Evaluating a multi-channel registration approach of FA and T1w on MS patients with simulated atrophy

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Target audience: Researchers interested in multi-modal MRI registration of data from people with multiple sclerosis (MS).

Purpose: Our goal was to evaluate a registration framework to register T1-weighted (T1w) and diffusion weighted (DW) images to a target space while maintaining the anatomical correspondence between them despite the presence of marked atrophy and white matter lesions.

Introduction: In MRI studies, registration of different scan type with each other and templates is a key stage in many image analysis pipelines. For example, extraction of tissue specific measures from scans offering insufficient contrast to allow reliable segmentation can still be achieved by registering them to an image that can be readily segmented, such as a T1w volumetric scan. However, one of the major challenges is to align all data to a common space. In this study we evaluate a multi-channel (MC) registration approach for scans from people with MS. Such scans are affected by white matter lesions and there may also be marked brain tissue atrophy. A particularly challenging task is to register T1w scans and diffusion weighted scans to a target space because of the geometrical distortions that affect the DW images and calculated maps. Multi-channel registration algorithms have the advantage of maintaining anatomical correspondence between T1w and DW images after registration to any target space (e.g. to another control of the same study or to a common standard space). This is true even when large-scale deformations are necessary to match patients' data to healthy targets. In this work, we tested the performance of a MC registration approach applied to T1w/DW data. Using simulated brain atrophy images (using control scans deformed to match scans from MS patients), we evaluated the MC approach when registering these to the unaltered control scans. Experimental results obtained from the MC approach are compared with standard single-channel registrations (SC) to their corresponding template (T1w/DW). Both qualitative and quantitative evaluations were carried out in this study.

Methods: <u>Subjects</u>: Ten healthy subjects (mean age = 39.1 years, 5 males and 5 females) and ten patients with MS (6 relapsing-remitting, 3 secondary progressive, 1 primary progressive, mean age = 49.4 years, 3 males and 7 females, mean disease duration = 18.3 years, median EDSS = 4.25) were scanned with local ethics committee approval.

<u>MRI</u>: Data was acquired on a 3T Philips Achieva scanner, with a 32-element head coil. The MRI protocol consisted of: 1) Dual echo proton density T2-weighted (T2w) scan: $1x1x3mm^3$, TR=3500ms, TE=19/85ms; 2) T1w structural scan: $1x1x1mm^3$, TR=6.9ms, TE=3.1ms; 3) Diffusion Tensor Imaging (DTI): Cardiac gated SE-EPI, TR = 24 RRs, TE = 68ms, number of DW directions = 61 (b=1200 s/mm2), number of non-diffusion weighted (b0) scans = 7, $2x2x2mm^3$ voxel size, SENSE = 3.1.

<u>Image analysis</u>: DTI indices, including Fractional Anisotropy (FA), were generated after eddy current correction (using eddy_correct from the FMRIB Software Library (www.fmrib.ox.ac.uk/fsl) and the Camino package[1] (www.camino.org.uk)). For each subject, T1w and FA volumes were co-registered after bias correction and intensity normalization[2] and skull stripping[3] using the pipeline described in Roura et al.[4]. NiftyReg software[5-7] was used to perform all registrations unless stated otherwise.

<u>Atrophy simulation</u>: We generated a range of plausible, atrophy-like deformations by registering each healthy T1w scan to each of the ten T1w MS patient scans. Each deformation was applied to the FA dataset, creating a total of 100 T1w/FA datasets with large range of simulated atrophy. We use the Demons registration[8] to generate the deformation to (a) avoid bias towards algorithm we use to overcome the simulated atrophy (the NiftyReg software we used to recover the deformation uses b-spline deformations) and (b) obtain an invertible deformation field, providing us with a gold standard deformation for each simulated dataset.

Figure 1 – Simulated atrophy images (T1w in row1 and FA in row 2): a)a') Healthy subject; b)b') MS patient; c)c') Simulated patient.

<u>Evaluation</u>: We tested three different registration strategies to assess the best method to overcome the simulated atrophy in both T1w and FA simultaneously: i) SC (the T1w and FA separately); ii) MC (the T1w and FA together); iii) T1w-based (using only the T1w SC registration results applied to both T1w and FA volumes). The three methods were compared against the gold standard registration and assessed qualitatively using difference image and checkerboards. We also quantify the mean intensity difference over the whole brain (WB) as well as separately in grey matter (GM) and white matter (WM) masks, which we derived from the T1w images using the SPM8 toolbox (http://www.fil.ion.ucl.ac.uk/spm/). We compute the average intensity differences for each method and simulation, grouping the 10 simulations for each patient and summarising as a mean and standard deviation for all simulations. We assessed significance of the mean intensity differences between the three methods for all simulations using the Student's t-test.

Results: When compared with the other registration pipelines, MC achieved a closer match (apparent as less intensity differences as shown in Figure 2). Most of the changes are concentrated near the ventricles, where the greatest transformations were required to bring features into alignment. Figure 3 shows the results for the SC, MC and T1w-based methods for T1w and FA respectively. Both SC and MC registrations were noticeably different for the WB, resulting in significant intensity differences for both T1w (p=0.0016) and FA (p<0.001). Moreover, FA was also found significantly different in both GM and WM (p<0.001). The T1w-based approach performed worse than both the MC and SC registrations.
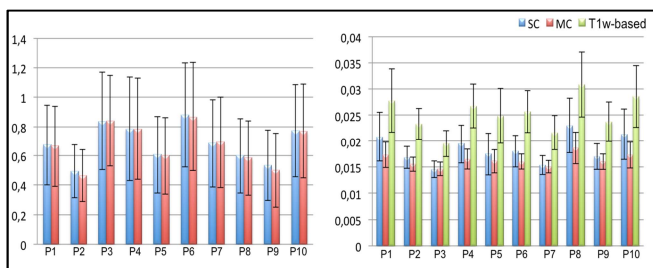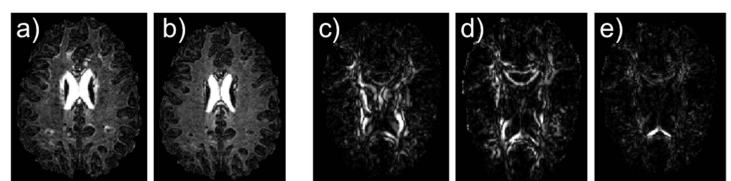

Figure 2 – Difference images: a) T1w SC; b) T1w MC; c) FA SC; d) FA OMB; e) FA MC.

Discussion: We found that when registering images with atrophy simulated to match that seen in people with MS, the MC approach used to simultaneously register T1w and FA images to a target yielded better results rather than SC or using the T1w transformations alone (for both the T1w and FA images). In our simulations we only took into account the atrophy, but we did not attempt here to simulate focal intensity changes such as white matter lesions which are usually seen in MS, and this is likely affect both T1w and DTI MS brains. Future work will extend the atrophy simulation framework to allow for focal differences in intensity, and evaluate the optimal registration approach to register to a common template space such as MNI or a group-based template.

Figure 3 – Bar plots of the mean intensity of the difference image for the WB (left T1w and right FA).

References: [1] Cook et al, ISMRM (2006); [2] Sled et al, TMI (1998); [3]Smith, HBM 17(2002); [4] Roura et al, ISMRM (2012); [5] Ourselin et al, Image Vision Comput 19 (2001); [6] Modat et al, CMPB (2010); [7] Daga et al, Biomed Imaging (2011); [8] Vercauteren et al, MICCAI (2008).