Published in final edited form as:

Magn Reson Med. 2017 August ; 78(2): 730–738. doi:10.1002/mrm.26461.

The Effects of Concomitant Gradients on Chemical Shift Encoded MRI

Timothy J. Colgan^{1,2}, Diego Hernando^{1,2}, Samir D. Sharma¹, and Scott B. Reeder^{1,2,3,4,5}

¹Department of Radiology, University of Wisconsin, Madison, WI

²Department of Medical Physics, University of Wisconsin, Madison, WI

³Department of Biomedical Engineering, University of Wisconsin, Madison, WI

⁴Department of Medicine, University of Wisconsin, Madison, WI

⁵Department of Emergency Medicine, University of Wisconsin, Madison, WI

Abstract

Purpose—To characterize the effects of concomitant gradients (CGs) on chemical shift encoded (CSE)-based estimation of B_0 field map, proton density fat fraction (PDFF), and R_2^* .

Theory—A theoretical framework was used to determine the effects of CG-induced phase errors on CSE-MRI data.

Methods—Simulations, phantom experiments, and in vivo experiments were conducted at 3T to assess the effects of CGs on quantitative CSE-MRI techniques. Correction of phase errors attributable to CGs was also investigated to determine if these effects could be removed.

Results—Phase errors due to CGs introduce errors in the estimation of B_0 field map, PDFF, and R_2^* . Phantom and in vivo experiments demonstrated that CGs can introduce estimation errors greater than 30 Hz in the B_0 field map, 10% in PDFF, and 16 s^{-1} in R_2^* , 16 cm off isocenter. However, CG phase correction before parameter estimation was able to reduce estimation errors to less than 10 Hz in the B_0 field map, 1% in PDFF, and 2 s^{-1} in R_2^* .

Conclusion—CG effects can impact CSE-MRI, leading to inaccurate estimation of B_0 field map, PDFF, and R_2^* . However, correction for phase errors caused by CGs improve the accuracy of quantitative parameters estimated from CSE-MRI acquisitions.

Keywords

concomitant gradients; chemical shift encoded MRI; PDFF; iron quantification; R_2^* estimation; B_0 field map estimation

Introduction

In recent years, there has been tremendous progress in the technical development and validation of chemical shift encoded (CSE)-MRI techniques. These techniques include: (i) mapping B_0 field inhomogeneity (estimating the B_0 field map) as required for quantitative susceptibility mapping (QSM) (1,2) and many other applications, (ii) water-fat separation (1,3–5) for mapping of proton density fat fraction (PDFF) as a quantitative biomarker of tissue triglyceride concentration (6–8), and (iii) R_2^* mapping as a quantitative biomarker of tissue iron concentration (9–11).

CSE-MRI techniques, particularly for PDFF and R_2^* estimation, can be performed using magnitude-based reconstructions, which discard the phase information from the complex source images. This has the advantage of avoiding confounding effects of phase errors in the underlying source data (8,12). However, magnitude-based techniques suffer from reduced signal to noise ratio (SNR) performance by discarding the phase information (12), and produce biased R_2^* estimates in high iron concentration settings due to noise floor effects (13). Complex-based algorithms have better SNR performance than magnitude-based techniques and are less affected by bias in high iron concentration settings (13). Further, complex-based algorithms can quantify PDFF over the full 0–100% dynamic range, which is desirable in applications where PDFF exceeds 50% such as adiposity imaging and bone marrow fat quantification. Additionally, complex-based techniques enable the measurement of B_0 field inhomogeneities. B_0 field inhomogeneity mapping has many important applications including shimming (14), off resonance correction techniques (15), and emerging QSM techniques (1,2). For all of these reasons, complex-based CSE-MRI techniques have important advantages over magnitude-based techniques.

However, there are several sources of phase error that affect the performance of complex-based CSE-MRI techniques. Previous work has shown that eddy currents corrupt the phase in multi-echo acquisitions, which leads to errors in water-fat separation if not accounted for in the signal estimation algorithm (16,17). Another important source of phase error in any MRI acquisition, including CSE-MRI, is the effect known as concomitant gradients (CGs). These additional magnetic field gradients, which appear simultaneously to the applied imaging gradients, arise by constraints imposed by Maxwell's equations (18). If unaccounted for, CGs lead to spatially dependent phase errors in the acquired images (18).

The impact of concomitant gradients has been investigated for several important MRI applications including: flow quantification (18), diffusion tensor imaging (19), R_2^* quantification (20), spiral acquisitions (21), and low-field MRI (22). Further, a technique to correct for CG phase errors was developed by Bernstein et al. (18) using knowledge of the imaging gradient waveforms. This correction is applied in post processing after the acquisition of the data and has been used to remove the effects of CGs for several applications (18,19,23).

Recently Ruschke et al (24) demonstrated the potential impact of phase errors due to CGs for CSE-MRI PDFF estimation. However, this previous work did not investigate the impact of different acquisition strategies (e.g., echo trains). Further, the effect of CGs on CSE-based

estimation of B_0 field map and R_2^* were not characterized. Therefore, the purpose of this work is to characterize the effects of CGs on CSE-based estimation of B_0 field map, PDFF, and R_2^* using different acquisition strategies. In this work, these effects are characterized using simulations, phantom experiments, and in vivo acquisitions. Additionally, the feasibility of CG correction prior to parameter estimation in CSE-MRI is evaluated.

