

SM1: overview of used techniques and parameters

**Multi-exponential T2 relaxation (Webb, Munro et al. 2003; MacKay, Laule et al. 2006; Laule, Vavasour et al. 2007)**

- **Myelin Water Fraction (MWF):**

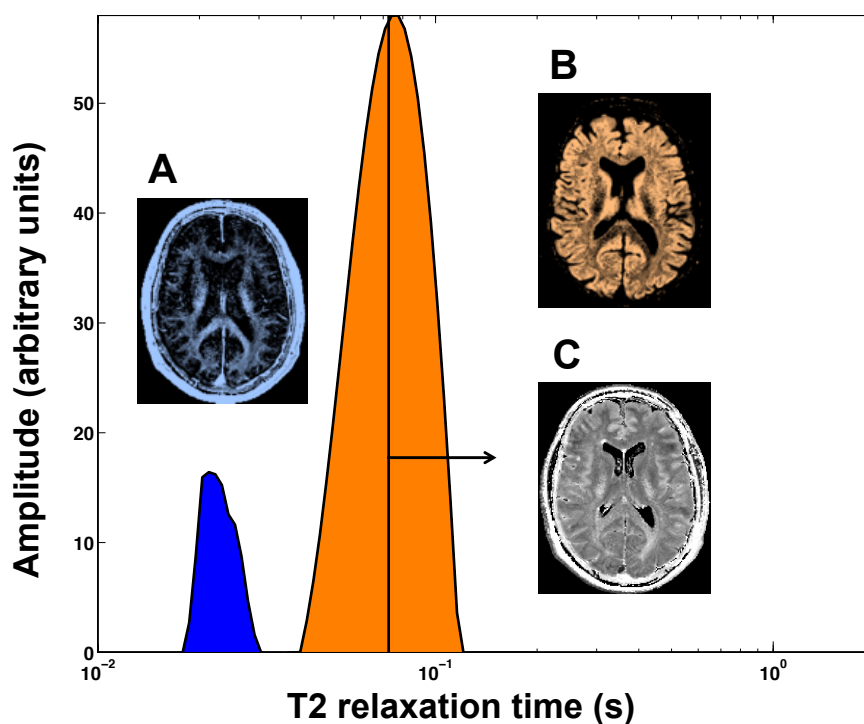
Area in the T2 distribution between 10ms and 35ms, divided by total area. MWF ranges between 0 and 1 and is an indication of the amount of myelin relative to total water. Blue peak (A) in figure 1, below.

- **Intra- and Extracellular Water Fraction (IEWF):**

Area in the T2 distribution between 35ms and 220ms, divided by total area. IEWF ranges between 0 and 1 and gives an indication of the amount of intra- and extracellular water relative to total water. Orange peak (B) in figure 1, below.

- **Intra- and Extracellular Water geometric mean T2 time (IEW-gmT2):**

Position of the intra- and extracellular water peak in the T2 distribution. IEW-gmT2 is expressed in seconds or milliseconds and typically has values around 80 ms. Vertical line (C) in figure 1, below.



**Figure 1 Example T2 distribution. A = Myelin Water Fraction, B = Intra-and Extracellular Water Fraction, C = geometric mean T2 of intra- and extracellular water. The cerebrospinal fluid pool is not shown in this distribution.**

## **Diffusion MRI (Tournier, Mori et al. 2011)**

### **Diffusion Tensor Imaging (Basser, Mattiello et al. 1994)**

- **Mean Diffusivity (MD):**

Mean of diffusion tensor eigenvalues. Indication of how much diffusion occurs, regardless of the direction of diffusion. Expressed in units of  $\text{mm}^2/\text{s}$ .

- **Axial diffusivity (AD):**

The largest diffusion tensor eigenvalue. This indicates how much diffusion occurs in the direction in which diffusion occurs most easily. This can be the direction in which axons are aligned, although it is discouraged to interpret AD like this (Wheeler-Kingshott and Cercignani 2009) Expressed in units of  $\text{mm}^2/\text{s}$ .

