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QUANTITATIVE TRACT INTEGRITY PROFILES (Q-TIPS): A NOVEL NEUROIMAGING TOOLBOX FOR ASSESSING ALONG-TRACT WHITE MATTER INTEGRITY

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INTRODUCTION

In this paper, we present a novel neuroimaging toolbox called "Quantitative Tract Integrity Profiles (Q-TIPs)", which performs tract-based analyses by quantifying the integrity of white matter along tracts. Q-TIPs extracts the orientation of any user-defined ROI mask or atlas using a novel 3D centerline extraction algorithm to automatically identify the principal orientation along the ROI. After extracting the centerline, quantitative white matter imaging values can then be extracted from any user-defined quantitative image (e.g., fractional anisotropy, mean diffusivity, T1w/T2w ratio, myelin water fraction, magnetization transfer ratio, etc.) along the fiber tract.

BACKGROUND

Quantitative magnetic resonance imaging (MRI) signals have long been analyzed using either region-of-interest (ROI) or voxel-wise approaches. ROI analyses [1][2][3][4] can be performed in hypothesis-driven studies, where pre-defined ROIs are selected. These are useful for studying global changes in cross-subject analyses, but sensitivity is reduced for small, localized changes. On the other hand, voxel-wise analyses [5][6] perform point-by-point statistical analyses, facilitating high spatial resolution. However, voxel-wise analyses suffer if image registration is not done properly or if small changes occur in different locations between subjects [7][8].

A few recent studies [9][10][11] have proposed performing analyses along white matter tracts in order to create quantitative curve or profile. This approach, called tract-based or along-tract analysis, has the ability to study large regions of interest while maintaining sensitivity to small and/or localized signal intensity changes. The results of these studies are promising; however, they are inherently limited due to the fact that they rely on diffusion tensor imaging (DTI) data in order to perform white matter fiber tracking (or "tractography") to define the tracts. As a result, the current approaches cannot be used for analyzing other white matter imaging modalities (such as T1w/T2w ratio, magnetization transfer imaging, multi-component T2-weighted myelin water imaging, etc.).

In this paper, the aim is therefore to create a novel, standalone toolbox – called "Quantitative Tract Integrity Profiles (Q-TIPs)"- to extract any white matter imaging metric along any 3D volume, thereby allowing the integration of multiple measures of white matter integrity along individual regions of interest.

METHODOLOGY

Any binary ROI mask and any quantitative image (such as a T1w/T2w ratio map – that are co-registered/aligned in the same coordinate space) are required as inputs for Q-TIPs. The Q-TIPs pipeline, from the binary ROI to the final along-tract (cross-sectional) slicing, is shown in Figure 1. The algorithms used in each step are briefly described in the following sections.

Dilation

Because white matter ROI masks may not be continuous, smooth objects with regular

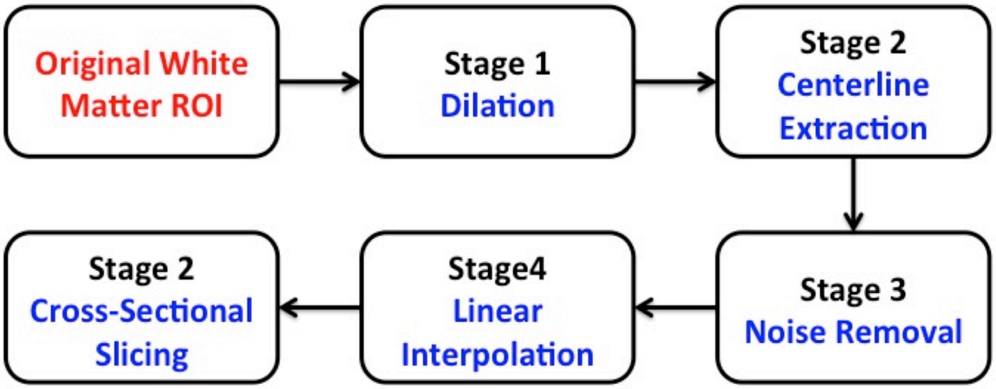

Figure 1: Image processing pipeline of Q-TIPs.

boundaries, they may have to be dilated and smoothed before the centerline can be extracted. Structure element of size 3x3x3 is applied on any ROI to fill unnecessary gaps.

