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Segmented Simultaneous Multi-Slice Diffusion Weighted Imaging with Generalized Trajectories

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Abstract

Purpose—The purpose of this work is to develop and evaluate a single framework for the use of Cartesian and non-Cartesian segmented trajectories for rapid and robust simultaneous multi-slice (SMS) diffusion-weighted imaging (DWI) at 3T.

Methods—A generalized SMS approach with intrinsic phase navigation using Multiplexed Sensitivity Encoding (MUSE) was developed. Segmented blipped-CAIPI Echo Planar Imaging (EPI) and z-gradient modulated spiral trajectories were examined using SMS DWI scans at 3T with a 32-channel head coil.

Results—The generalized SMS MUSE reconstruction framework was successful in significantly reducing artifacts for all trajectories. A DWI brain volume with a 67.5 mm height, 1.5 mm isotropic resolution, and 90 diffusion weightings was obtained in a scan time of six minutes.

Conclusions—The MUSE technique can be generalized to allow for reconstruction of both Cartesian and non-Cartesian segmented trajectories.

Keywords

Simultaneous multi slice imaging; diffusion weighted imaging

INTRODUCTION

Diffusion Weighted Imaging (DWI) is widely used in clinical and research studies for evaluating white matter structure (1). However, scan times for whole brain DWI with a large number of diffusion directions and higher resolutions can be prohibitive. Recent advances in parallel imaging with receiver arrays using Simultaneous Multi-Slice (SMS) imaging have allowed for significant acceleration of single-shot imaging techniques, such as Echo Planar Imaging (EPI), commonly used for DWI (2,3). One of the standard acquisition techniques for SMS imaging is Blipped-CAIPI EPI, which uses z gradient blips simultaneously with the EPI readout gradients to produce slice-dependent image shifts for better slice separation (4). Analogously, SMS using spiral trajectories with additional z gradient modulation has also

been proposed (5,6). The additional z gradient during spiral acquisitions makes the simultaneously acquired slices add up incoherently, which can be decoded using a 3D formalism for SMS imaging (7).

The low signal to noise ratio (SNR) in DWI due to diffusion gradients can make single-shot acquisitions with high resolution challenging. It is common with EPI and spiral trajectories to use multiple excitations with segments of k-space that are combined during image reconstruction. Segmentation makes it possible to increase spatial resolution, while also shortening readouts to reduce distortion and T_2^* decay-induced blurring. However, applying segmentation to DWI can be problematic as image phase modulation arising from motion during the strong diffusion-weighting gradients is generally inconsistent between segments. Consequently, methods have been developed for measuring and correcting these phase instabilities. For example, the phase information of each segment can be measured by implementing additional phase navigators (8), but this approach increases scan time and specific absorption rate (SAR) due to the need for an additional spin echo. Furthermore, phase information can be acquired using variable density techniques that oversample the center of k-space to resolve the phase distribution of each segment (9). An alternative approach termed Multiplexed Sensitivity Encoding (MUSE) (10,11) calculates the phase information in each segment from under-sampled data, and does not require additional scans. Recent work shows the utility of the MUSE technique for DWI without phase instability using SMS EPI (12).

Here, we extend the MUSE method for the use of any general Cartesian or non-Cartesian segmented SMS k-space trajectory. The 3D SMS k-space approach was modified to include MUSE phase correction in a generalized SMS Sensitivity Encoding (SENSE) reconstruction framework (7,13). Segmented blipped-CAIPI EPI and z-gradient modulated spiral trajectories were designed and implemented for DWI scanning at 3T. The data from both trajectories were successfully reconstructed within a single pipeline and provided diffusion-weighted images with minimal artifacts. A DWI volume 67.5 mm height was obtained at 1.5 mm isotropic resolution with 90 diffusion weightings in six minutes. The differences in the DWI results between the trajectories were also compared qualitatively.

