Multi-channel registration of FA and T1-weighted images to standard space: patients with Multiple Sclerosis

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Background Many medical image analysis pipelines, such as those used for quantitative magnetic resonance imaging (MRI) studies, include a registration step either between different modalities in subject's (native) space or different time-points in longitudinal studies. Registration is also of increasing interest for the study of multiple contrast MRI for cross-sectional and longitudinal group studies, where data needs to be co-registered to a common (standard) space. The co-registration of structural T1 weighted (T1w) scans and diffusion tensor imaging (DTI) derived fractional anisotropy (FA) maps to a common space is of particular interest as T1w scans can be used for brain segmentation while DTI maps inform the user about microstructural tissue properties. However, the registration of T1w and DTI is not a simple task since they contain complementary information with no clear functional mapping between the two. Furthermore, the two modalities are often differently affected by partial volume effects as a consequence of different voxel size or sequence specific image distortions (e.g. due to fast imaging such as EPI in DTI). Maintaining anatomic correspondence between these complementary modalities becomes even more challenging when patients with neurodegenerative disease are to be registered to a standard space (usually derived from a group of healthy subjects).

In this study we focus on multiple sclerosis (MS) subjects in whom both white matter and grey matter lesions, brain tissue atrophy (with sometimes marked ventricular enlargement) are seen. Figure 1 illustrates the disparity between the T1w Montreal Neurological Institute (MNI) template and an MS patient with severe structural damage and ventricle enlargement. Multi-channel (MC) registration algorithms such as proposed by Daga *et al.* [1] have the advantage of maintaining anatomical correspondence between, e.g. T1w and DTI, in atlas space even when large scale deformations are necessary (as shown in Figure 1). In this work, we tested the performance of an MC registration applied to a T1w/DTI data of healthy subjects and MS patients, choosing the Montreal Neurological Institute (MNI) space as target. We compare the results with standard single-channel registrations (SC) to their corresponding template.

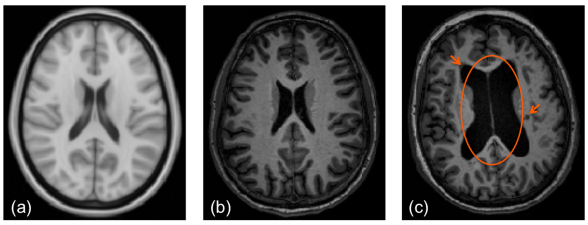

Figure 1 - T1w images: a) MNI atlas; b) Healthy subject; c) MS patient with ventricular enlargement and lesions marked.

Methods Subjects: Five healthy subjects (mean age = 41.8 years, 3 males and 2 females) and five people with MS (4 relapse remitting, 1 secondary progressive, mean age = 41.6, 2 males and 3 females, mean disease duration = 13.2 years, median EDSS = 2.5) were scanned on a 3T Philips Achieva scanner, with a 32 element head coil. MRI protocol: 1) Dual echo proton density T2 weighted (T2w) scan: 1*1*3mm, TR=3500ms, TE=19/85ms; 2) T1w structural scan: 1*1*1mm, TR=6.9ms, TE=3.1ms ; 3) DTI: Cardiac gated SE-EPI, TR = 24 RRs, TE = 68ms, number of diffusion weighting directions = 61 (7 b=0 and 61 b=1200 s/mm^2), 2*2*2mm voxel size, SENSE = 3.1. Image analysis: DTI indices, including FA, were generated after eddy current distortion correction (eddy_correct from the FSL library (www.fmrib.ox.ac.uk/fsl) and using the camino software package (www.camino.org.uk)[2]. The registration pipeline consisted of the following steps: i) skull stripping of the T1w MNI atlas using BET [3]; ii) bias correction and intensity normalization of the T1w scans using the N3 approach [4]; iii) lesion filling of the T1w scans (on MS patients only) according to [5] and iv) single channel (SC) or multi-channel registration (MC) to the predefined MNI T1w and FA templates from the International Consortium For Brain Mapping (ICBM) registered to the T1w in MNI space approach based on NiftyReg (www.sf.net/projects/niftyreg). SC registration of the T1w images to the T1w MNI template and SC registration of FA maps to the FA MNI template was performed on each subject. To perform the MC registration step, a MC volume composed of T1w and FA was first created by following these steps: the b0 (or non diffusion weighted) image was aligned to the T2w scan with non-rigid registration [7] to correct for EPI-induced distortions in the DTI data. The T2w scan provided a more accurate alignment due to both scans being T2w and the b0 scan being 3/8 the voxel size of the T2w scan compared to 1/8 the voxel size of the T1w scan. The T2w images were than aligned with the T1w images via affine registration [6]. The composition of the transformation matrix (T1w-T2w) and the deformation field (T2w-b0) allowed us to transform from the T1w space to the FA space (and vice-versa). The registered images were concatenated to generate a single MC volume of T1w and FA images in native (subject) space. The MC volume was used to transform the data to MNI space by means of a non-rigid registration to the composite T1w MNI/FA MNI template using the multi-channel registration of Daga *et al.* [1]. We use checkerboard images to assess the quality of the registration between the registered T1w image and the T1w MNI template, the registered FA map and the FA MNI template, and the co-registration between the registered T1w and registered FA in MNI space.

