Morphological standards for the human spinal cord – Validations and preliminary applications to patients

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Target audience: People involved in the characterization of spinal cord (SC) morphology, SC modeling and SC clinical research and practice

Introduction: MR-based *in vivo* studies have already described SC morphology, mainly SC cross-sectional area and diameters, at the cervical level [1,2]. *Post-mortem* studies have depicted the entire SC, including information on WM/GM proportions; however biases with *in vivo* data have not been investigated [3,4]. Moreover, large inter-individuals variations have been reported, limiting these morphological observations in their use as standards in clinical situations or as modeling input [5,6].

In this context, the objective of this study was to provide "invariant" morphological features of the complete *in vivo* human normal spinal cord that may be used as a database for individualized study of SC pathophysiological conditions, either for clinical practice and prognosis evaluation or to establish an accurate model of the SC that will open new perspectives to study compressive mechanisms such as encountered in SC injury or spondylotic myelopathy.

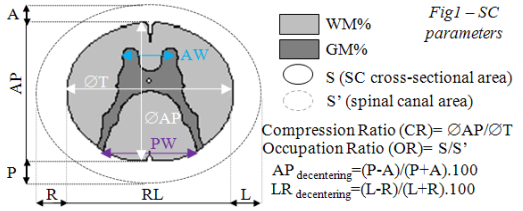


Fig1 – SC parameters

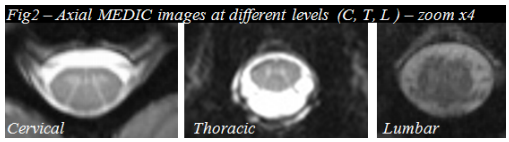


Fig2 – Axial MEDIC images at different levels (C, T, L) – zoom x4

Material and methods: Absolute SC parameters (ØT, ØAP, S, AW, PW and % of WM/GM) (*fig.1*) were first measured based on semi-automatically segmented (SliceOMatic, Tomovision) high resolution *in vivo* T_2*-w axial images acquired at 3T (21 slices, one slice per vertebral level from C1 to L2, resolution 0.5x0.5x5 mm^3 (*fig.2*), TE 27 ms, CSF-pulsatility synchronization, total acq time ~20min) on healthy young (27±5 yo, N=15, 9M/ 6F) and older (60±6 yo, N=8, 3M/5F) volunteers. Statistical differences (intra/inter-individual, age, sex, postmortem [3,4]) were investigated (JMP, SAS) and normalized-to-C3 ratios (S_{norm}, $ØT_{norm}$, $ØAP_{norm}$) were then derived and evaluated as "invariant". To test the hypothesis that the invariant database could be used to calculate any SC level of a subject given a single MR measurement (here C3), a leave one out analysis was performed using our 23 volunteers and root mean squared errors (RMSE) were calculated for each parameter. Spinal canal parameters (AP, RL, S', OR, as well as lateral and antero-posterior decentering, *fig.1*) were also measured and border values (average-2SD) were calculated. Patients were finally included in order to investigate the potentiality of our database.

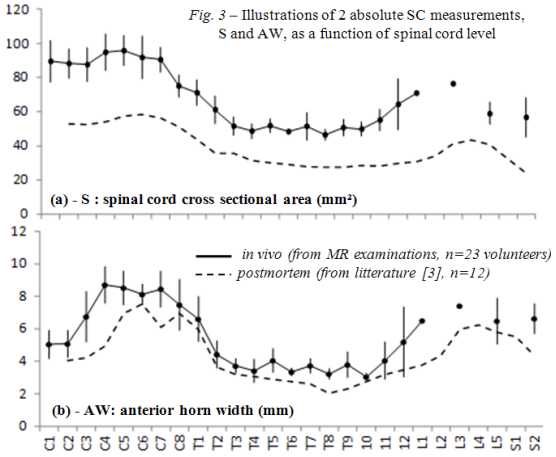


Fig. 3 – Illustrations of 2 absolute SC measurements, S and AW, as a function of spinal cord level

Results: Absolute measurements of SC morphology presented large intra- and inter-individual variations, up to 30% and 13% in average (*fig.3*). The main features when comparing aged group relative to young people were trends of decreased cross-sectional area (but not significant), lower ØAP ($p<0.03$) and higher WM% (ie. decrease GM surface, $p<0.05$). Gender had no influence on the parameters except for PW (higher for female, $p<0.01$). *Postmortem* data were statistically different from *in vivo* data (*fig.3*), except WM/GM%.

