Double-PFG MR as a novel means for characterizing microstructures in grey matter

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Aims. (1) To apply the angular d-PFG methodology to isolated grey matter and study the signatures of \(\mu_A\) and csA; (2) to compare the signatures in grey and white matter and (3) to apply d-PFG MRI and test the potential for delineating microstructures within grey matter regions.

Methods. Conventional s-PFG experiments were performed using a bipolar s-STE sequence with \(\Delta \delta = 50\,\text{ms}\). Angular d-PFG experiments in isolated pig grey matter were performed using a bipolar d-STE sequence following the experimental parameters: \(\delta_1 = \delta_2 = 4\,\text{ms}\), \(\Delta_1 = \Delta_2 = 50\,\text{ms}\) and \(t_m = 0\) or 28 ms. The same experiments were also performed on an isolated optic nerve. A double-PFG MRI sequence was written and calibrated using phantoms (data not shown). The imaging was performed on a rat brain using a d-PGSE sequence with \(\Delta_1 = 4\,\text{ms}\), \(\Delta_2 = 50\,\text{ms}\), and the matrix was 128x128, yielding an in-plane resolution of 141x141 \(\mu\text{m}\). The slice thickness was 1.5 mm and the number of scans was 24.

Results and Discussion. Figure 1A shows the conventional bp-s-PFG experiments in the grey matter specimen. Clearly, the signal decay is isotropic, manifesting the lack of EA in grey matter, and it is impossible to infer on underlying microstructure. However, when the bp-s-PFG experiment was performed with \(t_m = 0\,\text{ms}\) (Fig 1B), a pronounced modulation is observed, reporting on the presence of \(\mu_A\) and csA; at long \(t_m\), the modulations of \(\mu_A\) are decoupled from the \(E(\psi)\) peaks and the only anisotropy mechanism that can contribute to the signal decay is csA. The sharp modulation of \(\sim 20\%\) that is observed between \(E(0)\) and \(E(90)\) at long \(t_m\) (Fig 1B) clearly indicates that this grey matter specimen is comprised of randomly oriented, anisotropic compartments. When similar experiments were performed on white matter, the bp-s-PFG clearly indicated on the presence of EA (Fig 1C). The angular bp-d-PFG experiment at \(t_m = 0\,\text{ms}\) however revealed also the presence of \(\mu_A\) in the form of a bell shaped function, which is expected when EA exists (Fig 1D) and is in good agreement with previous studies as well. However, at long \(t_m\), a slight angular dependence still remained (Fig 1D), despite theoretical predictions for a \(\psi\)-independent curve for coherently organized cylinders. This modulation most likely arises from a population of undulating axons that are not exactly aligned perpendicular to the plane of the experiment; these can be expected to be randomly oriented. Since the degree of modulation is directly dependent on the compartment eccentricity, one can infer that the randomly oriented compartments in the grey matter specimen are much more eccentric than those in the optic nerve specimen. Taken together, the four panels in Figure 1 show novel means of characterizing grey matter, as well as new sources of contrast between grey and white matter that are based on local compartment shape anisotropy. To study whether indeed angular d-PFG MRI can provide new contrasts in MRI within GM regions, angular d-PFG MRI was performed on a rat brain. The individual images for each value of \(\psi\) are shown in Figure 2, showing robust signal differences at different values of \(\psi\). These regions of interest (ROIs) were chosen in the cortex, and the CA1 and CA3 regions of the hippocampus. Figure 3 shows an overlay of a d-PFG image with a rat brain atlas and the ROIs (for one side only), and the extracted \(E(\psi)\) plots. Clearly, the \(E(\psi)\) plots are symmetrical in both sides; however, the \(E(\psi)\) plots reveal different underlying microstructure for the three GM tissues. The modulation in the cortical grey matter is the largest, suggesting that it is characterized by very eccentric compartments, while the CA1 and CA3 regions of the hippocampus show a smaller modulation, suggesting that the microstructure is less eccentric there, with diffusion in the CA1 region experiencing the smallest compartment shape anisotropy. Mapping such parameters therefore should yield new forms of contrast in the GM.

Conclusions. The angular d-PFG appears very promising for characterizing underlying grey matter microstructures, showing different signatures for different GM regions in the brain based on \(\psi\) and \(\mu_A\). Future studies will focus on quantifying these parameters and mapping it as a new source of contrast in MRI.
