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Fasciculography: Robust Prior-free Real-time Normalized Volumetric Neural Tract Parcellation

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Abstract

Fiber tracking in Diffusion Tensor Magnetic Resonance Images (DTI) reveals 3D structural connectivity of the brain conveniently and thus is a viable tool for investigating neural differences. Unfortunately, local noise, image artifacts and numerical tracking errors during integration-based techniques are cumulative. Prematurely terminated fibers and under-sampled fiber bundles result in incomplete reconstruction of white matter fiber tracts and hence incorrect anatomical measurements. Quantitative cross-subject tract analysis, which is critical for abnormality detection, is complicated by inefficient and inaccurate tract reconstruction and normalization from fiber bundles. Because of the above problems, we propose a parcellation method that aims for lower sensitivity to initialization and local orientation error by directly segmenting full white matter tracts (Fasciculography), rather than reconstructing individual curves, from diffusion tensor fields. A fast, robust volumetric and intrinsically normalized solution is achieved by noise-filtering using a generic parametrized tract model to prevent premature tract termination. At the same time, orientation information reduces the search space, significantly speeding up the tract parcellation process with less human intervention. Detailed comparisons against streamline tracking, shortest-path tracking and non-rigid registration using synthetic and real DTIs confirmed the superior properties of Fasciculography. Since a normalized tract can be delineated interactively in a just few seconds using the proposed method, accurate high volume tract comparisons become feasible.

Index Terms

Fasciculography; FASC; Volumetric Tractography; DTI; White Matter; Interactive Tract Parcellation; Tract-based Morphometry

I. INTRODUCTION

WHITE Matter in the brain is composed of many neuronal fibers. Myelination of fibers restricts the water diffusion in response to magnetic gradients to specific patterns carried by

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This paper has supplementary downloadable material available at <http://ieeexplore.ieee.org> provided by the authors. This includes two multimedia MOV format movie clips, which show the interactive processing and dynamic 3D rendering from the Fasciculography software. This material is 7 MB in size. Software download @ <http://www.fasciculography.com>

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a set of diffusion weighted images (DWI) [1]. Diffusion Tensor Imaging (DTI) [2] reconstructs fiber orientations locally from the DWIs by fitting a tensor to the measurements. Since the size of neuronal fibers are much smaller than the voxel size of DTI, the measurements in DTI represent averaged orientations over a small region [3]. With an end goal of understanding and characterizing brain tracts in vivo, existing white matter parcellation methods from DTI can be summarized by two main steps: tracking and bundling. Virtual fiber pathways can be reconstructed as a set of streamlines by the orientations given by DTI using numerical tracking techniques. Streamlines that belong to the same anatomical structure can be selected and processed to create a streamline bundle. Therefore, a specific brain tract can be extracted and visualized by properly seeding, tracking and processing those virtual fiber pathways [4], [5], [6], [7], [8]. This selection process can be done manually or automatically using pattern recognition algorithms (classification/clustering).

Bundling and processing of streamlines is a major DTI research field. Automatic bundling [9] can be done with the help of proper prior models. The availability and appropriateness of a training set poses limitations to methods using prior models. Cross-subject analysis of fiber tracts is also complicated by the definition of point correspondence among bundles with varying fiber lengths and number of fibers. Various Tract-based Morphometry (TBM) methods [10], [11], [12] tackle the point correspondence issue mainly by generating a common parametrization through post-processing and registering fibers. The conversion from fibers to a common coordinate system can be avoided by using a tract-shape [13], [14], [15] directly for parcellation. Nevertheless, streamline tracking and bundling can be a convenient way to visualize a vector field which represents anatomic structure.

A. Fiber tracking

Fiber tracking methods such as Fiber Assignment Continuous Tracking (FACT) [4], [5], [16], [6] attempt to regenerate fiber pathways by repeatedly solving initial value problems (IVP) [17] on a vector field derived from DTI, where the initial values are called the seedings. Since oriented structures in the brain are observed to have high Fractional Anisotropy (FA) [18] values from DTI, the tracking of a fiber pathway terminates when it encounters a low FA region. Optimal seedings vary across tract types and subjects, and is very critical for accurate tract segmentation.

To reduce tracking error induced by local noise, front-propagating strategies have been employed in fiber tracking [19], [20], [21], [22], [23], [24]. In this class of methods, the tracking problem is solved by a shortest or minimum cost path solution. By propagating a wave front from a manual seed point under certain conditions that are favourable to the diffusion orientations, the time-of-arrival from the seed to each voxel is found. A Level Set formulation or the Fast Marching algorithm [25], [26], [19], [23] are commonly adopted to implement the front propagation. A probabilistic version has also been proposed [27]. Fibers are reconstructed by backtracking from multiple end points towards the initial seed point based on the local optimal direction given by the time-of-arrival map. The directions given by the time-of-arrival map are expected to be more robust than the original orientation field because the time-of-arrival map involves the processing of neighboring orientations and orientations from previous steps.

Note that front-propagating and back-tracking together require the specification of at least two points (typically manually) within the tract-of-interest and thus it is essentially a multi-ROIs (Region-Of-Interest) tracking method.

B. Fiber bundling

With the existence of image noise, partial volume effects, tracking errors, and seeding errors, fibers can diverge from the intended tract and travel into one or more neighboring tracts. Interactive parcellation [28], [29], [30], [31], [32] usually involves manual post-editing of tracking results, either using the whole brain seeding (placing seeds at all points in the white matter) or individual ROI seedings. While such methods are flexible and applicable to many tracts, they require extensive management of tens of thousands of fibers.

Different fiber classifiers have been proposed to reduce the complexity of the editing process [33], [34], [35], [9], [36]. Automatic grouping and matching of fibers is usually based on a similarity metric, also called fiber affinity, that measures the proximity of two fibers in terms of trajectory and location. By using an appropriate classifier, fibers that belong to a relevant anatomical structure are grouped together to become a bundle, while outlying (or irrelevant) fibers are discarded.

The atlas-based approach [9], [12] aims for fiber bundling solutions with the least amount of human intervention. Bundles can be identified by matching to labeled bundles on a fiber atlas. The introduction of a fiber atlas reduces the amount of human effort during parcellation; however, the creation of such a fiber atlas itself requires extensive human intervention. In addition, in order to match hundreds of thousand fibers with hundreds of thousands fibers from an atlas within a reasonable time frame, procedures such as simplification of fiber representations and down-sampling the number of fibers are typically necessary. The drawback of such methods is that smaller tracts would be easily under-represented if not completely neglected [12].

Most recently, a generalized cylinder approach has been proposed [37], but their tract solutions are limited to circular cross-sectional areas. This assumption is typically not valid for neural tracts. Moreover, their approach is a tubular-constrained level set surface evolution where the parameterization *within* the tract is not carefully considered and therefore tract normalization is still an issue.

