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B₁ Mapping of Short T₂* Spins Using a 3D Radial Gradient Echo Sequence

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Abstract

Purpose—To develop a method to acquire a radiofrequency (B₁) field map when the signal has a short T₂*.

Theory and Methods—The method is based on the actual flip angle imaging (AFI) technique and a radial 3D gradient-echo sequence known as CONcurrent Dephasing and Excitation (CODE) which preserves short T₂* signals. CODE was implemented with Gradient-modulated Offset-Independent Adiabaticity (GOIA) pulses to obtain high estimation sensitivity with AFI. The correlation method, that removes the quadratic phase from the frequency-modulated pulse excitation, was modified to handle gradient-modulated pulses. Validity of the modified correlation procedure was tested by Bloch simulations. CODE experiments with sinc, hyperbolic secant, and GOIA pulses were performed in order to see effects from the frequency- and gradient-modulation. Finally, GOIA-CODE AFI was conducted and compared with conventional AFI with 3D GRE.

Results—The modified correlation method developed to accommodate frequency- and gradient-modulations of GOIA performed well as judged by the minimal impact on reconstructed image quality. GOIA-CODE AFI provided flip angle maps consistent with those measured by GRE AFI when the T₂* was long (> 2 ms) and continued to perform well for short T₂* signals.

Conclusion—The proposed technique provides a means to obtain a 3D B₁ field map when imaging spins with short T₂*.

Keywords

actual flip angle imaging (AFI); B₁ mapping; frequency-modulated pulse; gradient-modulated offset-independent adiabaticity (GOIA); radial MRI; ultra-short TE; concurrent dephasing and excitation (CODE)

Introduction

Knowledge of the spatial radiofrequency (RF) field distribution is important in a number of MRI applications such as quantitative T₁ measurement (1) and correction of the B₁-dependent intensity variation (2). While overall distribution of the RF field for each coil can be obtained by measuring test objects or numerically solving the Maxwell equation based on the known coil geometry and sample model, the actual RF distribution is dependent on the conductivity, dielectric properties, and coil loading of each object. Therefore, direct

mapping of the spatial RF field for individual objects is always preferable especially for accurate outcomes in quantitative analyses.

A number of B_1 mapping methods have been introduced (3–7). Most methods estimate the RF field distribution as a function of the image intensities. A widely used method is the double-angle technique where two image datasets are acquired with spin echo or gradient echo (GRE) sequences at two different flip angles (mainly α and 2α) and the B_1 map is calculated from the intensity ratio of the two images (3, 4). In another method that acquires a spin echo and a stimulated echo during one repetition time (TR), similar to the double-angle technique, the actual flip angles are estimated from the ratio of the spin echo and stimulated echo images (5). Actual flip angle imaging (AFI) is a recently introduced technique that utilizes interleaved acquisitions of the dual TR steady-state that is formed by alternately changing TR in a spoiled GRE sequence (6). In this method, when the two TRs are sufficiently short relative to the longitudinal relaxation time T_1 the intensity ratio of the two TR images becomes a function of only the flip angle. Another technique based on spoiled GRE uses a linear dependence of the signal intensity on flip angle around the signal null point at 180° excitation (7). By acquiring a couple of images with different nominal flip angle around 180° and performing linear fitting to the model function, the B_1 field map is obtained independently with T_1 .

The RF field mapping methods introduced to date implicitly focus on relatively long-lived signals (i.e., spins with T_2 or T_2^* values greater than ~ 1 ms), since the minimum echo time (TE) achievable in those methods is generally greater than 1 ms. However, there is increasing need for quantitative evaluation of short T_2^* spins (8, 9) due to the recent expanded use of MRI methods that permit imaging of short T_2^* spins (10–13). While these sequences provide high sensitivity to short T_2^* spins, they suffer from restrictions on the achievable flip angle. This limitation is significant since large flip angles are preferred for increasing the sensitivity of the estimation in many of the B_1 mapping methods (14). To minimize the length of time between RF excitation and signal detection, the ultra-short TE (UTE) (10) and zero TE (ZTE) (11) methods utilize a short duration hard pulse followed by free induction decay (FID) acquisition. As a result, the maximum achievable flip angle in these methods is usually constrained by available peak RF power. Frequency-modulated (FM) pulses used in SWIFT alleviate this situation to some extent because sequential excitation in space distributes RF energy in time (12). However, broadband FM pulses still require high RF power (and SAR) to attain flip angles sufficient for B_1 mapping.

In this work, we propose a novel 3D B_1 mapping method for short T_2^* spins. This B_1 mapping method is based on an implementation of the AFI technique using the 3D radial sequence called CONcurrent Dephasing and Excitation (CODE) (13). CODE is a GRE sequence designed for short TE imaging ($TE < 500$ μs) with the added advantage of being relatively robust. However, as with other short TE sequences, the maximum flip angle achievable with standard CODE is constrained by the need to keep the pulse length short. To overcome the latter limitation, a low power FM pulse called Gradient-modulated Offset-Independent Adiabaticity (GOIA) (15) is used for excitation in CODE. The quadratic phase generated by the GOIA excitation pulse, like that produced by other FM pulses, is removed

using the correlation method (16). Validity of the correlation procedure for excitation with a GOIA pulse is evaluated for a wide range of flip angles using numerical Bloch simulations.

