Published in final edited form as:

Magn Reson Med. 2014 July ; 72(1): 93–102. doi:10.1002/mrm.24898.

Inter-slice Leakage Artifact Reduction Technique for Simultaneous Multi-Slice Acquisitions

Stephen F. Cauley¹, Jonathan R. Polimeni^{1,2}, Himanshu Bhat³, Dingxin Wang³, Lawrence L. Wald^{1,2,4}, and Kawin Setsompop^{1,2}

¹Athinoula A. Martinos Center for Biomedical Imaging, MGH, Charlestown, MA, USA

²Dept. of Radiology, Harvard Medical School, Boston, MA, USA

³Siemens Medical Solutions Inc, Malvern, PA, USA

⁴Harvard-MIT Division of Health Sciences and Technology, MIT, Cambridge, MA USA

Abstract

Purpose—Controlled aliasing techniques for simultaneously acquired EPI slices have been shown to significantly increase the temporal efficiency for both diffusion-weighted imaging (DWI) and fMRI studies. The “slice-GRAPPA” (SG) method has been widely used to reconstruct such data. We investigate robust optimization techniques for SG to ensure image reconstruction accuracy through a reduction of leakage artifacts.

Methods—Split slice-GRAPPA (SP-SG) is proposed as an alternative kernel optimization method. The performance of SP-SG is compared to standard SG using data collected on a spherical phantom and in-vivo on two subjects at 3T. Slice accelerated and non-accelerated data were collected for a spin-echo diffusion weighted acquisition. Signal leakage metrics and time-series SNR were used to quantify the performance of the kernel fitting approaches.

Results—The SP-SG optimization strategy significantly reduces leakage artifacts for both phantom and in-vivo acquisitions. In addition, a significant boost in time-series SNR for in-vivo diffusion weighted acquisitions with in-plane 2× and slice 3× accelerations was observed with the SP-SG approach.

Conclusion—By minimizing the influence of leakage artifacts during the training of slice-GRAPPA kernels, we have significantly improved reconstruction accuracy. Our robust kernel fitting strategy should enable better reconstruction accuracy and higher slice-acceleration across many applications.

Introduction

Single-shot two-dimensional (2D) EPI acquisition methods are routinely used for both diffusion-weighted and fMRI studies. Several methods for acceleration have been explored to reduce the long TR associated with high resolution full brain coverage imaging. Accelerated 2D parallel imaging techniques such as [1-3] are used to remove phase

encoding steps during an acquisition. While these methods have many benefits, such as a reduction of image distortion and T2* blurring, they cannot be used to shorten TR significantly as the TE value depends on the particular form of image contrast. Simultaneously acquiring multiple slices can significantly reduce the time required to acquire a fixed number of slices. This is accomplished through imaging multiple slices during a shared readout time. Due to the fact that the k-space lines are fully sampled, the simultaneously acquired slices do not exhibit typical $\sqrt{R}$ reductions in SNR observed with conventional parallel imaging acceleration techniques. Attempts have been made using wideband imaging [4, 5], simultaneous echo refocusing SER [6, 7], and parallel image reconstruction for simultaneously acquired multiple slices (SMS) [8-11]. Parallel imaging methods that incorporate SER have also been introduced for fMRI and diffusion applications [12, 13].

SMS is a promising parallel imaging modality that has been shown to work well when the simultaneously acquired slices have substantial distance between them. However, for brain imaging the smaller FOV along the slice direction limits the distance factor and the simultaneously acquired slices are more difficult to separate. Controlled aliasing (CAIPI) techniques have been introduced in [9] to perform shifts across the slices to more easily unalias the accelerated data. This method requires applying phase shifted RF pulses for excitation of each k-space line, which prohibits use of the method with EPI. The EPI compatible approach based on the wideband method [10] created CAIPI-like effects between excited slices. However, this method resulted in undesirably large voxel tilting artifacts. A recent work [14] examined using blipped-CAIPI to achieve spatial shifts in the PE direction, between simultaneously excited slices to avoid voxel tilting artifacts. This has enabled SMS acquisitions with high acceleration factors with a low g-factor penalty; allowing for significant gains in the temporal efficiency of diffusion imaging and fMRI acquisitions.

SENSE/GRAPPA [15], slice-GRAPPA (SG) [14], and auto-calibrating CAIPI [16] were proposed as k-space based methods for the reconstruction of CAIPI acquisitions. In this work we focus on the improvement of SG. Similar to GRAPPA [3], the SG method uses training data to fit a linear model that is used to unalias the simultaneously acquired slices. With SG, distinct kernels are used to unalias each of the simultaneously acquired imaging slices. It was illustrated in [14] that the fitted SG kernels showed a strong dependence on the static coil sensitivity profiles and not on the training data image contrast. This is a desirable property that allows the SG kernels to be used to accurately unalias SMS data that can have different contrast from the training data, e.g. in the case of diffusion encoding. However, in this work we will show that when using high slice acceleration together with in-plane accelerations the contrast independent property of the SG kernels will suffer. This results in an increased dependency of the kernels on the training data image contrast and causes increased signal leakage between the unaliased simultaneously acquired slices.