Motivation of the new volumetric approach—Tract parcellation based on fiber bundling relies on good fiber tracking results, while local orientation error from diffusion signals will significantly alter their trajectories [38]. Although many efforts have been made to offer better orientation information, such as higher angular resolution imaging (HARDI) [39], [40] or Q-ball [41], [42], [43], [24], signal noise is nevertheless unavoidable.

From a brain characterization point of view, the generation and processing of fiber pathways are intermediate procedures for extracting fiber bundles. Yet, the measurements derived from fiber bundles are the end goal. Common anatomical properties include length, surface area and volume, and statistics such as average FA within the structure. As tractography is a means of delineating anatomical tracts, we propose a novel algorithm based on a volumetric tract model instead of point-based fiber bundles designed to parcellate the entire tract or fascicle (Fasciculography). With the new volumetric tract representation, the aforementioned anatomical properties can be obtained directly and conveniently. Our idea is to develop a fast method that performs streamline tracking and anatomical segmentation simultaneously, with less dependence on seed points and local orientations.

Our target users would be researchers who need to analyze DTI data in order to identify and characterize tracts, especially those who are interested in group-wise study of individuals with a condition and/or characteristic (age, gender, etc.) where a training set is unavailable or yet to be constructed. Our implementation is a prior-free, platform-independent, single or double seeded, fast volumetric tractography/ segmentation/visualization tool without extra

tracking parameters or exhaustive parameter tuning or post-tracking editing necessary. Tracts are fully parametrized at the time of segmentation so that inspection can be done easily through an arc-length (tract axis) parameter; this property can only be obtained after additional processing steps using existing methods [13], [36], [12]. This parametrization will be particularly useful for multi-tract comparison.

We have packaged and extensively tested our implementation in a standalone application with a convenient user-interface so that users can perform volumetric tractography and verify the results of our method interactively, without the need of re-implementing the algorithm. The application can run on multiple OS platforms¹ [44]. We verified our method using third-party phantoms [45] and real DTI data, as described below: Comparisons were made among our method, single or double-ROIs FACT and tensorline deflection (TEND) [46], front-propagation tracking [21] and non-rigid registration [47], [48] to an atlas. Given a comparable amount of human intervention in terms of seed points, ROIs or time, our method can quickly accomplish desirable results in noisy and difficult situations where other methods would likely fail. We show that our method is robust with respect to a wide range of parameters and less sensitive to the positioning of manual seeds in Section V-D.

II. INTERACTIVE IMPLEMENTATIONS

We compare our Fasciculography (FASC) implementation [44] with other existing methods using working implementations provided by three different software packages: FACT tracking (integration based on the principal direction) in DtiStudio, [30] by John Hopkins University, TEND (integration based on the diffusion tensor) in the Diffusion Toolkit and TrackVis [49] by Massachusetts General Hospital, and the Diffusion Utility (front propagation) and Non-rigid Registration Tool (FA atlas mapping) in Bioimage Suite [50] by Yale University.

Interactivity is a key approach to achieve fast and reliable tractography in practice. Table I gives a summary of the deterministic factors for tracking performance of each method.

FACT and TEND software are interactive in terms of ROI selection while FASC is interactive in terms of seed selection. Seed points refer to the locations where tracks are initiated, while ROIs (in this paper) refer to locations where streamlines are expected to pass through. Fast and editable ROI selections implemented in DtiStudio/FACT and the Diffusion Toolkit/TEND localize tracts efficiently. These methods use whole brain seeding where tracks are initiated at all points in the white matter. These tracks are precomputed and thus sacrifice flexibility in varying parameters such as turning angle and FA threshold. Although seed points and ROIs are conceptually similar ideas, seed points and ROIs in this study play different roles in each implementation. As described by Catani et al. [6], streamline tracking methods perform better if dual-ROIs are given at the two ends of a tract. However, FASC uses a single point seed and performs better by seeding at the middle of a tract. Note that FASC and front-propagation/BioImage Suite do not require ROIs. Thus, for the later comparisons, we attempt to use the best possible seedings or ROIs for each method in order to achieve their best performance. For the sake of comparison, besides DtiStudio, we implemented our own interactively seeded and thresholded FACT; see Section V-D.

The seeding density, usually defined as the number of seeds per high FA voxel, for a whole brain tractography is an implicit but critical parameter which controls the number of fibers localized by interactive ROIs and ultimately affects tract thickness. Unfortunately, this seed density parameter is impractical to adjust interactively due to three reasons. First, it takes

¹Software download @ <http://www.fasciculography.com>

certain amount of time to compute the whole brain tractography. Second, the multiplying factor of the seed density is the number of voxels, where a small change scales up or down the resulting number of fibers significantly. Third, high fiber volume creates a huge computer memory burden that can quickly exhaust available resources.

The turning angle and FA thresholds play slightly different roles in each method. The tract thickness, which significantly determines the segmentation accuracy, is controlled by various factors or thresholds for each method; see highlighted terms in Table I. FACT/TEND tract thickness is mainly controlled by the size and shape of the ROIs and the fiber pathways. Since the fiber pathways are governed by orientation information, change of FA and turning angle thresholds for FACT/TEND affect only the number and the length of fibers but not their trajectories. However, FASC tract thickness is governed by the controlling FA and turning angle thresholds in Equation (4) and (5). Nevertheless, our study shows that the two thresholds do not significantly determine the tract quality in FACT/TEND/FASC while seeding and ROI selection directly influence tract quality, which confirms the design used in DtiStudio and Diffusion Toolkit.

III. RELATED FORMULATIONS

We would like to discuss two fundamental building blocks involved in our proposed volumetric parcellation: streamline tractography and coherence of orientation. Our method is not a replacement of either; rather, we integrate them with a volumetric tract model for tracking. Thus, any advancements in streamline tracking and tensor coherence research will benefit our method too. For simplicity and efficiency, we have adopted simple formulations for the two blocks. There are potentially better alternatives but they are not the key focus of this paper.

