Speciality area: Advanced Diffusion Acquisition

Speaker name: Ivana Drobnjak, University College London, i.drobnjak@ucl.ac.uk

Highlights:

- Oscillating gradient spin-echo (OGSE) acquisition enables a wide range of effective diffusion times by varying the frequency of its diffusion gradient waveform.
- OGSE acquisitions with varying frequencies measure the time dependance of the apparent diffusion coefficient (ADC) providing an insight into biological micro-environment.
- By providing access to short effective diffusion times, OGSE observes the onset of diffusion restrictions and can access very small micro-structural features such as intracellular properties, cellular size or surface-to-volume ratio.

Title: Oscillating Gradient Acquisition

Target Audience: Scientists and researchers who are familiar with basic diffusion MRI methodology and want to probe tissue microstructure in finer detail than possible with standard PGSE methods.

Outcome: Following this lecture, audience members should be able to understand the basic concept of oscillating gradients acquisition and how they can be used to characterise tissue structure at varying length scales.

Purpose: Imaging microstructural features of tissue can be of extreme importance in clinical applications, e.g. mapping axon radius in the brain affects nerve function and could provide insight into neuronal diseases; mapping cellular nuclear sizes could potentially characterize tumor progression; etc. In order to probe such small length scales most informatively, it is extremely promising to employ oscillating gradient approach, which provides access to short effective diffusion times. In this lecture we will introduce oscillating gradient acquisitions and demonstrate their ability to map microstructural parameters in biological tissue.

Methods: The apparent diffusion coefficient (ADC) depends on the effective diffusion time (observation time during which molecules are allowed to diffuse)[1]. In free diffusion ADC does not change with time and is equal to the intrinsic diffusivity, however once the spins start interacting with restrictions, ADC decreases and becomes time-dependent. Measuring this dependence can give an insight into the microstructure of biological tissues, e.g. surface-to-volume ratio [2]. This is not usually practical using standard pulsed gradient spin-echo (PGSE) methods because extremely strong gradients are needed to produce measurable diffusion attenuation for short effective diffusion times. Oscillating-gradient acquisitions, on the other hand, at higher frequencies can probe very short effective diffusion times and are hence capable of detecting restrictions to diffusion displacements over very small spatial scale i.e. sub-cellular level, thereby resulting in a greater sensitivity of the measured ADC [3].

A convenient framework for analysing OGSE method is Temporal Diffusion Spectroscopy in which the diffusion spectrum $D(\omega)$ is frequency dependent [4, 5, 3]. $D(\omega)$ is a a Fourier transform of a velocity auto-correlation function and hence its shape can provide unique information on the

microstructure of the sample. Appropriately designed oscillating-gradient waveforms can be used to sample $D(\omega)$ at well-defined frequencies and, by changing this frequency, the shape of $D(\omega)$ can be determined.

Above theory for measuring the time-dependent diffusion coefficients is very important in cases when we do not have any a-priori knowledge of the underlying restricted geometry. In cases when the a-priori model of restriction is known, the appropriate diffusion propagator is used to analyse the attenuation data and the estimated diffusion coefficient is not time-dependent. However, even in these cases, the optimisation results suggest that the use of the OGSE sequence in the acquisition protocol enhanced the sensitivity to microstructure parameter estimates such as axon diameter in the white matter [6, 7, 8, 9].

Results: Desirable diffusion gradient waveforms should have a narrow non-zero gradient power spectra peak in order to probe the diffusion spectrum precisely. For that purpose, cosine-OGSE and cosine-trapezoidal-OGSE have been found to be the most optimal waveforms [10, 11]. OGSE method has been applied for estimating ADC in beads in water [12], cancer tissue [13], rat brain [14, 15], and in-vivo human brain [16, 17]. OGSE use in model-based approach [4, 18, 11, 7] together with the interpretation of the optimisation results for estimating axon-diameter will be discussed as well.

Discussion: In practice, high frequency OGSE sequences are somewhat limited on human scanners with low gradient amplitudes. As the frequency of gradient modulation increases, the b-value decreases, so in order to keep echo times reasonable, the gradient amplitude must increase. This can potentially limit the extent to which we can sample the diffusion coefficients. However, OGSE sequences at even moderate frequencies can detect restricted diffusion over a spatial scale much smaller than the diameter of a single cell, thereby resulting in a greater sensitivity to the measured ADC [3].

