Simultaneous Acquisition of Gradient-Echo and Asymmetric Spin-Echo for Single-Shot Z-Shim: Z-SAGA

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This article describes the Z-SAGA pulse sequence, a technique for recovering susceptibility losses in EPI images for neuroimaging applications. The pulse sequence is based on an asymmetric spin echo EPI sequence and acquires a gradient echo image and an asymmetric spin echo image in a single shot. For one of the images, a z-shim gradient pulse is applied to compensate for susceptibility-related field distortions. The two images are combined to form an image with reduced signal loss. This sequence is simple to implement and experimentally demonstrated to be effective for BOLD imaging. Magn Reson Med 51:212–216, 2004. © 2003 Wiley-Liss, Inc.

Keywords: z-shim; susceptibility; fMRI; EPI

Susceptibility artifacts are a major cause of image distortion and signal loss. Various areas of the human head contain air pockets, such as the nasal cavity and the ear canals. The difference in magnetic susceptibility between different tissues causes significant magnetic field distortions near their interface. A vivid depiction of these distortions in three dimensions can be found in a study by Collins et al. (1), who numerically modeled the pattern of field distortion caused by human head susceptibility artifacts with a 3D head model.

Typically, field distortions are compensated by shims that are optimized online for each examination. Often the shim gradients are not capable of complete compensation, and residual magnetic field distortions remain in the sample. These distortions cause an artificial shortening of the transverse relaxation time in the region near large susceptibility changes, leading to a signal loss in gradient echo images. The susceptibility effect can be expressed as the relaxation time $T_2^*$, leading to an effective relaxation time $T_2$ as given by Eq. 1. This signal loss is of great consequence to fMRI studies, which utilize the BOLD (2) contrast and $T_2^*$-weighted imaging. Due to this signal loss, various areas of the brain, such as the orbital frontal cortex (OFC) and portions of the auditory cortex, are difficult to image.

$$\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_2}$$  \[1\]

A number of methods for compensating susceptibility-related signal loss, including passive techniques, such as placing shim material in the roof of the mouth (3), filling the nasal cavity with humidified nitrogen, or changing head orientation (4) have been introduced. Alternatively, the sample can be shimmed dynamically by applying slice specific shim settings (5), or by a technique known as z-shim (6–10). In the z-shim method, multiple images, some with additional slice gradient applied to capture signals in areas affected by susceptibility effect, are acquired and combined to produce a composite image having reduced signal loss. This multishot z-shim can also be viewed as an additional phase encoding in the slice direction and leads to a 3D approach, as demonstrated by Glover (11).

Z-shim pulse sequences require multiple shots, hence reducing the attainable temporal resolution of fMRI experiments. A single-shot technique described by Song (12) acquires a double echo EPI scan while z-shimming one of the echoes. That sequence collects two gradient echo images sequentially after each excitation, with z-shimming applied to one of them to recover the region of signal loss. A potential pitfall of Song’s approach is that the two images are acquired at different echo times and have different BOLD weighting, although partial Fourier imaging could be utilized to reduce the discrepancy in echo times. A technique introduced by Glover and Law (13) utilizes spiral in/out acquisitions without using z-shim, with spiral in acquisition generating an image having reduced susceptibility signal loss, while both spiral acquisitions are collected at comparable effective echo time. This article describes a technique that permits the acquisition of the z-shimmed image and standard image in a single repetition as well, and maintains comparable BOLD contrast between the two images. Specifically, a z-shimmed gradient echo EPI image is acquired before the acquisition of an asymmetric spin echo EPI image (14), and the sequence timing is such that the two images are acquired with identical $T_2^*$ weighting. This scheme is similar to that proposed by Song (12), but provides images having the same $T_2$ weighting. Furthermore, using partial Fourier acquisition in both images reduces $T_2$ decay between the effective echo times. Experimental results obtained with this approach demonstrate that it is robust and easy to use. Results also show that the BOLD contrast is consistent in the two images and that the method is easily applicable to fMRI studies.

