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Integrated SSFP for functional brain mapping at 7T with reduced susceptibility artifact

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Abstract

Balanced steady-state free precession (bSSFP) offers an alternative and potentially important tool to the standard gradient-echo echo-planar imaging (GE-EPI) for functional MRI (fMRI). Both passband and transition band based bSSFP have been proposed for fMRI. The applications of these methods, however, are limited by banding artifacts due to the sensitivity of bSSFP signal to off-resonance effects. In this article, a unique case of the SSFP-FID sequence, termed integrated-SSFP or iSSFP, was proposed to overcome the obstacle by compressing the SSFP profile into the width of a single voxel. The magnitude of the iSSFP signal was kept constant irrespective of frequency shift. Visual stimulation studies were performed to demonstrate the feasibility of fMRI using iSSFP at 7T with flip angles of 4° and 25°, compared to standard bSSFP and gradient echo (GRE) imaging. The signal changes for the complex iSSFP signal in activated voxels were 2.48 ± 0.53 (%) and 2.96 ± 0.87 (%) for flip angles (FA) of 4° and 25° respectively at the TR of 9.88ms. Simultaneous multi-slice acquisition (SMS) with the CAIPRIHNA technique was carried out with iSSFP scanning to detect the anterior temporal lobe activation using a semantic processing task fMRI, compared with standard 2D GE-EPI. This study demonstrates the feasibility of iSSFP for fMRI with reduced susceptibility artifacts, while maintaining robust functional contrast at 7T.

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Keywords

Integrated SSFP (iSSFP); fMRI; ultrahigh magnetic field; susceptibility artifact; semantic

1. Introduction

Blood oxygenation level dependent functional MRI (BOLD fMRI) has revolutionized the field of functional brain imaging since its inception [1–3]. Most existing fMRI studies used gradient-echo echo-planar imaging (GE-EPI), due to its whole-brain spatial coverage, fast imaging speed and relatively high contrast-to-noise ratio (CNR).

Although widely used, BOLD fMRI suffers from signal dropouts [4] and image distortions [5,6] that impair imaging in specific brain regions, such as the anterior temporal lobe and orbitofrontal cortex at the interface of air, bone and brain tissue. This susceptibility artifact becomes severe at ultrahigh magnetic fields, such as 7T. In recent years, balanced steady-state free precession (bSSFP) has been proposed, as an alternative of GE-EPI, for fMRI to overcome the aforementioned limitations. Initial studies utilized the transition band of the bSSFP signal profile that was sensitive to deoxyhemoglobin-induced frequency shifts [7,8], while more recent studies shifted focus towards the relatively flat passband for detecting microscopic diffusion related signal changes [9–11]. However, it remains difficult to achieve the whole-brain coverage using bSSFP due to the banding artifacts arising from the sensitivity of bSSFP signal to off-resonance effects. Although multiple bSSFP acquisitions with phase cycling increments can be combined to achieve full coverage, the scanning time will be multiplied by the number of phase cycling [12]. In addition to bSSFP, a few alternative SSFP sequences with unbalanced gradients to attain SSFP-FID and SSFP-echo signals, have been explored for fMRI [13–15]. The appeal of these SSFP methods is the whole-brain coverage without banding artifacts. However, these methods also have several important shortcomings. For traditional SSFP-FID with strong dephasing gradients, the functional contrast is sensitive to diffusion of spins in the field disturbances surrounding deoxygenated blood vessels (large draining veins) [13]. For the SSFP-echo signal, the functional contrast is susceptible to the effects of flow due to the strong dephasing gradient and the extravascular contribution from dynamic averaging around post-capillary vessels because of its long diffusion time[15].

