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Free-Breathing, Non-ECG, Continuous Myocardial T1 Mapping with CMR Multitasking

Jaime L. Shaw^{1,2,3}, Qi Yang¹, Zhengwei Zhou¹, Zixin Deng^{1,2}, Christopher Nguyen^{1,4,5}, Debiao Li^{1,2}, and Anthony G. Christodoulou¹

¹Biomedical Imaging Research Institute, Cedars-Sinai Medical Center, Los Angeles, CA

²Department of Bioengineering, University of California, Los Angeles, CA

³Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA

⁴Currently at: Cardiovascular Research Center, Massachusetts General Hospital, Charlestown, MA

⁵Currently at: Harvard Medical School, Boston, MA

Abstract

Purpose: To evaluate the accuracy and repeatability of a free-breathing, non-ECG, continuous myocardial T1 and extracellular volume (ECV) mapping technique adapted from the Multitasking framework.

Methods: The Multitasking framework is adapted to quantify both myocardial native T1 and ECV with a free-breathing, non-ECG, continuous acquisition T1 mapping method. We acquire interleaved high-spatial resolution image data and high-temporal resolution auxiliary data following inversion-recovery pulses at set intervals and perform low-rank tensor imaging to reconstruct images at 344 inversion times, 20 cardiac phases, and 6 respiratory phases. The accuracy and repeatability of Multitasking T1 mapping in generating native T1 and ECV maps are compared to conventional techniques in a phantom, a simulation, 12 healthy subjects, and 10 acute myocardial infarction (AMI) patients.

Results: In phantoms, Multitasking T1 mapping correlated strongly with the gold-standard spin-echo inversion recovery ($R^2 = 0.99$). A simulation study demonstrated that Multitasking T1 mapping has similar myocardial sharpness to the fully-sampled ground truth. In vivo native T1 and ECV values from Multitasking T1 mapping agree well with conventional MOLLI values and show good repeatability for native T1 and ECV mapping for 60 seconds, 30 seconds, or 15 seconds of data. Multitasking native T1 and ECV in AMI patients correlate positively with values from MOLLI.

Conclusion: Multitasking T1 mapping can quantify native T1 and ECV in the myocardium with free-breathing, non-ECG, continuous scans with good image quality and good repeatability in vivo in healthy subjects, and correlation to MOLLI T1 and ECV in AMI patients.

Keywords

T1 mapping; Tissue Characterization; Cardiac Imaging

INTRODUCTION

T1 mapping has emerged as a quantitative cardiac MRI technique capable of identifying both focal and diffuse myocardial fibrosis, as well as edema, amyloidosis, and fat infiltration¹. Native, or non-contrast, T1 changes have been shown with T1 mapping in myocardial infarction, hypertrophic and dilated cardiomyopathies, amyloidosis, and other diseases^{2–4}. Additionally collecting T1 maps after Gadolinium contrast administration enables calculation of the extracellular volume (ECV); elevated ECV has been shown in various disease states^{5,6}. Both native T1 and ECV have been shown to correlate with histological measures of myocardial fibrosis^{6–10}.

T1 mapping is most commonly performed by perturbing longitudinal magnetization, usually with an inversion recovery or saturation recovery pulse, and sampling along the recovery curve as the longitudinal magnetization recovers. Commonly-used techniques such as the Modified Look-Locker Inversion Recovery (MOLLI)^{11,12}, Shortened MOLLI (ShMOLLI)¹³, Saturation Recovery Single-Shot Acquisition (SASHA)¹⁴, and others^{15,16}, attempt to limit the effects of cardiac motion by acquiring one single-shot image per cardiac cycle, ECG-triggered to a specific cardiac phase (usually diastole). The short duration of diastole restricts the in-plane resolution for single-shot acquisitions. Furthermore, ECG triggering can misfire, especially at high fields. Respiratory motion effects are mitigated by utilizing breath-holds or respiratory navigators which, along with patient discomfort or compliance issues, may result in low imaging efficiency and potential respiratory motion artifacts.

We utilize an inversion recovery (IR) T1 mapping technique that achieves independence from ECG and respiratory control by continuously acquiring imaging data between IR pulses applied at set intervals during free breathing. This technique retrospectively resolves 3 separate types of temporal dynamics (each assigned to their own temporal dimension), namely cardiac motion, respiratory motion, and T1 recovery, with no reliance on an ECG signal. Nyquist sampling requirements and memory requirements increase exponentially with each additional dimension of interest, so imaging multiple time dimensions using conventional strategies would result in clinically infeasible scan times and prohibitive computational requirements. However, a recently proposed imaging framework called Cardiovascular Magnetic Resonance (CMR) Multitasking overcomes the dimensionality problem of resolving multiple image dynamics (“tasks”), allowing accelerated acquisition by employing a low-rank tensor image model, for which sampling requirements increase linearly with each added dimension¹⁷. This work is the first application of multitasking for ECV mapping and the first to explore the scan time needed for accurate and repeatable T1 and ECV mapping.

The Multitasking T1 mapping technique was first validated in a phantom study against the gold-standard spin-echo inversion-recovery method. A motion simulation was used to assess

the effect of motion on Multitasking T1 mapping accuracy and image quality. Subsequently, Multitasking T1 mapping was compared with a conventional ECG-gated, breath-hold, 2D T1 mapping method in healthy subjects for both native T1 and ECV. The accuracy and repeatability of native T1 and ECV values were assessed for three different Multitasking T1 mapping scan times: 60 s, 30s, and 15 s. Multitasking T1 mapping was also compared to MOLLI in 10 acute myocardial infarction (AMI) patients.