Theory

Concomitant gradients are variations in the magnetic field that appear as a byproduct of the applied imaging gradients. These concomitant gradients are orthogonal to the imaging gradients and can be derived analytically using Maxwell's curl and divergence equations (18). Unlike imaging gradients, CGs have significant first and second order spatially varying terms as follows:

$$B_{CG}(x, y, z, t) = \frac{1}{2B_0} \left[G_x^2(t) z^2 + G_y^2(t) z^2 + G_z^2(t) \frac{x^2 + y^2}{4} - G_x(t) G_z(t) xz - G_y(t) G_z(t) yz \right]$$

[1]

where $G_x(t)$, $G_y(t)$, and $G_z(t)$ are the imaging gradient waveforms generated in the x , y , and z directions respectively, and B_{CG} is the spatio-temporal concomitant gradient magnetic field (units in Tesla). At isocenter ($x=0$, $y=0$, $z=0$) the concomitant gradients are zero, but away from isocenter the CGs increase parabolically. Consequently, the edges of the field of view (FOV) will have the largest CGs. The magnitude squared of the gradient waveforms dictates the magnitude of the CGs, such that increasing the receiver bandwidth, decreasing the FOV, or increasing the number of echoes will increase the magnitude of concomitant gradients. Other pulse sequence parameters that increase gradient amplitude or duration (e.g., flow compensated gradients) can also increase the size of the CGs.

The presence of concomitant gradients affects the signal in CSE-MRI by introducing additional phase shifts. Specifically the signal at an individual voxel measured in a spoiled gradient echo (SGRE) acquisition in the presence of CGs can be modeled as follows:

$$s(TE) = \left[(\rho_W + \rho_F c_F(TE)) e^{-R_2^* TE} e^{i2\pi f_0 TE} \right] e^{i\phi_{CG}(TE)} \quad [2]$$

where

$$\phi_{CG}(TE) = \gamma \int_0^{TE} B_{CG}(\tau) d\tau \quad [3]$$

and ρ_W is the water signal component, ρ_F is the fat signal component, $c_F(TE)$ is the sum of complex exponentials reflecting the spectral model of fat (25,26), f_0 is the frequency shift (Hz) due to B_0 inhomogeneity at this voxel, $\phi_{CG}(TE)$ is the local phase error due to

concomitant gradients at this voxel, TE is the echo time, γ is the gyromagnetic ratio, and $B_{CG}(\tau)$ is the expression in Eq. 1 evaluated at this voxel's location (x,y,z) . In this model we are approximating the CG-induced phase offset as being constant across the voxel.

CSE-MRI techniques often rely on multi-echo acquisitions. For example, a typical acquisition for PDFF estimation might include a total of six echoes acquired in one or more interleaved echo trains. Eq. 2 highlights that CGs are a function of echo time, which could cause different phase errors in each echo of the multi-echo acquisition. Therefore, in this work we study how the temporal variation of CG phase errors affect multi-echo SGRE acquisitions for CSE-MRI applications.

Methods

Simulations

To characterize the effects of concomitant gradient phase errors on CSE-MRI, a simulated imaging scenario corresponding to an SGRE acquisition of a homogeneous water signal was assumed at 3T, with zero B_0 field map inhomogeneities (i.e. $f_0 = 0$ Hz), PDFF = 0%, and $R_2^* = 0$ s⁻¹, which will have no phase variation across echo times. Then representative CG phase shifts were calculated using Eq. 1 for several common CSE-MRI acquisitions (as shown in Figure 1a): (i) a single echo train with flyback readout, (ii) a single echo train with bipolar readout, and (iii) two interleaved echo trains with flyback readout. A single echo train with flyback readout is commonly used for water-fat separation at 1.5 T, whereas bipolar acquisitions are being investigated for many CSE-MRI applications at both 1.5 T and 3 T, and two interleaved trains are commonly used to obtain the shorter echo spacing required for water-fat separation at 3 T. For each acquisition, the concomitant gradient-induced phase terms were added as complex data at each echo time using Eq. 2.

These simulations were performed assuming a 3D axial acquisition with the timing of each echo shown in Figure 1a, including a readout gradient in the x (left/right) direction, phase encoding in the y (anterior/posterior) direction, and slice encoding in the z (superior/inferior) direction. According to Eq. 1, the largest concomitant gradient errors will be in the z (superior/inferior) direction since the x gradient has the largest squared area. Therefore a large FOV (48 cm) was chosen in the z-direction to highlight the potential magnitude of CG phase errors. In this work, we focused on axial acquisitions, which are typical in water-fat imaging. However, CG induced phase errors would apply to non-axial orientations as well. In a multi-echo acquisition, the readout gradient will always have the largest squared area so the CG phase error will be dominated by one of the first three terms in Eq. 1. With the readout gradient in the x- or y-direction the errors will grow parabolically in the z-direction, whereas a readout gradient in the z-direction will cause errors to grow in the x- and y-directions.

A complex fitting algorithm (6) was then used to jointly estimate the B_0 field map, PDFF, and R_2^* . PDFF was calculated as $\rho_F(\rho_W + \rho_F)$, including noise bias correction (27), and is typically reported as a percent. Note that noise bias correction was included to follow the usual processing pipeline in the estimation of PDFF (28,29), even though no noise was

added in these simulations. The errors in the estimated parameters were evaluated to assess the impact of CGs, for each of the three CSE-MRI acquisitions considered in this work.

The magnitude of CG induced phase errors depend on multiple parameters (e.g. echo times, field strengths, acquisition types, acquisition orientations, FOVs, receiver bandwidth, distance off isocenter). Therefore, similar protocols may result in different CG induced phase errors. Further, propagation of CG induced phase errors on the echo images into the subsequent parametric maps (B_0 field map, PDFF, and R_2^*) will depend on the echo time combination. To demonstrate this effect we also simulated the CG induced phase errors with a clinical protocol used in a clinical PDFF measurement scenario (30) with two interleaved echo trains and a flyback readout, 6 echoes, a receiver bandwidth (rBW) of ± 111 KHz, a first echo (TE_1) of 1.2 ms, echo spacing (ΔTE) of 1.0 ms, $FOV = 44 \times 40 \times 26$ cm, and a $256 \times 160 \times 32$ matrix size. We calculated the potential errors in parameter estimation with this protocol using the same procedure as above.

