

# Automated 3D fiber tracking based on two-ROI approach as a reliable tool for the detection of corticospinal tract degeneration in amyotrophic lateral sclerosis

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## Background and Objectives

While there is no objective diagnostic tool to demonstrate the corticospinal (CS) tract degeneration in various neurodegenerative disorders, several diffusion tensor MRI (DTI) investigations have revealed that there are statistically significant changes in diffusion properties along the CS tract in patients with amyotrophic lateral sclerosis (ALS). Previous studies (1-3), however, employed a region of interest (ROI) analysis of DTI maps, the result of which depends on critically on the approach to define ROI. Recently Aoki S et al (4) reported a quantitative result based on a tractography. In this study, we developed a so-called two-ROI approach in which 3D fiber bundle tracking was performed using two reference ROIs to delineate the CS tract. Reliability of this approach was analyzed, and the possible changes of diffusion properties were assessed in patients with ALS.

## Materials and Methods

DTI was performed using a single shot SE-EPI with 25 noncollinear diffusion gradient directions ( $b=1000 \text{ s/mm}^2$ ) and with no diffusion gradient on a 3.0-T MR system in 10 ALS patients (M:F=6:4,  $56 \pm 9$  years) and 8 healthy age and sex-matched controls who gave informed consents. The CS tract was identified on color-coded fractional anisotropy (FA) maps (FA threshold of 0.2) of fiber direction. Two ROIs were manually drawn including the CS tract and excluding voxels which contained anisotropic fibers with orientations inconsistent with known pyramidal tract orientation; one in the cerebral peduncle at the level slightly above the red nucleus (ROI-1), and the other in the lower pons (ROI-2). Fiber-tracking was performed using a home-made program based on the FACT method proposed by Mori. The 3D tracking results were superimposed on FA maps, so that sub-ROIs were determined automatically comprising the pixels which were penetrated by the 3D tracking results on each brain slice (tractoscope, Fig. 1). ROI analyses were conducted by two independent raters, and interrater variability was measured by coefficient of variation (CV).

## Results

FA was considerably variable along the CS tract with the highest values in the cerebral peduncle (CP) and posterior limb of the internal capsule (PIC) (Fig. 1). By contrast, MD was relatively constant above the lower pons, with a mild elevation in the CP and a large increase in the medulla. CV was significantly lower for both FA and MD in the ROIs which were automatically defined in the CP and PIC by the 3D fiber bundle tracking using two-ROI approach (Fig. 2, ANOVA with post-hoc test,  $p<0.01$ ). Average FA and MD values were lower and higher, respectively, in patients with ALS versus normal controls, with the statistical significance attained in the ROIs at the CP for FA (Fig. 3, ANOVA with post-hoc test,  $p<0.05$ ).

## Conclusion

FA is highly variable along the corticospinal tract in DTI maps, which indicates that possible mismatching in anatomical levels and boundary of ROI can affect the result in patients with ALS. Two-ROI approach may reduce such an operator-induced bias in defining ROI, and can be used as a reliable tool for demonstrating the corticospinal tract degeneration in ALS.

**References** 1) Hong YH, Lee KW, Sung JJ, Chang KH, Song IC. J Neurol Sci 2004 227(1):73-8 2) Brooks BR, Miller RG, Swash M, Munsat TL. Amyotroph Lateral Scler Other Mot Neuron Disord 2000;1:293 – 9. 3) Graham JM et al, Neurology 2004 14;2111-9 4) Aoki S et al, Radiation medicine 2005 23;195-9

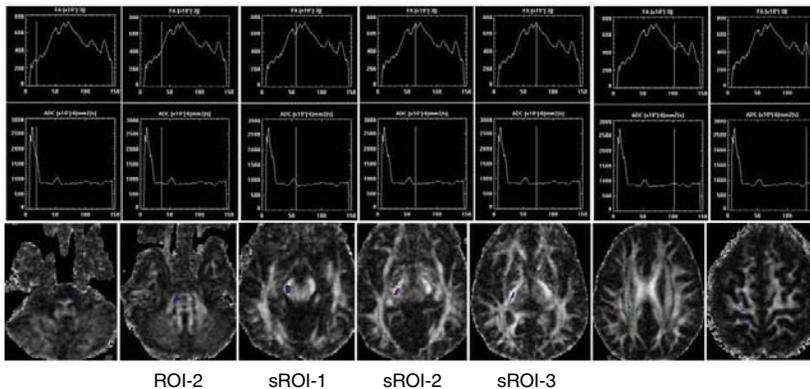


Fig. 1. Tractoscopes for FA (upper panel) and MD (middle). SubROIs (lower) were automatically determined at each brain slice (indicated by vertical bars in tractoscopes) by superimposing tracking results on FA maps. sROI-1 were defined at the level of ROI-1, while sROI-2 and sROI-3 were at the level of cerebral peduncle and posterior limb of internal capsule, respectively, having the highest FA values in those anatomical regions.

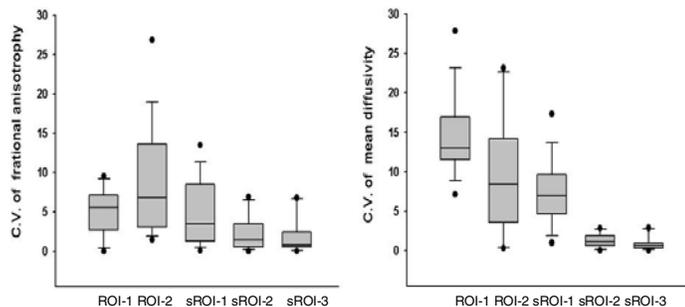


Fig. 2. Coefficient of variations (C.V.) of FA and MD in two operator-defined ROIs and three automatically determined sROIs.

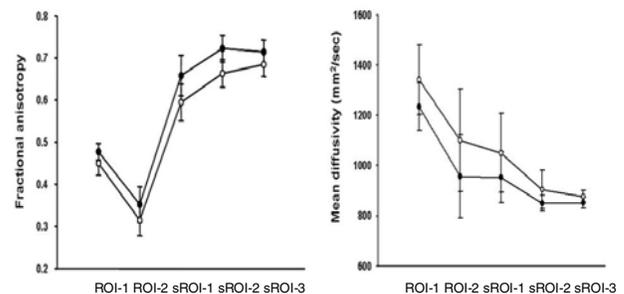


Fig. 3. Mean and standard deviation of FA and MD in patients with ALS (white circles) versus normal controls (black circles).