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Free-Breathing Slice-Interleaved Myocardial T₂ Mapping with Slice-Selective T₂ Magnetization Preparation

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Abstract

Purpose—To develop and evaluate a free-breathing slice-interleaved T₂ mapping sequence by proposing a new slice-selective T₂ magnetization preparation (T₂prep) sequence that allows interleaved data acquisition for different slices in subsequent heart beats.

Methods—We developed a slice-selective T₂prep for myocardial T₂ mapping by adding slice-selective gradients to conventional single-slice T₂prep sequence. In this sequence, 5 slices are acquired during 5 consecutive heartbeats, each using a slice selective T₂prep. The scheme is repeated four times using different T₂prep echo times. We compared the performance of the proposed slice-interleaved T₂ mapping sequence and the conventional single-slice T₂ mapping sequence in term of accuracy, precision and reproducibility using phantom experiments and in-vivo imaging in 10 healthy subjects. We also evaluated the feasibility of the proposed sequence in 28 patients with cardiovascular disease and the quality of the maps was subjectively scored. Furthermore, we investigated the impact of through-plane motion by comparing T₂ measurements acquired during end-systole vs. mid-diastole.

Results—T₂ measurements using slice-interleaved T₂ mapping sequence were correlated with spin-echo ($r^2 = 0.88$) and single-slice T₂ mapping sequence ($r^2 = 0.98$). The mean myocardial T₂ values were correlated between slice-interleaved (48 ms) and single-slice (51 ms) T₂ mapping sequences. Subjective scores of T₂ map quality were good to excellent in 81% of the maps in patients. There was no difference in T₂ measurements between end-systole vs. mid-diastole.

Conclusions—The proposed free-breathing slice-interleaved T₂ mapping sequence allows T₂ measurements of 5 left ventricular slices in 20 heartbeats with similar reproducibility and precision as the single-slice T₂ mapping sequence but with 4-fold reduction in acquisition time.

Keywords

Slice selective T₂prep; slice-interleaved T₂ mapping; Quantitative myocardial tissue characterization; myocardial T₂ mapping; Precision; Reproducibility

Introduction

T₂-weighted (T₂W) imaging is currently the standard clinical protocol for depicting changes in myocardial T₂ time for assessment of inflammation and edema (1). Commonly, a dark blood preparation pulse is combined with a turbo spin echo readout with or without fat saturation to image myocardial edema (2). However, there are several challenges in myocardial T₂W imaging including regional variations of signals due to phased-array coil, stagnant blood, and low signal and contrast to noise ratios (3–6). For example, in the study by Thavendiranathan (7) only 47% of patients had diagnostic T₂W image quality.

Myocardial T₂ mapping is an alternative technique to T₂W imaging (8–10). In this technique, several balanced steady-state free-precession images (bSSFP) are acquired immediately after a T₂ magnetization preparation (T₂Prep) pulses with different echo times. Subsequently, T₂ value for each voxel is estimated by a fitting a recovery curve of T₂ decays. To allow for full signal recovery before application of a new T₂prep pulse, a rest period of several heartbeats, during which no data is acquired, is inserted (8,9). For example, a 2 heartbeats rest was used in the T₂ mapping sequence proposed by Giri et. al. (9), resulting in the acquisition of only 3 T₂W images over 9 heartbeat (i.e. data acquisition efficiency of 33%). However, this short rest period could results in underestimation of myocardial T₂ values in patients with high heart rate (7). Therefore, higher number of rest-periods is required to reduce the sensitivity of T₂ measurements to heart rate. In addition, edema and inflammation could occur regionally which necessitates whole heart coverage, which results in high scan inefficiency. For example, to acquire T₂ maps from 5 short-axis slices of left ventricle, the scan time is 45 sec of which 30 sec are waiting time with no data acquisition.

3D myocardial T₂ mapping is an alternative to 2D T₂ mapping and have been recently proposed to improve spatial resolution and coverage of myocardial T₂ mapping (11–14). 3D T₂ mapping with 3D radial sampling allows myocardial T₂ quantification with an isotropic resolution of 1.7 mm³ but with a scan time of 18 min (11). Instead of waiting for full magnetization recovery after each T₂prep pulse, imaging every other heart-beat was proposed to reduce the scan time (13), but with reduced measurements accuracy (15). Application of a saturation pulse prior to T₂prep has been recently reported to reduce the scan time as the cost of loss of signal-to-noise (12). Despite ongoing advances in 3D T₂ mapping sequences, the scan duration remains long (>4 min), therefore 3D T₂ mapping has not yet been adapted for routine clinical scanning.

