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## Joint Myocardial $T_1$ and $T_2$ Mapping Using a Combination of Saturation Recovery and $T_2$ -preparation

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### Abstract

**Purpose**—To develop a heart-rate independent breath-held joint  $T_1$ - $T_2$  mapping sequence for accurate simultaneous estimation of co-registered myocardial  $T_1$  and  $T_2$  maps.

**Methods**—A novel preparation scheme combining both a saturation pulse and  $T_2$ -preparation in a single R-R interval is introduced. The time between these two pulses, as well as the duration of the  $T_2$ -preparation is varied in each heartbeat, acquiring images with different  $T_1$  and  $T_2$  weightings, and no magnetization dependence on previous images. Inherently co-registered  $T_1$  and  $T_2$  maps are calculated from these images. Phantom imaging is performed to compare the proposed maps to spin echo references. In vivo imaging is performed in ten subjects, comparing the accuracy and precision of the proposed technique to existing myocardial  $T_1$  and  $T_2$  mapping sequences of the same duration.

**Results**—Phantom experiments show that the proposed technique provides accurate quantification of  $T_1$  and  $T_2$  values over a wide-range ( $T_1$ : 260ms to 1460ms,  $T_2$ : 40ms to 200ms). In vivo imaging shows that the proposed sequence quantifies  $T_1$  and  $T_2$  values similar to a saturation-based  $T_1$  mapping and a conventional breath-hold  $T_2$  mapping sequence, respectively.

**Conclusion**—The proposed sequence allows joint estimation of accurate and co-registered quantitative myocardial  $T_1$  and  $T_2$  maps in a single breath-hold.

### Keywords

quantitative myocardial tissue characterization; myocardial  $T_1$  mapping; myocardial  $T_2$  mapping; myocardial inflammation; diffuse fibrosis

## Introduction

Measurement of the longitudinal ( $T_1$ ) and the transverse ( $T_2$ ) relaxation times in the myocardium enables a quantitative description of tissue characteristics and identification of various cardiomyopathies. Quantitative myocardial  $T_1$  mapping (1-5) provides a technique for non-invasive assessment of various cardiomyopathies (6) and interstitial diffuse fibrosis (7). When both native and post-contrast myocardial  $T_1$  maps are acquired, they can be used to measure the extracellular volume fraction (8), which has shown utility for detection of diffuse myocardial fibrosis (9). On the other hand, quantitative myocardial  $T_2$  mapping (10-16) enables detection of inflammation and edema (11,14).

Quantitative myocardial mapping approaches rely on acquiring multiple electrocardiogram (ECG)-triggered images with different contrast weightings, achieved by varying one or more sequence parameter(s). Then, a model describing the magnetization evolution, as a function of the unknown parameters of interest and the known sequence parameter(s) that is being varied, is fitted voxel-wise to these series of images.

Several myocardial  $T_1$  mapping approaches have been proposed for sampling of the longitudinal magnetization recovery curve. Look-Locker based inversion-recovery sequences (1,2,17) are commonly used (18-22), with a breath-hold acquisition of each slice, and provide high precision, albeit at the cost of accuracy (5,23). Recently, an inversion-recovery based multi-slice  $T_1$  mapping sequence has been proposed as well (24). As an alternative to the inversion-based sequences, saturation-recovery based myocardial  $T_1$  mapping was also investigated (25), which was recently revisited by introduction of the SATuration recovery single-SHot Acquisition sequence (SASHA) (3). Another saturation-recovery based approach called SAPPHIRE uses a combination of saturation and inversion pulses (4). These latter techniques have better accuracy compared to Look-Locker based sequences, although their precision tends to be worse (23).

For myocardial  $T_2$  mapping (10-16), several images are acquired with different  $T_2$ -weightings to generate a quantitative pixel-wise  $T_2$  map.  $T_2$ -preparation ( $T_2$ prep) (26) technique has been utilized to generate these varying  $T_2$ -weighted contrast. Multiple heart-beat rest periods are used in between these images in order to ensure sufficient magnetization recovery (11,14). An alternative technique, which eliminates the necessity for rest period was recently proposed (27). In this technique, a saturation pulse is used at every R-R interval, followed by a fixed  $T_1$  recovery period. After this recovery,  $T_2$ prep with different echo times are applied to generate a variety of  $T_2$  weighted images, which are acquired immediately afterwards. The fixed  $T_1$  recovery period ensures that all the images have the same longitudinal magnetization prior to the application of the  $T_2$ prep, and eliminates the need for rest periods, albeit at the cost of a reduced signal-to-noise ratio (27).

