiber orientation (Fig. 2b) Θ was found, that closely resembles the orientation dependence of T_{2b} of previous human *in-vivo* data (Fig. 2a) with a peak at approx. 38°.

Conclusion. The observed angular dependence in the *post-mortem* data for highly ordered WM supports the hypothesis of orientation dependence of the RF absorption lineshape that was observed in human brain *in vivo*. Here, variation of the orientation was achieved by rotating the sample in the magnetic field.

References. 1. C. Laule et al. *Neurotherapeutics* 4, 460 (2007). 2. R.M. Henkelman et al. *MRM* 29, 759 (1993). 3. C. Morrison et al. *MRM* 33, 475 (1995). 4. C. Morrison et al. *JMR(B)* 108, 103 (1995). 5. H. Wennerström. *CPL* 18, 41 (1973). 6. D.K. Müller et al. *Proc ISMRM* 2996 (2010). 7. A. Pampel et al. *Proc. ISMRM* 392 (2014). 8. R. Müller et al. *Proc. ISMRM* 4366 (2013). 9. D.K. Müller et al. *JMR* 230, 88 (2013). 10. H. Marschner, Proc. ISMRM 22:3336, 2014.

Acknowledgement. Funded by the Helmholtz Alliance ICEMED—Imaging and Curing Environmental Metabolic Diseases and by EU through the 'HiMR' Marie Curie ITN (FP7-PEOPLE-2012-ITN-316716).