Phantom Experiments

Phantom experiments were conducted using a 3T clinical MRI system (Discovery MR750, GE Healthcare, Waukesha, WI) and a 32-channel phased array torso coil (Neocoil, Pewaukee, WI). Complex data were acquired using a 3D multi-echo SGRE acquisition. Our experimental measurements focused on acquisition with two interleaved echo trains and flyback readout, due to the impact on parameter estimation that was observed in our simulations (see Results section). Complex echo images were reconstructed online, including eddy current compensation, coil combination, and nonlinear gradient correction. Similar to our simulations, estimates of B_0 field map, PDFF, and R_2^* were obtained using the complex fit algorithm described by Hernando et al. (6).

A homogeneous $NiCl_2$ - and $NaCl$ -doped water phantom of dimensions $37.2 \times 15.0 \times 14.8$ cm³ with 0% PDFF and homogeneous R_2^* was scanned to assess the effects of CGs on B_0 field map estimation. The phantom was scanned using a multi-echo 3D-SGRE acquisition in the axial direction, such that the readout gradient was oriented in the x-direction. The phantom was scanned twice, consecutively, without adjusting gradient shims and the center frequency between scans, in order to obtain similar B_0 field maps (f_0 in Eq. 2). However, the size of the FOV was changed between the two scans. The size of the FOV affects gradient amplitude and the area under the readout gradient, both of which will affect the CG amplitude, producing different amounts of CG phase errors for the two scans. Importantly, keeping the FOV constant but changing the receiver bandwidth will produce a similar effect. Both scans were acquired with two interleaved echo trains and a flyback readout, similar to the one shown in Figure 1a. Both scans had 6 echoes, flip angle = 3° , no parallel imaging, and a receiver bandwidth (rBW) of ± 142.86 KHz. The first scan had a first echo (TE_1) of 1.3 ms, echo spacing (ΔTE) of 1.0 ms, $FOV = 21 \times 21 \times 48$ cm, and a $128 \times 128 \times 60$ matrix size. The second scan had $TE_1 = 0.9$ ms, $\Delta TE = 0.7$ ms, $FOV = 35 \times 35 \times 48$ cm, and a $128 \times 128 \times 60$ matrix size. The B_0 field map was estimated for each of the two consecutive scans. These B_0 field map estimates were restricted to the smaller FOV (21×21 cm), and then interpolated to have the same voxel size to allow co-registration and direct comparison.

The B_0 field map estimates were then compared to determine the effects of CGs on B_0 field map estimation.

PDFF and R_2^* were estimated from an acquisition of the same doped-water phantom. The imaging parameters for this six-echo 3D-SGRE axial acquisition included: 6 echoes, flip angle = 3° , no parallel imaging, rBW = ± 125 KHz, $TE_1 = 1.3$ ms, $TE = 1.0$ ms, FOV = $21 \times 21 \times 48$ cm, and a $128 \times 128 \times 60$ matrix size.

Experimental Concomitant Gradient Correction

To further characterize the effects of CGs on CSE-MRI and to demonstrate the feasibility of CG correction, we also performed correction of CG induced phase errors before parameter estimation. To accomplish this, variables controlling the pulse widths and gradient amplitudes of the pulse sequence were saved for all three imaging gradient waveforms using the scanner's software. Subsequently, the CG induced phase errors for each echo were calculated using Eq. 3 and numerical integration of the stored gradient waveforms. This calculated phase was demodulated from the complex echo images prior to parameter estimation. The B_0 field map, PDFF, and R_2^* estimates were then calculated using this CG correction method and compared to the estimates without CG correction.

In Vivo Experiments

Two volunteers were scanned after receiving Institutional Review Board (IRB) approval and informed consent. The same scanner, coil, and data processing pipeline was used for the in vivo experiments as was used for the phantom experiments. We conducted three different in vivo experiments to highlight the effects of CGs on the B_0 field map, PDFF, and R_2^* individually even though all three parameters would be affected by CG induced phase errors in each experiment.

Two consecutive scans of a volunteer's thigh (male, age 25) were conducted to characterize the effects of concomitant gradients on B_0 field map estimation. Similar to estimating the B_0 field map in the phantom experiments, two axial multi-echo 3D-SGRE acquisitions were performed, without adjusting gradient shims and the center frequency in-between the scans. The FOV was varied between the scans, in order to introduce different CG-induced phase errors. In this case the thigh was chosen to minimize potential motion between the two scans. A 3D axial acquisition with two interleaved echo trains and a flyback readout was used with 6 echoes, flip angle = 3° , no parallel imaging, rBW = ± 125 KHz, and a $160 \times 128 \times 60$ matrix size for both scans. The first scan had $TE_1 = 1.3$ ms, $TE = 1.0$ ms, FOV = $23 \times 23 \times 48$ cm and the second scan had $TE_1 = 1.0$ ms, $TE = 0.8$ ms, FOV = $35 \times 35 \times 48$ cm. A low flip angle was used to minimize T1 related bias in the PDFF maps (27).

Additionally, two scans of the liver of a healthy volunteer (female, age 26) were also conducted to assess the effects of CG-induced phase errors on PDFF estimation. A 3D axial acquisition with two interleaved echo trains and a flyback readout was used with 6 echoes, flip angle = 3° , rBW = ± 166.67 KHz, $TE_1 = 1.3$ ms, $TE = 1.0$ ms, FOV = $35 \times 35 \times 48$ cm, a $192 \times 160 \times 48$ matrix size, and parallel imaging acceleration factors of 2 in the phase direction and 1.5 in the slice direction (31). One scan was performed with the liver located at isocenter and the other with the liver 12 cm away from isocenter in the superior (+z)

direction. Shifting the patient was achieved by moving the table. The slice at isocenter serves as a reference since there will be no CG errors at isocenter (Eq. 1). Each scan was performed in a 26 second single breath hold at end expiration.