A. Streamline tractography

Streamline tracking is the process of recovering line structures in a vector field. The vector field $\mathbf{F}(\mathbf{x})$ is provided by tensor orientations from DTI. The tracking problem can be written as an IVP of the partial differential equation [17]:

$$\frac{dL(s)}{ds} = \mathbf{F}(L(s)), L(s_0) = \mathbf{x}_0 \quad (1)$$

where $s \in \mathbb{R}$ is the arc-length parameter of the streamline $L(s) : \mathbb{R} \rightarrow \mathbb{R}^3$ in the 3D vector field $\mathbf{F}(\mathbf{x}) : \mathbb{R}^3 \rightarrow \mathbb{R}^3$, where $\mathbf{x} \in \mathbb{R}^3$ is a 3D point in the diffusion tensor image. Given an initial point $\mathbf{x}_0$, also known as the seed point, a streamline L can be recovered by line integration of Equation (1):

$$L(s) = \int_s \mathbf{F}(L(s)) ds$$

using first order numerical approximation:

$$L(s_{t+1}) = L(s_t) + \int_{s_t}^{s_{t+1}} \mathbf{F}(L(s)) ds \approx L(s_t) + \Delta s \mathbf{F}(L(s_t)) + E \quad (2)$$

where Δs is a constant numerical step and E is the error of numerical integration. In neural fiber tracking, fibers are expected to be located in high FA regions and smooth. Thus, the integration stops when the streamline turns abruptly or leaves the acceptable FA region. Therefore, the line integration is subjected to two constraints:

$$\begin{cases} \left\| \frac{d^2 L(s)}{ds^2} \right\| \leq \cos^{-1} \tau_{dp} \\ F_{fa}(L(s)) \geq \tau_{fa} \end{cases} \quad \forall s \in [s_0, s_n] \quad (3)$$

where τ_{dp} is a threshold for the rate of change of tangents $\left\| \frac{d^2 L(s)}{ds^2} \right\|$, and this rate is numerically implemented using the inner product of two tangent vectors at $L(s_i)$ and $L(s_{i+1})$. τ_{fa} is a scalar threshold of the FA values. Note that the indicator $F_{fa}(x)$ and the orientation map $\mathbf{F}(x)$ both serve as data inputs for the streamline tracking but the $F_{fa}(x)$ is a scalar map while $\mathbf{F}(x)$ is a vector field.

There are a number of numerical methods to recover L from $\mathbf{F}$ given $\times$ [17], but there is a trade-off between accuracy and efficiency. In our implementation, we used the Runge-Kutta Order 4 line integration method [17].

In addition to numerical error, streamline tracking suffers from noise in the vector field $\mathbf{F}$. Noise includes partial volume effects, imaging artifacts, motion error, tensor reconstruction error especially at cross-fibers, etc. In this regard, researchers have been actively developing better methods to generate improved orientation information, such as high-field MRI and Q-ball imaging [41], such that $\mathbf{F}$ in Equation (2) is more accurate. However, in any recursive numerical integration, errors due to local image noise are unfortunately cumulative. The longer the streamline, the higher the displacement error resulting in worse $L(s)$ for large s . If the line inadvertently hits the structural side-wall instead of the desired end point, the tracking will be terminated prematurely. Without post-editing of streamlines, accidental termination would result in incomplete reconstruction of line bundles and hence incorrect anatomical measurements.

B. Coherence of Orientation

DTI data, as a discrete representation of the underlying continuous orientation field, forms a set of vector samples. Since tract fibers are continuous, neighboring orientations within a tract should be consistent. Tract segmentation can be formulated as a classification problem where similar voxels are grouped according to their orientations. Coherence of orientation refers to the measure of agreement between two orientation samples which can be vectors or tensors. Various formulations of coherence have been investigated [51], [19], [52], [53], [54], [55], [56]. However, the grid resolution of front-propagating approaches or discretized connectivity definition by graph-based approaches limit the precision of these methods for tract segmentation.

We define our coherence of orientation in a slightly different way than voxel-wise formulations. We would like to quantify how relevant a voxel $x \in \mathbb{R}^3$ is to a streamline $L(s)$ based on its orientation. In this paper, the coherence between an oriented voxel and a streamline is defined as the inner product of the tensor orientation and the normalized tangent of the streamline:

$$C(x; L(s)) = \left(F(x) \cdot \frac{dL(s)}{ds} \right) \left\| \frac{dL(s)}{ds} \right\|^{-1} \quad (4)$$

Note that this coherence measurement is dependent on the streamline tangent at s . We cannot simply apply a threshold or perform a region growing type of operation on this measurement without knowing the streamline orientation at s for each x .

Taking the complementary strengths of streamline tractography and coherence of orientation, we designed our segmentation to be less sensitive to local orientation noise by simultaneously tracking and segmenting white matter structures. A fast and robust volumetric tractography is achieved by tract filtering using a generic tract model and recursive streamline extension to prevent premature tract termination. At the same time, orientation information is used to reduce the search space, significantly speeding up tract parcellation.

IV. METHODOLOGY

The oriented structure in our experiments are white matter fiber tracts in brain DTI. From experience with fiber tracking methods such as FACT, a collection of streamlines generated from reasonable seeds forms a limited representation of the tract. Due to tracking errors, such a collection can typically only be considered as a partial representation, see Figure 7(b).

We intend to maximize the length of the tract axis through iterative filtering (**Step 3**) and streamline extension (**Step 5**) of a tract volume. Our goal is to find a parametric volume $V(\alpha, \beta, \gamma): \mathbb{R}^3 \rightarrow \mathbb{R}^3$ where $\alpha, \beta, \gamma \in [0, 2\pi]$ and α, γ are symmetric, which best represents an oriented structure in a vector field [15]. The model $V(\alpha, \beta, \gamma)$ defines the coordinate system for the tract volume, indexing all points in the volume, facilitating (as described below) tract comparison and the use of the Fourier basis for filtering. Fibers for visualization can be generated by sampling the final $V(\alpha, \beta, \gamma)$ along the axial direction. Throughout this section, α, β , and γ refer to the axial, circumferential and radial parameters of a tract volume, respectively. We start with two formulations and then establish a feedback search system based on them.

Tract from Axis

Given knowledge of the true tract axis $Y(\alpha): \mathbb{R} \rightarrow \mathbb{R}^3$, we can extract the tract shape according to the orientation and FA values adjacent to the tract axis. A set of voxels can be found using a sweeping plane along the tract axis.

Let $P_{Y(\alpha)}(p) \in \mathbb{R}^2 \rightarrow \mathbb{R}^3$ be the orthogonal plane of $Y(\alpha)$, where p is the plane parameter. We find the cross-sectional area $A_\alpha(\beta, \gamma)$ of the tract by the intersection of the thresholded 2D coherence map and FA map computed based on $P_{Y(\alpha)}(p)$ and Equation (4)

$$A_\alpha(\beta, \gamma) = \{C(P_{Y(\alpha)}(p); Y(\alpha)) \geq \tau_{dp}\} \cap \{F_{fa}(P_{Y(\alpha)}(p)) \geq \tau_{fa}\} \quad (5)$$

Specifically, the tract axis is:

$$A_\alpha(\beta, 0) = Y(\alpha) \forall \beta$$

The boundary of $A_\alpha(\beta, \gamma) = A_\alpha(\beta, \pi)$ can be found by marching along the thresholded 2D coherence and FA map. The tract surface $S: \mathbb{R}^2 \rightarrow \mathbb{R}^3$ is recovered by sweeping along the tract axis:

$$S(\alpha, \beta) = A_\alpha(\beta, \pi) \quad \alpha \in [0, \pi] \quad (6)$$

Axis from Tract

Now we address the inverse problem: given knowledge of the tract shape, solve for the tract axis. Given a parametrized surface $S(\alpha, \beta)$, we would like to determine the tract axis. If we

hold the axial parameter α constant, $S(\alpha, \beta)$ becomes a contour. There are a few options to define the tract axis from a set of contours:

1. mathematical morphology for skeletonization [57] until one voxel is left.
2. contour shrinking through inward front-propagation using Level Set methods [25], [26].
3. compute contour centroids.