Signal leakage artifacts can have a significant impact on the data quality for fMRI and diffusion imaging acquisitions. The concept of signal leakage with its associated calculation and quantification was introduced in [17]. The L-factor metric was proposed to characterize the leakage signal through Monte Carlo simulation. The L-factor analysis begins with a

unique small frequency modulated signal being added to each of the imaging slices that are being acquired simultaneously. A frequency analysis of the slice-unaliased Monte Carlo time-series signal is used to determine the leakage artifact of the SMS slices. This artifact will appear at the unique frequencies added to the data in the simulation. We propose an improvement to the leakage characterization through the use of an alternative approach for calculating the leakage artifact. This method relies on the linearity of the image reconstruction process in order to rapidly calculate a leakage metric. Specifically, we show that linearity makes the addition of small frequencies in a simulation framework unnecessary for leakage analysis.

The main contribution of this work is an alternative optimization model for the fitting of SG kernels to reduce dependencies on image contrast and the associated signal leakage artifacts. We termed this technique “Split slice-GRAPPA” (SP-SG). While the standard SG kernel fitting produces kernels that minimize the image artifact, the SP-SG method takes a more balanced approach. The SP-SG method simultaneously minimizes errors coming from both image artifacts and leakage. This is accomplished by forming a new kernel fitting objective function to consider the importance of both sources of error. The benefits of SP-SG are illustrated through several human subject diffusion experiments. In particular, the robustness of the fitting kernel across b-values is demonstrated through reductions in artifacts and improved SNR. Based on this work, the SP-SG method has the potential to enable a more robust and less artifact prone SMS acquisitions at high acceleration factors. This should facilitate further improvements in temporal efficiency of fMRI and diffusion imaging acquisitions.

Theory

The slice-GRAPPA method is based upon a linear convolution model similar to the GRAPPA strategy used for in-plane acceleration. We begin by briefly reviewing the SG method for SMS acquisitions. We then examine the relationship between fitting errors for the SG kernels and inter-slice leakage. Here, we summarize the existing “L-factor” method that uses frequency analysis to produce a leakage metric. In addition, we offer a related artifact metric that can be more efficiently computed and is less sensitive to image phase variations. Finally, we introduce an alternative kernel optimization model for SG that is formulated to reduce the influence of inter-slice leakage artifacts.

Slice-GRAPPA Reconstruction

The channel j data from slice z can be described as the product of coil sensitivities $C_{j,z}(x, y)$ and a true magnetization $\rho_z(x, y)$. The simultaneously acquired multiple slices can be unaliased using SG reconstruction. SG reconstruction relies on the following relationship between all channel data from the aliased images:

$$I_{j,z}(x, y) = C_{j,z}(x, y) \rho_z(x, y) \approx \sum_{\ell=1}^L \left(\sum_{s=1}^S I_{\ell,s}(x, y) \right) K_{\ell,j,z}(x, y). \quad (1)$$

The fitting of the kernel parameters $K_{l,j,z}(x, y)$ can be calculated efficiently by first transforming (1) into k-space. Here, the kernel parameters are dependent on the total number of channels L and number of SMS slices S . By forming convolution matrices M_z across all channels for a given SMS slice z , the aliased SMS slices are written into the following system of equations:

$$(M_1 + M_2 + \cdots + M_S) K_{j,z} = I_{j,z}. \quad (2)$$

Here, we use the notation $I_{j,z}$ and $K_{j,z}$ to represent the vector form of the images and kernels respectively.

The explicit least squares solution of the SG formulation (2) is:

$$K_{j,z} = \left(\left(\sum_{s=1}^S M_s \right)^* \left(\sum_{s=1}^S M_s \right) \right)^{-1} \left(\sum_{s=1}^S M_s \right)^* I_{j,z}. \quad (3)$$

After the kernels have been determined they can be applied to each SMS data set. There is a trade-off between the memory required to store all of the kernels and computational cost to apply them. The most memory efficient method is to apply the kernels in k-space. This can be done by forming new 2D convolution matrices and performing the matrix-vector multiplication shown in (2). Alternatively, by transforming the kernels into image space they can be applied directly to the SMS channel data using (1).

When analyzing the quality of SG kernel fitting the typical metric would be to consider only the total artifact for the training data, i.e. the residual error in (2). However, this metric does not take into account that image contrast and structure will vary across a time series of images reconstructed with a fixed kernel, e.g. different b-values for diffusion weighted studies. As will be shown, fitting a robust kernel will allow for a trade-off between initial fitting error and stability across a wide range of image contrast. We now formalize representative metrics for inter-slice leakage artifacts that can be used to evaluate the quality of the fitted kernels.

Inter-slice Leakage Estimation

In [17] the authors introduced the “L-factor” procedure for analyzing inter-slice leakage artifacts of SMS acquisitions. The L-factor procedure utilizes Monte Carlo time-series analysis in conjunction with frequency modulated small signal perturbation. For simplicity we will refer to the method as the Frequency Modulation/Monte Carlo (FMMC) approach. The FMMC generates slice-aliased time-series data with an imposed slice-dependent sinusoidal modulation in time, see Figure 1 for an illustration of the two slice case. Here, channel j data for slice z , denoted as $I_{j,z}$, is modulated by the sinusoidal term $1 + \alpha \cos(\omega_z t)$. A CAIPI-like shift is applied to all of the channel data before the slices are aliased. SG fitted kernels $K_{j,z}$ can then be applied to produce estimates for each channel j and slice z . The channel estimates for each slice can subsequently be combined to form estimates of the slices. Assuming the kernel does not fully block inter-slice leakage one would expect to see ω_1 dependent frequency terms in the slice 2 estimate and ω_2 dependent terms in slice 1. Therefore, using frequency analysis each slice estimate can be separated into a pass-through

image for a slice z , $\tilde{I}_{z \rightarrow z}$, and leakage terms coming from all the other slices s onto slice z , $L_{s \rightarrow z}$.