METHODS

Segmented SMS trajectories were designed using the 3D SMS k-space framework as defined in Ref. (7). In 3D SMS k-space, the Field of View (FOV) along the slice or k_z -direction is given by $FOV_z = Nd$. The number of slices or equivalently the number of k_z planes needed for full sampling along the slice-select direction is denoted as N and d is the separation between slices. Using this definition for k-space sampling along the slice-select direction, SMS can be viewed as a standard 3D acquisition and any parallel imaging reconstruction methods, including 3D SENSE, can be used. Two trajectories were designed and are shown in Figure 1 (a, b). The first trajectory was a Cartesian blipped-CAIPI EPI where the z-gradient blips were applied between the phase encoding lines of a segmented EPI k-space. The second was an interleaved spiral trajectory with a sinusoidal z-gradient producing modulation along the k_z -direction. The sinusoidal modulation produces a slice

dependent spatial encoding similar to blipped-CAIPI and the trajectory was termed “wave-spiral.”

A segment of the 3D SMS k-space was acquired per acquisition. The number of segments L determines in-plane undersampling and the overall under-sampling R is given by $L \times N$. Since each segment can possess an arbitrary phase distribution after diffusion weighting, MUSE was used to combine the segmented SMS data. First, an image from each of $l=1$ to L segments $\rho_l(\mathbf{r})$ was reconstructed individually using iterative 3D SENSE. The signal equation for a general SENSE reconstruction can be written as

$$s_l(t) = \int C(\mathbf{r}) \rho_l(\mathbf{r}) e^{-i\mathbf{k}_l(t) \cdot \mathbf{r}} d\mathbf{r} \quad [1]$$

where $s_l(t)$ is the acquired signal and $\mathbf{k}_l(t)$ is the 3D SMS k-space from one segment and $C(\mathbf{r})$ is the receiver coil sensitivity for one array channel, which was acquired in an additional calibration scan. The integral can be written in matrix form including all channels and solved numerically as an inverse problem with a least-squares conjugate gradient algorithm and Non-Uniform Fast Fourier Transform (NUFFT) for increased speed (14). The images reconstructed from each under-sampled segment were then used to calculate the phase map of each segment $\phi_l(\mathbf{r})$. For each slice position, the phases were then combined with the coil sensitivities to perform a 3D SENSE reconstruction of the full data set leading to the final image $\rho(\mathbf{r})$. The system of equations that needs to be solved can be written as:

$$\begin{aligned} s_1(t) &= \int \left[C(\mathbf{r}) e^{i\phi_1(\mathbf{r})} \right] \rho(\mathbf{r}) e^{-i\mathbf{k}_1(t) \cdot \mathbf{r}} d\mathbf{r} \\ &\vdots \\ s_L(t) &= \int \left[C(\mathbf{r}) e^{i\phi_L(\mathbf{r})} \right] \rho(\mathbf{r}) e^{-i\mathbf{k}_L(t) \cdot \mathbf{r}} d\mathbf{r} \end{aligned} \quad [2]$$

The image reconstruction was performed in Matlab (The Mathworks, Natick, MA, USA) using the Image Reconstruction Toolbox (<http://web.eecs.umich.edu/~fessler/code/>). Gradient delays between readout lines (R-L/L-R) in the EPI trajectory were measured using navigators (3 lines) after the excitation pulse. For the spiral, time delays of approximately 5 μs were introduced to the k-space trajectories to compensate for ghosting artifacts in the reconstructed images.

All experiments were conducted on a Siemens 3T scanner (Siemens Healthcare, Erlangen, Germany) using a 32-channel head coil. A single spin echo DWI approach was chosen to minimize TE and the specific absorption rate (SAR). The blipped-CAIPI EPI sequence was constructed from the product EPI sequence and the spiral sequence was custom built using external spiral gradient files uploaded to the scanner. To reduce blurring of the spiral acquisition, a time segmented off-resonance correction (14) was used. The off resonance correction was performed in both reconstruction steps, incorporating the phase information calculated from the pre-scan for each slice position in Eqs. [1] and [2]. The pre-scan consisted of two 2D fast low angle shot (FLASH) measurements acquiring three echo times each for a total of six echoes with TE = 3.7, 4.7, 5.9, 7.0, 8.1, 10 ms. The off-resonance map

was then calculated using the method described in (15). The data were also used to provide coil sensitivity maps for the SENSE reconstruction. Since the single spin echo design leaves a gap between the end of the diffusion weighting period and the echo, the spiral acquisition included a short “spiral-in” sampling of the center of k-space followed by a “spiral-out”. This was added to oversample the center of k-space for improved image reconstruction and phase estimation. The EPI sequence used a partial Fourier sampling to shorten TE to make SNR comparable to the spiral sequence. Figure 1 (c) shows diagrams of the pulse sequences.

