Free-breathing 3D cardiac $T_1$ mapping with transmit $B_1$ correction at 3T

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Purpose: To develop a cardiac $T_1$ mapping method for free-breathing 3D $T_1$ mapping of the whole heart at 3 T with transmit $B_1$ ($B_1^+$) correction.

Methods: A free-breathing, electrocardiogram-gated inversion-recovery sequence with spoiled gradient-echo readout was developed and optimized for cardiac $T_1$ mapping at 3 T. High-frame-rate dynamic images were reconstructed from sparse $(k,t)$-space data acquired along a stack-of-stars trajectory using a subspace-based method for accelerated imaging. Joint $T_1$ and flip-angle estimation was performed in $T_1$ mapping to improve its robustness to $B_1^+$ inhomogeneity. Subject-specific timing of data acquisition was used in the estimation to account for natural heart-rate variations during the imaging experiment.

Results: Simulations showed that accuracy and precision of $T_1$ mapping can be improved with joint $T_1$ and flip-angle estimation and optimized electrocardiogram-gated spoiled gradient echo–based inversion-recovery acquisition scheme. The phantom study showed good agreement between the $T_1$ maps from the proposed method and the reference method. Three-dimensional cardiac $T_1$ maps (40 slices) were obtained at a 1.9-mm in-plane and 4.5-mm through-plane spatial resolution from healthy subjects ($n = 6$) with an average imaging time of 14.2 ± 1.6 minutes (heartbeat rate: 64.2 ± 7.1 bpm), showing myocardial $T_1$ values comparable to those obtained from modified Look-Locker inversion recovery. The proposed method generated $B_1^+$ maps with spatially smooth variation showing 21%–32% and 11%–15% variations across the septal–lateral and inferior–anterior regions of the myocardium in the left ventricle.

Conclusion: The proposed method allows free-breathing 3D $T_1$ mapping of the whole heart with transmit $B_1$ correction in a practical imaging time.

KEYWORDS
cardiac $T_1$ mapping, free-breathing, low-rank, myocardial $T_1$ mapping, spoiled gradient-echo, transmit $B_1$ inhomogeneity
INTRODUCTION

Cardiac $T_1$ mapping is a powerful cardiovascular MRI technique that allows quantitative assessment of tissue characteristics and underlying pathology of the myocardium. Native (i.e., without the use of exogenous contrast agent) myocardial $T_1$ characterizes alterations in the structure and intracellular/extracellular components of the myocardium. Native myocardial $T_1$ is a well-recognized biomarker for quantitative assessment of diseases that alter tissue composition, such as iron deposition, amyloid disease, Anderson-Fabry disease, and myocarditis.\textsuperscript{1–3} Extracellular volume fraction, measured from pre-contrast and post-contrast $T_1$ values, provides quantitative measurement of interstitial expansion and associated diseases, such as amyloidosis, fibrosis, or myocardial edema.\textsuperscript{2,3} Extracellular volume fraction is an emerging biomarker for diffuse fibrosis (e.g., heart failure, dilated cardiomyopathy, amyloidosis),\textsuperscript{3} which is challenging to detect using qualitative late-gadolinium enhancement methods.

Modified Look-Locker inversion recovery (MOLLI)\textsuperscript{4} is a widely used method for 2D cardiac $T_1$ mapping, which uses adiabatic inversion pulses for magnetization preparation and performs electrocardiogram (ECG)–gated balanced SSFP acquisitions through multiple cardiac cycles with breath-holding. Although MOLLI produces myocardial $T_1$ maps with high precision,\textsuperscript{5} the method is limited to a single-slice imaging per breath-hold. Methods have been developed to extend the conventional 2D MOLLI method to multislice 2D or 3D acquisitions with breath-holding by leveraging the state-of-the-art parallel imaging, simultaneous multislice acquisition, compressed sensing, and non-Cartesian sampling techniques.\textsuperscript{6,7} However, these methods suffer from limited through-plane resolution and coverage, often involving long or repetitive breath-holds to obtain volumetric $T_1$ maps of the heart, which imposes significant burden on patients.

Various methods have been developed to overcome the limitations of breath-holding and allow 3D cardiac $T_1$ mapping with free-breathing acquisitions. Respiratory and cardiac gating–based $T_1$ mapping methods have been developed to acquire interleaved multislice 2D\textsuperscript{8–10} or segmented 3D k-space data\textsuperscript{11–13} at end-diastole with free-breathing, in which effects from respiratory motion were mitigated by prospectively tracking respiratory motion using navigators or self-navigation techniques. Magnetic resonance fingerprinting approaches have been combined with free-breathing ECG-gated acquisitions for multi-parametric cardiac MRI.\textsuperscript{14} However, most of these methods are limited by spatial coverage, resolution in slice direction, or imaging time due to the low data-acquisition efficiency of gating. Recently, free-running (i.e., no cardiac or respiratory gating) continuous acquisition methods have been proposed for 2D or 3D cardiac $T_1$ mapping.\textsuperscript{15–20} Of note, Qi et al reported a free-running 3D whole-heart $T_1$ mapping method\textsuperscript{15} that uses translational respiratory motion correction and a patch-based low-rank tensor model to reconstruct 3D $T_1$ maps with isotropic resolution. The $T_1$ maps obtained by this method, however, were from 1.5 T, and the method may not translate well to 3 T for reasons discussed subsequently.

