Robust SENSE reconstruction of simultaneous multislice EPI with low-rank enhanced coil sensitivity calibration.

**Article** in *Magnetic Resonance in Medicine* · February 2018

**DOI:** 10.1002/mrm.27120

**CITATIONS**
0

**READS**
29

**7 authors**, including:

- **Mengye Lyu**
  The University of Hong Kong
  6 PUBLICATIONS  8 CITATIONS
  SEE PROFILE

- **Ed X Wu**
  The University of Hong Kong
  270 PUBLICATIONS  5,590 CITATIONS
  SEE PROFILE

Some of the authors of this publication are also working on these related projects:

Joint-Blade SENSE PROPELLER MRI [View project]
Robust SENSE reconstruction of simultaneous multislice EPI with low-rank enhanced coil sensitivity calibration and slice-dependent 2D Nyquist ghost correction

Mengye Lyu1,2 | Markus Barth3 | Victor B. Xie1,2,4 | Yilong Liu1,2 | Xin Ma1,2 | Yanqiu Feng1,5 | Ed X. Wu1,2

1 Laboratory of Biomedical Imaging and Signal Processing, the University of Hong Kong, Hong Kong SAR, People’s Republic of China
2 Department of Electrical and Electronic Engineering, the University of Hong Kong, Hong Kong SAR, People’s Republic of China
3 Centre for Advanced Imaging, University of Queensland, Brisbane, Queensland, Australia
4 Toshiba Medical Systems (China), Beijing, People’s Republic of China
5 School of Biomedical Engineering, Southern Medical University, Guangzhou, Guangdong, People’s Republic of China

Correspondence
Ed X. Wu, Department of Electrical and Electronic Engineering, The University of Hong Kong, Hong Kong SAR, China.
Email: ewu@eee.hku.hk

Funding information
Hong Kong Research Grant Council, Grant/Award Numbers: C7048-16G and HKU171103015; Lam Woo Foundation; Australian Research Council Future Fellowship, Grant/Award Number: FT140100865

Part of this work was presented at the 2017 Annual Meeting of International Society for Magnetic Resonance in Medicine.

Purpose: To improve simultaneous multislice (SMS) EPI by robust Nyquist ghost correction in both coil sensitivity calibration and SMS reconstruction.

Methods: To derive coil sensitivity and slice-dependent phase difference map between positive- and negative-echo images, single-band EPI reference data are fully sampled with EPI parameters matched to SMS acquisition. First, the reference data are organized into positive- and negative-echo virtual channels where missing data are estimated using low-rank-based simultaneous autocalibrating and k-space estimation (SAKE) at small matrix size. The resulting ghost-free positive- and negative-echo images are combined to generate coil sensitivity maps. Second, full-matrix positive- and negative-echo images are SENSE reconstructed from the reference data. Their phase difference or error map is then calculated. Last, SMS EPI is reconstructed using phase error correction SENSE (PEC-SENSE) that incorporates phase error map into coil sensitivity maps for negative-echo data. The proposed method was evaluated using both experimental data from 7T systems and simulations.

Results: Virtual coil SAKE eliminated Nyquist ghosts in the single-band EPI, yielding high-quality coil sensitivity maps and phase error maps. The subsequent PEC-SENSE robustly reconstructed SMS EPI under various conditions, including presence of in-plane acceleration, with lesser artifacts and higher temporal SNR than slice-dependent 1D linear correction method.

Conclusion: The proposed procedure of virtual coil SAKE calibration and PEC-SENSE reconstruction substantially reduces all ghost-related artifacts originating either directly from SMS EPI data or indirectly from EPI-based coil sensitivity maps. It is computationally efficient, and generally applicable to all SMS EPI-based applications.

KEYWORDS
EPI, ghost artifact, multiband, parallel imaging, SMS, virtual coil
1 | INTRODUCTION

EPI has been the preferred sequence for fast imaging in many important MRI applications, such as functional MRI and diffusion-weighted imaging. To achieve fast k-space transversal, the readout gradient polarity of EPI usually switches between 2 consecutive k-space lines. However, EPI acquisition scheme suffers from the inconsistencies between the readouts of opposing polarities. These inconsistencies can be caused by various hardware and subject-dependent imperfections, including gradient time delay, eddy current, and field inhomogeneity. Such inconsistencies periodically modulate the k-space and manifest as an artifact named Nyquist ghost in reconstructed images.

Simultaneous multislice (SMS) EPI, also known as multiband EPI, has shown great value in advancing spatial and temporal resolution in various EPI applications. Nyquist ghosts become more problematic in SMS EPI, because they are slice-dependent and interfere with slice separation process (i.e., SMS reconstruction). With multislice signals collapsed onto each other, Nyquist ghosts are mixed and cannot be slice-wise corrected before SMS reconstruction. If standard SMS reconstruction is used, the ghosted signals can be wrongly assigned within and across slices. Moreover, with SMS acquisition and reconstruction, Nyquist ghosts may not appear with the classic half FOV shift as in non-SMS EPI. The specific artifact pattern depends on many factors, including CAIPIRINHA shift, multislice ghost distribution, and reconstruction algorithms.

An additional factor in SMS EPI reconstruction is that single-band EPI with matching acquisition parameters is commonly used for coil sensitivity calibration, as it provides consistent geometric distortion to minimize reconstruction artifacts particularly in areas of large field inhomogeneity. This EPI-based reference scan can be acquired in a single shot if SMS EPI is not jointly accelerated in-plane, or in multiple shots where total number of shots equals the in-plane acceleration factor. However, Nyquist ghosts may also degrade such EPI-based reference scans, causing estimation errors in coil sensitivity maps or equivalently in GRAPPA kernels. The poorly estimated coil sensitivity maps will worsen SMS reconstruction by increasing artifacts and decreasing SNR. In addition, when using multiple shots, inter-shot phase variation can introduce extra ghosts, therefore further degrading coil sensitivity calibration. These multiple-shot-related ghosts appear similar to Nyquist ghosts yet manifest more nonlinearity and randomness associated with respiration and other subtle motions.

