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Super-Resolution Reconstruction of Diffusion-Weighted Images from Distortion Compensated Orthogonal Anisotropic Acquisitions

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Abstract

Increasing the spatial resolution in diffusion-weighted imaging (DWI) is challenging with a single-shot EPI acquisition because of the decreased SNR and T2* relaxation. Recently, acquisition of orthogonal anisotropic acquisitions and super-resolution reconstruction (SRR) of the underlying high-resolution image has been proposed to achieve higher resolution. Promising results have been shown with simulations. However, practical evidence that SRR enables resolution enhancement remains unclear. Particularly, real DWI scans acquired in orthogonal directions are subject to very different distortion. This makes the precise alignment of the images impossible and strongly perturbs the reconstruction.

In this work we propose to combine distortion compensation and SRR. Distortion compensation is achieved by acquisition of a dual echo field map, providing an estimate of the field inhomogeneity. The SRR is formulated as a maximum a posteriori problem and relies on a realistic image generation model. We evaluate our approach with real anisotropic acquisitions. Importantly, we demonstrate that combining distortion compensation and SRR provides better results than acquisition of a single isotropic scan for the same acquisition duration time. The SRR provides more detailed structures and better tractography results. This work provides the first evidence that SRR, which employs conventional SS-EPI techniques, may enable resolution enhancement in DWI, and may dramatically impact the way to achieve DW imaging in both neuroscience and clinical applications.

1. Introduction

Diffusion-weighted imaging (DWI) enables non-invasive investigation of the white-matter by probing the water diffusion in multiple directions and strengths in tissues. It requires a fast acquisition technique to ensure a moderate scan duration time and to ensure measurement of the DW-signal before it nulls out. Single-Shot Echo-Planar Imaging (SS-EPI) is the most commonly employed sequence in DWI. It acquires a whole slice after a single excitation. However, spatial resolution is limited with SS-EPI. It typically enables

acquisitions with spatial resolution on the order of $2 \times 2 \times 2\text{mm}^3$, leading to strong partial volume effect.

Resolution enhancement is challenging

Resolving finer structures, *i.e.* increasing the spatial resolution, requires sampling of higher frequencies in k -space¹. However, acquisition of higher frequencies –and consequently resolution enhancement– is challenging with an SS-EPI. First it makes the acquisition highly demanding on the scanner gradient coils, which have to switch as quickly and as linearly as possible when achieving the spatial encoding. Second, the time to encode a larger k -space in a single shot is not negligible and leads to a larger echo time (TE). This is fundamental in DWI because the DW-signal exponentially decreases with increasing TE, as described by:

$$S_i = S_{0,i} e^{-TE/T_2} e^{-bD_i},$$

where S_i is the diffusion signal in a voxel i , $S_{0,i}$ is the non-attenuated signal, TE is the echo time, T_2 the T_2 relaxation time in the tissue, b is the b-value and D_i is the Apparent Diffusion Coefficient (ADC) in the voxel i . Consequently, encoding a larger k -space leads to an increased TE which in turn leads to a drop in the SNR of the diffusion signal.

Another fundamental consequence of the increased TE is that SS-EPI is very sensitive to magnetic field inhomogeneities (T_2^* relaxation) caused by susceptibility changes at tissue interface, such as air and tissue. Particularly, areas in the temporal lobes and in the frontal lobe are commonly affected (see Fig. 1a, b). The field inhomogeneity gives rise to phase perturbation in k -space which accumulates during the acquisition of each slice. This results in severe distortion in the form of voxel shifts in the image space, mainly in the phase-encoding direction. Consequently, the increased TE due to the larger k -space encoding leads to increased accumulation of errors during the spatial encoding. This leads to severely increased geometric and intensity distortion in the phase encoding direction.

Recent works in ultra-high field DWI (7 Tesla or more) have investigated segmented EPI techniques, in which each slice is acquired in multiple shots, reducing the TE for each shot. These techniques, originally designed to attenuate the severe distortion at high field, can also be employed for encoding a larger k -space for resolution enhancement in DWI. However, phase inconsistencies resulting from even minimal physiological motion during the application of the sensitizing gradients are still challenging to correct in DWI. Additionally, such techniques multiply the scan duration time by the number of shots.