MATERIALS AND METHODS

A dual-echo EPI sequence is designed to incorporate the z-shim technique to compensate for susceptibility-related signal losses. The pulse sequence is depicted in Fig. 1. Essentially, the sequence uses a spin-echo RF pulse train and forms a gradient-echo EPI image from the FID signal.
Following the excitation pulse and another EPI image after the refocusing pulse. The center of the \( k \)-space, that of the EPI acquisition following the refocusing pulse, is shifted away from the spin-echo such that signal contrast is derived from an asymmetric spin echo that has a \( T_2^* \) weighting. In this configuration the center of both echoes are acquired with the same \( T_2^* \) weighting and slightly different \( T_2 \) weighting, and hence have similar BOLD weighting because \( T_2^* \) effects often dominate the BOLD contrast. If it is desired to have comparable \( T_2^* \) weighting in the two images, partial Fourier EPI acquisition can be used to move the echo centers of these images closer. Figure 1 also shows the zero-order gradient moments, or \( k \)-space traversal, for the phase-encoding direction (\( k_p \)) and the slice direction (\( k_s \)). These diagrams demonstrate the location of the echo centers for partial Fourier acquisition, as well as the \( z \)-shim and the rewinding on the slice direction. The \( z \)-shim is introduced before the acquisition of the first image by altering the strength of the slice refocusing gradient and the refocusing slice gradient. The \( k_s \) line depicts the \( z \)-shim and subsequent rewinding.

Several human experiments were performed to examine the utility of the Z-SAGA pulse sequence. The first experiment is a demonstration of the signal recovery achieved by the Z-SAGA sequence. The second experiment was designed to examine the BOLD contrast in the images of the Z-SAGA pulse sequence. The final study applies the Z-SAGA pulse sequence in an fMRI experiment where activation is expected in regions prone to susceptibility loss. The Z-SAGA pulse sequence is programmed in the Siemens IDEA pulse sequence environment for a 3 T Siemens Trio scanner with Sonata gradients capable of reaching 40 mT/m with a maximum rise time of 200 \( \mu \)sec. Images were reconstructed offline from raw data in the IDL programming environment, by echo reordering, application of phase reference scan correction, ramp sampling correction, and, if needed, an iterative partial Fourier reconstruction that restores the original complex \( k \)-space. A user interface is implemented in the sequence to allow online calibration of the \( z \)-shim gradient. The composite image is reconstructed by computing the square root of the sum of squares (SSQ) of the two acquired images (15). Prior to forming the SSQ image, the asymmetric spin-echo image is corrected for \( T_2^* \) decay by a correction factor \( f_c \) given by Eq. 2. In Eq. 2, \( T_2^* \) and \( T_2 \) are the echo times with respect to \( T_2^* \) decay given in Fig. 1, and \( T_2 \) is assumed to be 55 ms for the brain at 3T.

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f_c = e^{-\frac{\Delta T_2}{T_2}}
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Z-SAGA imaging was first performed on a normal volunteer to assess image quality and signal recovery. The imaging parameters consisted of a \( 64 \times 64 \) matrix, a 22 cm FOV, a bandwidth of 2056 Hz/pixel, a TR of 109 ms, a gradient echo time of 30 ms for the first echo, and an asymmetric spin echo time of 68 ms with an echo shift of 30 ms for the second echo. This timing results in a 38 ms interecho interval between the images. Five slices, 5 mm thick, positioned axially to cover the inferior frontal areas of the brain were imaged. Phase correction scans were acquired for both EPI readout trains. The \( z \)-shim gradient was calibrated online to optimize signal recovery in the inferior frontal lobe.

In order to examine the consistency of the BOLD contrast in the asymmetric spin echo image vs. that in the gradient echo image, a finger-tapping fMRI experiment was conducted. The fMRI paradigm consists of visually cued right-hand finger-tapping with three blocks of 30 sec on/off periods for a total scan time of 3 min. The subject was scanned with the partial Fourier Z-SAGA sequence with an echo time of 35 ms for the gradient echo EPI and

![Figure 1. Pulse diagram for the dual echo z-shim EPI sequence. The gradients are specified in standard read-phase-slice notation, as well as the zero order moments of the gradients that represent \( k \)-space traversal of the sequence. The \( k_s \) line infers that a partial Fourier EPI technique is applied for each image acquisition. The z-shim gradients are highlighted in gray as modifications to the slice refocusing gradient and the refocusing slice gradient. The z-shim is introduced before the acquisition of the first image by altering the strength of the slice refocusing gradient and the slice refocusing on the slice direction. The zero order gradient moments, or \( k \)-space traversal, for the phase-encoding direction (\( k_p \)) and the slice direction (\( k_s \)). These diagrams demonstrate the location of the echo centers for partial Fourier acquisition, as well as the \( z \)-shim and the rewinding on the slice direction.](image1.png)

