Published in final edited form as:

Magn Reson Imaging. 2008 June ; 26(5): 676–682. doi:10.1016/j.mri.2008.01.005.

Diffusion anisotropy indexes are sensitive to selecting the EPI readout-encoding bandwidth at high-field MRI

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Abstract

Diffusion tensor magnetic resonance imaging (DT-MRI) is generally performed using an echo planar imaging (EPI) acquisition to map directional water diffusion. However, the oscillating magnetic field gradients of the EPI acquisition can result in considerable mechanical vibrations, which lead, in turn, to magnetic field fluctuations causing Nyquist ghosting in the EPI data. The objective of this study was to investigate effects of EPI readout gradient modulation frequency, which is directly associated with the EPI readout bandwidth (BW), on the accuracy of DT-MRI measurements in a high magnetic field system. A spherical water phantom was used to study the relationship between the EPI BW and the Nyquist ghost for a spin-echo EPI acquisition with a matrix size of 128×128, complemented by diffusion sensitization gradients of up to $b=800$ s/mm² along six directions for DT-MRI. Nine volunteers (four males and five females) were studied using EPI at different BW acquisitions. Analysis of variance was used to investigate the EPI BW effects. The phantom studies demonstrated a systematic relationship between BWs and the intensities of Nyquist ghosts. In the human brain studies, EPI BW variations substantially corrupted diffusion anisotropy indexes (i.e., fractional anisotropy and relative anisotropy) ($F=10.5$, $P=.0001$) but were unrelated to diffusion-encoding directions ($F=0.14$, $P=.98$). It was possible to minimize BW dependence ($F=1.48$, $P=.25$) by tuning the modulation frequency of the EPI readout gradient. In conclusion, diffusion anisotropic indexes are sensitive to the readout BW of EPI due to associated Nyquist ghosting. However, the effect can be minimized by tuning the modulation frequency of the EPI readout gradient, that is, the EPI BW, to a range outside the harmonics of mechanical gradient vibrations.

Keywords

Echo planar imaging; Readout-encoding bandwidth; Diffusion tensor; High-field MRI

1. Introduction

Magnetic resonance imaging (MRI) systems with high static magnetic fields and rapidly oscillating magnetic field gradients have been developed for fast acquisition of high-resolution anatomical and functional imaging of the human body. Echo planar imaging (EPI) [1,2], which can accomplish single-shot imaging in less than 100 ms, is often used in blood-oxygenation-level-dependent functional MRI [1], arterial spin-labeling perfusion MRI [2] and diffusion tensor (DT) MRI [3]. The oscillating magnetic field gradients of EPI can result in considerable mechanical vibrations of the gradient coil assembly as the Lorentz forces exerted on the electric

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currents in the coil increase with increasing magnetic field strength. These mechanical vibrations, which are also the source of the loud acoustic noise in the scanner that often distresses patients, cause temporal magnetic field fluctuations that ultimately lead to phase modulations in EPI data and contribute to the well-known Nyquist (N2) ghosting [4,5]. The N2 ghost artifact arises from an asymmetry between odd and even echoes when positive and negative readout gradients are used to sample alternate lines of k -space. Upon image reconstruction, the phase asymmetry produces a ghost that is displaced by half the field of view (FOV) in the EPI phase encode direction relative to the correct image position. While the mechanical vibrations cannot be avoided, their amplitude and frequency are linked to the oscillatory magnetic field gradients of EPI [5,6]. Hence, the bandwidth (BW) and frequency of oscillations [i.e., echo spacing (ES)] of EPI acquisitions should be chosen carefully to avoid triggering resonant mechanical vibrations and to reduce acoustic noise [7]. One obvious solution to reduce the vibrations is lowering the BW and increasing the ES of the EPI readout gradients. At higher magnetic fields, however, lowering the BW inadvertently increases the vulnerability of EPI to susceptibility distortions in regions with inhomogeneous fields [8]. Similarly, increasing ES decreases signal-to-noise ratio because of transverse relaxation of the signal, while decreasing it may be prohibitive because oscillating gradients can induce peripheral nerve stimulation. Hence, the range of BW and ES variations at high magnetic fields can be too limited to effectively eliminate N2 ghosting with detrimental effects on quantitative MRI, such as DT-MRI.

