SUB MILLIMETER COREGISTRATION OF FUNCTIONAL MAPS ACROSS IMAGING SESSIONS

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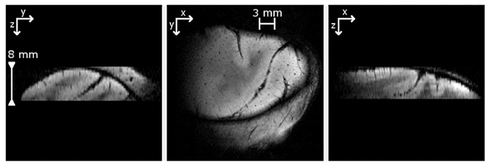
INTRODUCTION

fMRI is ideally suited for longitudinal studies of structural and functional brain plasticity. It is now feasible to collect functional brain maps with spatial resolutions of ~100 µm in ultra-high field systems. While these data sets are intrinsically coregistered for studies collected within a session from immobilized animals, the accuracy of coregistration across imaging sessions (or within, in the presence of head motion) is limited by the accuracy with which structural and functional images can be coregistered. The goal of this study is to develop an accurate and reliable registration process for longitudinal acquisitions of functional MRI scans providing partial brain coverage at very high resolution in order to quantify functional and structural changes over time using multiple imaging sessions.

DATA DESCRIPTION

• Data collected from 3 anesthetized squirrel monkeys using 9.4 T Varian MRI with 3 cm surface transceiver coil, under IACUC approved protocol.

•Slabs: 16 contiguous obliquely oriented 0.5 mm slices; FoV = 35 x 35 mm²; 512 × 512 in plane voxels; in-plane resolution: 68.35 × 68.35 µm²; 2D multi-slice gradient echo; flip angle 25°; TR/TE = 400/16 ms.



▲Figure 1. High resolution oblique slab

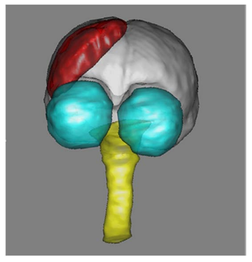


Figure 2. 3D rendering of brain (white), eyes (cyan), brain stem and spine (yellow) and slab (red). This shows the location of the slab relative to the whole brain. ▶

• Partial 3D head images: 128 × 128 × 128 isotropic voxels (resolution: 0.5 × 0.5 × 0.5 mm³); 3D gradient echo; FoV = 64 × 64 mm²; flip angle 15°, TR/TE = 5/2.39 ms

Figure 3. Partial 3D head MRI scans. Because the signal drops rapidly away from the coil, the contrast needs to be adjusted to permit visualization. Bottom row: two views with contrast adjusted in order to show details in regions of low intensity. Top row: Same images with contrast adjusted to show details in regions of high intensity. When the contrast is adjusted for high intensity regions, the rest of the head is not visible. When it is adjusted for low intensity regions, the area close to the coil is saturated. ▶

• BOLD and/or CBV-weighted functional echo planar images (EPI) runs: centered on the somato-sensory cortex, comprising 4 contiguous slices oriented obliquely with respect to the scanner frame of reference (in-plane resolution 273 x 273 µm, 2 mm slice thickness).

Focal single activations were generated in area 3b of primary somatosensory cortex by delivering seven 30 sec duration blocks of vibrotactile stimulation, alternated with 30 sec rest periods, to digits 1 and 3.

METHODOLOGY

We assume that geometric distortion is minimal in structural images due to the high bandwidth acquisition sequences used. Based on this assumption, all the transformations needed to register the various scans are rigid-body transformations, i.e., they only involve a translation vector and a rotation matrix . The easiest approach to compute these values would be to register directly slabs acquired during different sessions to each other with a standard intensity-based algorithm. This approach was tried but, as shown in the results section, did not lead to satisfactory results.

The solution we have developed to address this issue involves two main steps:

(1) register the slab to the partial 3D volume acquired during the same session.
(2) register the partial 3D volumes acquired longitudinally. Several intermediate steps are also required to achieve the desired accuracy.
(3) Apply distortion correction to activation maps to correct the misalignment with anatomical image arising from B0 inhomogeneities.

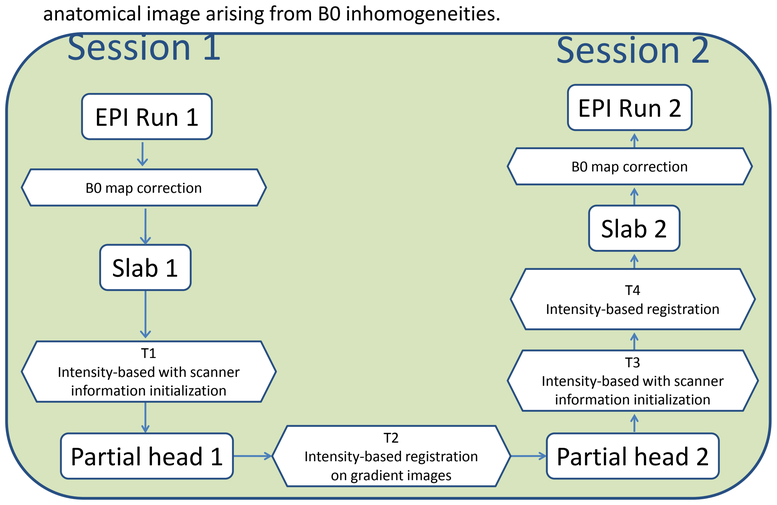


Figure 4. Overall process used in this study to register slabs acquired during two imaging sessions.

