Evidence for the Detection of Microscopic Diffusion Anisotropy in Human Brain Gray Matter in Vivo

Marco Lawrenz[1,2] and Juergen Finsterbusch[1,2]

[1]*Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Hamburg, Germany,* [2]*University Medical Centers Hamburg-Kiel-Luebeck, Neuroimage Nord, Hamburg-Kiel-Luebeck, Hamburg-Kiel-Luebeck, Germany*

Double-wave-vector diffusion-weighting (DWV) or d-PFG experiments [1] are experiments with two diffusion weighting periods, each characterized by a wave vector $\boldsymbol{q}$, applied successively in a single acquisition (Fig. 1). Such experiments offer access to microscopic tissue properties, in particular when varying the angle θ between the two wave vectors [1-3]. For a long mixing time τ_m between the diffusion weightings, the diffusion anisotropy present on a microscopic scale is reflected in a signal curve with maxima for parallel and antiparallel and minima for orthogonal wave vectors [1]. This anisotropy effect has been demonstrated in various samples and, more recently, in human brain white matter (WM) in vivo, even in a region-of-interest (ROI) that macroscopically appears isotropic [4]. Measuring this anisotropy in gray matter (GM) is very attractive, e.g. to unravel the background of GM microstructure differences or changes. Utilizing high-field gradients, the microscopic anisotropy has already been found in GM of the in vivo rat brain [5]. However, so far, it is unclear whether it can be assessed in GM with a standard whole-body MR system. In this study, first evidence for the detection of microscopic diffusion anisotropy in human cortical GM in vivo is reported.

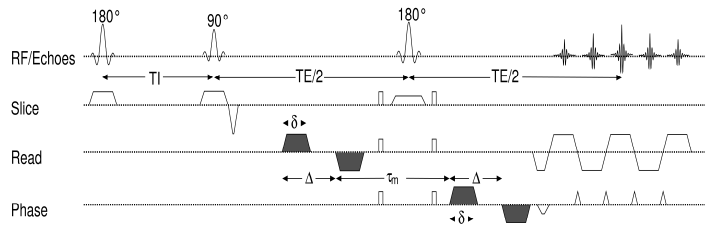

Fig. 1: Basic DWV pulse sequence with initial IR pulse and EPI readout.

Methods

Experiments were performed with a 3T whole-body MR system (TIM Trio, Siemens Healthcare) on young, healthy volunteers after their informed consent was obtained. Measurements were performed with spin-echo echo-planar imaging (Fig. 1) using an isotropic resolution of 4.0 mm (TE/TR = 155 ms/6.5 s). Only a single transverse slice was measured to minimize table vibration effects. In vivo it was positioned in the centrum semi-ovale to avoid regions with field inhomogeneities. Reference acquisitions were performed for a dodecane ($C_{12}H_{26}$) phantom that does not exhibit anisotropic diffusion.

The two diffusion-weighting periods were applied with a b value of 500 s mm^{-2} each, a diffusion time Δ of 25 ms, a mixing time τ_m of 45 ms, and a gradient pulse duration δ of 22 ms. An inversion-recovery pulse was applied prior to the excitation, the inversion time was adjusted to suppress WM signal contributions in vivo (TI = 530 ms). All 144 combinations of 12 directions sampling a circle in steps of 30° were applied for one coordinate plane. All three coordinate planes were covered in subsequent measurements. With one image without diffusion weighting, the total acquisition time was 16 min 9 s.

Averaged MR images of (i) parallel and antiparallel (Fig. 2a) and (ii) orthogonal wave vectors (Fig. 2b) and (iii) their difference (Fig. 2c) were calculated. Furthermore, in a phantom and a GM ROI (Fig. 2d), the signal variation with the angle θ between the two wave vectors was analyzed (Fig. 3).

Results and Discussion

Results of the experiments are summarized in Figs. 2 and 3. In the phantom, only a minor difference (Fig. 2c) between parallel/antiparallel and orthogonal wave vectors and a small deviation (below 1%) of the signal curve from a flat line is observed (Fig. 3a). This is in agreement with the absence of microscopic diffusion anisotropy in the phantom. In particular, no systematic artifacts seem to be present that could mimic an anisotropy effect. The in vivo data show the good suppression of WM signals close to the cortical surface (Fig. 2a and b), only a region that could contain the uppermost part of the pyramidal tracts yields significant signal but does not cause partial volume effects with the GM ROI considered. The difference map (Fig. 2c) reveals a slight difference in voxels containing gray matter while the difference in WM regions close-by is significantly lower, if any. Thus, it seems very unlikely that partial volume effects with WM cause the observed signal difference in GM. The individual signals (Fig. 3b) exhibit a large variability with θ because the signal-to-noise ratio in GM is also reduced due to the inversion recovery performed. However, the averaged signal curve (Fig. 3b) reveals the pattern typical for microscopic diffusion anisotropy, minima for orthogonal combination (90°, 270°) and maxima for parallel (0°) and antiparallel wave vectors (180°).