METHODS

Low-Rank Tensor Image Model

We adopt a low-rank tensor image model recently described by the Multitasking framework, which is capable of resolving multiple overlapping dynamics¹⁷. In this work, the image model specifically handles temporal dynamics corresponding to cardiac motion (t_c), respiratory motion (t_r), and T1 recovery (t_{T1}). Our multidimensional image $\rho(\mathbf{r}, t_c, t_r, t_{T1})$, a spatiotemporal image with 3 time dimensions, can be expressed in factorized form as:

$$\rho(\mathbf{r}, t_c, t_r, t_{T1}) = \sum_{\ell=1}^L u_{\ell}(\mathbf{r}) \phi_{\ell}(t_c, t_r, t_{T1}) \quad (1)$$

where $\{\phi_{\ell}(t_c, t_r, t_{T1})\}_{\ell=1}^L$ are temporal basis functions and $\{u_{\ell}(\mathbf{r})\}_{\ell=1}^L$ are spatial coefficients. Each 3D temporal function, $\phi_{\ell}(t_c, t_r, t_{T1})$, can itself be factored into temporal basis functions for each dimension and a core tensor term that governs the interactions between bases:

$$\phi_{\ell}(t_c, t_r, t_{T1}) = \sum_{m=1}^M \sum_{n=1}^N \sum_{p=1}^P c_{\ell mnp} v_m(t_c) w_n(t_r) g_p(t_{T1}) \quad (2)$$

where $c_{\ell mnp}$ is the core tensor, $v_m(t_c)$ is the m th of M cardiac temporal basis functions, $w_n(t_r)$ is the n th of N respiratory temporal basis functions, and $g_p(t_{T1})$ is the p th of P T1 recovery temporal basis functions.

There are multiple data acquisition and image reconstruction strategies available for low-rank tensor imaging. An “implicit” strategy could penalize the nuclear norm of each unfolding of the image tensor $\mathcal{X}$ with entries $X_{ijk\ell} = \rho(\mathbf{r}_i, t_{c,j}, t_{r,k}, t_{T1,\ell})$ ¹⁸. However, it is often impractical to store and process $\mathcal{X}$ when there are many time dimensions due to large memory requirements. A recent “explicit” strategy does not require storing $\mathcal{X}$, instead recovering each factor in separate steps: calculating the basis for each temporal dimension from the SVD of an appropriate subset of auxiliary data, then fitting these factors to the remainder of the data to recover the spatial components¹⁹. Unfortunately, this strategy requires full control of the auxiliary $(\mathbf{k}, t_c, t_r, t_{T1})$ -space sampling scheme. This control is not possible in free-breathing, ECG-free cardiac imaging, wherein subject physiological motion determines the passage of cardiac time t_c and respiratory time t_r .

Multitasking employs a mixed strategy¹⁷, exploiting the observation that the temporal functions $\{\phi_\ell(t_c, t_r, t_{T1})\}_{\ell=1}^L$ are themselves factorizable. As a result, implicit low-rank tensor completion can be applied to recover missing elements from the auxiliary data tensor $\mathcal{X}_{\text{aux}}$, e.g. by solving

$$\widehat{\mathcal{X}}_{\text{aux}} = \arg \min_{\mathcal{X}_{\text{aux}}} \|\mathbf{d}_{\text{aux}} - \Omega(\mathcal{X}_{\text{aux}})\|_2^2 + \lambda \sum_{i=1}^4 \|\mathbf{X}_{\text{aux},(i)}\|_*, \quad (3)$$

where $\mathbf{d}_{\text{aux}}$ contains the undersampled auxiliary data, Ω is an undersampling operator, $\mathcal{X}_{\text{aux}}$ is a low-rank tensor representing the now full auxiliary data, $\mathbf{X}_{\text{aux},(i)}$ is the tensor $\mathcal{X}_{\text{aux}}$ unfolded as a matrix with rows indexing the i th dimension and columns indexing all other dimensions, λ is a regularization parameter controlling the effective rank of the solution, and $\|\cdot\|_*$ is the nuclear norm which promotes low-rankness of each unfolded matrix. The auxiliary tensor $\mathcal{X}_{\text{aux}}$ is much smaller than the full image tensor $\mathcal{X}$ and can therefore be stored in memory, allowing practical implementation of Eq. (3). With the completed $\mathcal{X}_{\text{aux}}$ available, an explicit strategy can then be used to recover the individual temporal bases and the core tensor from the high-order SVD (HOSVD)²⁰. With $\{\phi_\ell(t_c, t_r, t_{T1})\}_{\ell=1}^L$ (or in matrix form Φ) known, the spatial coefficients (in matrix form $\mathbf{U}$) are then recovered by solving the optimization problem:

$$\widehat{\mathbf{U}} = \arg \min_{\mathbf{U}} \|\mathbf{d}_{\text{img}} - \Omega(\mathbf{E}\mathbf{U}\Phi)\|_2^2 + \lambda R(\mathbf{U}) \quad (4)$$

where $\mathbf{E}$ is the signal model including Fourier transform and coil sensitivities, and the product $\mathbf{U}\Phi$ generates the reconstructed image tensor unfolded along the first dimension.

Pulse Sequence

Multitasking T1 mapping was performed using a continuous-acquisition FLASH sequence, with repeated blocks consisting of: 1) 180° inversion recovery pulses and 2) interleaved golden-angle image data and auxiliary 0° radial spokes used for temporal subspace estimation. The imaging blocks are repeated after set intervals, as shown in Figure 1.