T₂prep sequence is used in myocardial T₂ mapping sequences to create images with different T₂ weighting (8–10,16,17). The T₂prep sequence consist of a non-selective 90° radio-frequency pulse to excite the magnetization into the transverse plane followed by a series of composite or adiabatic 180° pulses and a final –90° pulse to tip the magnetization back to the longitudinal direction (18,19). All the pulses in this sequence are non-selective, resulting in magnetization excitation and T₂ weighting over the entire volume of imaging. Therefore, this sequence requires a rest period after each T₂prep image acquisition to allow for magnetization recovery.

In this study, we hypothesize that combining slice-selective T_2 prep with interleaved slice acquisition will eliminate the need for rest period after each T_2 prep image acquisition, thereby reducing the overall scan time of T_2 mapping while increasing the spatial coverage. Based on that, we propose a novel slice-interleaved T_2 mapping sequence by developing a slice-selective T_2 prep sequence, which allows interleaving the data acquisition of different slices in subsequent heartbeats. Phantom and in-vivo studies in healthy and patients with cardiovascular disease are performed to investigate the performance of the proposed sequence.

Methods

Pulse Sequence

Figure 1 shows the schematic of the proposed free breathing slice-interleaved T_2 mapping sequence, illustrated for the acquisition of 5 slices, with the acquisition of 4 different T_2 prep echo times. For each T_2 prep echo time, each slice is acquired once using an ECG-triggered single shot acquisition. The first T_2 prep block usually corresponds to sampling the $TE_{T_2Prep} = 0$ time point, with presumably no T_2 prep pulses applied. This block is then repeated for different TE_{T_2Prep} echo times, where each image is now acquired after a slice-selective T_2 prep pulse. Finally, a last repetition of the block is performed by replacing each slice-selective T_2 prep pulses with a saturation pulse (I_{SAT}) to simulate the effect of a very long TE_{T_2Prep} (i.e. $TE_{T_2Prep} = \infty$) (15). For $TE_{T_2Prep} = 0$, we used T_2 prep pulses of zero time (i.e. 90° directly followed by -90° with no waiting time and no refocusing pulses in between) (15). In case of any flip angle imperfection, this method helps to uniformly having the same effect across all T_2 prep images, and thus minimizes its impact on the fitting process, and subsequently on the final estimated T_2 times. For the I_{SAT} acquisitions, we used a composite saturation pulse consisting of four rectangular 90° RF pulse train with crusher gradients in between the RF pulses (20). The RF pulses bandwidth was 1 kHz, and the composite total duration was 10 ms.

Figure 1.b illustrates the slice acquisition ordering, slice gaps, and slice thicknesses proposed for the T_2 prep and excitation pulses. The slice selective 90° pulses of the T_2 prep composite are applied with a slice thickness twice as large as the imaging slice to minimize the impact of slice profile imperfection. Data acquisition for different slices is interleaved to minimize slice cross-talk effects of both slice-selective T_2 prep pulse and excitation pulses. Furthermore, the acquisition of 5 slices provides a recovery time of 5 heart beats between two consecutive acquisitions of the same slice. Therefore, this approach removes the need for the additional 3–6 seconds rest periods commonly required in single-slice T_2 mapping sequences to guarantee full spin recovery before each T_2 prep pulse (9,10,15). To compensate for through-plane myocardial motion, a prospective slice tracking was performed using a pencil-beam respiratory navigator (NAV) positioned on the right-hemi-diaphragm and acquired immediately before each T_2 prep pulse. We note that the NAV was used only for slice tracking without any gating; therefore the scan time was not increased.

Figure 1.c shows the sequence diagram for the proposed slice selective T_2 prep sequence. It consists of a tip-down slice selective 90° pulse, followed by four non-selective 180° refocusing pulses and ends with a closing tip-up slice selective 90° pulse. A hard-pulse is used for the

opening and closing 90° pulses with a bandwidth of 2.4 kHz, and duration of 0.88ms. To minimize the stimulated echo artifacts that might result from playing the slice selection gradients in between the two T_2 prep 90° pulses (15), we reversed the refocusing lobe of the slice-selection gradient for the second 90° pulse, similar to (21), in order to achieve a perfect nulling for the gradients zeroth moments in between the two 90° pulses. For the refocusing pulses, composite refocusing pulses ($90^\circ_x, 180^\circ_y, 90^\circ_x$) are used to provide second order corrections to variations in B_1 , and are weighted in a Malcolm Levitt's (MLEV) opposing phase pairs scheme to compensate for RF pulse shape imperfections (22). The duration of each refocus pulse is 1.75 ms.