In this study, a special case of SSFP-FID sequences, termed integrated-SSFP or iSSFP was proposed for fMRI at 7T to achieve robust signal changes with negligible susceptibility artifacts [16,17]. The iSSFP sequence was modified from bSSFP by placing a gradient along the Z axis or X axis to dephase the spins across a 2π cycle within one voxel (herein referred as iSSFPz and iSSFPx, respectively). As a result, the magnitude of the iSSFP signal was kept constant while its phase varied linearly with the frequency, irrespective of the center frequency. The signal of iSSFP was expected to be less sensitive to diffusion and flow effects because of the relatively small dephasing gradient [18–20]. The iSSFP fMRI experiments with visual stimulation were performed at two flip angles of 4° and 25° and two different TRs of 5.03ms and 9.88ms respectively, in comparison with conventional bSSFP and GRE fMRI at 7T. The sensitivity, spatial specificity, and image quality of iSSFP fMRI

were investigated to demonstrate the feasibility of iSSFP for neuroimaging at ultrahigh magnetic field. In addition, the phase information was utilized to detect the functional activation based on complex iSSFP signals. The temporal lobe has been reported in literature as a critical neural substrate for semantic processing [21,22]. However, it is prone to be affected by susceptibility artifacts [23]. Subsequently, a comparative study between simultaneous multi-slice acquisition (SMS) accelerated iSSFP [24] and traditional standard 2D GE-EPI was conducted using a semantic processing task fMRI. SMS accelerated iSSFP showed reduced signal loss and distortion, and detected greater activation in the inferior part of left anterior temporal lobe compared to standard 2D GE-EPI. The limitations of iSSFP fMRI including relatively low SNR and temporal resolution were discussed.

2. Theory

In the bSSFP sequence, the total gradient area on any axis is zero during each TR ($TR \ll T_2 < T_1$) interval. Ignoring the diffusion effects, the transverse magnetization of bSSFP is given by [25,26] :

$$M_y^+(\theta) = M_0 (1 - E_1) \cdot \sin \alpha \cdot (1 - E_2 \cos \theta) / D \quad (1)$$

$$M_x^+(\theta) = M_0 (1 - E_1) \cdot E_2 \cdot \sin \alpha \cdot \sin \theta / D \quad (2)$$

with

$$D = (1 - E_1 \cdot \cos \alpha) \cdot (1 - E_2 \cdot \cos \theta) - E_2 (E_1 - \cos \alpha) \cdot (E_2 - \cos \theta) \quad (3)$$

where $E_{1,2} = \exp(-TR / T_{1,2})$, α is the flip angle of the radio frequency (RF) pulse and θ is the phase accrual across the TR between adjacent RF pulses. The signal $M_T(TE)$ acquired from one voxel at TE ($0 < TE < TR$) is given in the form of complex integral:

$$M_T(TE) = \exp(-TE/T_2) \left| \int_V p(\theta) \left(M_x^+(\theta) + i M_y^+(\theta) \right) \exp(i\theta TE/TR) d\theta \right| \quad (4)$$

where $p(\theta)$ is the dephasing distribution within the imaging volume V , reflecting the corresponding frequency distribution. As shown in the Fig. 1, the iSSFP sequence is modified from bSSFP by adding an extra dephasing gradient to cause a 2π phase dispersion across the width of a voxel along X axis or Z axis within a TR period.

$$\gamma \Delta L \int_0^{TR} G dt = 2\pi \quad (5)$$

where G is the extra dephasing gradient, and L is the width of a voxel. Thus, $p(\theta)$ in equation 4 is linearly distributed across one voxel. In order to understand the iSSFP signal

behavior intuitively, simulation of the iSSFP signal was performed in comparison with the bSSFP signal for flip angles of both 4° and 25°. In the simulation, the T_1 (2000ms) and T_2 (60ms) [14] values of gray matter at 7T were used, and TE was half of TR.

