Analysis Approaches of Diffusion MRI

The analysis pipeline of diffusion MRI usually have 3 major sections: data preprocessing, computation of the diffusion tensor and scalar maps, and quantitative analysis. Some common metrics used to compare DTI metrics are: mean diffusivity(MD), axial diffusivity(AD), radial diffusivity(RD), and fractional anisotropy(FA). They are all used to measure statistical comparison.

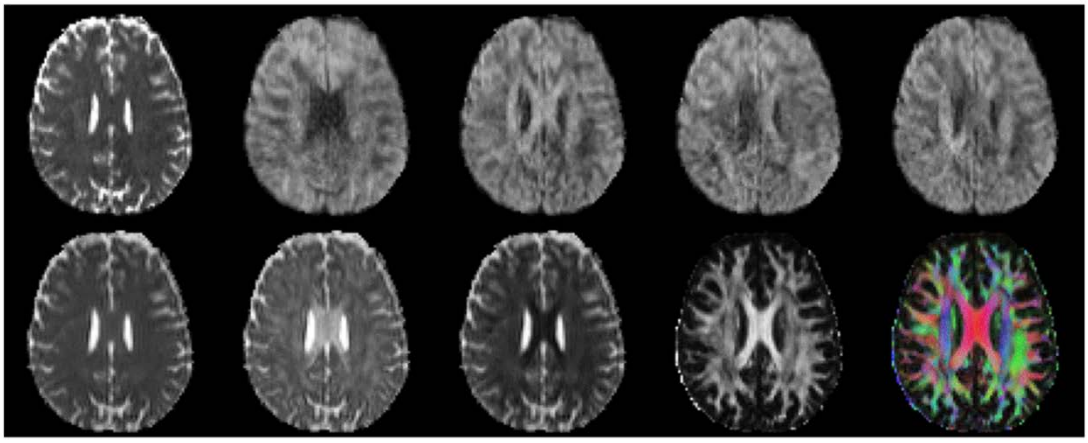

Figure 1. Top row shows b=0 s/mm² scan followed by 4 different slices with b=100 s/mm² and different gradient orientations.
Bottom row: mean diffusivity, axial diffusively, radial diffusivity, fractional anisotropy and tensor color map.

1. ROI (Region of Interest)

This approach is often used when the study has hypotheses involving specific brain regions of interest or pathways, which based on the manual delineation of specific regions of the brain or on an automatic parcellation method. Ideally, ROIs are determined on imaging data (T) independent from the DTI data and then registered onto the diffusion parametric map to avoid position bias. Then we can analyze summary statistic from the DTI scalar map of interest. We can also perform some statistical analysis on the resulting values.

Apart from automatic parcellation method, researches can also place ROIs manually. The main advantage of this way is the high sensitivity to small changes in DTI values in interested part of brains. But the disadvantages are also very apparent: labor intensive, require significant anatomic knowledge and so on.

2. Histogram Analysis

In the histogram analysis, the full range for a particular DTI metrics is divided into discrete bins and a count is performed within a region of interest to determine the

number of voxels with parameter values hat fall within the range of each bin. It is used to look for subtle changes that impact large areas or the entirety of the brain. We can compare some features of the histogram, such as peak location, mean, median as well as more complex representations of shape.

- **Advantages:** sensitivity to diffuse effects; have less need for manual intervention; provide fewer tests.

- **Disadvantages:** a lack of anatomic specificity, selection an appropriate bin size, normalization and smoothing level, decisions on how to handle partial volume voxel and the care needed to remove tissue of non-interest.

3. Voxel Based Method

In this method, subject images are registered to a common template space, Individual anatomy is distorted to achieve a voxel-wide correspondence across subjects, and then do a statistical analysis voxel-wisely to uncover group differences or correlations between DTI metrics and descriptor variables for the study populations.
Process for VBM: computation of the scalar map of interest in the data acquisition space; registration of the data to a common template space and spatial smoothing; performing statistical analysis (eg: multiple regression); multiple comparison corrections to reduce the type-1 error for the large number of voxels in the image space (eg: parametric and non-parametric methods).

- **Advantages:** automated; have the potential to be highly reproducible and scalable to large study samples; allows for testing across the whole brain while providing high anatomical specificity.

- **Disadvantages:** have a strong dependence on the details of the steps used in the analysis pipeline, i.e. the template chosen, the smoothing level used, the methods for image registration and the methods used to correct for multiple comparisons. More importantly, the automated registration methods may fail.

4. Tract Based Spatial Statistics

TBSS is a type of VBM which is included in the FSL package that is specifically designed for DTI analyses. The difference between the two method is TBSS does not require a highly accurate initial registration as with standard VBM but instead uses a template based on a skeletonize fractional anisotropy map that is derived from the nonlinearly aligned FA images of the population being studied.

- **Advantages:** allow more precise spatial comparison across subjects; prevent partial volume effects and prevent cross-contamination of different tissues.

- **Disadvantages:** its reliability is subject to preprocessing steps choice; it does not allow proper estimation of diffusion in voxel where there are crossing tracts or junctions; detection of signal in voxels that are father away from tract center is reduced.

5. Tractography

Diffusion tractography is currently the only non-invasive, in vivo method for studying structural brain connectivity.

- **Principle:** apart from producing scalar metric of diffusion, the tensor model also produces voxel-wise information of the local orientation of the primary diffusion vector, which for white matter is assumed to be the direction of the domain fiber bundle.

Based on the approach taken of how to connect the vectors and what other information is used, researches have developed various method of tractography.

