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Reproducibility of corticospinal diffusion tensor tractography in normal subjects and hemiparetic stroke patients

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ABSTRACT

Purpose: The reproducibility of corticospinal diffusion tensor tractography (DTT) for a guideline is important before longitudinal monitoring of the therapy effects in stroke patients. This study aimed to establish the reproducibility of corticospinal DTT indices in healthy subjects and chronic hemiparetic stroke patients.

Materials and methods: Written informed consents were obtained from 10 healthy subjects (mean age 25.8 ± 6.8 years), who underwent two scans in one session plus the third scan one week later, and from 15 patients (mean age 47.5 ± 9.1 years, 6–60 months after the onset of stroke, NIHSS scores between 9 and 20) who were scanned thrice on separate days within one month. Diffusion-tensor imaging was performed at 3 T with 25 diffusion directions. Corticospinal tracts were reconstructed using fiber assignment by continuous tracking without and with motion/eddy-current corrections. Intra- and inter-rater as well as intra- and inter-session variations of the DTT derived indices (fiber number, apparent diffusion coefficient (ADC), and fractional anisotropy (FA)) were assessed.

Results: Intra-session and inter-session coefficients of variations (CVs) are small for FA (1.13–2.09%) and ADC (0.45–1.64%), but much larger for fiber number (8.05–22.4%). Inter-session CVs in the stroke side of patients (22.4%) are higher than those in the normal sides (18.0%) and in the normal subjects (14.7%). Motion/eddy-current correction improved inter-session reproducibility only for the fiber number of the infarcted corticospinal tract (CV reduced from 22.4% to 14.1%).

Conclusion: The fiber number derived from corticospinal DTT shows substantially lower precision than ADC and FA, with infarcted tracts showing lower reproducibility than the healthy tissues.

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1. Introduction

Diffusion tensor tractography (DTT) enables noninvasive assessment and quantification of brain white matter tracts in vivo. Indices derived from diffusion tensor data include the widely used apparent diffusion coefficient (ADC), fractional anisotropy (FA), three eigenvalues of the diffusion tensor, as well as the less commonly reported fiber number which aims at providing a numerical estimate of the volume of intact fiber tracts [1]. DTT has been proven to be a valuable tool in the evaluation of the white matter changes and clinical outcome in stroke patients [1–5]. In previous DTI studies on wallerian degeneration (WD) of the CST, the ratios of the diffusion indices (rFA, rMD, $r\lambda_1$ and $r\lambda_{23}$) between the affected and unaffected sides of the CSTs have commonly been used based on the hypothesis that diffusion indices of the contralesional CST are unchanged after stroke. Several studies have reported the corticospinal DTT reproducibility in normal subjects [6–9], but none compares the results between the normal subjects, stroke side and normal appearing side of stroke patients. Before taking the corticospinal DTT as a non-invasive tool to monitor the therapy effect (such as pioneering stem cell therapy) in chronic stroke patients, it is essential to establish the reproducibility of corticospinal tractography in stroke patients, include quantitative indices of both stroke and normal appearing sides as a baseline.

Besides, if routine motion and eddy-current corrections are necessary, our concern is how the corrections may affect the values of DTT-derived indices in our measurements. Eddy currents can cause image distortions, which, together with the head motion, result in misalignment of the diffusion-weighted (DW) images. Methods to minimize the effects of eddy currents and motion have been described [10–12]. Quantitative assessment of motion correction is not extensive. Tijssen et al., [13] evaluated noise and motion effects by measuring the ROI-based and voxel-based FA and ADC in three regions (frontal gray matter, frontal white matter and splenium of corpus callosum) in six healthy volunteers and computer simulations. Ken and Mark [14] measured the motion correction of HARDI data. To our knowledge, quantitative measurements in the effects of eddy-current and motion correction on the reproducibility of DTT derived indices are not available in the literature.

