

## Speciality area: Diffusion Goes Mad

**Speaker Name:** Gareth J Barker, Gareth.Barker@kcl.ac.uk

### Highlights

- Water molecules, whether in a glass of water or in the brain, undergo a random motion known as diffusion; MR sequences can be sensitised to this, allowing diffusion to be quantified.
- In the brain, diffusion values differ depending on the direction in which they are measured, providing an insight into tissue structure.
- The *Diffusion Tensor* is the simplest description of the three dimensional diffusion process; many useful indices can be extracted from it, but these can sometimes be misleading, as the tensor model is not able to fully encapsulate all the complexity of brain tissue.

## From Diffusion Weighting to the Diffusion Tensor Indices

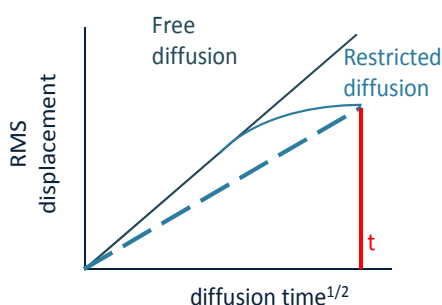
**TARGET AUDIENCE:** Physicists/technologists/clinicians who wish to understand the basics concepts of diffusion weighted imaging in general, and diffusion tensor imaging (DTI) in particular.

**OBJECTIVES:** Following this lecture, audience members should be able to:

- Discuss the basic concept of diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI)
- Recognise the limitations of DTI and the need for more complex diffusion models

**PURPOSE:** To provide the information necessary to allow audience members to appraise the applicability of DWI and DTI, and to apply them appropriately in their own clinical or research work.

**METHODS:** In a liquid, collisions between molecules lead to any particular molecule undergoing a 'random walk', with its mean square displacement from its initial position increasing with time according to  $r.m.s = \sqrt{\langle r^2 \rangle} = \sqrt{6Dt}$ , where D is the diffusion coefficient. (Einstein's equation). In an MR experiment, this motion leads to a loss of signal in the presence of magnetic field gradients given by  $S = S_0 e^{-bD}$ , where b is a function of the applied gradient strength, and duration and separation. For a simple "Stejskal Tanner pulsed field gradient" experiment<sup>i</sup>, in which identical diffusion encoding gradients (of amplitude G, duration  $\delta$  and separation  $\Delta$ ) are placed on either side of the 180° pulse of a spin echo pulse sequence,  $b = (\gamma G \delta)^2 (\Delta - \delta/3)$ . Diffusion weighted imaging (DWI) applies such diffusion weighting gradients to make image contrast sensitive to the mobility of water (in addition to the inherent T<sub>2</sub> weighting caused by the necessarily long echo time); this contrast may be of particularly useful in imaging of stroke<sup>ii</sup>, where vasogenic oedema leads to restricted diffusion and thus high signal on DWI<sup>iii</sup>.



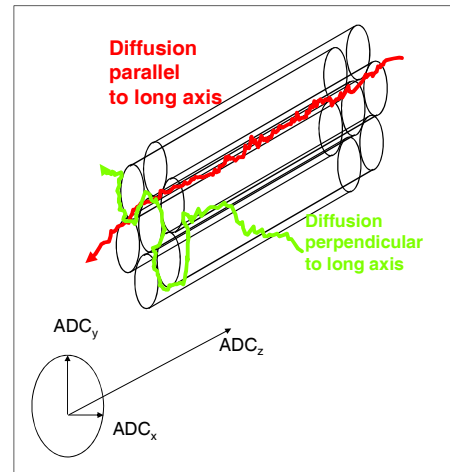
The Einstein equation assumes that diffusion is free or unhindered, but if diffusion is restricted or hindered (as is always the case in tissue, due to cell membranes and other structures, Einstein's equation is not valid anymore and changing the observation time (diffusion time) can change value that we measure for D. Despite this, we conventionally still estimate r.m.s displacement at a time t

(from the degree of signal loss), and calculate D from slope of curve. We refer to this (inherently underestimated) value as the *Apparent Diffusion Coefficient (ADC)*.

In a test tube, diffusion is largely isotropic, and is characterised by a single diffusion constant; in the brain diffusion may be anisotropic, as barriers to diffusion (e.g. axon walls and cellular microstructures) are oriented, and the system is characterised by different ADCs in different directions.