The second option is expected to give the most robust result, however, it is computationally expensive. To achieve fast segmentation, we pick the third option in our final implementation. Therefore,

$$Y(\alpha) = \frac{\int_{\beta} S(\alpha, \beta_i) d\beta_i}{\int_{\beta} d\beta_i} \quad (7)$$

Tract Optimization

We do not have the tract axis $Y(\alpha)$ nor the tract surface $S(\alpha, \beta)$ at the beginning. Even though we may allow manual seed selection, we still cannot expect those seeds to pass through the tract axis.

Since all geometric entities are unknown at the beginning, the search is implemented in a Gauss-Seidel fashion. To find a maximum length tract-axis streamline $Y(\alpha)$ under the influence of the tract surface $S(\alpha, \beta)$ and a generic model $V(\alpha, \beta, \gamma)$ and *vice versa*, we first begin with a manually seeded streamline $L^{(0)}(s)$ anywhere within the tract. The superscript ^(t) indicates the iteration number. There is a reparametrization from s to α since streamline tracking can move in both directions while we define α to be $[0, \pi]$. In the following discussion,

$$\alpha = \pi \left(\frac{s - \min(s)}{\max(s) - \min(s)} \right)$$

Since s and α are a one-to-one mapping, we assume $s = s(\alpha)$ for simplicity. The steps of the process are graphically illustrated in Figure 2.

Given a seed point x^0 on a vector field $\mathbf{F}$, we compute a streamline $L^{(0)}(s)$ using any numerical method solving Equation (1).

Step 1: Assume this line to be the initial tract axis:

$$V^{(0)}(\alpha, \beta, 0) = L^{(0)}(s) \quad \forall \beta \quad (8)$$

Step 2: Compute the surface using Equation (6) and assemble the volume:

$$V^{(0)}(\alpha, \beta, \pi) = S^{(0)}(\alpha, \beta) = A_{\alpha}(\beta, \pi)$$

Step 3: Filter the volume with $\mathcal{P}\mathcal{H}$ in the Fourier domain [58] removing frequencies higher than a tract length-dependent value $\mathcal{K}$ (see Appendix for details):

$$V_{filtered}^{(0)}(\alpha, \beta, \gamma) = \mathcal{F}^{-1}\{\mathcal{P}_{\mathcal{H}}\mathcal{F}\{V^{(0)}(\alpha, \beta, \gamma)\}\} \quad (9)$$

Step 4: Estimate the new tract axis using Equation (7):

$$Y^{(0)}(\alpha) = \frac{\int_{\beta} V_{filtered}^{(0)}(\alpha, \beta_i, \pi) d\beta_i}{\int_{\beta} d\beta_i}$$

Note that typically $Y^{(0)} \approx L^{(0)}$, and since it comes from a filtered volume which has taken tract smoothness and tensor coherence into account, it should be a better tract-axis estimation. However, it may be shorter than the optimal axis.

Step 5: Extend $Y^{(0)}(\alpha)$ to form $L^{(1)}(\alpha)$ by re-seeding and streamline tracking from the two end points of $Y^{(0)}(\alpha)$. Let $[s_{ext}^-, s_{ext}^+]$ be the range of parameters indicating the portions of the new $L^{(1)}$ which is copied from Step 4. We solve for $L^{(1)}(s)$ according to:

$$L^{(1)}(s) = Y^{(0)}(\alpha_1) \text{ if } s \in [s_{ext}^-, s_{ext}^+] \quad \frac{dL^{(1)}(s)}{ds} = \mathbf{F}(L^{(1)}(s)) \text{ otherwise} \quad (10)$$

where re-parametrization of the new tract axis is:

$$\alpha_1(s) = \pi\left(\frac{s - s_{ext}^-}{s_{ext}^+ - s_{ext}^-}\right) \quad (11)$$

The extended portion of $L^{(1)}(s)$ found by Equation (10) is subjected to the constraints defined in Equation (3). Repeat Step 1 to 5 until no further extensions can be found, i.e. for some $t > 0$, we stop iterating when

$$|L^{(t+1)}(\alpha)| = |Y^{(t)}(s)|$$

This algorithm always converges as it only allows increasing tract length and $\{x \in \mathbb{R}^3 | F_{fa}(x) \leq \tau_{fa}\}$ is finite.

V. RESULTS

We have implemented our method and extensively tested it on synthetic and real data. The implementation is fast enough to allow interactive execution. A typical long white matter tract Fasciculography, e.g. the cingulum, inferior longitudinal fasciculus (ILF) and inferior fronto-occipital fasciculus (IFO), requires 30–60 optimization iterations which takes less than 1 minute on a 2.4GHz duo core processor with 4GB RAM. For shorter tracts like the uncinate fasciculus (UNC), anterior commissure (AC) or pontine crossing tract (PCT), the tracking times are just a few seconds, including the processing for visualization. Figure 1 shows the Fasciculography surfaces and fibers for more than 30 tracts from a human DTI.

Existing fiber manipulation software (e.g. the two streamline tracking packages we are going to compare to in this section) can achieve a comparable speed to our method by pre-processing a whole brain tractography [32]. The user interaction is limited, however, to ROI modification; the fiber tracking parameters cannot be changed unless the preprocessing step is redone. Tract normalization procedures, for example, computing the mean fibers, are

performed as post-processing steps. The drawback of such methods is that tracts with low fiber coverage will be missing or under-represented, and therefore the resulting information will be inaccurate for cross-subject analysis.

On the contrary, Fasciculography allows interactive modification of tracking parameters, instantaneous validation of tract delineations and convenient tract editing (e.g. trimming and resampling). Fasciculography produces fully parametrized tract volumes which provide tract-to-tract point correspondence for all outputs. These properties make Fasciculography an ideal tract delineation tool for future cross-subject DTI analysis.

A. Interactive and non-interactive parameters

To provide a fair comparison between interactive implementations while attaining their best performances, our priority for parameter selection is outlined as follows:

1. We first consider a value which can be derived directly from the ground truth. Mean ground truth FA is used as the FA threshold (available in the synthetic cases). ROI's are derived from the ground truth tract boundary.
2. The coherence of orientation threshold τ_{dp} of FASC is manually selected since the corresponding FACT/TEND ROI size and shape are from the ground truth.
3. For the remaining non-interactive parameters, we accept the default value from the software.