Theory

The correlation procedure in GOIA-CODE

The sequence diagram of CODE with a FM pulse is shown in Fig. 1. The CODE sequence is composed of 3 segments: excitation, acquisition, and spoiling. In the excitation segment, a FM pulse with short pulse width T_p ($<500 \mu\text{s}$) is applied for slab selective excitation and the excited isochromats are simultaneously dephased by the excitation gradient. Immediately after the excitation, the gradient polarity is inverted to acquire an echo signal in the acquisition segment. Since the area under the excitation gradient is small relative to the area under the readout gradient, the acquired echo signal is asymmetric, which permits short TE for preserving short T_2^* signals. In CODE, the echo peak (i.e. the center of k-space) is sampled in every TR; therefore, the acquired signal is a radial k-space line that passes through the center of k-space. Accordingly, acquisition is repeated until the entire 3D k-space is sampled by changing the gradient direction, as is usually done in projection MRI (17). In the current implementation, a spoiling gradient is combined with the readout gradient.

Slab selective excitation with a FM pulse excites spin isochromats sequentially in space along with the frequency sweep; spin isochromats are assumed to be excited instantaneously at the time when the pulse is resonant with the spins. Therefore, the approximately linear frequency sweep combined with the linear magnetic field gradient produces a quadratic phase profile in the direction of the slab selection. This quadratic phase cannot be corrected by applying linear gradients. As such, local refocusing of isochromats takes place sequentially in time during readout, and this yields an unconventional echo formation called a “pseudo-echo” (18). In the case of such sequential signal refocusing, each isochromat has a different echo peak position in time (19). In 3D Cartesian MRI, the quadratic phase does not necessarily have a major impact on the reconstructed image, since all repetitions employ the same slab-selection direction and the quadratic phase distribution in space is common for all acquisitions. However, in the radial excitation of CODE, the slab-selection gradient changes its direction with each repetition and the quadratic phase distribution in space is no longer consistent between acquisitions. Hence, it is necessary to remove the quadratic phase by applying a specific procedure known as the correlation method (16), where the quadratic phase is compensated by dividing the measured profiles along the slab-selection direction by the known RF excitation profile.

The correlation method has been employed in sweep imaging with Fourier transformation (SWIFT) to remove the quadratic phase due to FM pulse excitation (12). However, the method reported in the previous works dealt only with FM pulses that are applied without gradient modulation, and thus it cannot be applied directly to GOIA pulses. Here a generalized formalism of the correlation method is derived to handle gradient modulated pulses.

Theoretical formalism of the correlation method can be derived from the Bloch equation by applying the low flip angle approximation ($M_z \approx M_0$). Under the low flip angle approximation, the Bloch equation is analytically integrated and the transverse magnetization at the end of the pulse T_p (i.e. excitation profile), $M_{xy} = M_x + iM_y$, is given by (20):

$$M_{xy}(\mathbf{r}, T_p) = i\gamma M_0 \int_K W(\mathbf{k}) S(\mathbf{k}) e^{i\mathbf{r} \cdot \mathbf{k}} d\mathbf{k}, \quad [1]$$

where

$$\mathbf{k}(t) = -\gamma \int_t^{T_p} \mathbf{G}_{ex}(t') dt', \quad [2]$$

$$W(\mathbf{k}(t)) = B_1(t) / |\gamma \mathbf{G}_{ex}(t)|, \quad [3]$$

$$S(\mathbf{k}) = \int_0^{T_p} \delta(\mathbf{k}(t) - \mathbf{k}) \left| \dot{\mathbf{k}}(t) \right| dt. \quad [4]$$

In these equations, γ , $B_1(t)$ and $\mathbf{G}_{ex}(t)$ are the gyromagnetic ratio, RF field and excitation gradient vector, respectively; $\mathbf{k}(t)$ is the excitation k-space coordinate; and $W(\mathbf{k})$ and $S(\mathbf{k})$ represent a weighted excitation k-space and a sampling trajectory function, respectively.

In CODE, since the excitation k-space trajectory is a straight line along the excitation gradient direction (but traversed non-uniformly in time), the sampling trajectory function $S(\mathbf{k})$ is constant for the employed one-dimensional (1D) excitation profile and, hence, can be omitted in the following. Based on Eq. [1], the Fourier transform of the signal in CODE, $\hat{s}(r)$, is expressed by (ignoring the gradient ramp time for simplicity):

$$\hat{s}(r) = \rho(r) \cdot \hat{b}_1(r), \quad [5]$$

where,

$$\hat{b}_1(r) = i\gamma \int_K W(k) e^{i\mathbf{r} \cdot \mathbf{k}} dk \quad [6]$$

In Eqs. [5] and [6], r and k express 1D spatial and excitation k-space coordinates along the excitation (readout) gradient direction. The $\rho(r)$ represents the projection of an object onto the constant readout gradient vector, and includes longitudinal relaxation effects (i.e., the projection of the steady-state magnetization). The spin density $\rho(r)$ that is to be obtained for image reconstruction is calculated as $\hat{s}(r) / \hat{b}_1(r)$.

Actual flip angle imaging (AFI)

In the AFI method, the spatial distribution of the flip angle is calculated based on a dual TR steady-state. The dual TR steady-state has been generated by alternately changing TR (TR_1 and TR_2) in conventional or radial spoiled GRE sequences (6, 21). As in conventional spoiled GRE sequences, when complete spoiling is realized in every TR, the CODE signal is

also described by the Ernst formula (22), and by replacing the imaging segment, AFI can be executed with CODE.

