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Nyquist Ghost Correction of Breast Diffusion Weighted Imaging using Referenceless Methods

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Abstract

Purpose: Correction of Nyquist ghosts for single-shot spin-echo EPI using the standard three-line navigator often fails in breast DWI due to incomplete fat suppression, respiration, and greater B_0 inhomogeneity. The purpose of this work is to compare the performance of the three-line navigator with four data-driven methods termed “referenceless methods”, including two previously proposed in literature, one introduced in this work, and finally a combination of all three, in breast DWI.

Methods: Breast DWI was acquired for 41 patients with SS SE-EPI. Raw data was corrected offline with the standard three-line navigator and four referenceless methods, which modeled the ghost as a linear phase error and minimized three unique cost functions as well as the median solution of all three. Ghost levels were evaluated based on the signal intensity in the background region, defined by a mask auto-generated from a T_1 -weighted anatomical image. Ghost intensity measurements were fit to a linear mixed model including ghost correction method and b-value as covariates.

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Results: All four referenceless methods outperformed the standard 3-line navigator with statistical significance at all four b-values tested ($b = 0, 100, 600, \text{ and } 800 \text{ s/mm}^2$).

Conclusions: Referenceless methods provide a robust way to reduce Nyquist ghosts in breast DWI without the need for any additional calibration scan.

Keywords

Nyquist ghost; breast; DWI; SE-EPI

Introduction

DWI of the breast is typically acquired using single-shot spin-echo (SS SE) EPI. Due to the alternating nature of EPI readout (RO) lines, eddy currents, imperfect gradients, and timing errors can cause inconsistencies between k-space lines of opposite polarity (RO+/RO-), which manifest as Nyquist, or N/2, ghosts. Nyquist ghosts are often corrected by acquiring a three-line navigator to measure the difference between alternating RO lines, which is modeled as a linear phase error. While the three-line navigator generally performs well for brain imaging, it often fails in body imaging due to insufficient fat suppression and increased B_0 inhomogeneity. Several other ghost correction methods have been proposed including a full-phase navigator (1), 2D phase-mapping approaches (2–8), acceleration-based techniques (9–11), methods that enforce low-rank structure of multi-channel data (12,13), and a class of methods, termed referenceless methods, that use the EPI data for self-correction (12,14–19).

These referenceless methods work by defining a cost function that is minimized when the data is ghost-free. The “Entropy” method (14,15,19) uses the image entropy after a 2D Fourier Transform as a heuristic cost function. The “SVD” method (16) defines a cost function based on a singular value decomposition of k-space after rearranging into GRAPPA-like kernels. Referenceless methods may be advantageous because they do not require the acquisition of any additional navigator or reference data, potentially allowing for decreased acquisition time and/or shortened TE, and easy integration with a wide range of acquisition strategies, including retrospective data. Because these techniques do not rely on coil sensitivity profiles, they should be suitable for combination with acceleration techniques, like in-plane parallel imaging (PI) and simultaneous multislice acquisition (SMS) (20–23); however, previous reports have suggested that the image-space-based referenceless methods may be limited by aliasing (16,19). Additionally, because they are data-driven, they may be limited by the low SNR of high b-values and high resolution DWI.

In this work we compare the performance of the standard 3-line navigator with referenceless methods for Nyquist ghost correction of breast DWI. We investigate previously proposed methods Entropy and SVD, introduce a referenceless method called Ghost/Object minimization (G/O), and assess a combination of all three. We also describe an iterative approach that allows these referenceless methods to be used in combination with PI. The methods are compared first using simulated data to assess their sensitivity to noise, and subsequently in an *in vivo* study to compare overall performance.

Methods

Linear Ghost Model and Correction

Nyquist ghosts arise due to differences between k-space lines with positive and negative polarity. The phase difference is often modeled in $X-k_y$ hybrid space as a 1st order polynomial: $\delta = \frac{\pi\kappa}{N_x}x + \phi$, where x refers to the discrete position in the RO dimension of the

spatial domain ϕ is a spatially constant phase shift between the RO+ and RO- lines, κ characterizes the slope ($\kappa = 1$) corresponds to a one pixel shift between RO+ and RO- in k-space), and N_x is the number of RO points. According to the Fourier shift theorem, and similarly described in Bernstein *et al.* (24), an image measured with SS SE-EPI can be described as:

$$I_{meas}(x, y) = I_0(x, y)\cos\left(\frac{\pi\kappa x}{N_x} + \phi\right) + iI'_0(x, y)\sin\left(\frac{\pi\kappa x}{N_x} + \phi\right) + \epsilon(x, y) \quad [1]$$