Regardless of physical sources, Nyquist ghosts can be mathematically described by the phase differences (i.e., phase errors) between positive-echo and negative-echo images. Most previous studies have adopted 1D linear phase error model. However, it is not uncommon to encounter 2D phase errors, which can arise from complex eddy current and local field inhomogeneity and exhibit non-linear distribution. 2D Nyquist ghost correction usually requires aliasing-free positive- and negative-echo images for phase error map estimation. This is typically achieved by temporally encoded EPI with proper data rearrangement of readout-inverted frames. The drawbacks of this approach are prolonged scan time and increased vulnerability to inter-shot phase variation.

Parallel imaging techniques have led to improved 2D Nyquist ghost correction methods. Positive- and negative-echo images can be separately reconstructed from a single-frame single-shot EPI using sensitivity encoding (SENSE). Phase error maps can then be calculated, denoised, and incorporated into coil sensitivity maps for robust 2D Nyquist ghost removal, as similarly implemented in multiplexed sensitivity encoding (MUSE) for multi-shot diffusion-weighted imaging. Nevertheless, these parallel-imaging-based correction methods still require coil sensitivity maps, which themselves can be compromised by 2D Nyquist ghosts if acquired using EPI.

Low-rank techniques explore data redundancy from a new perspective and can potentially enable fully self-referenced Nyquist ghost correction. A recent study has shown that the low-rank method ALOHA could correct 2D Nyquist ghosts on non-accelerated EPI without using coil sensitivity information. However, applying this approach to in-plane or SMS-accelerated EPI data may incur prohibitively heavy computation and serious ill-conditioning because acceleration will dramatically reduce data redundancy that underpins the low-rank properties.

This study aims to correct 2D Nyquist ghosts in both single-band EPI reference and SMS EPI data without using temporally encoded reference scans. A novel reconstruction procedure is proposed that uses low-rank and parallel imaging techniques. First, low-rank-based virtual coil SAKE is used to eliminate Nyquist ghosts from the single-band reference data fully sampled with matching EPI parameters, yielding ghost-free high-quality coil sensitivity maps. Then, full-matrix positive- and negative-echo images are SENSE reconstructed from the single-band reference data, and phase error maps are calculated slice-wise with denoising. Last, SMS EPI is reconstructed using phase error correction SENSE (PEC-SENSE), which removes slice-dependent 2D Nyquist ghosts by incorporating the pixel-wise phase error maps into coil sensitivity maps.

The procedure proposed above is based on the fact that single-band EPI data acquired using matching parameters not only provide distortion-consistent coil sensitivity maps, but also contain the same phase errors (associated with positive- and negative-echo inconsistencies) as the SMS EPI data. However, 2D Nyquist ghosts can reside in the single-band EPI data, in which case it is challenging to accurately
measure coil sensitivity maps. Most existing Nyquist ghost correction methods are not suitable here, because temporal-encoding-based methods suffer from increased scan time and inter-shot phase variation and parallel-imaging-based methods require coil sensitivity maps as a prior. Therefore, a new self-referenced virtual coil SAGE method is proposed here, which removes Nyquist ghosts by applying low-rank-based k-space estimation on positive- and negative-echo virtual channels. Moreover, it can remove inter-shot phase variation by separating shots into virtual channels.

2 | METHODS

2.1 | Virtual coil SAGE for ghost-free coil sensitivity calibration

Figure 1 illustrates the proposed coil sensitivity calibration procedure. The single-band EPI reference data are fully sampled with matching EPI parameters and corrected using 1D linear phase correction (LPC) first. Then virtual coil simultaneous autocalibrating and k-space estimation (VC-SAGE) is applied to eliminate the residual Nyquist ghosts. VC-SAGE includes 3 steps: virtual channel creation, SAGE iteration, and virtual channel combination. If reference scan is multi-shot EPI, different shots should also be separated into virtual channels with other steps unchanged. VC-SAGE presents a robust approach to removing both Nyquist and multiple-shot-related ghosts for accurate coil sensitivity calibration of EPI.

![Diagram](image1.png)

**FIGURE 1** The proposed coil sensitivity calibration procedure. Single-band EPI reference data are fully sampled with EPI parameters matched to simultaneous multislice (SMS) acquisition. After 1D linear phase correction (LPC), virtual coil simultaneous autocalibrating and k-space estimation (VC-SAGE) is applied to eliminate the residual Nyquist ghosts. VC-SAGE includes 3 steps: virtual channel creation, SAGE iteration, and virtual channel combination. If reference scan is multi-shot EPI, different shots should also be separated into virtual channels with other steps unchanged. VC-SAGE presents a robust approach to removing both Nyquist and multiple-shot-related ghosts for accurate coil sensitivity calibration of EPI.

