Efficacy of a Nonrigid Image-registration Method in Comparison to Readout-segmented Echo-planar Imaging for Correcting Distortion in Diffusion-weighted Imaging

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We evaluated the effectiveness of distortion correction using a nonrigid image registration method in diffusion-weighted imaging, comparing it with readout-segmented echo planar imaging (RS-EPI). Unlike the RS-EPI, the effectiveness of the distortion correction of the nonrigid registration method depended on the slice level, being most accurate at the level of the basal ganglia, lateral ventricle, and centrum semiovale.

Keywords: diffusion-weighted imaging, nonrigid image registration, echo planar imaging, brain, readout segmented echo planar imaging

Introduction

Diffusion-weighted image (DWI) plays an important role in MRI. It has high sensitivity and specificity for detecting acute stroke, and distinguishing it from other diseases.¹ Generally, echo planar imaging (EPI) is used for DWI. Image distortion often occurs due to both local magnetic field inhomogeneities and eddy current effects that arise from motion-probing gradients.

Recently, distortion reduction using readout segmented-EPI (RS-EPI) DWI for clinical diagnosis has been reported.² RS-EPI performs signal acquisition by dividing k-space in the readout direction, allowing reduction of echo space to reduce the image distortion caused by phase-dephasing.³ However, the scan time of RS-EPI DWI is longer than that of single shot-EPI (SS-EPI) DWI, and moreover, RS-EPI DWI is not available in all MRI scanners at present. Here, the non-rigid image registration method proposed by Ardekani and Sinha,⁴ which is a post-processing method that corrects the distortion of the b₀ images using T₂-weighted image (T₂WI) as reference, can be a solution for these problems. This is because the proposed method does not elongate the scan time and does not require a special MRI scanner as it is a post-processing for the scanned images. However, the effectiveness of the non-rigid image registration compared with RS-EPI DWI in regard of distortion correction is not yet reported. The purpose of this study was to evaluate the effectiveness of a nonrigid image registration compared to RS-EPI DWI for correcting the distortion in DWI.

Materials and Methods

MRI scans

This study protocol was approved by the Institutional Review Board of Kagawa University. Seven healthy volunteers (age: 31 ± 0.5 years) with no history of brain tumor or cerebrovascular disease were enrolled in this study. Informed consent was obtained from all individual participants included in the study. MR brain imaging was performed with a 3T scanner (MAGNETOM Skyra 3T; Siemens Healthcare, Erlangen, Germany) with a 20-channel head coil. Scan parameters of each sequence are shown in Table 1. DWI was obtained using SS-EPI and RS-EPI sequences. Fast spin-echo T₂WI (FSE-T₂WIs) was obtained as the reference image for the nonrigid image registration. The scanning plane of each MR image was set parallel to the anterior–posterior commissural (AC-PC) line (Fig. 1). For each subject, the scanning range was set so that the brainstem was included in slice numbers 1–10. In the RS-EPI DWI, the shortest echo space was 0.3 ms, which was achieved by setting the number of segments to 5.

Extraction of brain regions from each MR image

Figure 2 shows the schematics for extraction of brain regions from the images. Fiji software (version 2.0.0-rc-69/1.52p; National Institutes of Health, Bethesda, MD, USA) was used for this purpose.⁵ First, to create mask images, local thickness-processing was performed on each slice.⁶ The pixel value of the image after this processing depended on the thicknesses of the structures. Next, a radiological technologist manually set a threshold value within the range of 20–50 for each MR image to separate brain regions from other tissue, and confirmed the...
Table 1 Scan parameters of each MRI sequence

| Scan parameters | Setting values |
|-----------------|----------------|
| **SS-EPI DWI**  | **RS-EPI DWI** |
| TR/TE [ms]      | 5000/78        | 4180/77        | 5000/78        |
| FOV [mm]        | 256 × 256      | 192 × 192      | 256 × 256      |
| Matrix size     | 5              | 2              | 5              |
| Phase direction | A/P R/L        |                |                |
| Number of slices| 20             |                |                |
| Reduction factor| 2              |                |                |
| Echo space [ms] | 0.9 0.3        |                |                |
| b-Value [s/mm²] | 0 and 1000     | 0 and 1000     |                |
| Readout segments| – 5            |                |                |

FSE-T₂WI, fast spin-echo T₂-weighted image; RS-EPI DWI, readout segmented-echo planar imaging diffusion-weighted image; SS-EPI DWI, single shot-echo planar imaging diffusion-weighted image.