Ultimately, reducing the voxel size is challenging in MRI because of its direct relationship to the SNR. Additionally, because the SNR is proportional to the square root of the number of averages, decreasing the voxel size by a factor a (e.g. $a = 8$ to reduce the voxel size from $2 \times 2 \times 2\text{mm}^3$ to $1 \times 1 \times 1\text{mm}^3$) requires a^2 (e.g. 64) averages to ensure a similar SNR.

¹Intuitively, an edge is described by a rapid change in intensity over a short distance in the image and is consequently a high frequency spatial feature.

Increasing the resolution via super-resolution reconstruction

Another recent approach to enhance the resolution is to acquire multiple *anisotropic orthogonal* scans with a conventional SS-EPI sequence, and to recover the underlying isotropic high-resolution DW-images via super-resolution reconstruction (SRR). Proposing this technique, [6] have suggested to align each image in both k-space and q-space and have employed a Maximum *A Posteriori* (MAP) SRR approach based on a realistic image acquisition model. They show very promising results with simulated SRR scenarios, in which a real DWI acquisition is artificially under-sampled in the three orthogonal directions, reconstructed, and then compared to the underlying true high-resolution acquisition. However, a key problem when considering real orthogonal DWI scans is that they experience very different geometric and intensity distortion due to different phase-encoding directions. This makes the precise alignment of the images impossible. Locally, overlapping voxels across acquisitions may represent a different brain location, which strongly perturbs the reconstruction.

In this work, we propose for the first time to combine SS-EPI distortion compensation and super-resolution reconstruction. We correct for distortion by acquisition of a field map [5, 2]. It provides us with an estimate of the field inhomogeneity, which can in turn be employed to correct for the voxel shift in the image space. We then recover the underlying isotropic high-resolution images via SRR with a similar approach as in [6]. We evaluate our field-map corrected SRR approach (*FMC-SRR*) with *real* orthogonal acquisitions. First we demonstrate that distortion compensation is *essential* for an accurate SRR. Second we show that the SRR outperforms the acquisition of a single isotropic scan for the same acquisition duration time. It provides more detailed structures and better tractography results. This work provides the first evidence that SRR enables resolution enhancement in DWI.

2. Material and Methods

2.1. Data acquisition

We acquired $K = 3$ anisotropic DWI scans (axial, coronal, and sagittal) on a Siemens 3T Trio with a 32 channel head coil and the following parameters: FOV=220mm, matrix=176×176, in-plane resolution=1.25×1.25mm², slice-thickness=2.5mm, 5 $b=0$ s/mm², 30 directions at $b=1000$ s/mm². The number of slices was chosen to cover the whole brain, varying from 58 to 71 depending on the acquisition orientation. The total acquisition duration time for the three scans was 17min00.

For comparison, we acquired an isotropic DWI scan with parameters chosen to match the acquisition time of the three previous scans: matrix=146×146, resolution=1.5×1.5×1.5mm³, 100 slices, same sensitizing gradient orientations, two averages, 16min32.

Finally, a dual echo gradient echo field map image was acquired with $TE_{1/2} = 5.19/7.65$ ms, resolution=2×2×2.5mm³. The unwrapped *phase* field map was generated by the scanner.

2.2. Field-map based EPI distortion correction

We correct for geometric and intensity distortion by field-map unwarping, utilizing the phase field inhomogeneity map provided by the dual echo acquisition (see Fig. 1a). We

consider that the pixel mis-location due to T2* relaxation only occurs in the phase encoding direction and is negligible in the read-out direction [5]. The voxel shift y_r (in mm) at a location r was corrected from the phase value ϕ_r (in radians) of the phase field map via the following expression [5]:

$$\Delta y_r = (2\pi \cdot \Delta T_E \cdot B_{pe})^{-1} \phi_r \cdot \Delta q_y,$$

where ΔT_E is the difference in echo times of the dual echo gradient acquisition (in seconds), B_{pe} is the bandwidth per pixel (in Hz/pixel), and q_y is the voxel spacing (in mm/pixel) of the EPI image along the phase encoding direction. The image intensity values were corrected using the Jacobian of the unwarping model to account for the effect of signal stretching or shrinking.

