Apparent Indices in the Rat Brain by Angular Double-Pulsed-Field-Gradient MRI at Finite Mixing Time Collected With Different Experimental Conditions

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Introduction: Recently angular double-pulsed-field gradient (d-PFG) MRI has been suggested as an alternative mean for studying microstructures in the central nervous system (CNS). Double-PFG MR employs two diffusion sensitizing gradient pairs, G_1 and G_2, with durations δ_1 and δ_2, respectively and two diffusion time intervals exist between each gradient pair. These two gradient pairs are separated by a mixing time (t_m) and may be applied co-linearly or with an angle (φ) between them, resulting in radial or angular d-PFG, respectively [1-2]. In 1995 Mitra predicted that such angular d-PFG experiments would yield a bell-shaped dependence ($E(\varphi)$) [2]. This bell-shaped dependency was predicted to be proportional to the restricting length of the compartment and was observed experimentally in the d-PFG NMR experiments on different systems [3-5]. Theoretical predictions and experiments showed that angular d-PFG experiment at longt_m, provide a mean to distinguish between compartments with different eccentricities [6-7].

Objectives: To study and explore the effects of different experimental parameters, such as diffusion times, mixing times, diffusion gradient durations and gradient strength on the obtained aE and φ_{sym} maps obtained from angular d-PFG MRI performed on ex-vivo rat brains.

Methods: MRI experiments were conducted on a 7-T Biospec scanner (Bruker) capable of producing pulsed field gradients of 400 mT/m in each direction. Fixed ex-vivo rat brain was immersed in phosphate buffer solution (PBS) overnight and then placed in a 15 mm glass tube filled with Fluorinert. All d-PGSE MRI experiments were conducted with slice thickness of 800 μm and field of view (FOV) of 1.8 × 1.8 cm. A matrix of 148 × 148 was used, resulting in in-plane spatial resolution of 122 × 122 μm^2. The angular d-PGSE MRI experiments were performed when the G_1 was fixed in the x-direction and the orientation of G_2 was varied in the x-y plane, the measurements were conducted for 13 different values of φ between 0° and 360°. For the brain shown in Fig. 1A-D the following parameters were used: $\delta_1 = \delta_2 = 4$ ms, Δ_1 and Δ_2 were set to 17 ms and the t_m was set 15 ms, $|G_1| = |G_2| = 320$, 240 mT/m, resulting in the 2q-values of 1090 cm^{-1} and 817 cm^{-1}, respectively. For the brain shown in Fig. 1E-D, $\delta_1 = \delta_2$were set to 3.5 ms and $|G_1| = |G_2|$ to 172mT/m, resulting in the 2q-values of 513 cm^{-1}. For the brain shown in Fig. 2 the following parameters were used: $\Delta_1 = \Delta_2 = 10$ (Fig. 2A-B), 17 (Fig. 2C-D) and 22 (Fig. 2E-F) ms with a 2q-value of 1090 cm^{-1}. For Δ = 22 ms, the number of averages was 250**.** For the brain shown in Fig. 3 the following parameters were used: $\delta_1 = \delta_2 = 4$ ms, $|G_1| = |G_2| = 320$ mT/m, resulting in the 2q-values of 1090 cm^{-1}, $\Delta_1 = \Delta_2 = 17$ ms, the TR/TE of 2800/71 ms was used with 125 averages, G_1 and G_2 were X,X-Y (Fig. 3A-B), X,X-Z (Fig. 3C-D) and Y,Y-Z (Fig. 3E-F).

Results and Discussion: Fig. 1 shows aE and φ_{sym} maps obtained from angular d-PGSE experiments in three different 2q-values. Clearly, when the diffusion weighting is higher, more details are observed in the aE maps, in WM as well as GM regions. However, the φ_{sym} maps remain very similar throughout the different q values. Fig. 2 shows aE and φ_{sym} maps conducted with different diffusion times. Clearly, the aE increases with diffusion time, but the φ_{sym} remains almost without change. However, Fig. 2 shows also that a diffusion time of 10 ms seems to be sufficient for the distinction between different brain structures such as cortex, corpus callosum and striatum. Fig. 3 shows aE and φ_{sym} maps obtained from angular d-PFG MRI experiments performed in three different planes which were determined by varying the orientation of the second gradient pair. Clearly, each of the planes shows different microstructural information in both maps. This shows the strong orientation dependency of these parameters, emphasizing the need for a three dimensional non-variant acquisition scheme. We also found that aE and φ_{sym} maps are very similar when the mixing time is varied between 5 and 28 ms.

