Cervical Spinal Cord Template of Healthy Controls using High-Resolution Axial Gradient Echo Imaging

Daniel J. Tozer[1], Marios C. Yiannakas[1], Hugh Kearney[1], and Claudia A. M. Wheeler-Kingshott[1]

[1]NMR Research Unit, Department of Neuroinflammation, UCL Institute of Neurology, London, London, United Kingdom

Introduction: The use of brain templates, as targets to which all images are transformed when performing group analysis, is widely accepted (1). There are many templates for the healthy brain available such as the MNI152 (2) template based on conventional MR images and the FMRIB58 (www.fmrib.ox.ac.uk/fsl/data/FMRIB58_FA.html) template based on fractional anisotropy maps from diffusion tensor imaging. However, there is no such template for the spinal cord. The spinal cord is of interest in several neurodegenerative diseases as well as spinal cord injury as the location of lesions within the spinal cord often has a severe impact on disability (3). It is becoming recognised that study specific, rather than general, templates should be used (4). This work presents a method for creating an axial cervical cord template, which is tested on a small group of healthy controls.

Methods: *Subjects*: The data used in this study came from six healthy control subjects (mean age 28 years, range 26-31, 4 male, 2 female). Written informed consent was obtained from all subjects and the study was approved by the local institutional review board. *MRI protocol*: The subjects were scanned using a 3T Philips Achieva MRI system with RF multi-transmit technology (Philips Healthcare, Best, Netherlands) and the manufacturer's product 16-channel neurovascular coil. The sequence of interest was a high-resolution axial fat-suppressed 3D slab selective fast field echo (FFE) sequence with TR = 23 ms; TE = 5ms; flip angle α = 7°; FOV= 240 x 180 mm^2; voxel size = 0.5 x 0.5 x 5 mm^3; NEX = 8. Ten contiguous axial slices, orthogonal to the main axis of the spinal cord at the level of C2-3 intervertebral disc, were scanned in 13:34 min. The sequence was acquired 3 times in 5 of the subjects, on separate occasions. *Data analysis*: The template of the cervical cord was constructed from this data using the following steps: i) All data was trimmed to a volume of 50 x 50 mm^2 centred on the spinal cord. ii) For each of the 5 subjects scanned repeatedly the second and third scans were registered linearly to the first scan (using FLIRT (5)) and the three registered images were then averaged to produce a single averaged image for each subject. iii) Non-linear registration (using FNIRT (http://www.fmrib.ox.ac.uk/fsl/)) was then performed between the first scan of each subject and the 6th subject, used as an independent reference. The deformation field produced for each subject was then applied to the average spine for that subject. The five registered averaged cervical cords were then averaged to produce the template. This pipeline is shown schematically in figure 1.
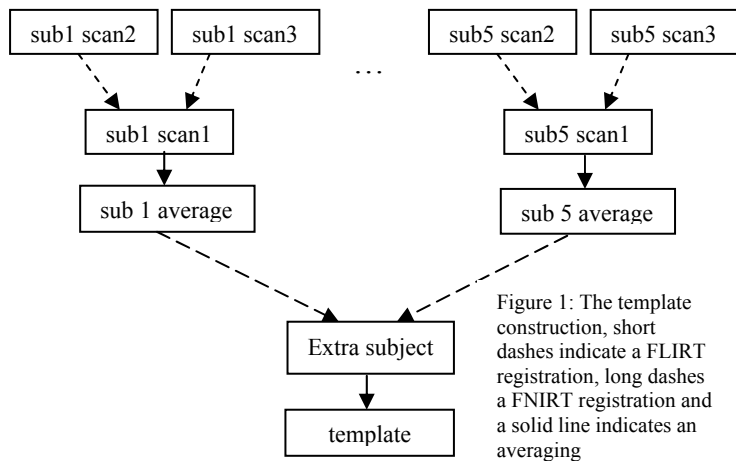

Figure 1: The template construction, short dashes indicate a FLIRT registration, long dashes a FNIRT registration and a solid line indicates an averaging
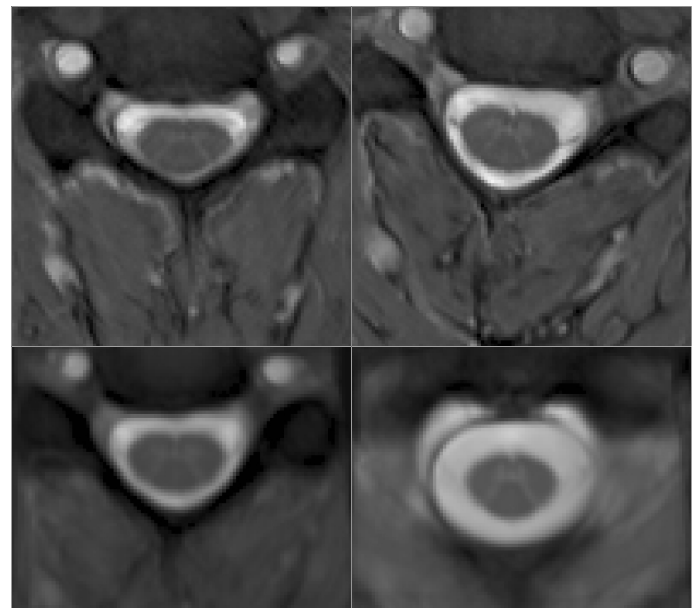

Figure 2: The two images on the top row show the lowest slice acquired for two of the subjects, the bottom left image shows the same slice from the template and the bottom right shows a slice from further up the cord

Results: Figure 2 shows two of the original spinal cord images and two slices from the final template. It can be seen from the template that the grey matter structure within the cord is well defined despite the low number of subjects, indicating that the registration and averaging has worked well.

Conclusions: The methodology presented here for the estimation of a template of the cervical spinal cord is straight forward and uses available software tools, yet appears to produce a template that can be used as a common space for spinal cord group analysis. The template is based on a small number of subjects; however this is augmented by the use of repeat scans for each subject. As the number of scans is identical for each subject this does not bias the template to a given subject, but does remove some of the variability associated with repeat scans. The use of a reference subject as the target for the non-linear registration may introduce a bias in the template to this subject, so when constructing a study template care should be taken in selecting the reference subject. The retention of the internal grey matter structure of the cord suggests that the registration and averaging steps do not introduce significant blurring in healthy controls. It remains to be defined, however, how to deal with groups involving patients and healthy subjects. The trimming of the images to a 50x50 mm^2 field of view improved the quality of the registration considerably, as it removes body structures highly dependent on the subject's size, which causes unhelpful stretching of the registered images, whilst still leaving enough detail to allow good estimation of the transformation matrix. This performed much better than extracting the spinal cord itself with the active surface model (6) and then registering the extracted cords (data not shown). In conclusion, the proposed method produces a good quality spinal cord template; although this could be improved by the use of more subjects the pipeline presented here can be retained to produce templates for use in group studies.

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