The AFI method relies on two fundamental assumptions: 1) complete spoiling of the transverse magnetization in every TR, and 2) sufficiently short TR as compared to T_1 . The requirement for perfect spoiling assures that the signal in each TR interval is proportional to the steady-state longitudinal magnetization arising purely from T_1 recovery (not containing occasionally coherent signals such as a stimulated echo). The second assumption for TR ($TR_{1,2} \ll T_1$) removes the T_1 dependence from the flip angle estimation. Under these assumptions, the flip angle distribution in space can be obtained according to the following equations (6):

$$R = \frac{S_2}{S_1} \approx \frac{1+n \cdot \cos \alpha}{n + \cos \alpha}, \quad [7]$$

$$\alpha = \arccos \left(\frac{R \cdot n - 1}{n - R} \right), \quad [8]$$

where α represents the actual flip angle, n is the ratio of the two repetition periods ($n = TR_2/TR_1$), and $S_{1,2}$ is the pixel intensity of images measured in intervals TR_1 and TR_2 . Provided that the first order approximation of T_1 relaxation terms, $e^{-TR_{1,2}/T_1} \approx 1 - TR_{1,2}/T_1$, is satisfied, flip angle estimation based on Eqs. [7] and [8] is robust for spins having a relatively wide range of T_1 values.

In the AFI method, the spatial distribution of the flip angle is determined from the difference of the image intensity ratio R given by Eq. [7]. Under a low flip angle condition, the intensity ratio R is relatively insensitive to the flip angle difference due to being a function of $\cos \alpha$, which means small intensity fluctuations, for example due to noise, potentially induce relatively large errors in the flip angle estimation (14). Furthermore, the flip angle variation in space, namely, the variability of R , is proportionally expanded as the nominal flip angle increases. Therefore, use of higher flip angles is desirable in the AFI method; flip angles of 40–80° have been suggested as nearly optimal conditions for AFI experiments (6).

Methods

Validation of the correlation method for relatively large flip angles

The derivation of the correlation method is based on the low flip angle approximation. Therefore, it is necessary to validate the correlation method for excitation with relatively large flip angles used in GOIA-CODE AFI. The general form of the Bloch equation, which cannot be integrated analytically, was numerically solved by use of the matrix notation (23). The numerical solution $m_{xy}(r, T_p)$ was compared with the analytical solution under the low flip angle approximation given by $M_{xy}(r, T_p)$ in Eq. [1]. In the analytical solution, the excitation profile is obtained as the Fourier transformation of the pulse, and thus the solution is independent of the flip angle (except for amplitude scaling). However, the spin system described by the Bloch equation inherently shows nonlinearity with respect to the flip angle, and therefore the performance of the correlation procedure may degrade as the flip angle

increases. Accordingly, in order to test the B_1 dependence, numerical integration of the Bloch equation was performed for five different flip angles: FA=5, 10, 20, 30, and 50°. Comparison of the numerical and analytical solutions, $m_{xy}(r, T_p)$ and $M_{xy}(r, T_p)$, was evaluated in accordance with the following function:

$$h(r) = a \cdot \frac{m_{xy}(r, T_p)}{M_{xy}(r, T_p)} \cdot e^{i(\phi r + \varphi)}, \quad [9]$$

where ϕ and φ are the zero and first order phase correction factors, and a is the constant scaling factor that is inversely proportional to the sine of the flip angle. The angles ϕ and φ were estimated by fitting $h(r)$ within the frequency sweep band to 1 in the least squares method. The phase correction term $e^{i\phi r + \varphi}$ which is equivalent to application of a linear gradient and constant phase offset, removed the linear component in the flip angle dependent phase. The correlation procedure was evaluated by comparing $h(r)$ with 1; that is, the correlation method should work better as $h(r)$ gets close to unity.

Simulation

First, 1D Bloch simulations for CODE with hyperbolic secant (HS1) (24) and GOIA (15) pulse excitation were performed. Common pulse parameters were employed for HS1 and GOIA pulses: $T_p=250 \mu\text{s}$, truncation factor $\beta=5.3$ ($\text{sech}(\beta)=0.01$), $bw=80 \text{ kHz}$. HS4 and HS2, which are flattened HS pulses (25), were employed as amplitude- and gradient-modulation functions of the GOIA pulse. The gradient modulation depth was set to 0.5 (the minimum gradient amplitude is half of the gradient in HS1 excitation). The frequency-modulation function was calculated based on the amplitude- and gradient-modulation functions (15). The HS1 and GOIA pulses were used in all simulations and experiments in this study. The CODE simulations were performed using a 1D theoretical spin density distribution. Simulated sequence parameters were $sw = 83 \text{ kHz}$ and $TE = 420 \mu\text{s}$. The evolution of the spins was calculated by numerically integrating the Bloch equation for each isochromat separately. The spin density was retrieved from the acquired signal according to Eq. [5] and then compared with the theoretical spin density.

3D Bloch simulations for CODE were performed with the HS1 and GOIA pulses in order to evaluate the performance of the correlation procedure in 3D imaging. The simulated parameters were common to those in the 1D simulation except $TE = 320 \mu\text{s}$. Projections onto excitation (readout) gradient directions were generated by analytically integrating a 3D theoretical phantom. CODE signals were obtained in the same way as the 1D simulation by using the projections as spin densities. 131,072 projections were calculated for 3D image reconstruction. The reconstructed image size was $256 \times 256 \times 256$. Details of the reconstruction processing are explained in the following “Imaging experiment” section. All simulations were performed with a home-built Bloch simulator running on Matlab (MathWorks Inc. MA).

Imaging experiment

The CODE sequence with FM pulse excitation was implemented on 9.4T 31cm bore MRI system equipped with 40 Gauss/cm gradients (Agilent Technologies Inc. CA). All data were

acquired with a single channel Helmholtz coil for transmit and receive. CODE is relatively sensitive to gradient system delays which cause the actual k-space trajectory to deviate from the ideal one. Therefore, before performing CODE experiments, the gradient system delays were adjusted by the following manner. First, three acquisitions of 1D CODE were performed, each of which used only one of the x, y, or z gradients. The acquired asymmetric echo signal was transformed to a projection and then the echo peak time was estimated from the linear phase in each projection. Based on the time mismatch among the echo peak positions, the gradient system delays were adjusted to align the echo peaks at the same time. Image reconstruction was done offline with a home-built program written with C language.