Since  $T_1$  and  $T_2$  values offer complementary information, a method for simultaneously mapping these quantities in a reduced amount of time is attractive. Furthermore, the inherently co-registered maps can potentially allow for better visualization of areas with abnormal  $T_1$  or  $T_2$  (28-30). These sequences employ different combinations of inversion

recovery and  $T_2$ prep techniques to generate different  $T_1$  and  $T_2$  weighted images for quantification.

In this study, we sought to develop a saturation-recovery and  $T_2$ -preparation based sequence that exhibits no heart-rate dependence, that can be acquired in a single breath-hold and that allows for accurate simultaneous estimation of myocardial  $T_1$  and  $T_2$  with a precision comparable to existing methods.

## Methods

### Proposed Sequence

In the proposed sequence, a saturation pulse is applied to eliminate the magnetization history at every heartbeat. The longitudinal magnetization then recovers based on the  $T_1$  value for a duration of  $T_{sat}$ . Subsequently, a  $T_2$ prep pulse (26) with echo length  $TE_{prep}$  is applied to generate the additional  $T_2$  weighting. A single-shot bSSFP image is then acquired using ECG-triggering. The schematic of this proposed joint  $T_1/T_2$  mapping sequence is depicted in Figure 1a. 4 heartbeats of the sequence diagram are shown in Figure 1b, along with the corresponding longitudinal relaxation curve. The longitudinal relaxation curve depicts the effects of the  $T_1$ - $T_2$  preparations, depicted by green circles, as well as the imaging pulses, where the red crosses indicate the acquisition of the k-space center. The mapping sequence acquires the first image with no preparation, followed by 12 heartbeats with various  $(T_{sat}^k, TE_{prep}^k)$  corresponding to heartbeat  $k$ , to sample images with different  $T_1$  and  $T_2$  weightings. These samples were distributed on the two-dimensional grid of possible  $T_{sat}$  and  $TE_{prep}$  times, where the  $T_{sat}$  values ranged between 0 and the maximum saturation recovery time within an R-R interval, and  $TE_{prep}$  values were limited to a range between 0 and 60 ms.

A composite saturation pulse, based on (31), with 1 kHz bandwidth and 10 ms duration is used.  $T_2$ prep uses non-selective opening and closing  $90^\circ$  hard pulses with 2.3 kHz bandwidth and 0.44 ms duration, to minimize  $T_2^*$  effects that might occur during the pulse (16), while the refocus pulses are weighted in a MLEV opposing phase pairs scheme to compensate for RF pulse shape imperfection (32). Additionally, for  $TE_{prep} = 0$ , a  $90^\circ$  followed immediately by a  $-90^\circ$ , followed by a crusher gradient was utilized, similar to the one proposed in (10), shown to reduce the effect of  $B_0$  and  $B_1$  variations of the excitation and refocusing pulses of the  $T_2$ prep sequence, and improving the  $T_2$  quantification accuracy (16).

### Joint $T_1$ and $T_2$ Map Reconstruction

The  $T_1$  and  $T_2$  maps are generated jointly by voxel-wise least-squares fitting of the magnetization evolution model to the image intensities. We use a 4-parameter model for fitting, which characterizes the effect of the bSSFP imaging pulses that are played until the acquisition of central k-space, on the magnetization measured after the  $T_1$  and  $T_2$  preparation. This model is given by:

$$M_{4\text{-parameter}}(T_{sat}, TE_{T2P}) = A \left(1 - e^{-T_{sat}/T_1}\right) e^{-TE_{T2P}/T_2} + B, \quad [1]$$

where the parameters, A and B do not depend on the saturation time,  $T_{\text{sat}}$  or the  $T_{2\text{prep}}$  time,  $TE_{T2P}$ . As detailed in (16), the B parameter captures the effect of the imaging pulses, and is a function of the steady-state magnetization, as well as sequence parameters. The A parameter is a function of the signal at full-recovery, and sequence parameters (flip angle, number of pulses, repetition time, etc).

