Probing tissue microstructure using oscillating diffusion gradients in the human calf

D. J. McHugh[1,2], P. L. Hubbard[1,2], S. Zhao[1,2], D. M. Higgins[3], G. J. Parker[1,2], and J. H. Naish[1,2]
[1]Imaging Sciences and Biomedical Engineering, University of Manchester, Manchester, United Kingdom, [2]The University of Manchester Biomedical Imaging Institute, Manchester, United Kingdom, [3]Philips Healthcare, Guildford, United Kingdom

Introduction: We present preliminary results of using diffusion MRI with oscillating gradient spin-echo (OGSE) sequences to measure the apparent diffusion coefficient (ADC) in human calf muscle as a function of effective diffusion time, Δ_e, on a clinical scanner. OGSE sequences have been shown to be sensitive to small-scale restrictions to diffusion in samples of packed beads [1] and to microstructure in the human brain [2] and rat brain, probing length scales shorter than single cell diameters [3,4]. Our approach provides, to the best of our knowledge, the first use of OGSE sequences as a probe of human tissue microstructure outside of the brain, using trapezoidal gradient waveforms similar to optimisations in [5] to look for evidence of restricted diffusion perpendicular to calf muscle fibres.

Method: The left legs of two subjects (one male aged 34 and one female aged 33) were imaged using a SENSE knee coil with a clinical 3 T Philips Achieva system. Trapezoidal gradients with N = 0,1,2,3,4,5 oscillations were used, where N = 0 corresponds to a standard PGSE sequence with Δ_e = 39.7 ms. Keeping the duration of each gradient pulse constant for all N, the effective diffusion time decreased with increasing N as the period of each oscillation decreased (as shown in Figure 1); oscillation frequency ranged from 23.2 to 116 Hz. The effective diffusion times in our sequences were defined by comparison with PGSE sequences, as in [4]. Gradient rise time was 0.9 ms and a maximum gradient strength of 70 mT/m enabled us to maintain a sufficient degree of diffusion weighting even with the shortest diffusion times. Images were acquired at 3 b values for each N, with b = 0, 50 and 600 s/mm^2 for N = 0,1,2 and the high b value changing to 424, 220 and 129 for N = 3,4,5 respectively (TR 3200 ms, TE 110 ms, FOV 180 mm x 180 mm, matrix 128 x 128). ADC maps were generated using the b = 50 s/mm^2 and high b value images for each N, avoiding the risk of perfusion effects in muscle for $b < 50$ s/mm^2, as reported in [6] and suggested by analysis of a standard multi-b value PGSE acquisition in the current study. Regions of interest (ROIs) corresponding to the medial and lateral gastrocnemii and the soleus muscle were drawn on four slices, with mean ADC values calculated for each N. Results were averaged over medial and lateral gastrocnemii because of their similar fibre composition: both have roughly an equal number of slow Type I and fast Type II fibres; in contrast the soleus muscle is composed primarily of Type I [7].

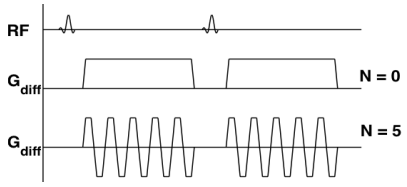

Fig 1. Comparison of diffusion gradients for PGSE (N = 0) and our highest frequency oscillation (N = 5).

Results and discussion: Figure 2 shows ADC as a function of effective diffusion time for each subject's gastrocnemii (averaged over medial and lateral) and soleus muscle (error bars show standard errors). The results in the gastrocnemii ROIs for both subjects show a general trend of increasing ADC with decreasing diffusion time, indicating less restricted diffusion as smaller length scales are probed. Qualitatively, a similar overall trend was observed in both subjects' gastrocnemii, characterised by an initial sharp rise in ADC between the two longest diffusion times (corresponding to N = 0 and N = 1) as well as a sharp rise at the shortest diffusion times. The general trend of increasing ADC with decreasing diffusion time (or, equivalently, with increasing frequency) is also seen in the soleus muscle for both subjects. The differences observed between ADC as a function of effective diffusion time in the gastrocnemii and in the soleus are likely to be due to the restrictive structures within the distinct muscle fibres, as the length scales probed with our oscillation frequencies are estimated to be between 6 and 14 μm, shorter than the mean muscle fibre diameters of between 48 and 66 μm in the gastrocnemii and between 66 and 71 μm in the soleus as measured in [8]. These intra-fibre restrictive structures could be expected to differ between the two muscle groups due to their differing composition in terms of Type I and Type II fibres, and this difference in structure may contribute to the differences observed in ADC as a function of effective diffusion time for each muscle group.

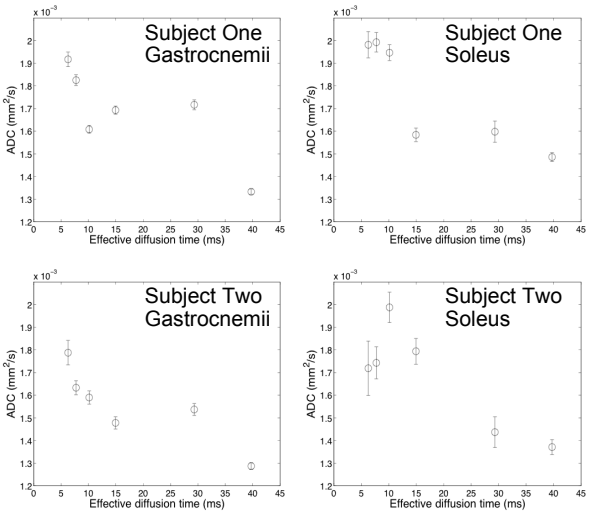

Fig 2. Top: ADC vs. effective diffusion time for subject one's gastrocnemii (left) and soleus (right). Bottom: ADC vs. effective diffusion time for subject two's gastrocnemii (left) and soleus (right).

This study provides the first use of oscillating gradients to probe the microstructure of human tissue outside the brain using a clinical scanner. We demonstrate increased ADC with decreasing effective diffusion time, as demonstrated pre-clinically in [3,4]. These results suggest the feasibility of using optimised OGSE sequences as sensitive probes of non-neural tissue microstructure in humans, with the potential for reaching shorter diffusion times and probing smaller length scales if higher gradient strengths are employed. Such techniques have applications in the study of pathological states, for instance understanding cell packing in tumours, as well as in making ADC a more specific measure of diffusion by differentiating between its various microstructural contributions.

References: 1. Schachter *et al. J. Magn. Reson.* 147: 232-237, 2000. **2.** Hosey *et al. Proc. Intl. Soc. Mag. Reson. Med.* 11: 2123, 2003. **3.** Colvin *et al. Cancer Res.* 68: 5941-5947, 2008. **4.** Does *et al. Magn. Reson. Med*. 49: 206-125, 2003. **5.** Drobnjak *et al. J. Magn. Reson.* 206: 41-51, 2010. **6.** Yanagisawa *et al. Magn Reson Imag.* 27: 69-78, 2009. **7.** Widrick *et al. J. Appl. Physiol.* 90: 2203-2211, 2001. **8.** Polgar *et al. J. Neurol. Sci.* 19: 307-318, 1973.