An agar gel phantom doped with 1% NaCl was measured to demonstrate the performance of the correlation procedure. Sequence parameters were common for both HS1- and GOIA-CODE: FA=5°, TR=4 ms, $sw=83$ kHz, FOV=6×6×6 cm³, 98,304 views and scan time=397 s. TE was slightly shorter for GOIA-CODE (309 μs for GOIA-CODE and 331 μs for HS1-CODE), since the area of the excitation gradient was smaller in GOIA excitation due to the gradient modulation. In order to uniformly sample the spherical k-space, the gradient directions were calculated using a semi-random Halton sequence (26). A uniform 2D distribution was generated using two sets of the Halton sequence, each of which had a different basis number (2 and 3), and then the 2D distribution was mapped onto a spherical surface. The points uniformly distributed on the spherical surface were sorted to pseudo-spirals so as to avoid big directional changes happening between successive TRs. Each spiral had 1,024 gradient directions (views). For comparison, data were also acquired using sinc-pulse excitation that does not generate quadratic phase. In sinc-CODE, an 11-lobe sinc pulse windowed with a cosine function was employed with $T_p=200$ μs and $sw\approx 60$ kHz. Other sequence parameters in sinc-CODE were common to GOIA-CODE except for TE=312 μs.

In image reconstruction of HS1- and GOIA-CODE, the quadratic phase was removed by the correlation procedure, i.e. according to Eq. [5]. For sinc-CODE, zero and first order phase corrections were performed. After the correlation or phase correction procedure, the obtained projection $\rho(r)$ was transformed back to k-space domain, and then the radial k-space line signal was gridded onto a 3D Cartesian k-space (27). In gridding, a Kaiser-Bessel window was employed as a convolution kernel; the kernel width was 3 pixels before grid oversampling, and the grid oversampling factor was 2. Sampling density correction factor was calculated by performing gridding back and forth iteratively between radial and Cartesian coordinates; 3 times iteration was employed (28). Applying Fourier transformation to the Cartesian k-space provided a 3D image followed by apodization correction. The image size was 256×256×256. For signal-to-noise ratio (SNR) comparison, two regions of interest (ROI) with a size of 16×16×16 pixels were selected from the background and a uniform part in the phantom. SNR was calculated according to $\bar{I} / \sqrt{\sigma}$, where $\bar{I}$ is mean signal intensity of the phantom ROI and σ is variance of the background noise region.

Tomato imaging was conducted with HS1- and GOIA-CODE in order to show its capability to capture short T_2^* signals. Some parts of the tomato, such as seeds and core region, have relatively short T_2^* which makes them difficult to visualize with conventional MRI sequences. The same sequence parameters as used in the CODE phantom experiments were

employed with the exception of $TR=4.7$ ms, $FOV=64\times64\times64$ mm³, number of views=131,072, and scan time=622 s. Three different flip angles of 4, 20, and 40° were used to get different T_1 weighted contrasts. Images were reconstructed with matrix size of $288\times288\times288$. For comparison, 3D GRE imaging was performed with the following parameters: $TR=6$ ms, $TE=2.6$ ms, $sw=83$ kHz, $FOV=64\times64\times64$ mm³, matrix= $256\times256\times256$, and scan time=394 s.

AFI

GOIA-CODE AFI implementation was done according to literature by replacing the imaging segment with GOIA-CODE (6). For comparison, 3D GRE AFI with non-selective hard pulse excitation was also performed as a reference standard. We employed $n=TR_2/TR_1=5$ for both GOIA-CODE and GRE. Sequence parameters for CODE were: $TR_1/TR_2=4.5/22.5$ ms, $TE=330$ μ s, nominal flip angle=45°, 32,768 views, matrix= $128\times128\times128$, and scan time = 450 s. Parameters for 3D GRE were: $TR_1/TR_2=12/60$ ms, $TE=1.7$ ms, matrix= $128\times128\times128$, and scan time = 1182 s. Because complete spoiling of transverse magnetization is critical for AFI, RF and gradient spoiling were used in both CODE and GRE. A recent analysis based on the diffusion propagator model demonstrated that the application of very large spoiling gradients yields nearly ideal spoiling regardless of the incremental phase in RF spoiling (29). Accordingly, very large gradient moments were employed for the GRE reference (163 and 814 gauss·ms/cm for TR_1 and TR_2). In GOIA-CODE, since the spoiling gradient combined with the readout gradient changes its direction in every TR, the spoiling effects in GOIA-CODE were evaluated. This assessment was performed by imaging a tomato, which contains water protons having a relatively large range of T_2^* values, under 3 different spoiling conditions: weak, intermediate, and strong spoiling corresponding to gradient moments of 8.8/74.4, 17.5/149 and 35.0/298 gauss·ms/cm (TR_1/TR_2), respectively. The capability of B_1 mapping for short T_2^* spins was evaluated by measuring solutions with 4 different iron oxide nanoparticle concentrations (0.2, 1, 2, and 4 mM) (Feridex, Bayer HealthCare Pharmaceuticals inc., NJ). T_1 and T_2^* values were measured by the least square fitting of inversion recovery and FID signal decay curves acquired without spatial encoding: $T_1/T_2^*=2022/8.4$, 687/3.0, 424/1.8 and 224/0.9 ms for the 0.2, 1, 2, and 4 mM solutions, respectively. For RF spoiling, an incremental phase of 117° was employed for both GOIA-CODE and GRE according to the original publication (30).

