

## Diffusion Imaging: Physics Applied to Body Applications Thomas L. Chenevert

Diffusion-weighted imaging (DWI) offers insight into cellular status, density, and structural organization by way of sequences sensitive to water mobility which is affected by these properties [1, 2]. Macroscopic tissue motion unrelated to diffusion can confound in vivo diffusion measurements therefore single-shot techniques are nearly exclusively used to mitigate extraneous bulk motion in the abdomen. Microcirculation flow through randomly-oriented capillaries in the presence of diffusion-sensitization gradients will also appear as a hyper diffusion-like attenuation in the low b-value regime [3-5]. Conversely, the high b-value extreme where true diffusion-based contrast is high, quantitative measurement of signal attenuation with increasing b-value is susceptible to noise limitations [6]. While not as pronounced as in neuro tissue, water mobility in body tissues may be directional due to true underlying cyto-architecture or appear anisotropic due to residual bulk motion artefact. Unlike DWI of the brain, an effective fat suppression method is clearly more crucial for successful body DWI sequences since lipid presents an anomalously low diffusion signal [7] that is spatially shifted relative to water signal on single-shot images, thus residual fat signal is an additional source of ADC error. In summary, diffusion imaging of the body requires organ site-specific customization of protocols to deal with: perfusion contamination at low b-values, SNR limitations in the high b-value regime, shim quality and fat suppression over a large FOV, multi-axis measurements to properly quantify isotropic diffusion (eg. ADC) or anisotropic features, as well as possible synchronization with cardiac/respiration to reduce residual bulk motion errors. Recent technical acquisition enhancements have successfully addressed many of these issues such that DWI of the body has gained rapid growth in a variety of applications.

Proper selection of b-values and gradient directions depend on the given body DWI application and objective [8]. Diffusion sensitization pulses on at least three orthogonal gradient axes are required to quantify a rotationally-invariant diffusion coefficient (ie, ADC or mean diffusion) [9, 10]. If anisotropic diffusion indices are sought (such as fractional anisotropy), at least 6 non-collinear directions are required although 9-16 directions are not uncommon. The quantity and range of acquired b-values also should be suited for the given application and signal quality properties. If simple quantification of ADC is desired, only two b-values are required as is typical in most clinical DWI studies to date. However, if one seeks to disentangle perfusion effects from molecular diffusion, or to detail true biophysical multi-exponential diffusion features then additional b-value samples are needed to fit DWI signals to a specified multi-exponential model. For example, diffusion may be modelled as a bi-exponential decay where characterization of "fast" and "slow" diffusion components, and their fractional contribution requires additional b-values to fit at least three model coefficients [11, 12]. Alternatively, the stretched-exponential implies a continuum of diffusion decays embodied in one "distributed diffusion coefficient" and involves only two model coefficients [13]. Perfusion influences are particularly relevant to diffusion measurements in vascular-rich lesions/tissues. In such instances, signal attenuation over the low b-value range (eg. 0 to 150s/mm<sup>2</sup>) are strongly affected by perfusion. It is empirically challenging to extract the "perfusion fraction" from measurements over the low and high b-value regime, although these concepts are being revisited [4]. Alternatively, one may effectively extinguish perfusion signals and their influence by only including b-values above 150s/mm<sup>2</sup> in diffusion calculations. The maximum b-value should be set such that signals recorded at that b-value are adequately above the noise floor. This maximum b-value depends on the SNR achievable for the target organ/tissue and the water diffusion coefficient of these tissues – the lower the diffusion value, the higher the b-value achieved before the signal approaches the noise floor. Field strength, receiver coil, acquired resolution and scan time provide some operator control to improve SNR and DWI quality, although reasonable guidelines for several body DWI protocols have been suggested [8].

One body DWI application that may have practical clinical value is lesion detection in a limited anatomical region, or over a "whole-body" survey scan [14, 15]. Pathology characterized by

relatively long T2 appear hyper-intense on DWI due, in part, to inherent high T2-weighting in DWI. Other normal long-T2 tissues such as blood and fluids, would also appear bright if not for incremental diffusion sensitization that attenuate high mobility fluid signals. Therefore lesions having long T2 and moderate to low water mobility, such as is common in solid lesions tend to exhibit conspicuous hyper intensity on moderate to high b-value DWI. Interestingly, despite their conspicuous hyper intense DWI signal, water mobility via ADC of these lesions often is not lower than normal tissues. If only "lesion detection" is desired, collection of multiple b-values is not strictly required. However, other applications such as lesion/tissue characterization or treatment response assessment via ADC[16], or multi-exponential analysis of DWI decays, or anisotropy study of organized tissues, then additional DWI conditions are required with commensurate increases in scantime. In this lecture, principles of body DWI measurements, protocol design, and biophysical models for analysis will be presented.

## References:

1. Norris, D.G., *The effects of microscopic tissue parameters on the diffusion weighted magnetic resonance imaging experiment*. NMR Biomed, 2001. **14**(2): p. 77-93.
2. Szafer, A., et al., *Diffusion-weighted imaging in tissues: theoretical models*. NMR Biomed, 1995. **8**(7-8): p. 289-96.
3. Le Bihan, D., et al., *MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders*. Radiology, 1986. **161**(2): p. 401-7.
4. Luciani, A., et al., *Liver cirrhosis: intravoxel incoherent motion MR imaging--pilot study*. Radiology, 2008. **249**(3): p. 891-9.
5. Lemke, A., et al., *An in vivo verification of the intravoxel incoherent motion effect in diffusion-weighted imaging of the abdomen*. Magn Reson Med. **64**(6): p. 1580-5.
6. Dietrich, O., S. Heiland, and K. Sartor, *Noise correction for the exact determination of apparent diffusion coefficients at low SNR*. Magn Reson Med, 2001. **45**(3): p. 448-53.
7. Ababneh, Z.Q., et al., *In vivo lipid diffusion coefficient measurements in rat bone marrow*. Magn Reson Imaging, 2009. **27**(6): p. 859-64.
8. Padhani, A.R., et al., *Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations*. Neoplasia, 2009. **11**(2): p. 102-25.
9. Alexander, A.L., et al., *A geometric analysis of diffusion tensor measurements of the human brain*. Magn Reson Med, 2000. **44**(2): p. 283-91.
10. Hasan, K.M., et al., *Analytical computation of the eigenvalues and eigenvectors in DT-MRI*. J Magn Reson, 2001. **152**(1): p. 41-7.
11. Clark, C.A. and D. Le Bihan, *Water diffusion compartmentation and anisotropy at high b values in the human brain*. Magn Reson Med, 2000. **44**(6): p. 852-9.
12. Lee, J.H. and C.S. Springer, Jr., *Effects of equilibrium exchange on diffusion-weighted NMR signals: the diffusigraphic "shutter-speed"*. Magn Reson Med, 2003. **49**(3): p. 450-8.
13. Bennett, K.M., et al., *Characterization of continuously distributed cortical water diffusion rates with a stretched-exponential model*. Magn Reson Med, 2003. **50**(4): p. 727-34.
14. Kwee, T.C., et al., *Diffusion-weighted whole-body imaging with background body signal suppression (DWIBS): features and potential applications in oncology*. Eur Radiol, 2008.
15. Takahara, T., et al., *Diffusion-weighted MR neurography of the sacral plexus with unidirectional motion probing gradients*. Eur Radiol, 2009.
16. Padhani, A.R. and D.M. Koh, *Diffusion MR imaging for monitoring of treatment response*. Magn Reson Imaging Clin N Am. **19**(1): p. 181-209.