Similarly, two scans of a volunteer's thigh (male, age 25) were performed to assess the effects of CGs on in vivo R_2^* quantification. The first scan was performed with an axial slice of the thigh located at isocenter and the second with the same slice away from isocenter, which was achieved by moving the table 14 cm in the superior (+z) direction. Once again, the slice at isocenter serves as a reference because it has no CG phase errors. The thigh was chosen to minimize additional sources of error in R_2^* quantification, including motion and the presence of nearby air-tissue interfaces. Both scans consisted of a 3D axial acquisition with two interleaved echo trains and flyback readout with 6 echoes, flip angle = 3° , no parallel imaging, $rBW = \pm 142.86$ KHz, $TE_1 = 1.3$ ms, $TE = 1.0$ ms, $FOV = 21 \times 21 \times 48$ cm, a $128 \times 128 \times 60$ matrix size, and averaged five times to improve SNR. The R_2^* estimates from the scan at isocenter, the scan off isocenter without CG correction, and the scan off isocenter with GC correction were compared.

Results

Simulations

Figure 1 demonstrates how concomitant gradient phase errors accumulate in multi-echo acquisitions as a function of echo time. Figure 1a contains a representative plot of a single echo train with flyback readout, a single echo train with bipolar readout, and two interleaved echo trains with flyback readout, all with six equally spaced echoes. Figure 1b is a plot of the accumulated CG phase error as a function of echo time for each acquisition type. In the single echo train case consisting of equally spaced echoes acquired within a single TR, a linear phase shift develops across subsequent echoes regardless of whether the readout is flyback or bipolar. In the case of two interleaved echo trains, however, each echo train acquisition has an identical phase evolution due to concomitant gradients. Since they are shifted and interleaved the resulting phase error contains an oscillatory nonlinear component as demonstrated in Figure 1b.

The B_0 field map estimates from the simulation are shown in Figure 2a. Note that the true B_0 field map inhomogeneity was 0 Hz for all positions, thus any deviation from 0 is due to CG-induced phase errors. For all three simulated acquisitions, the B_0 field map estimates are corrupted by the added CG phase errors even though this is not true B_0 inhomogeneity. As predicted by Eq. 1, the apparent B_0 field map follows a parabolic second order profile with no error at isocenter, but large errors up to 300 Hz at the edges of the field of view.

Error in the simulated PDFF estimates due to the presence of CGs is shown in Figure 2b. The CG phase error does not impact PDFF estimation in the case of the flyback and bipolar readout single echo trains. This is expected because the CG-induced phase errors accumulate linearly over the echoes, so $e^{i\phi_{CG}(TE)}$ will be completely absorbed into the estimation of B_0 inhomogeneity. However, the nonlinear oscillatory accumulation of phase error with the two interleaved echo train acquisitions cannot be completely mapped as B_0 inhomogeneity, and introduces errors up to 70% at 24 cm from isocenter in the PDFF estimates.

Simulated errors in the estimation of R_2^* for the homogenous water signal with true $R_2^* = 0 \text{ s}^{-1}$ are shown in Figure 2c. Similar to PDFF estimation, the concomitant gradient phase errors are completely absorbed into the B_0 field map estimation for the single echo train acquisitions so the R_2^* estimates are unaffected. However, the nonlinear oscillatory accumulations of CG-induced phase error results in the underestimation of R_2^* with errors up to 50 s^{-1} at 24 cm from isocenter.

Errors in the estimation of the B_0 field map, PDFF, and R_2^* were also simulated for the clinical imaging protocol of (30). With this protocol the CG induced phase errors had a max of 45° at the sixth echo, which is much smaller than all the other errors shown in Figure 1b. Also, the maximum errors for the estimated parameters was 25 Hz for the B_0 field map, 0.4% for PDFF, and 1 s^{-1} for R_2^* .

Phantom Experiments

Results for B_0 field map estimation in the doped water phantom are shown in Figure 3. The absolute value of the differences in the estimated B_0 field maps for the two scans are shown for a z-directed line through the center of the phantom. The differences are shown for B_0 field map estimates with and without CG correction. Changing the FOV, and subsequently the magnitude of the concomitant gradients, produced large differences in the estimated B_0 field maps, with errors up to 50 Hz at 12 cm off isocenter. However, these errors were predicted by our theoretical analysis and CG phase correction largely removed these B_0 field map differences, with a homogeneous error of around 15 Hz, which no longer has a second order shape indicative of CG errors. We believe this constant baseline error in the field was a result of temperature changes, long time constant eddy currents, or other unrelated errors. Regardless, the quadratic behavior of the B_0 field map is effectively removed by the CG correction.

Figure 4 plots estimates of PDFF along a profile in the z-direction through the center of the doped water phantom, for both uncorrected and CG corrected data. Errors in PDFF estimation of over 10% (absolute PDFF) at 11 cm from isocenter are observed. CG correction also removes the second order shape of the PDFF error and results in a more homogenous estimate close to the true 0% PDFF with the remaining error less than 1%.

Figure 5 plots estimates of R_2^* along a profile in the z-direction through the center of the doped water phantom, for both uncorrected and CG corrected data. Nonlinear CG phase accumulation across echoes corrupts the estimation of R_2^* and produces underestimation in R_2^* of up to 10 s^{-1} 12 cm away from isocenter. However, CG correction of the data before parameter estimation removes the underestimation and results in a uniform R_2^* estimate across the homogenous phantom.

