Diffusion spectrum MRI of cortical architectonics: visualization of cortical layers and segmentation of cortical areas by analysis of planar structure

V. J. Wedeen[1], S. Song[2], L. Wald[1], T. G. Reese[1], T. Benner[1], W. Tseng[3]

[1]Athinoula A. Martinos Center For Biomedical Imaging, Massachusetts General Hospital and the Harvard Medical School, Boston, MA, United States, [2]Washington University, St. Louis, MO, United States, [3]National Taiwan University, Taipei, Taiwan

Introduction This study investigates the capacity of diffusion spectrum MRI (DSI) to delineate the cytoarchitectonics of the cerebral cortex. While diffusion tensor imaging (DTI) is sensitive to aspects of gray matter architecture, as has been shown in deep gray nuclei [1] and in the developing cortex [2], DTI contrast is typically weak in the adult cortex, where tensors are relatively isotropic and uninformative. Recently, we have described an alternative and more general approach to diffusion MRI, diffusion spectrum imaging or DSI, which, by reconstructing a full 3D probability density function (pdf) of diffusion for each location, affords an extended capacity to detect and define neural cyoarchitectures of increased complexity [3,4].

This study presents methods for the creation and analysis of non-trivial intra-cortical contrast, based on DSI of the mouse brain *ex-vivo*. We describe a novel approach for analysis of DSI data, focusing on the planar or 2D structure of the diffusion pdf. After defining this approach to the mapping of cortical architecture, we test it in two ways. First, we use it to construct 3D graphics which we evaluate for their capacity to reveal known features of cortical architecture. Second, we use these data as the basis for an automated segmentation of the cortex, and evaluate whether this segmentation accurately defines known anatomy.

Methods and Results *1. Acquisition* Formalin-fixed coronal sections of mouse brain 2 mm thick were imaged within 72 hrs of fixation in a Brucker 4T imaging spectrometer with a custom RF coil. Using an *SE 2000/50* acquisition with spatial resolution of *180 x 180 x 240 μm*, or 5-10 pixels across the cortical thickness, DSI data were acquired with 591 *q*-encodings comprising a regular cubic lattice within the sphere of radius $|q| \le \sqrt{29}$ grid units, with diffusion mixing time $\Delta = 25$ *ms*, diffusional displacement resolution $(\pi q_{max})^{-1} \approx 3$ *μm*, and $b_{max} \approx 17000$ *s mm*$^{-2}$. For each voxel, the 3D pdf of diffusion *p(r)* was reconstructed by 3DFT of the signal amplitude *s(q)*. To define orientational dependence, the 3D function *p(r)* was mapped onto the sphere $|r| = 1$ and the signal amplitude *s(q)* onto $|q| = 1$ by radial projection ($\int p(r) d|r|$, etc.), and the local maxima of these spherical functions identified as vectors R_i and Q_i, respectively.

2. Visualization Except for single maximum of the pdf R_1 corresponding to the radially-oriented components of cortical architecture, the remaining maxima of the pdf cannot be consistently defined, and it is at least possible that their individual identities are in fact inconsistent. Accordingly, we may consider not individual maxima, but their aggregates, among the simplest of which are planes [5]. We will define planar structure within the diffusion pdf in 2 ways: planes of maximum diffusion, defined, by simple Fourier duality, as planes perpendicular to maxima Q_i of the raw data *s(q)* and, a more *ad hoc* definition, as planes that span pairs of orientation maxima $\{R_i, R_j\}$.

Figure 1 is a 3D rendering of mouse DSI with icons representing linear and planar structure: colored lines for maxima R_i, colored discs for planes of maximum dispersion perpendicular to Q_1, gray diamonds for planes that span the diffusion maxima $\{R_1, R_2\}$. Intracortical contrast corresponding to the cortical layers is immediately apparent. The cortex is delimited by layers 1 and 6, where we see sharp increases in horizontal structure. Between these, contrast corresponding to layer 2, then layers 3/4 and finally layer 5 appears as gradual intracortical variation in the density of planar architecture and of its orientation, particularly its orientation in horizontal directions. Medially, the cingulate cortex has a quite distinct appearance.