where $I_0(x, y)$ is the ideal, ghost-free image in the RO and PE directions, respectively and $\epsilon(x, y)$ is random thermal noise. The prime operator, $'$, indicates a circular shift in the image domain such that $I'_0(x, y) = I_0\left(x, y \pm \frac{FOV}{2}\right)$. In the case of multi-shot or PE-undersampled acquisitions, Equation 1 becomes less straightforward; the reconstructed image will contain multiple replicas of the object (ghosts) at locations given by:

$$I'_0(x, y) = \sum_{j=0}^{N_{seg}R-1} I_0\left(x, y \pm \frac{(2j+1)FOV}{2N_{seg}R}\right), \text{ where } N_{seg} \text{ is the number of segments and } R \text{ is the}$$

PE-undersampling factor. The ghosts will have an additional spatially-dependent signal modulation that varies with N_{seg} and sensitivity profiles.

Nyquist ghosts are commonly corrected using a three-line navigator (Method A) through $k_y = 0$ with polarity RO+/RO-/RO+. The linear phase difference between the positive and negative lines (δ) is fit in hybrid space to determine the correction parameters κ and ϕ (23–25).

In this work, the referenceless methods were also applied as a first order correction by estimating ϕ and κ solutions that minimize the cost function $f_{cost}(\phi, \kappa)$. The cost functions were defined as follows: “Entropy” (Method B) refers to the image entropy in the spatial domain, measured using Matlab’s (Mathworks, Natick, MA) “entropy” function (14,15,19). For “SVD” (Method C), single-channel k-space was reorganized into GRAPPA-like kernels before performing singular value decomposition and summing over the tail of the singular values (16). For Method D, we propose a ghost correction called “Ghost/Object minimization” (G/O), which is described in the following section. Finally, the “Median” solution (Method E) was defined as the median of the (ϕ, κ) values from the other three referenceless methods (B, C, and D).

Ghost/Object Minimization Theory

The cost function for the newly proposed Ghost/Object minimization (G/O, Method D) is calculated by taking the ratio of the magnitude of the measured image over one or more shifted copies, applying a 2D median filter, and *summing over the entire ratio image* in the image domain:

$$f_{cost}^{-1} = \sum_{x,y} F_{med2D} \left(\frac{|I_{meas}(x,y)|}{|I'_{meas}(x,y)|} \right) \quad [2]$$

where $I'_{meas}(x,y)$ is the sum of copies of the measured image, shifted to the expected location(s) of the ghost(s) as described above. The summation is taken over the entire image and does not require selection of the object or ghost regions, however, any pixels in $I'_{meas}(x,y)$ with very low noise values may bias the cost function by adding an overly large value to the summation. Thus, a 2D median filter, F_{med2D} , is applied to remove these outlier values. For simplicity, the summation in our implementation includes only the two ghosts ($j = 0$ and $j = R - 1$) that are located closest to the object, which tend to have largest intensity.

While the exact value of the cost function will depend on the image, it can be shown numerically that the region of the image containing the object without any overlapping Nyquist ghost dominates the cost function when κ and ϕ are near the correct solution. Due to the sine and cosine modulation of the signal intensity in the ghost and object (Eqn. 1), the inverse cost function can be approximated as:

$$f_{cost}^{-1} \approx \sum_{x,y_{object}} \left| \cot \left(\frac{2\pi\kappa x}{N_x} + \phi \right) \right| \quad [3]$$

where the sum is taken over the region of the measured image that contains only pure object and the noise is considered negligible. It is clear that f_{cost}^{-1} approaches ∞ when $\phi = \kappa = 0$, therefore, f_{cost} is minimized in the ghost-free image.

Simulation

To simulate the effect of varying noise, a synthetic image was generated in Matlab (modified Shepp-Logan (26)) and modified with a linear ghost artifact prior to adding noise. One hundred different phase values were randomly selected, with parameters in practical ranges ($-1.5 < \kappa < 1.5$ and $-0.3 < \phi < 0.3$), and Gaussian, complex noise was added to linearly sample 25 different SNR levels for each set of ghost parameters, where

$SNR = \langle |S_{max}| \rangle / (0.66 * \sigma_{noise} * \langle |S_{max}| \rangle)$ is the mean image intensity in the region of maximum signal (the phantom rim), and σ_{noise} is the standard deviation of the noise magnitude (27). The cost functions were calculated on the noisy data for Entropy, SVD, and G/O over a multi-resolution discrete search space. The solutions for each minimization were used to

correct the simulated ghost on the noise-free data and the RMS error was measured between the ideal and ghost-corrected images and averaged over all 100 trials for each noise level.