The above rule is applied to all discussed experiments on synthetic and real DTI. The maximum number of ROIs varies based on the tract geometry.

B. Comparison using synthetic DTI data

We verify our method using a set of DTI synthetic phantom images with ground truth, PISTE [45]. In PISTE, each tract has a different geometry posing its own tracking challenge. Three levels of noise are added for each tract geometry when synthesizing DTIs. We have selected 5 tracts with increasing levels of tracking difficulty from PISTE: branching, kissing, helix, orthogonal-cross and spiral (see Figure 3a). Branching and kissing phantoms are made by two tracts with different radii. It is usually more difficult to capture the smaller radius tract due to partial volume effects. The helix and spiral are long continuous tracts with increasing curvature. Here, it is usually more difficult to track the higher curvature portion. Each image represents a single tract (or double, for branching and kissing) with a homogeneous FA value. Therefore, good tract segmentations could be obtained by carefully selecting an appropriate FA threshold. Considering the high proximity among many white matter tracts in real data, for example the corpus callosum and the cingulum bundle, the last example, the spiral-cross tract, was created by combining the spiral and orthogonal-cross in the original dataset. This tract is designed to reflect a more realistic situation where simple thresholding and shortest-path approaches in general would not trivially succeed. To summarize, we ran four methods on 12 DTIs (4 tract types, 3 noisy DTIs each) to get 48 tracking results.

Tracking parameters and the three-ROIs rule

According to the rule defined in Section V-A, all methods use the mean FA value from the ground truth as the FA threshold and software default 0.5mm for the numerical integration step size. FACT/TEND use software default 30° as the maximum permissible turning angles. Given the Y-shape of the branching tract, we considered three ROIs sufficient without unnecessarily increasing the amount of human effort and the necessary resultant fiber coverage. In practice, ROIs are usually manually defined on orthogonal or oblique slices over a 2D display. For each phantom, we restricted the number of surface-type ROIs

to three. Tracking ROIs for FACT and TEND were manually selected from three cross-sectional areas of each of the ground truth tracts such that they maximized the resulting fiber coverage. FASC uses interactive turning angles. Seeding points of FASC and Front-propagation were manually selected by inspecting the color-coded DTI slices.

In general, each method has two interactive parameters, one for location and one for tract thickness: FACT/TEND has the ROI locations and ROI shapes. FASC has the single seed point and turning angle. Front-propagation has seed points and tube radius. We believe this rule is fair for all methods and it is practical in real world situations.

Qualitative comparison (Phantoms)—Figures 3 and 4 show the 3D appearance of the tracking results using the tested methods in high and low Signal-to-Noise Ratio (SNR) environments respectively. For FACT and TEND results, fibers appeared longer in high SNR cases than in low SNR cases. In low SNR cases, especially for the helix and spiral-cross tracts, low or missing fiber coverage is observed between or distant from ROIs. We can observe that fibers are diverted outside the expected tract, and therefore, adjusting the turning angle threshold cannot regain the missing coverage. This result shows the impact of premature termination of fibers due to accumulation of orientation errors.

We demonstrated the intrinsic weakness of shortest-path approaches in Figure 3 and 4. The overall appearance of the front-propagation tracking results are consistent in various SNR environments, which indicate its robustness with respect to orientation errors. However, tracks initiated far away from the source seed point often diverted to adjacent tracts.

Quantitative comparison (Phantoms)—We would like to investigate the degradation of tracking performance in response to more difficult tracts and in noisier environments. All fibers are quantized into binary images having the same resolution as the input DTI. All statistics in this section are computed based on voxel counting from the binary images and the ground truth which is derived from the noise-free phantom T2 images. Sensitivity values and Dice coefficients [59] are computed for the different tract types in different SNR environments. The Dice coefficient measures the tracking performance by considering the ratio between the correctly segmented portion over the total segmented volume adjusted by the ground truth volume. High true positive and low false positive values are both necessary to achieve a high Dice coefficient value. We report percentages (ranging from 0 to 100) in this paper, so that a perfect segmentation will score a 100. We also compute the mean FA from each segmented tract, as is commonly done. Reasonable front-propagation tracking results required many well-distributed seed points at all endings of a tract. However, this violates our three-ROIs rule for fair comparison, while using only three-ROIs does not produce reasonable results for shortest-path methods. Thus, their statistics are not included in this paper.

Figure 5 shows our method outperforms the other two methods in terms of sensitivity values in all cases, and has the highest Dice coefficients in 11 out of 12 cases. All FASC lines are relatively flat, as a function of tract difficulty, indicating the robustness of the method regarding difficult tract types, while the others exhibit steeper downward slopes. The heights of the FASC lines are all above 75% showing our method is robust in noisy environments, while the other lines are much lower (below 70%) at low SNR cases.

In Figure 5c, we can observe the TEND method giving good mean FA values (less than 15% error), however, this method provides the worst sensitivity values and Dice coefficients. This performance can be explained by the fact that the phantom tracts are constructed using homogeneous FA values for each branch. Thus, having fewer but correct voxel samples will give very accurate mean FA values. Note, such uniformity is not likely in real brain images.

Nevertheless, these results can also be viewed as demonstrating the high specificity of TEND. Unfortunately, low Dice coefficients (below 50%) caused by low tract coverage make this method unfavorable particularly for difficult tract types. FASC data points in the FA error vs. Dice coefficients plots stay in the same upper-right region showing that it is a better choice for difficult tracts.

C. Comparison using real DTI

We also test and compare, qualitatively and quantitatively, our method using real MR DTI data from the normal human brain. Figure 1 shows tract surfaces and fibers for more than 30 tracts from a human DTI. In the results below, we focus on the tracking of the cingulum bundle. In a normal human brain, the left and right cingulum bundles are a symmetric pair of fiber tracts located closely above the body (truncus) of the corpus callosum. The two bundles are separated by the interhemispheric (medial longitudinal) fissure. The cingulum has long fibers providing frontotemporal connections. It has an essential role in the neural system sub-serving emotional regulation, implicating it in the emotional dysregulation of bipolar disorder [60], [61]. The long cingulum fibers travel approximately parallel to the sagittal plane which allows qualitative evaluation of the tracking results with reference to the sagittal slices from the input images. The cingulum is challenging to track because it is thin especially at the ends and thus it is a good candidate for testing. Expert cingulum tracings which provide the ground truth for comparing tracking methods, are performed on the coronal slices. In this section, we compare FASC against FACT, TEND and the results of non-rigid registration [47], [48] to an FA atlas (NR-FA) which has the cingulum delineated. For each method, 18 cingulum tracts from 9 subjects were segmented. See Figure 6 and 7.