DT-MRI is generally performed using a diffusion-weighted spin echo (SE) followed by EPI detection [3]. The directional diffusion properties of tissue water are quantified by repeating the experiment with diffusion-weighting gradients applied along at least six different directions. However, artifacts induced by eddy current [9] and susceptibility distortions [10] are common artifacts in EPI, complicating accurate measurements and quantifications of DT-MRI data [11]. In addition to eddy currents and susceptibility distortions, N2 ghosting can distort apparent diffusion coefficients [12]. However, the impact of N2 ghosting on DT measures, especially on fractional anisotropy (FA) and mean diffusivity (MD; trace of the DT), has not been thoroughly evaluated. The objective of this study, therefore, was to investigate the effects of EPI BW on the accuracy of DT-MRI measurements on phantoms and studies of volunteers in a high magnetic field MRI system.

2. Materials and methods

EPI data were acquired using a 4-T MRI system (Bruker/Siemens MedSpec, Germany) equipped with a birdcage RF transmit head coil and an eight-channel phase array receiver head coil. DT-MRI acquisition was performed using parallel imaging with a factor 2 phase-encoding reduction and GRAPPA image reconstruction [13].

2.1. Phantom studies

A spherical water phantom provided by the manufacturer was used to study the relationship between the EPI BW and the N2 ghost for an SE EPI acquisition. SE EPI data were acquired with a matrix size of 128×128 and five 5-mm-thick transversal slices and 10-mm slice gaps, yielding a voxel resolution of $2 \times 2 \times 5 \text{ mm}^3$ across an FOV of $256 \times 256 \text{ mm}^2$. Repetition time (TR)/echo time (TE) was 3 s/80 ms with four averages. The phase-encoding direction of EPI was along the anterior–posterior direction. The EPI readout BW varied from 0.798 kHz/pixel (ES=1.32 ms) to 2.170 kHz/pixel (ES=0.71 ms).

The resulting data were analyzed by manual drawing of a region of interest (ROI) in the three middle slices in the background area where the N2 ghosts were most prominent, as shown in Fig. 1A. The mean and standard deviation of the magnitude in the ROI were recorded. The resulting data were plotted as a function of EPI readout BW for each study in order to determine

the relationship between the magnitude of the N2 ghost and the readout BWs and to select three ideal and nonideal BWs, which were applied to human brain studies for DT measurements. Repeated measures analysis of variance (ANOVA) was used to determine the extent to which the magnitude of the N2 ghost was associated with readout BWs under consideration of potentially additional effects from slice positions. Post hoc tests were used for pairwise comparisons. To account for multiple comparisons from multiple BWs in each test for three different slices, we adjusted the significance levels to $\alpha=.05/3$.

We also studied another phantom experiment with the application of diffusion gradients, used for the human brain. Forty imaging slices, each 3 mm thick and with a 1-mm gap between slices, were acquired. The matrix size was 112 (phase encoding) $\times$ 128 (readout encoding) with the 6/8 phase partial Fourier. The phase-encoding direction was set along the anterior–posterior direction. TR/TE=6 s/85 ms. FOV was 224 $\times$ 256 mm. For the DT-MRI encoding, diffusion weighting was achieved with two b values (0 and 800 s/mm²) along six diffusion-encoding directions. Twofold accelerated parallel imaging was used in combination with GRAPPA reconstruction, using 35 reference phase-encoding lines.

2.2. Human brain studies

Nine volunteers (four males and five females; mean age=47.2 years, S.D.=13.9 years, range=20 to 64 years) were recruited from the local community. The local institutional review boards approved this study. Informed consent was obtained from all participants prior to enrolling in this study. T_1 -weighted and T_2 -weighted structural images and DT-MRI images were obtained for each volunteer.

