Diffusion properties of cortical layers in fixed human brain tissue investigated with high-resolution STEAM

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Introduction The past few years have brought a tremendous increase in the number of studies performed on fixed tissue, human or animal, involving either normal tissue or tissue affected by pathological changes (e.g. MS, Alzheimer's) [1-3]. Although not all studies were performed at higher resolution than achievable *in vivo*, MRI of fixed tissue usually offers the possibility of achieving very high resolution since measurement time is not a major constraint. The relevance of fixed tissue properties to those *in vivo* have been carefully investigated [2,4] as has the dependence of diffusion properties of fixed tissue on the composition of fixative,and time between death and fixation. In tissue fixed directly after death, diffusion anisotropy is preserved [4,5] and this allows the acquisition of very-high-resolution diffusion data which also reflect the properties of the living brain. However, for brains kept in formalin solution and at moderately low temperatures (10-15C), the T1, T2 and T2* relaxation times [5] as well as the mean diffusivity [4,5] are strongly reduced with respect to *in vivo*. Unless T2 is lengthened by rehydrating the brain, diffusion methods relying on EPI are strongly affected by the shortened T2* leading to severe signal loss and blurring. Furthermore, the achievable matrix size is also limited by T2* decay, especially since the reduced diffusivity requires the use of high b-values and therefore long diffusion encoding times. Here, we use a method which is not affected by distortion or blurring and makes use of the longer T1 compared to T2/T2* relaxation times for the diffusion weighting. STEAM diffusion [6] is ideally suited to replace EPI-based methods at high fields and/or on anatomically accurate studies on samples with fast T2 and longer T1 relaxation.

Materials and methods Measurements were performed on a 16cm bore 9.4T animal scanner equipped with a 10cm ID, 270mT/m, 200μs rise time gradient coil and interfaced to a Varian UnityInova console. A 7cm surface coil was used for both RF excitation and signal receive. The brain samples were obtained from the brain donor programme of the University of Duesseldorf, Germany. Two brain samples were investigated, one containing the primary visual cortex (right occipital lobe), the other the auditory cortex (right temporal lobe). A STEAM diffusion sequence [7] was used with the parameters: FOV 64x64mm^2, matrix 192x192, 0.8mm slice thickness, 37 slices in two separate measurements (18+19 interleaved), TR=1200ms, TE=16ms, TM=42ms, α=50^o, BW=56kHz, 4 (occipital) or 2avgs (temporal lobe), diffusion encoding gradients of duration 4ms and 50ms apart, b=3000mm^{-2}s (occipital lobe) or b=2300mm^{-2}s(temporal lobe), either 60 (temporal lobe) or 30 (occipital lobe) encoding directions (Jones's scheme [8]), one b=0 image every 5 diffusion-weighted images. The temperature in the scanner bore before the measurements was 15C and kept constant due to water cooling of the gradient coil. The data were evaluated using the free software MedINRIA [9] as well as custom-written C++ software [10] for fibre tracking.

Results and Discussion We will concentrate in the following on results obtained from the occipital cortex; the results obtained on tissue from the temporal cortex were qualitatively similar, but displayed a greater variability due to lower SNR. Maps of the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) are shown in Fig.1 for a selected slice, together with the histogram showing the distribution of ADC and FA values over the whole sample. While all ADC values are extremely low, due primarily to the low temperature, the mean diffusivity of grey matter ($3.22x10^{-4}$) is about 70% higher than that of white matter ($1.9x10^{-4}$), where the ratio is comparable tovalues obtained *in vivo* [11] at higher b-values [12]. The FA values are also comparable to those obtained *in vivo* (0.05 for GM in occipital cortex, 0.21 occipital WM [11]), but higher. This might be due to the higher resolution of our data allowing for a better characterisation of the tissue microscopy.

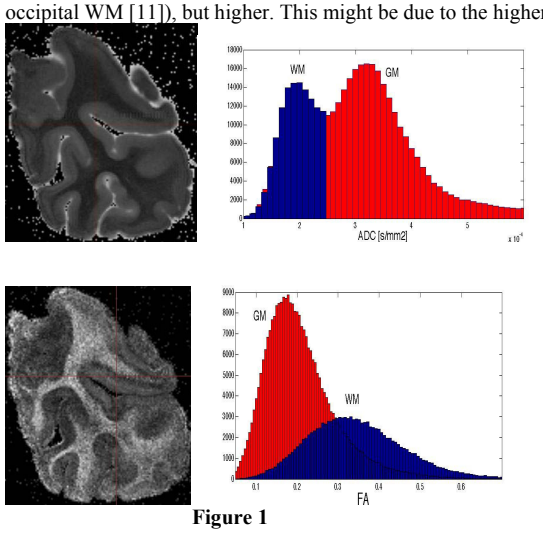

Figure 1

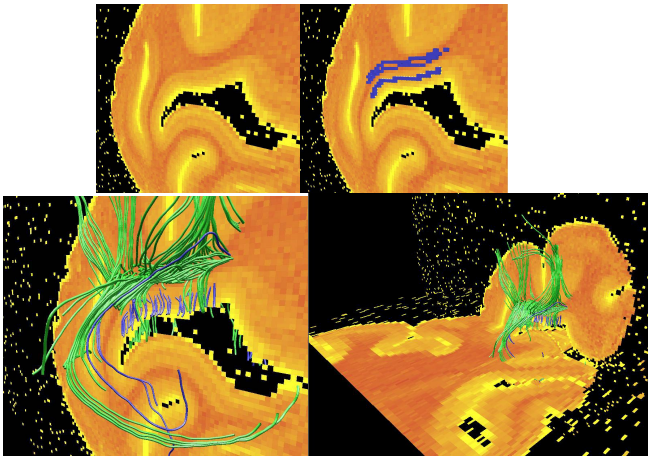

Figure 2

A striking feature of the ADC maps is the clear visibility of a myelinated cortical layer (stria of Gennari) and its distinct diffusion properties compared to the surrounding grey matter. Thus, the ADC value was found to be 10-20% lower in the stria of Gennari than that of the surrounding GM and the FA slightly higher, although the visibility of layers in the noisy FA maps was reduced. In order to further investigate the diffusion properties of the myelinated layer, a region of interest was placed in a cortical region where the layer was visible (Fig 2a), containing only voxels assumed to belong to the stria of Gennari (Fig 2b). A further region of similar size was placed in the adjacent white matter (Fig 2b) and fibres were tracked from these seed points (fibres tracked from the stria of Gennari are marked in blue, fibres from WM are green, Fig 2c-d). As seen in Fig. 2c most clearly, radial fibres emerge from the stria of Gennari through the cortex, thought to be due to pyramidal cells [1]. The visualisation of fibres which emerge from the grey matter and join the regular tracts of the white matter was also successful.

Conclusions In addition to the usual SNR challenge of high-resolution imaging, high-resolution diffusion studies on fixed tissue kept in formalin and at or below room temperature are very challenging due to the strongly reduced diffusivity and relaxation times of such samples. However, using a STEAM sequence with a large number of diffusion encoding directions and voxel size of 88nl, it was possible to characterise the diffusion properties of specific cortical regions and fibre structures (e.g. radial).

References

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