Phantom Imaging

All imaging was performed on a 1.5T Philips Achieva (Philips Healthcare, Best, The Netherlands) MRI system using a 32-channel cardiac coil.

In a phantom imaging experiment, we compared the estimated T_2 times obtained with the proposed sequence and a “conventional” single-slice sequence with no slice selective T_2 prep (15). Imaging was performed using 8 NiCl₂ doped agarose vials, whose T_2 and T_1 values spanned the ranges of values found in the blood and myocardium (46, 49, 50, 51, 54, 62, 70, 80 ms). A single-shot ECG-triggered SSFP sequence was used for imaging in the proposed slice-interleaved T_2 mapping sequence with the following parameters: 5-slices, FOV = $240 \times 240 \text{ mm}^2$, in-plane resolution = $2 \times 2 \text{ mm}^2$, slice thickness = 8mm, TR/TE = 2.2/1.1 ms, flip angle = 40° , 10 linear ramp-up pulses, SENSE rate = 2, acquisition window = 138 ms, number of phase encoding lines = 51, linear k-space ordering. Three different $TE_{T_2\text{Prep}}$ images were acquired at different $TE_{T_2\text{Prep}} = 0, 25, 50 \text{ ms}$, in addition to a single image after a saturation pulse to simulate $TE_{T_2\text{Prep}} = \infty$ (total of 4 images per slice). For comparison, a 2D single-slice T_2 mapping sequence was performed using the conventional non-selective T_2 prep sequence to image one slice of the phantom (which corresponded to the middle slice of the proposed sequence 5 slices). The same imaging and $TE_{T_2\text{Prep}}$ timing parameters were used for this non-selective T_2 prep sequence, but with a 4 seconds rest period after each image to allow for full spins recovery. T_2 values were calculated using a 3-parameter model fit (15). To assess for measurement reproducibility, each sequence was repeated 10 times in a random order.

Additionally, a Carr-Purcell-Meiboom-Gill (CPMG) spin-echo sequence with an echo train length of 32 and TE = 10 ms (i.e. TE = 10, 20, 30...320 ms) was performed as reference. The scan parameters were: FOV = $240 \times 240 \text{ mm}^2$, in-plane resolution = $1.25 \times 1.25 \text{ mm}^2$, slice thickness = 4 mm, TR = 6000 ms, flip angle = 90° , number of averages = 4. Reference T_2 values were obtained from a 2-parameter model fit to the spin echo signal.

In Vivo Imaging

The study was health insurance portability and accountability act (HIPAA) compliant and the imaging protocol was approved by our institutional review board with written informed consent obtained prior to each examination. Ten healthy adult subjects (29 ± 18 years, range: 19 – 70 years, 4 men) without contraindications to MRI were recruited. Additionally, 28 patients (59 ± 16 years, 18 males) referred for clinical CMR were recruited to undergo an

additional 20 sec free-breathing slice-interleaved T_2 mapping sequence in addition to clinically indicated CMR sequences to assess image quality of myocardial T_2 mapping. The clinical CMR indications varied and included: atrial fibrillation (N=12), cardiac sarcoidosis (N=5), hypertrophic cardiomyopathy (N= 2), apical non-compaction (N=1), mitral valve regurgitation (N=1), amyloid (N=1), and ischemic heart disease (N= 6). Each healthy subject was imaged with the proposed slice-interleaved T_2 mapping sequence with slice-selective T_2 prep and the “conventional” single-slice T_2 mapping sequence. To assess for reproducibility, each sequence was acquired 5 times for each subject. Both sequences were performed under free breathing conditions and used a two-dimensional pencil-beam NAV positioned on the right hemi-diaphragm (RHD) to track the breathing motion and prospectively correct for the slice position during imaging. The NAV tracking used a 2D spatially selective spiral pulse (23,24), with 16 spiral excitation turns in 10 ms, and a flip angle of 90° to excite the magnetization in a circular area centered on the RHD with a diameter of 50 mm. All scans were acquired in the short axis orientation.

The proposed sequence used a free-breathing single-shot ECG-triggered slice-selective T_2 prep bSSFP acquisition with the following parameters: 5-slices, FOV = $320 \times 320 \text{ mm}^2$, in-plane resolution = $2.5 \times 2.5 \text{ mm}^2$, slice thickness = 8 mm, slice gap = 4mm, TR/TE = 2.2/1.1 ms, flip angle = 40° , 10 linear ramp-up pulses, SENSE rate = 2, acquisition window = 140 ms, number of phase encoding lines = 67, linear k-space ordering. Similar to the phantom experiment, 3 images were acquired with $TE_{T_2\text{Prep}} = 0, 25, 50 \text{ ms}$, in addition to the SAT image (total of 4 images per slice). The nominal acquisition time of this sequence was 20 heartbeats.