(1) **Deterministic tractography:** reconstruction of a white matter tract by selecting a seed starting point and following a streamline based on the preferred direction of diffusion ellipsoids until an ending criteria is reached and the entire pathway is delineated.

Disadvantage: due to the resolution of dMRI is much larger than an axon, there are typically thousands of axons passing through a given voxel, and they may not all go in the same direction.

(2) **Probabilistic tractography:** In this method, the most likely fiber orientations are estimated at each voxel along with the probability distribution that a fiber would run along these directions. These probability distributions are then used to trace thousands of probable connections based on slightly jittered orientation.

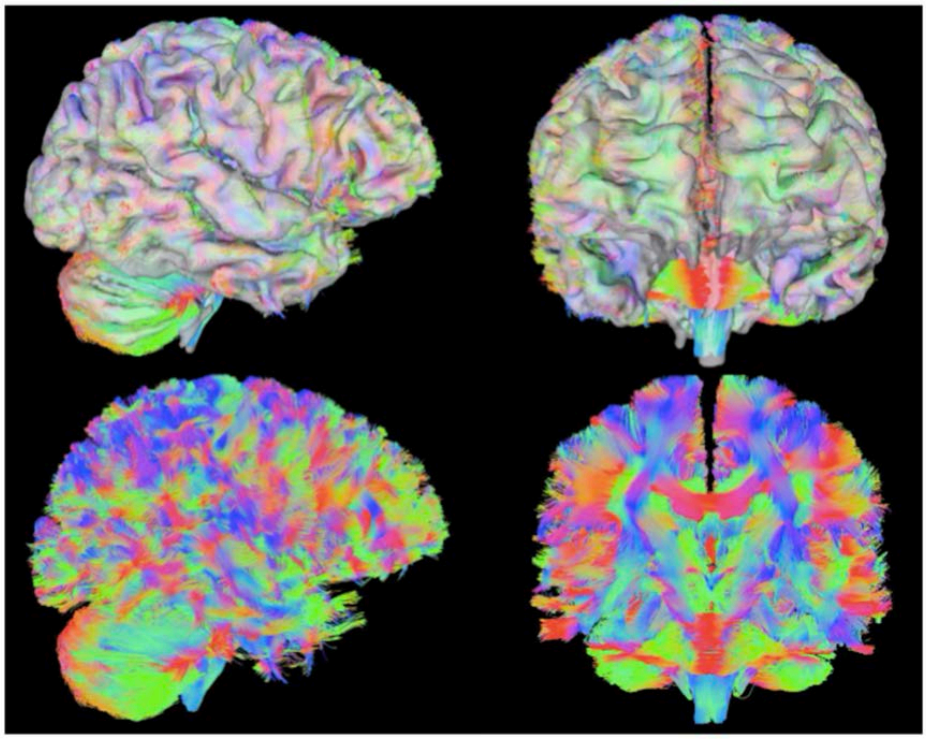

Figure 2. Using Deterministic tractography to estimate white matter streamlines from diffusion MRI data.

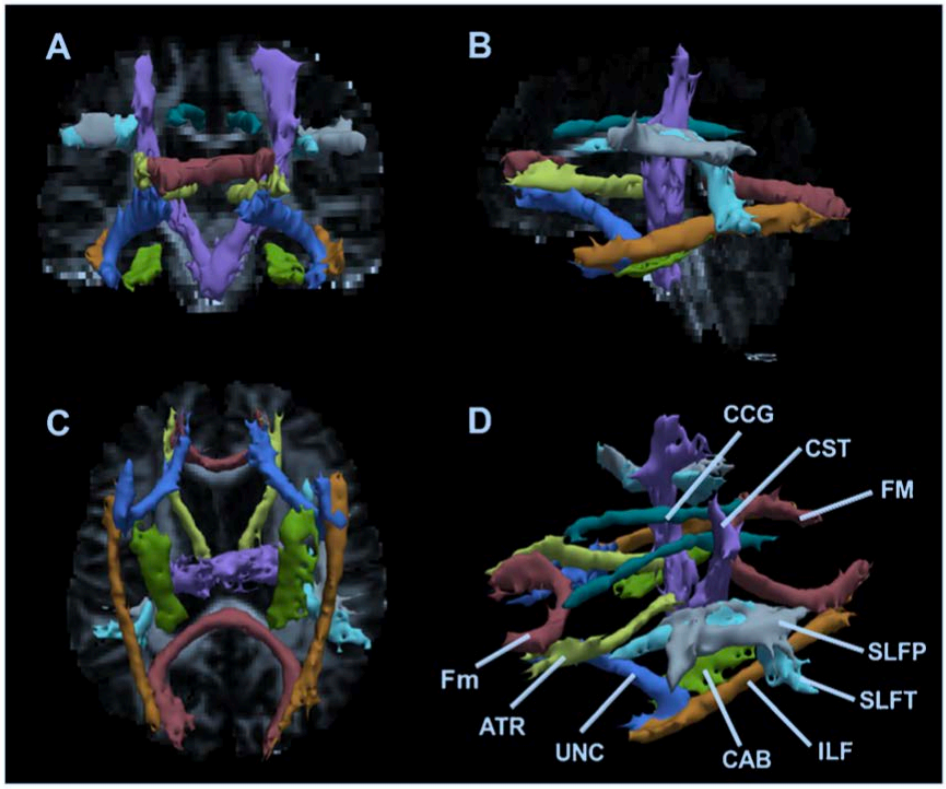

Figure 3. Using probabilistic tractography to estimate the paths of 18 specific white matter tracts.

References:

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