The simplest description is then given by the diffusion tensor:

$$\begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix}$$



The tensor can be diagonalised such that the *eigenvalues* of the tensor ( $\lambda_1, \lambda_2, \lambda_3$ ) describe the degree of diffusion along three perpendicular axes, while the *eigenvectors* ( $\epsilon_1, \epsilon_2, \epsilon_3$ ) indicate the orientation of these axes relative to the magnet coordinates.

$$\mathbf{D} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix} \begin{pmatrix} \epsilon_1 \\ \epsilon_2 \\ \epsilon_3 \end{pmatrix}$$

highest  
↑  
lowest

From tensor, various rotational invariant parameters can be calculated, describing the degree of diffusion:

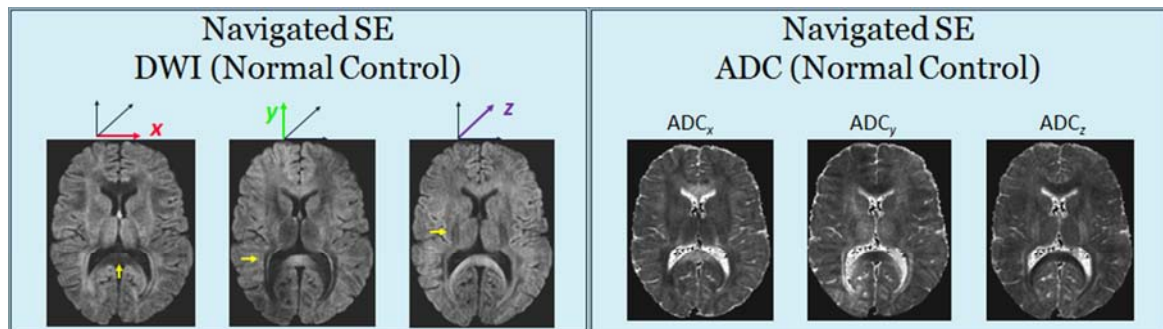
- mean diffusivity
- Trace =  $\lambda_1 + \lambda_2 + \lambda_3 = 3 * \text{ADC}_{\text{mean}}$
- axial diffusivity =  $\lambda_1$
- radial diffusivity =  $(\lambda_2 + \lambda_3) / 2$

... and how anisotropic it is:

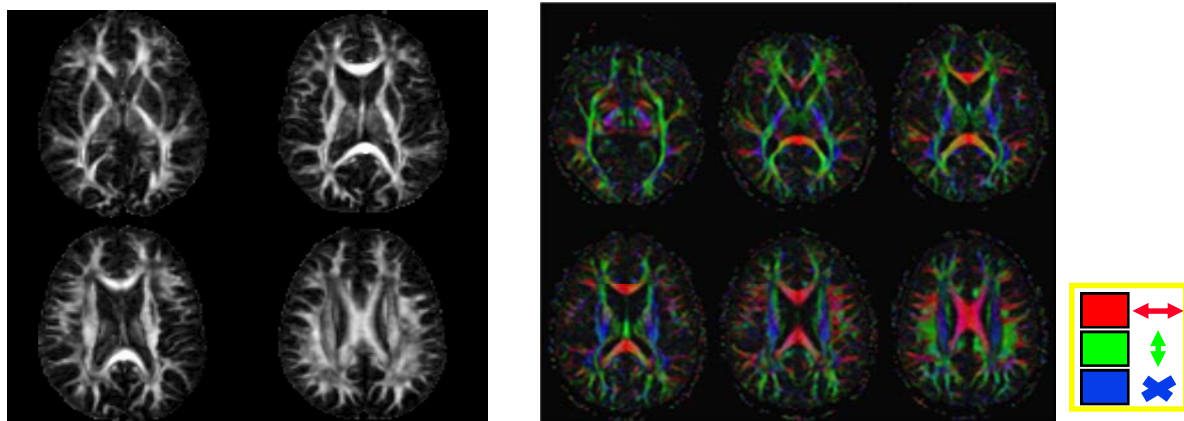
- fractional anisotropy<sup>iv</sup>  $FA = \sqrt{\frac{3}{2}} \frac{\sqrt{(\lambda_1 - \langle D \rangle)^2 + (\lambda_2 - \langle D \rangle)^2 + (\lambda_3 - \langle D \rangle)^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$
- relative anisotropy<sup>iv</sup>  $RA = \frac{\sqrt{(\lambda_1 - \langle D \rangle)^2 + (\lambda_2 - \langle D \rangle)^2 + (\lambda_3 - \langle D \rangle)^2}}{\sqrt{3} \langle D \rangle}$
- volume ratio<sup>v</sup>  $VR = \frac{\lambda_1 \lambda_2 \lambda_3}{(\frac{\lambda_1 + \lambda_2 + \lambda_3}{3})^3}$
- lattice index<sup>v</sup>  $LI_N = \frac{\sqrt{3}}{\sqrt{8}} \left( \frac{\sqrt{D_{\text{ref}} : D_N}}{\sqrt{D_{\text{ref}} : D_N}} + \frac{\sqrt{D_{\text{ref}} : D_N} \sqrt{D_{\text{ref}} : D_N}}{D_{\text{ref}} : D_N} \right)$
- ...