![Figure 2. Resulting images from a full Fourier Z-SAGA pulse sequence. The left image is the \( z \)-shimmmed echo and the center image is the standard EPI image. The right image is a sum of squares (SSQ) composite image. Signal recovery can be observed in the inferior frontal lobe, as well as in the temporal lobes. Sequence parameters include a full \( 64 \times 64 \) acquisition, a 4 mm thick axial slice, a bandwidth of 2056 Hz/pixel, a TR of 109 ms, and TE of 30. The time between echoes in the Z-SAGA sequence is 39 ms.](image2.png)
a 35 ms effective echo time for the asymmetric spin echo EPI. The inter-echo time between the two images was 22 ms. Ten 5-mm thick axial slices were acquired in 1 sec (TR \(= 100 \text{ ms}\)), covering the superior motor areas. The acquired partial Fourier matrix was \(64 \times 40\) with a 22 cm FOV. Two sets of fMRI data were reconstructed, one from the gradient echo images and the other consisting of the asymmetric spin echo images. Activation was detected by cross-correlating the data with a boxcar function coinciding with the paradigm. Activation maps of the cross-correlation as well as time courses were evaluated for the consistency of the BOLD response between the two datasets. Since the data were acquired simultaneously, direct comparison of the time course data were employed. Data processing was performed in IDL using custom processing routines. In addition to the fMRI study, a colocalized anatomical scan was acquired for functional overlay. The sequence used is a phase-sensitive true-IR imaging sequence.

Another fMRI experiment was performed to examine the ability of detecting BOLD activation in the areas recovered by the Z-SAGA sequence. The fMRI paradigm used for this task was a block-design visual-emotional response paradigm which evokes a strong emotional response in the subject (16). The imaging parameters consisted of a full Fourier \(64 \times 64\) matrix, a 22 cm FOV, a bandwidth of 2056 Hz/pixel, a TR of 109 ms, a gradient echo time of 30 ms for the first echo, an asymmetric spin echo time of 68 ms with an echo shift of 30 ms for the second echo, and 31 contiguous slices covering the whole brain. The z-shim was applied to the second echo and was optimized online for signal recovery in the inferior frontal areas using a scout. Once the z-shim is determined the fMRI run consisted of 34-sec alternating blocks of aversive photographs from the International Affective Picture System (IAPS), shown every 2 sec on a back-projection system installed in the bore. Four blocks were repeated with novel images in

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**Fig. 3.** Functional maps generated from a 30-sec block motor fMRI study and the Z-SAGA pulse sequence with z-shim gradients turned off. The left image is the functional map generated from the gradient echo acquisition and the right image is from the asymmetric spin echo acquisition. The maps are generated by cross-correlating the time course data with a reference time course from an activated pixel in the primary motor area. The maps are thresholded at a correlation value of 0.5.

**Fig. 4.** Average time course from the activated areas in Fig. 3 for the gradient echo data are plotted in a heavy line and the asymmetric spin echo data are plotted in a thin line. The average time courses are plotted in raw format in percent change from the mean. The ROI for creating the average is based on the activation map from the gradient echo data so that identical pixels are averaged.

**Fig. 5.** Functional maps resulting from a visual-emotional response paradigm. The maps are generated by using an activated pixel time course from the visual area as a linear correlation reference function. The resulting correlation map was thresholded at 0.2 and the minimum cluster size was fixed at 6. The maps are shown in overlay on a Z-SAGA image (top left), a standard EPI image (top right), and a high-resolution \(T_1\) weighted image (bottom row). The Z-SAGA data shows activation clusters in the amygdala region where the EPI data does not. The EPI data is generated from the Z-SAGA directly before image composition.
RESULTS AND DISCUSSION