Centerline Extraction

Once unnecessary gaps are filled by dilation, the centerline of the dilated ROI mask is extracted using a proprietary algorithm. This automated 3D centerline extraction algorithm uses a 'divide and conquer' technique, in which any 3D object is first sliced into a series of 2D images in X, Y and Z directions. Then, a geometric Voronoi algorithm is applied to each 2D image to extract the respective centerline information. This information is then combined to reconstruct the centerline of the original 3D object using an intersection technique.

Noise Removal

Although the extracted centerline is continuous and one voxel thin, it is not necessarily smooth, because it may contain small offsets (zigzags) between adjacent voxels. These offsets make it hard to perform cross-sectional slicing due to a high degree of variation in angle between adjacent points along the centerline. Therefore, in order to remove this noise, neighborhoods of points are defined and averaged in to smooth the line.

Linear Interpolation

In the previous step, some of the centerline information may unintentionally be removed along with the noise, creating discontinuities or gaps in the centerline. Therefore, gaps are automatically identified and filled using simple linear interpolation.

Cross-Sectional Slicing and Along-Tract Profiling

The last stage in the pipeline is to perform cross-sectional slicing along the extracted centerline, allowing tract-based analyses along the fiber tract. Cross-sectional slicing is accomplished by reslicing the ROI perpendicular to the direction of the centerline. Each resulting section is then masked using the original (undilated) ROI mask so that only accurate coordinates within the original ROI are included. Values from the user-defined (coregistered) quantitative MRI image(s) are then averaged for each cross-section along the length of the ROI, resulting in a quantitative tract integrity profile (or curve) along any desired ROI and any quantitative imaging method.

RESULTS AND DISCUSSION

In this section, we chose a random assortment of fiber tracts from the UManitoba-JHU Functionally-Defined White Matter Atlas [12] to show outputs at different stages of the Q-TIPs pipeline. Figures 2 and 3 show the results from two sample fiber tracts. The fiber tract in Figure 3 is more complex and also U-shaped as compare to one in Figure 2.

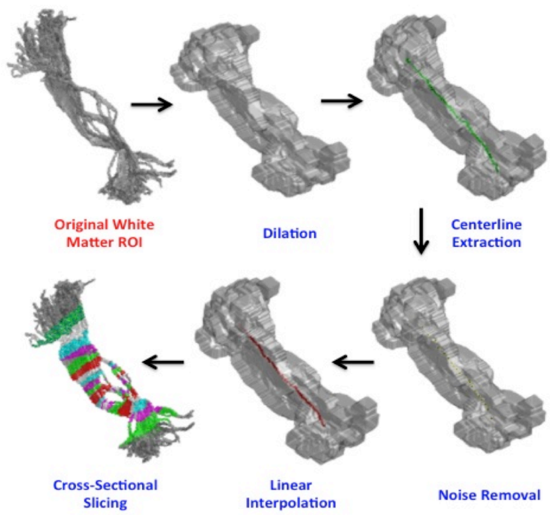

Figure 2: Outputs at different stages of Q-TIPs for a representative white matter ROI mask (from an existing atlas).

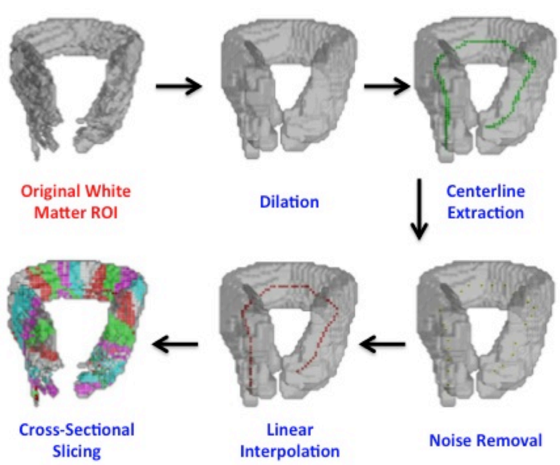

Figure 3: Outputs at different stages of Q-TIPs for a different white matter ROI mask (from an existing atlas).