The modulation amplitude found in GM (about 5%) is considerably lower than that observed in human brain WM (about 12%) [4]. This can mainly be related to the long pulse durations required on whole-body MR systems that are known to reduce the DWV signal modulation considerably for small cells [6].

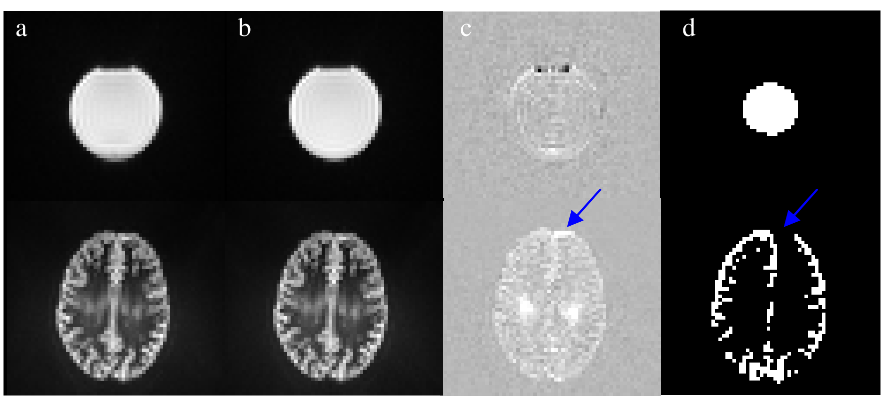

Fig. 2: Averaged MR images obtained for wave vectors in the *yz*-plane with (a) parallel and (b) orthogonal wave vectors and (c) difference of them for the phantom (upper) and the in vivo measurements (lower). (d) Masks used for the ROI analysis. A region in the frontal part of the brain (arrows) was discarded because the high difference values may indicate residual artifacts.

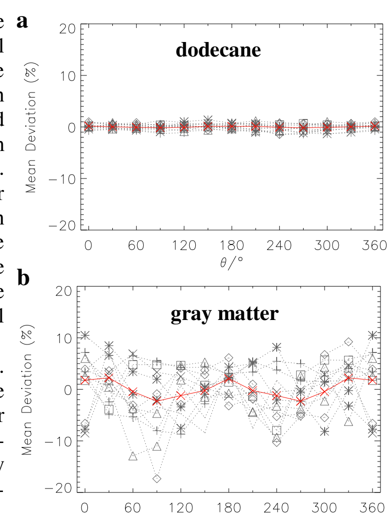

Fig. 3: The angular signal curves for the ROIs shown in Fig. 2d obtained in (a) the phantom and (b) in vivo. 144 wave vector combinations in the *yz*-plane were considered. The red curve is the mean over all measurements with a specific θ. In gray matter, the pattern typical for microscopic diffusion anisotropy is observed (W-shaped curve).

Conclusion

The diffusion anisotropy present on a microscopic scale seems to be detectable in human brain gray matter in vivo and could help to characterize gray matter tissue microstructure in the healthy and pathologic brain.

[1] Mitra PP, Multiple wave-vector extensions of the NMR pulsed-field-gradient spin-echo diffusion, Phys. Rev. B 51, 15074 (1995)

[2] Cheng Y, Multiple scattering by NMR, J. Am. Chem. Soc. 121, 7935 (1999)

[3] Özarslan E, Compartment shape anisotropy CSA revealed by double pulsed field gradient MR, J. Magn. Reson. 199, 56 (2009)

[4] Lawrenz M, Double-wave-vector diffusion-weighted imaging reveals microscopic diffusion anisotropy in the living human brain, Magn. Reson. Med. 69, 1072

[5] Shemesh N, Mapping apparent eccentricity and residual ensemble anisotropy in the gray matter using angular double-pulsed-field-gradient MRI. Magn. Reson. Med. 68, 794 (2011)

[6] Koch MA, Numerical simulation of double-wave vector experiments investigating diffusion in randomly oriented ellipsoidal pores. Magn. Reson. Med. 62, 247 (2009)