# Angular Double-PGSE spectroscopy of the Long Evans Shaker spinal cord

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**Introduction.** Conventional single-Pulsed-Field-Gradient (s-PFG) methodologies like diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI) are capable of faithfully depicting diffusion anisotropy in coherently ordered structures, providing important microstructural information. However, it is more difficult to characterize randomly oriented compartments using conventional s-PFG MR. In this case, diffusion is anisotropic on a microscopic scale but macroscopically, diffusion appears isotropic. Double-PFG (d-PFG) MR methodologies [1,2] were recently suggested as an alternative for studying microstructure in CNS [3-5]. The angular d-PFG is an experiment in which the angle $\psi$ is varied at a given q-value, while all of the other parameters are kept constant. These experiments yield an angular dependence $E(\psi)$, that resembles a bell-shaped function, from which the compartment size could be extracted even at low q-values but only for restricted, non-gaussian diffusion. For randomly oriented anisotropic compartments, this methodology, at a finite mixing time, could differentiate between spherical and nonspherical compartments [3-5]. This suggests that angular d-PFG may offer novel microstructural information that is not available from s-PFG. In the present study we used the angular d-PFG MRS to characterize the microstructure of the Long Evans Shaker (*les*) and their age-matched controls.

**Methods.** MR experiments were performed using an 8.4T NMR spectrometer (Bruker, Germany) equipped with a micro5 imaging gradient probe capable of producing pulsed gradients of up to 190 gauss $cm^{-1}$ in each of the three directions. Formalin-fixed spinal cords of 20, 33 and 180 days old *les* and their age matched control rats were used in this study. Angular bp-d-PFG experiments were conducted in the X-Y plane, when the fiber direction was aligned parallel to the $B_0$ direction (z direction) of the magnet. The first pair of gradient pulses ($G_1$) was set in the x direction and the orientation of the second gradient pair ($G_2$) was varied along 25 different values of $\psi$. The following parameters were used: Six different 2q-values (ranging between 393-2043 $cm^{-1}$), three different mixing times (0, 30 and 70 ms), $G_1max = G_2max = 80$ G/cm, $\delta_1 = \delta_2 = \delta_3 = 3$ ms and $\Delta_1 = \Delta_2 = 100$ ms.

**Results and discussion.** Figure 1 depicts a comparison between normalized $E(\psi)$ profiles of three different mixing times in all six q-values examined, in a 180 days old control rat. At $t_m$=0 ms, a bell-shaped function was found, indicative of microscopic anisotropy. As the q-value was increased, the bell function was more pronounced. At longer $t_m$s, however, the $E(\psi)$ profiles showed a $\cos(2\psi)$-like modulation which was also more pronounced at higher q-values. Interestingly, this modulation seems to represent mostly randomly oriented compartments. Figure 2 depicts, for comparison, the same data but for a 180 days old *les* spinal cord. Here, the bell shaped functions which were found with $t_m$=0 ms in the control, are very weak. Only a $\cos(2\psi)$-like modulation is observed in the *les* spinal cord at finite $t_m$s. These observations are consistent with much less restricted diffusion and a more isotropic morphology. This suggests that angular d-PFG experiments provide specific signatures for the control and *les* spinal cords and may provide a means for differentiating between the two groups.

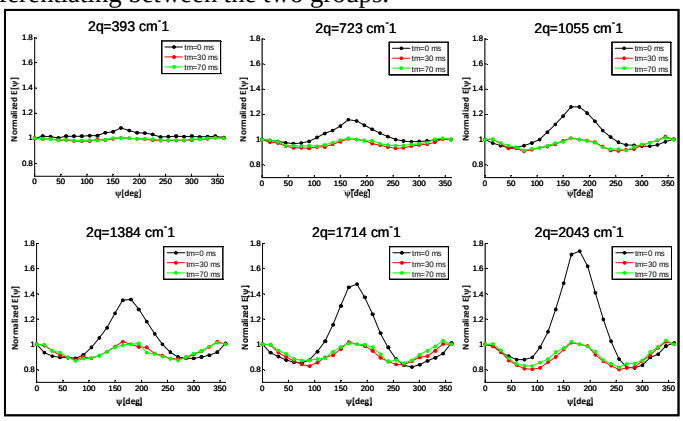


***Figure 1***

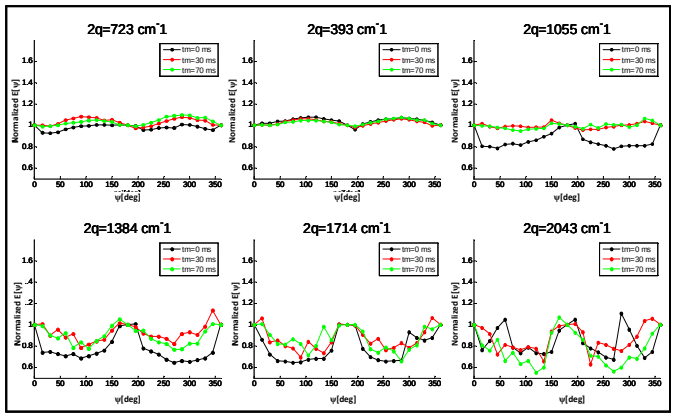


***Figure 2***

**Summary.** This study shows that d-PFG MR is a method that may be used to distinguish between control and *les* spinal cords. The angular d-PFG MR experiment offers specific signatures for the different tissue microstructures and may potentially provide, after appropriate modeling, accurate size measurements in such systems even at relatively low q-values. Angular d-PFG MR conducted in different $t_m$s may provide information on microscopic anisotropy and compartment shape anisotropy in randomly oriented systems.

**References.** [1] Mitra PP. Physical Review B, 1995; 51: 15074-15078 [2] Özarslan E., J. Magn. Reson., 2009; 199: 56-67 [3] Shemesh N. et al. NMR in Biomed, 2010; 23: 757-780 [4] Koch M., Finsterbusch J. NMR in Biomed, 2011; 24: 1422-1432 [5] Shemesh N., Cohen Y. Magn. Reson. Med., 2011; 65: 1216-1227