The single-slice T_2 mapping sequence (15) was performed to image one 2D single-slice (corresponded to the middle slice of the proposed sequence) using the same imaging and $TE_{T_2\text{Prep}}$ timing parameters as the proposed sequence but with non-selective T_2 prep pulses. This sequence used a 4-seconds rest period after each T_2W image acquisition to allow for a full spin recovery. The nominal acquisition time of this sequence was 13 heartbeats.

Sensitivity to cardiac motion

To assess the sensitivity of the slice-interleaved T_2 mapping sequence with slice-selective T_2 prep to the cardiac motion during systole, we acquired additional data in healthy subjects (N= 7, 31 ± 18 years, range: 22 – 71 years, 4 men) and patients with known or suspected cardiovascular disease (N= 8, 47 ± 14 years, range: 28–65 years, 4 men). In healthy subjects, we acquired T_2 maps using conventional single slice T_2 mapping sequence and slice-interleaved T_2 maps at end-systole and mid-diastole (4 different datasets). 5 slices in short axis view at the same location as slice-interleaved T_2 maps were acquired. The imaging parameters were: FOV = $320 \times 320 \text{ mm}^2$, in-plane resolution = $2.1 \times 2.1 \text{ mm}^2$, slice thickness = 8 mm, slice gap = 4mm, TR/TE = 2.8/1.4 ms, flip angle = 55° , 10 linear ramp-up pulses, SENSE rate = 2.3, acquisition window = 185 ms, 3 $TE_{T_2\text{Prep}}$ echo images were acquired with $TE_{T_2\text{Prep}} = 0, 25, 50 \text{ ms}$, in addition to the SAT image. In patients, only two datasets were acquired using slice-interleaved T_2 maps in mid-diastole and end-systole without any single-slice acquisition. Global and segmental myocardial T_2 values using 16-segment AHA model were measured from each dataset.

Data Analysis

All images were transferred to a separate workstation for analysis. In the phantom data, voxel-wise T_2 maps were generated using a 3-parameter model fit (15). Accuracy, precision and reproducibility were evaluated as follows. A region-of-interest (ROI) was manually defined for each vial in the spin echo data (ROI_{SE}). Similarly, a second ROI was defined for each vial in the data obtained with the two studied sequences (ROI_{seq}). Accuracy was measured for each vial (v) as the difference between the average (over the 10 repetitions) of the mean T_2 in $ROI_{seq}(v)$ and the mean reference T_2 in $ROI_{SE}(v)$. Precision was measured for each vial (v) as the average (over the 10 repetitions) of the T_2 standard deviation in $ROI_{seq}(v)$. Reproducibility was measured for each vial (v) as the standard deviation (over the 10 repetitions) of the mean T_2 in $ROI_{seq}(v)$.

For the in-vivo data, images were registered retrospectively using a non-rigid image registration algorithm (25) to compensate for residual in-plane motion. This algorithm simultaneously estimates a non-rigid motion field and intensity variations, and employs an additional regularization term to constrain the deformation field using automatic feature tracking. Upon registration, voxel-wise curve-fitting was performed, to generate T_2 maps using a 3-parameter fitting model (15). Then, a myocardial segment based analysis was performed following the AHA myocardial segment model. Epi- and endocardial contours were drawn manually by an experienced reader for each T_2 map in all slices. The myocardium was divided into 16 segments for the slice-interleaved results (using the three mid-ventricular slices), and 6 segments for the single-slice results. For each subject and segment, the average and standard deviation of T_2 values were calculated. The standard deviation served as a surrogate of the *precision*. For each subject, the standard deviation (over the five repetitions) of the mean T_2 values of each segment was calculated and served as a surrogate of the reproducibility. All calculations were performed using Matlab (v7.14, The MathWorks, Natick, MA).

For the patients data, the quality of the resulted T_2 maps were assessed by consensus of two experienced readers using a 4-point scale that addresses the T_2W image quality, registration quality, and the final T_2 maps quality: 1-nondiagnostic (very low confidence in the map due to severe motion artifacts or bad image registration), 2-fair (low confidence in two or three segments of the map, but high confidence in the rest), 3-good (most of the map is excellent except for small localized areas of artifact in at most one segment), and 4-excellent (high confidence in all segments in the map).