For gridding in the CODE reconstruction, 4 layer view-sharing between the two TR datasets was employed as was previously used in the k-space weighted image contrast technique and the temporal sliding-window technique (31, 32). The innermost layer was composed of views from only one TR dataset (TR_1 or TR_2) and the number of views from the other TR dataset gradually increased as the layer shifted to the outer ones. The number of views in each layer was 16384, 22938, 29492, and 32768 from inner to outer layers. Based on Perceval's principle, since the majority of signal energy is concentrated on the innermost layer, the data from the chosen TR (TR_1 or TR_2) predominately determined the contrast in the reconstructed image. The k-space data points from the other TR in the outer layers mainly play the role of reducing streaking artifacts due to k-space undersampling. Boundaries among the 4 layers were 0.5, 0.7, and 0.9 of the spherical k-space radius (64 pixel width). The lowest sampling density region (the outer edge of the spherical k-space)

had an undersampling factor of $\pi/2$ relative to the Nyquist criterion. A previous work has demonstrated that 3D radial reconstruction can be performed with undersampling by up to 8 without conspicuous artifacts (32).

Results

The GOIA pulse used in this study is shown in Fig. 2a. The peak power and SAR of the GOIA pulse were 40% (~ 8 dB voltage reduction) and 54% of the HS1 pulse, respectively, when using the same bw , T_p , FA, and β . To produce a flip angle of 40° , the peak B_1 amplitude of the GOIA pulse was 1,832 Hz (43 μ T). Under the low flip angle approximation (FA= 5°), the Fourier transformation of the GOIA pulse, $M_{xy}(r, T_p)$, as described by Eq. [1], perfectly matched the excitation profile obtained from numerical Bloch simulation, $m_{xy}(r, T_p)$ (Fig. 2b). The flip angle dependence of the correlation procedure was evaluated according to the metric, $h(r)$, expressed by Eq. [9] (Fig. 2c). The correlation procedure removed the quadratic phase in the excitation profile well regardless of the flip angle; the phase error was less than 5° ($\pi/36$ radian) within the frequency sweep band (80 kHz). A noticeable increase in an amplitude difference of the transverse magnetization at the edges of the profile occurred as the flip angle increased ($\sim 10\%$ for 50°), but the center 60 kHz region within the 80 kHz sweep band showed less than 2% error even for flip angle of 50° , demonstrating the correlation method works well for relatively high flip angles of the GOIA pulse.

Results of the correlation method for the 1D CODE simulation and experiment are shown in Fig. 3. It can be seen that the correlation method almost perfectly removes the quadratic phase. The ripples in the amplitude profile produced with both HS1- and GOIA-CODE are due to truncating one side of the echo tail in the CODE acquisition. These minor blips in the phase profile occur at sharp edges; however, such effects are minimal and the phase profile is mostly flat after the correlation process. The experimental data are highly consistent with the simulation results (Fig. 3c). Although there are minor phase errors around the edge of the phantom which are mainly due to susceptibility effects, the quadratic phase is removed well, resulting in a nearly flat phase profile.

Reconstructed images from 3D CODE simulations are shown in Fig. 4. Simulations were performed with a relatively low flip angle of 10° . The images without the correlation procedure commonly showed radially symmetric artifacts, although the artifact pattern was different for HS1- and GOIA-CODE (Fig. 4b,e). The correlation procedure nearly perfectly removed the artifacts (Fig. 4c,f). The artifacts from the quadratic phase and their removal by the correlation procedure are conspicuously shown along the line passing through the bright and dark stripe pattern region (Fig. 4d,h). In addition, an image from the GOIA-CODE simulation with flip angle of 50° is shown in Fig. 4g. The correlation procedure almost perfectly removed the radially symmetric artifacts even though FA = 50° (Fig. 4h).

CODE images from an agar gel phantom experiment are shown in Fig. 5a–c. All images from sinc-, HS1- and GOIA-CODE were highly consistent. The comparison with sinc-CODE, which does not have the quadratic phase from the pulse, demonstrates the capability of the correlation procedure to remove pulse effects nearly perfectly. In addition, the

consistency of images from HS1- and GOIA-CODE revealed that there were negligible effects arising from the gradient modulation in the GOIA excitation. The intensity profiles from all three images nicely overlapped with each other including the noise level in background as shown in Fig. 5d; SNR was consistent (65.9, 63.2, and 67.0 for sinc-, HS1-, and GOIA-CODE, respectively).

Tomato images acquired by GOIA-, HS1-CODE, and 3D GRE with flip angles of 4, 20, and 40° are shown in Fig. 6. With HS1, 40° flip angle could not be obtained due to the high peak power required which exceeded the RF power amplifier's capability under the current experimental setting. For 4 and 20°, the image contrasts were consistent between GOIA- and HS1-CODE. While GRE failed to preserve signals from the core region of the tomato, GOIA- and HS1-CODE had sufficient sensitivity for those signals due to their short TE (≈ 0.3 ms). Similarly, seed interiors were dark regardless of the flip angle in the GRE images, but in the CODE images, due to their short T_1 and the preservation of short T_2^* signals, the seeds became brighter as the flip angle increased.

Fig. 7 shows images and actual flip angle maps for a tomato obtained with AFI using GOIA-CODE and 3D GRE. While the images showed different contrasts due to different TE and TR (Fig. 7a,b), the flip angle scale maps were consistent with each other (Fig. 7c–f). GOIA-CODE AFI showed a slightly increasing trend in the flip angle estimate as the spoiling gradient moment increased. However, differences of the flip angle scales from GOIA-CODE were within 5% (2.25°) relative to the 3D GRE reference (Table. 1). In the core region of the tomato, the B_1 map from 3D GRE was very noisy (Fig. 7c) due to the low SNR resulting from the relatively long TE in 3D GRE (1.7 ms).