Data acquisition

Single-shot 2D SE-EPI DWI was acquired under IRB-approved protocols from 41 female subjects including 15 clinical patients undergoing breast cancer screening (age min/med/max = 40/52/68), 13 patients with biopsy-proven cancer receiving MRI for treatment monitoring (28/47/72), and 13 healthy volunteers (18/21/66). Four subjects undergoing screening had silicone implants in one or both breasts. All subjects were positioned headfirst prone in a Siemens Prisma^{fit} 3T scanner using a 16-channel Sentinelle breast coil. Diffusion images were acquired following the protocol used in the clinical trial ACRIN 6698, with TR = 8000 ms and TE 51 ms for monopolar diffusion (12 participants) or 74 ms for bipolar diffusion (29 participants), 36–50 4 mm axial slices with 320×320 mm in-plane FOV at 1.7×1.7 mm resolution, right-left phase encoding, in-plane undersampling of R = 3, 6/8 partial Fourier, SPAIR fat suppression, and total acquisition time ~5 minutes (28). One of the following three diffusion schemes was used to sample three orthogonal diffusion directions for each subject: b = 0, 100, 600, and 800 s/mm² (5, 9, 9, 9 averages = 32 volumes) [21 participants]; b = 0, 100, 600, and 800 s/mm² (4, 6, 6, 6 averages = 22 volumes) [5 participants]; b = 0, 100, and 800 s/mm² (5, 9, 9 averages = 23 volumes) [15 participants]. A 3-line navigator was acquired with phase encoding disabled for each coil, slice, and b-value/diffusion direction and for both the autocalibration scan (ACS lines) and undersampled data.

T₁-weighted anatomical images were acquired using a 3D VIBE sequence (RF-spoiled, 3D gradient echo) with fat suppression.

Image Reconstruction and Ghost Correction

Both ACS lines and undersampled data were reconstructed off-line with per-acquisition, per-coil, and per-slice ghost correction, followed by GRAPPA unaliasing (29). For the 3-line navigator correction (Method A), the phase difference between the center line and average of the 1st and 3rd lines of each navigator was smoothed with a Savitzky-Golay filter (sgolay, Matlab), weighted by the signal intensity to the fourth power, and fit to a first-order polynomial in x-k_y hybrid space.

The referenceless methods were first applied to the low-resolution ACS lines using a multi-resolution discrete search centered at $\phi = 0$ and $\kappa = 0.6$ in Matlab to determine ϕ_{ACS} and κ_{ACS} . The corrected ACS lines were used to calculate the GRAPPA weights. ϕ_{ACS} and κ_{ACS} were also applied as an initial correction for the undersampled diffusion-weighted data; to refine κ and ϕ a second iteration was performed using a non-linear minimization (fminsearch) including GRAPPA unaliasing in each step: i.e. a candidate (ϕ, κ) correction was performed on each channel of the undersampled data before GRAPPA unaliasing so the cost function could be evaluated on the unaliased reconstructed image.

Method D (Median) consisted of a combination of the four referenceless methods by taking the median of κ and ϕ from each method to reconstruct both ACS and undersampled data.

Assuming a monoexponential decay diffusion model, ADC maps were generated using a pixel-by-pixel linear fit of the natural log of the signal intensity across b-values.

Analysis

Due to the N/2 nature of Nyquist ghosts, $R = 3$ undersampling, and symmetric anatomy of axial breasts images, a large portion of the residual ghosts falls along the midline between the right and left breasts (Figure 1). Thus, the signal level of the background region was used as a surrogate measurement of the ghost level in the full image. To measure the signal in the background region, the T_1 -weighted anatomical image was resampled to match the DWI image matrix, thresholded, and dilated to automatically create a mask of object and background; all area posterior to the chest wall was automatically classified as object. We also measured the noise level for each case based on the average signal intensity of noise-only corner regions of the volume (Figure 1). We defined the ghost intensity for each method, acquisition, and subject over the whole volume as the average signal in the background region compared to the average noise level.

To compare the ghost correction performance, the whole-volume ghost measurements were averaged for each subject across averages at each b-value, and then a linear mixed model was applied with ghost correction method, b-value, and their interaction as covariates, adjusting for body mass index (BMI). A pairwise comparison was made between each correction method based on the model-estimated ghost intensity. To control type I error for multiple comparisons, Bonferroni correction was applied, and a two-sided p -value < 0.005 ($0.05/10$) was considered statistically significant for pairwise comparisons among five methods. The ghost intensity estimates were also compared between methods on a per-b-value basis in a pairwise way; statistical significance was set to $P < 0.00125$ ($0.05/40$) based on Bonferroni correction. SAS system (version 9.4; SAS Institute, Cary, North Carolina) was used in all statistical analyses.