As shown in Fig. 2, iSSFP signal has constant magnitude and linear phase across the frequency range of one cycle relative to bSSFP. The amplitude of iSSFP signal depends on T_1 , T_2 , TR, TE (TE=TR/2) and the flip angle α , but not the frequency offset, thus showing no sensitivity to the banding artifacts. The frequency shift and T_2^* increase accompanied by cortical activation can lead to phase and magnitude increase, respectively. The phase change is:

$$\Delta pha = \Delta f / (1/TR) * \pi \quad (6)$$

where pha is the phase change and f is the frequency shift. The signal change was the vector difference between the oxygenated and deoxygenated signal. So the fMRI based on iSSFP can combine the frequency shift and T_2^* BOLD effects. In the study, we performed iSSFP fMRI at TRs of 5.03 and 9.88ms and two different flip angles of 4° and 25° in comparison with conventional bSSFP on human brains at 7T.

3. Materials and methods

Experiments were performed to test the feasibility of the iSSFP sequence for fMRI on the 7T whole-body magnetom system (Siemens Medical Systems, Erlangen, Germany) with 1CP transmit/32 channel receiver head coil (Nova Medical, Cambridge, MA, USA). The earplugs were used to reduce the scanner noise and foam pads to limit the head motion. Participants provided written informed consent according to a protocol approved by the Institutional Review Board of the Beijing MRI Center for Brain Research.

In Exp.1, ten healthy subjects (21-25 years old, 5 males) were scanned using the iSSFP sequence in comparison with the bSSFP and GRE (five subjects for each) sequences respectively with flip angles of 4° and 25°. Three subjects were scanned with four different spatial resolutions to test the sensitivity of the iSSFP sequence to partial volume effects. After the scout scan, a 3D MPRAGE sequence was performed to acquire T_1 -weighted structural images which were used for localizing the calcarine sulcus and as the anatomic reference of fMRI. The imaging parameters of the iSSFP and bSSFP sequences for fMRI were the same: one axial oblique slice (5mm thickness) was oriented in the plane coincident with the calcarine sulcus, FA = 4°/25°, TR = 5.03/9.88ms (TE=TR/2), field of view (FOV) = 220*220mm², matrix size of 128*128, voxel size of 1.72*1.72*5mm³, bandwidth = 358/130 Hz/pixel for TR of 5.03/9.88ms. The acquisition time for one slice was 0.7s and 1.4s for TR of 5.03 and 9.88ms, respectively. A block-design visual stimulation with dark-gray and light-gray checkboard flashing at 8 Hz was used for task fMRI scans. The stimulus contained four 56-s blocks with 28 sec stimulus followed by 28 sec rest, and the total acquisition time for both task and resting scan was about 4 min. The subjects were asked to fixate at all time on the cross-hair located in the center of visual field during the experiments. For comparison, a GRE sequence was performed with the flip angle of 8°

(Ernst angle) for TE/TR=4.94/11ms. In addition, in order to investigate the sensitivity to partial volume effects, the iSSFPx and iSSFPz sequences were performed at TR of 9.88 ms with four different in-plane resolutions (1.72*1.72 mm², 1.72*1.15 mm², 1.72*0.86 mm², 1.72*0.69 mm²). The acquisition time for one slice was 1.4s.

Besides magnitude signals, phase maps were also reconstructed to calculate compound complex images. To reduce the effect of respiratory and cardiac pulsation on the phase images, the time course of phase in a region of interest (ROI) in white matter was used to regress out the potential interferences. Complex signal changes, I_{com} , were calculated from vector difference of signals between task and resting scans:

$$\Delta I_{com} = |\Delta I_{real} + i^* \Delta I_{ima}| \quad (7)$$

In Exp. 2, SMS accelerated iSSFP (TE/TR=4.26/8.51ms, SMS factor=4, readout bandwidth=162Hz/pixel) and traditional standard 2D GE-EPI (TE/TR=20/2000ms) were performed using a semantic processing task fMRI to detect the anterior temporal lobe activation [27]. The CAIPIRINHA (Controlled Aliasing In Parallel Imaging Results In Higher Acceleration) method was used to simultaneously excite four slices that were phase shifted of 0, $\pi/2$, π and $3/2\pi$ (0, FOV/4, FOV/2 and 3*FOV/4 shift in the phase encoding direction respectively). [28,29]. Magnitude images were reconstructed using the slice-GRAPPA technique with a kernel size of 2*2. The imaging parameters were: 8 slices with the resolution of 1.72*1.72*3mm³, FOV of 220*220 mm², FAs of 25° and 85°, and TRs of 3s and 2s for iSSFP and GE-EPI scans, respectively. In this fMRI experiment, eleven subjects performed semantic task versus font size task using Chinese characters in four on/off (18/18s) blocks, which were interleaved with 12s blocks of fixations. The scan time for one session was 4 minutes. Participants were required to identify one from three Chinese characters close to the target in meaning and font size in task and control groups shown in Fig. 3, respectively. Six sessions of 2D GE-EPI and six sessions of SMS accelerated iSSFP data for each participant were collected. The EPI and iSSFP sessions were interleaved during the experiment.

All data were analyzed using SPM8 on MATLAB 2012a (the MathWorks, Inc., MA, USA). In Exp 1, motion correction was applied to magnitude images and the transformation matrix was then applied on phase images. For the following statistics, general linear model was applied for visual activation detection with a threshold of $P < 0.001$ and spatial cluster size of at least 20 pixels. The MarsBar toolbox was used for ROI extraction and analysis, and the time courses were low-pass filtered to suppress the noise. In Exp 2, data preprocessing included image realignment, coregistration of structural and functional MRI data, normalization to the MNI space and spatial smoothing with a 4-mm full-width-at-half-maximum (FWHM) Gaussian kernel. Group analysis was performed to detect significant activation in the temporal cortex with a threshold of $P < 0.001$ and spatial cluster size of at least of 5 pixels.

4. Results

4.1. Simulation results

Figure 2 shows the signal profiles of bSSFP and iSSFP at flip angles of 4° and 25° respectively. The simulation results show that the magnitude of iSSFP, unlike bSSFP, stays constant across the frequency range of 2π cycle, indicating insensitivity to susceptibility artifacts. The phase of iSSFP signal varies linearly with the frequency. So the functional contrast of the iSSFP sequence can originate from the combination of T_2^* BOLD effect and frequency shift.

4.2. fMRI experiment 1

The functional images from one representative subject, obtained by iSSFPz, iSSFPx and bSSFP at different TRs of 5.03 and 9.88ms for flip angles of both 4° and 25° are presented in Fig. 4. Each slice acquisition took 0.7s and 1.4s for TR of 5.03 and 9.88ms, respectively. The images of iSSFPz, iSSFPx and bSSFP demonstrated increased SNR at the flip angle of 25° compared with 4° . For bSSFP, more severe distortion and chemical shift artifacts were observed at TR of 9.88ms relative to 5.03ms. For iSSFP, the TR of 9.88ms doesn't affect the image quality compared to the TR of 5.03ms.

As shown in Fig. 4, the images of the bSSFP sequence suffered from serious banding artifacts. There were more bandings at longer TR because of the great phase accrual. Meanwhile, the two iSSFP sequences were insensitive to frequency changes. For all the sequences, the average time courses of five subjects for different flip angles and TRs are shown in Fig. 5. Both iSSFP and bSSFP sequences exhibit higher signal changes at longer TR. In each case, although the bSSFP sequence presents higher signal changes, it has larger signal variations across subjects (standard deviation), especially for small flip angle and short TR. In other words, the iSSFP sequence shows more stable signal changes compared with the bSSFP sequence. In addition to signal changes, the T values of statistical analysis were also extracted from activated ROIs and compared across the different sequences (Table 1). The T values of iSSFP were larger than those of bSSFP except for the condition of FA/TR= 25° /5.03ms. In addition, Table 1 displays the signal changes for the iSSFP complex images that combined the magnitude and phase signals. Compared with the magnitude images, the complex signal changes are increased by about 1.0%, or higher and are comparable to those of bSSFP. The T values of iSSFP complex signal and bSSFP signal were also comparable at longer TR.