$N=3$ SMS excitation and refocusing pulses were generated as linear combinations of three sinc and refocusing SLR pulses respectively (16), using optimized relative phases to reduce peak RF (17). Peak RF power of the refocusing pulse was further minimized by reducing the amplitude of the slice-selective gradient using the variable rate selective excitation (VERSE) method (18). The excitation pulse was calculated online and the refocusing pulse was designed offline in Matlab and imported to the sequence during runtime. Figure 1 (d) shows a diagram of the SMS refocusing pulse.

Two *in vivo* DWI protocols were run on two healthy male volunteers after providing written consent using a protocol approved by the University of Hawaii/Queens Medical Center Institutional Review Board. In the first protocol, the EPI trajectory used a partial Fourier acquisition to reach a TE comparable to the spiral readouts and the second protocol was run without partial Fourier. The sequence parameters of the first protocol were 2000 ms TR, 75/85 ms TE (spiral/EPI), 1.5 mm isotropic resolution, two segments, 128×128 matrix, 45 slices ($15 \times N=3$), and diffusion weightings $b_1/b_2 = 300/1100$ s/mm² with 30/60 directions. The number of k_z samples was set to 2 (as shown in Figure 1 (a)), introducing a FOV/2 shift of simultaneously acquired slices. The scan time for each was 6:00 minutes. The sequence parameters of the second protocol were 1900/2200ms TR (spiral/EPI), 70/100 ms TE (spiral/EPI), 1.5 mm isotropic resolution, two segments, 128×128 matrix, 45 slices with $N=3$ simultaneous slices, diffusion weighting $b_1 = 1000$ s/mm² with 30 directions, and one scan without diffusion weighting. The scan time was 1:54 min for the spiral scans and 2:12 min for the EPI scans. The DWI data processing was performed using software developed in house.

RESULTS

Diffusion weighted brain images from the first protocol at $b_2 = 1100$ s/mm² are shown in Figure 2. The images were reconstructed without (top row) and with (bottom row) the generalized SMS MUSE method. The reconstruction without MUSE shows substantial image artifacts and signal dropouts due to the phase differences in the two k-space segments. The MUSE algorithm results in a robust reconstruction of the segmented DWI data. All images show qualitatively the same level of diffusion weighting however the spiral images are noticeably blurrier with moderately improved SNR.

Figure 3 shows diffusion weighted images of one SMS slice group for $b_1 = 300$ s/mm² and mean diffusivity (MD) for $b_1 = 300$ s/mm² and $b_2 = 1100$ s/mm² for both trajectories. All images were reconstructed using generalized SMS MUSE. Compared to the blipped-CAIPI EPI readout, the spiral images again appear to provide enhanced SNR at the cost of blurring.

Figure 4 shows Fractional anisotropy (FA) and the tensor color maps obtained from analysis using software developed in house. All methods show qualitatively similar results with no phase instability artifacts. Again, the blipped-CAIPI EPI scans exhibit sharper details compared to wave-spiral both in the FA and tensor images.

Tensor images from the second *in vivo* protocol, reconstructed with one and two segments are provided in Figure 5. A visible gain in SNR can be observed for the two-segment acquisition. In the single-segment results, the spiral acquisition provides enhanced SNR and a faster acquisition at the cost of blurring compared to the blipped-CAIPI acquisition. Note the EPI scans in this protocol did not use a partial Fourier acquisition and therefore had a longer TE.

DISCUSSION AND CONCLUSIONS

Our results demonstrate that it is possible to acquire robust high-resolution (1.5 mm isotropic) DWI at 3T using both Cartesian and non-Cartesian segmented SMS trajectories without additional phase navigators. The scan time for 90 diffusion directions was six minutes to cover a brain volume of 67.5 mm height, which is acceptable for a large number of clinical and research protocols. Previous research demonstrated that Cartesian MUSE could be applied to segmented SMS Blipped-CAIPI EPI (11,12). The generalized SMS MUSE reconstruction can be effectively applied to both blipped-CAIPI EPI and spiral readouts with additional gradient modulation along the slice-select direction. The MUSE approach allows shorter TR values compared to techniques that determine the phase of each k-space segment with additional navigators. On the other hand the number of segments achievable with MUSE is limited by accuracy of the phase generated from each segment. The presented data used an overall under-sampling factor of 6 (2 segments and 3 simultaneous slices) and not only measurement time but also the low SNR in the high-resolution diffusion weighted data prohibits higher segmentation factors.