Slab to partial 3D head scan

In principle, using image coordinates and scanning information retrieved from the image headers (Euler angles used to acquire the scan and center of the volume) should lead to an accurate registration but we have observed a small residual error, which we attribute to the hardware. To correct for this residual error we use AMIR [1], an in-house implementation of an intensity-based registration algorithm. This algorithm computes the transformation that maximizes the Normalized Mutual Information (NMI) [2] between the image volumes.

Partial head scans co-registration

Intensity variation across the images arising from the B1 inhomogeneities compromised the performance of intensity-based algorithms for the inter-session registration of partial 3D head scans. We therefore opted to work with the gradient images. Working with the gradient images alone led to accurate results for two reasons. First, sulci are clearly visible in the images and their edges provide strong registration features. Second, the rapid intensity drop-off visible in the images is attenuated in the gradient image. Figure 5 shows how gradient images attenuate intensity variations.

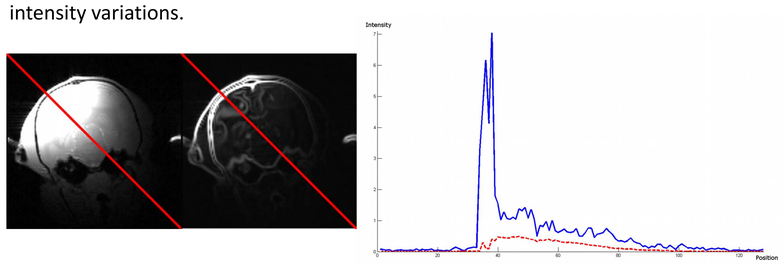


Figure 5. Left panel: original and gradient magnitude for one 3D head image. Right panel, intensity profiles along the red line shown on the left panel images. Solid blue: intensity profile for the original image. Dotted red: intensity profile for the gradient magnitude image.

Final refinement

While the slab to partial 3D and the 3D to 3D steps produce results that are visually correct, residual errors remain in the session to session slab registration due to the lower spatial resolution of the 3D volumes. However these transformations are sufficient to permit a final refinement by intensity-based registration of the slabs.

B0 map correction

The low bandwidth of the EPI readout in the phase encode direction makes the functional maps very sensitive to local B0 inhomogeneities. To correct for these effects, a B0 map was collected and used for prospective distortion correction of the functional maps as described by Jezzard et al.[3]

RESULTS

Direct slab-to-slab registration

Figure 6 shows results obtained when attempting to register directly one slab to the other for two different monkeys. Each row in this figure shows one slice in the first slab on the left panel and the corresponding slice in the second slab on the right panel. The middle panel shows the same slice in the volume obtained after registering the first slab to the second one. As can be seen, differences in the position of the slab during acquisition lead to substantial differences between the images. In particular, some sulci can be seen in one image and different sulci in the other image. Because sulci are strong features in these images, the lack of correspondence between these makes the registration difficult.

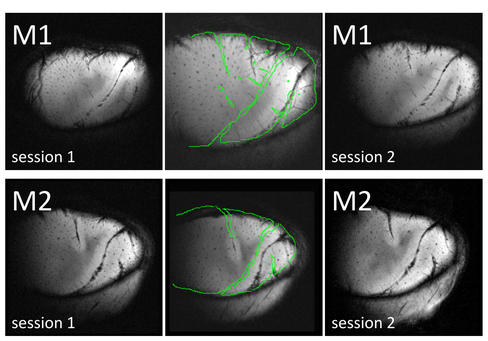


Figure 6. Direct slab-to-slab registration is not accurate. Two examples of different monkeys' slab registered with contours of the other slab projected. Left panels: slice of first slab. Right panels: corresponding slice of second slab. Middle panels: first slab registered to second slab. Lines in the middle panel are contours drawn on the second slab. Top: Total Registration Error (TRE) for monkey 1 (M1) is about 75 voxels. Bottom: TRE for monkey 2 (M2) is about 35 voxels. ▶

Slab-to-partial-3D registration

Slab-to-partial-3D registration results obtained with information derived from the image headers alone are shown in Figure 7 (left panels). An additional intensity-based registration permits the accurate registration of the slab (Figure 7 right panels).