## RESULTS:

Areas where diffusion in a particular direction is high show up as dark areas on simple diffusion weighted images, while ADC maps add quantitative measures:



If time allows data from a larger number of diffusion encoding directions (at least 6 non-collinear directions) to be measured, the full diffusion tensor can be estimated. From this fractional anisotropy (FA) can be extracted, which clearly highlights the white matter tracts within the brain. (FA maps are often also “colour coded” to show the principle direction of diffusion):



Mean diffusivity (MD), plus the radial and axial diffusivities (RD and AD, respectively), can also be calculated.

**DISCUSSION:** ADC values are affected by anything that can change the size of / shape of / barriers within the tissue compartment(s) we are measuring (see Fornasa<sup>vi</sup> for a useful qualitative review), while FA is often used as a marker of “structural integrity”. However results must be interpreted with caution in areas of crossing fibres and other areas in which the simple Gaussian diffusion process assumed by the diffusion tensor model is not valid. Similarly, RD and AD results can be misleading if the context in which the data were collected is not taken into account. In particular, RD is often used as a marker of myelination<sup>vii</sup>, but interpretation can be difficult in “real” tissue, with crossing fibres and other confounding issues.<sup>viii</sup>

**CONCLUSION:** DTI data are relatively straightforward to collect and process, and can give useful information about tissue microstructure; results must be interpreted with caution, however, and more complex models are required in order to more fully describe brain (and other) tissue.

## REFERENCES:

- 
- <sup>i</sup> E. O. Stejskal, J. E. Tanner, Spin diffusion measurements: spin echoes in the presence of time-dependent field gradient. *J. Chem. Phys.* 42, 288 (1965).
- <sup>ii</sup> S. Warach, D. Chien, W. Li, M. Ronthal, R.R. Edelman. Fast magnetic resonance diffusion-weighted imaging of acute human stroke. *Neurology.* 42(9), 1717 (1992).
- <sup>iii</sup> C. Pierpaoli, A. Righini, I. Linfante, J.H. Tao-Cheng, J.R. Alger, G. Di Chiro. Histopathologic correlates of abnormal water diffusion in cerebral ischemia: diffusion-weighted MR imaging and light and electron microscopic study. *Radiology.* 189(2), 439 (1993).
- <sup>iv</sup> P. J. Basser, C. Pierpaoli, Microstructural features measured using diffusion tensor imaging. *J. Magn. Reson. B* 111, 209 (1996).
- <sup>v</sup> C. Pierpaoli, P. J. Basser, Toward a quantitative assessment of diffusion anisotropy. *Magn. Reson Imag.* 36(6), 893 (1996).
- <sup>vi</sup> F Fornasa. Diffusion-weighted Magnetic Resonance Imaging: What Makes Water Run Fast or Slow? *J Clin Imaging Sci.* 1, 27 (2011).
- <sup>vii</sup> S.K. Song, S.W. Sun, M.J. Ramsbottom, C. Chang, J. Russell, A.H. Cross. Dysmyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *Neuroimage.* 17, 1429 (2002).
- <sup>viii</sup> C.A. Wheeler-Kingshott, M. Cercignani. About "axial" and "radial" diffusivities. *Magn. Reson. Med.* 61(5), 1255 (2009).