![Diagram](image2.png)

**FIGURE 2** (A) The proposed phase error calibration procedure. Positive and negative echoes are separately reconstructed from the single-band reference data using SENSE. The resulting positive- and negative-echo images are then slice-wise processed by ESPIRIT-based phase subtraction to generate phase error maps. (B) Phase error correction SENSE (PEC-SENSE) for SMS EPI reconstruction. SMS EPI data are first regrouped by separating the positive and negative echoes. Therefore, multiband factor (MB) stays the same yet the effective channel number and in-plane acceleration factor (R) are both doubled. The positive echoes are set to have the reference coil sensitivity maps without modification, and the coil sensitivity maps for negative echoes are slice-wise multiplied by the phase error maps. The positive and negative echoes are jointly reconstructed to produce final reconstructed slices.
SAKE) is applied to remove the residual Nyquist ghosts. Following VC-SAKE, eigenvector-based iterative self-consistent parallel imaging reconstruction (ESPIRiT) is used to calculate coil sensitivity maps.\textsuperscript{30} For simplicity, only the first set of ESPIRiT maps (i.e., the set with the largest eigenvalues) are used.

VC-SAKE consists of 3 steps: virtual channel creation, SAKE iteration,\textsuperscript{26} and virtual channel combination. In the first step, the input k-space data are organized into positive- and negative-echo virtual channels. To use existing SAKE implementation,\textsuperscript{26} the negative echoes are shifted in phase-encoding direction to match the locations of positive echoes, which ensures consistent sampling patterns across virtual channels. In the second step, missing data points in all virtual channels are initialized with 1D LPC results\textsuperscript{17,26} and then jointly updated in SAKE iterations based on the intrinsic low-rank property associated with multichannel k-space.\textsuperscript{26} Specifically, after initialization, virtual coil k-space contains residual Nyquist ghosts that 1D LPC fails to remove, therefore exhibiting abnormally high rank because of data inconsistencies. When SAKE iteratively updates the data with enforced low rank, virtual coil k-space becomes increasingly consistent and the Nyquist ghosts gradually diminish. In each SAKE iteration, virtual channels from the same physical channel are enforced to have identical image magnitude by replacing their original magnitude with averaged one. This extra constraint is not essential but improves convergence. After SAKE iterations, all virtual channels are ghost-free. In the last step, the positive- and negative-echo virtual channels are combined to increase SNR for the final ghost-free single-band EPI images. To prevent signal cancellation caused by the positive- and negative-echo phase difference, the virtual channel combination is performed with 2D linear phase alignment developed by Hoge et al.\textsuperscript{9} This algorithm is highly efficient and effectively eliminates signal cancellation although small nonlinear phase differences are present.
but negligible. Overall, VC-SAKE maintains the total channel number from input to output so that coil sensitivity maps can be readily calculated without special algorithm modification.

VC-SAKE can be applied to multi-shot reference data by similarly separating the shots into virtual channels and keeping other steps unchanged. In doing so, the number of virtual channels is equal to twice the number of shots, and multiple-shot-related ghosts are corrected together with Nyquist ghosts during SAKE iterations. Applying VC-SAKE to full k-space is usually time-consuming and in fact unnecessary because coil sensitivity maps are smooth in nature. Therefore, VC-SAKE can be applied to central k-space only.

2.2 Phase error correction SENSE for SMS EPI reconstruction

Similar to its in-plane version,11 SMS phase error correction SENSE (PEC-SENSE) reconstruction requires phase error maps in addition to coil sensitivity maps. Although low-resolution positive- and negative-echo images are already available as interim results of VC-SAKE as shown in Figure 1, they are not directly used for phase error maps because of the potential loss of nonlinear phase error information. Relying on VC-SAKE interim results may also compromise the flexibility and extensibility of the method as will be further elaborated in the Discussion. Therefore, we propose to extract phase maps from full-matrix positive- and negative-echo images using coil sensitivity maps11,23,24 as shown in Figure 2A.

In brief, positive- and negative-echo images are separately reconstructed from the (uncorrected) single-band reference data using SENSE at full matrix size. Then, phase error maps are estimated slice-wise as their phase differences through ESPIRiT-based phase subtraction. Specifically, the positive- and negative-echo images are treated as 2 coil channels, and the phase differences between their first set of ESPIRiT maps are taken as the estimated phase error maps. ESPIRiT-based phase error maps are denoised because of the denoising effects inherent in the ESPIRiT kernel formation and eigenvalue decomposition process.31 This approach also circumvents the practical implementation difficulties in fitting-based methods, such as identifying object areas and choosing fitting functions.14,15 The above procedure is described for single-shot EPI for simplicity. If the reference scan is multi-shot, which is required for SMS EPI with in-plane acceleration, positive- and negative-echo images are reconstructed from each shot, then averaged with phase alignment9 before ESPIRiT-based phase subtraction.

FIGURE 4 Demonstration of the proposed phase error calibration using the rat brain data. (A) SENSE reconstructed single-band positive- and negative-echo images. The positive- and negative-echo images had identical image magnitude but discrepant phase. (B) Different types of phase error maps corresponding to the 2 slices in (A). The white circles outline the object areas for easier comparison. The 1D linear phase error maps were generated using entropy minimization, and the raw phase error maps were the direct phase differences between SENSE reconstructed positive- and negative-echo images. The proposed phase error maps processed by ESPIRiT exhibited similar general distribution to the raw maps, yet with much reduced noise.
With coil sensitivity and phase error maps, ghost-free SMS EPI reconstruction is achieved by applying PEC-SENSE as outlined in Figure 2B. SMS EPI data are first regrouped by separating the positive and negative echoes with missing data points filled with zeros. Therefore, the effective channel number and in-plane acceleration factor (R) are both doubled. The positive echoes are set to have the reference coil sensitivity maps without modification, and the coil sensitivity maps for negative echoes are multiplied slice-wise by their phase error maps.\(^7,11,15\) Mathematically, the aliased images in \(i\)th channel can be expressed as

