

# Long Diffusion Time Improves DTI Tractography

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**INTRODUCTION:** Diffusion tensor imaging (DTI) tractography is gaining wide acceptance for mapping structural connectivity of the entire brain in a completely non-invasive manner. Most studies however use short diffusion time ( $t_{diff}$ ) and are generally limited to tracking large white-matter fibers. Diffusion measurements at long  $t_{diff}$  could sample more restrictive water motion and could thus be more sensitive to diffusion anisotropy. Apparent diffusion coefficient (ADC) and fractional anisotropy (FA) is dependent on  $t_{diff}$  [1, 2]. At longer  $t_{diff}$ , FA has been reported to be more sensitive to white-matter damages compared to the typical  $t_{diff}$  [3]. In this study, we hypothesize that long  $t_{diff}$  could improve fiber tracking. We used a modified STEAM EPI sequence to perform DTI measurements at long  $t_{diff}$ , avoiding significant signal loss due to T2 decay. DTI scans were acquired for 30 diffusion directions at multiple  $t_{diff}$  on fixed monkey brains. FA and DTI tensor field maps were analyzed for different diffusion times.

**METHODS:** DTI studies at multiple  $t_{diff}$  were performed on a phantom made up of mannitol in DMSO and on fixed monkey brains. [1H] Mannitol in DMSO was used to evaluate potential cross-term interactions at long  $t_{diff}$  because its ADC approximates the ADC of water in the fixed brain. The DTI parameters used in the phantom study were essentially identical to those used for the fixed brain studies.

DTI studies were performed on a 3T Siemens Trio scanner with a customized STEAM sequence. The DTI parameters were: TR = 3s, TE = 75 ms, 8 shot EPI, FOV = 76x76 mm, matrix = 64x64, two b values of 0 and 3950 s/mm<sup>2</sup>, 30 diffusion directions, and  $t_{diff}$  = 37, 120 and 250 ms, with corresponding averages of 6, 12 and 36. Diffusion time was varied by changing the mixing time, TM. Increased acquisitions were used for averaging at longer  $t_{diff}$  to minimize the effects of loss in SNR at different  $t_{diff}$  because the longer  $t_{diff}$  data has lower SNR due to T1 recovery. FA and tensor field maps were calculated. Tractography analysis was performed using line propagation techniques [4].

**RESULTS:** No significant  $t_{diff}$  dependence was observed for ADC obtained with the uniform mannitol phantom, indicating that cross-term interactions were negligible at long  $t_{diff}$ . In the fixed brains, ADC decreased with increasing  $t_{diff}$  as expected (data not shown). FA increased with increasing  $t_{diff}$  in both white (WM) and gray matter (GM) (Fig. 1).

In the corpus callosum, tensor magnitudes were large and tensor directions were identical between short (60 ms) and long (250 ms)  $t_{diff}$  (data not shown). Fig. 2 shows the tensor fields for two ROIs with smaller white-matter fibers for the short and long  $t_{diff}$ . Tensors of the long  $t_{diff}$  data had larger magnitude, were more directional and coherent with the neighboring pixels than those from the short  $t_{diff}$ . In other regions, the short  $t_{diff}$  tensors did not reveal ordered orientations whereas the long  $t_{diff}$  tensors revealed preferential directions that were coherent with the neighboring pixels. Fig. 2d shows an example of a tract terminated at a shorter distance in short  $t_{diff}$  data whereas the tracts continued in the long  $t_{diff}$  data, consistent with the expected structures.

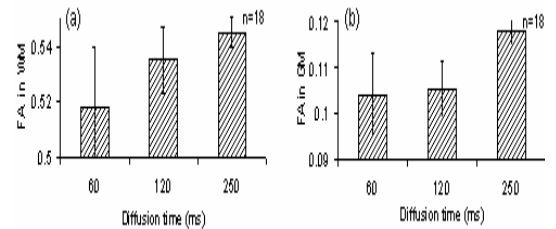


Fig. 1: FA as a function of  $t_{diff}$  of (a) WM and (b) GM from a fixed monkey brain.

**DISCUSSION & CONCLUSION:** Our results showed that DTI at long  $t_{diff}$  enhanced sensitivity to diffusion anisotropy, increased tensor strength and improved directionality in regions of smaller white-matter fibers. The coherence in tensor directions amongst neighboring pixels indicated that these findings were not noise. One limitation of long  $t_{diff}$  is SNR loss due to T1 recovery. This effect was significant on fixed brains because of its short T1 and required additional signal averaging at long  $t_{diff}$ . In live animals, T1 is significantly longer and the T1 effect from STEAM acquisition is small for  $t_{diff}$  ~250 ms as demonstrated previously [3]. In conclusion, these results suggested that DTI at long  $t_{diff}$  could improve tracking of smaller fibers. Future study will quantify reproducibility, validate tracking results against histology and include experiments on live monkeys.

**REFERENCES :** [1] Helmer et al, NMR Biomed 8:297 (1995). [2] Kim et al, MRM 54:1387 (2005) . [3] Nair et al., NeuroImage 28:165 (2005). [4] Mori S. et al., Ann. Neurol, 45:265 (1999)

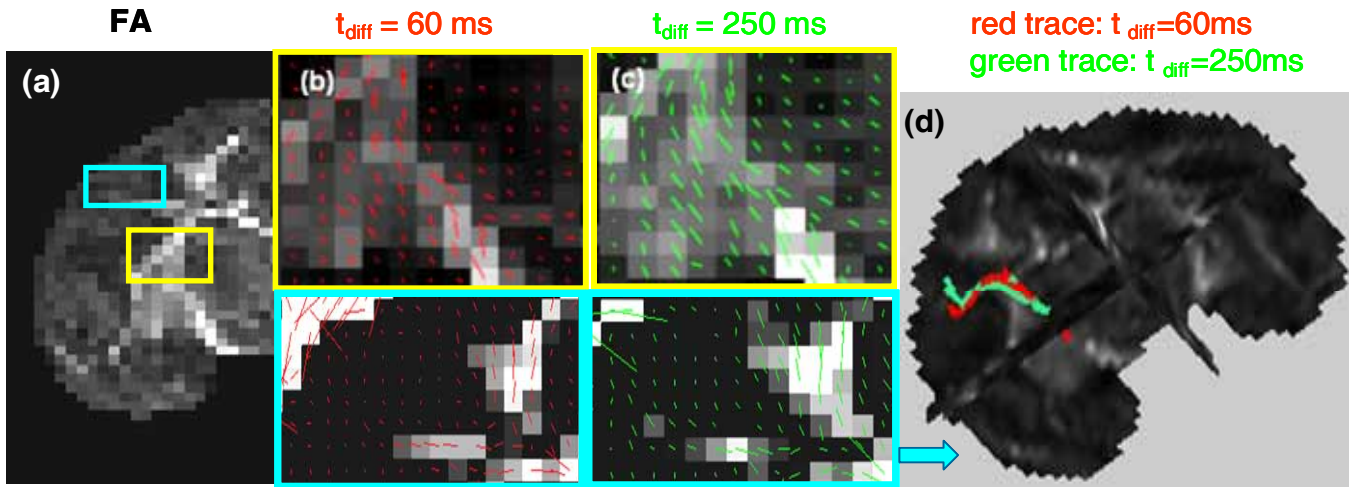


Fig. 2: (a) FA map of the left hemisphere and two overlaid ROIs. Tensor field maps for (b)  $t_{diff}$  = 60ms and (c)  $t_{diff}$  = 250ms overlaid on the corresponding FA maps. (d) Tractography at  $t_{diff}$  = 60 (red) and 250 ms (green) for the blue ROI.