In Vivo Experiments

In vivo B_0 field map estimates using scans of a volunteer's leg are shown in Figures 6 and 7. The differences in B_0 field map estimates for consecutive scans, each with a different FOV, were calculated with and without CG correction. Figure 6b contains differences between B_0 field map estimates obtained from consecutive scans, along a profile in the z-direction, through the muscles of the leg as shown in Figure 6a. Despite, maintaining constant shim

gradients and center frequencies between the scans, a large spatially varying difference, up to 40 Hz at a point 15 cm off isocenter with this acquisition, exists between the B_0 field map estimates using a 23 cm FOV and a 35 cm FOV. However, if the B_0 field map is estimated after CG correction the difference in B_0 field map estimates is reduced to less than 10 Hz. Figure 7 contains axial slices acquired 14 cm off isocenter and for the ROIs shown the differences in B_0 field maps is 34 Hz with the estimates without CG correction and 7 Hz after CG correction.

PDFF estimates are shown in Figure 8 for the healthy volunteer's liver. The same slice location through the volunteer's liver was acquired 12 cm off isocenter and at isocenter. The PDFF estimate with the liver off isocenter is shown in Figure 8a (no CG correction) and Figure 8b (with CG correction). Finally, that same slice acquired at isocenter (i.e. without CG errors), is shown in Figure 8c. All the ROIs had a standard deviation less than 3% and the average apparent PDFF values was -7.8% when the liver was 12 cm off isocenter, 2.5% with concomitant gradient phase errors removed before estimation, and 2.0% at isocenter. As expected, the concomitant gradient corrected PDFF estimate is more similar to acquiring the slice at isocenter with errors less than 1% while the slice away from isocenter has close to 10% absolute error.

Figure 9 contains R_2^* estimates for scans of a volunteer's thigh. The estimate of R_2^* in the volunteer's thigh muscle was 21 s^{-1} when acquired 16 cm off isocenter. CG correction before R_2^* estimation resulted in an estimate of 39 s^{-1} as shown in Figure 9b. At isocenter, where CGs have no effects, the R_2^* in the volunteer's thigh was estimated to be 37 s^{-1} . CGs corrupt the joint estimation of water, fat, and R_2^* off isocenter and create an underestimation in R_2^* of 18 s^{-1} compared to an isocenter acquisition but CG correction reduces this error to 2 s^{-1} . All of the ROIs in Figure 9 had a standard deviation of approximately 4 s^{-1} .

Discussion and Conclusions

In this work, we have demonstrated that concomitant gradients have a significant impact on the accuracy of CSE-based estimates of B_0 field map, PDFF, and R_2^* , by introducing phase errors into the acquired data. Phase errors caused by CGs are zero at isocenter but grow parabolically as a function of distance from isocenter. In this work we demonstrated that CGs can introduce B_0 field map errors for sequences involving either a single echo train or two interleaved echo trains. Our simulations and experimental measurements demonstrate that CG phase errors also corrupt complex CSE-based PDFF and R_2^* estimates when using a sequence with two interleaved echo trains. This is due to the nonlinear concomitant gradient phase error accumulation across echoes. Finally, we have also shown that calculation and demodulation of the CG phase terms improves the accuracy of estimating these three parameters.

CG phase errors can have a significant impact on various CSE-MRI applications. CGs do not create B_0 inhomogeneities but they create gradient dependent phase shifts that accumulate in the case of multi-echo acquisitions, leading to an apparent B_0 field inhomogeneity. These corrupted B_0 field map estimates would degrade the performance of algorithms that require estimates of the B_0 field inhomogeneity (32,33). B_0 field map errors

caused by CGs are also a potential confounder of the performance and accuracy algorithms for QSM based iron quantification (1,34–36) or other methods that require accurate measurement of a B_0 field map. Furthermore, we demonstrated error in liver PDFF estimation as high as 10% (absolute PDFF) at a location 12 cm off isocenter. This has significant potential impact on liver fat quantification and diagnosis of nonalcoholic fatty liver disease (NAFLD), considering that the PDFF thresholds between normal and abnormal levels are fat are approximately 3–6% (30,37). We also demonstrated that CG phase errors can lead to errors in R_2^* estimation, with errors in excess of 16 s^{-1} at 16 cm off isocenter in R_2^* , however other TEs or true PDFFs could result in different R_2^* errors with the same CG phase errors. Furthermore, the magnitude of CG phase errors depend on multiple factors as was shown in our simulations. However, if the gradient waveforms are known, CG effects can be accurately predicted, and therefore demodulated from the individual complex images at each echo time. Our data demonstrates that the correction for CG-induced phase errors can improve the accuracy of estimations for the B_0 field map, PDFF, and R_2^* .

In previous works, concomitant gradients have been identified as a source of error for several CSE-MRI applications. Ruschke et al (24) performed a preliminary investigation into PDFF estimation bias, due to several acquisition errors including concomitant gradients. They also demonstrated the need for CG phase error correction in PDFF estimation for multiple echo trains. Hofstetter et al. (20) demonstrated that CGs resulted in R_2^* overestimation using magnitude based R_2^* mapping, due to CG-induced macroscopic dephasing from large CGs across voxels. This effect was the opposite of what was observed using complex-based CSE-based joint PDFF and R_2^* estimation. There are two explanations for this apparent discordance. First, the echo trains used by Hofstetter et al. were designed for blood oxygenation level dependent (BOLD) applications and used significantly longer echo trains (12 echoes) than those typically used for fat and iron quantification (6 echoes). For example, the magnitude of the amplitude decay term due to concomitant gradients (Eq. 9 in Hofstetter et al. (20)) ranges from 0.999 at the first echo to 0.993 at the last echo in the two interleaved echo train sequence used in our in vivo R_2^* experiments in the thigh. This corresponds to a change in R_2^* at the first echo of 0.15 s^{-1} and 1.09 s^{-1} at the last echo. Consequently, with only six echoes we did not observe any significant effects due to macroscopic dephasing and were able to avoid large R_2^* errors by correcting the phase of the source images. It should be noted that intravoxel dephasing resulting from CGs should be amenable to correction by the method proposed by Hernando et al (32). Second, CG-induced phase oscillations observed with multi-shot CSE-MRI acquisitions lead to errors in R_2^* when joint estimation of B_0 field map, PDFF, and R_2^* is performed (in contrast to single species magnitude-based R_2^* estimation as performed by Hofstetter et al). Importantly, these R_2^* errors will occur even if the CG-induced phase errors are constant across each voxel. Also, for our particular simulation and experimental setup (eg: choice of echo times and true underlying PDFF and R_2^*), the CG effects observed in this work resulted in an underestimation of R_2^* (as opposed to an overestimation, as typically observed in the presence of macroscopic intra-voxel dephasing). The reason for this underestimation can be explained as follows. When fat is present, interference between water and fat and between the multiple peaks of fat during signal evolution leads to a decrease in the magnitude of the observed signal intensity, even in the absence of R_2^*