Although 3D cardiac $T_1$ mapping methods developed up until now have been applied mostly at 1.5 T, unique technical challenges arising from more severe $B_0$ and transmit $B_1$ ($B_1^+$) inhomogeneities need to be addressed at 3 T. For instance, spoiled gradient-echo (SPGR) readout with small flip angle (FA) is often used in 3D cardiac imaging at 3 T to avoid $B_0$ inhomogeneity–caused banding artifacts associated with balanced SSFP readout.\textsuperscript{7,16,17,19} However, $T_1$ mapping with SPGR readout is known to be sensitive to errors in FA caused by imperfect RF pulses and $B_1^+$ inhomogeneities.\textsuperscript{21} The latter is particularly problematic at 3 T, in which $B_1^+$ variation over the left ventricle with body-coil transmission is reported on the order of 30%–60%,\textsuperscript{22} leading to bias in $T_1$ estimation. Robustness of cardiac $T_1$ mapping methods with SPGR acquisitions needs to be thoroughly investigated in the presence of $B_1^+$ inhomogeneity.\textsuperscript{23,24}

In this work, we present a new cardiac $T_1$ mapping method for rapid 3D $T_1$ mapping of the heart at 3 T. A free-breathing, ECG-gated IR sequence with SPRG readout was developed and optimized in terms of acquisition protocol and excitation FA for accurate and precise cardiac $T_1$ mapping at 3 T. The optimized scheme was combined with sparse ($k,t$)-space sampling along a stack-of-stars trajectory to accelerate imaging. A subspace-based image-reconstruction method was used to recover high-frame-rate dynamic images from highly undersampled ($k,t$)-space data. The effects of FA errors on $T_1$ mapping were mitigated by joint estimation of $T_1$ and FA, in which the reconstructed dynamic images were first binned to different respiratory motion phases and then fitted voxel-by-voxel to a signal dictionary generated using Bloch equation simulations. The effects of heart-rate variations on $T_1$ mapping were reduced by generating signal dictionary with subject-specific timing of data acquisition recorded during imaging experiment. The performance of the proposed method was characterized and validated through numerical simulations, phantom studies, and in vivo experiments on healthy human subjects ($n = 6$). Preliminary accounts of this work have been presented previously in the form of conference abstracts.\textsuperscript{25–27}
2 METHODS

2.1 Data acquisition

The proposed ECG-gated cardiac T1 mapping sequence is shown in Figure 1. A nonselective inversion pulse was applied every N+M heartbeats with two different TIs. This scheme is referred to as the N-(M)-N-(M) protocol for simplicity, where N denotes the number of cardiac cycles for acquisition and M denotes the number of cardiac cycles for signal recovery. Data were acquired at end-diastole period using SPGR readout. A special data-acquisition scheme was used for sparse sampling (k,t)-space data along a stack-of-stars trajectory. A limited number of “training” data (e.g., along the kx, ky, and kz directions across the center of the k-space) were acquired with high sampling rate to determine the temporal changes of the underlying signal. Data at all other k-space locations were sparsely sampled over the entire (k,t)-space to ensure that sufficient number of measurements were acquired at each k-space location for subspace-based image reconstruction.

To track respiratory motion, one-dimensional (1D) respiratory navigator signals were acquired in the sagittal plane at the dome of the right hemi-diaphragm at the beginning and end of data acquisition of each cardiac cycle. A spatially selective inversion pulse was applied right after the nonselective inversion pulse to invert the magnetization signals in the same sagittal plane back to the equilibrium state, and therefore to mitigate the contrast changes caused by the nonselective inversion pulses in the navigator signals.

2.2 Image reconstruction

Image reconstruction of sparsely sampled data was performed by solving the following constrained optimization problem:

$$\hat{\rho}(x, t) = \arg\min_{\rho(x, t)} \| d(k, t) - \Omega \mathscr{F}_s \{ \rho(x, t) \} \|^2 + \lambda \| \mathscr{F}_t \{ \rho(x, t) \} \|_1,$$

s.t. $\rho(x, t) = \sum_{l=1}^{L} u_l(x) v_l(t)$

(1)

where $d(k, t)$ denotes the measured data; $\mathscr{F}_s$ denotes the Fourier transform in the spatial domain; $\Omega$ denotes the sampling mask in the (k,t)-space; and $\lambda$ denotes the regularization parameter, which was chosen based on the discrepancy principle.\textsuperscript{28} The first term of the cost function in Equation 1 penalizes data inconsistency, while the second term promotes sparsity of the reconstructed dynamic images $\rho(x, t)$ in the spatio-spectral domain.\textsuperscript{29} The constraint in Equation 1 represents $\rho(x, t)$ as a partially separable function,\textsuperscript{30,31} where $v_l(t)$ denotes the temporal basis function, $u_l(x)$ denotes the corresponding spatial coefficients, and $L$ is the model order. In this work, $v_l(t)$ was estimated separately from training data using singular value decomposition for simplified computation.\textsuperscript{29} Image reconstruction problem was then reduced

