

Human Brain White Matter Tractography with Diffusion MRI and DSI Studio

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Abstract: Diffusion-weighted magnetic resonance imaging (DW-MRI) based white matter tractography has become an indispensable tool in neuroscientific research and therapeutic neuroimaging. DSI Studio is a comprehensive diffusion MRI image reconstruction, fiber tracking, quantitative analysis and connectome mapping software package. DSI Studio offers quantitative anisotropy (QA) based tracking and supports a number of reconstruction models, including diffusion spectrum imaging (DSI), generalized q-sampling imaging (GQI) and diffusion tensor imaging (DTI), and is thus quite versatile. DSI Studio is a sophisticated software application designed for processing, analysing, and visualizing diffusion MRI (dMRI) data using Diffusion Spectrum Imaging (DSI) techniques. Fiber tractography is useful in clinical practice for surgical planning by neurosurgeons for avoiding important white matter tracts and lowering surgical risks. It helps with abnormality detection, diagnosis support, planning of treatments, and insights into neurological diseases.

Keywords: Diffusion Spectrum Imaging (DSI), White Matter tracts, Fiber Orientation Distribution (FOD), Diffusion MRI (dMRI), Diffusion Tensor Imaging (DTI)

I. INTRODUCTION

White matter tractography is a computer aided reconstruction of axonal fiber routes in brain from diffusion-weighted MRI data, has significantly evolved since its inception in the early 2000s. The ability to non-invasively map structural brain connectivity of human brain has transformed both basic neuroscience and clinical practice, allowing investigation of the human brain connectomics, brain surgical planning, and quantitative characterization of pathological change in neurological and psychiatric disorders.[1],[2].

A. Role of diffusion in Magnetic Resonance Imaging

Brain is highly anisotropic due to presence of white matter fiber tracts. Diffusion of water molecules shows high anisotropy in white matter regions as compared to gray matter regions. In Magnetic Resonance Imaging (MRI) diffusion coefficient in a particular part of brain for diffusion in a certain direction can be determined by applying a strong magnetic gradient in that direction. Diffusion based MRI provides many different imaging modalities with different capabilities. Major diffusion MRI based imaging methods are listed below:

B. Diffusion Weighted Imaging (DWI):

In DWI, less than six gradient directions are used to determine Mean Diffusivity (MD) or Average Diffusion Coefficient (ADC) of water molecules in different parts of the brain. This has many clinical applications including assessing brain stroke.

C. Diffusion Tensor Imaging (DTI)

DTI [2] is an extension of DWI that maps the directionality of water diffusion, useful for studying white matter tracts in the brain. DTI determines the full anisotropic diffusion tensor for diffusion of water molecules in each imaging voxel. By applying six different gradients all six independent components of the symmetric diffusion tensor can be determined in each imaging voxel in brain.

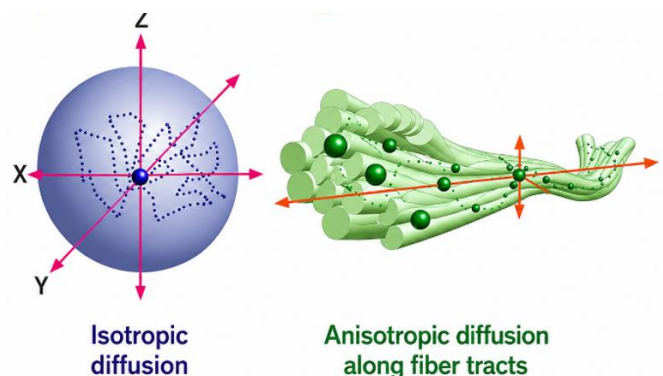


Fig. 1: Isotropic diffusion is prevalent in gray matter where water molecules diffuse equally in all directions. Anisotropic diffusion is prevalent in white matter fiber tracts.

Using DTI several scalar measures such as fractional anisotropy (FA), mean diffusivity (MD) and major diffusion directions can be determined from diffusion tensor's eigenvectors and eigenvalues.