For the DT-MRI study on the human brain, we used the same acquisition as the DT-MRI phantom experiments. Based on the phantom study with the application of diffusion gradients, DT-MRI was repeated with three different EPI readout-encoding BW settings [1.260 kHz/pixel (ES=0.86 ms), 1.446 kHz/pixel (ES=0.76 ms) and 2.170 kHz/pixel (ES=0.71 ms)]. Four scans were averaged to increase the signal-to-noise ratio.

Image files of DICOM formats were converted into Analyze format by using Osiris (<http://www.sim.hcuge.ch/osiris>) and MRICro (<http://www.sph.sc.edu/comd/rorden/mricro.html>) programs. Statistical Parametric Mapping Version 2 (SPM2; <http://www.fil.ion.ucl.ac.uk/spm/software/spm2/>) software was used for further postprocessing and data analyses. Maps of FA, relative anisotropy (RA) and trace (MD*3) were calculated from DT-MRI data using the DtiStudio program [14] and saved in Analyze format. Raw diffusion-weighted images were also saved in Analyze format, separately for each of the six diffusion directions with $b=800$ s/mm² and for each BW. All maps and images were put in the standard spatial normalization space using SPM2 with EPI.mnc as the template and the B0 image of each BW as the source using affine registration to estimate normalization parameters. After that, these parameters were applied to all maps and images to generate spatially normalized diffusion maps. Two ROIs were defined (the outside and inside brain areas on B0 images, $b=800$ s/mm² images, FA maps, trace maps and RA maps), using the MRICro program from Slice 20 to Slice 30, and saved in Analyze format of the ROI. The ROIs inside the brain were placed by visually inspecting regions for high N2 ghosting. The ROI was used to obtain mean and standard deviation of all maps and images.

We tested two issues: First, we tested whether N2 ghosting was a function of both directionality of diffusion encoding and BW variations, as well as their interaction. We used repeated measures ANOVA with the diffusion-weighted maps at $b=800$ s/mm² as the dependent variable and the encoding directions, BWs and their interaction as the independent variables. Second, we tested the extent to which composite indexes of diffusion, such as MD, FA and RA, were impacted by variations of BW. Similar to the phantom studies, ANOVA with diffusion indexes

as dependent variables and BW as independent variable was used to determine if DT-MRI differences were significant given the variance of the subjects. We independently tested for the effects of N2 ghosting in the ROIs placed inside and outside the brain. Following ANOVA, post hoc *t* tests were performed for pairwise comparisons between different BW settings. To account for multiple comparisons from three BWs in each test, we adjusted the significance levels to $\alpha=.05/3$.

3. Results

3.1. Phantom studies

Fig. 1 shows representative phantom images (Fig. 1A) from the middle (third) slice for different EPI readout BWs, depicting dependence of N2 ghost intensity on EPI BW (Fig. 1B) without applying diffusion gradients at all. Brightness was kept the same for all images to emphasize the N2 ghost. Using the ROI shown in Fig. 1A, we obtained the intensities of the N2 ghost on the three middle slices. ANOVA showed significant effects by both BWs ($F=168.7$, $P=.000001$) and slices ($F=24.4$, $P<.00001$). The post hoc test was not performed for the BWs because we thought that Fig. 1B was enough to demonstrate the BW effects. With the post hoc test for the three slices (Slices 2–4), there were significant differences between Slice 4 and Slice 2 or 3, but there was no significant difference between Slice 2 and Slice 3. Starting at low BW [BW=1.45 kHz/pixel (ES=0.77 ms)], the magnitude of the N2 ghost increased steadily with increasing EPI readout BWs until the intensity of the artifact stabilized at the BW=2.170 kHz/pixel, corresponding to an EPI ES of 0.71 ms.