![Figure 1](image-url)  
**Figure 1** Schematic diagram of the proposed data-acquisition scheme. The N-(M)-N-(M) protocol is shown with nonselective inversion pulse applied every N+M heartbeats (where N denotes the number of cardiac cycles for acquisition and M denotes the number of cardiac cycles for signal recovery) with two different TIs. Data acquisition consists of the “training” data set, acquiring a limited number of k-space lines with high sampling rate, and the “imaging” data set, sparsely sampling all other k-space locations for subspace-based image reconstruction. To track respiratory motion, one-dimensional respiratory navigator signals were acquired in the sagittal plane at the dome of the right hemi-diaphragm after a spatially selective inversion pulse was applied in the same sagittal plane to invert the magnetization signals back to the equilibrium state.
to determining the spatial coefficients \( u_t(x) \) from measured data. The optimization problem in Equation 1 was solved using an alternating direction method of multipliers-based algorithm. For fast computation of \( \mathcal{F} \), 1D Fourier transform was applied along the \( k_z \) direction first, and non-uniform fast Fourier transform was applied in the \( k_r-k_y \) plane for slice-by-slice reconstruction. The dynamic images were reconstructed in a coil-by-coil fashion and then combined using the sum-of-squares method to form the final reconstruction. We implemented the image reconstruction algorithm in Python and used the SigPy package to accelerate the computation using GPUs. Reconstructions were performed on four NVIDIA Tesla V100 SXM2 GPUs (parallelized over slice and coil dimensions) with reconstruction time around 1 minute for each slice and coil.

### 2.3 Estimation of \( T_1 \) and FA

Before parameter estimation, the reconstructed dynamic images were binned to different respiratory-motion phases based on diaphragm position information extracted from the navigator signals. Let \( \hat{\rho}_{n,m} \) denote the reconstructed dynamic signals at a voxel \( x_n \) in a selected respiratory phase and \( \eta_{n,m} = [T_{1,m}(x_n), \theta_{m}(x_n)] \) denote the nonlinear parameters (i.e., \( T_1 \) and FA). We estimated the \( \eta_{n,m} \) that best fit the dynamic signals as follows, using the variable projection method:

\[
\hat{\eta}_{n,m} = \arg \min_{\eta_{n,m}} \left| \frac{\hat{\rho}_{n,m} \mathbf{a}^H(\eta_{n,m})}{\| \mathbf{a}(\eta_{n,m}) \|_2} \right|^2
\]

(2)

where \( \mathbf{a}(\cdot) \) denotes an atom of a dictionary of signals calculated using Bloch equation simulation with varying \( T_1 \) and FA values defined on a discrete 2D grid and the actual timing of acquisition recorded during the imaging experiment. The evolution of the bulk magnetization vector was calculated excitation-by-excitation over the course of the entire scan by solving the Bloch equation numerically. The signal bases were formed using the simulated signals associated with the excitations where the spoke at the center of the \( k \)-space (e.g., \( k_z = 0 \)) was acquired at each frame. The bases were then binned to a motion phase to form the dictionary for joint \( T_1 \) and FA fitting. For the simulation and phantom studies, a dictionary was generated for a range of \( T_1 \) from 1 to 3000 ms in increments of 1 ms and for a range of FA from 0 to 2\( \times F_A_0 \) in increments of 0.01\( \times F_A_0 \), where \( F_A_0 \) is the nominal FA, in the case of joint estimation. For the in vivo study, the dictionary was generated for a range of \( T_1 \) from 500 to 2500 ms in increments of 10 ms and for a range of FA from 0.2\( \times F_A_0 \) to 1.5\( \times F_A_0 \) in increments of 0.01\( \times F_A_0 \) in the case of joint estimation, in consideration of expected smaller range of \( T_1 \) and FA values and for the sake of reducing computation time in dictionary generation and fitting. The time to generate the dictionary and to fit the data was 6.7 ± 2.1 minutes and 51.1 ± 2.8 seconds, respectively, using 8 Intel Xeon 2.4 GHz CPUs (4-core per CPU) on a workstation.