Diffusion tensor is geometrically represented as an ellipsoid and it is possible to calculate tract trajectories using deterministic or probabilistic streamlines along main eigenvectors of the diffusion tensor. Deterministic tractography uses a step-and-angle algorithm to propagate streamlines along the major eigenvector until the FA is below a threshold or the angular change exceeds a defined limit [3].

Despite its historical importance, DTI is afflicted by a well-documented and intrinsic limitation: it is incapable of distinguishing numerous crossing, touching, or spreading fiber populations inside a single voxel. Approximately 60-90% of white matter voxels comprise crossing fibers [2]. DTI's single-tensor approach falters in regions of complex fibre architecture. Crossing fibers give rise to circular or spherical tensors. This causes confusion about actual fiber orientations and distorts the streamlines and leads to inaccurate or incomplete tracts [4].

D. Multishell or Multi-b-value Diffusion Imaging:

Strength of applied magnetic field gradient is denoted by a parameter called b-value which can also be called the diffusion weighting factor. MRI images with non-zero b-values are able to capture information about diffusion of water molecules along the applied gradient direction. DWI and DTI use two b-values, one close to zero as a reference and one at a high b-value. Multi-b-value DWI acquires images with multiple b-values, allowing for more accurate assessment of tissue microstructure and diffusion properties. This can improve the differentiation between various tissue types and enhance sensitivity to subtle changes. This is also called multishell data acquisition.

Multi-shell diffusion imaging [5] is an advanced diffusion MRI acquisition technique that collects diffusion-weighted data at multiple b-values, enabling a more comprehensive characterization of tissue microstructure compared to single-shell diffusion imaging. By sampling diffusion signals across different diffusion sensitivities, multi-shell imaging supports sophisticated diffusion models such as neurite orientation dispersion and density imaging (NODDI) [6], constrained spherical deconvolution (CSD) [7] and diffusion kurtosis imaging (DKI) [8]. This approach improves the estimation of complex fiber architectures, tissue compartment properties, and microstructural organization in the brain, making it particularly valuable for studying neural connectivity, neurodevelopment, neurodegenerative disorders, and brain pathology. Multi-shell diffusion imaging has become increasingly important in modern neuroimaging research because it provides richer and more biologically meaningful information about tissue structure and connectivity.

E. Diffusion Kurtosis Imaging (DKI):

Diffusion Kurtosis Imaging (DKI) [8] is an advanced magnetic resonance imaging (MRI) technique that extends conventional Diffusion Tensor Imaging (DTI) by measuring the non-Gaussian diffusion behavior of water molecules in biological tissues. While DTI assumes that water diffusion follows a simple Gaussian distribution, DKI captures the complexity and heterogeneity of tissue microstructure, making it more sensitive to subtle pathological and developmental changes in the brain and other organs. DKI provides additional metrics such as kurtosis values, which reflect the degree of restriction and complexity in tissue environments, enabling improved characterization of white matter integrity, tumor heterogeneity, neurodegenerative diseases, stroke, and traumatic brain injury. Because of its ability to reveal microstructural information beyond standard diffusion imaging, DKI has become an important tool in both clinical research and biomedical imaging applications.

F. High Angular Resolution Diffusion Imaging (HARDI)

Advanced techniques like High Angular Resolution Diffusion Imaging (HARDI) [9],[10]. provide more accurate representations of complex fiber structures. Problems associated with DTI can be resolved by using more advanced MR imaging methods like HARDI using a large number of diffusion gradients applied at high angular resolution during imaging session. HARDI acquires data from a large number of gradient directions and reconstruct the orientation distribution function (ODF), which is a function that describes the likelihood of diffusion as a function of direction. DTI requires only six gradient directions, but HARDI approach can use hundreds of diffusion gradient directions.