Conclusion: Oscillating gradient acquisitions can selectively probe restricted diffusion environments using an extensive range of effective diffusion times. Hence, they can be used to produce much finer details of biological tissue microstructure compared to the standard PGSE method.

References

[1] W. S. Price, NMR Studies of Translational Motion, Principles and Applications, Cambridge University Press, 2009.

[2] L. L. Latour, P. P. Mitra, R. L. Kleinberg, C. H. Sotak, Time-Dependent Diffusion Coefficient of Fluids in Porous Media as a Probe of Surface-to-Volume Ratio, Journal of Magnetic Resonance, Series A 101 (3) (1993) 342–346.

[3] J. C. Gore, J. Xu, D. C. Colvin, T. E. Yankeelov, E. C. Parsons, M. D. Does, Characterization of tissue structure at varying length scales using temporal diffusion spectroscopy., NMR in Biomedicine 23 (7) (2010) 745–756.

[4] J. Stepisnik, Time-dependent self-diffusion by NMR spin-echo, Physica B: Condensed Matter 183 (4) (1993) 343–350.

[5] P. T. Callaghan, Translational Dynamics and Magnetic Resonance: Principles of Pulsed Gradient Spin Echo NMR, Oxford University Press, 2011.

[6] I. Drobnjak, B. Siow, D. C. Alexander, Optimizing gradient waveforms for microstructure sensitivity in diffusion-weighted MR., Journal of magnetic resonance (San Diego, Calif : 1997) 206 (1) (2010) 41–51.

[7] I. Drobnjak, D. C. Alexander, Optimising time-varying gradient orientation for microstructure sensitivity in diffusion-weighted MR., Journal of magnetic resonance (San Diego, Calif : 1997) 212 (2) (2011) 344–354.

[8] I. Drobnjak, G. Cruz, D. C. Alexander, Optimising oscillating waveform-shape for pore size sensitivity in diffusion-weighted MR, Microporous and Mesoporous Materials 178 (2013) 11–14.

[9] B. Siow, I. Drobnjak, A. Chatterjee, M. F. Lythgoe, D. C. Alexander, Estimation of pore size in a microstructure phantom using the optimised gradient waveform diffusion weighted NMR sequence, Journal of magnetic resonance (San Diego, Calif : 1997) 214 (2012) 51–60.

[10] E. C. Parsons, M. D. Does, J. C. Gore, Modified oscillating gradient pulses for direct sampling of the diffusion spectrum suitable for imaging sequences, Magnetic Resonance Imaging 21 (2003) 279–285.

[11] A. Ianus, B. Siow, I. Drobnjak, H. Zhang, D. C. Alexander, Gaussian phase distribution approximations for oscillating gradient spin echo diffusion MRI., Journal of magnetic resonance (San Diego, Calif : 1997) 227 (2013) 25–34.

[12] M. Schachter, M. Does, A. Anderson, J. Gore, Measurements of restricted diffusion using an oscillating gradient spin-echo sequence, Journal of magnetic resonance (San Diego, Calif : 1997) 147 (2) (2000) 232–237.

[13] J. Xu, M. Does, J. Gore, Sensitivity of MR diffusion measurements to variations in intracellular structure: Effects of nuclear size, Magnetic Resonance in Medicine 61 (2009) 828–833.

[14] M. Aggarwal, M. V. Jones, P. A. Calabresi, S. Mori, J. Zhang, Probing mouse brain microstructure using oscillating gradient diffusion MRI, Magnetic Resonance in Medicine 67 (1) (2011) 98–109.

[15] J. Kershaw, C. Leuze, I. Aoki, T. Obata, I. Kanno, H. Ito, Y. Yamaguchi, H. Handa, Systematic changes to the apparent diffusion tensor of in vivo rat brain measured with an oscillating-gradient spin-echo sequence, NeuroImage 70 (2013) 10–20.

[16] A. T. Van, S. J. Holdsworth, R. Bammer, In vivo investigation of restricted diffusion in the human brain with optimized oscillating diffusion gradient encoding, Magnetic Resonance in Medicine 71 (2014) 83–94.

[17] C. A. Baron, C. Beaulieu, Oscillating Gradient Spin-Echo (OGSE) diffusion tensor imaging of the human brain., Magnetic Resonance in Medicine.

[18] J. Xu, M. Does, J. Gore, Quantitative characterization of tissue microstructure with temporal diffusion spectroscopy, Journal of magnetic resonance (San Diego, Calif : 1997) 200 (2009) 189–197.