increases. However, the signal estimation algorithm misinterprets CG-induced phase oscillations in lean tissues as fat. Since these CG-induced phase shifts do not alter (decrease) the magnitude of the signal, the estimation algorithm incorrectly estimates the presence of fat and also introduces an underestimation of the apparent R_2^* . Note that this behavior may be different in adipose tissue or tissue with PDFF $\approx$ 50%, or for acquisitions with echo time combinations different from those used in this work. Future work using complex CSE-MRI to perform joint PDFF and R_2^* estimation with long echo trains should account for both the oscillatory phase shifts and intravoxel dephasing caused by CGs. A complete analysis accounting for both of these effects, however, is beyond the scope of this work.

There are multiple additional factors that can impact concomitant gradient phase errors that were beyond the scope of this work. The effects of nonlinear gradients, eddy current correction errors, and echo train lengths were not thoroughly analyzed in our study to determine their impact on concomitant gradient correction. Nevertheless, this work demonstrated that CG related errors are almost entirely mitigated using relatively straightforward calculations. These results suggest that CG correction should be performed routinely in CSE applications where complex images are used for parametric mapping of B_0 field map, PDFF, and/or R_2^* .

In conclusion, we have demonstrated the impact of concomitant gradient phase errors on the estimation of B_0 field map, PDFF, and R_2^* using CSE-MRI. For single or multiple echo trains, CG phase errors will create large erroneous B_0 field map estimates. CG phase errors with multiple echo trains also corrupt PDFF and R_2^* estimates using complex-based CSE-MRI. Importantly, correction of concomitant gradient errors in CSE-MRI applications is very straightforward, feasible and may improve the accuracy of these quantitative biomarkers.

Acknowledgments

The authors wish to acknowledge support from the NIH (UL1TR00427, R01 DK083380, R01 DK088925, R01 DK100651, K24 DK102595, and T32CA009206). We also wish to acknowledge GE Healthcare who provides research support to the University of Wisconsin.

References

1. Sharma SD, Hernando D, Horng DE, Reeder SB. Quantitative susceptibility mapping in the abdomen as an imaging biomarker of hepatic iron overload. *Magn Reson Med*. 2014; 74:673–683. [PubMed: 25199788]
2. Dimov AV, Liu T, Spincemaille P, Ecanow JS, Tan H, Edelman RR, Wang Y. Joint estimation of chemical shift and quantitative susceptibility mapping (chemical QSM). *Magn Reson Med*. 2015; 73:2100–10. [PubMed: 24947227]
3. Reeder SB, McKenzie CA, Pineda AR, Yu H, Shimakawa A, Brau AC, Hargreaves BA, Gold GE, Brittain JH. Water-fat separation with IDEAL gradient-echo imaging. *J Magn Reson Imaging*. 2007; 25:644–52. [PubMed: 17326087]
4. Berglund J, Ahlstrom H, Johansson L, Kullberg J. Two-point dixon method with flexible echo times. *Magn Reson Med*. 2011; 65:994–1004. [PubMed: 21413063]
5. Hardy PA, Hinks RS, Tkach JA. Separation of fat and water in fast spin-echo MR imaging with the three-point Dixon technique. *J Magn Reson Imaging*. 1995; 5:181–5. [PubMed: 7766980]

