Phase-based T₂ mapping with gradient echo imaging

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Purpose: Transverse relaxation time (T₂) mapping with MRI has a plethora of clinical and research applications. Current T₂ mapping techniques are based primarily on spin-echo (SE) relaxometry strategies that rely on the signal magnitude, and often suffer from lengthy acquisition times. In this work, we propose a phase-based T₂ mapping technique where T₂ information is encoded into the signal phase of rapid gradient echo (GRE) acquisitions.

Theory: Bloch equation simulations demonstrate that the phase of GRE acquisitions obtained with a very small inter-repetition RF phase increment has a strong monotonic dependence on T₂, resulting from coherent transverse magnetization. This T₂-dependent phase behavior forms the basis of the proposed T₂ mapping technique. To isolate T₂-dependent phase from background phase, at least 2 data sets with different RF phase increments are acquired. The proposed method can also be combined with chemical shift encoded MRI to separate water and fat signals.

Methods: The feasibility of the proposed technique was validated in a phantom experiment. In vivo feasibility was demonstrated in the brain, knee, abdomen, and pelvis. Comparisons were made with SE-based T₂ mapping, spectroscopy, and T₂ values from the literature.

Results: The proposed method produced accurate T₂ maps compared with SE-based T₂ mapping in the phantom. Good qualitative agreement was observed in vivo between the proposed method and the reference. T₂ measured in various anatomies agreed well with values reported in the literature.

Conclusion: A phase-based T₂ mapping technique was developed and its feasibility demonstrated in phantoms and in vivo.

KEYWORDS
gradient echo, magnetic resonance imaging, phase, quantitative imaging biomarker, relaxometry, RF spoiling, T₂ mapping
1 | INTRODUCTION

The transverse relaxation time ($T_2$) is associated with important microscopic tissue properties such as the concentration and cluster-size of paramagnetic particles and the mobility of hydrogen atoms. Importantly, $T_2$ is well known to characterize a plethora of important disease processes such as iron deposition, fibrosis, edema, malignancy, and inflammation, among others. As a result, quantitative $T_2$ mapping with MRI has many applications, including assessment of neuro-degenerative diseases and characterization of malignant lesions, detection of myocardial edema, detection of chronic rejection after heart transplant, detection of early cartilage degeneration, quantification of liver iron overload, and even identification of myofascial trigger points.

Spin-echo (SE)-based methods are commonly used to map $T_2$. By varying the TE and fitting the signals to a mono-exponential decay model (multi-exponential if a multi-component model is appropriate), $T_2$ can be estimated. Unfortunately, lengthy exams are needed because of the long TR to minimize $T_1$ weighting. Acquisition times can be reduced by acquiring multiple echoes (multi-echo SE) in a single TR, although the use of multi-echo methods may lead to different measurement of $T_2$.

Magnetization prepared $T_2$ contrast (“$T_2$-prep”) is a method used to encode $T_2$ relaxation into the longitudinal magnetization. This technique is advantageous for imaging blood vessels and the heart and relies on modulation of the longitudinal magnetization before a readout acquisition. Although faster than SE-based acquisitions, $T_2$-prep-based $T_2$ quantification also suffers from relatively long acquisition times.

Steady-state short TR methods based on spoiled gradient echo (SGRE), balanced-steady state free precession (bSSFP), and gradient-refocused acquisition in the steady-state (GRASS) are time efficient compared to SE $T_2$ mapping techniques. For example, 2 SGRE acquisitions with varying flip angle combined with bSSFP contain the necessary information for joint $T_1$ and $T_2$ estimation. Because of the use of short TR acquisitions, these methods can deliver simultaneous $T_1$ and $T_2$ quantification of spatially resolved 3D volumes within clinically acceptable acquisition times.

