SPATIAL NORMALIZATION OF CERVICAL CORD 3D T1-WEIGHTED IMAGES AND REGIONAL ASSESSMENT OF CORD ATROPHY WITH A VOXEL-BASED APPROACH

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Introduction. The spinal cord is a clinically eloquent site of the central nervous system and it is frequently involved in multiple sclerosis (MS). Studies assessing cervical cord atrophy in MS measured the cross-sectional area at a single anatomical level because coregistration of cord images in a common standard space and voxel-based analysis of cord atrophy are technically challenging. Recently, a new semi-automatic method has been proposed to spatially normalize cervical cord functional MRI scans [1]. Another semi-automatic method, which allows segmentation of the entire cervical cord from C1 to C7, has also been introduced [2].

Objective. To apply these two techniques on 3D T1-weighted high-resolution images of the cervical cord and to perform voxel-based assessment of cord atrophy in a group of MS patients compared with healthy controls.

Methods. High-resolution T1-weighted scans of the cervical cord were acquired from 41 healthy controls (15 males, mean age=39.8 years) and 31 relapsing-remitting (RR) MS patients (7 males, mean age=39.6 years). For each scan, a reference line was drawn along the anterior edge of the cord in the midsagittal slice. The caudal edge of the pons and the C7/T1 intervertebral disc were marked on this line as reference points (Figure 1A). After a 5-mm spatial smoothing filter was applied in a direction parallel to cord axis, images were normalized by reslicing them transverse to the reference line, and adjusting the distance between the two reference points in order to fit a 140-mm standard distance (Figure 1B). Anterio-posterior and left-right shifts were then corrected by rigid-body registration to align each slice with its nearest neighbour (Figure 1C). Cervical cord outlines on normalized images were drawn by using a semi-automatic approach based on an active surface [2] and were used to create cord masks (Figure 1D), which were then smoothed with 3, 4, and 5-mm full width at half maximum (FWHM) Gaussian filter. The resulting images entered a SPM5 second-level statistical analysis, to perform within- and between-group comparison of cord volumes. In RRMS patients, multiple regression models were used to assess the correlation between cord atrophy and cord lesion number and brain T2 lesion load (T2LL).

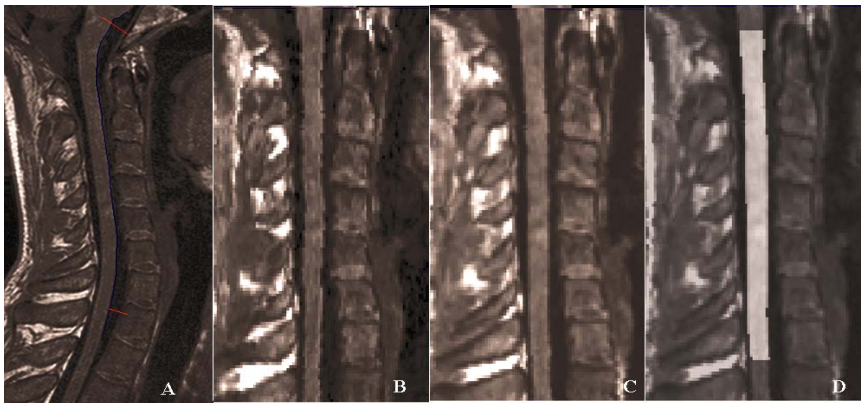

Figure 1. Post-processing applied to cervical cord images in order to perform spatial normalization of cord images.
A) Definition of a reference line along the cord anterior edge, and setting of caudal edge of pons and C7/T1 intervertebral disc as reference points.
B) Reformatting of image transverse to the reference line.
C) Rigid body registration of each slice with its nearest neighbour.
D) Segmentation of cord outlines at each slice with a semi-automatic method based on an active surface, and creation of the corresponding cord mask.

Results. Normalization of T1-weighted images was successfully run for all subjects and allowed the creation of a standard cervical cord template as an average of the 41 healthy subjects, which is shown in Figure 2 as the background image on which the SPMs are overlaid. Within-group average probability maps of the cervical cord were created for controls and patients (Figure 2A and 2B). Between-group comparison showed significant cord atrophy in RRMS *vs.* controls, which was mainly located in the posterior and lateral cervical cord regions at C2, C3, C6 and C7 levels (Figure 2C). Statistical comparison of images smoothed with different FWHMs gave very similar results. In RRMS patients, cervical cord atrophy was correlated with cord lesion number (r=-0.54, p=0.001) and T2LL (r=-0.27, p=0.001).

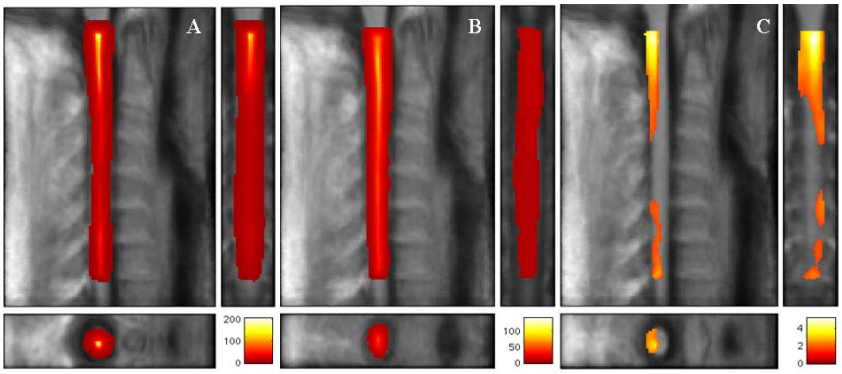

Figure 2. Within-group and between-group comparisons of cord volume, superimposed on a cervical cord template created as average image of the 41 control subjects.
A) Within-group cord probability map from healthy controls ($p<0.05$, family-wise error [FWE] corrected for multiple comparisons).
B) Within-group cord probability map from patients with RRMS ($p<0.05$, FWE corrected for multiple comparisons).
C) Between-group comparison: clusters showing significant cord atrophy in RRMS vs. healthy controls ($p<0.01$, uncorrected for multiple comparison).

Conclusions. Normalization of high-resolution T1-weighted cervical cord images was feasible and allowed the creation of an average standard template of the cervical cord. Voxel-wise assessment of cervical cord atrophy showed increased regional cord atrophy in RRMS patients *vs.* controls.

References. [1] Stroman P, et al. Magn Reson Imaging 2008;26:809-814; [2] Horsfield MA, et al. Neuroimage 2010; 50:446-455.