\[
I_{\text{aliased}}^{p,i} = \frac{1}{2} \sum_{z=1}^{MB} (C_{iz}I_z + C_{iz}'I_z')
\]

\[
I_{\text{aliased}}^{n,i} = \frac{1}{2} \sum_{z=1}^{MB} (C_{iz}E_zI_z - C_{iz}'E_zI_z'),
\]

where \(I_{\text{aliased}}^{p,i}\) and \(I_{\text{aliased}}^{n,i}\) are the aliased positive-echo image and negative-echo image, respectively, \(MB\) the multiband factor, \(z\) the slice index from 1 to \(MB\), \(C_{iz}\) the coil sensitivity map, \(E_z\) the phase error map, \(I_z\) the aliasing-free positive-echo image, and the superscript ‘’ denotes half FOV shift along phase-encoding direction. Note that aliasing-free positive- and negative-echo images only differ in phase by \(E_z\). With the latter substituted for \(E_zI_z\) in Eq. (2), the aliasing-free positive-echo image \(I_z\) is treated as the overall reconstruction target without loss of generality. By jointly solving Eqs. (1) and (2) in all channels, \(I_z\) can be reconstructed for the \(MB\) slices. The above equations assumes no CAIPIRINHA shift and in-plane acceleration for simplicity, but they can be easily incorporated. PEC-SENSE can be regarded as an extension of ghost correcting SENSE (GhC-SENSE),\(^7\) which was designed to correct slice-dependent 1D linear Nyquist ghosts in SMS EPI. In GhC-SENSE, SMS EPI data are also reconstructed by jointly solving Eqs. (1) and (2) but there \(E_z\) is assumed to be strictly linear in readout direction and constant in phase-encoding direction.

The complete code of our proposed SMS reconstruction procedure as described above can be obtained online (https://github.com/mylyu/SMS-EPI-Ghost-Correction) or from the authors.

2.3 Experiments

2.3.1 Rat brain imaging at 7T

The rat brain data were collected on a 7T Bruker scanner (70/16 Pharmascan, Ettlingen, Germany) equipped with a 4-
channel surface head coil. All experiments were conducted with the approval of local institutional animal ethics committee. Single-shot gradient-echo SMS EPI data were acquired with in-house programmed multiband pulses, which are standard sinc pulses multiplied by cosine waves. MB = 2 was used with no CAIPIRINHA shift and no in-plane acceleration. This coil has sufficient sensitivity variation along slice direction so that noise amplification is still acceptable without CAIPIRINHA shift. Other imaging parameters were TE/TR = 16/2000 ms, flip angle = 90°, FOV = 40 × 40 mm², matrix size = 96 × 96, echo-spacing = 0.24 ms, bandwidth = 4166 Hz/pixel, slice number = 20, slice thickness = 1 mm, and phase encoding along left-right direction. Standard geometry planning was used with the slices ~10° tilted from the orthogonal planes, and volume shimming up to the second order was applied. The reference scan was acquired by single-shot single-band EPI with matching parameters.

For all single-band and SMS EPI data, ramp sampling correction was done first. VC-SAKE was implemented based on original SAKE code in MATLAB (MathWorks, Natick, Massachusetts, USA).26 Because of the small channel number of 4, VC-SAKE was applied to full 96 × 96 k-space without experiencing significant computation burden. Based on simple empirical optimization, 100 SAKE iterations were chosen and performed with kernel size 6 × 6 and rank threshold ranging from 25 to 36. Note that a fixed rank threshold 36 was used for most slices, yet for optimal performance, smaller ranks were applied to few boundary slices.

**FIGURE 6**  Phase error maps and SMS EPI reconstruction of the phantom data from a large-bore 7T system. The SMS data were acquired at MB = 2 and R = 2 using a 32-channel coil, and the single-band reference scan was acquired by 2 shots. The phase encoding was along vertical axis. (A) Phase error maps. The white circles outline the object areas. This data set contained strong nonlinear phase errors beyond even 2D linear distribution, which was well represented by the proposed phase error maps. (B) SMS reconstruction. To compare phase error models, identical coil sensitivity maps from VC-SAKE corrected images were used for all reconstruction methods. Still, neither GhC-SENSE nor 2D LPC SENSE was capable of complete Nyquist ghost removal. In comparison, PEC-SENSE substantially improved the reconstruction, yielding almost no artifacts.
where the object size was relatively small. ESPiRiT was done using Berkeley Advanced Reconstruction Toolbox (BART), with kernel size $6 \times 6$, calibration region $48 \times 48$, and default null-space threshold of 0.001. PEC-SENSE was implemented in MATLAB with non-regularized least squares. For evaluation, VC-SAKE was compared with entropy-minimization-based 1D LPC and 2-frame phase labeling for additional coordinate encoding (PLACE). PEC-SENSE was compared with GhC-SENSE with and without using VC-SAKE corrected reference data.

**FIGURE 7**  (A) Nyquist ghost correction of the human brain single-band reference data acquired by 2-shot EPI from a large-bore 7T system. The phase encoding was along vertical axis. A single coil channel is displayed. Residual Nyquist ghosts were found in the 1D LPC images, whereas they were almost completely removed by VC-SAKE. As confirmed in Supporting Information Figure S2, VC-SAKE also effectively eliminated multiple-shot-related ghosts that 1D LPC failed to remove. (B) Phase error maps. The white circles outline the object areas. The proposed phase error maps captured the 2D phase errors without introducing apparent noise and artifacts.