### 2.4 Simulation study

We performed simulation studies to optimize the proposed data acquisition scheme in Figure 1. Bloch equation simulations were performed for various ECG-gated IR schemes with the following parameters in common unless otherwise mentioned: heart-rate = 80 bpm, acquisition window = 180 ms, inversion delay times = 100/180 ms (i.e., delays from the inversion pulse to the beginning of the first acquisition), FA = 6°, and SPGR readout. The effect of \( B_1^* \) inhomogeneity on the accuracy of \( T_1 \) estimation was investigated for 8-8, 5-(3)-5-(3), and 10-(3)-10-(3) protocols without noise at different \( B_1^* \) scenarios (i.e., \( B_1^* = 0.8/1/1.2 \)). Relative difference (in relation to the ground-truth \( T_1 \) value) was used to assess any bias in \( T_1 \) estimation. The precision of \( T_1 \) estimation was investigated for N-(M)-N-(M) protocols with noise and perfect \( B_1^* \) (i.e., \( B_1^* = 1 \)) using Monte Carlo simulations (i.e., 10 000 noise realizations). Normalized SD (nSD) (i.e., SD of estimated \( T_1 \) values normalized by SD of noise and inverse of square root of acquisition time) was used to assess the precision of the \( T_1 \) estimation. The SD of noise was assumed to be constant for all considered scenarios. Additionally, the effect of nominal FA on \( T_1 \) mapping was investigated for 8-8, 5-(3)-5-(3), and 10-(3)-10-(3) protocols with FAs ranging from 1° to 15° in 1° increments. Finally, the effect of heart-rate variation on \( T_1 \) mapping was investigated for 10-(3)-10-(3) protocol with heart-rate ranging from 50 to 120 bpm in 5 bpm increments.

Note that the \((k,l)\)-space is highly undersampled and the dynamic images are reconstructed with an explicit low-rank constraint in the proposed method. Therefore, different from MOLLI, in which the \( k \)-space of each frame can be fully sampled, the imaging time of the proposed method is given by:

\[
T_{\text{prop}} = \frac{P_p L}{Q_c} \times t_{\text{IR}} \times \frac{M+N}{N},
\]

where \( P_p \) and \( P_c \) denote the number of spokes in the \( k_r-k_y \) plane and phase encoding steps in the \( k_z \) axis, respectively, which are determined by the required spatial resolution; \( L \) is the rank of the dynamic images; \( t_{\text{IR}} \) denotes a fixed cardiac cycle duration; and \( Q_c \) denotes the number of spokes acquired per cardiac cycle. Here, \( P_p P_c L \) is the total number of unknowns of the low-rank model when the temporal basis is predetermined. Note that the inherent rank of the dynamic images reflects the spatial-temporal correlations of the temporal signal variations of all the voxels.
depends on the respiratory-motion pattern and the $T_1$ value distributions rather than protocol parameters $N$ and $M$. Because $t_{RB}$, $P_x$, $P_z$, $L$, and $Q_0$ were the same for different imaging protocols, the imaging time of the proposed method was calculated as $T_{Proposed} = \frac{M+N}{N}$ in our simulation study for simplicity.

### 2.5 Phantom study

A structured phantom consisting of 21 vials of deionized water doped with concentrations of gadolinium (Dotarem) varying from 0 to 0.5 mmol/L was built to validate the performance of the proposed method. Imaging experiment was performed using a 3T MR scanner (MAGNETOM Trio; Siemens Healthcare, Erlangen, Germany) with a body coil for transmission and a 12-channel head coil for reception. Acquisitions were performed using 8-8, 5-(3)-5-(3), and 10-(3)-10-(3) protocols for a simulated heart rate of 80 bpm. Common imaging parameters were FOV = 360 × 304 mm², matrix-size = 192 × 162, slice-thickness = 6 mm, FA = 9°, TR/TE = 3.0/1.5 ms, inversion delay times = 100/180 ms, and SPGR readout. Fully sampled $(k,t)$-space data were acquired on a Cartesian grid with a temporal resolution of 30 ms (i.e., 10 phase-encoding lines per frame) to evaluate the performance of different acquisition protocols. The 8-8, 5-(3)-5-(3), and 10-(3)-10-(3) protocols were repeated over 400, 400, and 640 cardiac cycles, respectively, to ensure full sampling of the $(k,t)$-space data. An IR sequence with fast spin echo (FSE) readout was performed to obtain reference $T_1$ maps with the following imaging parameters: FOV = 360 × 304 mm², matrix-size = 192 × 162, slice-thickness = 6 mm, TR = 10,000 ms, echo train length = 7, and TI = 50/100/250/500/750/1000/1500/2000/2500/3000 ms. An additional scan with MOLLI[37] was performed for comparison with the following parameters: FOV = 360 × 304 mm², matrix-size = 192 × 162, and slice thickness = 6 mm. Regions of interest were drawn within each vial, and the average $T_1$ value within each vial was used for analysis. Scatter plots were generated to show the correlation between the $T_1$ values from the different methods and those from the reference IR-FSE method. Bland-Altman analysis was performed to analyze the agreement between the $T_1$ values from the different methods and those from the reference IR-FSE method.