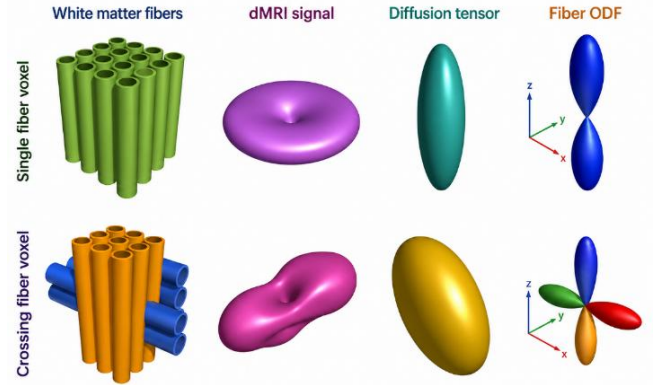


Fig. 2: DTI is unable to resolve fiber crossings, but ODFs are able to resolve fiber crossing areas.

HARDI refers to diffusion MRI imaging methods with high angular sampling and includes methods such as Q-ball imaging (QBI), diffusion spectrum imaging (DSI), constrained spherical deconvolution (CSD), diffusion spectrum imaging (DSI) and generalized q-sampling imaging (GQI). CSD as implemented in MRtrix3, deconvolves the fibre response function to provide fibre orientation density functions (fODFs) [9].

HARDI is an advanced neuroimaging technique used to study the complex microstructure of tissues, particularly in the brain's white matter. It is an extension of traditional diffusion-weighted imaging (DWI) and diffusion tensor imaging (DTI) that provides more detailed information about the orientation and connectivity of neural pathways. HARDI is especially valuable for imaging areas with crossing or branching nerve fibers, where the assumptions of the DTI model may not apply.

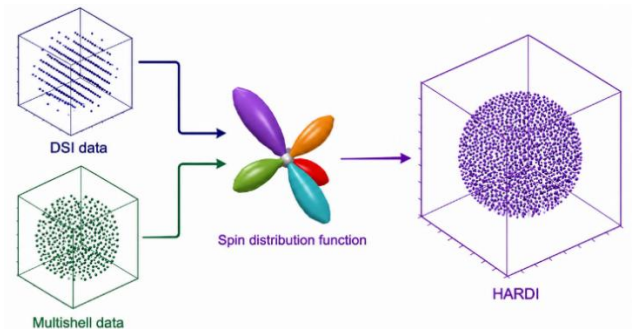


Fig. 3: HARDI imaging based on DSI and Multishell data

HARDI aims to overcome the limitations of DTI, which assumes a single dominant fiber orientation within each imaging voxel. In reality, many brain regions have complex fiber arrangements with multiple crossing or bending fibers. HARDI acquires diffusion data using a larger number of gradient directions and higher b-values (which affect the sensitivity to diffusion), allowing for the detection of more complex diffusion patterns[11]

G. White Matter Fiber Tractography

Tractography or fiber-tracking uses local fiber directions measured at each voxel to track the trajectory of a white matter pathway. The axonal directions allow for tracking the trajectories of fiber bundles. Fiber Tractography is a valuable tool for understanding the structural connectivity of the brain.

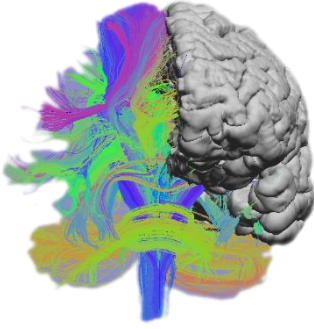


Fig. 4: White matter fiber bundles obtained using MR imaging based fiber tractography.

H. Tractography using DSI Studio

DSI Studio [12] is an advanced and widely used open source software platform which provides different advanced reconstruction methods for HARDI and a tracking algorithm based on quantitative anisotropy (QA). The software provides a single interface for diffusion spectrum imaging (DSI), generalized q-sampling imaging (GQI) and diffusion tensor imaging (DTI) reconstruction and includes tools for connectivity matrix analysis, tract-specific statistics and connectome visualization. It has been widely adopted in academic neuroimaging, spanning from clinical neurosurgery to population-level connectome studies.