**FIGURE 8**  SMS reconstruction of the human brain data at MB = 2 and R = 2. The images were cropped along left-right (readout) direction from 128 pixels to 90 pixels and displayed at brightness $\times 1$ and $\times 5$. Compared with 1D LPC-based reconstruction procedure (1D LPC reference + GhC-SENSE), the proposed method (VC-SAKE reference + PEC-SENSE) substantially reduced artifacts, as pointed by the arrows and enlarged in the insets.
2.3.2 | Phantom and human brain imaging at 7T

Phantom and human brain data were collected on a 7T Siemens whole-body research scanner equipped with a 32-channel head coil (Nova Medical, Wilmington, Delaware, USA). All experiments involving human subjects were approved by the local institutional review board and written informed consent was obtained. The SMS sequence distributed by Center for Magnetic Resonance Research (CMRR) at University of Minnesota was used.1,4,33,34 Single-shot gradient-echo SMS EPI was acquired on a spherical oil phantom (diameter = 165 mm) at MB = 2 and a healthy volunteer at MB = 4 and R = 2, with R = 2 and CAIPIRINHA shift of 1/4 FOV. At MB = 2, TR = 700/2170 ms (human/phantom), flip angle = 70°, and number of frames (time points) = 1; at MB = 4, TR = 539 ms, flip angle = 50°, and number of frames = 50. Other imaging parameters were TE = 30 ms, matrix size = 128 x 128, echo-spacing = 0.7–0.8 ms, bandwidth = 1628 Hz/pixel, slice number = 20/80 (human/phantom, after reconstruction), slice thickness = 2 mm, and phase encoding along anterior-posterior direction. For clear illustration of 2D phase errors, the slice orientation of phantom data was made largely oblique, and the shimming deliberately worsened by including the linear term only. The human data had standard slice orientation slightly tilted from orthogonal planes and standard shimming up to the third order. The reference scan was acquired by 2-shot single-band EPI with matching parameters.

Data were reconstructed with the same parameters as in rat brain experiments except for the minor modification described below. For all reference data, 1D LPC was applied twice to sequentially correct Nyquist ghosts and multiple-shot-related ghosts, and VC-SAKE was applied to central 48 x 48 k-space with 50 iterations, kernel size 3 x 3, and rank threshold ranging from 36 to 45. To fully capture nonlinear phase errors in the phantom data, ESPIRiT kernel size was increased to 9 x 9 with calibration region of 80 x 80. For optimal SNR performance, coil sensitivity maps were tailored to be slightly larger than the object.

Besides GhC-SENSE, PEC-SENSE was also compared with slice-dependent 2D LPC SENSE on the phantom data for demonstration of nonlinear phase error correction. The 2D LPC parameters were fitted from raw phase error maps with image magnitude as weighting. For evaluation, temporal SNR (t-SNR) maps were calculated using 50 frames of the human brain data at MB = 4 and R = 2.

2.4 | Assessments using simulations

In addition, the proposed method was quantitatively evaluated by well-controlled simulations. Two ghost-free slices acquired using FLASH sequence on the 7T Siemens (Erlangen, German) scanner with 32 channels were used as the gold standard, from which single-band EPI data were simulated to have 2 interleaved shots, and SMS EPI data were simulated to have a single shot at MB = 2 and R = 2. The phase errors added to
FIGURE 10  Quantitative evaluation of the proposed method in simulations. The 2 displayed slices formed one slice group in the simulated SMS acquisition. (A) Ghost correction of the single-band images. The error maps are displayed at bottom at brightness ×3, together with the root mean squared error (RMSE) values. The proposed VC-SAKE reduced the RMSE values from 0.0219 to 0.0077 as compared with 1D LPC only. (B) SMS EPI reconstruction. The error maps are displayed at bottom at brightness ×5. GhC-SENSE led to strong artifacts with RMSE = 0.2359/0.0273 using 1D LPC/VC-SAKE reference, whereas the proposed method was dramatically better with RMSE = 0.0063. (C) The g-factor maps. Standard SENSE, GhC-SENSE and PEC-SENSE had very similar g-factor maps. Their mean/max g-factors were 1.061/1.182, 1.058/1.173, and 1.058/1.175, respectively.

the 2 slices were $2\pi \left[ \frac{0.2}{N_x} - 0.5 \left( \frac{x}{N_x} \right)^2 + 0.5 \left( \frac{x}{N_x} \right)^3 + 0.1 \frac{N_y}{N_x} \right] + 0.3 \left( \frac{x}{N_x} \right)^2 - 0.3 \left( \frac{x}{N_x} \right)^3$ and $2\pi \left[ 0.1 - 0.7 \frac{N_y}{N_x} - 0.3 \left( \frac{x}{N_x} \right)^2 + 0.3 \left( \frac{x}{N_x} \right)^3 + 0.2 \frac{N_y}{N_x} + 0.2 \left( \frac{x}{N_x} \right)^2 - 0.2 \left( \frac{x}{N_x} \right)^3 \right]$, respectively, where $x \in \left[ -\frac{N_x}{2}, \frac{N_x}{2} - 1 \right], y \in \left[ -\frac{N_y}{2}, \frac{N_y}{2} - 1 \right], N_x = N_y = 128$. Besides, inter-shot phase variation $2\pi \left[ -0.05 + 0.1 \frac{x}{N_x} - 0.2 \left( \frac{x}{N_x} \right)^2 + 0.2 \left( \frac{x}{N_x} \right)^3 - 0.1 \frac{N_y}{N_x} + 0.1 \left( \frac{x}{N_x} \right)^2 - 0.1 \left( \frac{x}{N_x} \right)^3 \right]$ was added to the single-band data. CAIPIRINHA shift was not used.

