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T2* Measurement Bias Due to Concomitant Gradient Fields

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Abstract

Purpose—To demonstrate that concomitant magnetic fields can cause significant spatially dependent biases in T_2^* relaxometry measurements with implications for clinical applications such as BOLD and dynamic susceptibility contrast-enhanced MRI.

Methods—After developing a theoretical framework for intravoxel dephasing and signal loss from concomitant magnetic fields, this framework and the effect of concomitant fields on T_2^* are validated with phantom experiments and numerical simulation. In lower leg and renal T_2^* mapping, we quantify measurement bias for imaging protocols with high gradient amplitude multi-echo readouts, comparable to those used in clinical applications.

Results—Concordance between phantom experiment and numerical simulation validate the theoretical framework. Changes in T_2^* measured in the lower leg and kidney varied by up to 15% and 35%, as a result of concomitant gradient effects, respectively, when compared to the control measurements.

Conclusion—Concomitant magnetic fields produced by imaging gradient coils can cause clinically-significant T_2^* mapping errors when high amplitude, long duration gradient waveforms are used. While we have shown that measurement biases can be quite large, modification of imaging parameters can potentially reduce concomitant field-induced measurement errors to acceptable levels.

Introduction

Effective transverse relaxation time (T_2^*) mapping is frequently used to measure hepatic and myocardial iron content^{1–3}, the blood oxygenation level dependent (BOLD) effect in functional imaging of brain⁴, muscle^{5–7}, and kidney^{8–12}, and paramagnetic contrast agent concentration in dynamic susceptibility contrast imaging¹³. T_2^* measurements require sampling the transverse magnetization at various echo times following a radio-frequency

(RF) excitation. To minimize imaging time and reduce motion sensitivity, multi-echo gradient echo readouts are commonly used to efficiently sample the signal decay.

T_2^* is determined by a combination of several effects, including nuclear-nuclear and nuclear-electron interactions and static magnetic field (B_0) inhomogeneity. Magnetic susceptibility differences in the tissue microstructure cause varying field inhomogeneity levels and therefore varying T_2^* for different clinically relevant functional or structural tissue states¹⁴. For example, in BOLD imaging, the susceptibility difference between paramagnetic deoxyhemoglobin in red blood cells and diamagnetic surrounding fluid and tissue causes field inhomogeneity and a T_2^* relaxation time that is correlated with tissue oxygenation levels. Similarly, tissue iron in the form of superparamagnetic ferritin and hemosiderin increases field inhomogeneity and thus decreases T_2^* .

T_2^* contains a wealth of information about structural tissue properties and biological function; however, non-physiological sources of MR signal loss also contribute to the relaxation rate. For example, macroscopic B_0 inhomogeneity due to air/tissue interfaces and/or poor field shimming can cause significant field variation that results in intravoxel dephasing and signal decay^{15,16}. Properly shimming the volume of interest, using small imaging voxels, and postprocessing correction techniques can be used to reduce measurement bias from macroscopic B_0 inhomogeneity^{15,17–20}.

An additional source of signal loss can be due to concomitant gradient fields²¹. Concomitant gradient fields are time-varying and spatially-varying magnetic fields that are produced by the imaging gradient coils in addition to the desired linear field gradients²². The effects of these fields are typically small and are ignored in most MRI applications. However, concomitant fields can cause signal dropout, blurring, and artifacts in certain applications such as phase contrast, fast spin-echo, balanced steady-state free precession, EPI, spiral, and diffusion imaging techniques^{21–27}. To our knowledge, the effect of concomitant fields on T_2^* measurements has not been reported. In this study we hypothesize that concomitant fields can cause significant T_2^* measurement biases when a multi-echo readout is used. This effect is explored in phantom and in human muscle and kidney imaging experiments. Our analysis and experiments show how judicious choice of MRI parameters can minimize the deleterious effect of concomitant fields on T_2^* measurements.

Theory

An ideal gradient magnetic field for imaging would be oriented along the z axis with the ability to vary in amplitude linearly along any spatial dimension (x , y , or z). Gradient coils are designed to approximate such an ideal field as closely as possible. However, the principles of electromagnetics as described by Maxwell's equations dictate that an ideal gradient field must be accompanied by additional undesired field components known as concomitant fields. If we define the static B_0 to be oriented along z and if the x and y gradient coils are symmetrical and differ by a 90° coaxial rotation, the magnitude of the field in the z direction will vary from the ideal value of $B_0 + G_x x + G_y y + G_z z$ by a concomitant field term approximated by²²:

$$B_c(\vec{r}, t) = \frac{1}{2B_0} \left\{ G_x^2 z^2 + G_y^2 z^2 + G_z^2 \frac{x^2 + y^2}{4} - G_x G_z x z - G_y G_z y z \right\} \quad (1)$$

where G_x , G_y , and G_z are the gradient waveforms produced by the x , y , and z gradient coils and variables x , y , and z denote the distance along each axis from the center of the gradient system. The concomitant field term has a quadratic spatial variation and is time dependent since the gradient fields G_x , G_y , and G_z vary with time. This spatial variation can cause intravoxel dephasing and signal loss²¹. A voxel signal model that jointly accounts for intravoxel dephasing from macroscopic B_0 field inhomogeneity and concomitant gradient fields can be written as:

$$S(\vec{r}_0, t) = \int_V \rho(\vec{r}) e^{-t/T_2^*(\vec{r})} e^{i\gamma \Delta B_0(\vec{r})t} e^{i\gamma \int_0^t B_c(\vec{r}, t') dt'} d\vec{r} \quad (2)$$

where $\vec{r}_0$ is the voxel position, V denotes the voxel volume, t is the echo time, $T_2^*(\vec{r})$ is the relaxation time constant, $\rho(\vec{r})$ is proportional to the spin density, $\gamma \Delta B_0(\vec{r})t$ is the phase term

due to the macroscopic B_0 field inhomogeneity, and $\gamma \int_0^t B_c(\vec{r}, t') dt'$ is the phase term due to time-varying concomitant gradient fields.

If we assume that the tissue spin density and T_2^* are constant across the voxel, Equation (2) can be written as:

$$S(\vec{r}_0, t) = \rho(\vec{r}_0) e^{-t/T_2^*(\vec{r}_0)} \int_V e^{i\gamma \Delta B_0(\vec{r})t} e^{i\gamma \int_0^t B_c(\vec{r}, t') dt'} d\vec{r} \quad (3)$$

where the signal decay can be described as the exponential T_2^* decay modulated by an integral term that depends on both the static field inhomogeneity and the concomitant gradient fields. The integral in Equation (3) can be solved numerically if the static field and gradient waveforms are known. However, this equation provides little intuition into how concomitant fields influence signal decay and what imaging parameters or imaging orientations are most affected by concomitant field errors.

To help elucidate the effect of concomitant fields on intravoxel dephasing and signal decay, an analytic expression for the integral in Equation (3) is derived in the Appendix. This derivation only considers first-order spatial components of the static and concomitant fields and assumes an ideal “boxcar” voxel sensitivity function²⁸. However, this simplification provides useful insights into how specific MR scanner settings can impact concomitant field related T_2^* mapping errors. This intuition can be utilized to plan imaging protocols and experiments that minimize measurement bias due to concomitant fields. As derived in the Appendix, Equation (3) can be written as:

$$S(\vec{r}_0, t) = A(\vec{r}_0, t) \times \rho(\vec{r}_0) e^{-t/T_2^*(\vec{r}_0)} \quad (4)$$

where $A(\vec{r}_0, t)$ is,

$$A(\vec{r}_0, t) = e^{i\phi(\vec{r}_0, t)} \times \prod_{n=1}^3 \Delta x_n \operatorname{sinc} \left[\frac{\gamma \Delta x_n}{2} a_n(\vec{r}_0, t) \right] \quad (5)$$

and where $\phi(\vec{r}_0, t)$ is the image phase defined by Eq. (17) and x_1 , x_2 , and x_3 denote the voxel size along the principal x, y, and z dimensions of the gradient system. Coefficients $a_n(\vec{r}_0, t)$ in Equation (5) are equal to:

$$a_1(\vec{r}_0, t) = G_{0x}(\vec{r}_0) t + \frac{1}{2B_0} \int_0^t \left(\frac{G_z^2}{2} x_0 - G_x G_z z_0 \right) dt' \quad (6)$$

$$a_2(\vec{r}_0, t) = G_{0y}(\vec{r}_0) t + \frac{1}{2B_0} \int_0^t \left(\frac{G_z^2}{2} y_0 - G_y G_z z_0 \right) dt' \quad (7)$$

$$a_3(\vec{r}_0, t) = G_{0z}(\vec{r}_0) t + \frac{1}{2B_0} \int_0^t \left[2 \left(G_x^2 + G_y^2 \right) z_0 - G_x G_z x_0 - G_y G_z y_0 \right] dt' \quad (8)$$

where G_{0x} , G_{0y} , and G_{0z} is the spatial derivative (mathematical gradient) of the static macroscopic field along the three directions, and B_0 is the static magnetic field strength. Equation (5) shows that the classical T_2^* decay equation is modulated by the product of three **sinc** functions whose arguments are proportional to the voxel dimensions and the coefficients are defined by Eqs. (6)–(8).

Eqs. (6)–(8) illustrate how concomitant and macroscopic B_0 field inhomogeneity contribute to intravoxel dephasing and signal loss. These dephasing coefficients depend on the time integral of gradient waveform terms that are pair-wise multiplied or squared. For imaging protocols with a multi-echo readout, the read gradient waveforms contribute most significantly to the concomitant field (integral) terms because the total duration of the read gradient is much longer than either the slice-select or phase-encoding gradients. In the analysis below, only concomitant field terms due to the read gradient waveforms are discussed. We do this in order to clearly elucidate the effect of concomitant fields. Although the macroscopic field inhomogeneity terms ($G_{0x}(\vec{r}_0)$, $G_{0y}(\vec{r}_0)$, $G_{0z}(\vec{r}_0)$) also cause dephasing, they are neglected in the analysis below since their effect on T_2^* estimation has been shown previously^{15,18–20}.