Calibration of signal intensity in brain FSE-T₂WI

In each slice of the brain-extracted image data, to reduce the differences in signal intensities, a calibration process equalized the mean value and standard deviation of the signal intensities in the reference image (brain FSE-T₁WI) and that of the source image (b0 image of brain SS-EPI DWI) using the following Equation (1):

\[
SI_{c}(x,y) = \frac{\sigma_r}{\sigma_s} \left[ SI_s(x,y) - \overline{SI}_s \right] + \overline{SI}_c
\]  

where \(SI_{c}(x,y)\) is the signal intensity at each pixel of brain FSE-T₁WI after calibration (calibrated FSE-T₁WI), \(\sigma_r\) is the standard deviation of brain FSE-T₂WI, \(\sigma_s\) is the standard deviation of the b0 image of brain SS-EPI DWI, \(SI_{s}(x,y)\) is the signal intensity at each pixel of the b0 image of brain SS-EPI DWI, \(\overline{SI}_s\) is the mean value of signal intensities in the b0 image of brain SS-EPI DWI, and \(\overline{SI}_c\) is the mean value of signal intensities at the brain FSE-T₁WI. The calculation was performed similarly to the previously reported method.

Nonrigid image registration in SS-EPI DWI

We performed nonrigid image registration using the B-spline method with the b0 image of brain SS-EPI DWI as the source image and calibrated FSE-T₁WI as the reference image. The parameters were set as follows: Divergence Weight: 0.0, Curl Weight: 0.0, Landmark Weight: 0.0, Image Weight: 1.0, Stop Threshold: 0.01. Finally, the same deformation as the b0 image was applied to the b1000 image of brain SS-EPI DWI. We acquired the distortion-corrected DWI using a nonrigid image registration method (corrected brain SS-EPI DWI). This process was done using the Fiji software. Calculation time for this process was 13.0 ± 4.4 s per slice.

Evaluation of image distortion in SS-EPI DWI, corrected SS-EPI DWI, and RS-EPI DWI

In order to evaluate the effectiveness of the distortion correction, the mutual information compared with FSE-T₂WI in the previous report was calculated separately for each slice in each DWI volume. First, signal intensities were calibrated to 8-bit gray scale (range: 0–255, bin size = 256) by the following Equation (2) in b1000 image of brain SS-EPI DWI, corrected brain SS-EPI DWI, and brain RS-EPI DWI:

\[
SI_{post}(x,y) = \text{floor} \left( 255 \frac{SI_{pre}(x,y) - SI_{min}}{SI_{max} - SI_{min}} \right)
\]

where \(SI_{post}(x,y)\) is the signal intensity of each MR image at each pixel after 8-bit gray scale calibration process, \(SI_{pre}(x,y)\) is the signal intensity of each MR image at each pixel, \(SI_{min}\) is the minimum signal intensity of each MR image, and \(SI_{max}\) is the maximum signal intensity of each pixel.
MR image. Second, we calculated MI-$T_2$ using the following Equation (3):

$$MI - T_2(A, B) = \sum_{i=1}^{256} \sum_{j=1}^{256} p(a, b) \log \left( \frac{p(a, b)}{p(a)p(b)} \right)$$

where MI-$T_2$ ($A, B$) is the mutual information of image $A$ ($b1000$ images of brain SS-EPI DWI, corrected brain SS-EPI DWI, and brain RS-EPI DWI) and $B$ (brain FSE-$T_2$WI), $p(a, b)$ are 2D histograms ($256 \times 256$) from images $A$ and $B$, $p(a)$ is the histogram of image $A$, and $p(b)$ is the histogram of image $B$. We compared with MI-$T_2$ of $b1000$ images of brain SS-EPI (SS-EPI) DWI, corrected brain SS-EPI (corrected SS-EPI) DWI, and brain RS-EPI (RS-EPI) DWI.

The Friedman test with a Nemenyi multiple-comparison test was used to determine statistical significance. R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org/) was used to perform the statistical analysis, and a $p$-value <0.05 was considered to indicate statistical significance.

Results

Figure 3 shows SS-EPI DWI, corrected SS-EPI DWI, and RS-EPI DWI images at slice positions 3 (a, b, and c), 7 (d, e, and f), and 14 (g, h, and i) from a single subject. Edges derived from the FSE-$T_2$WI are overlaid in red on the SS-EPI (a, d, and g), corrected SS-EPI (b, e, and h), and RS-EPI (c, f, and i). The arrows indicate regions where the displacement from the red lines appears to be less in the corrected SS-EPI and RS-EPI than in the original SS-EPI.

Table 2 and Fig. 4 show the mean MI-$T_2$ for each image slice. The corrected SS-EPI or RS-EPI showed higher values than SS-EPI in all slices. The corrected SS-EPI showed the highest values in slice numbers 1–4 and RS-EPI showed the highest values in slices 5–10, with some differences being statistically significant ($p < 0.05$). For slices 11 and above, the corrected SS-EPI showed the highest values, which were significantly higher than values for SS-EPI ($p < 0.05$).

