

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 cancer¹ and stroke². 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 framework⁵ using biophysical models of tissue. An alternative, phenomenological approach, Filter Exchange Imaging (FEXI) has been used to quantify permeability in the human brain⁵. 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 compartments⁶. 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

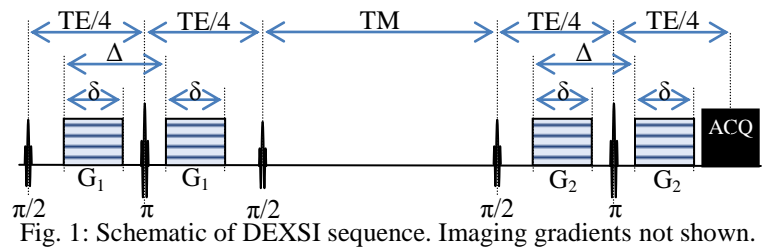


Fig. 1: Schematic of DEXSI sequence. Imaging gradients not shown.

perpendicular to axonal fibres in the mid-sagittal slice of the corpus callosum. 16x16 steps of G1 and G2 were taken (256 measurements in total). Parameters were: $\delta=5\text{ms}$, $\Delta=10\text{ms}$, $G_1=0$ to 0.7 T/m, $G_2=0$ to 0.7 T/m, $TM = 200\text{ms}$, 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 software⁷.

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 $(D_1, D_2) \sim (3,3)$ and $(2.5,0.4) \times 10^{-10} \text{m}^2/\text{s}$. There are also corresponding peaks with very low diffusion constants.

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 temperature⁸. Future work will decrease total acquisition time by fast imaging and optimising the diffusion protocol⁹.

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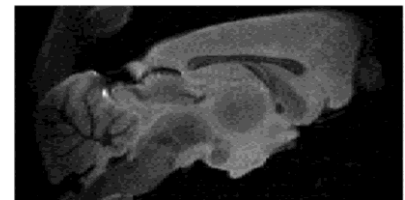


Fig. 2: Unweighted image of mid-sagittal slice

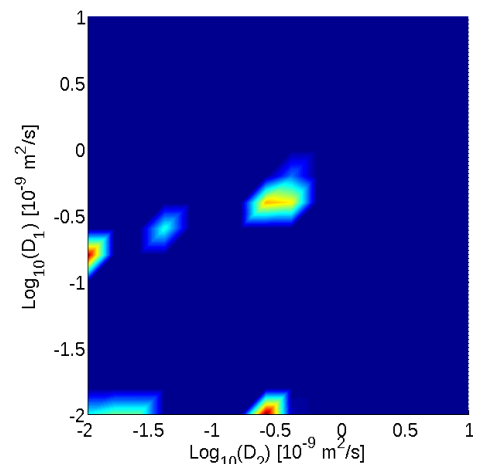


Fig. 3: 2D diffusion spectrum of rat corpus callosum