To further reduce acquisition time for $T_2$ mapping, Welsch et al. proposed a multi-echo gradient echo (GRE) acquisition known as double echo steady-state (DESS). This approach can also be extended for joint estimation of $T_1$ and $T_2$ using the triple echo steady-state (TESS) method proposed by Heule et al. In these methods, $T_2$ information is encoded into the relative magnitude between echoes. In vivo feasibility of these methods has been demonstrated. A variation of the DESS $T_2$ mapping technique developed by Staroswiecki et al. has demonstrated high potential for accurate in vivo $T_2$ mapping. Although only a single GRE acquisition is required, these methods rely on water-specific RF pulses for fat suppression, which may be unreliable in the setting of $B_0$ inhomogeneities. Differential $T_2^*$ weighting in the various echoes can also confound $T_2$ estimates.

We note that none of the above methods exploit signal phase to encode $T_2$ relaxation. In this work, we propose a major modification of an RF phase scheme first proposed by Zur et al. to achieve robust spoiling of transverse magnetization for GRE acquisitions. As we propose below, the use of very small RF phase increments, rather than large RF phase increments needed for RF spoiling, can create $T_2$-dependent changes in both the phase and magnitude of the GRE signal. In this work, we propose a novel quantitative $T_2$-mapping technique that encodes $T_2$ information into the phase of the GRE signal by manipulating the RF phase increment.

2 | THEORY

Complete spoiling of transverse magnetization is generally assumed when using SGRE acquisitions. RF spoiling is a well-known approach used for spoiling transverse magnetization. As first proposed by Zur et al., RF spoiling methods use a pseudo-random sequence of phases of the RF excitation. The phase sequence is defined by the difference between the $n^{th}$ and the $(n+1)^{th}$ RF excitation, i.e., $\Phi_R(n) = \Phi_R(n-1) + \Phi_0 + n \times \Delta \Phi \ (n = 0, \ldots)$. If the RF phase increment ($\Delta \Phi$) is chosen carefully, transverse magnetization accumulates in an incoherent manner and is effectively spoiled.

The choice of RF phase increment is important for effective RF spoiling. Specific choices of RF phase increment (e.g., $117^\circ$) lead to excellent RF spoiling, and the signal closely approximates the ideal SGRE signal magnitude. Other choices of RF phase increment may lead to less effective RF spoiling. Importantly, we note that the phase of GRE signals in the context of RF spoiling has not been well described.

In this study, we investigate the effects of the RF phase increment on the phase of the complex-valued GRE signal. Figure 1 plots the results of a Bloch equation simulation showing both the signal magnitude ($\eta$) and phase ($\theta$) of the GRE signal, using the RF phase increment method proposed by Zur et al.. In this computer simulation, an ensemble of 1000 spins periodically experienced a sequence consisting of an RF pulse, $T_1$ and $T_2$ relaxation, and at the end of each repetition, a $2\pi$ phase dispersion across the isochromats because of an unbalanced readout gradient. Note that the acquisition reference frame matches the excitation phase.

Figure 2 focuses on a narrow range of small RF phase increments, also with varying $T_1$, $T_2$, and flip angle. As can be seen in Figure 2, significant variations in the signal phase occur with changes in $T_2$ and flip angle, and to a much lesser extent with $T_1$. The largest signal phase was observed with small RF phase increments between $1-4^\circ$. 


Various combinations of $T_2$ (25 ms, 55 ms, 115 ms), $T_1$ (500 ms, 900 ms, 1400 ms), and flip angle ($5^\circ$, $10^\circ$, $15^\circ$) are used in the simulation assuming a TR of 10 ms and simulated TE of 0 ms to ignore the effects of $T_2^*$ decay, for simplicity.

The effects of $T_2$, $T_1$, and flip angle are also plotted in Figure 3, demonstrating not only a strong dependence of the signal phase on $T_2$ and flip angle, but also a relatively weak dependence on $T_1$. We can express the steady-state GRE signal acquired with an RF phase increment as
\[ S(\Delta \Phi, \alpha, \text{TR}; M_0, T_1, T_2) = M_0 \cdot |S(\Delta \Phi, \alpha, \text{TR}; T_1, T_2)| \cdot e^{i(\theta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) + \phi')}. \]  

(1)

where \( \eta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \) is the signal magnitude relative to \( M_0 \), \( \theta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \) is the signal phase immediately after excitation and is dependent on \( T_2, T_1, \) flip angle \( (\alpha) \), and \( \theta' \), which is the local background phase caused by complex coil sensitivity, eddy currents, magnetic field inhomogeneities, etc.