Z-SAGA imaging results in the human volunteer for a slice in the inferior frontal lobe is shown in Fig. 2. The three images in Fig. 2 correspond to the z-shimmed gradient echo image (left), the asymmetric spin echo image (center), and their composite SSQ image (right). The composite image shows a significant recovery in signal in the areas severely affected by the susceptibility effect. The z-shim gradient moment used for the acquisition of the gradient echo image was 2.8 ms • mT/m. Even with only a single z-shim acquisition, a significant amount of orbital frontal cortex is recovered in this image, as indicated by the arrows. With the balanced timing around the refocusing pulse, the $T_2$ weighting is identical in all three images and the BOLD contrast of the composite image is comparable to a gradient echo acquisition of the same effective echo time. $T_2$ weighting differences between the images are unavoidable, although the effect can be minimized by the application of partial Fourier acquisition.

Results from the motor fMRI study are shown in Figs. 3 and 4. The cross-correlation maps shown in Fig. 3 are thresholded with a cross-correlation value of 0.5. The activation patterns in the two datasets are comparable, although the spatial extent of the activation clusters in the asymmetric spin echo dataset is somewhat reduced due to the reduced SNR. The comparison in Fig. 3 is biased by SNR differences in the two datasets. A more pertinent comparison is made in Fig. 4, where time courses from both datasets in the same region of interest, which was defined based on activated pixels in the gradient echo dataset, are plotted. The y-axis represents the percent change from mean, which should be insensitive to $T_2$ losses. Here, the BOLD contrast in the two datasets are nearly identical. A reduction of approximately 0.3% in BOLD contrast was found in the asymmetric spin-echo data. This slight reduction in BOLD contrast may be due to a reduction of large vessel contributions in the asymmetric spin echo data (14).

Maps of activation to the emotional stimulus are shown in Fig. 5 for a slice containing the amygdala. The maps are overlaid on corresponding $T_2$ weighted EPI images (top) and a high-resolution $T_1$-weighted image (bottom). The Z-SAGA data exhibits activation clusters in the amygdala region where the EPI data does not. Bilateral amygdala activation for this paradigm is consistent with results from a PET study, where susceptibility losses are not a factor (16). The location of the susceptibility artifact in this subject is found to be more posterior than the subject in Fig. 2. This may be due to a difference in head orientation (4) and intersubject variability in anatomy.

This article reports a method for recovering susceptibility-induced losses for neuroimaging. The signal recovery is achieved through a single-shot z-shimming approach that acquires the standard image and the z-shimmed image after a single excitation. Furthermore, the BOLD contrast of the two images are nearly identical, as shown by the results in Fig. 4, in contrast to previous multiecho sequences (12). In addition, the method is robust for recovering signal in areas such as the amygdala, as shown in Fig. 5.

The pulse sequence described in Fig. 1 is compact, making efficient use of time within the TR. The use of partial Fourier acquisition moves the echo times of the two images closer. The second partial Fourier EPI train is reversed, mirroring the first readout with respect to the refocusing RF pulse, similar to the spiral-in/spiral-out sequence (13). The balanced structure of the sequence results in the reproducibility of the BOLD response between the two contrasts.

A drawback of the present pulse sequence design is a signal intensity reduction in the asymmetric spin echo image due to $T_2$ decay. The use of partial Fourier minimizes these losses. If the partial Fourier EPI readouts in the dual echo sequence shown in Fig. 1 were replaced by a reversed spiral acquisition (13,18), the echo centers with respect to $T_2$ of the two images could be moved closer to the refocusing pulse, resulting in much reduced $T_2$ losses in the second acquisition. Also important is that the composite image has a higher SNR compared to the standard single image approach.

Common to most z-shim sequences is an online calibration in order to determine the level of slice shim needed for a particular region. It is possible to encode multiple z-shim gradients using a multishot acquisition and acquire a subset of the full 3D z-shim encoding (11). These extra acquisitions decrease the temporal resolution of fMRI studies. The Z-SAGA sequence can be extended to a multispin echo approach such that the images with a multiple set of z-shims can be acquired with a single excitation. This scheme can reduce a 3D z-shim experiment by half by acquiring two z-shim encodings in one TR.

ACKNOWLEDGEMENTS

The authors thank Kyle Salem of Siemens Medical Solutions for technical support, and Stephan Hamann of Emory University for providing the paradigm for the aversive, emotional response fMRI study.

REFERENCES