### Phantom Imaging

All imaging was performed on a 1.5 T Philips Achieva (Philips Healthcare, Best, The Netherlands) system using a 32-channel cardiac coil array. Phantom imaging was performed using 14 NiCl<sub>2</sub> doped agarose vials, whose  $T_1$  and  $T_2$  values spanned a range of values ( $T_1$ : 260ms to 1460ms,  $T_2$ : 40ms to 200ms). A single-shot ECG-triggered bSSFP sequence with the following parameters was used for the proposed sequence for imaging at a heart-rate of 60 bpm: 2D single-slice, FOV = 280×280 mm<sup>2</sup>, in-plane resolution = 2×2 mm<sup>2</sup>, slice thickness = 8 mm, TR/TE = 2.8 ms/1.4 ms, flip angle = 70°, 10 linear ramp-up pulses, SENSE rate = 2.5, partial Fourier = 0.75, acquisition window = 121 ms, number of phase encoding lines = 43, linear k-space ordering. Furthermore, to establish the experimental heart-rate invariance of the method, the phantom imaging was repeated using the same imaging parameters at heart-rates of 70, 80, 90 and 100 bpm.

Spin-echo sequences were used to measure reference  $T_1$  and  $T_2$  values for each vial. For  $T_1$  values, an inversion spin-echo sequence was used with 16 inversion times between 100 and 3000 ms, as well as a TR/TE = 6000ms/10ms. For  $T_2$  values, a Carr-Purcell-Meiboom-Gill (CPMG) spin-echo sequence with an echo train length of 32 with TE 10 ms was performed with TR = 6000 ms. The scan parameters were: FOV = 240×240 mm<sup>2</sup>, in-plane resolution = 1.25×1.25 mm<sup>2</sup>, slice thickness = 4 mm, flip angle = 90°. Number of averages = 4.

Finally,  $T_1$  mapping was also performed using SASHA  $T_1$  mapping sequence (3) of the same duration, which is a saturation recovery based technique. For comparison  $T_2$  maps, a conventional  $T_2$  mapping sequence was used with 3  $T_{2\text{prep}}$  echo times (0, 25, 50 ms), whose acquisitions are separated by a 4 second rest period to allow for sufficient recovery, as well as an image acquired immediately after saturation pulse to simulate a very long  $T_{2\text{prep}}$  echo time (i.e.  $T_{2\text{prep}} = \infty$ ) (16). The duration of this acquisition was 4 heartbeats plus 8 seconds of rest period. The same imaging parameters, as the joint  $T_1/T_2$  sequence, were used for the imaging readout in both the SASHA  $T_1$  and the conventional  $T_2$  mapping acquisitions.

### In Vivo Imaging

The study was approved by the institutional review board, and written informed consent was acquired prior to each examination. In a prospective study, ten healthy adult subjects (31 ± 17 years, 4 men) without contraindications to MRI were recruited. For each subject, localizer scouts were acquired to define the mid-ventricular short-axis slice. The mid-ventricular short-axis slice was acquired using the proposed breath-held single-shot ECG-triggered bSSFP sequence with the same parameters as in phantom imaging. The acquisition took 13 heartbeats. Comparison  $T_1$  maps were acquired using the SASHA  $T_1$  mapping sequence of the same duration within a breath-hold; and comparison  $T_2$  maps were acquired

using the conventional  $T_2$  mapping sequence within a breath-hold, with the same parameters as in phantom imaging.

### $T_1$ and $T_2$ Map Analyses

All  $T_1$  and  $T_2$  maps were generated offline via a voxel-wise least-squares fitting using a Levenberg-Marquardt optimizer. The 4-parameter model of Equation [1] was used for the proposed joint mapping sequence. For phantom imaging, reference  $T_1$  times for the inversion-recovery spin-echo sequence was calculated using a 3-parameter inversion-recovery model,

$$M_{3\text{-parameter}}^{IR-SE}(T_{inv}) = A \left( 1 - 2e^{-T_{inv}/T_1} \right) + B. \quad [2]$$

The reference phantom  $T_2$  times for the spin-echo sequence was also calculated using a 3-parameter model,

$$M_{3\text{-parameter}}^{T_2}(TE_{T2P}) = Ae^{-TE_{T2P}/T_2} + B. \quad [3]$$

Comparison SASHA  $T_1$  maps were generated using a 3-parameter saturation-recovery model:

$$M_{3\text{-parameter}}^{T_1}(T_{sat}) = A \left( 1 - e^{-T_{sat}/T_1} \right) + B, \quad [4]$$

which was shown to capture the effects of the recovery-curve disturbance caused by multiple RF excitations before the k-space center, as well as reducing the susceptibility to magnetization transfer effects (3,33). Comparison conventional  $T_2$  maps were reconstructed using the 3-parameter model in Equation [3], which captures the effect of imaging pulses before the k-space center, and whose accuracy was shown to be independent of the  $T_2$ prep echo times (16).