We present an alternative, but related, metric for leakage that is motivated by the desired SG kernel properties presented in [14]. This method can be viewed as an update to the L-factor method that provides a more accurate representation of leakage artifacts. Specifically, an ideal fitting kernel $K_{l,j,z}$ will only allow for data from the slice of interest z to contribute:

$$0 = I_{l,s}(x, y) K_{l,j,z}(x, y), \quad s \neq z, \quad \ell = 1, \dots, L. \quad (4)$$

Thus, the Linear System Leakage Approach (LSLA) illustrated in Figure 1 individually passes each channel j data from all slices z through the SG kernels $K_{j,z}$. This directly results in a pass-through image $I_{z \rightarrow z}$ and leakage terms $L_{s \rightarrow z}$. LSLA utilizes the fact that each stage of the image reconstruction will be linear (including the coil sensitivity weighted combination). Linearity allows for each component of the slice-aliased signal to be analyzed separately, thereby bypassing the time-consuming time-series/frequency component analysis of FMMC. *We note that the pass-through and leakage signal calculated by the FMMC and LSLA methods are not identical but are related.* Their relationship can be understood by the vector diagram in Figure 1. Here, the LSLA estimate for slice 1 is created by combining the pass-through image from slice 1 and leakage signal components from slice 2,

$I'_1 = I_{1 \rightarrow 1} + L_{2 \rightarrow 1}$. In FMMC, a small sinusoidal modulation of amplitude α is imposed on the slice 2 data. This would create a modulation of amplitude $\alpha L_{2 \rightarrow 1}$ on the leakage signal (green arrow) parallel to $L_{2 \rightarrow 1}$. Based upon the relative phase difference θ between I'_1 and $L_{2 \rightarrow 1}$, taking the magnitude of the coil combined image and performing the FMMC analysis will result in a scaling factor of $\alpha L_{2 \rightarrow 1} \cos(\theta)$. Therefore, the leakage calculated using FMMC and LSLA are related by $L_{2 \rightarrow 1} = L_{2 \rightarrow 1} \cos(\theta)$ (Both methods were implemented and this relationship was verified). This informs us that the leakage from FMMC is dependent on the relative phase between the slices. In fMRI acquisitions, spatially varying phase evolution can occur due to drift, cardiac/respiratory changes, and fMRI activation, while in diffusion imaging, small amounts of tissue motion can lead to dramatic phase changes. The leakage calculated from LSLA does not depend on the relative phase between the slice's signal and thereby provides a less biased metric.

Having described the leakage metrics, we will now motivate our alternative kernel optimization SP-SG model through comparison with the standard SG model. The drawback of the SG approach will be explained through the use of pass-through and leakage notation defined within the LSLA framework. In this context, the total image artifact for the first slice from a two slice multi-band accelerated (MB=2) acquisition will be defined using the true image I_1 :

$$\begin{aligned} E_{total} &= \|I_1 - I'_1\| = \|(I_1 - I_{1 \rightarrow 1}) - L_{2 \rightarrow 1}\| \\ &\leq \|I_1 - I_{1 \rightarrow 1}\| + \|L_{2 \rightarrow 1}\| \\ &= E_{intra} + E_{inter} \end{aligned} \quad (5)$$

The intra-slice error (E_{intra}) is associated with the estimation error between the pass-through signal and the true image. The inter-slice error (E_{inter}) corresponds directly to the leakage components. In standard SG, the kernels minimize the total image artifact by reducing the total error shown in (5). However, reducing the total artifact without placing restrictions on the intra- and inter-slice artifacts can lead to a dependency on artifact cancellations. With the SG method the intra- and inter-slice artifacts might be arbitrarily large but combine to help reduce the total artifact, i.e. the leakage component $L_{2 \rightarrow 1}$ can be tailored to match (but of opposite sign) the intra-slice artifact ($I_1 - I_{1 \rightarrow 1}$). However, changes to inter-slice relationships observed across a time-series of images can disturb this condition and result in larger total error.

Split Slice-GRAPPA Reconstruction

We begin by re-formulating the SG formulation (2) in order to balance each possible artifact:

$$\begin{pmatrix} M_1 \\ \vdots \\ M_z \\ \vdots \\ M_S \end{pmatrix} K_{j,z} = \begin{pmatrix} 0 \\ \vdots \\ I_{j,z} \\ \vdots \\ 0 \end{pmatrix}. \quad (6)$$

This unconstrained optimization can be solved in the least squares sense, where the explicit solution will have the form:

$$K_{j,z} = \left(\sum_{s=1}^S M_s^* M_s \right)^{-1} M_z^* I_{j,z}. \quad (7)$$

This solution differs from the solution to the SG formulation (3) in both the projection operation as well the Semi-positive Definite (SPD) matrix used to describe the kernel. The SPD matrix shown in (7) requires forming individual correlation matrices based upon each slice calibration matrix, i.e. $M_s^* M_s$ for each slice s . This is an additional computational cost when compared to (3). However, the time to actually solve for the fitting kernels will be identical as it involves a pseudo-inverse operation with the same number of kernel parameters. We will refer to the method (6) as the split slice-GRAPPA (SP-SG) solution based upon the optimization across concatenated/split slices as opposed to the optimization across the aliased slices in SG. Specifically, in the SP-SG formulation, for each channel, the intra-slice artifact $M_z K_{j,z} - I_{j,z}$ is weighted against each inter-slice artifact $M_s K_{j,z}$ from a slice $s \neq z$.