Imaging

All imaging was performed on a 3T scanner (Verio, Siemens Healthcare, Erlangen, Germany) with a 12-channel receive coil. The Multitasking T1 mapping sequence consists of: interleaved image and auxiliary data as described above, matrix size: 160×160, FoV: 270×270 mm, voxel size: 1.7×1.7×8 mm³, flip angle: 5°, TR/TE: 3.6/1.4 ms, time between IRs: 2.5 s. MOLLI¹² was performed with the following sequence parameters: steady-state free-precession (SSFP), TR/TE: 2.4/1.05 ms, flip angle: 35°, voxel size = 1.7×1.7×8 mm³,

minimum inversion time (TI): 110 ms, TI increment: 80 ms, ECG-triggered to diastole. MOLLI pixel-wise T1 maps were generated online following automatic motion correction.

Image Reconstruction

Real-time Image Reconstruction—Following data collection, the first image reconstruction step was to generate a “real-time” image used expressly for motion identification. We used an explicit low-rank matrix imaging strategy, estimating the real-time temporal basis, analogous to ϕ_ℓ in Eq. 1 with one time dimension, from the SVD of the auxiliary data, followed by least-squares fitting of the real-time temporal basis to the undersampled image data to recover $\{u_\ell(\mathbf{r})\}_{\ell=1}^L$ ²¹. Following this step, we have a “real-time” image (Figure 2) which shows cardiac motion, respiratory motion, and T1 recovery progressing along one time dimension.

Motion Identification—From the “real-time” image created in Step 1, we identify cardiac and respiratory motion and place the corresponding images into 20 and 6 bins, respectively. As recently described¹⁷, we use an unsupervised machine learning approach to automatically cluster respiratory and cardiac motion states, an approach which incorporates a low-rank T1 recovery model to address the changing contrast weightings after IR pulses. The number of cardiac bins was chosen as 20 to be comparable to typical cine images (potentially enabling functional analysis). The number of respiratory bins was chosen as 6 based on analysis of the within-cluster sum of squared error curve aggregated from all subjects. The T1 recovery dimension was sorted according to TI, which is known for each readout of the acquisition (segment number $\times$ echo spacing); no binning or grouping of TI times is used.

Tensor Formation and Subspace Estimation—Following motion identification, we form a 4-way auxiliary data tensor with one k-space readout dimension and three time dimensions: cardiac motion, respiratory motion, and T1 recovery. Because auxiliary data are not available from every combination of cardiac phase, respiratory phase, and corresponding TI (i.e., the auxiliary data is fully sampled in 1D time but undersampled in 3D time), we complete the auxiliary data tensor $\mathcal{X}_{\text{aux}}$ by low-rank tensor completion (Eq. 3). The T1 recovery temporal basis functions $\{g_p(t_{\text{T1}})\}_{p=1}^P$ can be predetermined (as will be described later), so we constrain $\mathcal{X}_{\text{aux}}$ to the subspace spanned by $\{g_p(t_{\text{T1}})\}_{p=1}^P$ and extend Eq. 3 to:

$$\widehat{\mathcal{X}}_{\text{aux}} = \arg \min_{\mathcal{X}_{\text{aux}} \in \text{span}\{g_p(t_{\text{T1}})\}_{p=1}^P} \|\mathbf{d}_{\text{aux}} - \Omega(\mathcal{X}_{\text{aux}})\|_2^2 + \lambda \sum_{i=1}^4 \|\mathbf{X}_{\text{aux},(i)}\|_* + R(\mathcal{X}_{\text{aux}}), \quad (5)$$

Where $R(\cdot)$ is an optional regularization functional which can be used to exploit complementary properties of $\mathcal{X}_{\text{aux}}$ (such as temporal finite difference sparsity²²). The

cardiac and respiratory temporal basis functions and the core tensor are determined from the HOSVD of the cardiac and respiratory dimensions of $\mathcal{X}_{\text{aux}}$.

As previously mentioned, the T1 recovery temporal basis functions $\{g_p(t_{\text{T1}})\}_{p=1}^P$ can be predetermined, which we define from the SVD of a dictionary of Bloch equation curves. The Bloch dictionary was created by generating signals from a FLASH-IR steady-state equation:

$$M_{z\text{IRFLASH}} = A \frac{1 - e^{-TR/T1}}{1 - e^{-TR/T1} \cos \alpha} \left[1 + (B - 1) (e^{-TR/T1} \cos \alpha)^n \right] \quad (6)$$

where $M_{z\text{IRFLASH}}$ is the longitudinal magnetization from inversion recovery FLASH, A contains contributions from proton density, $T2^*$, and coil sensitivity, TR is the repetition time, α is the FLASH flip angle, B represents inversion efficiency, and n is the readout index. The dictionary comprises T1 values ranging from 100 ms to 3000 ms, α ranging from 0.5° to 7.5° degrees, and B ranging from -1 to -0.5 . The SVD of this dictionary produces the T1 recovery temporal basis functions.

Multidimensional Image Reconstruction—Image reconstruction is performed by solving the optimization problem in Eq. 4 with R chosen as the spatial total variation functional¹⁷. E includes coil sensitivities and the nonuniform fast Fourier transform (NUFFT) with golden-angle radial trajectories. The regularization parameter, λ , was chosen empirically to balance between blurring and noise artifacts in the T1 maps. The result of this reconstruction (Figure 3) gives us a five-dimensional cardiac image (two spatial dimensions, 3 temporal dimensions) with full T1 recovery curves for multiple cardiac and respiratory combinations, for a total of 41,280 images (344 inversion times $\times$ 20 cardiac phases $\times$ 6 respiratory phases).