6. Hernando D, Kellman P, Haldar JP, Liang ZP. Robust water/fat separation in the presence of large field inhomogeneities using a graph cut algorithm. *Magn Reson Med*. 2010; 63:79–90. [PubMed: 19859956]
7. Berglund J, Kullberg J. Three-dimensional water/fat separation and T2* estimation based on whole-image optimization—application in breathhold liver imaging at 1.5 T. *Magn Reson Med*. 2012; 67:1684–93. [PubMed: 22189760]
8. Bydder M, Yokoo T, Hamilton G, Middleton MS, Chavez AD, Schwimmer JB, Lavine JE, Sirlin CB. Relaxation effects in the quantification of fat using gradient echo imaging. *Magn Reson Imaging*. 2008; 26:347–59. [PubMed: 18093781]
9. Wood JC, Enriquez C, Ghugre N, Tyzka JM, Carson S, Nelson MD, Coates TD. MRI R2 and R2* mapping accurately estimates hepatic iron concentration in transfusion-dependent thalassemia and sickle cell disease patients. *Blood*. 2005; 106:1460–5. [PubMed: 15860670]
10. Hankins JS, McCarville MB, Loeffler RB, Smeltzer MP, Onciu M, Hoffer FA, Li CS, Wang WC, Ware RE, Hillenbrand CM. R2* magnetic resonance imaging of the liver in patients with iron overload. *Blood*. 2009; 113:4853–5. [PubMed: 19264677]
11. Anderson LJ, Holden S, Davis B, Prescott E, Charrier CC, Bunce NH, Firmin DN, Wonke B, Porter J, Walker JM, et al. Cardiovascular T2-star (T2*) magnetic resonance for the early diagnosis of myocardial iron overload. *Eur Heart J*. 2001; 22:2171–9. [PubMed: 11913479]
12. Hernando D, Liang ZP, Kellman P. Chemical shift-based water/fat separation: a comparison of signal models. *Magn Reson Med*. 2010; 64:811–22. [PubMed: 20593375]
13. Hernando D, Kramer JH, Reeder SB. Multipeak fat-corrected complex R2* relaxometry: theory, optimization, and clinical validation. *Magn Reson Med*. 2013; 70:1319–31. [PubMed: 23359327]
14. Schar M, Vonken EJ, Stuber M. Simultaneous B(0)- and B(1)+-map acquisition for fast localized shim, frequency, and RF power determination in the heart at 3 T. *Magn Reson Med*. 2010; 63:419–26. [PubMed: 20099330]
15. Olafsson VT, Noll DC, Fessler JA. Fast joint reconstruction of dynamic R2* and field maps in functional MRI. *IEEE Trans Med Imaging*. 2008; 27:1177–88. [PubMed: 18753040]
16. Hernando D, Hines CD, Yu H, Reeder SB. Addressing phase errors in fat-water imaging using a mixed magnitude/complex fitting method. *Magn Reson Med*. 2012; 67:638–44. [PubMed: 21713978]
17. Yu H, Shimakawa A, Hines CD, McKenzie CA, Hamilton G, Sirlin CB, Brittain JH, Reeder SB. Combination of complex-based and magnitude-based multiecho water-fat separation for accurate quantification of fat-fraction. *Magn Reson Med*. 2011; 66:199–206. [PubMed: 21695724]
18. Bernstein MA, Zhou XJ, Polzin JA, King KF, Ganin A, Pelc NJ, Glover GH. Concomitant gradient terms in phase contrast MR: analysis and correction. *Magn Reson Med*. 1998; 39:300–8. [PubMed: 9469714]
19. Baron CA, Lebel RM, Wilman AH, Beaulieu C. The effect of concomitant gradient fields on diffusion tensor imaging. *Magn Reson Med*. 2012; 68:1190–201. [PubMed: 22851517]
20. Hofstetter LW, Morrell G, Kaggie J, Kim D, Carlston K, Lee VS. T2* Measurement bias due to concomitant gradient fields. *Magn Reson Med*. 2016
21. King KF, Ganin A, Zhou XJ, Bernstein MA. Concomitant gradient field effects in spiral scans. *Magn Reson Med*. 1999; 41:103–12. [PubMed: 10025617]
22. Volegov PL, Mosher JC, Espy MA, Kraus RH Jr. On concomitant gradients in low-field MRI. *J Magn Reson*. 2005; 175:103–13. [PubMed: 15869890]
23. Meier C, Zwanger M, Feiweier T, Porter D. Concomitant field terms for asymmetric gradient coils: consequences for diffusion, flow, and echo-planar imaging. *Magn Reson Med*. 2008; 60:128–34. [PubMed: 18581353]
24. Ruschke, S., Eggers, H., Kooijman, H., Baum, T., Settles, M., Haase, A., Rummeny, EJ., Karampinos, DC. Addressing phase errors in quantitative water-fat imaging at 3 T using a time-interleaved multi-echo gradient-echo acquisition; Proceedings of the 23rd Annual Meeting of ISMRM; Toronto, Ontario, Canada. 2015. p. 3657
25. Hamilton G, Yokoo T, Bydder M, Cruite I, Schroeder ME, Sirlin CB, Middleton MS. In vivo characterization of the liver fat (1)H MR spectrum. *NMR Biomed*. 2011; 24:784–90. [PubMed: 21834002]

26. Yu H, Shimakawa A, McKenzie CA, Brodsky E, Brittain JH, Reeder SB. Multiecho water-fat separation and simultaneous $R2^*$ estimation with multifrequency fat spectrum modeling. *Magn Reson Med*. 2008; 60:1122–34. [PubMed: 18956464]
27. Liu CY, McKenzie CA, Yu H, Brittain JH, Reeder SB. Fat quantification with IDEAL gradient echo imaging: correction of bias from $T(1)$ and noise. *Magn Reson Med*. 2007; 58:354–64. [PubMed: 17654578]
28. Hines CD, Frydrychowicz A, Hamilton G, Tudorascu DL, Vigen KK, Yu H, McKenzie CA, Sirlin CB, Brittain JH, Reeder SB. $T(1)$ independent, $T(2)$ (*) corrected chemical shift based fat-water separation with multi-peak fat spectral modeling is an accurate and precise measure of hepatic steatosis. *J Magn Reson Imaging*. 2011; 33:873–81. [PubMed: 21448952]
29. Meisamy S, Hines CD, Hamilton G, Sirlin CB, McKenzie CA, Yu H, Brittain JH, Reeder SB. Quantification of hepatic steatosis with $T1$ -independent, $T2$ -corrected MR imaging with spectral modeling of fat: blinded comparison with MR spectroscopy. *Radiology*. 2011; 258:767–75. [PubMed: 21248233]
30. Rehm JL, Wolfgram PM, Hernando D, Eickhoff JC, Allen DB, Reeder SB. Proton density fat-fraction is an accurate biomarker of hepatic steatosis in adolescent girls and young women. *Eur Radiol*. 2015; 25:2921–30. [PubMed: 25916386]
31. Brau AC, Beatty PJ, Skare S, Bammer R. Comparison of reconstruction accuracy and efficiency among autocalibrating data-driven parallel imaging methods. *Magn Reson Med*. 2008; 59:382–95. [PubMed: 18228603]
32. Hernando D, Vigen KK, Shimakawa A, Reeder SB. $R^*(2)$ mapping in the presence of macroscopic $B(0)$ field variations. *Magn Reson Med*. 2012; 68:830–40. [PubMed: 22161866]
33. Sharma SD, Artz NS, Hernando D, Hornig DE, Reeder SB. Improving chemical shift encoded water-fat separation using object-based information of the magnetic field inhomogeneity. *Magn Reson Med*. 2015; 73:597–604. [PubMed: 24585487]
34. Schweser F, Deistung A, Lehr BW, Reichenbach JR. Quantitative imaging of intrinsic magnetic tissue properties using MRI signal phase: an approach to in vivo brain iron metabolism? *Neuroimage*. 2011; 54:2789–807. [PubMed: 21040794]
35. de Rochefort L, Liu T, Kressler B, Liu J, Spincemaille P, Lebon V, Wu J, Wang Y. Quantitative susceptibility map reconstruction from MR phase data using bayesian regularization: validation and application to brain imaging. *Magn Reson Med*. 2010; 63:194–206. [PubMed: 19953507]
36. Liu J, Liu T, de Rochefort L, Ledoux J, Khalidov I, Chen W, Tsiouris AJ, Wisnieff C, Spincemaille P, Prince MR, et al. Morphology enabled dipole inversion for quantitative susceptibility mapping using structural consistency between the magnitude image and the susceptibility map. *Neuroimage*. 2012; 59:2560–8. [PubMed: 21925276]
37. Szczepaniak LS, Nurenberg P, Leonard D, Browning JD, Reingold JS, Grundy S, Hobbs HH, Dobbins RL. Magnetic resonance spectroscopy to measure hepatic triglyceride content: prevalence of hepatic steatosis in the general population. *Am J Physiol Endocrinol Metab*. 2005; 288:E462–8. [PubMed: 15339742]