The comparison between iSSFP and conventional GRE was also carried out. Although the Ernst angle of 8° and slightly longer TR of 11ms were used in the GRE protocol, the SNR and contrast were still inferior to those of the iSSFP technique as shown in Fig. 4. In addition, the signal change of GRE, shown in Fig. 5b, is just about 1.6% which is obviously lower than that of the iSSFP with the flip angle of 25° and TE/TR of 4.94/9.88ms.

The iSSFP sequences were also performed at four different spatial resolutions on three subjects for the two flip angles (4° and 25°). As shown in Fig. 6, the functional contrasts of iSSFP were lower than those of bSSFP, and the iSSFP sequences produced almost the same signal changes for different resolutions. Although the traditional bSSFP sequence showed

smaller signal change at lower resolutions for the FA of 4°, the difference across resolutions for bSSFP was not statistically significant. Meanwhile, both T values and activation volumes for iSSFP and bSSFP did not show significant monotonous changes with the four spatial resolutions (Table S1 in the supplementary material).

4.3. fMRI experiment 2

Four representative images of the SMS accelerated iSSFP and standard 2D GE-EPI for different slice positions at the temporal lobe along with group activation results in Exp. 2 are shown in Fig. 7. In comparison with GE-EPI, which is seriously affected by signal dropout and image distortion induced by susceptibility artifacts, SMS accelerated iSSFP demonstrates excellent visualization of the anterior temporal lobe. The activation results detected by group analysis were overlaid on the normalized T1 anatomic images (MNI space). As shown in Fig. 8, similar activations were found in inferior temporal sulcus in the group results of both GE-EPI (coordinate: $[-58, -44, -8]$; T: 5.92) and SMS accelerated iSSFP (coordinate: $[-64, -40, -10]$, $[-60, -30, -14]$; T: 5.46, 6.38). Greater activations within the inferior portion of the anterior temporal lobe (coordinate: $[-42 -26 -24]$; T: 5.13) were detected by SMS accelerated iSSFP compared to GE-EPI fMRI (uncorrected $P < 0.001$). Small volume correction within a 10-mm-radius sphere at the inferior part of temporal lobe was conducted and the P value corrected by FWE was less than 0.05. Values of the single voxel located at the local peak ($[-42 -26 -24]$) were extracted and Z score of the time courses were analyzed for all the subjects, as shown in Fig. 8(e). The statistical results showed significant difference ($P < 0.05$) between semantics and font size judgments, supporting that the detected area in anterior temporal region is related to semantic processing.

5. Discussion

This study presents a special case of the SSFP-FID technique termed iSSFP for fMRI at ultrahigh magnetic field. It was modified based on the traditional bSSFP by placing a specific dephasing gradient on the Z axis or X axis to compress the bSSFP magnitude profile into each voxel. The results of Bloch equation simulation and fMRI experiments show that iSSFP 1) has more stable signal changes than bSSFP; 2) can utilize larger flip angles, thus higher SNR and better tissue contrast, than GRE; 3) can be accelerated by SMS to improve temporal resolution and imaging coverage, which is difficult for SMS based bSSFP with banding artifacts; and 4) can achieve better image quality with reduced susceptibility artifacts and higher sensitivity to functional activation in the inferior temporal lobe and orbitofrontal cortex, compared with bSSFP and GE-EPI.

As an important index of the performance of the fMRI technique, SNR influences the image quality and fMRI sensitivity. The SNR efficiency (η) of the fMRI sequence is measured by [7,30]:

$$\eta \propto \sqrt{\frac{T_{read}}{T_{ima}}} * \frac{|M_{xy}|}{M_0} \quad (8)$$

where T_{read} is the readout time, and T_{ima} is the imaging time. As a modification of bSSFP by placing a dephasing gradient, iSSFP had relatively lower SNR because of reduced M_{xy} . Since SNR increases with field strength [31–33], this study was performed at ultrahigh field of 7 Tesla, which could also suppress signal contribution from large vessels [34,35].