To the best of our knowledge, simple analytical forms of \( \eta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \) and \( \theta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \) have not been derived. In this work, calculation of these 2 functions is based on the use of a lookup table. Lookup tables are constructed from Bloch equation simulations based on wide ranges of possible \( T_1 \) and \( T_2 \) values and the known acquisition parameters used in the experiment: \( \Delta \Phi, \alpha, \text{TR} \). All lookup tables used in this work are constructed using the same Bloch equation simulation described above.

Figure 3 depicts in greater detail the dependence of the signal phase with respect to \( T_2, T_1, \) and flip angle over a few small RF phase increments. A pronounced monotonic increase in the observed phase with \( T_2 \) is noted over a wide range of physiological \( T_2 \) values \(^{21} \) with RF phase increments between 1° and 4°. For an RF phase increment of 2°, the signal phase is consistently sensitive to \( T_2 \) over a wide range of \( T_2 \) values (Figure 3A). Unlike the strong dependence on \( T_2 \), the signal phase changes minimally over a wide range of \( T_1 \) values between 1000 ms and 2000 ms (Figure 3B). Given these observations, a small RF phase increment such as 2° will encode the tissue \( T_2 \) into the signal phase.

In actual MRI acquisitions, the received signal phase contains an additional background phase term, i.e., \( \theta' \) (Equation 1). Estimates of the signal phase resulting from \( T_2 \) of the tissue must be isolated from the background phase. In this work, we propose the following method to isolate \( \theta \) from \( \theta' \) and subsequently estimate tissue \( T_2 \).

### 2.1 Proposed phase-based T₂ mapping

In principle, 2 identical acquisitions with equal and opposite RF phase increments will generate equal but opposite phase responses (Figure 2), i.e., \( \theta(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) = -\theta(-\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \). Using 2 such acquisitions, \( \theta \) can be isolated from \( M_0, \eta \), and \( \theta' \) in Equation 1 by taking the phase difference of 2 GRE signals acquired with opposite RF phase increments and with all other acquisition parameters identical, i.e.

\[
\hat{\theta}(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) = \left( \angle S(\Delta \Phi, \alpha, \text{TR}; T_1, T_2) - \angle S(-\Delta \Phi, \alpha, \text{TR}; T_1, T_2) \right) / 2.
\]

(2)

Using a well-chosen RF phase increment (e.g., \( \Delta \Phi = 2° \)) and a relatively large flip angle (e.g., \( \alpha = 18° \)), the estimated signal phase can be used to estimate T₂. Based on the model presented above, it is expected that only a small error might occur in the T₂ estimate related to T₁ and unanticipated errors in flip angle (Figure 3B,C). Note that the same figure shows a maximum signal phase of 50°, which will result in a phase difference of 100° between 2 signals. This phase difference is well below 2π, suggesting that even with higher T₂ values, there should be no risk of phase wrap in the proposed method.

In this work, we propose to estimate T₂ from \( \hat{\theta} \) through the use of a lookup table generated from a Bloch equation simulation that uses the known TR and flip angle of the acquisition. We note that the phase is weakly-dependent on T₁, and therefore T₁ values measured using other methods or values reported in the literature for the anatomy of interest can be used to generate the lookup table.