2.3. Super-resolution reconstruction of the diffusion-weighted images

The super-resolution reconstruction (SRR) was achieved by using a similar approach as in [6], summarized in this section. The $K = 3$ anisotropic DWI scans were affine-registered to a reference volume to account for possible patient motion. The $b=0\text{s/mm}^2$ image of the first anisotropic acquisition was chosen as the common reference volume. Each gradient orientation was compensated for the rotation component of the transformation. In the presence of motion, the DW-images may represent different gradient-sensitization directions in the patient coordinate system among the acquisitions. Consequently, the three acquisitions were aligned in q -space to ensure that each triplet of DW-images corresponded to the exact same gradient orientation, and showed identical diffusion-attenuation patterns. This alignment was performed by interpolation in q -space.

Following the *MAP* approach of [6] we considered an image acquisition model to describe how the acquired low resolution volumes are obtained from the unknown high-resolution DWI we aim at recovering. Based on a model including motion, signal averaging, and resampling, the high-resolution DW-image $\mathbf{x}^g$ for a gradient direction g was estimated from the K low-resolution images $\{\mathbf{y}_k^g, k = 1, \dots, K\}$ via the following expression:

$$\hat{\mathbf{x}}^g = \arg \min_{\mathbf{x}} \sum_{k=1}^K \|\mathbf{y}_k^g - \mathbf{D}_k \mathbf{B}_k \mathbf{M}_k \mathbf{x}^g\|^2 + \lambda \|\mathbf{Q} \mathbf{x}^g\|^2,$$

where the volumes $\mathbf{y}_k$ and $\mathbf{x}^g$ are expressed as column vectors by a lexicographical reordering of the pixels, $\mathbf{D}_k$ is a down-sampling matrix, $\mathbf{M}_k$ is the warping matrix that maps the HR volume $\mathbf{x}^g$ to the LR volume $\mathbf{y}_k^g$, $\lambda = 0.001$ controls the regularization strength, $\mathbf{Q}$ is the 3-D discrete Laplacian, and $\mathbf{B}_k$ is the blur, or point spread function (PSF) of the MRI signal acquisition process (See [6] for more details). As in [4, 6], we considered a PSF in the slice-selection direction only, described by a Gaussian slice selection profile of standard deviation $\sigma_{\text{PSF}} = (\text{slice thickness}) / (4 \sqrt{2 \ln 2})$.

2.4. Experimental setup

Both the anisotropic and the isotropic acquisitions were corrected for distortion by utilizing the field-map unwarping technique described in Section 2.2. The SRR of each DW-image was achieved to create an isotropic volume of $1.25 \times 1.25 \times 1.25 \text{ mm}^3$ (*FMC-SRR*). To investigate the effect of the distortion compensation, we also achieved the SRR without any field-map correction (*SRR*) at the same isotropic resolution. We compared the SRR technique to the isotropic acquisition by resampling the $1.5 \times 1.5 \times 1.5 \text{ mm}^3$ DW-images to $1.25 \times 1.25 \times 1.25 \text{ mm}^3$ as well (*ISO*). Finally, we investigated the effectiveness of applying a postprocessing denoise correction technique to the isotropic acquisition (*dISO*). We employed the Joint Linear Minimum Mean Squared Error (LMMSE) noise filter proposed by [7].

Tensors were estimated by linear least-squares fit on the logarithm of the DW-images. Color fractional anisotropy (color-FA) maps were computed by considering the normalized primary eigen-vector of each tensor as a vector in the RGB space, modulated by the tensor FA. We qualitatively compared the color-FA maps of *ISO*, *dISO*, *SRR* and *FMC-SRR*.

We qualitatively compared the four experiments via *residual bootstrapping* [1]. The residual bootstrap is a model-based resampling technique. From an estimated tensor-field, it generates a set of virtual new DWI acquisitions by randomly sampling the model residuals, simulating new acquisitions with a different but realistic noise. A new tensor-field was estimated from each virtual acquisition, and the corresponding variance of the FA assessed. The obtained FA variance is related to the estimation uncertainty. A lower value indicates a lower uncertainty, indicating a better quality of the data. The average FA variance for the four experiments *ISO*, *dISO*, *SRR* and *FMC-SRR* was compared in a common 3-D region of interest (Fig. 4a).

Finally, tractography of the corpus callosum was achieved. The same seeding region was employed in the four experiments. The streamlines were color-coded with the color-FA map and compared.