Results For healthy subjects the MC approach performed as well as the SC approach when co-registering T1w and FA images to MNI atlas space independently of each other (see Figure 2). However, there was a distinct improvement when co-registering MS patient data to the MNI atlas using the MC approach compared to the SC approach. Figure 3 shows the results from a patient registered to the MNI space in whom the enlarged ventricles and MS lesions mainly drive the misalignment in the brain outline and internal structure displacement (see red arrows in Figure 3). Misalignments were present in all patients included in this pilot study. Figure 3.c illustrates that both SC and MC registration produce misalignments even though MC registration improves co-registration in the boundaries of the ventricles, corpus callosum and cortex (green arrows in Figure 3).

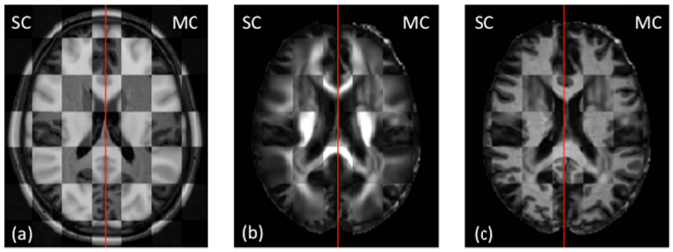

Figure 2. Co-registration results for a healthy subject in MNI atlas space presented as checkerboard images (left side SC registration / right side MC registration): a) registered T1w and T1w MNI ; b) registered FA and FA MNI c) registered T1w and registered FA in MNI space.

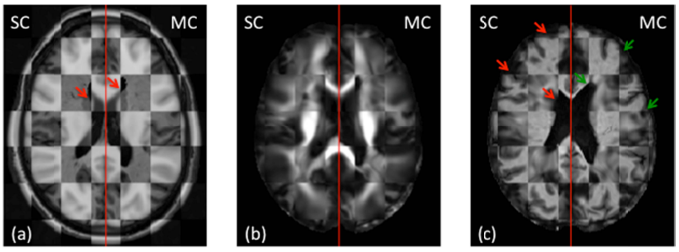

Figure 3. Co-registration results for a MS patient in MNI atlas space presented as checkerboard images (left side SC registration / right side MC registration): a) registered T1w and T1w MNI; b) registered FA and FA MNI; c) registered T1w and registered FA in MNI space.

Conclusion We have developed a pipeline to perform a simultaneous co-registration of T1w and FA images to standard space. In application, the MC registration on MS patients (with brain atrophy and lesions) yields better results in terms of the alignment between the T1w and FA images in standard space. However, it should be noted that registration to standard space in the presence of brain atrophy and ventricular enlargement is difficult because of the large deformations required to match a healthy brain template. A possible way to tackle this issue and improve the co-registration is to create a group specific atlas for healthy controls and patients separately.

References [1] Daga et al, Biomed Imaging (2011); [2] Cook et al, ISMRM (2006): [3] Smith, HBM 17(2002); [4] Sled et al, TMI (1998); [5] Chard et al, JMRI (2010); [6] Ourselin et al Image Vision Comput 19 (2001); [7] Modat et al, CM PB(2010);

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