2. Materials and methods

2.1. Subjects and image acquisition

Institutional review board approval and written informed consent were obtained prior to examination. 10 normal subjects (3 females, 7 males; mean age 25.8 ± 6.8 years; range 21–45 years) and 15 patients (3 females, 12 males; mean age 47.5 ± 9.1years; range 31–56 years) with chronic stroke (mean of NIHSS scores 9.5 ± 0.7) were prospectively enrolled in this study (during June 2009–July 2010). The inclusion criteria of enrolled patients were: with hemiparetic stroke in the one-sided middle cerebral artery territory and lesion-free in the opposite side, 6–60 months after the onset of stroke, NIHSS scores between 9 and 20, age between 35 and 70 years old, no malignant or other major disease. Two scans of the 10 healthy subjects were obtained in one session (without re-positioning of the subjects) and the third scan was obtained one week later on a 3 T MR scanner (GE, Signa, Excite, HDx 3.0 T, Wisconsin, USA). Three scans of the 15 patients were obtained on three separate days within one month. Diffusion-weighted echo-planar imaging (EPI) sequence with twice-refocused spin echo was performed with the following parameters: TR/TE/NEX, 7000/min/2; number of sections, 31; section thickness, 4.0 mm; section separation, 0 mm; matrix 128×128; FOV, 240×240 mm; total scan time, 7 min 58 s. Diffusion weighting was encoded along 25 non-collinear directions using a b value of 1000 s/mm^2 and another one without diffusion weighting ($b = 0$).

2.2. Slice prescription

One well-trained technologist (C.W.L., with eleven-year experience in MR) performed all scans with landmark localization, with axial slices prescribed parallel to the AC–PC (anterior commisure–posterior commisure) line using a sagittal localizer. The sagittal images of the first scan of each patient were saved on the console of MR scanner together with the axial slices marked out. In the follow-up studies, these first sagittal images were recalled from the hard disk and the positions of the target axial slices were placed to be as close as possible to the first scan. The between-session change of the slice postion was calculated by the mutual information method [15] using the first slice of the T2-weighted images without diffusion-sensitizing gradient ($b = 0$) in the first scan as a reference.

2.3. Fiber tracking and ROI drawing strategy

All raw data were transferred to a workstation and analyzed with nICE software (Nordic ICE v2.3.8, NordicNeuro Lab, Norway). The corticospinal tracts were reconstructed using the fiber assignment by continuous tracking (FACT) method [16] with multi-ROI and brute-force approach [17,18]. Fibers belonging to the corticospinal tracts were defined as those passing both the cerebral peduncle at the level of optic tract and pons at the level of superior cerebellar peduncle, for which the ROIs were chosen as shown in Fig. 1. Fiber tracking was terminated with FA below 0.2 [19] or turning angle greater than 45°. Obviously spurious reconstructed projections were removed afterwards. Although this operation was rather subjective, the occurrence rate of spurious tracts was not high and thus should have minor effects on the results. The fiber number, FA, and ADC of reconstructed corticospinal tracts were recorded. One well-trained technologist (C.Y.W. with three-year MR experience) and a neuroradiologist (C.C.L, with eight-year experience in neuroradiology) performed the fiber tracking in the 10 normal subjects. The data of patients were analyzed by C.Y.W.

2.4. Motion and eddy-current correction

The motion and eddy-current correction protocol implemented in the nICE imaging processing software was used prior to tract reconstruction, because it was once suggested that motion correction may improve tract reproducibility [13,20,21]. The correction using T2-reference follows that of Rohde et al., [12] in its use of normalized mutual information as a cost function for comparing images with different contrast. The limits with respect to motion were set to 4 mm in translation and 4° in rotation, respectively, using b_0 images as a reference in each scan. On the other hand, the eddy current correction algorithm estimates the translation, shearing, and scaling along the phase-encoding direction due to residual gradient along the slice, readout, and phase encoding directions, respectively [12]. The maximum shear limits were set to 0.1 pixels per column, while the accepted scaling range was from −0.06 to 0.02. The maximal correction in the translation, rotation, and shear/scaling were presented with column plots. The mean and standard deviation of the maximal correction were also recorded. Bilateral corticospinal tracts in each scan of all healthy subjects and stroke patients were reconstructed twice: one with motion and eddy-current correction and the other without, to compare the effects of corrections.