3. Results

Fig. 1 illustrates the field-map distortion compensation. It depicts how orthogonal EPI acquisitions are subject to different geometric distortion depending on the phase-encoding direction (Fig. 1b,d). Fig. 1c,e shows that the field-map unwarping successfully corrects for most distortion.

Fig. 2 reports the color-FA maps for *ISO*, *dISO*, *SRR* and *FMC-SRR*. Particularly, the color-FA of *ISO* (Fig. 2a) is much more noisy, which is corrected when de-noising in post-processing (*dISO*, Fig. 2b). Fig. 2c shows that non-compensation of the distortion (*SRR*) leads to a blurred color-FA map, particularly in the region R2. Fig. 2b,d show that *dISO* and *FMC-SRR* provide similar structures. Interestingly, fine structures far smaller than the slice thickness (2.5mm) of the anisotropic acquisitions are well conserved with *FMC-SRR* (region R1) but lost with *dISO*. Importantly, structures in the region R2 appear to be more detailed with *FMC-SRR* than with *dISO*.

Fig. 3 shows a zoom of the color FA maps in a region of the brain stem. Consistent with Fig. 2a, it shows that *ISO* provides a highly noisy color-FA (Fig. 3b). *dISO* provides more smooth results (Fig. 3c) but with interpolation artifacts (region R3) and more blurred structures than *FMC-SRR* (region R1). Fig. 2d (*SRR*) shows that misalignment of the uncorrected acquisitions leads to a missing structure (R2).

Fig. 4 reports the bootstrap results. It shows the estimation uncertainty to be much higher with *ISO*. The uncertainty with the other techniques is comparable.

Finally, Fig. 5 reports the tractography results for the corpus callosum. *ISO* (Fig. 5a) provides poor results due to the high noise corruption. The noise filtering in *dISO* (Fig. 5b) enables a better connectivity assessment. However, a number of streamlines remain disorganized (regions R1 and R2). *FMC-SRR* (Fig. 5d) outperforms the other approaches. Particularly, streamlines in the frontal part (region R3) better represent the anatomy. Without distortion correction (*SRR*, Fig. 5b), the anisotropic scans were poorly aligned in the frontal region (see Fig. 1a,b) and the tracts prematurely stopped.

4. Conclusion

Increasing the resolution requires sampling of higher frequencies in k -space which is very challenging in DWI. Sampling of a larger k space *along each* axis is difficult (1) because of the dramatically low SNR associated with a small voxel size and (2) because of the increased TE, which in turn leads to higher distortion and a lower SNR. Instead, we used anisotropic orthogonal acquisitions which can be seen as an over-sampling of k -space along only two axes. It achieves a better SNR due to the larger voxel size and reduces the spatial encoding burden. The underlying isotropic high-resolution image is then recovered by SRR in the image space, relying on a realistic image generation model and a MAP formulation.

We have proposed to compensate for SS-EPI distortion before achieving the SRR and have presented the first extensive investigation of the effectiveness of SRR in DWI. We have shown that EPI distortion compensation is essential when achieving SRR. Without correction, overlapping voxels across acquisitions do not represent the exact same brain location, which severely perturbs the SRR. It leads to blurred (Fig. 2c-R2) and missing (Fig. 3d-R2) structures. Ultimately, it leads to prematurely stopped tractography streamlines (Fig. 5c).

We have shown that for the same scan duration time, acquisition of an isotropic scan (*ISO*) instead of three anisotropic scans and SRR provides lower results. It provides a much lower SNR impacting the color FA (Fig. 2a, 3b), the FA (Fig. 4) and the tractography (Fig. 5a). De-noising the isotropic acquisition (*dISO*) successfully corrects for noise (Fig. 2a) and provides lower estimation uncertainty (Fig. 4). However, it leads to blurred structures (Fig. 2b-R2, 3c). This might be due to both the noise filtering and the interpolation necessary to resample the $1.5 \times 1.5 \times 1.5 \text{ mm}^3$ images to the resolution obtained by SRR ($1.25 \times 1.25 \times 1.25 \text{ mm}^3$). Additionally, we observed artifacts caused by the interpolation with *dISO* (Fig. 3c-R3). In contrast, *FMC-SRR* provides more detailed structures (Fig. 2d-R2, 3e). The two ascending columns in the brain stem (Fig. 3e) were better separated because SRR enables sampling of higher frequencies in k -space and consequently enables a better

representation of fine edges. The estimation uncertainty was low with *FMC-SRR* (Fig. 4). Ultimately, *FMC-SRR* provides the best tractography results (Fig. 5d).