Figure 1.

Concomitant gradient phase error accumulation across multiple echoes depends on the readout gradient acquisition strategy. (a) Readout gradients for six-echo CSE gradient waveforms for a single echo train with flyback (monopolar) readout (top), a single echo train with bipolar readout (middle), and two interleaved echo trains with flyback readout, where echo times are marked with a black diamond. (b) Concomitant gradient phase errors as a function of echo time. Note the linear CG phase accumulation in single echo train acquisitions, and the non-linear phase accumulation in interleaved echo train acquisitions.

Figure 2.

Concomitant gradient phase errors can result in large errors in (a) B_0 field map estimation, (b) proton density fat fraction (PDFF) estimation, and (c) R_2^* estimation. Simulation results are shown for a single echo train with flyback readout, a single echo train with bipolar readout, and two interleaved echo trains with flyback readout. The errors in the estimates are shown as a function of position along the z-axis. All three acquisition types have B_0 field map errors but only the two interleaved echo trains has errors in PDFF and R_2^* due to nonlinear concomitant gradient phase accumulation across echoes.

Figure 3.

Large differences in the B_0 field map estimated between two scans can be removed with concomitant gradient phase correction. Two scans, one with a 21 cm FOV and the other with a 35 cm FOV, were repeated consecutively while maintaining the shim gradients. The absolute differences between the B_0 field map estimates (solid blue) and the differences after applying concomitant gradient correction (dashed red) are shown for a z-directed line extending through the center of the phantom. The residual B_0 field map differences after CG correction are likely due to temperature effects and other unrelated errors and not due to CGs since they no longer have a parabolic profile and are similar in regions with and without concomitant gradient effects.

Figure 4. Significant errors in PDFF that are removed when concomitant gradient induced phase errors are demodulated from source images. The PDFF estimate using uncorrected data (solid blue) and the estimate after concomitant gradient correction (dashed red) are shown for a line through the center of a water phantom with 0% PDFF.

Figure 5.

Significant errors in R_2^* estimation are observed in a doped water phantom. These errors can be removed by correcting for concomitant gradient induced phase errors. The R_2^* estimate obtained from uncorrected data (solid blue) and the estimate after concomitant gradient correction (dashed red) are shown for a line through the center of a water phantom with a homogenous R_2^* .

Figure 6.

Differences in B_0 field map estimates that can be removed with concomitant gradient correction. (a) The difference between B_0 field map estimates for a 23 cm axial FOV and a 35 cm axial FOV are shown for consecutive scans, with no shimming in between, of a volunteer's leg. (b) Difference between B_0 field map estimates after CG correction, which no longer has the parabolic shape of (a). (d) The differences in the B_0 field map estimates are shown for the Z-directed line shown in the coronal cross-section of the volunteer's leg as shown in (c). The raw data (solid blue) and the CG corrected data (dashed red) are shown. The dashed line in (c) represents the cross section shown in Figure 7.

B₀ field mapping

Figure 7.

Differences in B₀ field map estimates that are removed with concomitant gradient correction. The B₀ field map estimate for an axial thigh slice 14 cm off isocenter that was acquired with consecutive scans, and no shimming in-between, for a 23 cm FOV (a) and a 35 cm FOV (b). B₀ field map estimates after CG correction are also shown for the 23 cm FOV (c) and 35 cm FOV (d). The average value and standard deviation in Hz of the ROI was 169 ± 3.6 Hz in (a), 135 ± 2.7 Hz in (b), 78 ± 3.7 Hz in (c), and 85 ± 2.7 Hz in (d).

Figure 8.

Significant PDFF errors can be avoided through correction of concomitant gradient induced phase errors for multiple echo train CSE-MRI acquisitions. The PDFF estimate for (a) the liver 12 cm off isocenter, (b) concomitant gradient correction with the liver 12 cm off isocenter, and (c) the liver at isocenter. The average value and standard deviation in each of the ROIs was $-7.8 \pm 2.6\%$ in (a), $2.5 \pm 2.1\%$ in (b), and $2.0 \pm 2.9\%$ in (c). This example was acquired in a healthy volunteer with no liver disease.

Figure 9.

In vivo errors in R_2^* quantification that are removed with concomitant gradient correction. The R_2^* estimate for (a) an axial thigh slice 16 cm off isocenter, (b) concomitant gradient correction of that slice, and (c) the same slice at isocenter. The average value and standard deviation (in s^{-1}) of the ROI was 21 ± 3.1 (a), 39 ± 3.1 (b), and 37 ± 3.6 (c).