Parameter Fitting—Parameter fitting was first performed by least-squares fitting to Eq. 6 for A , B , $T1$, and α , with 344 inversion time images at 1 respiratory phase and 1 cardiac phase, corresponding to end-expiration and end-diastole, respectively. Myocardial T1 values were extracted from this map. Blood pool T1 values were extracted from a second map wherein A , B , and $T1$ were fit from Eq. 6, but α was held constant at a low flip angle such that $M_{z\text{IRFLASH}}$ approached that of unperturbed inversion recovery, to better model the mixing of distant non-excited spins in the blood pool during the continuous acquisition²³. Example T1 maps created from fitting for T1 at different motion states are shown in Figure 4.

Phantom

The accuracy of the proposed Multitasking T1 mapping technique was evaluated in vitro in phantoms. Two T1 phantoms were created by doping water in vials with varying concentrations of Optimark (Gadoversetamide), one consisting of 13 vials with T1 values in the native myocardium and blood T1 range (948 to 1748 ms) and the other consisting of 12 vials with T1 values in the post-contrast myocardium and blood T1 range (75 to 564 ms).

Reference T1 values for each phantom were obtained with a gold-standard spin-echo inversion recovery sequence with 17 inversion times (TI) ranging from 50 to 5,000 ms and a repetition time (TR) of 10 s. Multitasking T1 mapping was performed in each phantom and compared with the reference T1 values. For Multitasking T1 mapping, data were reconstructed as described above, but with singleton cardiac and respiratory dimensions.

Simulation

A simulation study was performed using a numerical motion phantom to assess the effect of motion on Multitasking T1 mapping accuracy and image quality. A cardiac and respiratory motion phantom was created from the XCAT phantom with 20 cardiac phases for each of 6 respiratory phases²⁴. The cardiac motion was assigned a simulated heart rate of 54 bpm, and the respiratory motion ranged from end-expiration to end-inspiration with a diaphragm displacement range of 10 mm at 15 breaths per minute. Typical T1 values at 3T were assigned to each tissue type in the phantom: for example, myocardial T1 was 1200 ms and blood pool T1 was 1900 ms. Using Eq. 5, an MRI acquisition was simulated following our inversion-recovery pulse sequence with programmed cardiac and respiratory motion states, from which k-space data was generated for both image and auxiliary data. Partial volume effects were included in the simulation by averaging signals from 16 adjacent 0.5 mm slices to make an 8 mm slice, the same thickness used in vivo. To test the motion identification accuracy and the effect on the resulting image quality, the Multitasking reconstruction was performed using the simulated k-space data using: 1) the programmed cardiac and respiratory motion (i.e. the known motion), and 2) the unsupervised machine learning method for motion identification as described above (learned motion). Multitasking T1 maps were calculated for an end-expiration respiratory phase and an end-diastolic cardiac phase. For comparison, ground truth T1 maps were calculated from fully-sampled k-space data from end-diastole and end-expiration.

In vivo study

Multitasking T1 mapping and MOLLI were performed in 12 healthy subjects. The study was approved by the Institutional Review Board and all subjects provided written informed consent before scanning. Repeated measurements were acquired with MOLLI in diastole, each scan requiring a separate breath-hold. Multitasking T1 mapping was acquired with two successive 60 second scans. Repeatability was analyzed between the first and second 60 second scans. Additionally, the first 60 second scan (Multitasking₆₀) was split into two 30 second datasets and the first 30 second scan (Multitasking₃₀) split into two 15 second datasets (Multitasking₁₅) to determine the effects of scan time on T1 estimation and repeatability. Both methods were prescribed at the same 2D mid-ventricular short-axis slice. For native T1 mapping, Multitasking T1 mapping and MOLLI were acquired prior to contrast administration in all subjects; for ECV mapping, both methods were acquired 15–20 minutes after contrast administration to obtain post-contrast T1 maps in a subset of 8 subjects. For subjects undergoing contrast administration, hematocrit was determined from a blood sample taken directly prior to imaging. ECV values were calculated for the 8 subjects who had both native and post-contrast T1 maps.

In addition to the healthy subjects, ten patients with acute myocardial infarction were recruited and scanned on a separate clinical scanner using the same scanner platform and hardware setup. Multitasking T1 mapping and MOLLI were acquired before contrast administration in all patients for native T1 mapping and 15–20 minutes after contrast administration in a subset of 7 patients to enable ECV mapping as described above. Based on the healthy subject results, a 30 second scan time was chosen for Multitasking T1 mapping in patients (Multitasking₃₀). Because this was part of a clinical scan, MOLLI T1 maps were acquired at the conventional spatial resolution of $2.1 \times 1.4 \times 8 \text{ mm}^3$. Additionally, in one AMI patient, a conventional phase-sensitive inversion recovery (PSIR) late gadolinium enhancement (LGE) image in a mid-ventricle slice was acquired post-contrast administration ($1.8 \times 1.4 \times 8 \text{ mm}^3$) and compared to phase-sensitive T1-weighted images from the post-contrast Multitasking T1 mapping scan. For the multitasking scan, the TI with nulled myocardium was retrospectively selected, and PSIR processing was performed using the phase of the longest TI image as a co-registered, full-resolution phase correction map.

Data Analysis

For the phantom study, regions-of-interest (ROIs) were drawn in each vial on the T1 map. For the simulation, myocardial sharpness was measured for 3 line profiles drawn across the septum and lateral wall on the T1 maps at an end-expiration respiratory phase and diastolic cardiac phase²⁵. The average sharpness of the 3 line profiles is reported. The percent error of the myocardium in the T1 maps was calculated compared to the ground-truth T1 maps.