Axial Imaging

For a multi-echo single-slice axial imaging protocol with Cartesian readout, the read gradient can be oriented along either x or y. For either read-gradient orientation the amplitude decay term, Eq. (5), due to concomitant gradient fields can be written as:

$$A(\vec{r}_0, t) = e^{i\phi(\vec{r}_0, t)} \times \Delta x \Delta y \Delta z \operatorname{sinc} \left[\frac{\gamma \Delta z z_0}{2B_0} \int_0^t G_R^2 dt' \right] \quad (9)$$

where G_R^2 is the read gradient waveform squared and z is the slice thickness. For small argument of the **sinc** term, the amplitude decay is largely unaffected by concomitant fields.

Equation (9) shows that the amplitude decay term $A(\vec{r}_0, t)$ is similar at all echo times for slice locations near isocenter ($z_0 = 0$), high main magnet field strengths, small slice thicknesses, low gradient amplitudes and durations, and short readout echo-trains. For imaging protocols where slice location is far from isocenter, slice thickness is large, and the gradient amplitude, duration, and echo-train are large, the amplitude decay due to concomitant fields will be most pronounced. Equation (9) demonstrates that the amplitude decay term is independent of voxel position within a given axial slice and that all voxels in a given slice are affected equally. The impact of these amplitude decay trends on the measured T_2^* is depicted in Figure 1.

Coronal Imaging

For a multi-echo single-slice coronal imaging protocol with Cartesian acquisition, the read gradient can be oriented along either x or z. If the read gradient is chosen along x, the amplitude decay term is identical to Eq. (9). However, the interpretation is slightly different than the axial case since z now corresponds to the in-plane voxel dimension and z_0 denotes a particular pixel location in the 2D image. If the read gradient is chosen along z, the amplitude decay term becomes:

$$A(\vec{r}_0, t) = e^{i\phi(\vec{r}_0, t)} \times \Delta x \Delta y \Delta z \operatorname{sinc} \left[\frac{\gamma \Delta x x_0}{8B_0} \int_0^t G_R^2 dt' \right] \cdot \operatorname{sinc} \left[\frac{\gamma \Delta y y_0}{8B_0} \int_0^t G_R^2 dt' \right] \quad (10)$$

where y is the slice thickness and x is the in-plane voxel length in the x direction. Unlike the axial orientation, amplitude decay terms differ depending of the direction of the read gradient. If the read gradient is oriented along x, slice location does not impact the amplitude decay term. Instead the amplitude decay term will vary across the image with increasing distance from isocenter in the z direction. As shown by Eq. (10), if the read gradient is chosen along the z-direction the amplitude term will depend on both the slice location and in-plane positioning along y.

Sagittal Imaging

For a multi-echo single-slice sagittal imaging protocol with Cartesian acquisition, the read gradient can be oriented along either y or z. If the read gradient is chosen along y, the

amplitude decay term is identical to Eq. (9). This term does not depend on slice position and will vary across the image along the z dimension. For a read gradient along z, the amplitude decay term is described by Eq. (10), which depends on both slice location and in-plane position along z.

Equations (9) and (10) illustrate the nuanced effect that concomitant fields have on intravoxel dephasing. The amplitude decay terms depend on a number of factors that include the shape and duration of the read gradient waveforms, voxel dimensions, main magnet field strength, and image slice orientation (see online supplement for simulation results depicting these effects). All these parameters can play a role in the amount of concomitant field induced signal dephasing.

Methods

Phantom, muscle, and kidney imaging experiments were performed to evaluate T_2^* estimation errors caused by concomitant field effects. All imaging was performed using a 1.5T Avanto scanner with the SQ-gradient system (Siemens Medical Solutions, Erlangen, Germany). Phantom imaging was performed using the body coil. Muscle and kidney imaging was performed using a combination of body matrix and spine arrays. All human imaging was Institutional Review Board approved (University of Utah), and written informed consent was obtained.

Phantom Experiment

A cylindrical phantom (6.3cm diameter, 108cm length) was filled with deionized water and doped with 15.3 millimolar copper (II) sulfate pentahydrate and 50 millimolar sodium chloride. The long axis of the phantom was oriented parallel to the main field direction (z direction) and phantom center was positioned at the center of the gradient coil system (isocenter). The phantom and MR table remained fixed for all imaging experiments. Axial imaging was performed at 7 different slice locations along the length of the phantom ($z = -90\text{mm}, -60\text{mm}, -30\text{mm}, 0\text{mm}, 30\text{mm}, 60\text{mm}, 90\text{mm}$). At each position, two T_2^* imaging protocols were used. The first protocol used a multi-echo gradient recalled echo (MGRE) sequence to acquire data for 12 echoes during a single sequence repetition. For control, the second protocol acquired 12 echoes using twelve separate single-echo gradient recalled echo (GRE) sequence repetitions. We note that a single-echo acquisition is largely insensitive to concomitant gradients. Except for this difference in multi-echo vs. single-echo, imaging parameters for the two protocols were identical. The following scan parameters were used: $TE_1/TR = 2.4/100\text{ms}$, $TE = 2.5\text{ms}$, flip angle = 68° , FOV = 10.5cm, matrix 64×64 , 4 averages, number of echoes 12, 10mm slice thickness, and bandwidth 1953 Hz/pixel. For the MGRE acquisition, an oscilloscope (RIGOL DS1052E, Beijing China) was used to record the read-gradient waveform. Using each 12-echo set of images, T_2^* maps were computed on a pixel-by-pixel basis by fitting the magnitude of the image signal intensity to the exponential function $S = S_0 e^{-t/T_2^*}$ using two fit parameters (S_0 and T_2^*). Calculation was performed using the nonlinear fitting routine, lsqnonlin, in MATLAB (MathWorks, Natick, MA). For phantom and human images, signal to noise ratio (over regions of interest) of the