Quantitative tract profiles are then made once the cross-sectional slicing is done using the orientation of the extracted centerline. Figure 4 and 5 show the quantitative tract profiles of the fiber tracts used in Figure 2 and 3, respectively, created by averaging over each cross-sectional slice along the length of desired ROI.

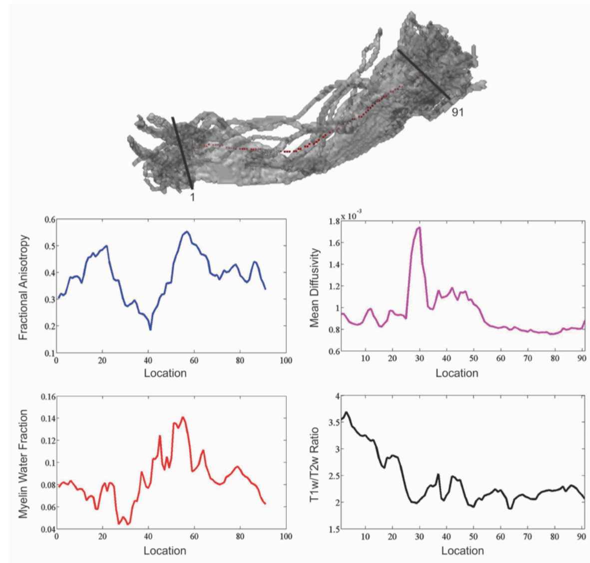

Figure 4: Tract-profiles (fractional anisotropy, mean diffusivity profile, myelin water fraction, and T1w/T2w ratio) are generated using Q-TIPs.

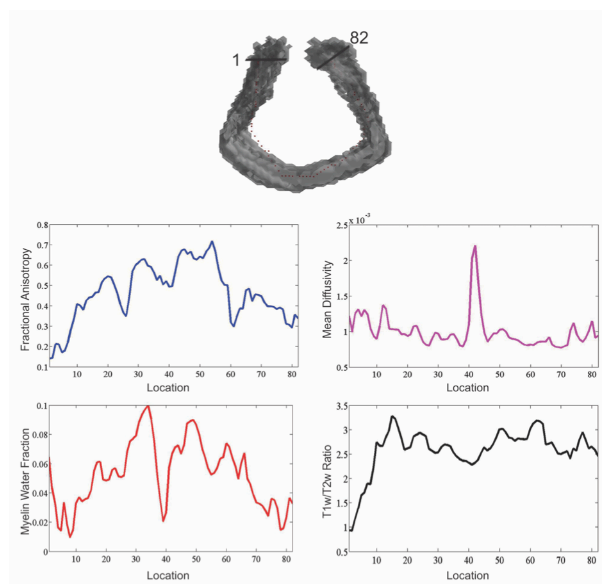

Figure 5: Tract-profiles (fractional anisotropy, mean diffusivity profile, myelin water fraction, and T1w/T2w ratio) are generated using Q-TIPs.

Our results show that the Q-TIPs pipeline is able to perform tract-based analyses on complex white matter ROIs from existing white matter atlases without relying on diffusion MRI or tractography. Instead, Q-TIPs extracts the cross-sectional slices using the orientation of an extracted centerline from any ROI atlas, thereby making it a flexible and generalizable tool that can be used to assess any quantitative imaging modality.

CONCLUSION

In this paper, we have briefly described a novel "Quantitative Tract Integrity Profiles (Q-TIPs)" toolbox for assessing the integrity of white matter tracts using along-tract analysis. Q-TIPs addresses a major limitation that existed in previously reported tract-based analysis studies, and is compatible with any white matter imaging modality. Moreover, Q-TIPs is a standalone MATLAB toolbox, and can therefore be run on most major operating systems.

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