For in vivo measurements, T1 maps were analyzed from a cardiac phase identified as end-diastole and a respiratory phase identified as end-expiration. ROIs were drawn in Matlab (Mathworks, Natick, MA) within the entire myocardium in the short-axis slice (“global”) as well as in the septum alone, using conservative ROIs to avoid partial-volume effects. In AMI patients, the myocardium was divided into 6 segments according to the AHA 17-segment model. On the separate blood T1 maps, an ROI was placed in the left ventricular blood pool, taking care to avoid papillary muscles. To compare T1 map image quality, the resolution-matched T1 maps from MOLLI and Multitasking with different amounts of data in controls were blinded and pooled and scored by a radiologist using a 4-point scale (4: excellent, 3: good, 2: fair, 1: poor).

Statistical Analysis

Simulation sharpness measurements from the fully-sampled ground-truth, and Multitasking T1 mapping with known and learned motion were compared using repeated measures one-way ANOVA analysis followed by Tukey’s multiple comparisons test. Multitasking T1 mapping values and image quality scores for different amounts of data were compared with MOLLI using repeated measures one-way ANOVA analysis with Tukey’s multiple comparisons test. Multitasking T1 mapping native T1 and ECV values were also compared to MOLLI using Bland-Altman analysis. Intra-study repeatability was assessed for each method using the root mean square of the coefficient of variation (CoV) for two repeated measurements. Differences between Multitasking T1 mapping native T1 and ECV in six AHA segments were assessed using two-way ANOVA analysis. Statistical analyses were

performed with GraphPad Prism (GraphPad Software, La Jolla, CA). Statistical significance was set at $p < 0.05$.

RESULTS

Phantom Study

Multitasking T1 mapping was compared to T1 values from the gold-standard spin-echo inversion recovery in 2 phantoms, one representing native T1 values and one representing post-contrast T1 values. The T1 phantoms show strong correlation with the gold-standard T1 values, shown in Supporting Figure S1, with a linear regression slope of 0.965 and R^2 value of 0.990, $p < 0.001$. Across all phantom vials, the T1 values calculated using the proposed Multitasking T1 mapping were not different from the spin-echo reference values (Student's t-test, $p = 0.10$).

Simulation

Supporting Figure S2 shows the ground-truth fully-sampled T1 map along with Multitasking T1 maps using known motion and motion learned using the machine learning algorithm. The average sharpness of the myocardial septum was not significantly different: $0.27 \pm .03 \text{ mm}^{-1}$, $0.27 \pm .03 \text{ mm}^{-1}$, and $0.26 \pm .04 \text{ mm}^{-1}$ ($p = 0.291$) for fully-sampled, Multitasking with known motion, and Multitasking with learned motion, respectively. The average sharpness of the myocardial lateral wall was not significantly different: $0.27 \pm .02 \text{ mm}^{-1}$, $0.26 \pm .01 \text{ mm}^{-1}$, and $0.27 \pm .02 \text{ mm}^{-1}$ ($p = 0.180$) for fully-sampled, Multitasking with known motion, and Multitasking with learned motion, respectively. The percent error of the myocardium T1 values compared to the fully-sampled ground-truth were 0.13% for Multitasking using known motion and 1.7% for Multitasking using learned motion.

In Vivo Study

T1 maps were successfully acquired in all 12 healthy subjects (age 37 ± 9 , 6 female) with both Multitasking T1 mapping and MOLLI. Representative native and post-contrast T1 maps and ECV maps for one subject are shown in Figure 5 and demonstrate similar quality using both methods. Estimated ventricular septal native T1 values showed good agreement between for MOLLI and Multitasking₆₀, Multitasking₃₀, and Multitasking₁₅, as well as global ventricular T1 values (Table 1). No significant difference was found between MOLLI and myocardial Multitasking T1 mapping values from any scan duration, for both septal and global ventricular native T1 ($p = 0.674$, $p = 0.064$). No significant difference was found among native ventricular blood T1 values ($p = 0.112$). A significant ANOVA p value was determined for septal myocardium ECV for MOLLI and all Multitasking T1 mapping lengths; however, multiple comparison testing showed no significant differences for each Multitasking T1 mapping length compared to MOLLI for both septal and global ECV.

Intra-study repeatability was assessed for MOLLI and each length of Multitasking T1 mapping using the coefficient of variation (CoV), shown in Table 2. Native and ECV measurements showed excellent repeatability for both septal and global myocardial segments for MOLLI and all Multitasking T1 mapping lengths. For ECV, Multitasking T1 mapping measurements demonstrated better repeatability compared to MOLLI.

A Bland-Altman analysis was performed to assess the agreement between Multitasking T1 mapping and MOLLI for native T1 and ECV (Figure 6). For Native T1, all measurements except one subject outlier for septal native T1 with Multitasking₃₀ were within the 95% limits of agreement for Multitasking₆₀, Multitasking₃₀, and Multitasking₁₅. The mean bias between methods was slightly higher for global native T1 measurements than septal: 44 ms vs 17 ms for Multitasking₆₀, 40 ms vs 15 ms for Multitasking₃₀, and 39 ms vs 9 ms for Multitasking₁₅. For ECV, all measurements except one subject outlier for global ECV with Multitasking₁₅ were within the 95% limits of agreement for Multitasking₆₀, Multitasking₃₀, and Multitasking₁₅. ECV measurements had similar biases for septal and global regions: 1.3% vs 1.3% for Multitasking₆₀, 0.66% vs 0.65% for Multitasking₃₀, and -0.84% vs 0.07% for Multitasking₁₅.