### 2.6 In vivo study

Six healthy volunteers (4 males and 2 females; 32 ± 3 years) were recruited under a study protocol approved by our local institutional review board. Written informed consent was obtained from all subjects before study participation. Imaging experiments were performed using a 3T MR scanner (MAGNETOM Trio) with a body coil for transmission and spine and surface coils for reception. Imaging was performed using 10-(3)-10-(3) protocol with data sampling following a stack-of-stars trajectory. Two frames were acquired per cardiac cycle, each consisting of k-space spokes along the same angle in the $k_x$-$k_y$ plane over all $k_z$ encodings and three additional training lines at the center of the k-space along the $k_x$, $k_y$, and $k_z$ direction, respectively (Figure 1). The spoke angle varied randomly from frame to frame following uniform random distribution. The other imaging parameters were FOV = 308 × 308 × 180 mm³, matrix size = 160 × 160 × 40, image orientation = short-axis view, FA = 9°, TR/TE = 3.4/1.7 ms, and inversion delay times = 100/180 ms. A relatively large through-slice coverage was chosen to mitigate errors in FA due to imperfect slab excitation profile in the presence of both respiratory and cardiac motions. Data acquired over the first 800 cardiac cycles (corresponding to anticipated scan time of 10 minutes considering average adult heart rate of 80 bpm) were used for reconstruction and analysis. The dynamic images were reconstructed using temporal basis functions $\psi(t)$ estimated from training data with model order $L = 15$. The model order was chosen based on the singular value decay of the Casorati matrix formed by the training data as in the previous work on using low-rank constraints for image reconstruction.29,33 The reconstructed dynamic images were then binned into eight respiratory motion bins using the acquired 1D respiratory navigator signals. The number of respiratory bins was chosen to be eight based on our previous experience on using MR for respiratory motion correction in PET.33 The diaphragm position was first estimated for each frame by fitting a logistic function to the 1D spatial profile near the interface between the liver and lung. Frames were then grouped into bins according to the estimated diaphragm position while ensuring a similar number of frames within each bin. Results obtained from respiratory motion phase at or near end-exhalation were used for analysis. The short-axis view slices were divided into ROIs of 16 segments according to the American Heart Association recommendations for analysis. For comparison, 2D $T_1$ maps were acquired using MOLLI[37] for five slices in the short-axis view over the apical, midcavity, and basal regions of the heart and for one slice in the long-axis four-chamber view with the following parameters: FOV = 360 × 304 mm², matrix size = 192 × 162, and slice thickness = 4.5 mm. All of the five short-axis slices were categorized into apical, midcavity, and the basal regions based on location and were used for analysis. The mean and SD of the $T_1$ and $B_1^+$ (defined as the ratio between the measured and nominal FAs) were calculated for each ROI.
and were visualized through bull’s-eye plot and bar plot. Statistical analysis was performed using Wilcoxon signed-rank test to compare $T_1$ values obtained by MOLLI and the proposed method.

3 | RESULTS

Results from the simulation study are shown in Figures 2 and 3. When estimating $T_1$ only with the assumption of perfect $B_1^+$ (i.e., $B_1^+ = 1$), noticeable bias in $T_1$ estimation was found in all the investigated imaging protocols in the presence of typical $B_1^+$ inhomogeneities at 3 T (the blue dashed lines in Figure 2). The 8-8 protocol, which has the highest data-acquisition efficiency (i.e., number of k-space lines acquired per unit time) among all the schemes, showed the highest sensitivity to $B_1^+$ inhomogeneity (Figure 2A). Insertion of cardiac cycles for signal recovery reduced this bias in $T_1$ estimation at the cost of imaging time (Figure 2B,C). Joint $T_1$ and FA estimation led to unbiased $T_1$ estimation in the simulation study as expected (the red solid lines in Figure 2). Figure 3A shows the precision of $T_1$ estimation for different imaging protocols. The nSD of the proposed method with joint $T_1$ and FA estimation was minimized and plateaued around $N = 13, 14, 14,$ and $13$ for $N-N, N-(1)-N-(1),$ $N-(2)-N-(2),$ and $N-(3)-N-(3)$ protocols, respectively. The nSD of the proposed method with $T_1$ estimation only was minimized and plateaued around $N = 12, 8, 10,$ and $12$ for $N-N, N-(1)-N-(1), N-(2)-N-(2),$ and $N-(3)-N-(3)$ protocols, respectively. Although resulting in unbiased estimation of $T_1,$ joint $T_1$ and FA estimation led to larger nSD than the case of estimating $T_1$ only. Increasing the number of cardiac cycles for signal recovery reduced the nSD observed in joint $T_1$ and FA estimation, eventually to a level similar to those observed in the case of estimating $T_1$ only with 10-(3)-10-(3) protocol. Note that joint $T_1$ and FA estimation was unstable for the 8-8 protocol despite the desired data-acquisition efficiency. Figure 3B shows the effects of FAs on the precision of $T_1$ estimation for different imaging protocols. The nSD was minimized and plateaued around $FA = 9^\circ$ in the case of joint $T_1$ and FA estimation for both 5-(3)-5-(3) and 10-(3)-10-(3) protocols. Based on the results, $FA = 9^\circ$ was used for the ECG-gated IR sequence with SPGR readout in the phantom and in vivo experiments. Figure 3C further shows that heartbeat rate has only marginal effects on the precision of $T_1$ estimation for 10-(3)-10-(3) protocol, which is the protocol selected for the in vivo experiments.