### 2.2 Synthetic T₂-weighted images

In addition to the phase maps used to generate the T₂ map, magnitude images are also acquired. By multiplying these magnitude images with the inferred T₂ decay from the phase-based T₂ map, synthetic T₂-weighted images can be generated. The synthesis of the signal in each voxel can be expressed as

\[
S_{\text{syn}} = |S| \times e^{-\frac{TE}{T_2}},
\]

(3)

where \( S_{\text{syn}} \) is the synthesized T₂-weighted signal, TE is the virtual echo time, S denotes the signal acquired with 1 (or a combination) of the images acquired at the 2 phase increments, and \( \hat{T}_2 \) denotes the estimated phase-based T₂ value.

### 3 METHODS

#### 3.1 Phantom experiments

The accuracy of the proposed method was evaluated using a phantom constructed with varying concentrations of agarose and NiCl₂ to modulate the T₂ and T₁ relatively independently. \(^{24} \) The T₁ was varied such that the confounding effect of T₁ variation in the proposed method can be demonstrated. A 4 \( \times \) 4 grid of cylindrical vial agarose gel phantom was constructed for this experiment. Each vial is ~3 cm in diameter and 4.8 cm in height. Each column was constructed with a varying concentration of agarose (0.5%, 1%, 2%, 4%) to modulate T₂. Each row is doped with a varying concentration of NiCl₂ (0 mM, 0.5 mM, 1 mM, 2 mM) to modulate T₁.
All phantom experiments were performed on a clinical 3.0T MRI system (Signa Premier, GE Healthcare, Waukesha, WI) using a high channel density posterior and anterior receive array coil with up to 90 independent coil elements (Air Coil, GE Healthcare). Single-echo SE-based T2 mapping was performed to provide a reference standard. TEs of 11 ms, 50 ms, 100 ms, and 150 ms were acquired with TR of 6000 ms. Other acquisition parameters include: axial acquisition; FOV = 18 cm × 18 cm; matrix = 128 × 128; slices = 1; slice thickness = 15 mm; receiver bandwidth = ±83.33 kHz. Signals were fit to a mono-exponential decay signal model offline in MATLAB (The MathWorks, Natick, MA) to estimate T2 on a voxel-by-voxel basis. A circular region of interest (ROI) was drawn in each vial. The T2 measurements were averaged in each ROI for comparison with the proposed method.

T1 maps of the phantoms were generated using inversion recovered fast spin-echo (FSE-IR) MRI. Acquisition parameters were as follows: inversion time = 50 ms, 500 ms, 1000 ms, 1500 ms, 2500 ms, 3500 ms, 4000 ms; TR = 6000 ms; FOV = 18 cm × 18 cm; matrix = 256 × 256; slices = 1; slice thickness = 15 mm; receiver bandwidth = ±25 kHz. T1 estimation was performed on a voxel-by-voxel basis. A circular region of interest (ROI) was drawn in each vial. The T2 measurements were averaged in each ROI for comparison with the proposed method.

For each reconstruction by the proposed method, T2 measurements were averaged inside ROIs drawn directly on the T2 maps in the following regions described by Liu et al27: medial femoral central (MFC) condyle, lateral femoral posterior (LFP) condyle, and lateral tibial plateau (LTP), as well as patella-deep (PAT-D), patella-superficial (PAT-S), lateral oral posterior (MFP) condyle, medial tibial plateau (MTP), and gastrocnemius muscle (MUS). For each individual region, box-whisker plots were created to demonstrate the distribution of T2 measurements by the 2 compared methods. A Student’s t-test was performed for paired samples. For measurements across all the regions, the Pearson coefficient was computed.

A brain study was performed on 1 volunteer (male, age 30 y). The acquisition parameters of the proposed method were as follows: 3D acquisition; sagittal plane; FOV = 14 cm × 14 cm × 9.6 cm; TR = 5.9 ms; matrix = 256 × 256 × 32; bandwidth = ±90.91 kHz; signal averages = 3; acquisition time = 4:48 min. Because of the difficulty of limiting motion over long acquisition times, a commercial multi-echo SE T2 mapping was used as reference instead of single-echo SE. Acquisition parameters include: sagittal plane; FOV = 14 × 14 cm; slice thickness = 2.7 mm; gap = 0.3 mm; slices = 28; TR = 1.0 s; acquisition matrix = 256 × 256; TEs = 8.6 ms, 14.8 ms, 22.2 ms, 29.5 ms, 36.9 ms, 44.3 ms, 51.7 ms, 59.1 ms; bandwidth = ±31.25 kHz; signal averages = 1; exam time = 12:56 min. The acquisition volumes of the 2 methods were precisely co-localized.