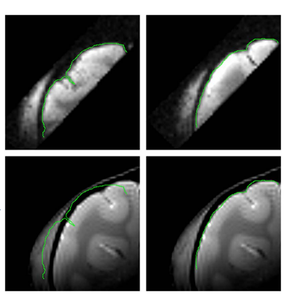


Figure 7. Registration of a slab with its corresponding partial head image. Left column with scanner-derived information only; Right column after an additional intensity-based step. Top row shows the slab image, the bottom row the partial head image. Contours have been drawn on the top images and copied on the bottom ones ▶

Partial-3D scans coregistration

The NMI can be viewed as a measure of the spread of the joint intensity histograms. Figure 8 shows the value of the NMI as a function of misalignment for the original images (dotted lines) and the gradient magnitude images (solid lines). NMI has a peak that is much more pronounced for the gradient magnitude images than for the original images. This facilitates convergence to a local maximum, and explains the improved coregistration performance results using gradient images.

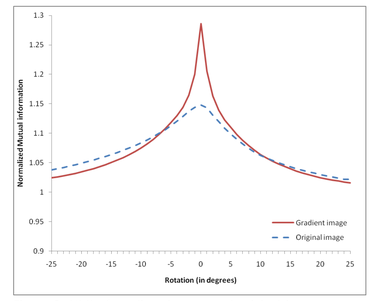


Figure 8. NMI of gradient images and original images versus rotation. The joint histogram of the gradient image spreads less than the other one, showing a better correspondence of the voxels intensities. The NMI function of the gradient image is sharper and allows a better registration.

Result on the activation maps

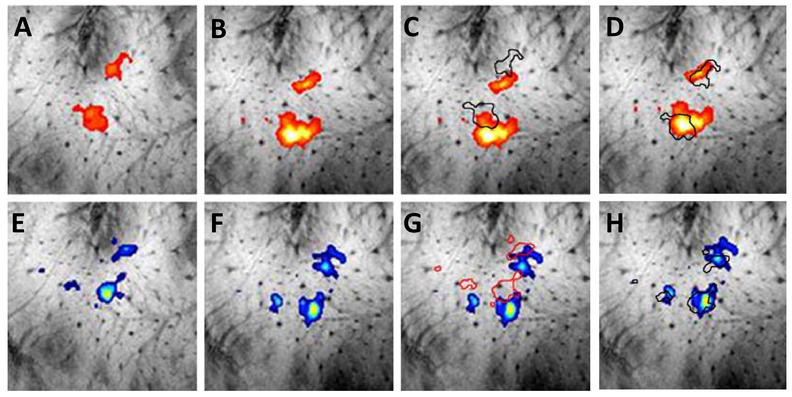


Figure 9. Results of registration for GE-BOLD (top) and CBV (bottom). From left to right: activation map of session 1 (A,E), activation map of session 2 (B,F), contour of activation map of session 1 overlaid on session 2 before (C,G) and after (D,G) B0 correction.

Fig. 9 A-D show the same slice of both slabs with the BOLD functional maps overlaid following registration of raw and distortion-corrected functional maps. Fig. 9 E-H present the equivalent results for the CBV-based functional maps. As shown in Fig. 9 C, E, the rigid body coregistration of raw functional maps, while accurate to ~1 mm across sessions, nonetheless significant exhibited significant misregistration, reflecting the effect of residual distortion in the EPI images. Correction of these residual distortions (as shown in Fig. 9 D, H) led to excellent (< 150 µm) coregistration of the activation centers maps obtained by BOLD and CBV mapping.

Table 1 summarizes the distances between the t-score weighted centroids of single digit activations in maps collected in two sessions using GE-BOLD and CBV mapping within and across animal. Registration error was 131 ± 46 µm (mean ± sd) for GE-BOLD and 121 ± 19 µm for CBV maps.

		Monkey 1	Monkey 2	Monkey 3	All (n=6)
BOLD	D1	175	186	152	
	D3	87	83	102	
	mean	131	135	127	**131**
	sd	63	73	36	**46**
CBV	D1	144	133	125	
	D3	129	92	105	
	mean	137	113	115	**121**
	sd	11	29	14	**19**

Table 1. Distance (µm) between t-value weighted centroids of single digit activation foci for D1 and D3 activations collected in two different functional mapping sessions in three monkeys. Top panel: Gradient echo (GE) BOLD maps. Bottom panel: CBV maps.

CONCLUSION

To the best of our knowledge, this is the first registration method proposed for the longitudinal registration of ultrahigh resolution functional maps with sub-millimeter coregistration accuracy. Furthermore, these results suggest that high resolution fMRI mapping has the capability to identify functional reorganization in cortex with sub-millimeter accuracy in longitudinal studies.

ACKNOWLEDGEMENTS

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