Researchers use DSI Studio to map the connections of white matter tracts in the brain. It reveals information about tissue microstructure and connectivity, it helps researchers understand how the brain changes with age, psychiatric diseases, and neurological problems. Clinically, DSI Studio reveals abnormalities in white matter tracts that help in the diagnosis and characterization of brain illnesses like traumatic brain injury, stroke, epilepsy, and multiple sclerosis.

The DSI Studio reconstruction pipeline includes importing MRI image file in DICOM or NIFTI format and multiple preprocessing steps, including Gibbs ringing correction, eddy current correction, and signal-to-noise ratio (SNR) estimation. The software implements GQI reconstruction by estimating the spin distribution function (SDF) from the diffusion-weighted signal by means of a sampling method defined by the diffusion sampling length ratio (DSL), a critical parameter controlling the spatial resolution of fiber orientation estimates. A simplified pipeline is shown in Fig. 5.

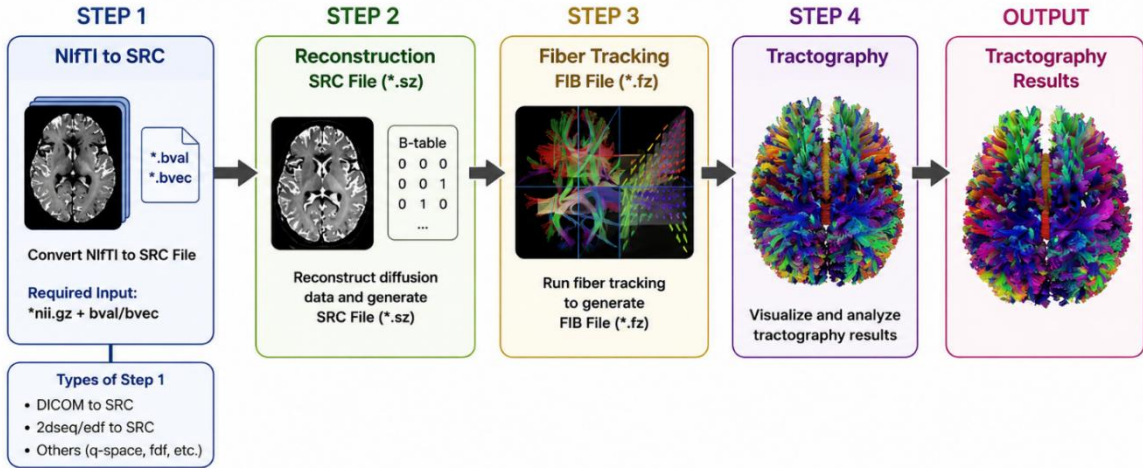


Fig. 5: Fiber tractography analysis pipeline using DSI-Studio.

A metric called quantitative anisotropy (QA) is constructed from the SDF maxima, normalized against an isotropic template, and reflects the anisotropic component of limited diffusion along each fiber orientation. Unlike FA, QA is additive across several fiber populations in a voxel, which makes it robust in detecting and differentiating crossing fiber compartments. This characteristic is crucial in that it allows DSI Studio to resolve complicated fiber architecture which is impossible in the single tensor approach under DTI[13].

DSI Studio employs an optimal propagation approach based on the fiber orientations extracted from the peaks of SDF. The approach determines the closest SDF fiber orientation to the current propagation direction at each point along a streamline using Runge-Kutta 4th order integration for numerical precision and terminates based on QA criteria, angular deviation limits or tract length limitations. The use of QA as the termination criterion instead of FA is especially important: FA is confounded by partial volume effects, and is diminished at crossing fiber interfaces,

leading to premature termination of streamlines. Quality assurance retains sensitivity in these regions, allowing reconstruction of tracts usually truncated by diffusion tensor imaging approaches[8]

I. Fiber tract shape measures

Various shape measures for fiber tracts can be determined from tractography analysis which have emerged as valuable descriptors that provide additional insights into anatomical variability and correlations with cognitive and clinical phenotypes, representing quantitative geometric characteristics that traditional diffusion metrics such as fractional anisotropy and mean diffusivity [14]

The principal fiber tract shape measures [15] that can be determined using tractography analysis encompass the following:

- Length (mean length of the bundle),
- Span (linear distance between bundle endpoints),
- Curl (length-to-span ratio),
- Elongation (length-to-diameter ratio),
- Diameter (projected width assuming a cylindrical form),
- Volume (aggregate occupied space),
- Total surface area (external surface area of the bundle),
- Total radius of end regions (mean radius at both extremities).
- Total surface area of end regions (surface area at both ends)
- Irregularity (degree of deviation from a smooth cylindrical shape)

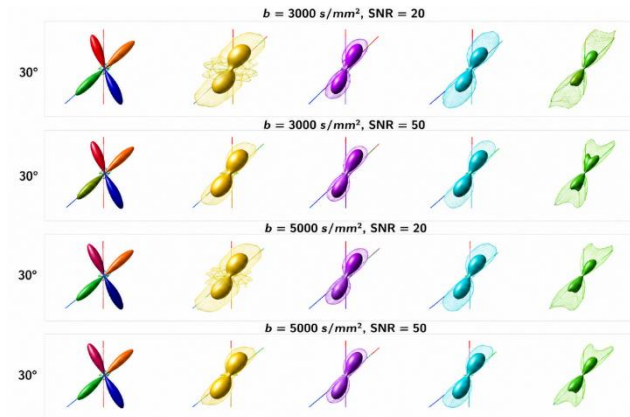


Fig. 6: Multishell imaging with different b-values

II. DATA FORMATS

Diffusion MRI (dMRI) data is typically acquired and stored in specific image formats that are suited for preserving the multidimensional and spatial information of the diffusion data. The most common image formats used for diffusion MRI data include:

A. DICOM (Digital Imaging and Communications in Medicine):

DICOM is most commonly used for storing and transmitting medical images enabling the integration of medical imaging devices such as scanners, servers, workstations, printers, network hardware, and picture archiving and communication systems (PACS) from multiple manufacturers. DICOM files often come with specific headers containing metadata about the acquisition parameters, patient information, and more. The DICOM format provides flexibility and compatibility with medical imaging systems.

B. NIfTI (Neuroimaging Informatics Technology Initiative)

The NIfTI format is a widely used standard used by researchers for storing neuroimaging data. NIfTI files usually have the ".nii" or ".nii.gz" extension. It supports both 3D and 4D data (such as multiple diffusion-weighted volumes over time). NIfTI files store not only the image data but also relevant metadata like image orientation, voxel dimensions, and other header information.

III. METHODOLOGY

Diffusion MRI data typically DTI or HARDI, can be used for white matter fiber tractography and related analysis.

A. DSI-Studio as software tool for diffusion MR data

DSI-Studio is a software application primarily used for processing and visualizing diffusion MRI (dMRI) data. Diffusion MRI is a specialized imaging technique that provides insights into the microstructural organization of tissues, especially the white matter tracts in the brain. It is primarily used for advanced diffusion imaging techniques, such as Diffusion Spectrum Imaging (DSI) and High Angular Resolution Diffusion Imaging (HARDI). DSI Studio provides a range of features for processing, visualizing, and analysing dMRI data, making it a valuable tool for researchers and clinicians working in the field of neuroimaging. These are below steps for tractography processing.

DSI Studio is a popular tool for tractography analysis and mapping white matter connections in neuroscience and clinical research. It facilitates the study of neurological and psychiatric illnesses, brain development and aging, multiple sclerosis, cognitive function and brain plasticity by analyzing structural connection patterns. The program enables neurosurgical planning, the interpretation of functional connectivity, assessment of drugs and treatments, and personalized medicine through the analysis of patient-specific connectivity. Also, DSI Studio is a vital instructional and training tool for diffusion imaging,

tractography, and neuroanatomy studies. DSI Studio's versatility and advanced capabilities make it a valuable resource for researchers and medical professionals seeking to delve into the intricate details of brain structure and connectivity. However, it's important to note that while DSI Studio provides powerful tools, its findings should be interpreted alongside other clinical information and imaging modalities in medical practice.