S_{norm}, $ØAP_{norm}$, $ØT_{norm}$ were similar for both young and older groups, meaning that they could represent good invariants. However, only S_{norm} in *postmortem* studies was non statistically different from *in vivo* data. The leave one out analysis conducted to mean RMSE <10%. One example of real and calculated parameters along the entire SC for one healthy subject is given on *fig.4.* One example of invariant application to a clinical case (41 yo with osteophytes at C5 and C6 vertebral level) is illustrated in *fig.5*. In this particular case, ØAP and S were locally significantly reduced of 25% and 36% compared to expected normal situation. The advantage of using the invariant database to calculate the expected normal SC morphology is that the patient is his own control.

Finally, mean canal occupation ratio (OR) was found equal to (0.42±0.05, 0.35±0.02, and 0.25±0.09 at C, T, L levels, respectively), with influence of age and sex, which also influence $AP_{decentering}$ (data not shown). Mean OR border values were evaluated to 0.29, 0.22 and 0.12 at C, T, L levels resp., meaning that below these numbers, the investigated person may be considered at risk, as illustrated on *fig. 6* (68 yo with spastic gait and sensory ataxia). Further correlations with SC impairment, clinical score and validations of border values as risk factors should be conducted.

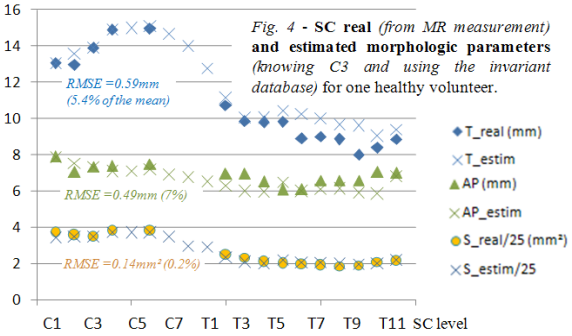


Fig. 4 - **SC real** *(from MR measurement)* **and estimated morphologic parameters** *(knowing C3 and using the invariant database)* for one healthy volunteer.

Conclusion: In this study, we have shown that 1) high quality axial SC images with good GM/WM contrast can be acquired at all SC levels, 2) because of shrinkage during fixation, care should be taken when modeling from *postmortem* data, 3) age influences SC morphology, however, 4) SC morphological invariants exist. Such invariants could be applied to pathological cases in order to extrapolate the "normal" SC morphology. This should help in modeling compressive pathologies, such as SC trauma, spondylotic myelopathy, etc .. This database should also further help in the personalized diagnosis, and in the longer term, to protect from SC impairment and to build predictive models of disease and progression. Further clinical cases are under investigation in order to fully evaluate the potentiality offered by the SC morphological database for prognosis or surgical decision. Finally, influence of age and sex on GM geometry and proportion should be further investigated in order to build specific templates.

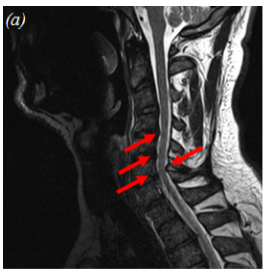
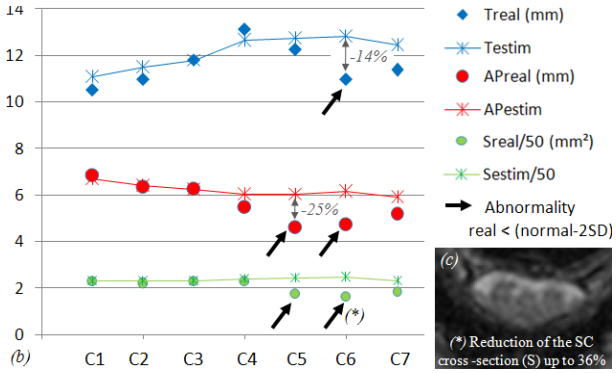


Fig. 5 – Applied to a patient with osteophytes, the invariants allow to estimate how should normally be the healthy SC (baseline -✶-).



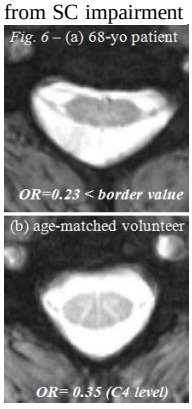


Fig. 6 – (a) 68-yo patient

References: [1]Sherman, AJNR 1990 [2]Kato, E Spine J 2012, [3]Kameyama, Spine 1996, [4]Ko, Spinal Cord 2004, [5]Maikos, J Neurotrauma 2008, [6]Greaves, Biom Eng 2008.