- **Radial Diffusivity (RD):**

The mean of the smallest two diffusion tensor eigenvalues. This indicates how much diffusion occurs in the direction perpendicular to the direction in which most diffusion occurs. Expressed in units of  $\text{mm}^2/\text{s}$ .

- **Fractional Anisotropy (FA):**

Ratio of standard deviation and root mean square of diffusion tensor eigenvalues. FA ranges between 0 and 1 and gives an indication of how strong preferred directions of Gaussian diffusion are present in a voxel.

### **Diffusion Kurtosis Imaging (Jensen, Helpert et al. 2005; Hui, Cheung et al. 2008)**

- **Mean Kurtosis (MK):**

Kurtosis is a unitless statistical measure with a value of 3 in a normal (Gaussian) distribution. In diffusion MRI, the excess kurtosis is calculated (kurtosis - 3). Positive values then indicate a distribution profile that is more sharply peaked than a Gaussian distribution. Mean kurtosis is the mean of kurtosis tensor eigenvalues and gives an indication of how much the diffusion deviates from the Gaussian profile, regardless of direction of

diffusion.

### **Neurite Orientation Dispersion and Density Imaging (Zhang, Schneider et al. 2012)**

In the NODDI model, the diffusion signal is split into signal from tissue and signal from cerebrospinal fluid (CSF, modeled as Gaussian isotropic diffusion). The signal from tissue is again split into contributions from neurites (modeled as a set of sticks with unhindered diffusion along them and highly restricted diffusion perpendicular) and extracellular space (modeled as Gaussian anisotropic diffusion).

- **ISotropic fraction (FISO):**

Fraction of signal corresponding with Gaussian isotropic diffusion relative to total signal. FISO ranges between 0 (no Gaussian diffusion) and 1 (only Gaussian diffusion) and represents the cerebrospinal fluid compartment. 1-FISO conversely yields the total tissue fraction.

- **Neurite Density Index (NDI):**

Fraction of signal corresponding with unhindered diffusion along, and highly restricted diffusion perpendicular to a range of directions. NDI ranges between 0 and 1 and represents the intracellular tissue fraction (relative to total tissue). 1-NDI represents the extracellular tissue fraction.

- **Orientation Dispersion Index (ODI):**

Dispersion of orientations along which diffusion occurs with properties adhered to the intracellular compartment. ODI ranges between 0 (no dispersion, i.e. neurites mainly oriented in one single direction) and 1 (complete dispersion, i.e. neurites are organized along many directions)

For further details about these techniques and parameters, please refer to:

Basser, P. J., J. Mattiello, et al. (1994). "Estimation of the effective self-diffusion tensor from the NMR spin echo." Journal of magnetic resonance. Series B **103**(3): 247-254.

Hui, E. S., M. M. Cheung, et al. (2008). "Towards better MR characterization of neural tissues using directional diffusion kurtosis analysis." Neuroimage **42**(1): 122-134.

Jensen, J. H., J. A. Helpert, et al. (2005). "Diffusional kurtosis imaging: the quantification of non-gaussian water diffusion by means of magnetic resonance imaging." Magnetic resonance in medicine : official journal of

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- Laule, C., I. M. Vavasour, et al. (2007). "Magnetic resonance imaging of myelin." Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics **4**(3): 460-484.
- MacKay, A., C. Laule, et al. (2006). "Insights into brain microstructure from the T2 distribution." Magnetic resonance imaging **24**(4): 515-525.
- Tournier, J. D., S. Mori, et al. (2011). "Diffusion tensor imaging and beyond." Magn Reson Med **65**(6): 1532-1556.
- Webb, S., C. A. Munro, et al. (2003). "Is multicomponent T2 a good measure of myelin content in peripheral nerve?" Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine **49**(4): 638-645.
- Wheeler-Kingshott, C. A. and M. Cercignani (2009). "About "axial" and "radial" diffusivities." Magnetic resonance in medicine : official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine **61**(5): 1255-1260.
- Zhang, H., T. Schneider, et al. (2012). "NODDI: practical in vivo neurite orientation dispersion and density imaging of the human brain." Neuroimage **61**(4): 1000-1016.