last echo was greater than 30 and 5.4, respectively, ensuring that noise statistics are zero mean and Gaussian^{29–31}.

To confirm that intravoxel dephasing from B_0 inhomogeneity was minimal, a 3D field map of the phantom was acquired using the following scan parameters: $TE_1/TE_2/TR = 6.87/17.93/25$ ms, flip angle = 25° , FOV = 21.8×50 cm, matrix $112 \times 256 \times 32$, 2mm slice thickness, and bandwidth 100 Hz/pixel. Field map (B_0) and numerical gradient along three principal directions (G_{0x} , G_{0y} , G_{0z}) were calculated over the phantom volume.

Phantom Simulation

To confirm that T_2^* measurement bias was due to read gradient concomitant fields, theoretical signal decay was calculated using Equation (3), the oscilloscope-measured MRGE read gradient waveform, voxel size, imaging plane, slice location, and echo times used in the phantom experiment. The following parameter values, $\rho(\vec{r}_0)=1$, $T_2^*=78.17$ ms, and $B_0(\vec{r})=0$, were also used. The theoretical signal intensity in each voxel was calculated numerically according to Equation (3) by discretizing each image voxel into 1813 ($7 \times 7 \times 37$) sub-voxels. For each sub-voxel, numerical integration (1 μ s time step) of the inner gradient term in Equation (3) was performed for the real and imaginary components using the trapezoid rule. The complex valued signal for each sub-voxel was summed to obtain the signal for the entire voxel. This calculation was performed for the twelve echo times and for axial slice positions along z between ± 100 mm. T_2^* maps were calculated for these simulated images using the nonlinear fitting technique described above.

Evaluation in the Lower Leg

Axial imaging of the right calf was performed on one healthy volunteer (22 yr female). A shim volume 20cm in length along the S/I direction and centered on landmark position was placed around the right calf. Local shimming was performed to minimize static field inhomogeneity over a selected region of the lower right leg. Two T_2^* measurements were acquired using protocols A and B whose imaging parameters and gradient waveforms are shown in Table 1 and Figure 2, respectively. Protocol A consisted of one 12-echo GRE acquisition. Protocol B consisted of two separate 6-echo GRE imaging acquisitions (odd and even echoes). Aside from splitting protocol B into two separate acquisitions, imaging parameters for the protocols were identical. The purpose of protocol B was to reduce dephasing from concomitant fields so that it could be used as a measurement control for protocol A. Protocol B acquired the same images as A, albeit the dephasing due to concomitant fields was markedly less for the later echo times. Imaging was performed over 8 uniformly spaced slices ranging from ± 80 mm from magnet isocenter. Coil combined magnitude images were generated, and T_2^* maps for protocol A and B were computed using the nonlinear fitting method described above. For verification, oscilloscope measurements of the gradient waveforms were obtained during imaging (Figure 2).

Evaluation in the Kidney

Axial imaging of the kidney was performed on two healthy volunteers (subject 1: 38 yr female, subject 2: 25 yr female). Subjects were positioned so that a central axial slice

through the right kidney was located at the center of the gradient system along z ($z=0\text{mm}$). An ROI enclosing the right kidney was selected, and local shimming was performed over the selected region during free breathing. Two single-slice T_2^* measurements were acquired at position $z=0\text{mm}$ using protocols A and B. For all kidney imaging, protocol A and B scan parameters were identical to those listed in Table 1 except for the following changes: flip angle = 15° , TR = 34ms, water only excitation.

Both protocol A and B were acquired sequentially during the same 20 second breath-hold at end-expiration. Imaging was repeated six times during six separate breath-holds. To eliminate biases due to the potential for increased motion near end of breath-hold, ordering of three acquisitions was permuted for each breath-hold. Raw data from the six separate breath-holds were averaged prior to image reconstruction to minimize variations due to inconsistent breath-holds.

Next, the MR table was moved so that the kidney position was shifted by 80mm in the superior direction relative to the gradient coil center. Shim volume and axial slice location were shifted by this amount to maintain the same anatomical positioning. While the anatomic position and imaging slice were kept the same, slice location relative to the gradient system isocenter changed by 80mm. Shimming was repeated and T_2^* measurements using protocol A and B were performed as described above. This same procedure of moving table, shim volume, and slice location was repeated for a third location: 40mm superior relative to the gradient coil isocenter. T_2^* maps from both protocols were computed using the nonlinear fitting method described above. Read gradient waveform shape was again confirmed with oscilloscope readings.