To further investigate the T_1 - and T_2^* -insensitivity of the method, experiments were performed on phantoms containing iron oxide solutions of different concentrations. Images and flip angle scale maps of the phantoms obtained with GOIA-CODE are shown in Fig. 8, along with a standard reference from 3D GRE. GOIA-CODE preserved short T_2^* signals for the highest concentration that had T_2^* less than 1 ms (Fig. 8d). All maps obtained from GOIA-CODE showed a consistent flip angle distribution regardless of the T_1 and T_2^* combinations. There was a slightly decreasing trend of the estimated flip angles as T_1 and T_2^* decreased (Fig. 8f–h). However, differences of the estimated flip angle scales from GOIA-CODE were less than 10% (4.5°) compared with the GRE reference (Table. 2).

Discussion

The main innovations of the introduced B_1 mapping method involve the short TE acquisition scheme (CODE) combined with a low power FM pulse (GOIA) for high flip angle excitation. The use of the short TE sequence is advantageous not only for capturing short T_2^* signals, but also for sustaining SNR. In most cases, B_1 mapping does not require high spatial resolution imaging because the B_1 distribution is usually smooth and slowly varying; as a result, SNR often is not the limiting factor in B_1 mapping. In AFI, however, high flip angles and a relatively short TR significantly reduce the steady-state magnetization particularly for long T_1 spins; in many cases, the flip angle is far from the optimal one like the Ernst angle in the single TR steady-state (22) (although the dual TR steady-state in AFI

does not exactly follow the Ernst formula). Thus, due to its ability to minimize signal loss from rapid T_2^* decay, the short TE sequence permits closer to optimal acquisition conditions as compared with most conventional MRI sequences (e.g., short TE maximizes SNR and reduces scan time).

In this study, the quadratic phase generated by GOIA excitation was removed with the correlation method that was linked to the excitation k-space originally introduced in the 2D selective RF pulse design (20). The modified correlation method can be applied to all types of gradient-modulated pulses, including variable-rate selective excitation (VERSE) that also introduces gradient modulation so as to reduce RF power and SAR (33). Moreover, the previous excitation k-space analysis demonstrated that the link between the k-space and image domains via Fourier transformation also exists between the RF pulse (excitation k-space) and the excitation profile, even in two- and three-dimensional cases. Therefore, in theory the generalized correlation method works for any k-space trajectory, including a spiral gradient readout and 2D selective FM pulse excitation.

The CODE sequence in this study was chosen based on its robustness and ease of implementation for B_1 -mapping, despite the fact that some of the other short-TE sequences can achieve even shorter echo times. The robustness of CODE arises from the fact that the acquired signal is in the form of a gradient echo, rather than FID as used by the majority of ultra-short TE sequences. By acquiring the echo peak, it is possible to obtain accurate data at the center of k-space with CODE. In contrast, FID-based acquisition techniques such as UTE and ZTE may have some difficulties in k-space center registration. UTE requires ramp sampling, which is sensitive to eddy currents and gradient system delays, to capture k-space center (10). With ZTE, the first few points of the FID (k-space center) are usually not collected, since the readout gradient is turned on before the receiver gate opens (11). For recovering the missing k-space center, it is necessary to perform additional measurements (34, 35) or special processing in reconstruction (36). In either of the cases, errors in k-space center registration can have a significant impact on image contrast, since the majority of k-space energy is concentrated near the center.

The GOIA pulse used herein allowed a significant reduction of RF peak power and SAR as compared with the HS1 pulse using the same pulse parameters. In the current setting with a 9.4T animal scanner, the GOIA pulse needed the relatively large peak power of 1832 Hz (43 μ T) to achieve a 40° flip angle, which may exceed the achievable value with some clinical scanners. However, parameter optimization in the GOIA pulse design enables further reduction of the pulse power and SAR. For example, the peak power can be reduced to 787 Hz (18.5 μ T), which is applicable to clinical scanners, by changing the pulse parameters as follow: $T_p=400$ μ s, $bw=32$ kHz, and gradient modulation depth=0.75. With this pulse, the SAR becomes ~30% of the GOIA pulse used herein, while TE remains less than 500 μ s.

To obtain a stable steady-state in AFI with radial MRI sequences, the excitation profile should be uniform. Without a flat excitation profile, spins experience a different flip angle during each TR, since the excitation slab direction rotates with the gradient vector which changes from view to view. Consequently, the magnetization is no longer stable when TR is not long enough as compared to T_1 . The GOIA pulse used in the current experiments has a

flat excitation profile (Fig. 2b) and thus satisfies this requirement. However, ZTE shows some difficulties in this regard, since hard pulse excitation in the presence of the constant gradient yields a sinc-shaped excitation profile. While the effects from the sinc-shaped profile can be corrected for relatively long TR acquisitions (37), it is not suitable to the steady-state based quantification methods such as AFI and the variable flip angle T_1 measurement.

Complete spoiling at the end of every TR is another concern for the steady-state formation in AFI. Ideally, optimized spoiling is desirable, since spoiling efficacy is determined by the complex interplay between various factors such as flip angle, TR, T_2 diffusion, and resonance offsets (21, 29, 38). However, detailed spoiling optimization is beyond the scope of the current study. As an alternative and simple solution, in the GRE reference we applied very large spoiling gradient moments, as previously suggested (29), to achieve a nearly optimal spoiling condition at the expense of time (i.e. lengthy TR). In AFI with GOIA-CODE, we tested the performance of three gradient spoiling conditions (weak, intermediate and strong spoiling) and the obtained maps were consistent with the map from the GRE reference regardless of the spoiling gradients. In GOIA-CODE, the spoiling gradient combined with the readout gradient changes its direction in every TR and the semi-random view ordering generated with Halton sequences (26) introduces extra randomness in gradient spoiling. In this case, radial k-space acquisition may help to eliminate signal fluctuations around the steady-state that are induced by the random-gradient-like spoiling; the randomly fluctuating signals are averaged out in the gridding process in reconstruction (21), which is similar to the mechanism that makes radial imaging tolerant to motion artifacts (39).