MRI Acquisition—Magnetic resonance imaging acquisition diffusion-weighted images were acquired on a 3T Trio MR scanner (Siemens, Erlangen, Germany) with a single-shot echo planar imaging sequence in alignment with the anterior commissure–posterior commissure plane (AC-PC). Diffusion sensitizing gradients were applied along 32 non-collinear directions uniformly distributed on a unit sphere, with b -value = 1000s/mm^2 , together with an acquisition without diffusion weighting (b -value = 0) (repetition time (TR) = 7400ms , time to echo (TE) = 115ms , field of view (FOV) = $256 \times 256\text{mm}^2$, matrix = 128×128 , slice thickness = 3mm without gap, 40 slices, 1 average). The resulting image resolution was $2\text{mm} \times 2\text{mm} \times 3\text{mm}$. The tensor fitting was performed using BioImage Suite [50].

Tracking parameters and ROIs—According to the rule defined in Section V-A, FACT and TEND tracking ROIs are derived from expert tracings of the cingulum. We use tracings from two coronal slices located 50mm anterior and 50mm posterior to the mid-point between the anterior commissure and the posterior commissure. Expert tracings also serve as the ground truth.

Common default parameters for FACT/TEND/² Fixed-thresholds FASC: turning angle = 30° , FA = 0.3, step size = 0.5mm and FASC tract filter period $\mathcal{K}$ = 15mm . The interactive FASC parameters used were: turning angles = $[22^\circ - 35^\circ]$, FA = $[0.25, 0.35]$ and remaining defaults. NR-FA is a multi-level spline-based normalized mutual information registration based on the FA maps of the test image and the atlas. These registrations were performed using Bioimage Suite [50] using the default settings.

²We fixed the FASC thresholds in some of the experiments for comparison only. Interactive threshold selection is one of the improved properties of FASC over classical tractography.

Qualitative comparison (Real DTI)—In Figure 7, we show the worst and best tract results from each method. As shown in the worst cases of FACT and TEND, severely inadequate fiber coverage was observed between the two ROIs resulting in a complete failure to locate the tract. Modifying the non-interactive FA and turning angle parameters cannot improve the situation because those fibers are not terminated inside the tract. Visualization of regional fiber trajectory patterns can be found in Figure 9. In fact, they ran outside the tract due to orientation noise. This inadequate fiber coverage matches the same phenomenon seen in the low SNR synthetic phantoms. NR-FA produces stable results for all subjects since the grid deformation in registration ensures a certain degree of tract integrity, however, it cannot produce large bending and significant tract shift relative to the reference atlas. FASC does not suffer from any of the above problems.

Quantitative comparison (Real DTI)—In Figure 8 we show the performance of FASC versus FACT, TEND and NR-FA in terms of sensitivity and Dice coefficients. Since we allowed two ROIs for FACT and TEND, there are four possible combinations of ROIs tracking: anterior ROI only, posterior ROI only, fibers passing through either ROI and fibers passing through both ROIs. Other factors such as seed density, fiber samplings, tract geometry and noise could also affect the tracking results; therefore, any one of the four combinations could be the best. In the plots, we show the best single-ROI and dual-ROIs results out of the four in terms of Dice coefficients. In each plot, the performance of FACT, TEND and NR-FA do not appear to have significant differences. However, we observe a clear separation of FASC points in the upper-right relative to the lower-left FACT, TEND and NR-FA points demonstrating the superior performance of FASC. Using interactive FASC thresholds slightly improve their results about 1–4%. Table II outline the overall performance of each method for cingulum parcellation. FASC, regardless of default or interactive thresholds, has the highest minimum, maximum and averaged values. The main problem for FACT/TEND, is actually not because of the selection of thresholds, is the orientations at the thin endings of cingulum that are severely and consistently corrupted by partial volume effect. As we can see in Figure 9, all the FACT/TEND fibers are consistently and coherently being diverted outside the tract volume. FASC captured the coherence but not being diverted because of the volumetric tract model.

D. Seeding Sensitivity

1) Tract quality vs. seeding locations—In Figure 9, we show the FASC tracts using three different locations along the cingulum bundles of Subjects 1, 5 and 9. We also generate FACT fibers using those three locations and additional surrounding points as the seeds. Note that these tract-specific FACT seedings are denser than those in previous comparisons which are generated for a whole brain tractography. The FACT seeds with density = 4mm^{-2} are defined on a plane passing through the three points and thresholded by FA = 0.3. All maximum turning angles are set to be 30° and FA threshold = 0.3. The results show that FACT only achieves a partial cingulum depiction for Subject 1 and varying tract thickness depending on the seed locations. Modifying the FA and turning angle parameters do not affect the depiction because those fibers are not terminated inside the tract. The FACT fibers of Subject 5 and 9 cover three different regions of the same tract and appear to be non-overlapping. Hence, using any of these seed locations or even the union of them provides very misleading results because the fibers representing the tract are not continuous or consistent along the tract. The seeding sensitivity for FASC is lower. FASC 1A, 1B and 1C appear very similar, while 5A and 5B look slightly different from 5C at the end which is seeded outside 5A and 5B. In addition, FASC fibers are always continuous since they are just sampling a continuous tract model (see the Appendix).

2) Accuracy vs. change of major parameters (including seed locations)—Our FASC method is robust in terms of tracking parameters. In this section, we show the Dice coefficients of cingulum parcellation using FASC with systematic variation of parameters. The manual segmentations are the same used in Figure 8. Major tracking parameters of FASC include FA threshold (τ_{fa}), turning angle threshold (τ_{dp}), tract filter ($\mathcal{K}$) and seed location (x^0). Table III summarizes the parameter settings for the experiments presented in this section. An example set of seed locations is shown in Figure 10.

Figure 11 shows the variations of Dice coefficient against a range of FASC parameter values. Each subfigure shows the result of perturbing one of the major tracking parameters. For non-varying parameters, the default parameters in Table III are used. In general, FASC works similarly for cingulum tracts using $\tau_{fa} \in [0.15, 0.4]$, $\tau_{dp} = 10^\circ$ and $K \in [10, 35]$. In Figure 11, a change of seed location along the diffusion direction does not significantly change the tract accuracy. The accuracy of parcellation maintains similar levels as long as the seeds are placed within the tract. Accuracy falls sharply when the seeds are right outside the tract. Figure 12 plots the average values over 9 subjects for each major FASC parameter. The plots for average Dice vs. Seeding along cross-sectional axes have a smoother fall off of Dice coefficients due to the variation of tract thickness in different subjects.