Note that the SP-SG formulation will result in higher total artifact error (5). That is, for SG reconstruction each convolution matrix M_s will directly contribute toward reducing the RMSE while no condition is placed on the inter-slice artifact $M_s K_{j,z}$ from a slice $s \neq z$. For SP-SG reconstruction we attempt to limit the influence of inter-slice artifacts with the desired condition of $M_s K_{j,z} = 0, s \neq z$. This additional condition for SP-SG can increase the

kernel fitting RMSE with respect to the SG objective. However, with the SG method, using all of the slice convolution matrices M_s to improve the kernel fitting RMSE can result in artifacts during the application of those kernels to images with different contrasts. This is caused by changes in the inter-slice leakage that no longer contribute toward reducing RMSE. By limiting the dependency on inter-slice leakage artifacts during the training process the SP-SG method is less vulnerable to produce artifacts based upon image contrast change. Note that the trade-off between the intra- and inter-slice artifacts can be tuned through a generalization of the SP-SG formulation that adds weighting parameters α :

$$\begin{pmatrix} \alpha_1 M_1 \\ \vdots \\ \alpha_z M_z \\ \vdots \\ \alpha_S M_S \end{pmatrix} K_{j,z} = \begin{pmatrix} 0 \\ \vdots \\ \alpha_z I_{j,z} \\ \vdots \\ 0 \end{pmatrix}. \quad (8)$$

Methods

In order to accurately compare the SG method against the proposed SP-SG model, experiments were performed in both a spherical water phantom and in two human subjects. The experiments were designed to highlight the importance of inter-slice and intra-slice artifacts as well as to examine time series SNR. Institutionally approved protocol consent was obtained from the two healthy subjects prior to the experiments being performed. All acquisitions were completed on the MGH-UCLA 3T Siemens Skyra CONNECTOM scanner equipped with the AS302 “Connectom” gradient with $G_{\max} = 300\text{mT} / \text{m}$ and Slew = $200\text{T} / \text{m} / \text{s}$. A custom-built 64-channel RF head array [18] was used for reception. For all experiments the Stejskal-Tanner diffusion single-shot EPI acquisition was used.

The first experiment was performed on a uniform spherical water phantom to demonstrate the significant increase in total artifact error that can result with changes to image contrast. The uniform water phantom produces images with similar but not identical image characteristics for the slices that are to be aliased in a SMS acquisition. That is, there will be a substantial overlap between the convolution matrices for two SMS slices s and z . This situation will create a strong dependence on the training image contrast for the SG kernels, which can cause contrast dependent leakage artifacts that result in a large total artifact error across a time-series. To examine this proposition, the training data for the SG kernels were acquired with no diffusion encoding and the SMS acquisition performed at $b = 1000\text{s/mm}^2$, where significant spatial phase and some magnitude variations will occur. The imaging parameters were $200 \times 200\text{mm}^2$ FOV, 2.0mm isotropic resolution, 63 slices with a MB factor of 3, FOV/3 shift between the simultaneously acquired slices, in-plane acceleration factor of 2, no partial Fourier, and TE/TR = 62ms/3s. The training data was acquired across each individual slice with the same imaging parameters except the TR = 9s. The training data was used to fit the kernels for both the SG and SP-SG models, and the resulting unaliasing performance was compared at $b = 1000\text{s/mm}^2$.

Data was collected in-vivo on two subjects. For the first subject, a time-series of non-slice accelerated diffusion data was acquired and used to quantify the total image artifact, intra-slice artifact, and inter-slice leakage artifact for both the SG and SP-SG models. The imaging parameters were $220 \times 220 \text{ mm}^2$ FOV, 2.0mm isotropic resolution, in-plane acceleration factor of 2, no partial Fourier, $b = 3000 \text{ s/mm}^2$, 63 slices, and $\text{TE/TR} = 80 \text{ ms/8s}$. 64 repetitions were acquired along a single diffusion direction and an initial $b = 0 \text{ s/mm}^2$ image was used as training data for both the SG and SP-SG kernel fitting. For total image artifact calculation, the unaccelerated slice data was used to synthesize a MB=3 acquisition with FOV/3 inter-slice shift. The accelerated data was then unaliased using either the SG or SP-SG kernels to produce the estimate of the single slice data. This estimate was then compared to the original unaccelerated slices to calculate the total image artifact. In addition, the LSLA technique was used for intra- and inter-slice artifact estimation. Here, the SG and SP-SG kernels were applied to each single slice independently. In all cases, the average artifact maps were calculated from averaging across the 64 repetitions. The temporal averaging was performed on the magnitude of the artifact in order to avoid issues with averaging across data with large shot-to-shot phase variation (caused by small motion during diffusion encoding).

For the second subject, a time-series of MB=3 diffusion encoded data was collected to examine the difference in time-series SNR produced by the kernel fitting strategies. The MB=3 acquisition included 50 repetitions at $b = 0 \text{ s/mm}^2$ followed by 50 repetitions at $b = 1000 \text{ s/mm}^2$ (with the diffusion encoding direction remaining unchanged throughout the acquisition). The imaging parameters were the same as those used for the first subject, but with a $\text{TE/TR} = 66 \text{ ms/3s}$. A inter-slice shift of FOV/3 was imposed on the simultaneously acquired slices.

