A COMBINED APPROACH FOR THE ELIMINATION OF PARTIAL VOLUME EFFECTS IN DIFFUSION MRI

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Introduction

Partial volume is a major confounding factor in the analysis of diffusion tensor imaging datasets. The mixing effects of different tissue types, CSF, or different tracts within each voxel are non-linear, acquisition dependent, and could exceed the effect of subtle pathology or microstructural alterations of interest [1]. The tract-based spatial statistics (TBSS) method aims at avoiding CSF contaminated voxels by reducing its analysis to the centerline (skeleton) of structures [2]. This approach, however, requires non-contaminated tract thickness that exceeds the size of a voxel. On the other hand, if many uncontaminated voxels exist, TBSS loses statistical power by selecting a single voxel with the maximal FA. In this work, we combine two approaches to ameliorate these problems: (1) Free-water elimination (FWE) that eliminates intra-voxel CSF contamination [3] and (2) Partial volume clustering that classifies and probabilistically selects all non-contaminated voxels [4]. We demonstrate this method on a tract specific analysis of the corpus callosum in the mid-sagittal plain. We find that our method increases the sensitivity of recognizing abnormalities with a clinical dataset of Alzheimer's disease (AD).

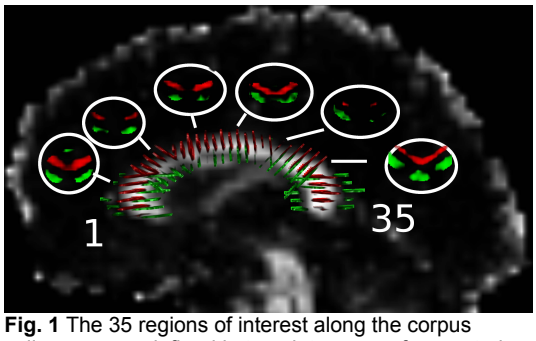

Fig. 1 The 35 regions of interest along the corpus callosum were defined in template space, from anterior (1) to posterior (35). Fiber (red), CSF (green), and partial volume were classified.

Methods

Imaging: Diffusion weighed imaging was performed on a 1.5T (Symphony, Siemens) for 15 AD patients and 15 matched healthy controls, using twice refocused EPI-DTI with the following parameters: TR/TE 4700/78 ms, FOV 240 mm, data matrix of 96 x 96 yielding an in-plane resolution of 2.5 mm, 50 axial slices with a thickness of 2.5 mm and no gap, with 6 gradient directions (b=1000 s/mm²) and a b=0 image. This scheme was repeated 10 times.

Diffusivities estimation: All images were corrected for motion and eddy currents (FSL, FLIRT), while compensating the gradient directions. Images were masked (FSL, BET) and the tensor toolkit was used for tensor estimation (https://gforge.inria.fr/projects/ttk). Free-water corrected tensors and free-water maps were calculated following the methods in [3].

TBSS analysis: The full TBSS pipeline was applied using the parameters suggested in [2]. The projection of the TBSS skeleton was applied to obtain radial diffusivities and FWE radial diffusivities.

Cluster analysis: Registration was performed in three steps directly on the tensor datasets using DTITK (http://www.nitrc.org/projects/dtitk): First, a template was bootstrapped using the IXI aging template. Then, a population specific template space was created with means of affine and diffeomorphic registration. The probabilistic clustering [4] was performed in 35 regions of interest (ROIs) that were manually defined in template space using the open-source MITK Diffusion 2011 (www.mitk.org). The clustering parameters were upsampling=5, number of histogram bins=255, thickness=7.

Group statistics: A two-sample unpaired t-test controlled for age was applied to compare the two groups, with p=0.05 as the threshold for significance.

Results

Fig. 1 shows the mid-sagittal plane of one of the subjects and the corresponding clustering results. The central slice in each of the ROIs was extracted and visualized using volume rendering (MITK). Fig. 2a shows group average radial diffusivity values extracted along the mid-sagittal plane of the TBSS skeleton. Significant differences (indicated by black circles), were found at one position. Fig. 2b shows the same analysis for FWE corrected radial diffusivities. While group differences are enhanced by the correction in the posterior region, they are reduced anteriorly. The group-wise, region-based clustering results, from anterior to posterior, are shown in Fig. 3a and Fig. 3b presents the results of clustering with FWE. The clustering strongly enhances group differences in the posterior part of the corpus callosum (ROIs 18-25). In the Anterior, group differences remain insignificant. Applying FWE reduced the differences in the Genu and Splenium below the significance level.

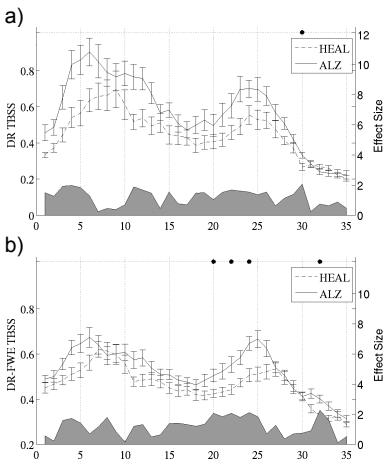

Fig. 2 Group differences along the TBSS skeleton of radial diffusivity (a) and FWE radial diffusivity (b). Black circles indicate significance of p<0.05; effect size is shown in grey.

Discussion

We propose a method for controlling the effect of partial-volume on diffusion measures and apply it on the mid-sagittal axis of the corpus callosum. Alzheimer's disease seems to cause true microstructural changes in the posterior part of the corpus. The changes become clearly visible using the clustering approach and survive/get enhanced by FWE. In the Anterior, differences did not reach significance and effect size was decreased/not enhanced by FWE, suggesting possible involvement of extra-cellular differences. Future work should consider the use of statistical techniques like threshold-free cluster enhancement (TFCE) and evaluate the applicability of the approach in other tracts in the brain.

[1] Vos *et al.*, NeuroImage 2011 [2] Smith *et al.*, NeuroImage 2006 [3] Pasternak *et al.*, MRM 2009 [4] Schlüter *et al.*, Int J Med Robot 2005

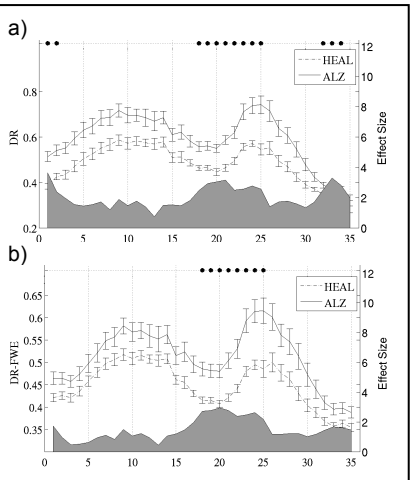

Fig. 3 Radial diffusivity estimated using partial volume clustering (a) and clustering combined with FWE (b). Black circles indicate significance of p<0.05; effect size is shown in grey.