Fig. 2 shows the amplitude of the Nyquist (N2) ghost on the 112×128 matrix for $b=0$ and $b=800 \text{ s/mm}^2$ on phantom data averaged over the three middle slices for the same acquisition as the human experiments. For applications on the human brain, we only selected three readout BWs: BW=1.26 kHz/pixel (ES=0.86 ms), BW=1.446 kHz/pixel (ES=0.76 ms) and BW=2.170 kHz/pixel (ES=0.71 ms). In the DT-MRI of the phantom study, the magnitudes of the N2 ghost obtained from $b=0$ and $b=800 \text{ s/mm}^2$ were measured for each BW for the three middle slices using the ROI shown in Fig. 1A. The ANOVA test shows no significant effects on slice positions for the $b=800 \text{ s/mm}^2$ data ($F=3.952$, $P=.02$) and for the $b=0 \text{ s/mm}^2$ data ($F=3.20$, $P=.05$). The *P* values here were not adjusted for multiple comparisons. However, there were significant effects on the BWs for the $b=800 \text{ s/mm}^2$ data ($F=2035$, $P<.000001$) and for the $b=0 \text{ s/mm}^2$ data ($F=207.4$, $P<.000001$). The magnitudes of the N2 ghost between the six diffusion-encoding directions were not significantly different ($F=0.753$, $P=.58$) for the $b=800 \text{ s/mm}^2$ data. The magnitude of the N2 ghost between $b=0$ and $b=800 \text{ s/mm}^2$ was significantly different ($F=223.4$, $P<.000001$).

3.2. Human studies

Fig. 3 shows representative DT-MRI maps obtained on a volunteer. Two ROIs were defined outside the brain (background) and inside the brain regions. The magnitude of the N2 ghost was dominant at the BW=2.170 kHz/pixel (ES=0.71 ms) and consistent with the result of the phantom study. The N2 ghost effect was shown in the DT-MRI maps.

Table 1 lists signal intensities of the two ROIs on the B0 images and DT-MRI maps for the three EPI readout BWs. On the B0 images, signal intensities were normalized to the N2 ghost intensity of the BW=1.260 kHz/pixel, and therefore, values have no unit.

N2 ghosting in B0 images was associated with variations of BW ($F=10.38$, $P=.0006$). The post hoc test shows that there were significant differences between the high BW [BW=2.170 kHz/pixel (ES=0.71 ms)] and the lower BWs [BW=1.260 kHz/pixel (ES=0.86 ms) and BW=1.446 kHz/pixel (ES=0.76 ms)], while differences between lower BWs (BW=1.260 kHz/pixel and

BW=1446 kHz/pixel) diminished, as expected from the phantom study. On the B0 images with the ROI of the inside brain, there was no significant difference ($F=0.34$, $P=.71$).

The composite diffusion indexes MD, FA and RA were analyzed separately, because they represent different tensor properties. In regions of N2 ghosting, the values of FA and RA did not differ significantly for any BW ($P>.02$) as tested by pairwise comparisons. However, both FA and RA significantly varied as a function of BW ($F=10.5$, $P=.0001$). The post hoc test shows that there were significant differences between the high BW (BW=2.170 kHz/pixel) and the lower BWs (BW=1.260 kHz/pixel and BW=1.446 kHz/pixel) for FA and RA, while differences between the lower BWs (BW=1.260 kHz/pixel and BW=1.446 kHz/pixel) diminished, similar to the results from B0 images. In contrast to FA and RA, MD did not significantly vary as a function of BW ($F=1.48$, $P=.25$).

On the $b=800$ s/mm² images with the inside brain ROI, the ANOVA test with the signal intensities as a dependent variable and BWs and the six diffusion-encoding directions as independent variables showed a significant effect by BWs ($F=8.57$, $P=.0003$), independent of diffusion-encoding directions ($F=0.14$, $P=.98$). The post hoc test for BWs showed again that there were significant differences between the high BW (BW=1.260 kHz/pixel) and the lower BWs (BW=1.446 kHz/pixel and BW=2.170 kHz/pixel) and no significant difference between lower BWs (BW=1.446 kHz/pixel and BW=2.170 kHz/pixel). There were no significant interactions between BWs and diffusion-encoding directions ($F=0.004$, $P=1.00$).