The average time courses and T values of iSSFP, bSSFP and GRE were compared for different combinations of flip angles and TRs. The signal changes of iSSFP and bSSFP scaled with both flip angle and TR, and the average signal changes of iSSFP were lower than those of bSSFP. When the passband of bSSFP was utilized to detect the functional contrast, the SNR efficiency for iSSFP was about 0.6 times of that for bSSFP at the flip angle of 25°. Nevertheless, the signal changes were more stable with smaller standard deviations across subjects compared to those of bSSFP. As indicated in the results of simulation, the signal of bSSFP was T_2/T_1 weighted and in cycle of $1/TR$. The visual cortices of different subjects might be located at different position of the passband. Thus, the bSSFP magnitude variation relative to frequency change was different across the subjects, causing larger signal variability. Under the condition of short TR and small flip angle, the variation became more severe due to lower SNR. The T values of iSSFP were larger than those of bSSFP except for the condition of FA/TR=25°/5.03ms, suggesting a higher or comparable sensitivity to functional activation using iSSFP compared to bSSFP. The highest T value was obtained using bSSFP with FA/TR=25°/5.03ms, probably because of highest SNR with larger FA and reduced temporal noise due to magnetic field fluctuation and physiological noise at shorter TE. The T values for iSSFP was greatest when FA/TR was 25°/5.03ms, while the highest signal change was observed for FA/TR of 25°/9.88ms. This observation suggests that while a longer TR results in a larger functional signal change in iSSFP, the temporal noise (due to field fluctuation and physiological noise) also increases resulting in smaller T values at FA/TR of 25°/9.88ms. Due to the small sample size in the present study, these findings need to be replicated in future studies.

Past studies have shown that the functional contrast for passband bSSFP is primarily T_2 based BOLD at short TE/TRs [19,36]. For traditional non-balanced SSFP, e.g. FISP, a strong gradient is utilized to completely spoil the transversal magnetization, resulting in T_2^* -weighted signal [37]. Nevertheless, the dephasing gradient for iSSFP is small enough and there is still T_2 -weighted component in the iSSFP signal. Thus, the functional contrast of iSSFP signal is both T_2 and T_2^* weighted. In addition to magnitude, phase information of iSSFP could also be used due to its linear relationship with frequency shift. The complex signal changes reflect combined effects of T_2 and T_2^* based BOLD effects and frequency shift. The iSSFP complex images provided almost the same effect size of, but more stable functional contrast compared to that of bSSFP, as shown in Table 1. Another property of iSSFP is stable functional signal changes across different spatial resolutions, suggesting that it may be originated from microvasculature instead of larger vessels that would cause reduced fMRI signal changes with lower spatial resolutions [34]. Ultrahigh magnetic field also contributes to the stable iSSFP signal changes across different spatial resolutions [38].

In previous non-balanced SSFP fMRI studies [13,15], diffusion and flow had great effect on the signal of SSFP-FID and SSFP-echo because of the strong dephasing gradient. According to the Figure 1 shown by Oliver Bieri, et al. 2012, diffusion effects predicted to barely affect

the SSFP-FID signal when spoiling moments was below 20mT/m*ms [20]. Due to the relatively small dephasing gradient and short TR (spoiling moments of 13.6 and 4.7mT/m*ms) used in our study, the magnitude of iSSFP signal was reduced slightly, and the linear phase distribution across one voxel for iSSFP would not be affected significantly [19]. As shown by simulation and experiment in a previous study [18], blood flow has almost no effect on the signal magnitude at the passband, but leads to flow-related signal increase due to frequency offsets at the transition band for bSSFP and non-balanced SSFP. Thus, for iSSFP, the blood flow has barely any effect on the magnitude, but may cause phase changes due to the frequency shift. This might partly explain why the signal changes of complex (magnitude + phase) images had larger standard deviation compared to that of magnitude images alone in our study.