E. Interactive Implementation

The tract optimization loop from Equation 8–10 generates a tract volume from the streamline $L^{(t)}(s)$ and then regenerates the streamline to $L^{(t+1)}(s)$ by re-tracking at the two ends of the tract. Due to the existence of noise, branching or crossing of fiber tracts, $L^{(t)}(s)$ may not travel along the desired path. In actual implementation, we provide tools for manually constraining $L^{(t)}(s)$ before or after the tract optimization loop. In [62], we delineated multiple crossing tracts around the brainstem area using $L^{(0)}(s)$ created by manual point pairs which force the reconstructed tract to pass through specified locations. Examples tracts are shown in Figure 13. This two-points constraint can handle some of the situations where a small portion of tensors are corrupted due to crossing tracts. Figure 14 shows the normalized tract voxels [63] of the cingulum, inferior fronto-occipital (IFO) and uncinate (UNC) fasciculus using the α parameter of the model.

VI. CONCLUSIONS

Fasciculography (FASC) is the first interactive real-time volumetric tracking method for DTI tract parcellation. Our implementation demonstrated interactive execution rates and our testing on synthetic and real data demonstrated the improved performance of the method compared with existing methods. The interactive abilities of our method allow convenient flexibility in terms of tracking parameter modification, editing, and instantaneous visualization and validation of tract delineations. The FASC parcellation is less sensitive to seed and parameter selections compared to existing methods, and applicable to difficult tract geometries. The tract-to-tract correspondence provided by the fully parametrized volumes make Fasciculography an ideal tool for cross-subject DTI analysis, as will be explored in future work.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

APPENDIX

We here explain the details of Equation (9). Recall that $\alpha, \beta, \gamma \in [0, 2\pi]$ are parameters of the tubular volume $V(\alpha, \beta, \gamma)$ with symmetric α and γ samplings. k_1, k_2, k_3 are non-

negative integers for frequency numbers and $K_\alpha, K_\beta, K_\gamma$ are integers for maximum frequencies along each dimension. $\alpha_{ij}(k_1, k_2, k_3) \in \mathbb{R}$ are volumetric Fourier coefficients.

The Fourier Tract Model

We assume our target tract is tubular and therefore can be decomposed by a set of Fourier basis functions:

$$\mathbf{B}_{k_1, k_2, k_3}(\alpha, \beta, \gamma) = \begin{bmatrix} \cos(k_1\alpha)\cos(k_2\beta)\cos(k_3\gamma) \\ \cos(k_1\alpha)\sin(k_2\beta)\cos(k_3\gamma) \\ \sin(k_1\alpha)\cos(k_2\beta)\cos(k_3\gamma) \\ \sin(k_1\alpha)\sin(k_2\beta)\cos(k_3\gamma) \\ \cos(k_1\alpha)\cos(k_2\beta)\sin(k_3\gamma) \\ \cos(k_1\alpha)\sin(k_2\beta)\sin(k_3\gamma) \\ \sin(k_1\alpha)\cos(k_2\beta)\sin(k_3\gamma) \\ \sin(k_1\alpha)\sin(k_2\beta)\sin(k_3\gamma) \end{bmatrix}$$

and Fourier coefficient matrices:

$$\mathbf{A}(k_1, k_2, k_3) = \begin{bmatrix} a_{11}(k_1, k_2, k_3) \dots a_{18}(k_1, k_2, k_3) \\ a_{21}(k_1, k_2, k_3) \dots a_{28}(k_1, k_2, k_3) \\ a_{31}(k_1, k_2, k_3) \dots a_{38}(k_1, k_2, k_3) \end{bmatrix}$$

The inverse Fourier Transform of $V(\alpha, \beta, \gamma)$ is defined as:

$$V(\alpha, \beta, \gamma) = \sum_{k_1=0}^{K_\alpha} \sum_{k_2=0}^{K_\beta} \sum_{k_3=0}^{K_\gamma} \mathbf{A}(k_1, k_2, k_3) \mathbf{B}_{k_1, k_2, k_3}(\alpha, \beta, \gamma) \quad (12)$$

The Tract filter $\mathcal{P}_{\mathcal{H}}$

In Section IV, our volumetric tract model $V(\alpha, \beta, \gamma)$ has been fit to 2D contours. As we can see from Figure 15d, DTI noise and artifacts diverts some of the FACT fibers from the main tract body. Similarly, the samples of cross-sectional areas $A_\alpha(\beta, \pi)$ are noisy due to orientation noise and therefore a tract filter $\mathcal{P}_{\mathcal{H}}$ is used. $\mathcal{P}_{\mathcal{H}}$ is an ideal low-pass filter with a cutoff frequency along axial dimension of the $V(\alpha, \beta, \gamma)$ (i.e. the α direction). We demonstrate the effect of the tract filter in Figure 15 by running the FASC algorithm without the filter. In Figure 15b, the tract optimization (see Section IV) has been terminated earlier and resulted in a shorter tract than the normal FASC tract shown in Figure 15a.

The tract filter $\mathcal{P}_{\mathcal{H}} V(\alpha, \beta, \gamma)$ is actually implemented by setting $K_\alpha = 2\mathcal{P}^{-1}|L^{(t)}(s)|$, $K_\beta = 20$ and $K_\gamma = 1$ during inverse Fourier transform described by Equation (12). K_α is designed to be dependent on the length of the tract axis so that we do not over-fit the tract model when the initial streamline $L^{(t)}(s)$ is short at the early stage of tract optimization. The parameter $\mathcal{H}$ which is the minimum period or equivalently the maximum permissible Fourier frequency along the axial direction (the α parameter), is set to be 15mm for the experiments presented in this paper.

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Figure 1.

Fasciculography of major white matter tracts from a human brain DTI. One of the advantages of Fasciculography is that it offers both the fibers view and tract view without additional processing. All tracts are intrinsically normalized and ready for cross-subject analysis. A video clip of a dynamic 3D Fasciculography visualization is available online at <http://ieeexplore.ieee.org>.

Step 1: Seeding $L^{(0)}(s)$

Step 2: Surface $S^{(0)}(\alpha, \beta)$

Step 4-5: Extended axis $L^{(1)}(s)$

Step 3: $V_{filtered}^{(0)}(\alpha, \beta, \gamma)$

Example of extended volume $V_{filtered}^{(1)}(\alpha, \beta, \gamma)$

Figure 2.

Visualization of the output of each step in the tract optimization algorithm in Section IV. This example shows the first two iterations of the reconstruction of the Tapetum portion of the corpus callosum bundle from real DTI. A video clip demonstrating a complete Fasciculography operation through a graphical user interface is available online at <http://ieeexplore.ieee.org>.

Figure 3.

Qualitative comparison among Fasciculography (FASC), FACT, tensorline deflection (TEND) and front-propagation trackings using synthetic DTI images with Signal-to-Noise (SNR) Ratio 30:1. (Left to Right) Increasing tract difficulty with the same SNR. All methods perform well for the left two tracts. FASC and FACT is able to segment the helix, while only FASC can obtain the spiral.

Figure 4.