Results

Phantom Experiment and Simulation

Phantom T_2^* maps, measured with the MGRE and GRE imaging protocols, are depicted in Figure 3. Substantial measurement variation along the length of the phantom was seen for the multi-echo readout (MGRE). However, for each echo acquired using a separate excitation (GRE), the T_2^* measurement was independent of slice positioning. This result is consistent with the interpretation provided by Eq. (9), namely intravoxel dephasing due to concomitant fields is most pronounced when imaging away from isocenter with high amplitude multi-echo gradient waveforms. When imaging at center of gradient system, T_2^* measurements for the two protocols coincide. Concomitant fields altered T_2^* measurements by as much as 24% at 9 centimeters from isocenter.

Median values of the T_2^* maps (calculated over the phantom cross-section in Figure 3) are compared to theoretical calculations in Figure 4. The dotted line denotes the simulated T_2^* values that were calculated from the measured MGRE read gradient waveform. Simulated and measured T_2^* maps for the MGRE protocol are in close agreement.

A coronal static field map (B_0) and numerical gradients of the static field (G_{0x} , G_{0y} , G_{0z}) are depicted in Figure 5. The field map is gradually varying along the phantom length and

gradient maps show that this variation is small and similar for all voxels. Average values of G_{0x} , G_{0y} , and G_{0z} over the center coronal phantom slice for $-90\text{mm} < z < 90\text{mm}$ are 0.003 ± 0.1 , 0.12 ± 0.09 , and $0.05 \pm 0.08\text{Hz/mm}$, respectively. Field variations of this magnitude are small, confirming that T_2^* measurement bias from static field inhomogeneity is not significant in the phantom experiment.

Evaluation in the Lower Leg

T_2^* maps at five different positions along the lower leg are shown in Figure 6. The difference maps (bottom row in Figure 6) demonstrate that measurements using the two protocols (lower and higher concomitant fields) coincided at isocenter but differed with increasing distance from isocenter. T_2^* values for the medial gastrocnemius muscle using protocol B and A differ by 3.7ms at the 80mm position, a 15% decrease for protocol A when compared to protocol B. This difference is explained by the signal amplitude decay term in Equation (9). Whereas protocol A utilized a 12-echo acquisition, splitting protocol B into two separate 6-echo acquisitions reduced concomitant field induced intravoxel dephasing for the later echoes. T_2^* values in the medial gastrocnemius, for all five slice location (8cm span) are shown in Table 2.

Evaluation in the Kidney

Figure 7 shows T_2^* maps for subjects 1 and 2. Protocol B (lower concomitant field) was less sensitive to distance from isocenter along the z-direction when compared to protocol A (higher concomitant field). The difference between protocol B and A measurements were particularly pronounced for the 80mm measurement. In subject 1, the median difference in T_2^* for the whole right kidney was 23.4ms, a 35% difference when compared to protocol B. In subject 2, the median difference for the right kidney was 16.2ms, a 28% measurement difference when compared to protocol B. For ROIs drawn in the cortex (shown in Figure 7) protocol A underestimated T_2^* values measured by protocol B by as much as 20ms. A complete listing of T_2^* values is shown in Table 3.

Discussion and Conclusions

Like static macroscopic B_0 inhomogeneity, concomitant magnetic fields can cause intravoxel dephasing and signal dropout in MR images. Resulting T_2^* estimation errors can be problematic when using T_2^* as an indicator of underlying physiology. Inoue et al. demonstrated a significant correlation between renal cortex T_2^* and estimated-glomerular filtration rate (eGFR) in patients with non-diabetic chronic kidney disease⁹. Slope of the linear correlation shows that a 1ms change in T_2^* is approximately equivalent to a 5 ml/min per 1.73m^2 change in eGFR. In this paper, we have shown that the average cortical T_2^* in the kidney was underestimated by as much as 21.8ms when performing off-isocenter (8cm) axial imaging with a 12-echo readout. Taken in the context of the work by Inoue et al.⁹, eGFR would be underestimated by 109 ml/min per 1.73m^2 , an amount that is equivalent to the total eGFR of a healthy subject.

Concomitant field effects are relevant to other T_2^* application in the abdomen, such as hepatic iron quantification. A strong linear correlation between $1/T_2^*$ and iron concentrations in the liver (measured via biopsy) has been demonstrated by a number of investigators^{2,32}. Clinically relevant values of T_2^* for liver iron quantification range from 0.5 – 30ms at 1.5T¹. To ensure sensitivity over this very broad range of T_2^* values, high-bandwidth imaging protocols with closely spaced echoes are frequently used to ensure sufficient sampling of the signal decay. A multi-echo readout is also standard in the abdomen because it enables acquisition during a single breath-hold. A high bandwidth multi-echo readout in combination with the large liver span in the cranial to caudal direction (potential for off-isocenter imaging) can create scenarios in which iron quantification is overestimated (T_2^* underestimated). However, this effect is likely to only be relevant when quantifying mild to moderate tissue iron content elevation (longer T_2^* values). For high iron concentration states (very short T_2^*), signal decay from concomitant fields is small in comparison to significant iron induced signal dephasing.

