# Diffusion Time Dependence of DTI Measurements

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## Introduction

Restricted diffusion is the primary mechanism causing diffusion anisotropy in the nervous system (1). It has also been postulated to play a central role in the marked decline of water apparent diffusion coefficient (ADC) in neural tissue following the onset of ischemia (2–3). In a recent study, Takahashi et al. reported that the intra-axonal longitudinal ADC is not restricted while the transverse ADC is significantly restricted by the axolemmas (4). In another study, Weglarz et al. suggested that anisotropic diffusion in the spinal cord might be entirely explained by the presence of the slow transversal component, arising from the restricted diffusion (5). The effect of restricted diffusion has been investigated by performing diffusion tensor imaging (DTI) as a function of diffusion time ($t_D$). Clark et al reported that DTI parameters are $t_D$-independent in human brains in the range of 8–80 ms (6). However, the degree of diffusion weighting may be affected differently by increasing $t_D$. It is possible to maintain a constant b value by reducing the q value. Alternatively, one could also maintain a constant q value by increasing the b value. In the present study, DTI data with short and long $t_D$ were conducted on fixed mouse brain. Both constant q value and constant b value weighting approaches were examined. Each line of k-space data was acquired in an interleaved fashion for collecting short-$t_D$ and long-$t_D$ DTI data to eliminate the inter-measurement variation.

## Materials and Methods

Four 6-week-old male Swiss Webster mice underwent, after euthanasia, intra-cardiac perfusion fixation with 4% paraformaldehyde in phosphate buffered saline (PBS). After fixation, the excised brain was placed in 4% paraformaldehyde/PBS at 4°C for one week then switched to PBS at 4°C for an extra week before imaging. The experimental parameters concerning the $t_D$, g, b-value, and NEX are listed in the following table:

| | | short $t_D$ DTI | | long $t_D$ DTI with constant b value | | long $t_D$ DTI with constant q value | | | |
|---|---|---|---|---|---|---|---|---|---|
| Exp. Conditions | | (a) | | (b) | | (c) | | (d) | |
| b ($\mu s/\mu m^2$) | | 1889.5 | | 1889.5 | | 4466.1 | | 4466.1 | |
| Δ (ms) | $t_D$ (ms) | 20 | 18.3 | 45 | 43.3 | 45 | 43.3 | 45 | 43.3 |
| δ (ms) | | 5 | | 5 | | 5 | | 5 | |
| g (gauss/cm) | | 24 | | 19 | | 24 | | 24 | |
| NEX | | 2 | | 2 | | 2 | | 6 | |

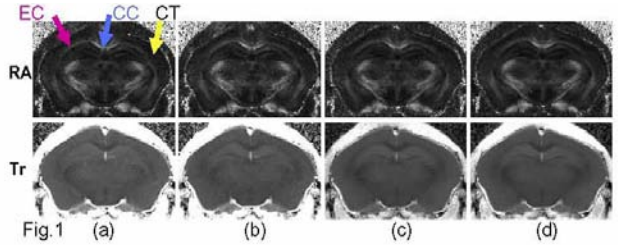

Fig.1

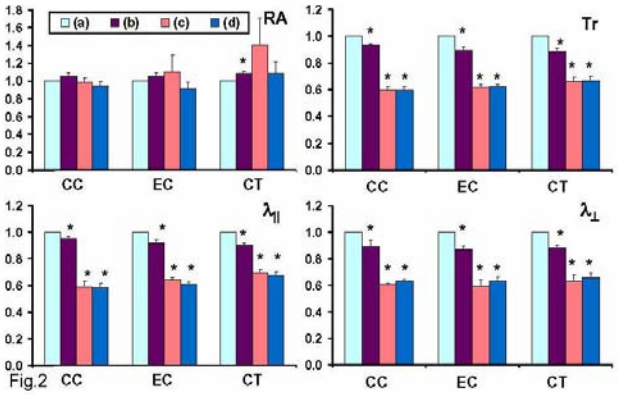

Fig.2

Data were acquired using a spin-echo diffusion weighted imaging sequence with TR 1.5 sec, TE 70 ms, slice thickness 1 mm, field-of-view 3 cm, and data matrix 256 × 256 (zero filled to 512 × 512). Diffusion sensitizing gradients were applied along six directions: [Gx,Gy,Gz] = [1,1,0], [1,0,1], [0,1,1], [-1,1,0], [0,-1,1], and [1,0,-1]. Interleaved acquisitions were performed on each line of k-space data for all experimental conditions, including the b = 0 image. Relative anisotropy (RA), Tr ($=\lambda_1+\lambda_2+\lambda_3$), $\lambda_{\parallel}$ ($=\lambda_1$), and $\lambda_{\perp}$ ($=(\lambda_2+\lambda_3)/2$) were measured in tissues of different degrees of anisotropy: Corpus Callosum (CC, RA = 0.75), External Capsule (EC, RA = 0.35), and Cortex (CT, RA = 0.15). A paired t-test was used to compare the DTI parameters obtained from (a) with those from other conditions. $P < 0.05$ is considered significant.

## Results

Region of interest analyses of CC, EC, and CT were performed on the derived maps under all conditions (Fig. 1). In order to minimize the inter-animal variation, the measurements of the data with longer diffusion time (b, c, and d) were normalized to the measurements with short diffusion time as shown in Fig. 2. Comparing to condition (a), there were no significant changes in RA within the CC or EC. However, a slight increase of RA was seen in the CT. Tr, $\lambda_{\parallel}$, and $\lambda_{\perp}$ exhibited the similar trend showing significant decreases in all three tissues with increasing diffusion time. Substantially more significant decreases were observed when a constant q value was applied, as in (c) and (d). Since the SNR of diffusion weighted images in (c) was 40% lower than that in (a), the comparable SNR was achieved in (d) by tripling the number of averaging. There were no significant differences in all parameters measured between (c) and (d) suggesting that the observed changes are not due to the difference in SNR.

## Discussion and Conclusion

ADC decreased with increasing diffusion time whether constant q or b value was maintained. A more significant ADC reduction was observed in constant q value approach. The preservation of RA with a significant reduction of directional diffusivities suggest that intra-axonal structures such as neurofilaments and microtubules may play a role in the observed restricted diffusion of central nervous system white matter in addition to axolemmas and myelin sheaths. Further studies are required to investigate the origin of the diffusion anisotropy and the restricted diffusion.

## References

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