Conventional GE-EPI based fMRI methods that detect brain activation are generally based on T_2^* BOLD effects. However, the relatively long TEs and readout durations make the images sensitive to signal dropout and image distortions. In Fig. 4 and Fig. 7, the images of iSSFP are not affected by the off-resonance and susceptibility artifacts compared with bSSFP and GE-EPI. This result is consistent with the theory and simulation and coincides with the experimental observation that greater activations within inferior portion of the anterior temporal lobe were detected by SMS accelerated iSSFP compared to EPI. It is possible to achieve the whole brain coverage using iSSFP without careful shimming or multi-frequency acquisitions, which is demonstrated in Exp. 2.

However, there are a few limitations of the iSSFP technique. The temporal resolution of iSSFP was low. Rather long acquisition time was needed to obtain higher functional contrast (about 1.4s for one slice with TR of 9.88ms), which will hinder the widespread application of iSSFP to achieve higher spatiotemporal resolution, larger space coverage and fMRI based on event-related design. Future work will focus on acceleration techniques for iSSFP. The SMS acquisition technique based on phase modulation of CAIPIRINHA has been utilized to alleviate the problem in the present study. Preliminary results (3s for 8 slices with TR of 8.51ms) showed that the temporal resolution of iSSFP without periodic bands was effectively improved. Its application in bSSFP, however, has been limited because the phase modulation of CAIPIRIHNA results in shifted off-resonance profiles and subsequent banding artifacts in simultaneously excited slices [10,37,39].

6. Conclusions

As a unique case of the SSFP-FID sequence, iSSFP has been shown to be a feasible technique for fMRI at 7T. The functional contrasts can originate from the magnitude and phase change related to T_2 and T_2^* based BOLD effects and frequency shift respectively. In comparison with bSSFP, iSSFP provides almost the same effect size of, but more stable functional contrasts and does not need careful shimming and acquisition at specific frequency band. The SMS technique has been utilized to alleviate the limitation of low temporal resolution. In good agreement with simulation results, the experimental results indicate excellent image quality for SMS accelerated iSSFP with no susceptibility artifacts. Although, in comparison with the 6% or higher signal change for GE-EPI[40], the sensitivity of iSSFP to visual cortex activation is lower, it is suitable for specific fMRI tasks

to visualize activations in temporal and orbitofrontal cortices at high and ultrahigh magnetic fields.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Diagram of the iSSFP sequence modified from bSSFP (solid line). A spoiling gradient (dotted line) is placed right before the slice selective gradient (a) or after the readout gradient (b) to dephase the spins across a 2π cycle within one voxel. The gray shaded region corresponds to the 2π difference.

Fig. 2.

The results of simulated signal magnitude and phase profile for iSSFP (red line) compared with bSSFP (blue line). The iSSFP sequence shows constant magnitude and linear phase along the frequency for both of high (a) and low (b) flip angles. Because of the dephasing gradient, the SSFP profile is averaged into the size of one single voxel represented by the green box in (a) and (b).

Fig. 3.

Schematic illustration of the experimental procedure and stimuli. Participants were required to identify one from three Chinese characters (lower) close to the target (upper) in meaning and size and to indicate by keypress during task (red cross-hair) and control (green cross-hair) sessions, which were interleaved with 12s blocks of fixations (black cross-hair).

Fig. 4.

The visual fMRI activation maps ($t > 4$) of iSSFP (magnitude and complex) and bSSFP (magnitude) at 7T for different flip angles and TE/TRs overlaid onto corresponding baseline images of a representative subject. All three sequences exhibit high GRE contrast with higher flip angles and better image quality with short TE/TRs. iSSFP shows insensitivity to susceptibility changes without banding artifacts, compared with bSSFP. The activation map of GRE (FA/TE/TR=8°/4.94ms/11ms) is also displayed.

Fig. 5.