T1 maps were successfully acquired in all 10 AMI patients (age 55 ± 13 , 2 female). The native T1 values over all 6 segments for MOLLI and Multitasking₃₀ were 1268 ± 107 ms and 1152 ± 85 ms, respectively; ECV values over all 6 segments for MOLLI and Multitasking₃₀ were $28.5\% \pm 5.2\%$ and $26.9\% \pm 4.2\%$, respectively. Multitasking₃₀ measurements positively correlated with MOLLI for native T1 ($r = 0.562$, $p < 0.001$) and ECV ($r = 0.811$, $p < 0.001$). Figure 7 shows correlation and Bland-Altman plots for MOLLI and Multitasking₃₀ for native T1 and ECV for AMI patients. For native T1, all measurements except four outliers were within the 95% limits of agreement between MOLLI and Multitasking₃₀. For ECV, all measurements except two outliers were within the 95% limits of agreement between MOLLI and Multitasking₃₀. The mean bias between methods was 115 ms for native T1 ($p < 0.001$, 2-way ANOVA) and 1.6% for ECV ($p = 0.146$, 2-way ANOVA). Figure 8 shows Multitasking inversion time images together with conventional PSIR LGE images and both conventional and Multitasking₃₀ ECV maps from a 29-year-old male patient with acute myocardial infarction acquired in the same imaging session. The varying contrasts available with Multitasking T1 mapping (bright-blood and dark-blood shown) allow visualization of the infarct lesion with both bright and dark blood in a cardiac phase chosen to match the conventional method. The infarct lesion in the septal wall showed increased ECV compared to a remote region in the lateral wall for both Multitasking T1 mapping ($45.1 \pm 1.6\%$ vs $26.0 \pm 2.8\%$) and MOLLI ($53.4 \pm 2.3\%$ vs $25.8 \pm 1.8\%$). Supporting Figure S3 shows native T1, post-contrast T1, and ECV maps for an AMI patient acquired with both MOLLI and Multitasking₃₀.

Image quality scores for both native and post-contrast T1 maps from healthy subjects are shown in Supporting Figure S4. None of the 80 total T1 maps were scored with a 1 (poor) and only 1 T1 map was scored with a 2 (fair); the remaining 79 T1 maps were either good or excellent quality. For native T1 the average image quality scores for MOLLI, Multitasking₆₀, Multitasking₃₀, and Multitasking₁₅ were 3.83, 3.75, 3.75, and 3.5 ($p = 0.286$); for post-contrast T1 the scores were 3.88, 3.75, 3.75, and 3.88 ($p = 0.806$). Neither one-way ANOVA nor multiple comparisons testing found a significant difference between image quality scores for native or post-contrast T1 maps. Image quality scores for native and post-contrast T1 maps from AMI patients are shown in Supporting Figure S5. In patients, average image quality scores for native T1 for MOLLI and Multitasking were 3.90 vs 3.10 ($p = 0.010$); for post-contrast T1 the scores were 3.71 vs 3.00 ($p = 0.047$).

DISCUSSION

In this study, we have shown a Multitasking T1 and ECV mapping method which is acquired without ECG triggering and without respiratory navigators or breath holds. Conventional T1 mapping techniques sample the longitudinal recovery curve after magnetization preparation with a sampling pattern determined by the preceding R-R intervals and typically must be completed within a breath hold; in comparison, our technique acquires data with an acquisition that is independent of heart rate and respiration. We determined the accuracy and repeatability of native T1 and ECV quantification from Multitasking T1 mapping with different lengths of scans in 12 healthy subjects. Multitasking T1 and ECV mapping was also compared to MOLLI in 10 AMI patients.

In a phantom study, we showed good accuracy with Multitasking T1 mapping compared to gold-standard spin-echo inversion imaging. A simulation of Multitasking T1 mapping using a numerical motion phantom showed accurate myocardial T1 estimation, with percent errors smaller than our reported in vivo coefficient of variation for repeatability. The simulation also demonstrated that Multitasking T1 mapping has similar myocardial sharpness to the fully-sampled ground truth using either known or learned motion patterns. We compared in vivo T1 measurements to MOLLI, which also uses inversion recovery¹². We showed similar in vivo myocardial native and blood pool T1 values with Multitasking T1 mapping compared to MOLLI in control subjects, all of which were within reported ranges²⁶. In control subjects, ECV values had no significant differences with multiple comparison testing between MOLLI and each Multitasking T1 mapping length despite significant ANOVA p values for ECV. All ECV values were within the reported range for control subjects^{26,27}. Native T1 values from healthy controls and AMI patients were not directly compared due to known differences between T1 normal ranges measured on different scanners.²⁸ In AMI patients, native T1 and ECV were correlated between MOLLI and Multitasking, with only native T1 showing a statistically significant bias between methods. These observations are consistent with the known behavior of the bSSFP MOLLI sequence, in which the calculated T1 values are artificially increased in AMI patients due to increased T2 values and decreased magnetization transfer (MT) effects²⁹ in edematous tissue occurring after acute myocardial injury^{23,30}. Conversely, low-flip-angle FLASH sequences are more robust to T2 and MT effects, so no such overestimation is expected to occur when used for Multitasking T1. Confounding biases from T2 and MT effects would be canceled by the subtraction operations during the ECV calculation, restoring agreement between sequences.

Multitasking T1 mapping shows good repeatability for native T1 and ECV. We showed good T1 map image quality scores with Multitasking in healthy subjects; however, overall image quality was slightly reduced compared to MOLLI. In patients, Multitasking T1 mapping showed image quality scores in the “good” range and MOLLI showed scores in the “excellent” range. One potential reason for reduced image quality with Multitasking in general is the use of FLASH versus MOLLI’s bSSFP, leading to a lower SNR acquisition. The reduced Multitasking image quality specifically in the AMI cohort may be due to irregular cardiac and respiratory motion patterns, as commonly seen in patients. While the Multitasking framework provides an avenue to handle these variations in motion, further improvements may improve motion robustness including alternative auxiliary data

trajectories to better capture motion and adapting the motion identification step to specifically handle arrhythmia.

