Diffusion-diffusion Exchange Spectroscopic Imaging (DEXSI) MRI in a rat corpus callosum

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Introduction: The permeability of membranes within tissue microstructure is abnormal in a number of pathologies, for example in cancer[1] and stroke[2]. We adapt the Diffusion-diffusion Exchange Spectroscopy (DEXSY)[3,4] NMR technique for MRI biological samples to quantify permeability. Previous studies that estimate permeability have adapted the Karger framework[5] using biophysical models of tissue. An alternative, phenomenological approach, Filter Exchange Imaging (FEXI) has been used to quantify permeability in the human brain[5]. The FEXI study assumed a two site system and that the rate of exchange between sites was mono-exponential. A recent study suggests white matter can be better described by at least three compartments[6]. Diffusion-diffusion exchange techniques are inherently able to detect multiple diffusivities and thus the exchange of water between them. We demonstrate the first use of diffusion-diffusion exchange spectroscopy in an imaging application and, furthermore, the first use with biological tissue.

Methods: The DEXSI pulse sequence is shown in Fig 1. For this study, a single spin-echo readout was used and implemented on a 9.4T Agilent small bore scanner equipped with 1T/m gradients and 26mm r.f. volume coil. Diffusion gradients were aligned perpendicular to axonal fibres in the mid-saggital slice of the corpus callosum. 16x16 steps of G1 and G2 were taken (256 measurements in total). Parameters were: δ=5ms, Δ=10ms, G_1=0 to 0.7 T/m, G_2=0 to 0.7 T/m, TM = 200ms, TE was minimized, 12x24mm FoV, 128x128 matrix. A rat brain was perfused fixed and immersion fixed for 1 week in 4% aqueous formaldehyde from paraformaldehyde, then immersed in phosphate buffer solution for 1 week. The sample was immersed in perfluorosolv PFS-1 (Solvay Solexis) prior to scanning. Temperature was maintained at 18°C throughout the experiment. 2D diffusion spectra were generated using 2D inverse Laplace transform software[7].

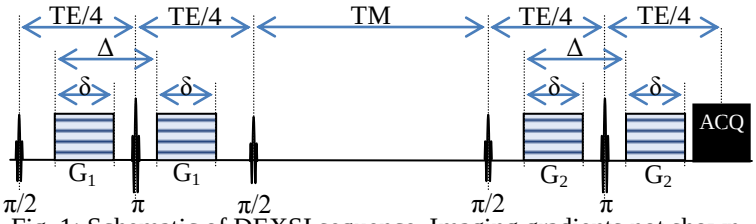

Fig. 1: Schematic of DEXSI sequence. Imaging gradients not shown.


Fig. 2: Unweighted image of mid-sagittal slice

Results: An unweighted image of the mid-sagittal slice and 2D diffusion spectra of the corpus callosum are shown in Fig. 2&3 respectively. Peaks in the 2D diffusion spectrum are seen at (D_1,D_2) ~ (3,3) and (2.5,0.4) x10^{-10}m^2/s. There are also corresponding peaks with very low diffusion constants.

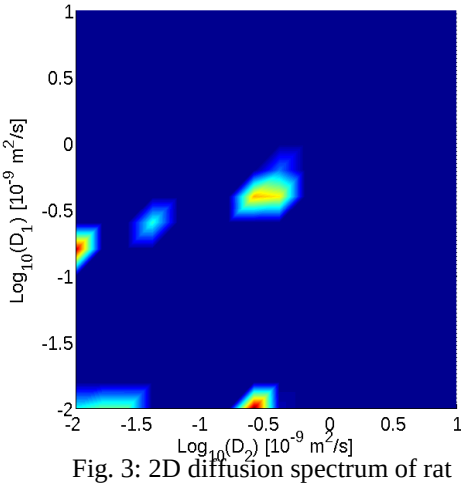

Fig. 3: 2D diffusion spectrum of rat corpus callosum

Discussion: For the first time we have applied diffusion-diffusion exchange spectroscopy in an imaging application in biological tissue. Diffusion constants are consistent with fixed tissue at room temperature[8]. Future work will decrease total acquisition time by fast imaging and optimising the diffusion protocol[9].

References: 1. Lätt J et al. NMR Biomed 22: 619–628 **2.** Nilsson M et al. Magn Reson Med, 69: 1572–1580 **3.** Qiao Y et al. J Chem Phys 122:214912 **4.** Hubbard PL et al. J Phys Chem B 110, 20781-20788. **5.** Kärger J, Adv Coll Interf Sci 23, 129–148 **6.** Panagiotaki E et al. Neuroimage 59(3), 2241-2254 **7.** Godefroy S, Ryland B and Callaghan PT, Victoria University of Wellington, Wellington, New Zealand. Provided courtesy of Petrik Galvosas. **8.** Alexander DC et al. NeuroImage 52, 1374–1389. **9.** Alexander DC, Magn Reson Med 60, 439–448.