T_2^* has been increasingly used to explore muscle function during exercise, ischemia, and postocclusive reactive hyperemia⁶. Analyses are based on T_2^* changes before and after application of a stressor or event. Due to long cranio-caudal range along the extremities, imaging scenarios that cause substantial concomitant field effects are possible. While such effects are likely too small to impact T_2^* difference measurements, our results suggest that absolute T_2^* , a potentially useful measurement in skeletal muscle, could be substantially affected.

Our work suggests some simple principles to minimize T_2^* measurement bias from concomitant fields. First, concomitant field effects are small in regions near the center of the gradient system, so imaging near the magnet isocenter is optimal. Second, decreasing maximum gradient amplitude (often achieved by decreasing readout bandwidth) can significantly reduce T_2^* measurement error from concomitant fields (see Figure 1). Third, coronal and sagittal imaging planes tend to have less significant concomitant field effects when compared to axial protocols (see Figure S1 in online supplement). We can suggest two reasons for this last point. When imaging in an axial plane, the readout gradient amplitude and slice thickness dimension are uncoupled, enabling scenarios with strong readout gradients and large voxel dimensions along the through-slice direction. In contrast, for coronal or sagittal imaging protocols described by Equation (9), the readout gradient amplitude is often coupled to and limits the size of the relevant (in-plane) voxel dimension. The second reason is shown by Equation (10). For this case (sagittal or coronal imaging plane with readout gradient along z), the argument of each **sinc** term has been decreased by a factor of 4 when compared to Equation (9). Finally, B_0 field strength is another consideration that should be taken into account when planning T_2^* imaging protocol since the effects of concomitant fields decrease with increasing field strength. However, imaging at higher field strengths, while minimizing concomitant field effects, may increase B_0 field inhomogeneity and associated measurement error.

Isolating concomitant field effects from B_0 inhomogeneity, patient motion, and other confounding factors can be challenging for *in vivo* experiments. Since it was impossible to ensure complete elimination of these factors, protocol B, consisting of two separate 6-echo acquisitions, provided the primary control for all measurements in the kidney and leg studies. Separate “odd” and “even” imaging sequences were used to acquire all twelve echoes. While some level of intravoxel dephasing from concomitant fields is present in protocol B, the effect is markedly less when compared to the 12-echo protocol A. In kidney imaging experiments, both protocol A and B were acquired during the same breath-hold at end-expiration to ensure that measurement differences were not due to B_0 inhomogeneity or inconsistent breath-holds. The principal analysis of concomitant field effects consisted of comparing the difference between protocol A and B measurements at different axial slice positions relative to gradient isocenter. In both the lower leg and kidney imaging experiments, concomitant field-induced T_2^* measurement errors for protocol A are highlighted in these difference maps.

The phantom experiment was designed to isolate concomitant field effects from other confounding sources of intravoxel dephasing. A long cylindrical phantom design was chosen to achieve a uniform B_0 field over a significant portion of the phantom. The field map and its derivative along the three principal directions (Figure 5) confirmed that the average B_0 field variation was small (less than 0.12Hz/mm) for distances up to 90mm from isocenter. In addition to this control, the GRE imaging protocol provided an additional assurance that other confounding factors did not impact T_2^* measurements. Since the GRE protocol acquired each of twelve echoes independently, the amount of intravoxel dephasing from concomitant fields was identical for each echo. The stability of this control measurement in addition to the close concordance between MRGE and simulated T_2^* values demonstrate the effect of concomitant fields in the absence of other confounding factors. Although GRE and MRGE protocols acquired images at identical echo times, it is possible that eddy current differences also contributed to differences in T_2^* values. However, close agreement of experimental and simulated results suggest that eddy current differences between GRE and MGRE protocols, if present, were relatively minor. Evaluation of eddy-currents on T_2^* measurement accuracy was beyond the scope of this study.

In subject 1 (Figure 7), T_2^* measurements for protocol A and B increased at the 40mm station location when compared to measurements at isocenter. This may be due to inconsistent shimming between imaging station locations. There is precedent in the literature for widely varying measured T_2^* values in the kidney.³³ The factors causing this variability are not fully understood at this time and need to be explored further in future work. Despite this limitation, use of control measurement (protocol B) enabled concomitant field effects to be demonstrated independently from other factors affecting T_2^* in the kidney.

Concomitant fields are just one of many factors that can cause inaccurate T_2^* estimation. Macroscopic B_0 field inhomogeneity can also cause significant measurement error. Recent work by Hernando et al.¹⁸ demonstrated that slice profile and the voxel sensitivity function should be considered when designing robust post-processing correction techniques for macroscopic field effects. Although a T_2^* protocol and post-processing technique that jointly

and robustly corrects for all known sources of error would be extremely useful, development of such algorithms was beyond the scope of this work. Since the effect of concomitant field on T_2^* estimation is not widely known, the goal of this paper was to characterize this effect and provide a theoretical framework to assist in understanding this error source. Despite this study limitation, we have shown that modification of imaging parameters can substantially reduce concomitant field induced T_2^* measurement errors. In addition, the theoretical framework presented provides a foundation for potential post-processing correction techniques.