All of the data was processed through online reconstruction, where the standard vendor's implementation of in-plane GRAPPA and complex coil combination were used. The vendor's coil combination assumes a fixed set of coil sensitivities that are acquired through a adjustment acquisition prior to the experiments. The acquired low-res array coil images are divided by the body coil image to produce smooth sensitivity maps. These complex coil sensitivity maps are used through a linear set of operations to combine all coil data. In all cases, in-plane GRAPPA was applied after the slice unaliasing was performed using either the SG or SP-SG kernels. The synthesis of accelerated data and the estimation of the intra- and inter-slice artifacts (computed using the LSLA technique) were also performed online. The time-series results for each subject were independently registered for comparison using FSL-FLIRT motion correction [19].

Results

Figure 2(A) shows the results of SG reconstruction of MB=3 phantom data at $b = 1000 \text{ s/mm}^2$, where significant residual slice-aliasing artifacts can be observed in most slices of the phantom. In comparison, Figure 2(B) shows the increased uniformity and reduced artifacts for the SP-SG reconstruction. It is important to note that this is a difficult reconstruction case due to the small contrast differences between the simultaneously acquired slices.

Using in-vivo data from subject one, Figure 3(A) highlights the significant amount of similarity in the calibration matrices for simultaneously acquired slices, for MB=3 training data (with an in-plane acceleration factor of 2). The magnitude of the 64 largest singular values are plotted for each slice calibration matrix M_i . Additionally, the singular values are recalculated for each slice calibration matrix after excluding the range from each M_j , $i \neq j$. The substantial decrease in singular values for each M_i demonstrates the strong linear dependence between the slice calibration matrices across different MB factors. This has the potential to cause significant signal leakage artifacts when the standard SG kernel model is used.

Figure 3(B) illustrates the fitting error trade-off between the SG and SP-SG strategies, using in-vivo data from subject one. The figure shows the differences in the total artifact and inter-slice artifact errors for the two methods. The mean error is computed across each receive channel and the SMS slices for the training data. For all channels, the total artifact error is decreased for the SG method while the inter-slice error is decreased for the SP-SG method. This highlights the difference in the optimization model for the two methods: *the SP-SG method trades-off higher total artifact error in the training data for reduction in leakage.*

Comparisons of the time-series artifacts from the SG and SP-SG models, using the data from subject one, are shown in Figure 4 and Figure 5. Figure 4 compares the temporal average total artifact error at $b = 3000\text{s/mm}^2$ for the SG and SP-SG models. The error is computed for the center slice group of the MB=3 acquisition. Of the MB=3 slices groups, the center group contains that highest artifact error for both models and was chosen to highlight the largest error level in the acquisition. The average total artifact errors are shown starting at an intensity value of 10, which was determined to be slightly above the estimated noise level for the time-series magnitude image, see Figure 4(D). Significant total artifact reductions can be observed for the SP-SG model, in comparison to the SG model, when applied to this diffusion encoded image time-series (6.8% reduction in the mean artifact level). Figure 5 shows the inter- and intra-slice artifact error for the center slice group, using the SG and SP-SG methods. Significant intra-slice and inter-slice leakage error can be observed when the standard SG model is used. The SP-SG method reduces the mean intra-slice error from 8.7 to 5.7 and the mean inter-slice leakage errors from 9.2 to 5.5 and from 9.7 to 5.5.

Figure 6 shows the magnitude and phase of a representative aliased slice group that was used to generate the artifact maps in Figure 4 and Figure 5. Here, images from three consecutive repetitions for the three slices are shown. While the magnitude images do not exhibit significant variation across the repetitions, large variations can be observed in the phase images. In addition, the temporal phase variations across the slices are extremely different.

Figure 7 contains a comparison of the SNR for the SP-SG and SG reconstructions of the MB=3 acquisition performed on the second subject. Figure 7(A) shows the ratio of the SNR at $b = 0\text{s/mm}^2$ for the center slice group and Figure 7(B) shows this result at $b = 1000\text{s/mm}^2$. At $b = 0\text{s/mm}^2$, small deviations from the SNR ratio of 1 are observable. However, the average SNR ratio for this non-diffusion weighted image series is approximately one.

When considering the case of $b = 1000 \text{ s} / \text{mm}^2$, a much larger deviation in SNR ratio can be observed, with the SP-SG method exhibiting over 10% gains in SNR for many areas.

Discussion and Conclusion

In this work, the SP-SG method has been proposed as an alternative to train slice-GRAPPA kernels. The SP-SG model is formulated to improve the reconstruction of simultaneous multi-slice acquisitions. The development of SP-SG has been motivated by the LSLA leakage calculation model, which has also been proposed as part of this work to allow for the rapid and accurate analysis of signal leakage. The SP-SG method has been shown to significantly reduce image artifacts for phantom and in-vivo acquisitions. It was also demonstrated that the SP-SG technique can provide a significant boost in time-series SNR for in-vivo diffusion weighted SMS acquisitions. We demonstrate this improvement in SNR through acquisitions that combine an in-plane acceleration factor of 2 and MB=3 for a total acceleration of 6. We have focused on this type of 6 fold acceleration, since in-plane acceleration is widely used in diffusion acquisitions to reduce image distortion, while not significantly affecting the SNR (for low in-plane acceleration factors, the SNR lost from in-plane acceleration is generally smaller than, or comparable to, a SNR gain from TE reduction [20]). In-plane acceleration reduces the effective amount of PE shift that can be applied in a SMS acquisition. In this work, a FOV/3 shift was used within the in-plane accelerated “reduced” FOV. This corresponds to a FOV/6 shift in the full FOV, which results in relatively small distances between the aliased voxels. Therefore, with our combined acceleration approach, we expect the contrast dependency property of the SG kernel to be similar to MB=6 acquisitions with no in-plane acceleration (and significantly larger than the MB=3 only case).