Results

Figure 2 demonstrates the performance of the referenceless methods with increasing levels of SNR. While the error increases at lower levels of SNR for all four methods, all four referenceless methods are tolerant to noise down to an SNR levels of about 3 – 5; entropy is most sensitive to noise, followed by SVD, Median, and finally G/O. This sensitivity is reflected in the shape of the cost functions (example in Figure 2 inset). As SNR decreases, the minimum regions spread out and additional local minima develop that do not correspond to the ghost-free image, especially for Entropy and SVD. While all three referenceless cost functions have clear global minima at low noise levels, the cost functions vary in shape, especially as the noise level increases, suggesting that they each contain some unique information.

The performance of all five ghost correction methods varied across cases and slices. The 3-line navigator tended to fail more frequently than the referenceless methods in the 41 breast cases tested. An example is shown in Figure 3 that represents a typical case where the 3-line navigator failed and the referenceless methods significantly reduced the ghost at both $b = 0$ and $b = 800 \text{ s/mm}^2$, as well as the resulting ADC map.

The overall effects of ghost correction method are shown in Figure 4, which plots the ghost intensities measured over the whole volume for each subject and acquisition. The mean ghost levels estimated according to the adjusted linear mixed model are overlaid including 95% confidence intervals. All four referenceless methods generally reduce ghost levels compared to the standard approach. According to the adjusted linear mixed model, the performance of all four referenceless methods (B-E) is statistically superior ($p = 0.0002$) to the standard linear correction (A). While there is no statistical difference between the performance of the entropy, SVD, and G/O referenceless methods (B-D), the median combination of referenceless methods (E) is estimated to significantly outperform any single referenceless method alone ($p < 0.0001$).

The mean ghost intensities for each method separated by b-value according to the full linear mixed model are plotted in Figure 5; p -values less than 0.00125 are indicated. The mean ghost intensity of all referenceless methods (B-E) is lower than that of the standard 3-line navigator at all four b-values ($P < 0.001$). The differences between entropy, SVD, and G/O referenceless methods are not statistically significant regardless of b-value. The median method (E) yields the lowest ghost intensity value at all four b-values, however, E only outperforms B-C with statistical significance compared to Entropy and SVD at $b = 0 \text{ s/mm}^2$ and to Entropy at $b = 100$ and 800 s/mm^2 .

Discussion

One potential source of Nyquist ghosts is eddy currents induced by the diffusion gradients. The 3-line navigator is independent of b-value because it is acquired before diffusion weighting is applied and cannot correct for eddy currents caused by the diffusion gradients. The referenceless methods depend on the diffusion-weighted data and do include effects from the diffusion gradients, but they may be more sensitive to the signal loss at high b-values. We have shown here, however, that all four referenceless methods perform well in low SNR down to $\sim 3\text{--}5$ in simulated phantom data and outperform the 3-line navigator at all four b-values up to $b = 800 \text{ s/mm}^2$. If used for images with even lower SNR (e.g. very high resolution or large b-values), adding additional denoising filters could improve the performance of all the referenceless methods.

All five ghost correction methods estimated and applied two linear parameters on a per-coil, per-slice, and per-acquisition basis. In a small number of cases none of the ghost correction methods fully suppress the ghost, suggesting that it may be necessary to use higher-order correction. The referenceless methods may be extended to include higher-order parameters or correction that varies over the RO train if the necessary correction can be modeled by a small number of parameters. However, the computational time will quickly grow as the model increases in complexity.

The referenceless methods represent a data-driven approach to correct Nyquist ghosts. They can be applied retrospectively to a wide variety of data acquisitions without the need for any additional reference scan as methods like phase labeling for additional coordinate encoding (PLACE) and phase mapping require (2–8). Ghost correction by referenceless methods also does not rely on coil-sensitivity profiles, as methods like phase array ghost elimination

(PAGE) do (9–11), and therefore preserve all information about coil-sensitivity for the purpose of maximizing acceleration. Additionally, by removing the three-line navigator, it may be possible to shorten the TE. However, one limitation of the referenceless methods is the increased computational requirement for optimization of the nonlinear cost functions. In our implementation, SVD is the slowest referenceless method; a full static SVD reconstruction takes about 1.3 times longer than the three-line navigator correction and further increases to about 100 (G/O) to 300 (SVD) times when the iterative approach, which includes GRAPPA unaliasing in the cost function minimization, is used to determine dynamic corrections. It should be possible to reduce computation requirements to clinically practical times with further optimization of the processing.