Phase-based T2 maps were reconstructed as described in the Theory section. T1 of 1198 ms was assumed (midpoint between the T1 of the medial femoral cartilage and patella).26 The reference T2 map from multi-echo SE images were calculated by fitting the signal to a single-exponential decay model to minimize least square error on a voxel-by-voxel basis. To compare the proposed method and the reference, T2 measurements were averaged inside ROIs drawn directly on the T2 maps in the following regions described by Liu et al27: medial femoral central (MFC) condyle, medial femoral posterior (MFP) condyle, medial tibial plateau (MTP), patella-deep (PAT-D), patella-superficial (PAT-S), lateral femoral central (LFC) condyle, lateral femoral posterior (LFP) condyle, and lateral tibial plateau (LTP), as well as T2 measurements from the gastrocnemius muscle (MUS). For each individual region, box-whisker plots were created to demonstrate the distribution of T2 measurements by the 2 compared methods. A Student’s t-test was performed for paired samples. For measurements across all the regions, the Pearson coefficient was computed.
as reference for $T_2$ measurements, acquisition parameters include: axial plane; FOV = 24 cm × 24 cm; slice thickness = 3.6 mm; slice spacing = 0.4 mm; number of slices = 22; TR = 5 s; acquisition matrix = 256 × 256; TEs = 11 ms, 70 ms; bandwidth = ±31.25 kHz; signal averages = 1; acquisition time = 24:00 min. The acquisition volumes of the 2 methods were precisely co-localized.

Phase-based $T_2$ maps were reconstructed as described in the theory section. $T_1$ of 915 ms was assumed (midpoint between the $T_1$ of white matter and the putamen at the age of 20). The reference $T_2$ map was reconstructed using least-square error fitting to a single-exponential model. Synthetic $T_2$-weighted images were also generated with virtual $T_2$ values of 70 ms and 100 ms as described in the Theory section.

For imaging in the abdomen and pelvis, separation of water and fat signals was performed by combining the proposed method with a multi-echo 3D GRE chemical shift encoded (CSE) acquisition. Abdomen (male, age 54 y) and pelvis (male, age 47 y) experiments were conducted on 1 volunteer, respectively. The acquisition parameters in the abdomen included: axial plane; FOV = 40 cm × 32 cm × 26 cm; TR = 6.5 ms; acquisition matrix = 100 × 80 × 26; 5 echoes with TEs = 0.9 ms, 2.0 ms, 3.0 ms, 4.0 ms, 5.1 ms; bandwidth = ±100 kHz; signal averages = 1; exam time = 20 s in a single breath-hold. In the pelvis, the same acquisition parameters were used with the following exceptions: slice thickness = 8 mm; slices = 32; TR = 6.4 ms; bandwidth = ±90.91 kHz; exam time of 25 s in a breath-hold.

For the image reconstruction, the proposed method was combined with CSE-MRI. Using complex fitting with single $R^2$ least-squares fitting reconstruction from the ISMRM Fat-Water Toolbox (http://ismrm.org/works hops/FatWa ter12/data.htm), water and fat signals were separated. The magnitude and phases of each chemical species were then used to reconstruct individual $T_2$ maps for each chemical species.

Single voxel multi-TE STEAM-MRS was acquired in the liver and the spleen to provide reference values for phase-based $T_2$ measurements. STEAM-MRS data was acquired with the following parameters: TR = 3500 ms; TE = 10 ms, 15 ms, 20 ms, 25 ms, 30 ms; number of points = 2048; spectral width = 5000 Hz; 5 ms mixing time. The voxel size was 15 mm × 15 mm × 20 mm in the liver and 15 mm × 15 mm × 10 mm in the spleen. Signal magnitude as well as $T_2$ of water and fat signal was estimated jointly using non-linear least square fitting.