Conclusion: These results show that angular d-PGSE MRI performed with a long t_m, provide a mean to distinguish between compartments with different eccentricities under a wide range of experimental conditions making such experiments clearly feasible in vivo.

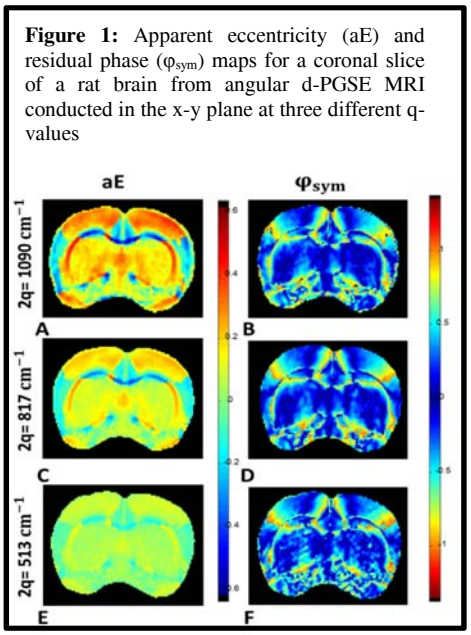

Figure 1: Apparent eccentricity (aE) and residual phase (φ_{sym}) maps for a coronal slice of a rat brain from angular d-PGSE MRI conducted in the x-y plane at three different q-values

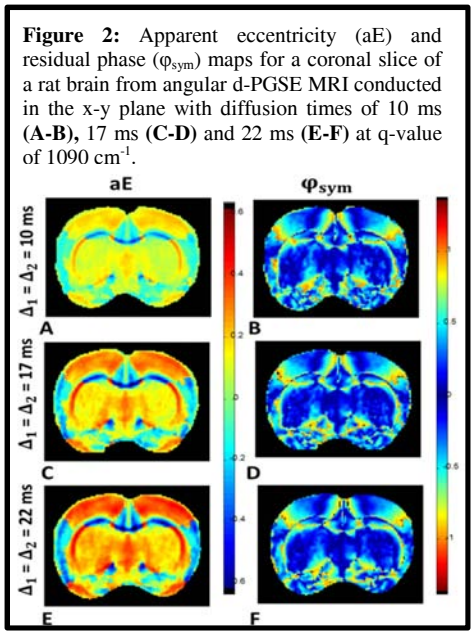

Figure 2: Apparent eccentricity (aE) and residual phase (φ_{sym}) maps for a coronal slice of a rat brain from angular d-PGSE MRI conducted in the x-y plane with diffusion times of 10 ms **(A-B),** 17 ms **(C-D)** and 22 ms **(E-F)** at q-value of 1090 cm^{-1}.

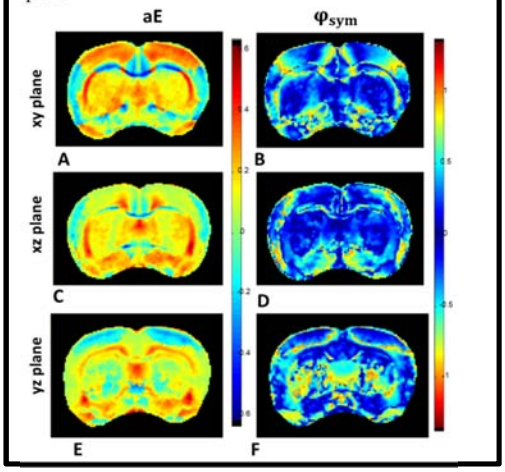

Figure 3: Apparent eccentricity (aE) and residual phase (φ_{sym}) maps for a coronal slice of a rat brain from angular d-PGSE MRI performed in three different planes which were determined by varying the orientation of the second gradient pair.

References: **[1]** D.G. Cory et al., Polymer Preprints, 3,149-150 **(1990)**. **[2]** P.P. Mitra, Phys. Rev. B, 51 15074–15078 **(1995)**. **[3]** Komlosh M.E. et al., NeuroImage, 78, 210-216 (2013). **[4]** Lawrenz M. et al., Magn. Reson. Med., 69, 1072-1082 (2013). **[5]** N. Shemesh et al, NMR in Biomed., 23, 757-780 **(2010)**. **[6]** E. Özarslan, J. Magn .Reson, 199, 56-67 **(2009)**. **[7]** N. Shemesh el al, Magn. Reson. Med. 68, 794–806 **(2012).**