While the summation in Equation 2 is performed over the entire image, the cost function is dominated by the object-only region due to the sine and cosine signal modulation. While the method does not explicitly select regions of interest, it could be limited by the amount of object/ghost overlap if the object lacks signal variation in the PE direction, which would flatten the shape of $f_{cos}(\phi, \kappa)$. Additionally, G/O requires the removal of outlier values prior to taking the summation, which is not necessary for Entropy or SVD. In this implementation we removed these outliers by applying a 2D median filter, which also produces some denoising in $f_{cos}(\phi, \kappa)$. While this filtering does add a small bias to the comparison of the referenceless methods, median filtering did not improve the entropy metric in our data, and cannot be used with SVD as it requires complex data. However, all of the methods used, including the linear navigator, may be further optimized using other denoising techniques (e.g. Gaussian) and additional tuning.

Previous reports have claimed that referenceless methods performed in the image domain were limited by the amount of overlap and aliasing that arise when acceleration techniques or multi-shot acquisition are used (16,19). In this work, we overcome the limitation of PE undersampling by incorporating the GRAPPA reconstruction in the optimization; this strategy may be useful in combination with other acceleration methods as well.

Nyquist ghost artifacts can modulate the true image signal and lead to errors in ADC estimation via two distinct mechanisms. The first is simple overlap – if any portion of a Nyquist ghost overlaps the object it can increase or decrease the object signal. Secondly, an incorrect phase produces a spatially-varying cosine modulation of the object signal (Eqn. 1). In this work we used the ghost signal in the image background as an estimate of the overall ghost level. Although ghost signal in the image background does not directly produce ADC errors, it is an objective measure of the overall ghost level.

In this study, we used the 3-line navigator as the reference standard ghost correction method. Our implementation of this method gives somewhat different results than the vendor's proprietary implementation, but the average performance of the two implementations is similar.

Conclusions

Referenceless methods provide a data-based alternative to the three-line navigator for 1st-order ghost correction, which often fails in breast DWI. We proposed an additional referenceless method, Ghost/Object (G/O) minimization, which defines a cost function in the image domain that exploits the cosine and sine modulation in the ghosted image and the N/2 nature of the ghost. All four referenceless methods show low sensitivity to noise levels, especially G/O and SVD in a simulation at increasing noise levels and perform well at b-values up to 800 s/mm². In this work, all three referenceless methods were successfully combined with accelerated imaging of R = 3 and outperformed the 3-line navigator correction at all four b-values. Additionally, because each of the three cost functions employed contain some unique information, combining the referenceless methods with the median of 1st-order parameters showed a trend of improved ghost correction performance.

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Figure 1. Measurement of ghost levels.

Nyquist ghosts in a $b = 0 \text{ s/mm}^2$ image (A) can be seen in the background region between the breasts. The T_1 -weighted anatomical image (B) is used to create an object mask, which is applied to the $b = 0 \text{ s/mm}^2$ image (C). The signal in the background region (D) reflects the intensity of the residual ghost. Red boxes indicate the regions used to measure the average noise level in root sum of squares images.

Figure 2. Simulation of noise effect on cost functions.

This plot shows the accuracy of each method, averaged over 100 trials, for increasing SNR levels. Example images are shown for 4 (of 25 tested) sample SNR values. The inset plots show the cost functions for a single trial at two SNR levels, indicated on the x-axis by * and °. With decreasing SNR, additional local minima develop and minimum regions spread out. White and red circles indicate the correct and estimated ghost parameters, respectively.

Figure 3. Single-slice DWI from an example case.
A single acquisition of $b = 0$ and 800 s/mm^2 images and an ADC map are shown. The example highlights a case in which the referenceless methods perform well and the 3-line navigator fails in the ACS lines.

Figure 4. Whole-volume ghost intensity plotted over method.

Colored points indicate ghost intensity measured over the volume of each subject and acquisition; color indicates b-value. The black circles indicate the ghost intensities estimated according to the adjusted linear mixed model with 95% confidence intervals. Plotted over two y-scales for detail.

Figure 5. Ghost intensity by method and b-value.

Ghost intensity and its 95% confidence interval estimated by the linear mixed model given b-value and ghost correction method. Threshold for statistical significance is set to $P < 0.00125$ based on Bonferroni's method for multiple comparisons.