Another area for potential improvement is intra-bin respiratory motion. Because Multitasking is a free-breathing technique there is a potential for intra-bin respiratory motion even with accurate binning – which a breath-hold technique like MOLLI is not subject to. There are two possible sources of intra-bin motion to contend with: misclassification of data to bins or motion within the bin due to the size of the bin (bin width). Our simulation demonstrated minimal differences in T1 and sharpness between Multitasking T1 maps using known and learned motion with possible misclassification errors ruling out inaccurate binning as a source of reduced image quality, but we have not explored the effect of bin width, which was optimized in this study based on an aggregate analysis of all healthy subjects, or noise which may affect motion classification in vivo. Strategies to mitigate the effect of intra-bin motion due to bin width include increasing the number of bins, excluding outliers within bins, or using a weighted reconstruction to emphasize data near the bin centers as well as improving motion identification, all of which will be the subject of future study.

Compared with other inversion or saturation recovery T1 mapping techniques which sample recovery curves with four (3D-QALAS³¹) to 11 (MOLLI¹¹) sampling points, Multitasking T1 mapping has 344 sampling points ranging from 3.6 ms to ~2500 ms along the recovery curve for any length of scan, which avoids temporal blurring that may result from combining neighboring radial projections, such as with a KWIC filter^{32,33} and allows retrospective viewing of images at any inversion time (to within 7.2 ms). Our acquisition utilized alternating image and auxiliary data lines with an echo spacing of 3.6 ms, giving the auxiliary data a temporal resolution of 7.2 ms, thus Multitasking T1 mapping can detect changes in cardiac, respiratory, and T1 dynamics with the temporal resolution of the auxiliary data. Respiration typically occurs with a frequency of 0.1–0.5 Hz, while cardiac motion occurs in the range of 0.6–3 Hz³⁴, suggesting that it may be possible to still achieve good results with even less auxiliary data, which currently has a sampling frequency of 139 Hz. Further studies will examine the effect of collecting the auxiliary data less often, which may result in shorter scan times.

In a clinical setting, patients typically undergo a multitude of breath-holds throughout a cardiac MRI scan which may result in reduced compliance. For those who have difficulty holding their breath and in whom T1 mapping is of interest, breath-hold techniques are simply not possible. Similarly, patients who have abnormal heart positions are challenging to image with traditional ECG gating due to poor signal, difficulty placing leads, and potential ECG misfires. In these instances, Multitasking T1 mapping may be capable of imaging where other methods may fail because it utilizes a continuous acquisition which does not use ECGs or breath-holds. Removal of the need for ECGs also becomes more important for imaging at higher field strengths, where good quality ECG signals are known to be difficult to obtain. Multitasking T1 mapping further allows us to quantify T1 throughout the cardiac cycle, for example in both diastole and systole and at different respiratory states, appearing consistent with diastolic and systolic T1 mapping previously possible only with a multitude of breath holds (with two breath holds typically used to collect systole and diastole at end-

expiration^{35,36}) with a recent study demonstrating the capability for T1 mapping in multiple cardiac phases during a breath-hold and using ECG gating³⁷. In this study, we have limited our analysis of Multitasking T1 mapping to end-diastole and end-expiration to be consistent with the ECG-gated, breath-held technique used as a reference measurement. While we show that simultaneous T1 mapping at multiple cardiac and respiratory phases is possible with Multitasking, further study is warranted beyond this initial study to determine if there is any clinical value in analyzing T1 maps from different motion states.

Multitasking T1 mapping has the ability to produce different types of diagnostic images simultaneously. For example, for functional imaging, cine images with dark blood, bright blood, nulled fat, or any other available contrast can be created from any desired inversion time throughout all the cardiac phases. Using post-contrast data, inversion times can be chosen for bright blood or dark blood with the myocardium signal nulled, mimicking bright blood or dark blood late gadolinium enhancement images. Further work will examine the accuracy and reproducibility of simultaneous functional data and late gadolinium enhancement from Multitasking T1 mapping. The ability to simultaneously produce additional images (which usually require separate scans and breath-holds) demonstrates how Multitasking T1 mapping has the potential to change the cardiac MR imaging paradigm. Specifically, Multitasking T1 mapping represents a move towards push-button MRI, wherein a dataset comparable to several conventional techniques combined can be recovered retrospectively from one scan with limited set up.

We were able to demonstrate Multitasking T1 mapping for 10 subjects with acute myocardial infarction; however, further evaluation is needed to characterize myocardial tissue in the presence of other disease states with expected native T1 and ECV elevations. In this study, the patient MOLLI T1 map spatial resolution could not be changed because they were acquired according to the protocol ordered for the clinical scan; to remove potential confounders from this mismatch, future studies will compare T1 maps with matched resolutions. While we expect our technique to be fully heart-rate independent, future work will assess the performance of Multitasking T1 mapping during arrhythmia. The current reconstruction time for Multitasking T1 mapping is about 1–2 hours per 2D slice using a GPU with two 2.70 GHz 12-core Intel Xeon CPUs, an NVIDIA Quadro K6000 GPU, and 256 GB of RAM. Note that the low-rank tensor imaging method used in Multitasking T1 mapping reduces not only the degrees of freedom, but also the computational requirements: all calculations are performed directly on the compressed tensor factors, meaning that the uncompressed tensor never has to be held in memory. In contrast, although compressed sensing methods such as XD-GRASP²² find an image that is compressible, they perform calculations on the uncompressed form of the image, requiring it to be held in memory in full. In this paper, for example, the factored low-rank tensor representation of the multidimensional image required 1,290x less memory than the uncompressed tensor, allowing multitasking reconstruction where compressed sensing was not possible.