4. Discussion

As expected, we found that N2 ghosting increased over a certain range with increasing EPI readout BW. In EPI, a higher readout BW is associated with a higher modulation frequency of the gradient. When the modulation frequency approaches the harmonics of the mechanical resonance characteristic of the gradient system, the magnitude of mechanical vibrations increases, which, in turn, can lead to measurable fluctuations of the magnetic field and, thus, to interferences with data acquisition, giving rise to N2 ghosting. The results of this study show that the induced artifacts can substantially affect diffusion measurements, especially diffusion anisotropy. A practical solution to reduce these artifacts is to tune the EPI BW and, correspondingly, the modulation frequency of the gradients to a range outside the harmonics of mechanical gradient vibrations. As the results show, the approach is sufficiently effective in minimizing the effect that N2 ghosting has on sensitive measures, such as anisotropy indexes of DT-MRI.

Fig. 1B shows that the magnitude of the N2 ghost is fairly constant (about 50) for BWs up to about 1.45 kHz/pixel. In general, this range depends on the gradient system in the magnet. Theoretical analysis of the N2 ghost is complicated. Several sources of MRI signal interference have been identified as contributing factors in the EPI N2 ghost, such as eddy currents, concomitant fields, oblique imaging, imaging filters, imperfect pulse sequence timing, B0 field inhomogeneity, susceptibility differences, chemical shift and the influence of the frequency response [4,7,15]. For example, Delakis et al. [7] found that the N2 ghost depended on the MRI receiver frequency response. Zhou et al. [4] evaluated the concomitant field effect on the N2 ghost.

Therefore, our results may not be the same for all 4-T MRI because different vendors use different gradient systems. MRI users should therefore evaluate the best EPI BW to use in their DT-MRI experiments to minimize the N2 ghost. Currently, both 1.5- and 3.0-T MRI systems are most commonly used in clinical applications. The N2 ghost effect could also depend on the magnetic field strength [16] because the oscillating magnetic field gradients of EPI can result in considerable mechanical vibrations of the gradient coil assembly as the Lorentz forces

exerted on the electric currents in the coil increase with increasing magnetic field, causing the N2 ghost [17]. Therefore, we expect that the N2 ghost effect could be less on both 1.5- and 3.0-T MRI systems than on the 4.0-T MRI system if the gradient system is identical. We also expect that the N2 ghost effect could be greater on the 3.0-T MRI system than on the 1.5-T MRI system with the same gradient system.

The in vivo studies showed that diffusion anisotropy indexes, that is, FA and RA, were more confounded by the presence of N2 ghosting than MD. Therefore, the selection of the EPI readout-encoding BW is critical to measuring diffusion anisotropy. The results further showed that N2 ghosting induced by BW variations was unrelated to the diffusion-encoding directions. This should substantially simplify potential retrospective corrections of diffusion measurements in the presence of N2 ghosting.

Finally, in addition to N2 ghosts, there are several factors of data acquisition that can affect the quantification of DT-MRI data. When strong diffusion gradients are switched rapidly, a time-varying magnetic field of the gradients results in eddy currents. Eddy currents can produce geometric distortions of contraction or dilation, shift and shear in diffusion-weighted images [9,18]. This artifact can be reduced by using a double refocusing SE sequence [19], by image postprocessing [20-22] or by using stimulated echo sequences [23]. Another type of artifact generated during diffusion studies is the susceptibility artifact caused by an inhomogeneous magnetic field when an EPI sequence is used to obtain data. The susceptibility artifact generates a local imaging distortion or signal dropout [10]. Because of the use of a relatively low phase-encoding BW, a severe artifact can occur in EPI acquisition along the phase-encoding axis when a local frequency shift happens [11]. However, as this study shows, the selection of readout-encoding (or frequency-encoding) BW and the corresponding ES should be one of the factors that need to be optimized when designing a DT-MRI protocol.

5. Conclusion

This study shows that EPI N2 ghosting can markedly interfere with measurements of diffusion anisotropy. To the extent to which N2 ghosting is related to characteristic mechanical vibrations of the gradients during EPI, the effects can be effectively minimized by tuning the modulation frequency of the EPI readout gradient, that is, the EPI BW, to a range outside the harmonics of mechanical vibrations.

