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

Virginie Calloët1, Léo Fradet2,3, Jean-Philippe Ranjeva2, Guillaume Duhamel1, Olivier Girard4, Pierre-Jean Arnaux5, and Yvan Petit6

1Centre de Résonance Magnétique Biologique et Médicale (CRMBM, UMR 7339), CNRS / Aix-Marseille Université, Marseille, France, 2Laboratoire de Biomécanique Appliquée (LBA, UMRT 24), IFSTTAR / Aix-Marseille Université, Marseille, France, 3Department of Mechanical Engineering, École de technologie supérieure, Montreal, Quebec, Canada

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 pathophysiologic 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.

Material and methods: Absolute SC parameters (∅T, ∅AP, S, AW, PW and % of WM/GM) (fig. 1) were first measured based on semi-automatically segmented (SliceOMatic, Tomovision) high resolution in vivo T2-T1w axial images acquired at 3T (21 slices, one slice per vertebral level from C1 to L2, resolution 0.5x0.5x5 mm (vivo), TE 27 ms, CSP-pulsatility synchronization, total acq time ~20min) on healthy young (27±5 yo, N=15, 9M/6F) and older (60±16 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 (Snorm, ∅Tnorm, ∅APnorm) 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.

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 ∅AP (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%

Snorm ∅APnorm ∅Tnorm were similar for both young and older groups, meaning that they could represent good invariants. However, only Snorm in postmortem studies was not 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, ∅AP 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 (0.4±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 APmax (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.

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.

References: [1]Sherman, AJNR 1990