Averaged time courses with standard deviations (across subjects) for iSSFPz (red line), iSSFPx (green line) and bSSFP (blue line) with flip angles of 25° and 4° and TE/TRs of 2.52/5.03ms and 4.94/9.88ms. (Five subjects for bSSFP and GRE, ten subjects for iSSFP, where one was not activated at flip angle of 4° and TE/TR of 4.94/9.88ms due to head motion.) For the four conditions in (a), (b), (c) and (d), compared with bSSFP, the signal changes (%) of the iSSFPz and iSSFPx tend to be lower, but with smaller standard deviation. The signal change of GRE (black line; FA=8°, TR=11ms) with longer TR in (b) is lower than that of the corresponding iSSFP sequence.

Fig. 6.

Functional contrasts comparison among four different resolutions for both flip angles of 25° and 4°. The acquisition time for one slice (TR) was all 1.4s. Results for three subjects at each flip angle are collected and pooled. The functional contrasts of iSSFP were lower than those of bSSFP. For the four different resolutions, the signal changes of the three sequences are almost the same except that the bSSFP with 4° FA shows lower signal change at low resolution. However, this difference is not statistically significant.

Fig. 7.

Comparison of the quality of the first to the fourth slices at temporal lobe between SMS accelerated iSSFP (a) and 2D GE-EPI (b). There are less signal loss and distortion for the images of iSSFP than GE-EPI with the same spatial resolution ($1.72 \times 1.72 \times 3 \text{ mm}^3$).

Fig. 8.

Group analysis showed activations (uncorrected $P < 0.001$, cluster size > 5) at inferior temporal sulcus for both iSSFP (a, $[-64, -40, -10]$, $T: 5.46$; $[-60, -30, -14]$, $T: 6.38$) and GE-EPI (c, $[-58, -44, -8]$; $T: 5.92$) and more activation (red arrow; $[-42 -26 -24]$, $T: 5.13$) at the lower part of anterior temporal lobe for iSSFP (b), compared with GE-EPI (d). Averaged signal changes and standard errors for the activated voxel with peak value in (b) are shown in (e). And t-test shows significant difference ($P < 0.05$) between semantics and size judgments.

Table 1

The signal changes (mean $\pm$ std, %) and T values (mean $\pm$ std) for iSSFP (magnitude and complex), bSSFP (magnitude) and GRE (magnitude).

FA(deg.)/TR(ms)	Signal changes (%)				T values			
	25/5.03	25/9.88	4/5.03	4/9.88	25/5.03	25/9.88	4/5.03	4/9.88
iSSFPz magnitude	1.33 $\pm$ 0.17	1.75 $\pm$ 0.33	0.91 $\pm$ 0.19	1.33 $\pm$ 0.32	14.14 $\pm$ 2.53	11.11 $\pm$ 1.25	8.51 $\pm$ 1.70	8.98 $\pm$ 1.09
iSSFPx magnitude	1.09 $\pm$ 0.17	1.81 $\pm$ 0.32	0.68 $\pm$ 0.13	1.01 $\pm$ 0.39	10.80 $\pm$ 1.44	10.96 $\pm$ 1.90	7.60 $\pm$ 1.39	9.58 $\pm$ 2.04
bSSFP magnitude	1.60 $\pm$ 0.38	2.71 $\pm$ 0.77	1.37 $\pm$ 1.55	2.53 $\pm$ 1.06	14.49 $\pm$ 3.28	7.42 $\pm$ 0.97	6.00 $\pm$ 1.96	5.66 $\pm$ 0.73
iSSFPz complex	1.94 $\pm$ 0.75	2.49 $\pm$ 0.44	--	2.48 $\pm$ 0.53	6.76 $\pm$ 0.84	7.00 $\pm$ 1.43	--	5.68 $\pm$ 0.74
iSSFPx complex	2.15 $\pm$ 0.53	2.96 $\pm$ 0.87	--	1.70 $\pm$ 0.64	5.47 $\pm$ 0.29	6.54 $\pm$ 1.41	--	6.53 $\pm$ 1.19
GRE	0.77 $\pm$ 0.18 *				10.53 $\pm$ 1.54 *			

means that there are no activations above the threshold in some subjects

* means that the FA/TR of GRE are 8°/11ms.