Qualitative comparison among fasciculography (FASC), FACT, tensorline deflection (TEND) and front-propagation trackings using synthetic DTI images with Signal-to-Noise (SNR) Ratio 5:1. (Left to Right) Increasing tract difficulty with the same SNR. Under the three-ROIs constraints (Section V-B) in noisy environment, only FASC succeeds in all cases.

Figure 5. Quantitative comparison of the tracking performance among Fasciculography (FASC), FACT and tensorline deflection (TEND) using synthetic DTI images. In (5a) and (5b), each plot shows the tracking performance under the same Signal-to-Noise Ratio with increasing tract difficulty (data points from left to right).

(a) 3D surfaces by cingulum Fasciculography

(b) 2D views of the cingulum Fasciculographies (white). The background is diffusion encoded color scaled by FA values.

Figure 6.

Cingulum Fasciculography of 8 DTIs. The total processing time for each tract pair is less than 5 minutes, including visualization, computations, human intervention and retrieval if necessary.

(a) Best FASC, FACT, TEND and NR-FA cingulum pairs.

(b) Worst FASC, FACT, TEND and NR-FA cingulum pairs.

Figure 7.

Qualitative comparison of the best and worst cingulum pairs, in terms of Dice coefficients, by Fasciculography (FASC), FACT, tensorline deflection (TEND) and non-rigid FA registration (NR-FA).

Figure 8.

Quantitative comparison of cingulum fasciculography (FASC) against FACT, tensorline deflection (TEND) and non-rigid FA registration (NR-FA) using 9 real DTIs and expert segmentations of 18 tracts as ground truth.

(a) FACT fibers and FASC tracts 1A, 1B and 1C from DTI of Subject 1

(b) FACT fibers and FASC tracts 5A, 5B and 5C from DTI of Subject 5

(c) FACT fibers and FASC tracts 9A, 9B and 9C from DTI of Subject 9

Figure 9.

Comparing the tracking results of FASC versus FACT from different seedings of the cingulum tracts of 3 subjects. All thresholds are identical. Each FASC tract uses one seed point located at the center of the red ellipse. FACT fibers are seeded around the FASC seed. Inconsistent regional fiber trajectory patterns are observed by seeding the front, the middle and the back portion of the tracts.

(a) Three seeding axes

(b) Seed set

Figure 10.

An example set of seed locations for quantitative evaluation of seeding sensitivity. Samples (in yellow, on right) are taken along three different axes (in red, on left) based on the main diffusion direction at the center seed.

Figure 11. Change of Dice coefficients of cingulum parcellations DTIs under perturbation of parameters. This figure shows the result using one subject. Averaged results can be found in Figure 12.

Figure 12.

Average Dice coefficients of 9 left cingulum and 9 right cingulum parcellations in response to change of major FASC parameters. The first column is by major tracking parameters: FA threshold (τ_{fa}), turning angle threshold (τ_{dp}) and tract filter ($\mathcal{K}$). The second column is by moving the seed location (x^0) along different directions.

(a) Adult Subject

(b) Child Subject

Figure 13.

FASC tracts around brainstem area using manual point pairs and the 2D axial slices parallel to the MCP. Abbreviations: Inferior/Middle/Superior Cerebellar Peduncle (ICP/MCP/SCP), Corticospinal Tract (CST), Medial Lemniscus (ML) and Pontine Crossing Tract (PCT).

Figure 14. Normalized cingulum (first row), inferior fronto-occipital and uncinate fasciculus voxels (second row) of 4 subjects from DTI Fasciculography [63].

(a) $V(\alpha, \beta, \gamma)$ with tract filtering (b) $V(\alpha, \beta, \gamma)$ without tract filtering (c) FASC fibers within $V(\alpha, \beta, \pi)$

(d) FACT fibers

Figure 15.

Comparison between Fasciculography (a) with and (b) without tract filtering using the same seed point. The contours represent the boundary of cross-sectional areas $V(\alpha, \beta, \pi)$. In (b), the noisy contours $V(\alpha, \beta, \pi) = A_\alpha(\beta, \pi)$ of Equation (6) since the tract filter is not used. FASC fibers are shown in (c). In (d), FACT fibers stray and without editing are unsuitable for tract normalization.

Table I

Deterministic factors affecting tracking performance. Abbreviated terms: FA thresholds (FA), maximum turning angle (angle), first seed point (source) for front-propagation (Front-Prop.) method, deformation (def.) grid, similarity metric (metric) and the quality of the reference atlas (atlas) for non-rigid registration. **Factors in bold** letters control the tract thickness the most.

	interactive	non-interactive
FACT/TEND	ROI locations, size, shape	FA, angle, seed density
FASC	seed point, FA, angle	
Front-Prop.	seed points after source	source, front smoothness
Non-rigid Reg.		def. grid , metric, atlas

Table II

Average and range of cingulum delineation performance of FASC (Fixed Thresholds), FACT (Two ROIs), TEND (Two ROIs) and non-rigid registration to FA atlas (NR-FA) over 9 subjects.

Left cingulum	FASC	FACT	TEND	NR-FA
Avg. Sensitivity (%)	84.0	50.0	59.2	47.2
Avg. Dice Coeff.	68.8	37.6	39.4	39.0
Right cingulum				
Avg. Sensitivity (%)	83.5	52.4	71.0	46.1
Avg. Dice Coeff.	68.3	45.9	44.8	38.5
Left cingulum	FASC	FACT	TEND	NR-FA
Sensitivity Range (%)	74–93	38–78	24–87	32–60
Dice Coeff. Range	63–74	24–58	33–59	31–44
Right cingulum				
Sensitivity Range (%)	68–92	16–73	53–84	30–59
Dice Coeff. Range	59–74	37–56	38–54	29–49

Table III

Major FASC parameters and ranges of variation for the parameter sensitivity evaluation. The initial seed is placed manually near the tract axis. Seed displacements are in *mm*.

Parameters	Default value	Feasible range/direction	Evaluated samples
FA (τ_{fa})	0.3	[0.0, 1.0]	0, 0.05, 0.1, ..., 0.5, 0.55
Turning angle (τ_{dp})	30°	(0°, 90°]	0°, 5°, 10°, ..., 60°, 65°
Tract filter (κ)	15mm	(0–∞]	1, 5, 10, ..., 50, 55, 80, 90
Seed point (x_0)	manual	diffusion axis	$\pm 0.2, 0.4, 1.0, 2.0$
		cross-sectional 1	$\pm 0.2, 0.4, 0.8, 1.6, 3.2, 6.4$ *
		cross-sectional 2	$\pm 0.2, 0.4, 0.8, 1.6, 3.2, 6.4$ *

* Additional seed locations are used to show the contrast between seeding inside and outside of the tracts. Since tract thickness varies across different subjects, only the listed samples are used for the averaged plots in Figure 12.