Discussion

MI-$T_2$ was used to evaluate the image distortion in this study. MI is used as a cost function in image registration, and maximized MI is used for image registration between different imaging modalities (i.e., between CT and MRI). In FSE-$T_2$WI, there is very little image distortion because the FSE sequence is not subject to a narrow bandwidth in the phase-encode direction. Therefore, we consider that if the MI-$T_2$ showed a high value, the similarity of an image to the FSE-$T_2$WI was high, and the image distortion was low. Teruel et al. reported distortion-correction of $b0$ DWI images using a method based on opposite but symmetrical image distortion with reversed polarity phase-encoding, and showed that the corrected SS-EPI showed higher MI-$T_2$ than the original SS-EPI. We assume that the degree of MI-$T_2$ represents the image distortion at each slice in this study.
Nonrigid image registration based on the B-spline method has been previously used for distortion correction in DWI.\(^4,11\) In this method, control points are typically arranged in a grid pattern on source images, and deformations to the source images are performed by moving the points, with B-spline interpolation being used to predict the signal intensity of other points.\(^8,11\) Nonrigid image registration based on the B-spline method was used in this study, and the mean MI-\(T_2\) of the corrected SS-EPI showed higher values than the SS-EPI in all image slices. Therefore, we conclude that effective image distortion correction was obtained using the nonrigid image registration method in this study.

Treiber et al.\(^12\) reported that severe distortion of brain DWI occurred at the brainstem. Our slice numbers 1–4 corresponded to the inferior cerebellum in each subject. In these slices, the mean MI-\(T_2\) values of the corrected SS-EPI showed the highest values of the three DWI image sets, and the apparent displacement of the brainstem was improved in most subjects (Fig. 3). Moreover, because the difference between the MI-\(T_2\) of RS-EPI and SS-EPI was small, we consider that the image distortion of the SS-EPI was lower in these slices than in other slices. Therefore, the nonrigid image registration method made it possible to largely correct for the image distortion that occurred in the brainstem.

The mean MI-\(T_2\) of RS-EPI showed higher values than the corrected SS-EPI in slice numbers 5–10, corresponding to the pons and midbrain in each subject. Moreover, the mean MI-\(T_2\) of RS-EPI showed significantly higher values than the SS-EPI in slice numbers 7–10. Pronounced image distortion occurred due to B\(_0\) inhomogeneity derived from the air contained in the nasal cavity and the mastoid air cells at these levels. Ardekani and Sinha\(^4\) reported that nonrigid image registration correction of severe image distortion in areas subject to susceptibility artifact areas was limited by the requirement that the Jacobian of the deformation field be positive. Therefore, we consider that the nonrigid image registration method used in this study might be limited at these slice levels. In comparison with the nonrigid image registration, a technique based on \(k\)-space trajectory enabling short echo space setting, such as RS-EPI, seems to more effectively reduce image distortion and artifacts at these levels.

The mean MI-\(T_2\) of corrected SS-EPI was significantly higher than that of SS-EPI at slice number 11 and above \((p < 0.05)\). These slices corresponded to the basal ganglia,

![Fig. 3 SS-EPI DWI, corrected SS-EPI DWI, and RS-EPI DWI images from a single subject. Edges from the FSE-T\(_2\)WI are overlaid in red on SS-EPI (a, d, and g), corrected SS-EPI (b, e, and h), and RS-EPI (c, f, and i). The displacement from the red line in each corrected DWI is less than that in the SS-EPI (arrows). FSE-T\(_2\)WI, fast spin-echo T\(_2\)-weighted image; RS-EPI DWI, readout segmented-echo planar imaging diffusion-weighted image; SS-EPI DWI, single shot echo planar imaging diffusion-weighted image.](image-url)
Fig. 4  Mean values of MI-$T_2$ at each slice in each DWI image set. The corrected SS-EPI showed significantly higher values than the SS-EPI at slice numbers 4, 7, 11 and above ($P < 0.05$). The RS-EPI showed significantly higher values than SS-EPI at slice numbers 7–11, 13, 14, and 18. DWI, diffusion-weighted image; MI, mutual information; RS-EPI, readout segmented-echo planar imaging; SS-EPI, single shot-echo planar imaging.
Conclusion

To evaluate the effectiveness of a nonrigid image registration method, we compared SS-EPI DWI before and after application of nonrigid image registration methods and RS-EPI DWI. The effectiveness of the nonrigid image registration method varied according to the level of the image slices, and distortion-corrected images could be obtained at the level of the basal ganglia, lateral ventricles, and centrum semiovale without using RS-EPI.

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Conflicts of Interest

The authors have no conflicts of interest to declare.

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