VC-SAKE was applied with 100 iterations and rank threshold 32, and all other parameters for VC-SAKE and ESPIRiT were identical to those used for the in vivo human brain data. Root mean squared errors (RMSE) were calculated to assess the overall quality of single-band ghost correction as well as the final SMS reconstruction. G-factor maps were computed to quantified noise amplification.

3 | RESULTS

Figure 3 compares VC-SAKE with 1D LPC and 2-frame PLACE on the rat brain single-band EPI data. 1D LPC failed to fully remove Nyquist ghosts, leaving severe residual artifacts overlapping with the true object. Consequently, coil sensitivity maps were erroneously estimated in the affected areas. In contrast, VC-SAKE dramatically improved the Nyquist ghost correction, leading to well-estimated coil sensitivity maps. The VC-SAKE corrected images and resulting coil sensitivity maps were essentially identical to 2-frame...
PLACE results, indicating that VC-SAKE is comparable to temporal-encoding-based methods regarding Nyquist ghost correction ability with the advantage of only a single reference acquisition.

The proposed phase error calibration on the rat brain data is demonstrated in Figure 4. As shown in Figure 4A, SENSE reconstructed positive- and negative-echo images had nearly identical magnitude but discrepant phase. No noticeable aliasing, Nyquist ghosts and other artifacts were observed. As displayed in Figure 4B, the proposed phase error maps were well estimated using ESPiRiT, whereas the raw phase error maps were rather noisy.

SMS EPI reconstruction of the rat brain data is shown in Figure 5. Using reference data corrected by 1D LPC (1D LPC reference) led to dark artifacts pointed by orange arrows in the first row. These artifacts disappeared in the second and third rows when VC-SAKE corrected reference data (VC-SAKE reference) were used. As pointed by blue arrows in the second row, even if VC-SAKE was used, GhC-SENSE reconstructed images still contained residual artifacts, which were directly caused by the 2D phase errors in SMS data. In the third row, the combination of VC-SAKE and PEC-SENSE effectively reduced all artifacts mentioned above. The necessity of phase error map denoising is illustrated in Supporting Information Figure S1, where raw phase error maps were used, leading to increased noise and spotty artifacts.

Figure 6 further compares PEC-SENSE with 2D LPC SENSE using the phantom data. As shown by the phase error maps in Figure 6A, this data set had strong nonlinear phase errors beyond 1D or even 2D linear distribution. To examine and compare phase error models, identical coil sensitivity maps obtained from VC-SAKE reference were used for all reconstruction methods. 2D LPC SENSE improved Nyquist ghost correction over GhC-SENSE, yet the residual artifacts were still visible. Only PEC-SENSE produced nearly artifact-free images.

Nyquist ghost correction of the human brain single-band reference data is demonstrated in Figure 7A. Residual Nyquist ghosts were found in the 1D LPC images, whereas they were almost completely removed by VC-SAKE. Apart from Nyquist ghosts, multiple-shot-related ghosts also resided in the 1D LPC images, which arose from the 2D nonlinear inter-shot phase variation shown in Supporting Information Figure S2B. Nevertheless, all ghosts were well corrected because VC-SAKE created virtual channels to account for positive- and negative-echo inconsistencies, as well as the inter-shot phase variation. The corresponding phase error maps are shown in Figure 7b. Although the phase errors could be largely 1D linear on some slices, 2D phase error components were present.

Figure 8 shows SMS reconstruction of the human brain data at MB = 2 and R = 2. Obvious artifacts were found using conventional 1D LPC reconstruction procedure (1D LPC reference). The proposed method (VC-SAKE reference + PEC-SENSE) eliminated these artifacts, leading to considerably improved image quality. SMS reconstruction and t-SNR maps of the human brain data at MB = 4 and R = 2 are displayed in Figure 9. Similar to MB = 2 results, 1D LPC reconstruction procedure suffered from ghost-related artifacts with t-SNR decrease in multiple areas. In contrast, the proposed method led to nearly artifact-free reconstruction and therefore improved t-SNR maps.

Figure 10 shows the simulation results with quantitative assessments. For ghost correction of the single-band data (Figure 10A), applying VC-SAKE effectively reduced the RMSE values from 0.0219 to 0.0077 as compared with 1D LPC only. For SMS reconstruction (Figure 10B), using 1D LPC reference and GhC-SENSE led to strong artifacts (RMSE = 0.2359). With VC-SAKE, GhC-SENSE result could be improved with yet the artifacts remained visible (RMSE = 0.0273). In contrast, the proposed method combining VC-SAKE and PEC-SENSE provided considerably better reconstruction (RMSE = 0.0063). As shown in Figure 10C, the g-factor maps from standard SENSE, GhC-SENSE and PEC-SENSE were very similar. Their mean/max g-factors were 1.061/1.182, 1.058/1.173, and 1.058/1.175, respectively, indicating that PEC-SENSE will not cause apparent increase of noise amplification with the typical phase error distribution.

4 | DISCUSSION

In this study, PEC-SENSE was applied to slice-dependent 2D Nyquist ghost correction in SMS EPI. More importantly, VC-SAKE was proposed to reconstruct ghost-free single-band EPI images and offered a general solution to remove not only Nyquist ghosts but also inter-shot phase variation for accurate coil sensitivity calibration. Their combination led to a considerably improved performance over slice-dependent 1D linear correction method under various experimental conditions, including different phase error patterns, acceleration factors, and channel numbers, as well as animal and human scanners.