Statistical Analysis

The quality of the curve fitting process, used to estimate the T_2 values, is evaluated using the Chi-Square goodness of fit model and the corresponding p values are reported. Wilcoxon signed rank tests were used to compare the accuracy, precision and reproducibility of the proposed sequence, and the single-slice sequence in both the phantom study and the in-vivo measurements with statistical significance threshold defined at $p < 0.05$. In the in-vivo study, a one-way Kruskal–Wallis analysis of variance test was used to compare the T_2 measurements at different myocardial levels (specifically, basal, mid and apical levels) with the same statistical significance threshold defined at $p < 0.05$.

Results

Phantom Imaging

Figure 2 shows the accuracy, precision and reproducibility of T_2 measurements obtained in the phantom study using the single-slice and the proposed slice-interleaved T_2 mapping sequences. For the vials with T_2 times matching the range of normal myocardium (i.e. $T_2 = 40$ to 60 ms), the slice-interleaved T_2 values were within 5ms from the spin echo measurements and within 9 ms for the single-slice sequence. Across all vials, the slice-interleaved T_2 measurements were lower than the single-slice measurements ($p < 0.05$) but similar to the spin echo measurements ($p = 0.31$). No significant differences were found in the precision and reproducibility between the two sequences ($p = 0.09, 0.13$ respectively). The goodness of fit for the fitting process was $\chi^2 = 0.7$ – 1.3 , which corresponds to $p = 0.25$ – 0.43 .

Figure 3.a shows a cross sectional image for the phantom with representative ROIs drawn on the vials for measurements. Figure 3.b–3.d depict the regression analysis performed between the reference T_2 values measured from the spin echo images (x-axis) and the mean of the estimated T_2 values across repetitions using the single-slice (Figure 3.a) and the slice-interleaved (Figure 3.b) sequences. Figure 3.c shows the regression analysis between the T_2 values obtained with the slice-interleaved and the single-slice T_2 mapping sequences. Figure 3.e–3.g shows the Bland-Altman plots corresponding to each of the previous regression plot. The slice-interleaved and single-slice measurements exhibit a good correlation with the spin echo measurements ($r^2 = 0.88$ and 0.94 respectively). There is a strong correlation ($r^2 = 0.98$) between the T_2 values measured from single vs. slice-interleaved sequences with a regression slope of 0.8 indicating slightly lower T_2 values when using the slice-interleaved sequence compared with the single-slice one.

In Vivo Imaging

Figure 4 shows example in-vivo T_2 maps obtained with the five repetitions of the proposed sequence in a healthy subject. The maps visually appear homogeneous over all slices and myocardial segments suggesting a low spatial variability of T_2 values. The quality of the proposed slice-interleaved T_2 mapping sequence appears visually similar over the five repetition scans suggesting a good reproducibility of the method.

Figure 5 shows an example of the T_2 quantifications based on the proposed slice-interleaved sequence. Figure 5.a shows the bullseye of the T_2 quantifications obtained in a healthy subject from one of the 5 repetitions. Figure 5.b shows the average T_2 values at different slices (basal, mid and apical levels) for all healthy subjects between slice-interleaved vs. single-slice T_2 mapping sequence. The Kruskal–Wallis test resulted in non-significant differences between the T_2 values across the three ventricular slices ($p = 0.39$).

Figure 6 shows an example comparison between the single and slice-interleaved sequences in 3 healthy subjects. For each subject, the T_2 map generated from the single-slice sequence is compared to the T_2 map generated for the corresponding slice in the slice-interleaved sequence. The T_2 measurements, precision, and reproducibility are shown for each map. The goodness of fit was $\chi^2 = 0.9$ – 1.7 for the single-slice sequence and $\chi^2 = 1.1$ – 2.0 for the slice-

interleaved sequence across all subjects. This corresponds to $p = 0.37$ – 0.21 and 0.31 – 0.17 respectively.

Figure 7 presents the subject-based analysis of in-vivo T_2 quantifications over the whole myocardium in 10 healthy subjects. Over the entire myocardium, similar T_2 (48 ± 5.6 ms vs. 51 ± 3.4 ms using single-slice sequence, $p=0.07$), precision (11 ± 4.0 ms vs. 10 ± 1.5 ms, $p=0.7$), and reproducibility (3 ± 1.8 ms vs. 1.7 ± 1 ms, $p=0.19$) values were obtained in the slice-interleaved sequence compared to the single-slice sequence.