Although a thorough comparison between SMS EPI and spiral methods is beyond the scope of the work, visual differences between the images and resultant diffusion maps from the different acquisitions were observed. The spiral images had noticeable blurring compared to the EPI results even with the segmented off-resonance correction. On the other hand, the EPI data shows some Gibbs-ringing artifacts in the diffusion weighted images as well as in the FA maps. The field map required a fit to six echo times (as opposed to two) to be visually effective, possibly indicating a large degree of sensitivity of off resonance in SMS spiral. Especially close to cavities, residual distortions were present in the spiral data even after correcting for off-resonances. Off-resonance effects in EPI are also more visibly benign because artifacts are geometric distortions rather than blurring. The shorter TE of the spiral in addition to the oversampling of the k-space center provided for increased SNR compared to EPI, which could be partially offset using a partial Fourier EPI approach. It is also important to note that the EPI sequence was obtained from an optimized commercial product and the spiral sequence was developed in-house using external gradient files. Image quality and dimensions are extremely dependent on the exact knowledge of the applied gradient. Despite blurring, the direct comparison of EPI and spiral data shows a notable change in the object size. Combined with an A-P compression of the EPI data (due to the applied phase

encode direction), this leads to an apparent compression of the spiral data in the R-L direction. Future optimization may be required to either measure or estimate the k-space trajectories used in the generalized reconstruction.

A drawback of the proposed method is that reconstruction times using iterative SENSE with off-resonance correction can be prohibitively slow. In our case, the reconstruction of one DWI spiral SMS set (3 simultaneously acquired slices) with off-resonance correction required 1 hour on an Intel® Xeon(R) CPU E5-1620 v2 @ 3.70GHz. This leads to a total reconstruction time of 56 days for 90 diffusion-weighted volumes (with 15 times 3 slices). However, since all volumes are independent, there exists a high potential for parallelization given the necessary computational power leading to an achievable reconstruction time of 1 hour. In our case the limiting factor was the available number of MATLAB licenses and reconstruction of all three datasets was performed in 3 days on a high performance cluster from the Information Technology Services at the University of Hawaii.

In conclusion we demonstrate that it is straightforward to extend the MUSE technique to any arbitrary trajectory including non-Cartesian spiral for rapid DWI with reduced artifacts. A generalized SENSE picture allows the use of MUSE for any segmented two- or three-dimensional acquisition including SMS, multi-slab, or volumetric scans. In particular the perspective of SMS as a 3D acquisition is an intuitive tool putting SMS techniques in context of what is already well known about volumetric imaging.

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REFERENCES

1. Basser PJ, Mattiello J, LeBihan D. MR diffusion tensor spectroscopy and imaging. *Biophysical J.* 1994; 66:259–267.
2. 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. *J Magn Reson Imaging.* 2001; 13(2):313–317. [PubMed: 11169840]
3. 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.
4. 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. *Magn Reson Med.* 2012; 67(5):1210–1224. [PubMed: 21858868]
5. Chu, A., Noll, D. Simultaneous multislice spiral imaging using z-gradient modulation and parallel receive coils.. *Proceedings of the 21st Annual Meeting of ISMRM; Salt Lake City, Utah, USA.* 2013; Abstract 3317
6. Zahneisen B, Poser BA, Ernst T, Stenger VA. Simultaneous multi-slice fMRI using spiral trajectories. *Neuroimage.* 2014; 92:8–18. [PubMed: 24518259]
7. Zahneisen B, Poser BA, Ernst T, Stenger VA. Three-dimensional Fourier encoding of simultaneously excited slices: generalized acquisition and reconstruction framework. *Magn Reson Med.* 2014; 71(6):2071–2081. [PubMed: 23878075]
8. Frost R, Jezzard P, Douaud G, Clare S, Porter DA, Miller KL. Scan time reduction for readout-segmented EPI using simultaneous multislice acceleration: Diffusion-weighted imaging at 3 and 7 Tesla. *Magn Reson Med.* 2015; 74:136–149.

