DISTINGUISHING RESTRICTED DIFFUSION AND FLOW USING PULSED AND OSCILLATING DIFFUSION GRADIENTS AT 1.5 T

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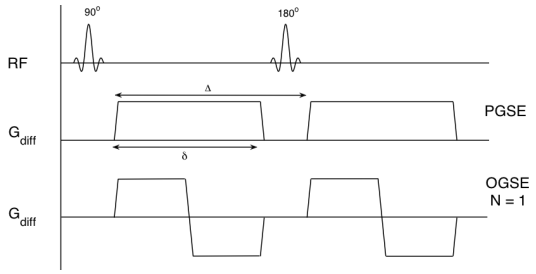
Introduction: Measurements of the time-dependent diffusion coefficient *in vivo* provide sensitivity to diffusion over a range of length scales, and can be used to probe tissue microstructure [1,2]. In particular, it has been shown that such time-dependence has the potential to distinguish between restricted diffusion and flow [3]. The former is characterised by an increase in diffusivity at shorter diffusion times as fewer structures are encountered and diffusion is less restricted [3]; in contrast, flow exhibits a 'diffusivity' proportional to the diffusion time as the motion remains coherent over the diffusion time [4]. Here we present preliminary results of using PGSE sequences with different effective diffusion times (Δ - δ/3), as well as an oscillating gradient spin-echo (OGSE) sequence to reach a shorter diffusion time, to look for evidence of restricted diffusion and a time-dependent flow component in the human liver.



Sequence, Δ - δ/3 (ms)	δ (ms)	Δ (ms)
PGSE (48)	6.0	50
PGSE (36)	15	41
PGSE (26)	22	34
OGSE (f = 43 Hz)	22	34

Fig 1. Pulse sequence diagram and parameters

Method: The livers of two healthy volunteers (one female aged 26 and one male aged 23) were imaged using a Philips 1.5 T Intera system (Philips Healthcare, Best, The Netherlands). PGSE sequences with effective diffusion times of 48, 36 and 26 ms were performed, along with a single-oscillation trapezoidal OGSE sequence at 43 Hz, corresponding to an approximate effective diffusion time of 16 ms (estimated as in [5]). For all sequences the gradient rise time was 0.9 ms, and a maximum gradient strength of 61.7 mT/m was achieved by using three orthogonal diffusion gradients simultaneously, measuring diffusion along one direction. Images were acquired at b = 0, 150, 500 s/mm^2 for each sequence with TR = 6000 ms, TE = 69 ms, FOV = 375 x 281 mm^2, matrix = 128 x 128, slice thickness = 8 mm and 4 signal averages. Maps of the apparent diffusion coefficient (ADC) were calculated using voxel-wise signal intensities from the b = 150 and 500 s/mm^2 images assuming a mono-exponential decay, providing measurements of flow-insensitive diffusivity at each diffusion time [6]. With diffusion measurements in the liver being sensitive to perfusion at b-values lower than 150 s/mm^2 [6], maps of perfusion-sensitive 'pseudo-diffusion' were produced for each diffusion time by using voxel-wise signal intensities from the b = 0 and 150 s/mm^2 images and assuming a mono-exponential decay. A region of interest (ROI) in the right lobe was drawn on a single slice b = 0 s/mm^2 image for each diffusion time, allowing mean ADC and mean perfusion-sensitive diffusivity values to be calculated.

Results and discussion: Figure 2 shows mean ADC (blue) and mean perfusion-sensitive diffusivity (red) as a function of effective diffusion time for both subjects, with error bars showing the standard deviation over the ROI. For both subjects we can see a trend of increasing ADC as shorter diffusion times are probed, providing evidence of restricted diffusion with fewer hindrances to diffusion encountered as the diffusion time is reduced. Conversely, for the perfusion-sensitive measurements we can see for both subjects a trend of decreasing diffusivity as the diffusion time is reduced, characteristic of what Callaghan terms stationary random flow [4]. The larger error bars on the flow measurements are likely to reflect the inclusion in the ROI of some voxels which do not contain a flow component, where it is the lower true diffusion coefficient which is measured instead. The results also indicate that as the diffusion time is reduced, the diffusivities measured by the two fits converge towards the true underlying diffusion coefficient, suggesting that short diffusion times suppress the sensitivity to perfusion. Probing the diffusion-perfusion relationship may therefore be a further application of clinical OGSE sequences, in addition to their utility for probing small-scale restrictions to diffusion.

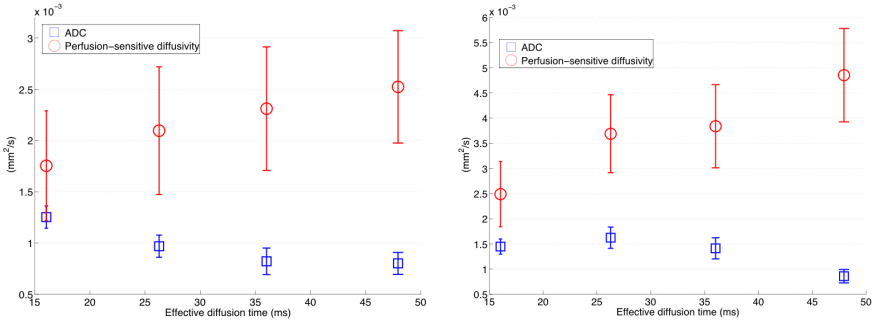


Fig 2. ADC and flow-sensitive diffusivity as a function of effective diffusion time for two subjects.

These results provide, to the best of our knowledge, the first measurements utilising the time-dependent diffusivity to distinguish between restricted diffusion and flow in humans, as well as the use of OGSE sequences at low field strength to reduce the effective diffusion time. Measurements of the time-dependent diffusion coefficient have been shown to provide information about cellular size [2], with the results presented here showing that information about perfusion can also be obtained from similar measurements. Such techniques may therefore have application in studying healthy or pathological tissues where features such as cellular size and density as well as perfusion are of interest.

References: 1. Latour et al. *Proc. Natl. Acad. Sci.* 91:1229-1233, 1994. **2.** Fieremans et al. *Proc. Intl. Soc. Magn. Reson. Med.* 19:1153, 2011. **3.** Parsons et al. *Magn. Reson. Im.* 21:279-285, 2003. **4.** Callaghan, Principles of Nuclear Magnetic Resonance Microscopy, OUP, New York, 1991. **5.** Does et al. *Magn. Reson. Med.* 49:206-125, 2003. **6.** Koh et al. *Eur. Radiol.* 16:1898-1905, 2006. **Acknowledgements:** AstraZeneca and MRC for funding.