RF spoiling is another important factor in magnetization spoiling. We employed a simple RF spoiling with 117° phase increment. The quadratic phase from FM pulse excitation combined with the gradually changing gradient direction may help spoiling, since the quadratic phase is never refocused perfectly with linear gradients. However, the changing gradient direction makes RF spoiling analysis complex because the incremental phase is not constant in space. That is, the phase increment depends on spatial position due to the variable resonance frequency of each isochromat in different TRs. Therefore, detailed analysis of RF spoiling in GOIA-CODE AFI needs to include the conventional incremental RF phase analysis as well as the quadratic phase from FM pulse excitation and gradient view ordering. Further considerations to the RF spoiling strategy will be handled in future applications.

Conclusions

A new AFI approach has been demonstrated for B_1 -mapping using a short TE radial 3D GRE sequence (CODE). In this technique, a GOIA pulse is employed in order to excite spins to higher flip angles (40 – 80°) which increases the sensitivity for flip angle estimation. In order to remove the quadratic phase derived from the GOIA pulse, the theoretical formalism of the correlation method has been modified and then validated using numerical Bloch simulations. As compared with the HS1 pulse, the GOIA pulse permits a significant decrease in RF power in CODE, thereby enabling high enough flip angles to gain high sensitivity in AFI. GOIA-CODE AFI yields B_1 estimations that are consistent with

conventional AFI methods (using a Cartesian GRE sequence), but extends B_1 -mapping capability to include spins with very short T_2^* values.

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List of symbols

<i>a</i>	Italic lower case “ay”
$\hat{b}_1$	Italic lower case “bee” under hat with subscript Roman “one”
B_1	Italic upper case “bee” with subscript Roman “one”
B_{1x}	Italic upper case “bee” with subscripts Roman “one” and italic lower case “ex”
B_{1y}	Italic upper case “bee” with subscripts Roman “one” and italic lower case “why”
G_{ex}	Italic bold upper case “jee” with subscripts italic lower case “ee” and “ex”
<i>h</i>	Italic lower case “aych”
	Italic upper case “eye” under bar
<i>k</i>	Italic lower case “kay”
$\dot{k}$	Italic bold lower case “kay”
$\underset{\cdot}{k}$	Italic bold lower case “kay” under dot
<i>K</i>	Italic upper case “kay”
<i>K</i>	Italic bold upper case “kay”
<i>m</i>	Italic lower case “emm”
m_{xy}	Italic lower case “emm” with subscripts italic lower case “ex” and “why”
M_0	Italic upper case “emm” with subscript Roman “zero”
M_x	Italic upper case “emm” with subscript italic lower case “ex”
M_y	Italic upper case “emm” with subscript italic lower case “why”
M_z	Italic upper case “emm” with subscript italic lower case “zee”
M_{xy}	Italic upper case “emm” with subscripts italic lower case “ex” and “why”
<i>n</i>	Italic lower case “en”
<i>r</i>	Italic lower case “are”
<i>r</i>	Italic bold lower case “are”
<i>R</i>	Italic upper case “are”
<i>s</i>	Italic lower case “ess” under hat
<i>S</i>	Italic upper case “ee”

S_1	Italic upper case “ess” with subscript Roman “one”
S_2	Italic upper case “ess” with subscript Roman “two”
t	Italic lower case “tee”
t'	Italic lower case “tee” with superscript “prime”
T_1	Italic upper case “tee” with subscript Roman “one”
T_2	Italic upper case “tee” with subscript Roman “two”
T_2^*	Italic upper case “tee” with subscript Roman “two” and superscript “asterisk”
TE	Upper case “tee” and “ee”
TR	Upper case “tee” and “are”
TP	Italic upper case “tee” with subscript italic lower case “pee”
W	Italic upper case “doubleyou”
α	Italic lower case “alpha”
δ	Italic bold lower case “delta”
γ	Italic lower case “gamma”
κ	Italic lower case “kappa”
ϕ	Italic lower case “phi”
ψ	Italic lower case “psi”
σ	Italic lower case “sigma”
ρ	Italic lower case “rho”

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Figure 1.

Sequence diagram of CODE with frequency-modulated pulse excitation. CODE is composed of 3 modules: excitation, acquisition and spoiling. Signal dephasing happens simultaneously with excitation. Since the dephasing part in the excitation gradient is much shorter than the readout gradient, an asymmetric echo is acquired in CODE. The spoiling gradient is combined with the readout gradient.

Figure 2.

(a) A GOIA pulse used in this study (HS4 amplitude modulation, HS2 gradient modulation, gradient modulation depth=0.5, $T_p=250\ \mu\text{s}$ and $bw=80\ \text{kHz}$) and (b) comparison of the GOIA excitation profiles from the analytical solution under the low flip angle approximation $M_{xy}(r, T_p)$ given by Eq. [1] and the numerical Bloch simulation $m_{xy}(r, T_p)$ (FA=5°). Shaded regions represent 80 kHz frequency sweep range of the pulse (amplitude (top) and phase (bottom)). (c) Validity of the correlation procedure was evaluated for flip angles of 5, 10, 20, 30 and 50° by calculating $h(r)$ according to Eq. [9] (top: amplitude ratio $|h(r)|$, bottom: phase difference $\arg(h(r))$). While amplitude of the excitation profile slightly degraded around the edge of the sweep band for higher flip angles (~10% for 50°), the quadratic phase was almost completely removed regardless of the flip angle. The spatial position r is shown in kHz unit for clarity of the frequency sweep range of the pulse.