### Simulation experiment to evaluate the sensitivity of phase to motion

Although no apparent effect of motion was observed in vivo (below), it is well known that GRE acquisitions with unbalanced gradients and no RF spoiling (i.e., unspoiled GRE) can be sensitive to motion. In the presence of unbalanced gradients, moving spins will accrue a different phase during each TR. This phase accrual may impact the $T_2$-dependent phase of the method proposed in the current work, potentially confounding $T_2$ measurements.

For the proposed method, phase accrual resulting from the unbalanced readout gradient is a linear function of the voxel location. Assuming that the phase dispersion from the unbalanced gradient is $2\pi$ across the voxel in the readout direction, the additional phase accrual from the overall voxel can be written as: $n \times TR \times Vx \times 2\pi / \Delta X$, for a voxel moving from the image isocenter, where $Vx$ is the velocity of the voxel in the readout direction and $\Delta X$ is the voxel dimension in the readout direction. This effect potentially confounds quantification of the phase shift used to encode $T_2$.

To assess the magnitude of velocity effects on $T_2$ quantification, we performed a Bloch equation simulation experiment where the effects of the first order motion (velocity) in the readout direction were modeled. This simulation was performed using a modification of the simulation described in the Theory section. In addition to a $2\pi$ phase dispersion, a velocity-dependent common phase was added to all isochromats in a voxel at the end of each repetition. This simulation experiment was conducted with velocity values ranging from −1 mm/s to 1 mm/s, with a 2 mm voxel dimension. Other parameters used in the simulation included: flip angle = 18°, TR = 5 ms, $\Delta \Phi = \pm 2^\circ$, $T_2 = 50$ ms, and $T_1 = 1000$ ms. Signal phase attributed to $T_2$ was estimated from the phase difference between the 2 signals (i.e., with $\Delta \Phi = \pm 2^\circ$) divided by 2 and compared with a $T_2$ lookup table for $T_2$ estimation, using the proposed method described in the Theory section. The lookup table was generated using Bloch equation simulation without motion and the same acquisition parameters over a wide range of tissue relaxation parameters.

### RESULTS

#### Phantom experiments

In the phantom experiment the $T_1$ of the phantom vials were estimated by FSE-IR to be 873 ms, 932 ms, 829 ms, and 925 ms, corresponding to agar concentrations of 0.5%, 1%, 2%, and 4% in phantoms with 2 mM NiCl$_2$; 1390 ms, 1315 ms, 1279 ms, and 1332 ms in phantoms with 1 mM NiCl$_2$; 1725 ms, 1698 ms, 2053 ms, and 1792 ms in phantoms with 0.5 mM NiCl$_2$; 2848 ms, 2902 ms, 2788 ms, and 2888 ms in phantoms with 0 mM NiCl$_2$. The proposed method (that did not correct for $T_1$ effect in the signal phase) demonstrated close agreement with reference $T_2$ estimates (Figure 4) (slope = 1.03 ± 0.07, intercept = −3.24 ± 5.67). For vials of vastly different $T_1$ measurements (2 mM NiCl$_2$ and 0.5 mM NiCl$_2$), the $T_2$ measurements show slightly higher deviation from the reference at high $T_2$ values.
In the knee imaging experiments, the proposed method produced high quality $T_2$ maps in all knees (Figure 5), including high apparent SNR and excellent depiction of anatomic detail. In areas where water signal is dominant (cartilage and muscle), similar $T_2$ values were observed between the proposed method and the multi-echo SE $T_2$ map used as a reference. In Figure 6, the box-whisker plot and scatter plot showed strong correlation between the phase-based $T_2$ and the reference $T_2$ measurements (Pearson correlation coefficient = 0.86), with slope = 0.78 ± 0.12 and intercept = 3.24 ± 4.84. Quantitative $T_2$ values measured using the proposed method were very similar to the multi-echo SE-based $T_2$ measurements, although many of these measurements showed statistical differences.