The results from phantom studies are shown in Figure 4 and Supporting Information Figures S1 and S2. Banding artifacts were observed in the estimated $T_1$ maps.
from MOLLI, whereas no noticeable artifacts were shown in the estimated $T_1$ maps from the proposed method (Figure 4A). The 5-3-5-3 and 10-3-10-3 protocols both showed accurate $T_1$ mapping in relation to the reference IR-FSE method when $T_1$ and FA were estimated jointly, as shown in the correlation plots in Figure 4B and Bland-Altman plots in Figure 4C. The 8-8 protocol produced $T_1$ maps with large variations when $T_1$ and FA were estimated jointly (Figure 4A), which matched with the simulation results in Figure 3. Supporting Information Figure S1 shows the results obtained from the same experiment but with estimation of $T_1$ only assuming perfect $B_1^+$ (i.e., $B_1^+ = 1$). $B_1^+$ inhomogeneity–caused bias was found in the estimated $T_1$ maps from IR sequence with SPGR readout as expected. Compared with the case of estimation of $T_1$ only, joint $T_1$ and FA estimation reduced the limits of agreement by 77.7, 44.7, and 49.4 ms for the 10-3-10-3 protocol, respectively (Figure 4C and Supporting Information Figure S1C). Supporting Information Figure S2 shows results from another phantom study with variation in $B_1^+$ field strength via control of transmitter voltage. The 5-3-5-3 protocol achieved robust $T_1$ mapping when $T_1$ and FA were estimated jointly, despite the variation in $B_1^+$ field strength. The estimated $T_1$ from each vial were in good agreement with those estimated from the reference IR-FSE method. Ratios between different nominal FAs and estimated average FAs from each vial were also in good agreement.

Results from the in vivo study are shown in Figures 5–10 and Supporting Information Figures S3 and S4. The average heart-rate of the 6 volunteers was 64.2 ± 7.1 bpm (min: 53.7 bpm, max: 73.5 bpm). The acquisition time for the 6 volunteers was 14.2 ± 1.6 minutes (min: 12.2 minutes, max: 16.4 minutes). Figure 5 shows representative reconstructed images at various slice positions and TIs from subject 1 using the proposed method. Figure 6 also shows four-chamber-view $T_1$ maps that were generated by reslicing the 3D $T_1$ map from the proposed method. For comparison, $T_1$ maps from MOLLI at the same slice position and orientation are shown at the bottom of each subfigure. Overall, the $T_1$ maps from the proposed method were comparable to those from MOLLI. Note that the nominal in-plane and through-plane resolution from the proposed method was 1.9 mm and 4.5 mm, respectively. Figure 7 further shows 3D $T_1$ maps from subject 2, covering the whole left ventricle from base to
apex. As can be seen, high-quality 3D T₁ maps of the heart were produced using the proposed method. Figure 8 shows a quantitative comparison of T₁ maps from all subjects using the proposed method (with and without joint T₁ and FA estimation) and MOLLI, respectively. The bull’s-eye plot and bar plot of the mean and SD of T₁ values from each ROI show a very good agreement between the two methods. This observation is also supported by the Bland-Altman plots shown in Supporting Information Figure S3. Compared with the case of estimation of T₁ only, joint T₁ and FA estimation reduced the SD of T₁ values across 16 myocardial segments by 30.5 ms. Statistical test showed that the T₁ values of the 16 myocardial segments from the proposed method with joint T₁ and FA estimation were not statistically different from MOLLI at 5% significance level (p = .08). The mean and SD of septal T₁ values between MOLLI and the proposed method across subjects is compared in Supporting Information Table S1.

Figure 9 shows representative T₁ and B₁⁺ maps from subject 2 obtained by the proposed method. Notice the similarity in estimated T₁ values for each tissue type (e.g., myocardium, liver, muscle) even with significant variations in estimated B₁⁺ across different regions (Figure 9A). The 3D B₁⁺ maps of the heart (Figure 9B) show larger B₁⁺ values in lateral/anterior regions than septal/inferior regions, which is consistent with literature. Group analysis of B₁⁺ maps acquired from all subjects is shown in Figure 10. B₁⁺ variation ranged from 21%–32% and 11%–15% across the septal–lateral and inferior–anterior regions of the myocardium in the left ventricle, respectively. When such B₁⁺ inhomogeneities were ignored in T₁ estimation, T₁ values in the septal and inferior regions were overestimated (Supporting Information Figure S4). This was consistent with the simulation results in Figure 2.
In this work, a new free-breathing cardiac $T_1$ mapping method is proposed for robust $T_1$ mapping of the heart at 3 T. The $T_1$ maps obtained using the proposed method have a strong correlation and good agreement compared with reference and comparison methods in both the phantom experiments with various conditions (Figure 4 and...

**FIGURE 5** In vivo study results of reconstructed images from the proposed method. Representative reconstructed images from subject 1 are shown at various slice positions for a fixed TI of 1343 ms (top row) and various TI times for slice position index of 18 (bottom row). Note that the images were selected from reconstructed images in clock time and may be at different respiratory motion phase.