Multitasking T1 mapping uses a continuous acquisition to image a 2D mid-ventricular short axis slice. Due to the nature of cardiac and respiratory motion, this means that the tissue may move in and out of the slice during the acquisition. We compensate for this effect by fitting for the flip angle along with T1, as the motion manifests as a lower effective flip angle;

however, parameter fitting has the potential to be improved. To increase sensitivity to AMI, similar to MOLLI, T2 and/or MT mapping could be added to the imaging framework to increase sensitivity to these effects. Whole-heart mapping approaches are ideal to fully characterize the tissue of the entire myocardium. This study was limited to a single slice; however, Multitasking T1 mapping is easily extendable to 3D in which another dimension (z) is added to the spatial basis ($\mathbf{U}$) and the temporal basis (Φ) remains the same. Practically speaking, this means the framework essentially stays the same for 3D imaging.

CONCLUSION

The proposed Multitasking T1 mapping method enables T1 mapping free of ECG and prospective respiratory monitoring in different cardiac and respiratory phases. Multitasking T1 mapping shows similar T1 and ECV values to MOLLI with good image quality and good repeatability in vivo in healthy subjects, and correlate to MOLLI T1 and ECV in AMI patients. Multitasking T1 mapping can obtain accurate and repeatable T1 maps of the myocardium with a free-breathing, non-ECG, continuous technique.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Schematic diagram of the proposed Multitasking T1 mapping continuous IR sequence. The IR pulses (gray blocks) are repeated every 2.5 seconds and readouts are applied continuously until the next IR with no gaps. Solid readouts represent image data incremented by the golden angle and acquired every odd readout. Dotted line readouts represent auxiliary data, a repeated 0 degree radial spoke, collected every even readout. The longitudinal magnetization (M_z) recovery curve for a typical non-contrast myocardial T1 of 1200 ms is shown in blue.

Figure 2.

Example images resulting from the real-time image reconstruction, showing the profile for a horizontal line drawn through the myocardium and liver (yellow dotted line). Throughout the 60 seconds, the dome of the liver moves in and out of the profile with respiration (blue). Systole and diastole can be observed as periodic contraction and relaxation of the LV (green).

Figure 3.

Example images resulting from the multidimensional image reconstruction. a) A horizontal profile (yellow dotted line) drawn through the myocardium at 5 example inversion times (TI) with all inversion times shown for the horizontal profile shown on the right, b) the same horizontal profile through the myocardium showing cardiac phase changes from systole (S) to diastole (D) with corresponding images, and c) a vertical profile (not shown) through the liver/air border showing respiratory phase changes and corresponding images at end-expiration and end-inspiration.

Figure 4.

Example T1 maps at multiple motion states: Diastole and systole T1 maps with a horizontal line profile (white dotted line) drawn through the heart for all cardiac phases (top). End-expiration and end-inspiration T1 maps with the white dotted line showing different liver positions (bottom).

Figure 5. Example native (top row) and post-contrast (middle row) T1 maps and ECV maps (bottom row) from one healthy subject acquired with MOLLI and Multitasking T1 mapping with 60 seconds, 30 seconds, and 15 seconds.

Figure 6.

Bland-Altman plots comparing septal and global native T1 values a) and ECV values b) between MOLLI and Multitasking T1 mapping with different scan lengths. The dotted lines indicate the 95% limits of agreement and mean bias.

Figure 7.

a) Bland-Altman plots comparing native T1 values (left) and ECV values (right) between MOLLI and Multitasking T1 mapping in acute myocardial infarction (AMI) patients. The dotted lines indicate the 95% limits of agreement and mean bias. b) Correlation of native T1 values (left) and ECV values (right) measured with MOLLI and Multitasking T1 mapping in AMI patients.

Figure 8.

Images from a patient with acute myocardial infarction. a) conventional PSIR LGE image (left) along with inversion time images showing the different contrast (bright-blood, dark-blood) available with Multitasking T1 mapping (right). b) ECV maps from conventional MOLLI (left) and Multitasking (right) collected in the same scan as the multitasking images in a).

Table 1.

Native T1 and extracellular volume (ECV) from healthy subjects using MOLLI and Multitasking T1 mapping with 60 seconds, 30 seconds, and 15 seconds of data.

		MOLLI	Multitasking₆₀	Multitasking₃₀	Multitasking₁₅	ANOVA
Native T1 (ms)	Septal	1263 ± 48	1246 ± 35	1247 ± 37	1253 ± 58	p = 0.674
	Global	1239 ± 46	1195 ± 43	1199 ± 46	1200 ± 69	p = 0.064
	Blood	1928 ± 77	2043 ± 122	1963 ± 220	1940 ± 223	p = 0.112
ECV (%)	Septal	27.6 ± 2.9	26.2 ± 2.8	26.9 ± 2.2	28.4 ± 2.9	p < 0.01 *
	Global	27.1 ± 2.4	25.7 ± 2.5	26.4 ± 2.1	27.0 ± 2.6	p = 0.091

* No significant differences were found with multiple comparisons testing.

Table 2.

Coefficient of Variation (CoV) values for repeated measures of MOLLI and Multitasking T1 mapping with 60 seconds, 30 seconds, and 15 seconds of data.

CoV (%)		MOLLI	Multitasking ₆₀	Multitasking ₃₀	Multitasking ₁₅
Native T1	Septal	0.61	1.3	1.9	2.2
	Global	0.69	1.2	1.3	2.0
ECV	Septal	5.6	5.2	2.0	3.6
	Global	3.9	3.8	3.1	3.6