# Assessment and improvement of fMRI normalization based on inversion-recovery prepared high-resolution EPI

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***Introduction***

Echo-planar imaging (EPI), used in most functional MRI (fMRI) studies, has several major limitations, including 1) geometric distortion, 2) low spatial-resolution, and 3) low anatomic resolvability, as compared with structural MRI data. Because of these limitations, it is difficult to accurately register EPI based fMRI data to structural images. For the same reasons, it remains challenging to accurately normalize fMRI data to a standard template (e.g., MNI template), which is needed for group analysis of fMRI data. Additionally, because the pattern of EPI distortions is dependent upon head position in the magnetic field, the registration and normalization of fMRI data become even more difficult if the subjects move between fMRI and structural MRI scans.

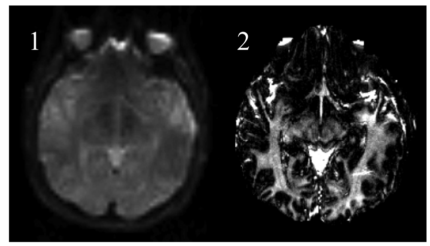
Different approaches have been developed to address these challenges. First, field map based EPI distortion correction has been used to reduce fMRI distortions, making the registration between functional and structural data more reliable [1]. However, because of the limited spatial resolution and anatomic resolvability in fMRI data, it is difficult to assess the accuracy of registration for small anatomic structures even after EPI distortion correction. Second, nonlinear normalization algorithms have been developed so that the structural MRI data (with superior anatomic resolvability) can be much better aligned to the standard template [2]. However, it is not clear how the nonlinear normalization algorithms perform on raw EPI data with distortions, limited resolution, and anatomic resolvability.

Our aims in this study are twofold. The first aim is to develop an imaging protocol based on high-resolution inversion-recovery (IR) prepared segmented EPI (with identical distortion patterns as in single-shot EPI), enabling accurate assessment of the performance for distortion correction and linear / nonlinear normalization algorithms for EPI data. The second aim is to suggest an integrated acquisition and post-processing pipeline, to improve the accuracy of fMRI data registration and normalization.

***Methods and Results***

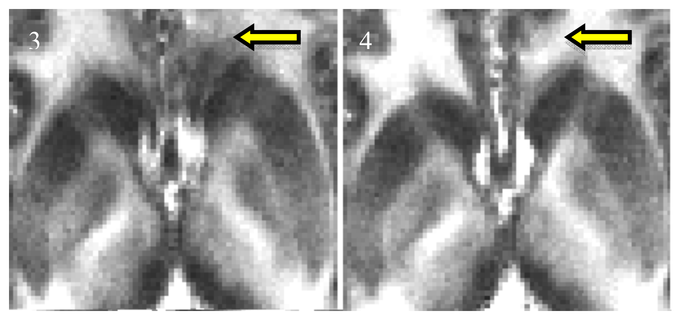
<u>*1. Development of high-resolution IR-prepared EPI for improved anatomic resolvability*</u>

Single-shot EPI, IR-prepared segmented EPI, and field inhomogeneity maps (based on 6 asymmetric spin-echo EPI with different T2*-weightings) were acquired from a healthy volunteer at three head positions (center, tilted left, and tilted right) on a 3T GE MRI scanner. The in-plane matrix size for single-shot EPI and field map is 64 x 64 (i.e., 3.75 x 3.75 x 3.8 mm voxel size), and the matrix size for IR-prepared segmented EPI is 256 x 256 (i.e., 0.94 x 0.94 x 3.8 mm voxel size). In comparison with single-shot EPI (Figure 1), the developed IR-EPI protocol has a significantly improved contrast, resolution and anatomic resolvability (Figure 2). Note that the inter-ky line echo spacing time in IR-segmented EPI was adjusted to a level that the geometric distortions in single-shot EPI and IR-EPI were identical, making it possible to directly compare the anatomic structures from both data sets.




<u>*2. Assessing the performance of EPI distortion correction*</u>

We used IR-EPI to compare the accuracy of registration between EPI data acquired at different head positions (with inconsistent distortions), before and after field map based distortion correction. EPI images from different head positions were registered using linear registration before and after distortion correction. From visual inspection of the aligned low-resolution EPI images, it is very difficult to assess the quality of alignment for different neural structures. On the other hand, by applying the same affine transformation matrices to the IR-EPI, we could see that that some structures are not very well aligned (e.g., caudate and putamen). Figure 3 shows the summation of three aligned IR-EPI images, showing blurring effect and inaccurate gray-white matter contrast (indicated by an arrow) due to residual mis-alignment after affine transformation.




When EPI distortions are corrected before applying the registration procedure described above, the residual misalignment is significantly reduced. Figure 4 shows the summation of three IR-EPI images with distortion correction and affine transformation, showing that the gray-white matter contrast is correctly reflected. The IR-EPI data enables assessment of EPI distortion correction performance, confirming that EPI distortion correction improves alignment of neural structures at both a cortical and a subcortical level. Our results indicate that field mapping is a valuable technique for improving EPI registration and normalization.

<u>*3. Assessing the performance of nonlinear registration algorithms on EPI and IR-EPI*</u>

We also investigated the accuracy of image alignment based on nonlinear registration, since previous studies indicated that the local deformations used in nonlinear warping could be more successful than linear registration for addressing position-dependent distortion changes across scans.

First, nonlinear warp coefficients were calculated from the single-shot EPI data at different head positions and applied to the IR-EPI images. However, there is limited anatomic resolvability in single-shot EPI data to register and evaluate the alignment of the images. As seen with the linear registration, although the EPI images appear to be in the same space, inspection of the IR-EPI images indicates that some small structures are not well-aligned after nonlinear registration (similar to that shown in Figure 3).

Second, we applied nonlinear registration directly to the IR-EPI data before and after field-map based correction. In both cases, nonlinear registration was qualitatively successful in alignment of structures between different head positions (similar to that shown in Figure 4). Note that even though the uncorrected IR-EPI from different head positions can be well aligned by nonlinear registration, the aligned images remain in distorted coordinates and may not be directly compared with other types of structural images (e.g., SPGR or MP-RAGE). On the other hand, the corrected- and aligned IR-EPI data are in non-distorted coordinates and thus can be directly registered to other types of structural MRI data. The transformation matrices derived from IR-EPI alignment can be directly used to align the single-shot EPI data. Thus, the fMRI data is well aligned even for small anatomic structures.

***Discussion***

The IR-EPI protocol described here makes it possible to evaluate the effects of EPI distortion and distortion correction on small neural anatomic structures, and evaluate and improve the registration of fMRI images. The low spatial resolution of the single-shot EPI data precludes assessment of these characteristics in detail using the single-shot EPI alone. By examining the IR-EPI data, we can see that field-map based distortion correction of the EPI scans is able to correct distortion that impacts neural structures within the brain. Furthermore, addition of an IR-EPI acquisition offers the potential to improve the registration of fMRI data. We recommend that IR-EPI scans be acquired along with fMRI and field mapping scans to address EPI distortion and improve image registration.

***References:*** [1] Jezzard P, Balaban RS. Magn Reson Med. 1995. 34(1):65-73. [2] Tahmasebi AM et al. Neuroimage. 2009. 47: 1522-1531.