Similarly, high quality $T_2$ maps were generated by the proposed method in the brain (Figure 7). However, some discrepancies in $T_2$ values were observed between the 2 methods, especially in the gray matter. Average $T_2$ values in ROIs were 39 ms (phase-based) and 53 ms (SE) in the genu of corpus callosum; 40 ms (phase-based) and 61 ms (SE) in the splenium of corpus callosum; 47 ms (phase-based) and 59 ms (SE) in the white matter; 35 ms (phase-based) and 40 ms (SE) in the globus pallidus of basal ganglia; 45 ms (phase-based) and 54 ms (SE) in the putamen of basal ganglia.

Synthetic $T_2$-weighted images generated from the phase-based $T_2$ map and the simultaneously acquired magnitude images are also shown with 2 different virtual echo times (70 ms, 100 ms). Compared with a $T_2$-weighted SE image with TE of 70 ms, the synthesized $T_2$-weighted image with virtual TE of 70 ms showed overall similar appearance, although with slightly reduced apparent gray–white matter contrast.

In the abdomen and pelvis, 3D spatially resolved $T_2$ maps generated from separated water signal were successfully reconstructed after water–fat separation (Figure 8). Close agreement between $T_2$ value of the water signal estimated by the proposed method and MRS was observed, with estimates of 20 ms and 22 ms, respectively, using a co-localized voxel. Similarly, in the spleen, the proposed method measured a $T_2$ value of 38 ms compared to 34 ms with MRS.

Finally, in the peripheral zone of the prostate, phase-based $T_2$ measurements (72 ms) were comparable to values reported in literature (74 ± 9 ms in the prostate).23

### 4.3 Simulation experiment to study the sensitivity of signal phase to motion

As shown in Figure 9, the signal phase in the proposed method was sensitive to motion. For example, a velocity of 1 mm/s lead to a 3.6° change in the signal phase, relative to no motion. Accordingly, the apparent $T_2$ estimation was reduced from 50 ms to 42 ms.

5 | DISCUSSION

We have proposed and successfully demonstrated preliminary feasibility of a phase-based $T_2$ mapping technique based on GRE imaging. The theory and technique for encoding
T₂ information into the signal phase of a GRE acquisition were developed. We demonstrated that using a small RF phase increment in GRE acquisitions, a signal phase that increases monotonically with the transverse relaxation time can be generated. This behavior forms the basis of the proposed method for encoding information into the GRE signal phase. The feasibility of the proposed method was successfully demonstrated in phantoms and in vivo experiments, including in combination with chemical shift encoded water–fat separation. Further, the proposed approach can be used to generate high quality synthetic T₂-weighted images that can be acquired in relatively short acquisition times.

Compared with traditional SE-based T₂ mapping and T₂-prep-based methods, the proposed method reduces acquisition time and would potentially render quantitative T₂ mapping feasible for many clinical applications, including those...
that require short breath-holds. Compared with DESPOT2, the proposed method requires fewer GRE source images for parametric mapping and consequently shorter acquisition time. Further, the proposed method is also immune to signal voids caused by banding artifacts seen with bSSFP methods. Compared with the TESS $T_2$ mapping technique, $T_2$-weighting and $T^*_2$-weighting in the signals of the proposed method are naturally separated, because the $T_2$ information is contained in the signal phase, which is not affected by $T^*_2$ effects. The proposed technique is also compatible with CSE-MRI, which is useful in many extra-cranial imaging applications, particularly in the abdomen and pelvis. This feature would enable simultaneous generation of $T_2$ maps for both water and fat signals as well as the $R^*_2$ and $B_0$ field map.