In conclusion, we have demonstrated that concomitant magnetic fields can cause substantial spatially-dependent T_2^* estimation errors. While these errors are most pronounced for thick slice, off-isocenter axial imaging, images acquired in other imaging planes can also be affected. As is the case with other concomitant field-induced artifacts, imaging at lower field strengths and utilizing high amplitude and long duration imaging gradients can be particularly problematic. Although measurement biases can be quite large, the following methods can be used to reduce the magnitude of T_2^* errors caused by concomitant gradient fields:

- Reduced readout bandwidth of multi-echo acquisition.
- Reduce slice thickness when imaging in the axial plane.
- Image near isocenter when possible.
- Image at higher field strengths (i.e. 3T rather than 1.5T).

Given the potential effects of concomitant magnetic fields, reducing this source of error through better protocol design may contribute to more robust and accurate T_2^* measurements across a range of clinical applications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Appendix

A simplified form of the integral in Equation (3) is derived below. The following derivation considers the ideal case of a “boxcar” voxel sensitivity function, i.e. considering the signal at an image pixel to represent the unweighted integral of the signal arising from a perfect rectangular cube of spins with no contribution from adjacent voxels. If we consider first-order variation in the static and concomitant fields across a voxel, we can expand the following terms using a first order Taylor expansion³⁴:

$$\Delta B_0(\vec{r}) = \Delta B_0(\vec{r}_0) + (\vec{r} - \vec{r}_0) \cdot \nabla(\Delta B_0(\vec{r}_0)) \quad (11)$$

$$B_c(\vec{r}, t) = B_c(\vec{r}_0, t) + (\vec{r} - \vec{r}_0) \cdot \nabla B_c(\vec{r}, t) \quad (12)$$

To simplify notation, let us write the gradient of the static and concomitant fields terms as

$$\vec{G}_0(\vec{r}_0) = \nabla(\Delta B_0(\vec{r}_0)) \quad (13)$$

$$\vec{G}_c(\vec{r}_0, t) = \nabla B_c(\vec{r}_0, t) \quad (14)$$

respectively.

Substituting Eq. (11) and (12) into Eq. (3) and using the notation defined by Eqs. (13) and (14) gives the following expression:

$$S(\vec{r}_0, t) = \rho(\vec{r}_0) e^{-t/T_2^*(\vec{r}_0)} \int_V e^{i\gamma[\Delta B_0(\vec{r}_0)t + \int_0^t B_c(\vec{r}_0, t') dt']} e^{i\gamma(\vec{r} - \vec{r}_0) \cdot [\vec{G}_0(\vec{r}_0)t + \int_0^t \vec{G}_c(\vec{r}_0, t') dt']} d\vec{r} \quad (15)$$

The first exponential inside the integral does not depend on $\vec{r}$ and can be factored outside the volume integral. Equation (15) then simplifies to:

$$S(\vec{r}_0, t) = \rho(\vec{r}_0) e^{-t/T_2^*(\vec{r}_0)} e^{i\phi(t)} \int_V e^{i\gamma(\vec{r} - \vec{r}_0) \cdot [\vec{G}_0(\vec{r}_0)t + \int_0^t \vec{G}_c(\vec{r}_0, t') dt']} d\vec{r} \quad (16)$$

where

$$\phi(t) = \gamma[\Delta B_0(\vec{r}_0)t + \int_0^t B_c(\vec{r}_0, t') dt'] \quad (17)$$

denotes the image phase due to static and concomitant gradient fields. For a voxel located at $\vec{r}_0$ with dimensions x , y , and z along the 3 principal axes, Eq. (16), the signal from voxel located at $\vec{r}_0$, can be written as:

$$S(\vec{r}_0, t) = \rho(\vec{r}_0) e^{-t/T_2^*} e^{i\gamma\phi(t)} \times \int_{x_0 - \Delta x/2}^{x_0 + \Delta x/2} \int_{y_0 - \Delta y/2}^{y_0 + \Delta y/2} \int_{z_0 - \Delta z/2}^{z_0 + \Delta z/2} e^{i\gamma(\vec{r} - \vec{r}_0) \bullet [\vec{G}_0(\vec{r}_0)t + \int_0^t \vec{G}_c(\vec{r}_0, t') dt']} dz dy dx$$

(18)

Using the expression for the concomitant fields, Eq. (1), and solving the triple integral simplifies Eq. (18) to

$$S(\vec{r}_0, t) = \rho(\vec{r}_0) e^{-t/T_2^*} e^{i\gamma\phi(t)} \times \Delta x \Delta y \Delta z \cdot \text{sinc}\left(\frac{\gamma \Delta x t a_1(\vec{r}_0, t)}{2}\right) \text{sinc}\left(\frac{\gamma \Delta y t a_2(\vec{r}_0, t)}{2}\right) \text{sinc}\left(\frac{\gamma \Delta z t a_3(\vec{r}_0, t)}{2}\right)$$

(19)

where the coefficient terms $a_1(\vec{r}_0, t)$, $a_2(\vec{r}_0, t)$, and $a_3(\vec{r}_0, t)$ are defined by Eqs. (6)–(8).

