Dependence of White Matter Orientation to Magnet Field on Gradient-Echo Imaging at 17.2 Tesla in Mice.

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Introduction: When gradient echo weighted images at UHF were first examined in detail, an heterogeneous signal was observed in human white matter [1]. Various mechanisms were proposed for this, including degree of myelinisation, iron content, microvasculature, etc. It was later shown that there exists a correlation between the orientation of fibre bundles (relative to the applied field) and the observed signal, both on T2* weighted [2-4] and phase (5-8] images. The origin of this signal change is not yet fully understood.

While studies so far have examined mainly both human and macaque models, there are difficulties in obtaining numerous orientations. In humans and in a conventional MRI scanner, it is difficult to vary the angle of the head to the magnet field more than about 30 degrees. With a macaque model, a human size MRI system is still required, and even then accurate positioning of the head at a range of angles is difficult.
With the availability of a 17.2 Tesla pre-clinical scanner, with a large horizontal bore (26cm diameter warm bore, 8.5cm diameter gradients), the ability to image small animals (mice) in different orientations may provide another model to examine these effects. What is more, the extremely high applied field provides both improved SNR (and thus resolution) and presumably amplifies the orientation effect.

Materials and Methods: The most obvious tracts of white matter in the mouse brain extend across the brain in a nearly flat sheet, with the main fibre directions running laterally. Thus when the mouse is positioned on its belly but transverse to the bore of the magnet, the white matter tracts are nearly axially aligned. However in the coaxial position (regardless of how the mice lies) the tracts run transverse to the main field. From the previous studies at lower field in humans, it is expected that the coaxial body position should yield a shorter T2*, compared to neighbouring brain regions, than the transverse position.

Two 5 week old (20 g) Swiss mice were examined, in each case in two positions: transverse to the magnet bore and along the magnet axis. A 3 cm single loop transceive coil was used. Both single echo and multiple echo scans were acquired, with the latter allowing for the calculation of T2* maps. The latter avoids potentially confounding issues of B1 homogeneity from the surface coil affecting the tissue contrast. Scan parameters were 256x256 matrix, 1.6cm FOV, 250um slice thickness, yielding images of 63x63x250um voxel size. For single echo, anatomical imaging the parameters were TR=350ms, TE=9.2ms, FA=45 BW=20kHz and 8 averages. For T2* mapping the parameters were TR=800ms, first TE=3.5ms, echo spacing 4.5ms with 7 echoes, FA=30 BW=78.125kHz, and 4 averages. The mice were first imaged with their bodies positioned transverse to the bore of the magnet. They were then repositioned in the more classical position, i.e. co-axially with the main magnetic axis.

Results: As can be seen in Fig. 1, the white matter clearly appears darker, i.e. has a shorter T2*, when the mouse is in the coaxial position. This indicates a similar behavior to that found in macaques [2] and the trends found in humans [3,4] that show decreasing T2* as white matter fibre bundles are oriented transverse to the applied field. While magic angle effects have been observed in peripheral nerves [9], such a behavior usually shows shorter relaxation times (on T2) when the nerves are parallel with the field than when transverse, which is opposite to what is seen here.

Also interesting is that there appears, at this very high field strength, to be some orientation effects in the grey matter signal. This may prove to be a tool to allow even greater resolution of cortical structures.

Body position	Grey matter		White matter	
	Mouse 1	Mouse 2	Mouse 1	Mouse 2
Transverse	18.3ms	15.8ms	15.7ms	15.9ms
Parallel	17.3ms	16.4ms	11.6ms	12.4ms

Table 1: Calculated values of T2 in grey and white matter in two mice, as a function of their orientation relative to the applied magnetic field. For each measurement the standard error was less than 2ms.*

What mechanisms underlie these orientation effects is still unknown. On the one hand, it may be that the simplistic models of isolated cylinders imbedded in a medium of differing susceptibility need to be extended to more properly model the real tissue (many parallel cylinders, etc.). On the other hand, it is possible that certain constituents of the tissue, such as myelin, may have anisotropic susceptibility, and thus produce quite different effects than isotropic modeling suggests.

Conclusions: The high sensitivity and available bore size on this 17.2 Tesla, 26cm magnet allows examination of white matter orientation influence on T2* signals in mice. The availability of mice models increases greatly the experimental range, not only from the perspective of measurements at multiple orientations, but also the ability to observe this signal behavior as a function of brain development.

References: [1] Li et al. NeuroImage 32 :1032-1040 (2006) ; [2] Wiggins et al. Proc ISMRM 237 (2008); [3] Cherubini et al. MRM 61:1066-1072 (2009); [4] Bender et al. NMR Biomed. 23:1071-1076 (2010); [5] Hernández et al. Proc ISMRM 953 (2009); [6] Schäfer et al. Proc ISMRM 956 (2009); [7] Lee et al. PNAS 107:5130-5135 (2010); [8] He et al. PNAS 106:13558-13563 (2009); [9] Chappel et al. AJNR 25:431-440 (2004)

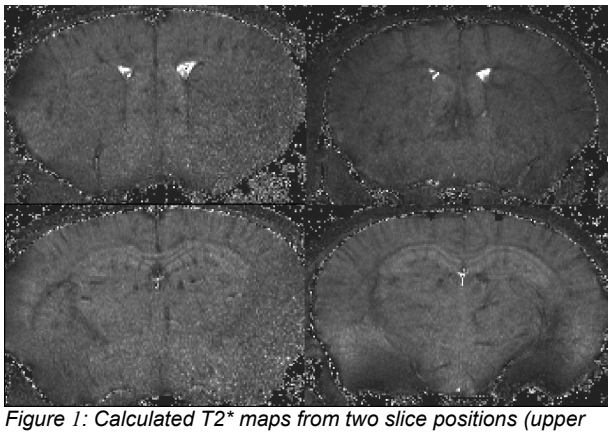

Figure 1: Calculated T2 maps from two slice positions (upper vs lower rows) with different head orientations: transverse (left column) vs. coaxial (right column). Of note is the the significantly darker appearance of white matter in the right column, indicating a shorter T2* when the fibre directions are perpendicular to the main field.*