In this work, the proposed GRE-based method was able to shorten the minimum acquisition time compared to SE-based $T_2$-mapping methods. Among the steady-state methods, DESPOT2 requires at least 3 or more acquisitions. The proposed phase-based $T_2$ mapping technique requires 2 acquisitions, whereas DESS and TESS require only 1. The number of acquisitions required would normally determine the minimum acquisition time needed to create a $T_2$ map of a certain resolution and FOV. However, it is worth noting that the relative advantage of DESS and TESS in this comparison is offset by their generally longer TR (14 ms, 20 ms, 26 ms, 21 ms)\textsuperscript{17-20} compared to DESPOT2 (e.g., 3.6 ms)\textsuperscript{16} and the phase-based $T_2$ mapping (e.g., 5.9 ms, 5.6 ms, and 6.5 ms in this work). Further, depending on the application, multiple signal averages are often acquired, when there is sufficient acquisition time (e.g., in the knee and in the brain). In such applications, the SNR efficiency is a more important measure of acquisition speed. Rigorous evaluation of the SNR performance of the proposed method is beyond the scope of this work but will be an important component of future investigations.

Small discrepancies between the $T_2$ measured with the proposed method and SE-based methods were observed, particularly in the brain. Although the reasons for these discrepancies are unclear, possible reasons include multi-component $T_2$ effects, magnetization transfer, $B_1$ inhomogeneities, motion, or combinations of these factors. Further work will be needed to determine the cause of these discrepancies.

Previous studies have demonstrated that motion can lead to change in the signal magnitude in steady-state acquisitions using unbalanced GRE acquisitions and pseudo-random RF phase spoiling. In this work, we have performed preliminary Bloch equation simulations modeling constant linear motion, demonstrating that small changes in the signal phase may result from motion, leading to underestimation of $T_2$. Although no definite effects of motion on artifacts or $T_2$ estimation...
accuracy were observed in the experimental studies, some underestimation of $T_2$, relative to references standard measurements was observed in cartilage and in the brain. It is uncertain whether this apparent underestimation in $T_2$ was related to motion or not. Future rigorous evaluation of the potential effects of motion on $T_2$ estimation is warranted, especially for applications where tissue motion may be an important factor (e.g., heart, flowing blood).

There are several limitations of this work. First, although the feasibility of this method has been successfully demonstrated, considerable technical optimization and substantial further clinical validation is needed. Further studies will be needed to evaluate the technical accuracy and noise performance of the proposed method, as well as to optimize acquisition parameters. In addition, the precise impact of $B_1$ inhomogeneities, motion, variation in $T_1$ of the tissues, magnetization transfer effects, and multi-exponential relaxation requires further evaluation. These effects may explain the apparent discrepancies between the $T_2$ measurements in the brain between the proposed phase-based method and conventional SE-based $T_2$ mapping.

Another major limitation of the proposed method is that the $T_2$ mapping algorithm requires knowledge or assumption of the $T_1$ of tissue to map the signal phase into a $T_2$ value. Although the signal phase is relatively independent of $T_1$ for long $T_1$ values, this is not the case for shorter $T_1$ values. Therefore, the overall accuracy of this method is unknown for $T_2$ quantification, especially in tissues with short $T_1$ values.

Further, the proposed method can be used to generate synthetic $T_2$-weighted images. However, because of the relatively large flip angle in the proposed method, the source magnitude images are $T_1$-weighted. For this reason, the $T_2$-weighted images synthesized from the phased-based $T_2$ maps and simultaneously acquired magnitude images will be $T_1$-weighted as well, similar to short tau inversion recovery (STIR)-based methods.

In addition, the proposed method currently requires the use of 3D acquisitions, because of the need for a uniform flip angle across the tissue of interest. Extension to 2D imaging should be feasible but will require more complex lookup table construction that accounts for acquisition slice profiles.

6 | CONCLUSIONS

We have presented and successfully demonstrated the feasibility of a novel phase-based $T_2$ mapping method based on GRE imaging. This approach has the potential for rapid, 3D mapping of $T_2$ in tissue. Further technical development, optimization, and clinical validation are needed.

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