Are SHORE-based biomarkers suitable descriptors for microstructure in DSI?

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Introduction. Micro-structural indexes based on a novel reconstruction method for diffusion MRI data (SHORE)[1] have recently been proposed. Nevertheless, such numerical biomarkers require proper validation and so far, no attempt has been done to apply the SHORE method to human magnetic resonance imaging (MRI) data. In this work, we derive and analyze SHORE descriptors on a group of human Diffusion Spectrum Imaging (DSI) data. The study aimed at determining their descriptive power, reliability and relations with established indexes of connectivity microstructure.

Methods. Ten healthy subjects (Age: 57.2±14.5; female:male=7:5) underwent 2 MRI scans at 3T (Siemens Tim Trio equipped with a 32-channel coil). The scans were within a 1 month interval (± 1 week, tp1c and tp2c). We refer to Obertino[2] for further details. The Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) model was used for signal reconstruction and the related biomarkers including Return to the Origin (RTOP), Axis (RTAP) and Plane (RTPP) probability as well as Propagator Anisotropy (PA) were calculated as in Ozarslan[1]. These represent the zero net displacement probabilities in the three- (RTOP), two- (RTAP) and mono-dimensional (RTPP) cases, respectively, providing an estimation of the mean pore geometry (volume, cross-sectional area, length) irrespectively of the pore shape. In consequence, from RTAP, an estimation of the mean ensemble value of the axons' radius (R) can be inferred[1]. Segmentation was performed by Freesurfer (http://surfer.nmr.mgh.harvard.edu/) and the Generalized Fractional Anisotropy (GFA) was calculated as in reference[2]. The corpus callosum (CC) and corona radiata (CR) were detected by means of the ICBM-DTI-81[3] WM parcellation (Figure 1). Histograms of the SHORE-based biormarkers were extracted for each region in order to assess their descriptive power as well as the repeatability of the measurements across time points. Focusing the analysis on the CC and CR allowed characterizing the behavior of the biomarkers in regions having a specific a-priori known structure (e.g. parallel fibers in the CC and crossings in the CR, respectively) and thus shading light on their ability on distinguishing the two conditions. Histograms were compared quantitatively both subject-wise across time points on healthy controls for assessing the reliability of the measurements by measuring the mean square error between the corresponding envelops, and qualitatively across subjects to eventually put forth inter-subject variations. Furthermore, group descriptors were derived for both patients and controls.

Results. Results revealed that 1) none of the considered biomarkers is normally distributed neither in WM nor in GM (Lilliefors test); 2) the intra-subject distributions of the SHORE derived biomarkers are very close across time points (MSE: 8.3x10^-09±8.56x10^-05 for RTAP); 3) the histograms are similar in shape across subjects at each time point (see Figure 2 for RTAP); 4) RTAP and R are strongly correlated to GFA in all regions (rho>0.8, Pearson); 5) the pdf of the estimated values for the radius are consistent with those reported in references[4] and are slightly overestimated (Figure 3); 6) R histograms have different shape in WM, GM, CC and CR in controls (see Figure 4). 5) The ensemble average estimates of R are consistently different in the CC and CR for all healthy controls (see Figure 5). Noteworthy, R is sistematically larger in crossing areas. Similar findings hold for RTPP and RTOP.

Discussion and Conclusions. Overall, results provide evidence on the suitability of RTAP, RTOP and RTPP as biomarkers. While RTOP map is hyperintense at crossings, RTAP provides an estimation of R that is consistent with the values reported in literature for humans[5,4]. Future work includes the analysis of the discriminative power of such biomarkers in differentiating patients from controls at group level.

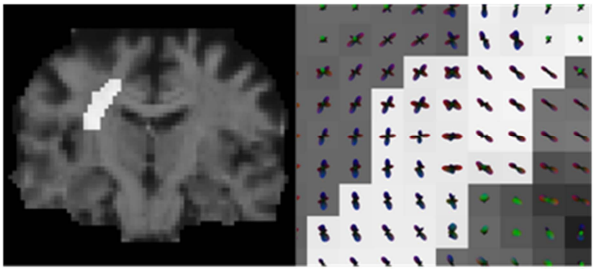

Figure 1. CR mask (left) and ODFs in the CR.

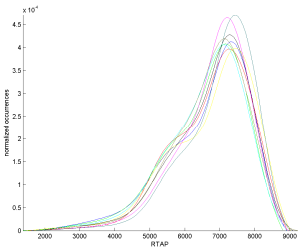

Figure 2: RTAP in WM.

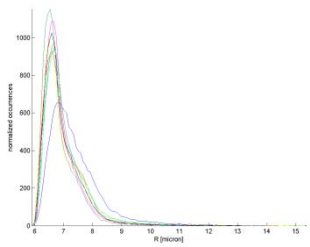

Figure 3: Histograms of the radius estimation in WM.

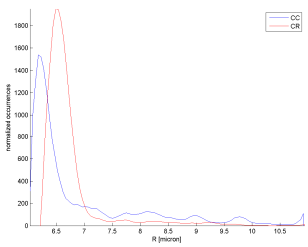

Figure 4: Histograms of the radius estimation in CC and CR.

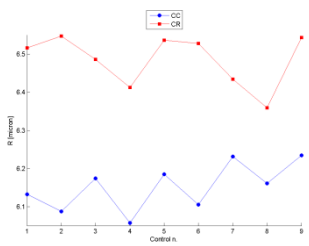

Figure 5. Estimates of R across controls in CC and CR.

References. [1]E. Ozarslan et al. Neuroimage. 2013; 78: 16:32. [2]S. Obertino et al., ISMRM DPTM Workshop 2013. [3]K. Oishi et al. Neuroimage. 2008; 43(3):447-57. [4]D. C. Alexander et al. Neuroimage. 2010: 52; 1374-1389. [5]F. Aboitiz et al. Brain Research. 1992; 598; 154-161.