**FIGURE 6** $T_1$ maps from subjects 1 and 2 obtained by the proposed method. Representative $T_1$ maps are shown for various slice positions in the short-axis view and four-chamber view. $T_1$ maps from MOLLI at the same slice position and orientation are shown at the bottom of each subfigure for comparison. Note that for the four-chamber view, the $T_1$ map from MOLLI were acquired with in-plane resolution of 1.5 mm, whereas the $T_1$ map from the proposed method was generated by reslicing the 3D $T_1$ map acquired with through-plane resolution of 4.5 mm.
Supporting Information Figure S2) and the in vivo experiments across all subjects (Figures 6 and 8 and Supporting Information Figure S3). Robust $T_1$ mapping was achieved despite significant $B_1^+$ variations at 3 T. This is most noticeable by the fact that uniform $T_1$ distributions for each tissue type (e.g., myocardium, liver, muscle) were achieved across the entire FOV (Figure 9A) and is further supported by the close agreement of $T_1$ maps between the proposed method and MOLLI (Figure 8), despite the observed $B_1^+$ variation across the septal–lateral and inferior–anterior regions of the myocardium in the left ventricle (Figure 10). Noticeable bias in $T_1$ estimation was otherwise observed when $B_1^+$ inhomogeneities were ignored in $T_1$ estimation (Figures 2, 4, 8, and 10; Supporting Information Figures S1 and S4). These observations were consistent throughout simulation, phantom, and in vivo results. The estimated $B_1^+$ values of the myocardium show spatial variations that are consistent with those reported in literature (i.e., the $B_1^+$ values in the lateral/anterior regions were 10%–30% larger than the septal/inferior regions). However, the $B_1^+$ distributions within the blood pool should be carefully interpreted, as flow effects were not considered in joint $T_1$ and FA estimation. As a result, the estimated $T_1$ and FA values of blood may be biased.

This method has several novel features. First, the proposed method mitigates bias in $T_1$ estimation caused by errors in FA through joint estimation of $T_1$ and FA. We carried out systematic numerical simulation studies to optimize the ECG-gated IR sequence with SPGR readout in terms of acquisition protocols and nominal FAs, with the goal of minimizing the SD of the estimated $T_1$. Second, the proposed method uses the special $(k,t)$-space sampling scheme and subspace-based image reconstruction to recover dynamic images from undersampled data (i.e., two 3D volumes for every cardiac cycle with data acquisition). This allows mitigating the effects of natural heart-rate variations on $T_1$ mapping by fitting the reconstructed dynamic signals to a signal dictionary generated with subject-specific timing of data acquisition recorded during imaging experiment. Third, the proposed method is robust to $B_0$ inhomogeneities, as it uses adiabatic nonselective pulse for inversion and SPGR acquisitions. Altogether, the proposed method achieves free-breathing $T_1$ mapping in the presence of $B_1^+$ and $B_0$ inhomogeneity at 3 T in a practical imaging time.

The proposed method may be potentially useful for quantification of post-contrast $T_1$ and extracellular volume fraction mapping, in which accurate and precise estimation of $T_1$ is important. Although results from simulation and phantom studies show that the proposed method can estimate short $T_1$ values with accuracy and precision, further investigation is necessary to evaluate the performance of proposed method for post-contrast $T_1$ estimation. Because $T_1$ relaxation in the tissue changes over time in vivo after contrast agent is injected, the performance of the proposed method needs to be carefully examined for these applications, including investigations in the context of subspace-based reconstruction. An interesting next step would be to investigate the feasibility as well as the performance of the proposed method for these applications in vivo.

In this work, a subspace-based image reconstruction method was used to recover dynamic images in clock time for ECG-gated acquisitions, and respiratory motion was resolved by subsequently binning reconstructed images to different respiratory motion phases. A potentially interesting future work would be to investigate the possibility of treating respiratory motion as an additional temporal dimension using the low-rank tensor model for ECG-gated acquisitions. In the ideal case with constant heart-rate, this would be feasible, as $T_1$-weighted contrast changes can then be modeled by IR at fixed number of inversion delay times. In reality, however, natural variations of heartbeat rate will require modeling the $T_1$-weighted contrast changes in clock time for ECG-gated acquisitions over the entire imaging experiment. This can impose technical challenges when attempting to represent the underlying dynamic images using a low-rank tensor model.

Results from the in vivo study showed that $T_1$ values from the proposed method were not statistically different from MOLLI at 5% significance level ($p = .08$). This indicates that the proposed method has similar bias as MOLLI in the in vivo study. Several factors contribute to the apparent underestimation of $T_1$ when the proposed method is
used for in vivo cardiac $T_1$ mapping. First, magnetization-transfer effects can lead to underestimated $T_1$ values in the proposed method as in MOLLI, because both methods use IR-based acquisition schemes for $T_1$ mapping. Second, the proposed method currently assumes perfect inversion pulse. Adding inversion efficiency to parametric fitting may potentially improve the accuracy of $T_1$ estimation at the cost of computation time (i.e., a larger dictionary of bases needed for parametric fitting). Further investigation is necessary to study the potential source of bias in the proposed method in the in vivo settings.