Using x_1 , x_2 , and x_3 to denote x , y , and z , Eq. (19) can be written in the compact form shown in Eqs. (4) and (5).

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Fig. 1.

Calculated $T2^*$ measurement variation due to concomitant fields for an axial, multi-echo imaging protocol (12-echoes) with a 40cm field of view and 1.56×1.56 mm inplane voxel resolution. $T2^*$ measurement variation is shown for three different scenarios: slice position varied along z while 10mm slice thickness maintained (top), slice position fixed at 80mm along z while slice thickness varied from 0 to 15mm (middle), and readout bandwidth varied while 10mm slice thickness maintained (bottom). In top and middle plot, results are shown

for both 1.5T and 3T field strengths. Dotted horizontal line denotes 50ms T2* value that would be measured in the absence of concomitant field errors.

Fig. 2.

In-vivo experiments: Read gradient waveforms for imaging protocols A and B where data sampling occurs on the negative polarity lobe. Echo times for protocol A were acquired in a single excitation. Echo times for protocol B were acquired in two 6-echo sets: one “odd” and one “even” readout. Because the concomitant gradient effect depends on the integral of the readout gradient squared, protocol A results in much more severe shortening of T_2^* than protocol B.

Fig. 3.

Phantom experiment: Axial T2* maps acquired along phantom length. Top and bottom row show maps from multi-echo (MGRE) and single echo (GRE) imaging protocols, respectively. T2* values using MRGE protocol decreased with increasing distance from isocenter along z. Values using GRE protocol did not change with distance from gradient system isocenter.

Fig. 4. Phantom experiment: Median T2* for MGRE and GRE protocols showing marked shortening of T2* (up to 24% at 9 cm from isocenter) caused by concomitant fields. The dotted line represents the simulated T2* for the MGRE protocol. Phantom experiment results match the simulated results.

Fig. 5.

Phantom experiment: Fieldmap (B_0) and numerical gradient of B_0 along three principal directions (G_{0x} , G_{0y} , G_{0z}). Only a minor field variation along length of phantom exists within region where T_2^* maps were acquired, ± 90 mm along the z dimension. Field inhomogeneity within this region is insufficient to cause significant intravoxel dephasing, ensuring that intravoxel dephasing from concomitant fields dominate experiment.

Fig. 6.

In-vivo human experiments: Axial T2* and difference maps at 5 locations in the lower right leg showing a decrease in T2* caused by concomitant field effects. Top and middle rows were acquired using protocol A and B, respectively. Bottom row is difference between protocol B (lower concomitant fields) and protocol A (higher concomitant fields) maps. T2* values measured using protocol B were less sensitive to offsets along the z direction when compared to protocol A. Median T2* values in medial gastrocnemius ROIs (outlined in black in upper row) are reported in Table 2.

Fig. 7.

In-vivo human experiments: Axial T2* and difference maps of the right kidney of subject 1 (left) and subject 2 (right) at three different table locations showing strong effect of concomitant gradients on T2*. Top and middle rows were acquired using protocol A and B respectively. Bottom row is difference map between protocol B and protocol A T2* maps. Median T2* values in cortex ROI (outlined in upper left image of each series) are reported in Table 3.

Table 1

Imaging parameters for protocol A (high concomitant field) and B (low concomitant field). Bolded values in table highlight key protocol differences.

	Protocol A	Protocol B	
Description	All Echoes	Odd Echoes	Even Echoes
First Echo Time	2.81ms	2.81ms	5.08ms
Echo Spacing	2.27ms	4.54ms	4.54ms
Number Echoes	12	6	6
Readout Bandwidth	1776Hz/Pixel	1776Hz/Pixel	1776Hz/Pixel
Matrix	256×152	256×152	256×152
FOV	400×237.5mm	400×237.5mm	400×237.5mm
Slice Thickness	10mm axial	10mm axial	10mm axial
Flip	42°	42°	42°
TR	289ms	289ms	289ms

Table 2

Median T_2^* values in the medial gastrocnemius measured at 5 positions along the calf. Values for protocols A, B and the difference are reported for each location. T_2^* values in msec.

	iso	20mm	40mm	60mm	80mm
A	29.0	28.8	27.7	24.8	21.0
B	29.0	28.6	28.4	27.1	24.7
B-A	0.0	-0.2	0.7	2.3	3.7

Table 3

Median T_2^* values in the kidney for Subjects 1 and 2 at three different station locations. Values were computed over entire right kidney and cortex ROIs shown in Figure 6. T_2^* values in msec.

		Right Kidney		Cortex ROI	
		Subject 1	Subject 2	Subject 1	Subject 2
iso	A	63.3	70.3	73.6	73.2
	B	60.5	68.7	70.3	70.7
	B-A	-2.8	-1.6	-3.3	-2.5
40mm	A	64.9	63.5	74.8	72.0
	B	68.9	67.7	80.4	75.5
	B-A	4.0	4.2	5.6	3.5
80mm	A	43.9	40.8	53.4	45.6
	B	67.3	57.0	75.2	65.6
	B-A	23.4	16.2	21.8	20.0