The first subject in-vivo experiment was used to analyze the kernel fitting process. It was observed that during the kernel fitting the standard SG method results in less total artifact error than the SP-SG method. This is a result of the SP-SG method trading-off the total artifact error for reduced leakage error, as highlighted in Figure 3(B). In the diffusion weighted time-series data, where the image contrast differs significantly from the training data, reducing leakage during the kernel fitting corresponded to a smaller total artifact error. The improvement of the SP-SG method over the standard SG method is shown in Figure 4. The larger total artifact error for the SG optimization formulation is caused by a dependence on leakage in the kernel fitting. In diffusion time-series data, where the image contrast has changed, the leakage signal will no longer contribute correctly to forming the image and reducing the total artifact error. The SP-SG method explicitly optimizes the kernels to minimize the leakage error rather than the total error. This will allow for more accurate reconstruction of diffusion-weighted acquisition with high slice and in-plane accelerations.

It is important to note that, with the SP-SG method, we have effectively constrained both magnitude and phase variations from contributing to the leakage signal. First, there is a significant difference in magnitude images when comparing the fitting data acquired at $b=0$ and the higher b -values used for the time series. In addition, at high b -values bulk motion, dynamic blood flow changes, and non-rigid tissue related pulsatility during the diffusion encoding can cause large spatially varying changes to the image phase. If leakage due to

variations in only the magnitude or in only the phase were constrained for the kernel calculation, the resulting kernels are unlikely to be robust for standard DWI protocols where both can change rapidly from shot-to-shot. Finally, by removing contrast dependencies, with respect to the training data, the SP-SG method makes the kernels primarily dependent on the coil sensitivities. This could potentially reduce the effects of small motion, during the data acquisition, on the reconstruction accuracy.

In this work, the analysis of the image artifacts was performed on an in-vivo diffusion weighted dataset. In high b-value diffusion weighted acquisitions, the spatial variation of image phase can change significantly from shot to shot, see Figure 6. The total artifact error for the reconstruction of SMS slices is dependent on the interaction between the inter- and intra-slice artifacts. Therefore, spatial phase variations can cause a significant change in the interaction of these artifacts across a time-series. The resulting changes to the artifacts can lead to a significant increase in total artifact error across the time-series. These variations were mainly caused by differences in motion due to cardiac and respiratory activity. Therefore, accurate calculation of the temporal average for the total artifact error can only be obtained using in-vivo datasets with realistic temporal phase variation.

A decrease in temporal variation of the total artifact error will result in an increase to the time-series SNR. Figure 7 illustrates the potential increase in SNR when employing the SP-SG method. In a non-diffusion weighted acquisition ($b = 0 \text{ s} / \text{mm}^2$), with no significant change to image contrast/phase in the time-series, the total artifact error does not change significantly. Thus, the SNR ratio between SP-SG and SG methods is close to one in all spatial locations. For the $b = 1000 \text{ s} / \text{mm}^2$ acquisition, with significant variation to image phase, the total artifact variation of the SG reconstruction will be larger than the total artifact variation of the SP-SG reconstruction. This is reflected in a SNR ratio that on average is significantly above one.

In fMRI acquisitions the image contrast does not change significantly for a time-series. Therefore, the total artifact error of the standard SG method should be lower than that from the SP-SG method. However, the SG method will still result in more signal leakage because of the kernel fitting dependency. Signal leakage can cause fMRI activation from one slice to leak into another, resulting in false positives in the detected functional activation. In [17] the authors performed a detailed analysis of signal leakage using the FMMC model. The L-factor was used as a metric to describe the leakage level and also as a guide in choosing acceptable slice-acceleration factors for a given protocol. With the reduction in signal leakage afforded by the SP-SG method, acquisitions with higher slice-acceleration factors should be possible. This will allow for further improvement in the achievable temporal sampling rate and efficiency.

As the SMS acceleration is pushed well beyond the slice-acceleration factor considered in this work, the choice of kernel size will be critical. This is due to the restriction on inter-slice leakage imposed through the SP-SG formulation. An increase to the kernel size will provide more fitting degrees of freedom to help balance out the additional inter-slice leakage errors (due to the higher MB factor). Without an increase to the kernel size the SP-SG formulation may become overly constrained and produce reduced quality reconstructions.

The generalized SP-SG formulation allows for a flexible trade-off between the inter- and intra-slice artifacts by tuning the weighting parameters. For example, in fMRI applications it might be desirable to sacrifice intra-slice artifact performance to reduce the inter-slice leakage artifact. This can be viewed as a specificity and sensitivity trade-off. The inter-slice leakage artifact can cause a reduction in specificity by creating displaced false positives due to signal leakage. On the other hand, the intra-slice artifact will cause a spatially varying signal attenuation/amplification for a given slice. This will affect the sensitivity to activation detection and with large attenuation false negatives can occur. However, small modulation on signal level is not particularly harmful while a small leakage can result in a large displacement of detected activation. This is particularly evident when the acquisition is physiological noise dominated. In this regime, the relatively small attenuation/amplification due to the intra-slice artifact will affect both the signal and noise equally and there should be no net effect on the sensitivity to activation.