The current work has several limitations that warrant further investigation. First, the proposed method involves ECG-gated acquisition, which is susceptible to ECG mistriggering and may suffer from image blurring due to cardiac motion. The former could be addressed by adaptive heartbeat-rate prediction as in the double-gating technique. The latter can be mitigated by retrospectively discarding k-space data acquired outside the end-diastole window based on recorded ECG signals. Free-running (i.e., no cardiac or respiratory gating) based continuous acquisition scheme may be preferable over the ECG-gated acquisition schemes for maximizing data-acquisition efficiency. However, in the free-running continuous acquisition scheme, apparent inversion recovery rate is strongly coupled with FA. Therefore, accurate estimation of FA is expected to be critical for accurate $T_1$ estimation with free-running acquisition in the presence of $B_1^+$ inhomogeneity at 3 T. This research direction is currently under investigation. Second, FA estimation by the proposed method was validated using a phantom experiment with variation in $B_1^+$ field strength by changing the transmitter voltage (Supporting Information Figure S2). Validation with a reference cardiac FA or $B_1^+$ mapping method (e.g., actual flip-angle imaging.

**FIGURE 8** In vivo study results showing quantitative comparison of estimated $T_1$ from MOLLI and those from the proposed method. (A) Sixteen-segment American Heart Association (AHA) bull’s eye plots of mean $T_1$ from MOLLI, proposed method with $T_1$ estimation only assuming perfect $B_1^+$ (i.e., $B_1^+=1$), and proposed method with joint $T_1$ and FA estimation. (B) Bar plots showing mean and SD of estimated $T_1$ from MOLLI and proposed method. Cases of proposed method with $T_1$ estimation only assuming perfect $B_1^+$ (i.e., $B_1^+=1$) and joint $T_1$ and FA estimation are shown. BA, BAS, BIS, BI, BIL, BAL, MA, MAS, MIS, MA, MIL, AA, AS, AI, AL each denotes basal anterior, basal anteroseptal, basal inferoseptal, basal inferior, basal inferolateral, basal anterolateral, midcavity anterior, midcavity anteroseptal, midcavity inferior, midcavity inferolateral, midcavity anterolateral, apical anterior, apical septal, apical inferior, and apical lateral regions of the myocardium in the left ventricle.

| BA | BAS | BIS | BI | BIL | BAL | MA | MAS | MIS | MA | MIL | MAL | AA | AS | AI | AL |
|----|-----|-----|----|-----|-----|----|-----|-----|----|-----|-----|----|-----|----|----|
| 1189 | 1165 | 1159 | 1142 | 1130 | 1210 | 1197 | 1197 | 1185 | 1185 | 1176 | 1176 | 1164 | 1164 | 1152 | 1152 |
| 1204 | 1161 | 1170 | 1186 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 | 1206 |

**FIGURE 8** In vivo study results showing quantitative comparison of estimated $T_1$ from MOLLI and those from the proposed method.
In human subject studies is necessary to further verify the performance of FA mapping results from the proposed method. Third, performance of the proposed method was validated in vivo with a small number of healthy subjects (n = 6). Studies with a larger number of healthy subjects and patients are necessary to assess the accuracy and reproducibility of the proposed method and to evaluate its value in clinical applications. Future work can also include investigation with different sparsity constraints (e.g., finite difference or wavelet transform), investigation with different sampling schemes, and multisite/multivendor validations of the proposed method and findings from this work.

5 | CONCLUSIONS

A new free-breathing cardiac $T_1$ mapping method was proposed and optimized for fast 3D $T_1$ mapping of the
whole heart at 3 T with transmit $B_1$ correction in practical imaging time.

**CONFLICT OF INTEREST**

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher’s website.

FIGURE S1 Phantom results of electrocardiogram (ECG)-gated inversion-recovery (IR) schemes with spoiled gradient-echo (SPGR) readout and T1 estimation only assuming perfect B1+ (i.e., B1+=1). (A) Estimated T1 maps from the different methods. (B) Scatter plots showing comparison of estimated T1 from the different methods with those from IR-fast spin echo (FSE). Solid line represents line of identity, and dashed line represents line of regression. (C) Bland-Altman plots showing comparison of estimated T1 from different methods with those from IR-FSE. Solid line represents the mean difference and dashed line represents the 95% confidence interval for limits of agreement

FIGURE S2 Phantom study results with variation in B1+ field strength via control of transmitter voltage. (A) Estimated T1 maps from IR-FSE and 5-(3)-5-(3) protocol with 80%, 100%, and 120% of reference transmitter voltage. (B) Vial number positions. (C) Estimated B1+ maps (defined as the ratio between the measured and nominal flip angles [FAs]) from the 5-(3)-5-(3) protocol with 80%, 100%, and 120% of the reference transmitter voltage. (D) Estimated average FA within each vial from the 5-(3)-5-(3) protocol with 80% (green line and circle), 100% (blue line and circle), and 120% (red line and circle) of reference transmitter voltage. Note that the ratio between the different B1+ field strength and the estimated average FAs from each vial are in good agreement

FIGURE S3 In vivo study results of Bland-Altman plots comparing estimated T1 from the proposed method with those from modified Look-Locker inversion recovery (MOLLI). Results from the anterior, septal, inferior, and lateral regions of the myocardium in the left ventricle are shown. Solid line represents the mean difference and dashed line represents the 95% confidence interval for limits of agreement

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