Future work will investigate the comparison of other EPI distortion correction techniques. Perfect compensation of the distortion is indeed essential to ensure that overlapping voxels in each acquisition represent the exact same brain location. The field-map unwarping is effective for moderate distortion but is known to be limited in highly distorted regions, in which it is difficult to compute smooth phase maps. Particularly, we will investigate a hybrid approach combining deformable registration and field-map unwarping, which has been reported to provide the best results [3].

This work is the first report that SRR from distortion compensated orthogonal anisotropic acquisitions outperforms a single isotropic acquisition for the same scan duration time. DWI with SRR reveals more detailed structures and provides a better connectivity assessment. It shows that SRR, which employs conventional SS-EPI techniques, may dramatically impact the way to achieve DW imaging in neuroscience and clinical applications.

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References

1. Chung S, Lu Y, Henry RG. Comparison of bootstrap approaches for estimation of uncertainties of DTI parameters. *Neuroimage*. Nov; 2006 33(2):531–541. [PubMed: 16938472]
2. Cusack R, Brett M, Osswald K. An evaluation of the use of magnetic field maps to undistort echo-planar images. *Neuroimage*. 2003; 18(1):127–142. [PubMed: 12507450]
3. Gholipour, A.; Scherrer, B.; Warfield, SK. On the Accuracy of Unwarping Techniques for the Correction of Susceptibility-Induced Geometric Distortion in Magnetic Resonance Echo-Planar Images. *IEEE International Conference on Engineering in Medicine and Biology*; 2011.
4. Greenspan H. MRI inter-slice reconstruction using super-resolution. *Magn Res Imag*. 2002; 20(5): 437–446.
5. Jezzard P, Balaban RS. Correction for geometric distortion in echo planar images from b0 field variations. *Magn Reson Med*. 1995; 34(1):65–73. [PubMed: 7674900]
6. Scherrer, B.; Gholipour, A.; Warfield, SK. Super-Resolution in Diffusion-Weighted Imaging. *Proceedings of the 14th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI)*; 2011.
7. Tristán-Vega A, Aja-Fernández S. DWI filtering using joint information for DTI and HARDI. *Med Image Anal*. 2010; 14(2):205–218. [PubMed: 20005152]

Figure 1.

Field-map based distortion correction. (a): Phase field-map generated from the dual-echo sequence. (b): Axial acquisition with EPI distortion ($b=0\text{s/mm}^2$, phase-encoding direction: anteroposterior). (c): Corrected image. (d): Coronal acquisition with distortion (sagittal view, phase-encoding direction: head to foot). (e): Corrected image. The red circles highlights regions of high distortion.

Figure 2.

Color-FA maps for (a):*ISO*, (b):*dISO*, (c):*SRR* and (d): *FMC-SRR* (axial view). R1 points out that fine structures are well conserved with *FMC-SRR*, despite the large slice thickness employed for each anisotropic acquisition. R2 highlights a region in which *SRR* (without distortion compensation) provides blurred results. Importantly, the structures in the region R2 are more detailed with *FMC-SRR* than with *dISO*.

Figure 3.

Zoom on the color-FA maps in a region of the brain stem. (a): T1-weighted image showing the zoom location (axial view). Color-FA maps for (b):*ISO*, (c):*dISO*, (d):*SRR* and (e): *FMC-SRR*. The color-FA for *ISO* is highly noisy, while the noise reduction technique employed in *dISO* makes the structures fuzzy (region R1) and produces artifacts (R3). In *SRR* some structures are missing due to the non-correction of distortion (R2). *FMC-SRR* provides the most detailed structures (R1).

Figure 4.

Assessment of the estimation uncertainty by averaging the FA variance from the residual bootstrap in a 3-D region of interest. (a): region of interest considered, in the external capsule. (b): average of the FA variance in the ROI.

Figure 5. Tractography results for the corpus callosum from (a): *ISO*, (b): *dISO*, (c): *SRR* and (d): *FMC-SRR*.