The improvement made by the proposed method arises from both VC-SAKE enhanced coil sensitivity calibration and PEC-SENSE-based slice-dependent 2D Nyquist ghost correction. Their relative contribution depends on ghost characteristics in individual datasets. In this study, VC-SAKE and PEC-SENSE showed comparable contribution on reconstruction of the rat brain (Figure 5) and phantom data (Figure 6). When significant inter-shot phase variation occurred, the contribution from VC-SAKE could be more dominant (e.g., for the improved reconstruction of human brain data) (Figures 8 and 9). We used VC-SAKE and PEC-SENSE at
calibration and reconstruction stage, respectively, because of their own pros and cons. Specifically, VC-SAKE is self-referenced but requires fully sampled data and iterative computation, whereas PEC-SENSE needs coil sensitivity and phase error maps but can reconstruct accelerated data with efficient least-squares solutions.

### 4.1 Comparison with existing Nyquist ghost correction methods

Several recent SMS EPI reconstruction methods have considered slice-dependent Nyquist ghosts under 1D LPC framework and made improvements over slice-averaged correction. However, they cannot handle 2D phase errors, which are frequently encountered at high fields and cause artifact increase and SNR decrease as shown by the present study and others. It is possible to perform self-referenced 2D phase error correction with simplified phase error models and exhaustive parameter search. However, some data sets, such as the oblique phantom data in Figure 6, can contain highly nonlinear phase errors in both directions, in which case, simplified phase error models may cause residual artifacts.

As a potential alternative to VC-SAKE, temporally encoded EPI can be used to acquire single-band reference data and provide ghost-free coil sensitivity and phase error maps. Doing so takes twice the acquisition time than the proposed method at calibration stage, which is not necessarily a major issue for acquisition of time series (e.g., functional MRI). But, importantly, temporally encoded EPI is vulnerable to the inter-shot phase variation induced by physiological motions, which is difficult to correct for being nonlinear and random. In contrast, our proposed calibration using non-temporally-encoded EPI and VC-SAKE is inherently robust against this issue. When a multi-shot reference scan is needed, VC-SAKE can fully remove the potential inter-shot phase variation as demonstrated in Figure 7A and Supporting Information Figure S2. In this sense, VC-SAKE constitutes a post-processing-based alternative to FLEET technique, which reduces inter-shot phase variation by consecutively acquiring all shots within each slice. It is also possible to use double FOV EPI for ghost-free coil sensitivity and phase error calibration, but this approach inevitably incurs certain mismatch in eddy current and geometric distortion because of the smaller phase-encoding blips. It might be a choice only if the mismatch is insignificant.

VC-SAKE exploits low-rank properties of EPI positive and negative echoes. In principle, it is similar to the recently proposed ALOHA method, where the positive and negative echoes are organized into concatenated Hankel matrices with 2 levels of pyramidal decomposition. However, VC-SAKE is relatively simple in procedure and additionally accounts for inter-shot phase variation. Furthermore, VC-SAKE focuses on correcting the reference data, so it strategically avoids the computation burden associated with repetitive measurements (e.g., frames in functional MRI) and b-values and directions in diffusion-weighted imaging. Unlike original SAGE that was mostly demonstrated with random sampling, VC-SAKE is applied to Cartesian trajectory. Two crucial reasons have ensured its robustness. First, all missing data can be well initialized because of the fully sampled k-space and 1D LPC. According to our experience, VC-SAKE cannot converge if initialized with all zeros and converges slowly if initialized with uncorrected data. Second, all virtual channels are jointly estimated such that the data redundancy between positive and negative echoes is exploited. In general, many existing low-rank techniques can be adapted to Nyquist ghost correction. Their optimization and evaluation remain to be explored in future studies.

### 4.2 Noise robustness and flexibility of the proposed method

One may argue that the proposed phase error calibration in PEC-SENSE (Figure 2A) is subject to noise amplification during SENSE reconstruction of double in-plane accelerated data. This concern is negligible in most practical SMS EPI applications for the following reasons. First, the targeted SMS EPI acquisition with total acceleration MB × R is supposed to be affordable for the given coil array, therefore the SENSE reconstruction in Figure 2A with effective acceleration 1 × 2R (≤ MB × R) can be similarly or more easily achieved without pronounced noise amplification. Second, phase error maps can be effectively denoised by ESPIRiT or other filters under smoothness assumption. Third, the reference scan acquires multiple (i.e., R number of) shots with in-plane acceleration. Therefore, more positive- and negative-echo images are available for averaging to compensate for the increased noise amplification. For the final reconstruction, PEC-SENSE forms separate equations for positive and negative echoes yet all equations are jointly solved. As shown in Figure 10C with g-factor maps, the noise amplification is typically very similar to standard SENSE. More discussion of this issue can be found in several earlier studies.

It is possible to directly estimate phase error maps from VC-SAKE generated positive- and negative-echo images (Figure 1). However, we consider the proposed SENSE-based phase error calibration (Figure 2A) to be more flexible and extensible. First, VC-SAKE usually corrects central k-space only, therefore the produced images may be over-smoothed and degrade nonlinear phase error measurements. Second, the SENSE-based phase error calibration can be easily re-done or repeated if necessary. For example, gradient coil heating may cause phase error change in multi-trial
experiments such as functional MRI, yet coil sensitivity maps can be mostly unaffected and be re-used to update phase error maps. Third, it is possible to integrate the SENSE-based phase error calibration with alternative reference scans. For example, if FLASH\textsuperscript{12,38} or single-band EPI with mismatching acquisition parameters\textsuperscript{8} is used for coil sensitivity calibration, phase error maps can still be derived using such coil sensitivity maps together with a single EPI shot acquired with matching parameters.