Figure 3.

Demonstrations of the correlation procedure for 1D Bloch simulations on (a) HS1- and (b) GOIA-CODE and (c) a 1D GOIA-CODE experiment. No significant change was shown for amplitude before and after the correlation process due to the flat excitation profiles of HS1 and GOIA, whereas asymmetric echo acquisition in CODE generated ripples on the profile due to the truncating echo tail in one side (top row). The quadratic phase generated by HS1 or GOIA excitation was nicely removed for both simulation and experiment (bottom row). The simulations were performed with $FA=10^\circ$ and $TE=420\ \mu s$. The experimental GOIA-CODE data was acquired with an agar gel phantom.

Figure 4.

A 3D theoretical phantom used in CODE simulations (a) and reconstructed images from (b,c) HS1- and (e,f,g) GOIA-CODE. The images were reconstructed (b,e) without and (c,f) with the correlation process. The images reconstructed without the correlation procedure showed radially symmetric artifacts around the center of FOV. Those artifacts disappeared in the images reconstructed with the correlation procedure. The correlation procedure worked well even for a flip angle of 50° (f). The radially symmetric artifacts derived from the quadratic phase and the improvement of the image quality due to the correlation procedure were clearly shown on the intensity profile along the dashed line on the theoretical phantom image (a) (d: HS1-CODE, h: GOIA-CODE).

Figure 5.

Agar gel phantom images acquired with (a) sinc-, (b) HS1- and (c) GOIA-CODE, and (d) intensity profile along the dashed line on the sinc-CODE image. Boxes on the image (a) are regions of interest used for calculating signal-to-noise ratio (65.9, 63.2 and 67.0 for sinc-, HS1- and GOIA-CODE, respectively). Sequence parameters were common for all cases: TR=4 ms, TE=0.3 ms, and FA=5°.

Figure 6.

Tomato images from (a,d,g) GOIA-CODE, (b,e) HS1-CODE, and (c,f,h) 3D GRE with different nominal flip angles (FAs) of 4, 20, 40°. 40° flip angle could not be obtained for HS1-CODE, because the RF peak power exceeded the RF amplifier's capability. The images from FA=20 and 40° were scaled by 1.5× and 2.5× relative to those from FA=4°.

Figure 7.

TR_1 (S_1) images from 3D GRE (a) and GOIA-CODE (b), and flip angle scale maps from the actual flip angle imaging (AFI) with 3D GRE (c) and GOIA-CODE (d–f). For GOIA-CODE AFI, 3 different gradient spoiling conditions were tested; (d) weak, (e) intermediate and (f) strong spoiling (8.8/74.4, 17.5/149 and 35.0/298 gauss·ms/cm for TR_1/TR_2). For 3D GRE reference, a spoiling gradient moment of 163/814 gauss·ms/cm was employed. Boxes shown in the 3D GRE map (c) are the ROIs for quantitative comparison (Table. 1). Actual flip

angles are given by κ FA; FA=45°. TR₂=5·TR₁ and FOV=64×64×64 mm³ were used in all cases. Scan time was 450 and 1182 s for GOIA-CODE and 3D GRE, respectively.

Figure 8.

TR_1 (S_1) images (a–d) and flip angle scale maps (f–i) from iron oxide nanoparticle solutions with 4 different concentrations and reference image (e) and map (j) from 3D GRE. T_1/T_2^* values were 2022/8.4, 687/3.0, 424/1.8 and 224/0.9 ms for 0.2, 1, 2 and 4 mM solutions, respectively. The GRE map was acquired with the 0.2 mM solution. Spoiling gradient moments in TR_1/TR_2 were 35.0/298 and 163/814 gauss·ms/cm for GOIA-CODE and 3D GRE. Boxes shown in the 3D GRE map (j) are the ROIs for quantitative comparison (*Table. 2*). Actual flip angles are given by κFA ; $FA=45^\circ$. $TR_2=5 \cdot TR_1$ and $FOV=64 \times 64 \times 120$ mm³ were used in all cases. Scan time was 450 and 1182 s for GOIA-CODE and 3D GRE, respectively.

Table 1

Estimated actual flip angle scale under 3 different gradient spoiling conditions.

	GOIA-CODE AFI			3D GRE AFI
	weak	intermediate	Strong	
ROI1	0.69±0.08	0.69±0.08	0.70±0.09	0.67±0.07
ROI2	1.11±0.03	1.13±0.02	1.17±0.02	1.13±0.02

mean±standard deviation. Gradient moments for weak, intermediate and strong spoiling were 8.8/74.4, 17.5/149 and 35.0/298 gauss-ms/cm (TR₁/TR₂), respectively. In 3D GRE reference, the gradient moment was 163/814 gauss-ms/cm. Nominal flip angle was 45°. The size of the ROIs shown in Fig. 7c was 5×5×5.

Table. 2

Estimated actual flip angle scale for iron oxide solutions with 4 different concentrations.

T ₁ /T ₂ ^a [ms]	GOIA-CODE AFI				3D GRE AFI	
	2022/8.4	687/3.0	424/1.8	224/0.9	2022/8.4	2022/8.4
ROI1	0.75±0.02	0.72±0.02	0.68±0.02	0.64±0.01	0.72±0.02	0.72±0.02
ROI2	1.08±0.02	1.04±0.02	1.02±0.02	1.00±0.02	0.99±0.02	0.99±0.02

mean±standard deviation. Spoiling gradient moments were 35.0/298 and 163/814 gauss-ms/cm (TR₁/TR₂), respectively. Nominal flip angle was 45°. The size of the ROIs shown in Fig. 8j was 5×5×5.