Acknowledgment

We thank Dr. Yu Zhang for helpful advice to processing DT-MRI data. We also thank Miss Sun-Hee Lee (East-West Neo Medical Center, Seoul, Korea) for the technical assistance. The authors appreciate the help provided by Dr. Stephen Pickup (Department of Radiology, University of Pennsylvania) in revising the manuscript. This research was supported by a grant from the Korean Health 21 R&D Project, Ministry of Health and Welfare, Republic of Korea (A062284).

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Fig. 1.

Representative images of the phantom scans (A) for a few EPI readout BWs (kHz/pixel) and the Nyquist (N2) ghost behaviors (B) on the 128×128 matrix of the SE EPI sequence without applying diffusion gradients. In Panel A, the display windows were the same for each row of images to show the Nyquist (N2) ghost. The magnitudes of the N2 ghost on the three middle slices are shown in Panel B, and data were obtained from the ROIs in Panel A. The magnitude of the N2 ghost increased with increasing EPI readout BWs after the BW=1.45 kHz/pixel. The corresponding echo spaces related to the EPI BW were as follows: 1.14 ms (BW=0.930 kHz/pixel), 0.99 ms (BW=1.086 kHz/pixel), 0.83 ms (BW=1.302 kHz/pixel), 0.76 ms (BW=1.446 kHz/pixel), 0.71 ms (BW=1.698 kHz/pixel) and 0.71 ms (BW=2.710 kHz/pixel).

Fig. 2.

The amplitude of the Nyquist (N2) ghost on the 112×128 matrix for $b=0$ and $b=800 \text{ s/mm}^2$ on phantom data averaged over the three middle slices for the same acquisition as the human experiments. For applications on the human brain, we only selected three readout BWs [BW=1.26 kHz/pixel (ES=0.86 ms), BW=1.446 kHz/pixel (ES=0.76 ms) and BW=2.170 kHz/pixel (ES=0.71 ms)] based on this phantom study.

Fig. 3. Representative DT-MRI data with the three different EPI readout BWs (kHz/pixel) and two ROIs obtained from the DT-MRI study on a volunteer. The magnitude of the Nyquist (N2) ghost was dominant at the EPI BW=2.170 kHz/pixel. The white arrow indicates the region of the N2 ghost. The corresponding echo spaces related to the EPI BW were as follows: 0.86 ms (BW=1.260 kHz/pixel), 0.76 ms (BW=1.446 kHz/pixel) and 0.71 ms (BW=2.170 kHz/pixel). B0 denotes SE EPI images acquired without diffusion gradients and DWI is the diffusion-weighted imaging acquired with the application of diffusion gradients. Trace is a diffusion isotropic index, that is, MD*3.

Table 1

Signal intensities (mean±S.D.) for the B0 images (*b* value=0 s/mm²) and DT-MRI maps for the three EPI readout BW's on the two ROIs shown in Fig. 3

BW (kHz)	B0 images		DT-MRI maps (inside brain ROI)		
	Outside brain ROI ^a	Inside brain ROI	Trace ^b	FA ^b	RA
1.260	1.00±0.23	5.96±1.46	1.27±0.29	0.10±0.02	0.09±0.02
1.446	0.93±0.18	6.40±1.53	1.38±0.29	0.10±0.02	0.09±0.02
2.170	1.39±0.27	6.47±1.45	1.53±0.29	0.15±0.04	0.13±0.04

On the B0 images, signal intensities obtained from the BW=1.446 kHz/pixel (ES=0.76 ms) and the BW=2.170 kHz/pixel (ES=0.71 ms) were normalized by using the magnitude of the Nyquist ghost (outside brain ROI) of the BW=1.260 kHz/pixel (ES=0.86 ms).

^aThe ANOVA test shows significant BW effects (*F*=10.38, *P*=.0006). The post hoc test shows that there were significant differences between the BW=2.170 kHz/pixel and the BW=1.260 kHz/pixel or the BW=1.446 kHz/pixel.

^bThe ANOVA test shows significant BW effects (*F*=10.5, *P*=.0001). The post hoc test shows that there were significant differences between the BW=2.170 kHz/pixel and the BW=1.260 kHz/pixel or the BW=1.446 kHz/pixel.