FULLY AUTOMATED SEGMENTATION OF THE CERVICAL CORD USING PROPSEG: APPLICATION TO MULTIPLE SCLEROSIS

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TARGET AUDIENCE: Physicians and scientists interested in spinal cord imaging in neurodegenerative conditions.

PURPOSE: To evaluate a recently developed fully automated cord segmentation method in a large cohort of patients with multiple sclerosis (MS).

INTRODUCTION: Loss of axons in the spinal cord, with a consequent reduction in cord cross-sectional area (CSA), represents the main pathological substrate of irreversible physical disability in multiple sclerosis (MS) and this has been demonstrated both in *post mortem* studies[1] and *in vivo* investigations.[2] Imaging methods that offer accurate and reliable estimation of cord CSA over time are therefore warranted as they provide a biologically plausible endpoint to clinical trials. Over the years, methods to measure cord CSA on MRI have evolved from the manual outlining of the cord on axial images[3] to highly reproducible semi-automated methods.[2,4] More recently, a fully automated method (PropSeg) has been developed, which requires no manual intervention and is based on an iterative propagation of a deformable model with adaptive contrast mechanisms.[5] The method offers fast and reliable measurements of the cord CSA in a matter of seconds, as demonstrated in a pilot study of healthy volunteers and spinal cord injury patients; importantly, the method has been reported in conjunction with its use with T1-, T2- and T2*- weighted acquisitions and at any level of the spinal cord, unlike previously reported methodologies which work mainly with T1-weighted contrast at cervical level. In this work, the method is evaluated in a large cohort of people with MS by comparing its measurements of cervical cord CSA with those obtained through an established semi-automated method based on an active surface model (ASM).[4]

METHOD: A) Imaging dataset: One hundred and fifteen cases were processed for the purpose of this study: 27 healthy control subjects, 21 with clinically isolated syndrome (CIS), 25 cases with relapsing remitting MS (RRMS), 22 cases with primary progressive MS (PPMS) and 20 cases with secondary progressive MS (SPMS). Informed consent was obtained from all study participants and the study was approved by the local institutional review board. The dataset was collected using a 3T Philips Achieva MRI system (Philips Medical Systems, Best, Netherlands) and the manufacturer's product 16-channel neurovascular (NV) coil; the whole cervical spine was imaged in the sagittal plane using a T1w 3D-TFE acquisition and the following imaging parameters: TR = 8.1 ms; TE = 3.7 ms; TI = 867 ms; flip angle α = 8°; FOV= 256 x 256 mm^2; voxel size = 1 x 1 x 1 mm^3; NEX = 1; 128 contiguous slices; scanning time 6:30 min. B) Image analysis: For the ASM method, the 'cord finder' option available with the Jim Software (Xinapse systems, www.xinapse.com) was used to segment a 15 mm section of the cervical spinal cord, firstly by reformatting the 3D-T1w volume in the axial plane (middle slice through the C2-3 intervertebral disc) and then processing 5 slices (2 above and 2 below the middle slice) re-sampled to a 1 x 1 x 3 mm^3 resolution, manually inserting seed points as previously described.[4] For the PropSeg method, the entire 3D-T1w volume was processed by simply specifying the directory path containing the image data; all CSA values for each slice in the axial plane (1 x 1 x 1 mm^3) were output and only the slices corresponding to those analysed with the ASM method were averaged and compared. C) Reproducibility assessment: Using both image segmentation methods, 10 control cases and 10 cases with MS (3 x CIS, 3 x RRMS, 2 x PPMS, 2 x SPMS) were analysed 3 times by the same rater (intra-rater) on 3 separate occasions with a minimum of one week gap between measurements. D) Statistics: Analysis was performed using SPSS 11.0 (SPSS, Chicago, Ill., USA); correlations between CSA measurements obtained with PropSeg and ASM were investigated for each patient group separately using the Pearson correlation coefficient; for the assessment of intra-observer reproducibility, the coefficient of variation (COV) was calculated using the mean and standard deviation from the repeated measures and the equation COV= [SD/mean] × 100%. Sample size calculations within each patient group and with each method were also performed.

Group	n=	CSA (ASM[4]) (Mean ± SD, mm^2)	CSA (PropSeg[5]) (Mean ± SD, mm^2)	R^2	p-value
Control	**26**	**75.8 ± 7.8**	**70.2 ± 7.5**	**0.98**	**0.0001**
CIS	**21**	**81.9 ± 8.5**	**75.9 ± 7.9**	**0.98**	**0.0001**
RRMS	**23**	**73.8 ± 7.8**	**68.7 ± 7.9**	**0.96**	**0.0001**
PPMS	**22**	**66.0 ± 11.2**	**60.4 ± 10**	**0.98**	**0.0001**
SPMS	**20**	**61.4 ± 11.0**	**56.1 ± 10.5**	**0.99**	**0.0001**

Table 1. Cross-sectional area (CSA) measurements and correlation coefficients.

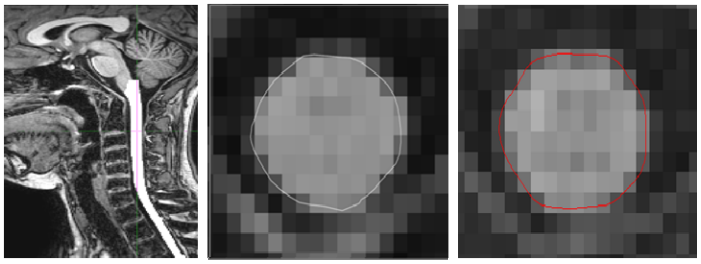

Figure 1. Single slice at C2/3 level (left; shown in green) segmented using PropSeg (middle; contour shown in white) and ASM (right; contour shown in red)

RESULTS: Using PropSeg, all cases were processed within minutes (each individual case requiring a few seconds depending on the processor used). Out of a total of 115 cases analysed, PropSeg failed to correctly segment the cervical cord only in 3 cases (1 x control and 2 x RRMS) and these cases were excluded from the analysis. Figure 1 shows an example of the segmentation for each method. Table 1 shows mean CSA measurements obtained in each group using both image segmentation methods and also the correlation coefficients identified between these measurements. On average, CSA values using PropSeg were 8.4% lower as compared to those obtained with the ASM method. Intra-rater COVs for the ASM method in 10 controls and 10 patients were 0.29% and 0.63%, respectively; as expected, no variation between repeated measurements was identified using PropSeg. Based on the analysis method and preliminary results presented herein, the difference in the sample size required to detect a 2% reduction in CSA with 80% power at 5% significance between the two methods is 8.6% (CIS 3.3%, RRMS 18.4%, PPMS 4.6%, SPMS 8.2%).

CONCLUSION: In this pilot study, PropSeg has been shown to offer fast and reliable segmentation of the cervical spinal cord in a large cohort of MS patients with favourable intra-rater COV values and with CSA measurements that are highly correlated with those obtained with the currently established ASM method. The systematic CSA difference between both methods can be explained by larger partial volume effect in the ASM case related to the averaging of adjacent slices. Another possible explanation is a difference in contrast adaptation mechanism. The effect of slice thickness and anatomical coverage will be investigated in future work, which will also include a more comprehensive reliability assessment e.g. multi-center as well as longitudinal investigations. In conclusion, the results from this study suggest that PropSeg is a user-friendly, reliable and time-efficient way of obtaining CSA measurements in MS and its use in clinical trials involving large datasets is warranted.

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