We used ESPiRiT to denoise the phase error maps. In our experience, use of kernel size from $6 \times 6$ to $9 \times 9$ and null-space threshold of 0.001 can consistently provide decent results for typical data sets.\textsuperscript{30} For very noisy data (e.g., with high in-plane acceleration), relatively small kernel size and high null-space threshold can be used to derive smoother phase error maps. However, caution should be taken here as this may compromise the estimation accuracy of nonlinear phase errors to some extent.

### 4.3 Computational efficiency of the proposed method

Using a personal desktop (4-core i7-4790K CPU and 32-GB RAM) and MATLAB 2016, VC-SAKE took $\sim 5/120$ s per slice for 2-shot 4/32-channel data using $48 \times 48$ k-space, yet the time could be dramatically reduced to $\sim 1/5$ s using $24 \times 24$ k-space with sufficient coil sensitivity map quality.\textsuperscript{31} For SMS reconstruction, PEC-SENSE took $\sim 15$ s for the 50-frame data in Figure 9. With coil compression\textsuperscript{39,40} and numerical optimization,\textsuperscript{41,42} the entire procedure may achieve near real-time reconstruction.

### 4.4 Future studies

The proposed VC-SAKE procedure remains to be systematically optimized for parameters including kernel size, rank threshold and iteration numbers. Future studies may investigate the feasibility of automatic parameter determination, e.g., based on signal-ghost ratio\textsuperscript{35} or image entropy.\textsuperscript{17} Further, nonstationary Nyquist ghosts may remain as a challenge because of the fixed reference data. If multiband and in-plane acceleration factors are low, phase error maps can be dynamically updated for frames by separately reconstructing their positive and negative echoes before joint reconstruction.\textsuperscript{11} For nonstationary Nyquist ghost correction at high acceleration factors, simultaneously applying low-rank and coil sensitivity constraints\textsuperscript{29} may offer a promising direction for exploration in the future.

It is also possible to adapt the proposed method to GRAPPA-based implementation.\textsuperscript{1,6,8,43} The VC-SAKE corrected single-band images can be Fourier transformed into k-space with and without multiplying the phase error maps, synthesizing the autocalibration signal (ACS) lines for positive and negative echoes. A similar strategy has been adopted in dual-polarity GRAPPA,\textsuperscript{10,44} yet the k-space implementation of our proposed method will not require temporally encoded scans.

### 5 CONCLUSION

2D Nyquist ghosts not only directly contaminate simultaneous multislice EPI data, but also degrade the EPI-based coil sensitivity calibration. The proposed virtual coil SAKE can correct 2D Nyquist ghosts as well as inter-shot phase variation for accurate coil sensitivity calibration, whereas the proposed PEC-SENSE enables slice-dependent 2D Nyquist ghost correction for the final reconstruction. Such combination of virtual coil SAKE and PEC-SENSE can substantially reduce all ghost-related artifacts originating either directly from SMS EPI data or indirectly from coil sensitivity maps. This general approach can be readily applied to all SMS EPI-based applications, including functional MRI and diffusion-weighted imaging.

### ACKNOWLEDGMENTS

This work was supported by the Hong Kong Research Grant Council (grants C7048-16G and HKU17103015 to E.X.W.), Lam Woo Foundation (to E.X.W.), and Australian Research Council (Future Fellowship FT140100865 to M.B.). We thank BART developers, Dr. Michael S. Hansen of US National Institutes of Health and Dr. W. Scott Hoge of Brigham and Women’s Hospital and Harvard Medical School for sharing the code and toolboxes online. We also thank Dr. Jonathon Polimeni of Athinoulia A. Martinos Center for Biomedical Imaging of Harvard Medical School for the helpful discussions.

### ORCID

Markus Barth \(\text{http://orcid.org/0000-0002-0520-1843}\)

### REFERENCES


**SUPPORTING INFORMATION**

Additional Supporting Information may be found in the online version of this article.

**FIGURE S1.** (A) Differences between the phase error maps in Figure 4B. Results are presented with 2 display ranges. Differences between the proposed phase error maps and raw maps were mostly noise. In addition, the proposed phase error maps successfully captured the 2D phase error components missing in the 1D linear maps. (B) Similar to the third row in Figure 5 but using raw phase error maps without any denoising. Increased noise and spotty artifacts were observed as indicated by the boxes and circles, respectively.

**FIGURE S2.** Examination of residual phase errors and inter-shot phase variation in VC-SAKE corrected single-band human brain data. SENSE was applied to separately reconstruct the 2 readout polarities of the 2 shots using central $48 \times 48$ k-space, and their raw phase differences were calculated. For comparison, the same reconstruction and calculation were applied to uncorrected and 1D LPC single-band data using $128 \times 128$ and $48 \times 48$ central k-space. (A) Raw phase error maps between positive- and negative-echo images for each shot. The results from the 2 shots were consistent. Positive- and negative-echo phase errors were nearly invisible after VC-SAKE, whereas they were more or less presented in uncorrected and 1D LPC data. (B) Raw inter-shot phase variation maps for each readout polarity. The results from the 2 readout polarities were consistent. Inter-shot phase variation was almost fully removed by VC-SAKE, whereas it remained detectable after 1D LPC. Altogether, the results in (A) and (B) suggest that the human brain data contained not only positive- and negative-echo phase errors but also inter-shot phase variation, and they were both well corrected by VC-SAKE.

**How to cite this article:** Lyu M, Barth M, Xie VB, et al. Robust SENSE reconstruction of simultaneous multislice EPI with low-rank enhanced coil sensitivity calibration and slice-dependent 2D Nyquist ghost correction. *Magn Reson Med.* 2018;00:1–15. [https://doi.org/10.1002/mrm.27120](https://doi.org/10.1002/mrm.27120)