Figure 8 shows the in-vivo myocardial segment-based analysis of T_2 mapping in healthy subjects. The proposed slice-interleaved sequence provided lower segment-wise T_2 values compared to the single-slice sequence in all segments (48 ± 2.6 ms vs 51 ± 1.8 ms, $p<0.05$). In average over all subjects, both sequences led to similar precision (9.8 ± 2 ms vs. 9.5 ± 2.5 ms, $p=0.43$) and reproducibility (3.3 ± 0.5 ms vs. 3.7 ± 1.2 ms, $p=0.16$) values. High precision of T_2 measurements was obtained in septal segments when compared to free-wall segments for both sequences (7.5 ms vs 11.5 ms, $p<0.05$ in the single-slice, and 6.5 ms vs 12 ms, $p<0.05$ in the slice-interleaved). Reproducibility is also better in the septal segments compared to the free-wall segments in both slice-interleaved sequence (2.5 ms vs 5 ms, $p<0.05$) and single-slice sequence (3 ms vs 4 ms, $p<0.05$).

Figure 9 shows examples of T_2 maps with associated subjective scores used for the qualitative evaluation in patients. 81% of maps received a subjective score of good to excellent image quality. Only 6 slices (4%) were of poor/non-diagnosable quality, 3 of those were most apical slices. Figure 10 shows example T_2 maps obtained in patients with elevated T_2 times in one or more myocardial segment, which demonstrates the feasibility of this technique in detecting regional T_2 elevation.

Supporting Figure S1 shows example T_2 maps at end-systole and mid-diastole acquired using single-slice and slice-interleaved T_2 mapping sequences. Supporting Figure S2 shows Bland-Altman plots for the segment based T_2 measurements at end-systole and mid-diastole in healthy subjects using the single-slice T_2 mapping sequence (Fig. 12.a) and the slice-interleaved sequence (Fig. 12.b), and in patients using the slice-interleaved T_2 mapping sequence (Fig 12.c). The different symbols represent different myocardial levels (i.e. basal, mid, and apical slices). There was no difference between global T_2 measurements acquired using slice-interleaved T_2 mapping sequence in end-systole and mid-diastole phases in healthy or patients ($p=0.4$, 0.35 respectively).

Discussion

In this study, we developed a novel free-breathing slice-interleaved myocardial T_2 mapping sequence by implementing a slice-selective T_2 prep sequence in combination with an interleaved slice acquisition scheme. This significantly reduces the scan time and improves data acquisition efficiency allowing the coverage of more slices in a comparable scan time of one slice acquired using the single-slice T_2 mapping sequence without slice-selective T_2 prep sequence. A 20 heartbeat free-breathing T_2 mapping sequence with 5-slices of LV coverage

can be easily integrated in any clinical CMR imaging protocol as we demonstrated in our initial clinical feasibility study.

Although, there was no statistically significant difference between T_2 measurements from the single-slice vs. the slice-interleaved sequence, the proposed sequence led to reduced T_2 values compared to the single-slice sequence in both phantom study ($\sim 4\text{ms}$) and segment-based analysis of the in-vivo subjects ($\sim 3\text{ms}$). However, “true” myocardial T_2 value is unknown, therefore, it is unclear if the proposed slice-interleaved sequence under-estimate the actual T_2 or it is closer to the *true* myocardial T_2 . In our phantom experiment, we found the T_2 values measured by slice-interleaved sequence to be closer to spin-echo measurements and lower than single-slice sequence.

To allow for signal recovery of at least 5 heart-beat ($\sim 5\text{ s}$ for a heart rate of 60 bpm), the number of slices has to be ≥ 5 slices to maximize the throughput of the sequence in term of acquisition time vs. slice coverage. If the number of acquired slices is less than 5, rest cycles will become necessary, and the time efficiency of the sequence will be reduced. On the other hand, more slices can be acquired, which results in more time between subsequent data acquisitions for the same slice.

The proposed slice-interleaved T_2 mapping sequence is acquired during free breathing. Although single-slice T_2 mapping sequences are performed in one breath-hold, it has been shown over 50% of patients cannot sustain a stable 12–15sec breath-hold and retrospective motion correction is needed (25,26). Considering that we have to perform retrospective motion correction, we did not limit the scan time to the duration of a single breath-hold. A combination of prospective slice-tracking to minimize through plane motion and retrospective motion correction to reduce the impact of in-plane motion allows us to acquire free-breathing T_2 mapping.

The proposed sequence can easily be adapted for segmented data acquisition for myocardial T_2 mapping to acquire higher spatial resolution 2D mapping (27). The data acquisition for different k-space segments will be interleaved in exactly the same fashion the slices are interleaved in the proposed sequence, and thus can be used in a time-efficient way to acquire the entire 2D k-space data. Further studies are needed to implement and evaluate the performance of a segmented T_2 mapping sequence using slice-selective $T_2\text{prep}$ sequence.