B. Data preprocessing with DSI-Studio

1) Data Import and Preprocessing

DSI Studio allows users to import dMRI data in various formats, including *DICOM*, *NIfTI*, and others. It includes preprocessing tools to correct for motion artifacts, eddy current distortion, and other sources of noise commonly encountered in dMRI data. Preprocessing in DSI Studio refers to a series of essential steps that are performed on raw diffusion-weighted imaging (DWI) data before they are further processed, analyzed, or visualized using DSI Studio software.

2) Gradient Correction: :

DWI data are acquired using gradient pulses that induce diffusion sensitization. However, hardware imperfections can lead to variations in the gradient strength and direction. Gradient correction involves adjusting the DWI data to account for these imperfections, ensuring that the diffusion sensitization is accurately represented.

3) Eddy Current Correction:

When strong gradients are applied during MRI scans, eddy currents can be induced in the imaging hardware, leading to distortions in the DWI data. Eddy current correction aims to correct these distortions by estimating and compensating for the effects of eddy currents, resulting in more accurate and undistorted DWI images.

4) Motion and Distortion Correction:

Patient motion during the MRI scan can introduce artifacts in the DWI data. Motion correction algorithms align the DWI images to correct for motion-related discrepancies. Geometric distortions caused by susceptibility effects (e.g., air-tissue interfaces) can also be corrected to ensure accurate diffusion measurements.

5) Image Registration:

DWI data are acquired in multiple directions, and they need to be aligned (registered) to a common coordinate space for accurate analysis. Image registration involves aligning all DWI volumes to a reference image, enabling the combination of data acquired from different directions.

6) B0 Volume Extraction

In DWI data, images are acquired with and without diffusion sensitization ($b=0$ images). B_0 images provide information about the static tissue and can be used as a reference for registration and distortion correction.

7) Diffusion Gradient Table Adjustment:

The diffusion gradient table, which specifies the directions and strengths of diffusion sensitization gradients, should be accurately aligned with the acquired data. Adjustments ensure that the gradient directions are correctly associated with the corresponding DWI volumes.

8) Noise Reduction: :

Noise reduction techniques, such as spatial averaging or filtering, can be applied to improve data quality.

9) Data Resampling:

This involves interpolating or resampling the data to a common voxel grid or resolution.

C. Image reconstruction with DSI-Studio

The reconstruction step processes an SRC file to generate the FIB file, which can be further used in fiber tracking.

DSI Studio supports advanced diffusion models beyond traditional Diffusion Tensor Imaging (DTI). It can handle DSI and HARDI data, allowing users to explore complex fiber configurations, such as crossing fibers and complex orientation distributions. Diffusion reconstruction in DSI Studio refers to the process of generating a diffusion spectrum from the raw diffusion-weighted imaging (DWI) data. Limitation and future work

Image reconstruction steps are listed below:

1) Raw DWI Data:

Diffusion-weighted imaging (DWI) data are acquired using MRI scanners with gradients applied in multiple directions. These gradients sensitize the MRI signal to water diffusion in different orientations.

2) Diffusion-Weighted Signal Measurements:

Each diffusion-weighted image provides information about the MRI signal attenuation due to water diffusion. The signal attenuation is influenced by factors such as tissue microstructure and the direction of diffusion.

3) *Diffusion Spectrum Representation:*

The diffusion spectrum represents the probability distribution of water diffusion displacements in different directions and distances. It captures a more comprehensive view of water diffusion behavior compared to simpler models like diffusion tensor imaging (DTI).

4) *Q-Space Sampling and Calculation:*

DSI Studio processes the acquired DWI data using a technique called q-space sampling. This involves collecting diffusion-weighted signals across a range of diffusion distances (q-values) and gradient directions. The software employs mathematical techniques to calculate the diffusion spectrum based on the collected signal measurements.

5) *Mapping Displacements and Probabilities:*

The diffusion spectrum consists of a 3D array in which the three dimensions correspond to different spatial dimensions. The values within the array represent the probability of water diffusion displacements occurring in different directions and distances.