3. Segmentation Automated segmentation of the DSI data of Fig. 1 is carried out by coding the 1D and 2D structures defined by the pdf as a single data vector for each voxel, and then applying a simple k-means segmentation routine to these data [1]. More specifically, for each voxel, we form a data vector $\{x, y, R_1, R_2, \ldots, Q_1, Q_2, \ldots, R_1 \times R_2, \ldots\}$, where *x* and *y* are the 2D image coordinates of the voxel. To suppress effects of gross cortical orientation, all vectors at each point are given an identical an in-plane rotation to align the $\{x,y\}$-components of the principal radial orientation at that location R_1 with the image *y*-axis. To eliminate the effect of orientation sign ambiguity of diffusion contrast, every local vector *V* is then converted to the 3 x 3 symmetric tensor $V^T V$ before segmentation, whose one nonzero eigenvalue has eigenvectors $\pm V$. The k-means algorithm was initialized with $N = 80$ seed points, this approximately the number of principal segments classically identified by histology for this mouse brain section [6].

Figure 2 shows the result one trial of an automated segmentation. Comparing this segmentation with a standard histological atlas indicates considerable capacity of the automated procedure to identify established cytoarchitectonic areas, both cortical and subcortical.

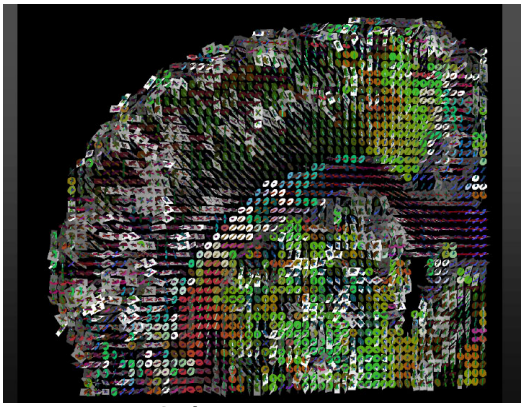

Fig. 1. Mouse DSI planar structure.

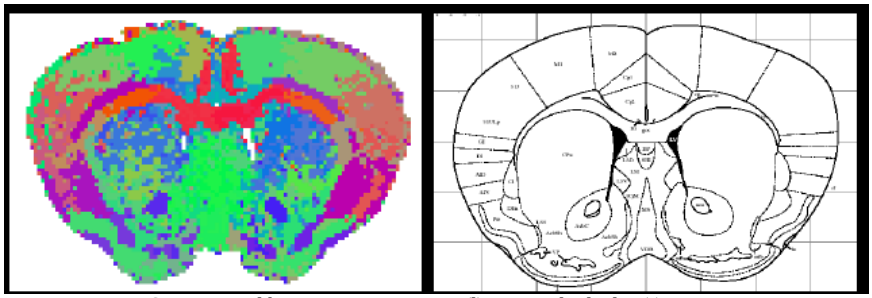

Fig. 2. Mouse DSI automated k-means segmentation (l) vs. standard atlas (r).

Discussion DSI with display and analysis of the planar or 2D structure of the diffusion pdf affords a new window into the architecture of the neocortex, enabling the visualization of laminar architecture of the cortex and the delineation of regional architecture by automated segmentation. The detection of planar structure within the diffusion pdf amounts to a kind of geometric filter matched to fiber dispersion, more coherent than pdf maxima, and yet particularly informative about the horizontal components that may furnish crucial intracortical contrast. As such, this approach goes beyond the paradigms of fiber orientation mapping that have held sway in most previous diffusion MRI of neural architecture. This study suggests that DSI holds promise for the mapping cerebral gray matter architecture, and potential for the discovery of novel types of order within cerebral architectonics.

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