

# Effects of Diffusion Times on Diffusions-Tensor-Imaging Contrast

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## INTRODUCTION

Diffusion tensor imaging (DTI) has gained wide acceptance for tracking white matter projections non-invasively. Recent studies suggested that DTI has the potential to trace fiber projections into the gray matter using multi-b values approach in which the “slow” component of the DTI data was found to be more suited for this purpose (1). Another potential window of improvement was to optimize diffusion time ( $t_{diff}$ ) for DTI sensitivity. Diffusion-time dependence on the apparent diffusion coefficient (ADC) in the brain had been exhaustively studied. At short  $t_{diff}$ , ADC is relatively large and quickly plateau beginning at  $t_{diff}$  of 15-20 ms. However, the diffusion-time dependent effect on DTI sensitivity has not been explored. It was hypothesized that the “effective” diffusion distance for fiber tracking due to its structural size is larger than the distance covered by a  $t_{diff}$  of 15-20 ms reported for “cellular”-level microstructures. Consequently, for  $t_{diff}$  relevant for DTI could be considerably longer. An optimized  $t_{diff}$  could potentially improved sensitivity for fiber tracking in both white and gray matters. Unfortunately, longer diffusion generally requires long echo times which results in unacceptable signal loss. In this study, we implemented a DTI protocol based on Stimulated Acquisition Mode (STEAM) sequence for making long diffusion time measurements ranging from 30 to 280 ms. The effect of anisotropic index as a function of diffusion times was evaluated for gray and white matter using multispectral analysis of  $T_2$  and DTI data.

## METHODS

Mice, anesthetized at 1% isoflurane, were secured in a stereotaxic head restrainer with tooth-, ear- and shoulder-bars. Rectal temperature and respiration rate were monitored and maintained within normal physiological ranges. MRI was performed on a 9.4T, 89mm vertical bore magnet with a 100 G/cm gradient insert (100  $\mu$ s rise time) and a small RF transceiver surface coil optimized for imaging mouse brain. Diffusion Weighted Images were acquired using bipolar Stejskal-Tanner diffusion gradients (2) added to either side of the TM period of a STEAM sequence. The gradients were applied in six directions (3) to calculate the eigen vectors, eigen values and anisotropy maps of the diffusion of water (4, 5) using program written in Matlab®. DWI images were acquired at seven different diffusion times ranging from 30 ms to 280 ms. The imaging parameters were TR = 2.5 s, TE = 14 ms, 90° flip angle, matrix of 64x64 zero filled to 128x128, FOV = 1.28 x 1.28 cm, 7 slices of 0.9-mm thickness with interslice gap of 0.1 mm and a spectral width of ~50 kHz. The low b-value image was acquired with b = 5 cm<sup>2</sup>/s and high b value images were acquired with b = 1200 cm<sup>2</sup>/s. In addition, heavily  $T_2$  weighted images (TE = 45ms) were acquired. From these measurements, one set of  $T_2$  map and ADC maps at different diffusion time were calculated. Gradient on each axis was adjusted to eliminate the gradient-interaction cross terms at each diffusion time, such that the ADC measured in 6 directions were within 5% of each other in a spherical water phantom.

All data analysis was performed on Matlab®. Volume ratio (VR) was chosen as the measure of diffusion anisotropy as it is relatively more sensitive to the eccentricity of diffusion ellipsoid. VR is defined as the volume of the diffusion ellipsoid to the volume of the sphere of diameter  $(\lambda_1 + \lambda_2 + \lambda_3)/3$ , where  $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$  are the three Eigen values corresponding to the diffusion ellipsoid (6, 7). VR varies from 0 to 1 where 0 indicates anisotropic diffusion and 1 indicates isotropic diffusion.

## RESULTS & DISCUSSION

Figure 1 shows the pixel-by-pixel scatterplots of  $T_2$  versus VR for two diffusion times from an ROI that include both gray and white matters (red ROI). Two  $T_2$  range was used, namely  $T_2 > 27$  ms (gray matter, green) and  $T_2 < 27$  ms (white matter, red). Data were obtained from pixels that include corpus callosum and cortical gray matter. An increase in anisotropy (decreased VR) in white matter was observed with increasing diffusion time, with VR ranging from 0.68 to 0.45.

Figure 2 shows similar analysis from an ROI that covers only the cortical gray matter. An increase in anisotropy (decreased VR) in gray matter was also observed with increasing diffusion time, indicative of the presence of microstructures.

Anisotropy changes with increasing diffusion times is more evident in the fractional anisotropy maps. Some of these structures are better delineated at longer diffusion times (white matter of internal capsule and cortical grey matter shown with white arrows in Figure 3). DTI by summing data from different DTI could provide different sensitivity to different fiber compartments (red arrow in Fig. 3c).

## CONCLUSION

Cortical gray matter and white matter showed increased diffusion anisotropy with increasing diffusion time, as indicated by VR and DTI maps. Longer diffusion time shows better sensitivity to some fiber tracks that was not evident in short diffusion time. DTI by summing data from different DTI could provide different sensitivity to different fiber compartments.

## References

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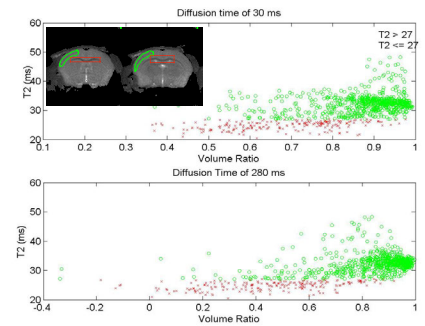


Fig 1.  $T_2$  vs VR scatter plot of corpus callosum at different diffusion times. Inset shows ROI

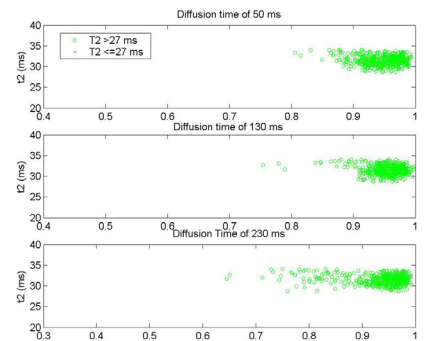


Fig 2.  $T_2$  vs. VR scatter plot of cortical grey matter at different diffusion times.

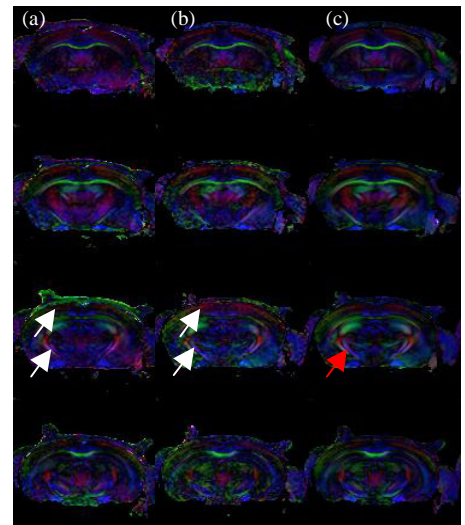


Fig 3. FA color maps at (a) 30, (b) 230 ms  $t_{diff}$  and (c) average of 7  $t_{diff}$