6) *Complex Fiber Configurations:*

The diffusion spectrum is particularly advantageous when dealing with complex fiber configurations, such as crossing or kissing fiber bundles. These configurations are challenging to represent accurately using simpler diffusion models like DTI.

7) *Fiber Orientation Distribution (FOD) Estimation:*

From the diffusion spectrum, DSI Studio estimates the Fiber Orientation Distribution (FOD) within each voxel. The FOD provides information about the density of fiber orientations within a voxel.

8) *Advanced Analyses:*

The diffusion spectrum and FOD information serve as the basis for subsequent analyses such as fiber tractography, which reconstructs white matter pathways, and connectivity mapping, which studies brain networks.

D. Fiber Tracking:

DSI-Studio offers powerful fiber tractography capabilities, allowing users to reconstruct white matter tracts in the brain. It supports both deterministic and probabilistic tractography algorithms and provides options for adjusting tracking parameters.

1) *Connectivity Analysis:*

DSI Studio provides tools for connectivity analysis, enabling researchers to study the structural connectivity of the brain. Users can perform region-of-interest (ROI)-based analyses and generate connectivity matrices.

2) *Fiber Orientation Distribution (FOD) Visualization:*

The software allows users to visualize the Fiber Orientation Distribution (FOD) within voxels, which is crucial for understanding complex fiber orientations in the brain. It provides visualization options such as spherical harmonics rendering and orientation distribution functions.

3) *ROI Based Analyses or Atlas Based Analyses:*

Users can define regions of interest (ROIs) and perform analyses based on specific brain regions or anatomical atlases. This is useful for studying connectivity patterns in specific brain regions.

4) *Batch Processing:*

DSI Studio supports batch processing, allowing users to automate repetitive tasks and Analyse multiple datasets simultaneously.

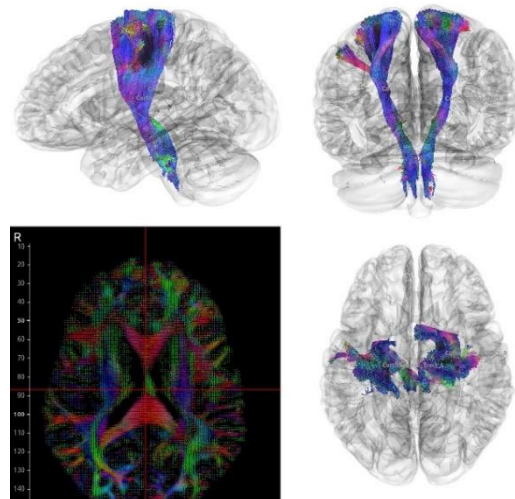


Fig. 7: White matter fibers from cortico-spinal tract identified using MR imaging based tractography

IV. CONCLUSIONS

DSI Studio is a powerful MRI image processing tool to represent, analyze and visualize brain white matter tracts. DSI Studio offers a range of tractography algorithms, including deterministic and probabilistic techniques. It allows determination of structural connectivity in the brain and examination of neural network integrity. It includes many data processing, analysis and visualization tools that greatly help in generating brain connectomics related insights. It can handle a wide range of types of files that are often used in MRI research. The reconstructed tracts of the brain can be viewed via DSI Studio's simple user interface. Users can rotate, zoom, and explore the pathways in real-time while dealing with the 3D visualization. To look into the relationship between patterns of specific parts of the brain, researchers may choose regions of interest (ROIs). The tracts running through these ROIs can be examined by quantitative analysis by users. On the basis of the results of the tractography, connectivity matrices and diagrams could be generated. These matrices indicate the degree of connectivity between different parts of the brain. Furthermore, information about the structure of the brain networks could also be derived. DSI Studio incorporates sophisticated tools which includes fibre bundle clustering, statistical analysis, and virtual dissection for significant white matter pathways. These characteristics make it easier to study neural networks at a deeper level. DSI Studio is a flexible and effective tool that is useful for comprehension of brain structure, connectivity, and pathology. Because of its wide range of applications, it is an invaluable tool for both researchers looking to understand the neurological system and medical practitioners making therapeutic decisions.

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