# In Vivo Measurement of Intra-Voxel Crossing Fibers in the Cerebral Cortex Using Diffusion MRI

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**Target Audience:** Physicists, neuroscientists and clinicians who are interested in using diffusion MRI to study cerebral cortical fiber patterns.

**Introduction:** Conventional diffusion tensor imaging (DTI) provides information about the orientations of white matter pathways but is not a very good model for gray matter. Coherent patterns of diffusion anisotropy in the cerebral cortex were first observed in high-resolution postmortem DTI and more recently in higher resolution *in vivo* acquisitions[1-4] It has been shown that the principal diffusion orientation within most regions of cortex is radial (perpendicular to the cortical surface) [1-4]. Histology shows, however, that there also exist coherent fiber patterns within cerebral cortex oriented tangential (along the laminae) to the cortical surface (e.g. inner and outer stripes of Baillarger and the dendritic tufts[5]. Here we present an *in vivo* diffusion MRI protocol that has been optimized for detection of cortical fiber orientations. We compare four different analysis strategies for characterizing radial and tangential fiber patterns in an region-of-interest (ROI) containing the primary motor (M1) and primary somatosensory (S1) cortices.

**Methods:** *Data Acquisition.* The study was performed with IRB approval and written consent was obtained from three healthy volunteers (one 25 y.o. female, one 26 y.o. male, one 35 y.o. make). Data were acquired on a 3T MR750 MRI scanner (GE Healthcare) with $G_{max}$=50 mT/m, SR=200 T/m/s equipped with a 32-channel receive coil (Nova Medical). A 2D single-refocused diffusion-weighted (DW) SE-EPI sequence with 50% increased crusher gradients (to eliminate spurious echo artifacts in the high resolution images) was used to acquire HARDI data (960 directions at b = 1,000 s/mm$^2$ ). Images with b = 0 s/mm$^2$ (69 in total) were interspersed every 14 DW images. The protocol parameters were: TE/TR = 70/3500 ms, FOV = 21×21 cm$^2$, matrix size = 210×210, spatial resolution=1×1×1 mm$^3$, 28 contiguous axial slices directly above the corpus callosum, ASSET R = 3, BW = 2604 Hz/pixel, acquisition time = 1h. *Data Analysis*. The data were first corrected for field drift, bulk motion and eddy current distortions using the function EDDY from the FMRIB Software Library (FSL)[6]. Diffusion tensor (DT) and BEDPOSTX (2 sticks) models were fitted using the FSL function dtifit and bedpostx. Constraint spherical deconvolution (CSD)[7] and constant solid angle q-ball methods were performed to reconstruct orientation distribution functions (ODFs) using dipy software[8]. DT and CSD model were compared based on their accuracy in fitting the diffusion signal through 8-fold cross-validation[9]. In each voxel included in the ROI, a random 12% of the diffusion signal samples (~100 samples) were chosen for each iteration of the cross-validation, and the model was fit to the remaining 88% of the data. A prediction of the unused samples was performed based on the model. To evaluate and compare the models, model predictions of the q-space samples in each voxel from 8 iterations of the algorithm,were compared to all of the q-space measurements and the correlation between the predicted data and the original data were computed.

**Reults and Discussion:** Figure 1 displays the model fitting results from four methods: a) the diffusion tensor, b) bedpost, c) CSD d) peaks detected by CSD ODF, e) CSA[10] and f) map of the indicating the voxels (in red) in which the CSD model provided a better prediction accuracy compared to the diffusion tensor. The diffusion tensor results (Fig. 1a) clearly show that the principal diffusion direction is orthogonal to the cortical surface in M1. The tensors fan out from the white matter to the cortex. However, the tensors fail to capture the diffusion orientations that are tangential to the surface of the cortex. These tangential oreintations are visualized only with the other three methods (bedpost, CSD and CSA). The two sticks from the bedpostx method (Fig. 1b) demonstrate nearly orthogonal crossings in most cortical voxels. ODFs from CSA method are less sharp since CAS is a model-free method but still crossing fibers are shown. The fiber ODF from the CSD method not only capture the orientation information but also the response intensity such that the ratio between the tangential versus radial diffusion response can be can determined. For Figure 1f, the voxels locations (in red) in which the CSD model provided a better prediction accuracy compared to the diffusion tensor are largely constrained to the cortex. This is likely a reflection of the fact that the DT model fails to capture the crossing fibers in the cortex.

**Conclusion:** We studied cortical diffusion patterns in the *in vivo* human brain. The DT model clearly shows the principal diffusion orientation in the cortex is orthognonal to the cortical surface. The CSD and bedpostx model show that the crossing fibers can be detected reliably *in vivo* and are nearly orthogonal to each other.

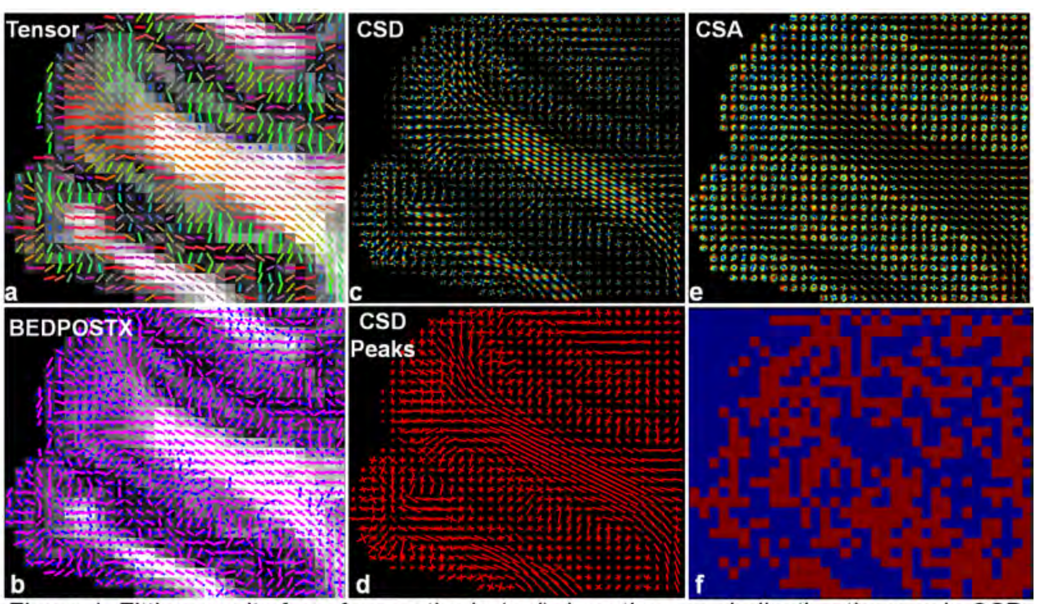

Figure 1, Fitting results from four methods (a-d). Location map indicating the voxels CSD better performs DT model predicting diffusion signal (in red).

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