

# IMAGING THE GRID STRUCTURE OF THE BRAIN WITH DSI AND QBI WITH THE 3T CONNECTOM INSTRUMENT: CONDITIONAL VALIDATION OF IN VIVO MRI TRACTOGRAPHY IN HUMANS

Van J Wedeen<sup>1</sup>, Ruopeng Wang<sup>1</sup>, Timothy G Reese<sup>1</sup>, Thomas Witzel<sup>1</sup>, Julian Cohen-Adad<sup>2</sup>, Bruce R Rosen<sup>1</sup>, and Lawrence L Wald<sup>1</sup>

<sup>1</sup>Martinos Center for Biomedical Imaging, Mass General Hospital, Harvard Medical School, Charlestown, MA, United States, <sup>2</sup>Department of Electrical Engineering, Institute of Biomedical Engineering, Ecole Polytechnique de Montreal, Montreal, Quebec, Canada

**Background:** Diffusion MRI of the structure of the brain ventures to discover a reality scarcely known in other ways. This poses several challenges. One is uncertainty as to how to represent such data, recognize salient features, and describe human variation. Perhaps more fundamental is uncertainty as to how to know the accuracy and value of this data, given the deficit of exterior standards to which it can be compared. Recently, it has been shown, with MRI, that the brain pathways adhere to a curvilinear coordinate system derived from the three axes of development [1]. This finding potentially can contribute to the resolving these difficulties, first, as a framework for analysis - the natural coordinate system of the brain - and second, as a means to validate MRI of brain pathways by testing it against an exceptional constraint on pathway imposed by this structure. Here we test the practicability of grid imaging in humans, acquiring data with several diffusion MRI methods and analyzing grid structure with a new operator-independent algorithm.

**Methods:** High angular resolution diffusion MRI - diffusion spectrum and Q-ball imaging (DSI, QBI) - were obtained in normal human subjects. Scans were performed in a Siemens 3T Connectom, a modified Skyra platform notable for a 2-meter insert gradient of peak intensity  $G_{\max} = 300 \text{ mT m}^{-1}$ . Scans were acquired with a 1 or 2 echo SE diffusion-weighted pulse sequence, TE equal to the minimum allowed by the gradient encoding, with spatial resolutions of 1 - 2 mm isotropic, DSI acquired with 514 diffusion encodings and  $b_{\max} = 15000 \text{ s mm}^{-2}$  and QBI with 128 or 256 encodings and sensitivity  $1000 \leq b \leq 12000 \text{ s mm}^{-2}$ . For reference DSI with  $b_{\max} 15000 \text{ s mm}^{-2}$  required TE 65 ms. With acquisition of one slice per excitation, scan durations were 10-60 min per cerebral hemisphere. Grid structure was reconstructed without operator intervention using a new algorithm, as follows. Its plan is to create two fields of crossing fibers and then select the segments that fulfill the grid constraint. At each voxel, two maximum vectors of the diffusion ODF are chosen, and a path from each extended, by streamline tractography, to serve as the axis of a local 2D grid. On each of these axis curves an array of paths is seeded, each initially parallel to the other axis. The distances between these two families are then computed, and segments retained where this is below a threshold, usually 1 voxel, so that these fibers cross in a 2D sheet per the grid thesis. The result is an image volume occupied not by simple paths but sets of paths that cross as 2D surfaces. In an ideal study, the brain would be filled with broad 2D grids in three orthogonal orientations.

**Results:** Rigorous analysis of this complex varied data collection is not yet possible, however preliminary qualitative conclusions may be ventured. In all cases, the great preponderance of grid regions constructed appeared consistent with known anatomy and with the hypothesis of grid structure of the brain. The density and extent of the grid domains increased consistently with image quality, as defined by SNR, diffusion b-value, and spatial resolution. Compared with the rhesus brain ex vivo, the human data generally do not achieve similar grid densities, except in notable regions including the *centrum semiovale*, where human and rhesus data both show

structure previously defined in detail [2]. Comparing diffusion methods, DSI appears more robust in compact white matter of central areas and 3-way crossing, while QBI occasionally shows more extensive structure within gyral "blades" not previously identified. Rarely, different methods could produce plausible but incompatible structure, indicating the methodology as defined is not infallible.

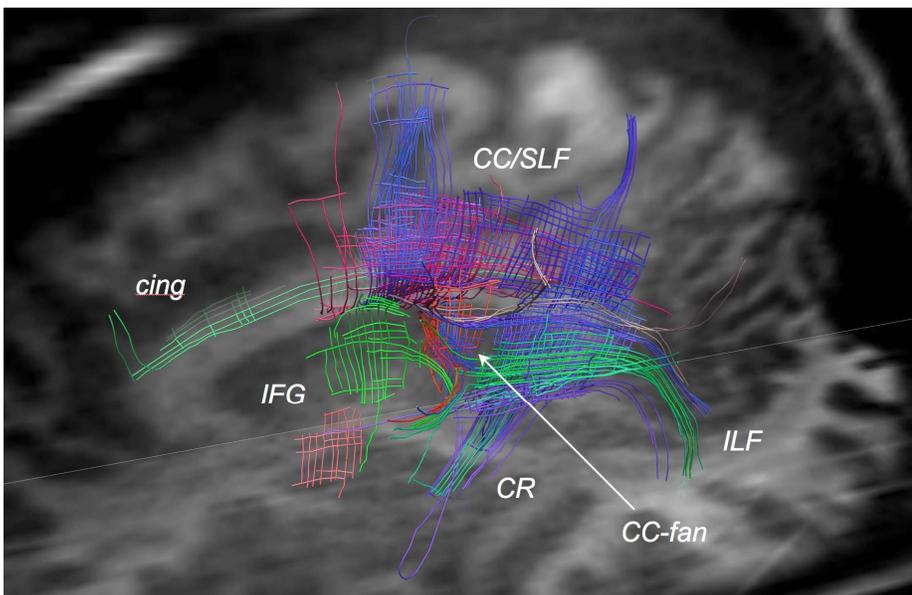


Fig 1. Components of frontal grid structure of a normal human subject QBI  $b=8000 \text{ s mm}^{-2}$  1.5mm isotropic resolution constructed as described in the text. Identified domains include *cingulum* bundle (cing), *inferior frontal gyrus and sulcus* (IFG), *corona radiata* (CR), *corpus callosum* and SLF1 (CC/SLF), *inferior longitudinal fasciculus* (ILF) and the *transverse fan of the corpus callosum* within the *centrum semiovale* (CC-fan).

**Conclusions:** The grid structure of the brain is easily detected across a range of high angular resolution diffusion MRI methods in human subjects. While these grid data are highly incomplete and their analysis preliminary, evidence is highly encouraging that grid analysis will be useful in humans both as a metric of scan value and as a framework for structural analysis.

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