In the slice-selective $T_2\text{prep}$ composite design, we did not use slice-selective gradients for the refocusing pulses. The underlying assumption to allow this approach is that the time between the refocus pulses (i.e. $TE_{T_2\text{Prep}}/4$ for 4 refocus pulses) is very small (e.g. 12.5ms for a $TE_{T_2\text{Prep}} = 50\text{ms}$) compared to the myocardium T_1 time ($\sim 1200\text{ms}$ at 1.5T), and thus the T_1 recovery that occurs in the non-imaged slices, experiencing the multiple 180° refocus pulses without the 90° , -90° tipping pulses, is negligible especially that the next slice to be imaged is in the next cardiac cycle allowing enough time for the spins that might be inverted by the end of the composite to be recovered.

Slice-selective preparation pulses are typically more sensitive to through-plane motion. To minimize this impact, we have chosen a larger slab size for the $T_2\text{prep}$ pulse in addition to the prospective slice-tracking scheme. However, there may be still residual through-plane

motion that could impact the T_2 measurements, which might explain the lower precision values in subjects #1 and #3. To study the overall effect on the final T_2 measurements, we compared between the T_2 measurements at end-systole and mid-diastole on a separate group of subjects, however we did not find any differences between T_2 values measured in systolic vs. diastole.

The recovery time for magnetization of each slice depends on the heart-rate. In our implementation of 5 slices, the time difference between two subsequent images for each slice is 5 heartbeats (i.e. $5 \times (\text{R-R interval})$ seconds). Thus, the relaxation time is reduced for elevated heart rates (i.e. shorter R-R interval), allowing less time for recovery, which in turns could affect the T_2 weighting of the subsequent images. In two subjects (#1 and #9), the heart rate was varying significantly during the scans (between 60 and 90 bpm), which resulted in low reproducibility in the slice-interleaved T_2 measurements. One potential solution is to increase the number of slices to allow for more relaxation time for each slice. Another alternative solution is to use a minimum rest cycle between data acquisition for the same slice.

We observed 10–20% variations in the myocardial T_2 values among different myocardial segments. Similar variability ranges were reported in 3D T_2 mapping (11,12). In (11), a T_2 values ranges between 35 ms to 45 ms was reported across segments. In (12), the standard deviation of myocardial T_2 measurements was 3.5–5 ms across the entire myocardium. We also note that this variability is in the same range as the measurements reproducibility (an average of 4 ms standard deviation among different repetitions), which suggests that these variations could be attributed to the imaging and physiological confounders of myocardial T_2 mapping including sensitivity to field inhomogeneities.

We have investigated the proposed sequence only on a 1.5T system. Further studies at higher magnetic field are needed to assess the proposed slice-interleaved T_2 mapping sequence in the presence of increased B_1 and B_0 inhomogeneities.

The slice-interleaved T_2 mapping sequence uses a slice-selective T_2 prep sequence. Inflow and through-plane motion will adversely impact the T_2 prep. For myocardial T_2 mapping, we have used a slice-tracking approach and a larger slice-selective gradient to minimize this impact. However, we expect blood T_2 measurements to be affected with this sequence, which will result in inaccurate T_2 measurements in the blood pool. Since T_2 values of the left ventricular blood pool will not change at different location, a single scan using conventional single-slice T_2 mapping may be sufficient if blood pool T_2 measurement is needed.

Conclusion

The free-breathing slice-interleaved T_2 mapping sequence allows T_2 measurements of 5 left ventricular slices in 20 heartbeats with similar reproducibility and precision as a single-slice T_2 mapping sequence but with 4-folds reduction in acquisition time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

a) Schematic of the proposed slice-interleaved T_2 mapping sequence using slice-selective $T_2\text{Prep}$ with b) an interleaved slice acquisition scheme. The imaging sequence uses a respiratory navigator (NAV) pulse for slice tracking by measuring respiratory motion of the right-hemi-diaphragm. The sequence consists of several $T_2\text{Prep}$ blocks, each with a specific $T_2\text{Prep}$ echo time. In each block, all slices are subsequently acquired in an interleaved fashion using ECG triggered T_2 -prepared single shot imaging. The first block usually corresponds to $T_2\text{Prep} = 0$, and the last block corresponds to $T_2\text{Prep} = \infty$, where each image is acquired immediately after a saturation pulse (I_{SAT}). c) Schematic of the slice-selective T_2 magnetization preparation composite using 2 slice-selective 90° and -90° pulses with four non-selective composite Malcolm Levitt's (MLEV) refocusing pulses. The refocusing gradient for the second 90° pulse is reversed to achieve a perfect nulling for the gradients zeroth moments in between the two 90° pulses. SS is the slice selection direction.