The improved reconstruction accuracy afforded by the SP-SG method has implications across a variety of other applications such as arterial spin labelling, dynamic susceptibility contrast perfusion, neurological and whole body diffusion, and fMRI. The method not only allows for higher slice acceleration through improvements in reconstruction accuracy, but also enables high fidelity reconstruction at modest levels of acceleration, which will be important for clinical applications of the SMS technique. Future work will explore the ability to tailor parallel imaging reconstruction, through modifications of the SP-SG weighting scheme to allow for improved reconstruction accuracy for a specific application.

Acknowledgments

We would like to thank Steen Moeller and Essa Yacoub from the University of Minnesota Center for Magnetic Resonance Research for giving valuable advice on quantification of related optimization methods. This work has been supported through the NIH Human Connectome Project NIH U01MH093765, and grants NIBIB R00EB012107, R01EB006847, NCRR P41RR014075.

References

1. Sodickson DK, Manning WJ. Simultaneous acquisition of spatial harmonics (SMASH): fast imaging with radiofrequency coil arrays. *Magnetic Resonance in Medicine*. 1997; 38(4):591–603. [PubMed: 9324327]
2. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. SENSE: sensitivity encoding for fast MRI. *Magnetic Resonance in Medicine*. 1999; 42(5):952–962. [PubMed: 10542355]
3. Griswold MA, Jakob PM, Heidemann RM, Nittka M, Jellus V, Wang J, Kiefer B, Haase A. Generalized autocalibrating partially parallel acquisitions (GRAPPA). *Magnetic Resonance in Medicine*. 2002; 47(6):1202–1210. [PubMed: 12111967]
4. Weaver JB. Simultaneous multislice acquisition of MR images. *Magnetic Resonance in Medicine*. 1988; 8(3):275–284. [PubMed: 3205156]
5. Paley MN, Lee KJ, Wild JM, Griffiths PD, Whitby EH. Simultaneous parallel inclined readout image technique. *Journal of Magnetic Resonance Imaging*. 2006; 24(5):557–562.
6. Feinberg DA, Reese TG, Wedeen VJ. Simultaneous echo refocusing in EPI. *Magnetic Resonance in Medicine*. 2002; 48(1):1–5. [PubMed: 12111925]
7. Reese TG, Benner T, Wang R, Feinberg DA, Wedeen VJ. Halving imaging time of whole brain diffusion spectrum imaging and diffusion tractography using simultaneous image refocusing in EPI. *Journal of Magnetic Resonance Imaging*. 09; 29(3):517–522.

8. Larkman DJ, Hajnal JV, Herlihy AH, Coutts GA, Young IR, Ehnholm G. Use of multicoil arrays for separation of signal from multiple slices simultaneously excited. *Journal of Magnetic Resonance Imaging*. 2001; 13(2):313–317. [PubMed: 11169840]
9. Breuer FA, Blaimer M, Heidemann RM, Mueller MF, Griswold MA, Jakob PM. Controlled aliasing in parallel imaging results in higher acceleration (CAIPIRINHA) for multi-slice imaging. *Magnetic Resonance in Medicine*. 2005; 53(3):684–691. [PubMed: 15723404]
10. Nunes RG, Hajnal JV, Golay X, Larkman DJ. Simultaneous slice excitation and reconstruction for single shot EPI. *International Society for Magnetic Resonance in Medicine*. 2006:293.
11. Moeller S, Yacoub E, Oelman CA, Auerbach E, Strupp J, Harel N, Ugurbil K. Multiband multislice GE-EPI at 7 Tesla, with 16-fold acceleration using partial parallel imaging with application to high spatial and temporal whole-brain fmri. *Magnetic Resonance in Medicine*. 2010; 63(5):1144–1153. [PubMed: 20432285]
12. Feinberg DA, Moeller S, Smith SM, Auerbach E, Ramanna S, Glasser MF, Miller KL, Ugurbil K, Yacoub E. Multiplexed echo planar imaging for sub-second whole brain fmri and fast diffusion imaging. *PLoS One*. 2011; 5(12):e15710. [PubMed: 21187930]
13. Setsompop K, Gagoski BA, Polimeni JR, Witzel T, Wedeen VJ, Wald LL. Blipped caipirinha for simultaneous multi-slice EPI with reduced g-factor penalty. *International Society for Magnetic Resonance in Medicine*. 2010:551.
14. Setsompop K, Gagoski BA, Polimeni JR, Witzel T, Wedeen VJ, Wald LL. Blipped-controlled aliasing in parallel imaging for simultaneous multislice echo planar imaging with reduced g-factor penalty. *Magnetic Resonance in Medicine*. 2012; 67(5):1210–1224. [PubMed: 21858868]
15. Blaimer M, Breuer FA, Seiberlich N, Mueller MF, Heidemann RM, Jellus V, Wiggins G, Wald LL, Griswold MA, Jakob PM. Accelerated volumetric MRI with a SENSE/GRAPPA combination. *Journal of Magnetic Resonance Imaging*. 2006; 24(2):444–450. [PubMed: 16786571]
16. Zhu K, Kerr A, Pauly J. Autocalibrating CAIPIRINHA: Reformulating CAIPIRINHA as a 3D Problem. *International Society for Magnetic Resonance in Medicine*. 2012:518.
17. Moeller S, Xu J, Auerbach EJ, Yacoub E, Ugurbil K. Signal leakage(l-factor) as a measure of parallel imaging performance among simultaneously multi-slice (sms) excited and acquired signals. *International Society for Magnetic Resonance in Medicine*. 2012:519.
18. Keil B, Blau JN, Biber S, Hoecht P, Tountcheva V, Setsompop K, Triantafyllou C, Wald LL. A 64-channel 3T array coil for accelerated brain MRI. *Magnetic Resonance in Medicine*. 2012; 1002/mrm.24427
19. Jenkinson M, Bannister P, Brady JM, Smith SM. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage*. 2002; 17(2):825–841. [PubMed: 12377157]
20. Jaermann T, Crelier G, Pruessmann KP, Golay X, Netsch T, van Muiswinkel AMC, Mori S, van Zijl PCM, Valavanis A, Kollian S, Boesiger P. SENSE-DTI at 3T. *Magnetic Resonance in Medicine*. 2004; 51:230–236. [PubMed: 14755645]