9. Liu C, Bammer R, Kim DH, Moseley ME. Self-navigated interleaved spiral (SNAILS): application to high-resolution diffusion tensor imaging. *Magn Reson Med*. 2004; 52(6):1388–1396. [PubMed: 15562493]
10. Chen NK, Guidon A, Chang HC, Song AW. A robust multi-shot scan strategy for high-resolution diffusion weighted MRI enabled by multiplexed sensitivity-encoding (MUSE). *Neuroimage*. 2013; 72:41–47. [PubMed: 23370063]
11. Chang HC, Gaur P, Chou YH, Chu ML, Chen NK. Interleaved EPI based fMRI improved by multiplexed sensitivity encoding (MUSE) and simultaneous multi-band imaging. *PLoS One*. 2014; 9(12):e116378. [PubMed: 25549271]
12. Chang HC, Guhaniyogi S, Chen NK. Interleaved diffusion-weighted improved by adaptive partial-Fourier and multiband multiplexed sensitivity-encoding reconstruction. *Magn Reson Med*. 2015; 73(5):1872–1884. [PubMed: 24925000]
13. Pruessmann KP, Weiger M, Bornert P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. *Magn Reson Med*. 2001; 46:638–651. [PubMed: 11590639]
14. Sutton BP, Noll DC, Fessler JA. Fast, iterative image reconstruction for MRI in the presence of field inhomogeneities. *IEEE Trans Med Imaging*. 2003; 22(2):178–188. [PubMed: 12715994]
15. Funai AK, Fessler JA, Yeo DT, Olafsson VT, Noll DC. Regularized field map estimation in MRI. *IEEE Trans Med Imaging*. 2008; 27(10):1484–1494. [PubMed: 18815100]
16. Pauly JM, LeRoux P, Nishimura DG, Macovski A. Parameter Relations for the Shinnar-LeRoux Selective Excitation Pulse Design Algorithm. *IEEE Trans Med Imaging*. 1991; 10:53–65. [PubMed: 18222800]
17. Wong, E. Optimized phase schedules for minimizing peak RF power in simultaneous multi-slice RF excitation pulses.. *Proceedings of the 20th annual meeting of ISMRM; Melbourne, Australia*. 2012; Abstract 2209
18. Conolly S, Nishimura D, Macovski A, Glover GH. Variable-rate selective excitation. *J Magn Reson*. 1988; 78:440–458.

FIG. 1.

This figure shows diagrams of the (a) blipped-CAIPI EPI and (b) wave-spiral 3D SMS k-space trajectories. Pulse sequence diagrams of the RF, x-gradient, and z-gradient for the two sequences are displayed in (c). The wave-spiral gradients are shown in blue. Note that the EPI sequence used a partial Fourier EPI acquisition. Also shown is the (d) $N=3$ SMS refocusing pulse used for the DWI experiments. The pulse was designed using a modulated SLR pulse with phase optimization and variable rate selective excitation for lower peak RF amplitude.

FIG. 2.

Multi-shot (2 segments) diffusion weighted (a, c) blipped-CAIPI EPI and (b, d) wave-spiral images from the human subject ($b_2=1100\text{s/mm}^2$). The images were reconstructed with and without using the MUSE method.

FIG. 3.

Diffusion weighted images (a, b) for $b_1 = 300 \text{ s/mm}^2$ and mean diffusivity (MD) for (c, d) $b_1 = 300 \text{ s/mm}^2$ and (e, f) $b_2 = 1100 \text{ s/mm}^2$ are shown for both trajectories. The blipped-CAIPI EPI images are shown in (a, c, and e) and the wave-spiral in (b, d, and f). All simultaneously acquired slices ($N = 3$) are shown, the center slice being enlarged. All images were reconstructed using generalized SMS SENSE with MUSE.

FIG. 4.

This figure shows DWI data from the first *in vivo* protocol. The data were processed using software developed in house. Fractional anisotropy (FA) and the tensor color maps are shown for the data acquired with both trajectories. The multi-slice data was reformatted to show sagittal and coronal views of the acquired volume.

FIG. 5.

This figure shows tensor images reconstructed with SENSE from one segment as well as with SENSE MUSE from two segments from the second *in vivo* protocol. A visible gain in SNR can be observed for both trajectories when a multi-shot acquisition is used.