Figure 2.

(a) Cross-sectional image for the phantom consisting of multiple cylindrical vials of different T_1 and T_2 values. Representative ROIs are shown to illustrate how measurements were calculated, and which vials were considered. The rest of the vials have $T_2 > 100$ ms which is beyond the myocardium T_2 range, (b) Accuracy, precision and reproducibility of the single-slice and the slice-interleaved T_2 mapping sequences in a set of phantom vials with different T_1/T_2 values. Each sequence was repeated 10 times. Accuracy is defined as the difference between the averaged T_2 times over all 10 repetitions and the spin echo T_2

measurements. Precision is defined as the average over all 10 repetitions of the T_2 standard deviation within each vial. Reproducibility is defined as the standard deviation over all 10 repetitions of the mean T_2 times within each vial. The proposed slice-interleaved sequence yields similar absolute accuracy ($p=0.915$), precision ($p=0.26$), and reproducibility ($p=0.29$) compared with the single-slice sequence.

Figure 3.

(a–c) Regression analysis between the reference T_2 values measured from the spin echo images (x-axis) and the mean of the estimated T_2 values across repetitions (y-axis) using a) single-slice and b) slice-interleaved sequences. c) Regression analysis obtained between the single-slice and the slice-interleaved measurements. The slice-interleaved measurements exhibit a strong correlation with both spin echo and single-slice measurements ($r^2 = 0.88$ and 0.98 respectively), (d–f) Corresponding Bland-Altman plots.

Figure 4.

Example T₂ maps obtained in one subject with the slice-interleaved T₂ mapping sequence.

The maps are shown for all five slices and five repetitions of the sequence. All T₂ maps show homogeneous T₂ signal over all myocardium, slices, and repetitions.

Figure 5.

a) Example T_2 maps obtained in one healthy subject with the associated bullseye of the myocardial segment-based quantification. The average T_2 over the whole myocardium is shown in the center of the bullseye view. b) Basal, mid, and apical T_2 values for different subjects. No significant difference was found in T_2 values across the different slices ($p=0.54$).

Figure 6. Example myocardial T₂ measurements, accuracy and precision of T₂ maps obtained using the single-slice and the slice-interleaved sequences in 3 healthy subjects. The values in each bullseye center represent the average T₂ times over the whole myocardium. Comparable image quality and T₂ quantifications were obtained with the two sequences.

Figure 7.

T_2 measurements, precision, and reproducibility of the slice-interleaved and single-slice sequences obtained for each subject. Accuracy, precision and reproducibility were measured over the entire mid-ventricular slice in the slice-interleaved and the single-slice sequence. On average, similar T_2 values measurements (48 ± 5.6 ms vs. 51 ± 3.4 ms using single-slice sequence, $p=0.1$), precision (11 ± 4.0 ms vs. 10 ± 1.5 ms, $p=0.6$) and reproducibility (3 ± 1.8 ms vs. 1.7 ± 1 ms, $p=0.11$) were obtained in the slice-interleaved sequence compared to the single-slice sequence.

Figure 8.

Myocardial segment-based quantification of T_2 values over all healthy subjects for a) measurements, b) precision, c) reproducibility. d) Bland-Altman plot of the T_2 differences between the single-slice and the slice-interleaved sequences. The values in each bullseye center represent the average T_2 times over the whole myocardium not the average of the segments values. The slice-interleaved sequence measurements led to lower segment-wise T_2 values (48 ± 3 ms vs 51 ± 2 ms, $p < 0.05$) and similar range of precision (9.8 ± 2 ms vs. 9.5 ± 3 ms, $p = 0.36$) and reproducibility (3.3 ± 0.5 ms vs. 3.7 ± 1.2 ms, $p = 0.08$) when compared with the single-slice sequence measurements.

Figure 9.

Subjective qualitative analysis of T₂ map quality in patients. a) Illustration of the four-point scale used for the assessment: 1-nondiagnostic (very low confidence in the map due to severe motion artifacts or bad image registration), 2-fair (low confidence in two or three segments of the map, but high confidence in the rest), 3-good (most of the map is excellent except for small localized areas of artifact in at most one segment), and 4-excellent (high confidence in all segments in the map). b) Overall scores on 28 patients with 140 slice maps.

Figure 10. Overlaid T_2 maps on magnitude images in three patients with dilated cardiomyopathy (subject 1) and suspected sarcoidosis (subject 2 and 3), which shows regional elevation of T_2 values compared to normal myocardium.