Figure 1.

Metrics for inter-slice leakage. (Top) The Frequency Modulation/Monte Carlo (FMMC) approach generates slice-aliased time-series data with an imposed slice-dependent sinusoidal modulation in time. Channel j data for slice z , denoted as $I_{j,z}$, is modulated by sinusoidal term. Frequency analysis separates each slice estimate into a pass-through image $\tilde{I}_{z \rightarrow z}$ and leakage terms from another slice s $L_{s \rightarrow z}$. (Bottom) The Linear System Leakage Approach (LSLA) individually passes each channel j data from all slices z through the SG kernels $K_{j,z}$. Based upon the relative phase difference θ between I_1' and $L_{2 \rightarrow 1}$, taking the magnitude of the coil combined image and performing the FMMC analysis will result in a scaling factor of $\alpha L_{2 \rightarrow 1} \cos(\theta)$. Therefore, the leakage calculated using FMMC and LSLA are related by $L_{2 \rightarrow 1} = L_{2 \rightarrow 1} \cos(\theta)$.

Figure 2.

Comparison of artifacts for SG and SP-SG reconstruction of a MB=3 with FOV/3 slice shift acquisition. The SG and SP-reconstructions of a uniform water phantom at $b = 1000\text{s/mm}^2$ are shown in (A) and (B) respectively. The uniform water phantom produces images with similar but not identical image characteristics for the slices that are to be aliased in a SMS acquisition, i.e. a substantial overlap exists between the convolution matrices for SMS slices. This situation will create a strong dependence on the training image contrast for the SG kernels, which can cause contrast dependent leakage artifacts that result in a large total artifact error across a diffusion weighted time-series.

Figure 3.

The relationship between (A) linear independence of calibration matrices and (B) reduction to the SG objective function. MB=3 with FOV/3 shfit is illustrated, where the SMS slices have 42mm of slice separation. (A) The change in singular values for a slice M_i calibration matrix when excluding the range of all other calibration matrices associated with SMS slices M_j , $i \neq j$. The substantial decrease in singular values for each M_i demonstrates the strong linear dependence between the slice calibration matrices across different MB factors. This has the potential to cause significant signal leakage artifacts when the standard SG kernel model is used. (B) Trade-off of fitting error and inter-slice dependencies for the SG and SP-SG methods. The mean difference in RMSE across the MB=3 slices is shown at each channel. For all channels, the total artifact error is decreased for the SG method, while the inter-slice error is decreased for the SP-SG method. This highlights the difference in the optimization model for the two methods: *the SP-SG method trades-off higher total artifact error in the training data for reduction in leakage.*

Figure 4.

Total artifact comparison for synthesized MB=3 with FOV/3 shift data. (A) The center slices used as the gold standard. (B) and (C) The total artifacts of SG and SP-SG at $b = 3000\text{s/mm}^2$ averaged for 64 repetitions. The total artifact corresponds to the influence of all slices $z = 1, 2, 3$ onto slices $z = 2$. The histogram of total artifacts at $b = 3000\text{s/mm}^2$ is shown in (D). Significant total artifact reductions can be observed for the SP-SG model, in comparison to the SG model, when applied to this diffusion encoded image time-series (6.8% reduction in the mean artifact level).

Figure 5.

Intra- and inter-slice artifact comparison for synthesized MB=3 with FOV/3 shift data. Significant intra-slice and inter-slice leakage error can be observed when the standard SG model is used. The SP-SG method reduces the mean intra-slice error from 8.7 to 5.7 and the mean inter-slice leakage errors from 9.2 to 5.5 ($L_{2 \rightarrow 1}$) and from 9.7 to 5.5 ($L_{2 \rightarrow 3}$).

Figure 6.

Magnitude (A) and phase (B) evolution for three $b = 3000\text{s/mm}^2$ MB=1 acquisitions. The slices are each separated by 44mm. While the magnitude images do not exhibit significant variation across the repetitions, large variations can be observed in the phase images. In addition, the temporal phase variations across the slices are extremely different.

Figure 7.

Ratio of SNR between SP-SG and SG methods for MB=3 with FOV/3 shift acquisitions, a consistent mask is applied across each slice. The average across 50 repetitions of $b = 0 \text{ s/mm}^2$ and $b = 1000 \text{ s/mm}^2$ are shown in (A) and (B) respectively. At $b = 0 \text{ s/mm}^2$, small deviations from the SNR ratio of 1 are observable. However, the average SNR ratio for this non-diffusion weighted image series is approximately one. When considering the case of $b = 1000 \text{ s/mm}^2$, a much larger deviation in SNR ratio can be observed, with the SP-SG method exhibiting over 10% gains in SNR for many areas.