A region-of-interest (ROI) analysis was performed for both phantom and in vivo imaging. The mean value and standard deviation in the ROI were recorded for each calculated  $T_1$  and  $T_2$  maps. For phantom imaging, circular ROIs were drawn across each of the 14 vials, starting from the center of the vial and containing ~300 pixels. For in-vivo imaging, epi- and endocardial contours were drawn manually by two independent experienced readers blinded to the acquisition type for each map. The  $T_1$  and  $T_2$  values were recorded in the septum (example ROIs are depicted in Supporting Figure S1), where the segments show the smallest variation in measurements (34,35). Furthermore, a segment-based analysis was also performed to compare the regional variations of the methods. This included the six segments (anterior, anteroseptal, inferoseptal, inferior, inferolateral, anterolateral) for the mid-ventricular short-axis slice. The standard deviations within these regions were assessed as a surrogate for precision.

For phantom imaging, accuracy was assessed by comparing the mean of the vial for the spin echo reference  $T_1$  (respectively  $T_2$ ) map, and the mean of the vial for the  $T_1$  (respectively  $T_2$ ) map from the proposed sequence. The null hypotheses that there was no difference in the mean value for a vial in the spin echo reference and in a map generated using the proposed sequence was tested using a paired t-test across all vials. A  $P$  value of  $<0.05$  was considered to be significant. Additionally, Bland-Altman analysis was performed to compare the individual reference  $T_1$  (and  $T_2$ ) values with those calculated from the proposed sequence. The correlation between the estimated  $T_1$  or  $T_2$  times and the heart rate was studied using Pearson's linear correlation coefficient.

For both phantom and in-vivo imaging, the proposed method was compared with SASHA  $T_1$  and conventional  $T_2$  mapping, in terms of the measured  $T_1$  or  $T_2$  values, and the associated precision. These values were taken as the average of those of the two independent observers. The null hypotheses that there was no difference in the measured values (or precision) between the maps generated by the proposed  $T_1$  (or  $T_2$ ) map and the corresponding comparison map were tested using a paired t-test across all vials. A  $P$  value of  $<0.05$  was considered to be significant. Bland-Altman analysis was performed to characterize the inter-observer variability. Furthermore, Pearson's linear correlation coefficient was used to compare the overall inter-observer variability.

## Results

### Phantom Imaging

Comparison of the proposed method and the reference values in phantom imaging shows a high level of correlation among the two approaches. The correlation coefficients were 0.99 for both the  $T_1$  and  $T_2$  measurements, and these correlations are depicted in Figure 2a ( $T_1$  in the top, and  $T_2$  in the bottom row respectively). The  $T_1$  and  $T_2$  values calculated using the proposed sequence were not different than the reference values ( $P = 0.49$  in both cases). Bland-Altman analysis shows the variation observed between the  $T_1$  and  $T_2$  values (top and bottom rows respectively) calculated from the proposed method versus the reference values are within the acceptable range ( $-3.1 \pm 13.9$  ms for  $T_1$ ;  $0.4 \pm 11.1$  ms for  $T_2$ ), as shown in Figure 2b. Finally, the proposed method shows a maximum difference of 1.2% and 2.6% for  $T_1$  and  $T_2$  measurements respectively as a function of the heart-rate. There was no significant correlation between the  $T_1$  or  $T_2$  values and the heart-rate, with correlation coefficients  $< 0.2$  and  $P > 0.95$  for both  $T_1$  and  $T_2$  measurements, demonstrating heart-rate invariance. This heart-rate invariance is depicted in Figure 2c in representative vials for different heart rates for  $T_1$  and  $T_2$  values (top and bottom rows respectively). The vials are color-coded consistently for the  $T_1$  and  $T_2$  graphs.

Additional comparisons with existing mapping sequences show that for  $T_1$  mapping, both SASHA and proposed  $T_1$  mapping sequences have similar accuracy and precision ( $P = 0.11$  and  $0.34$  respectively). For  $T_2$  mapping, the proposed mapping sequence has similar accuracy and precision compared to the conventional  $T_2$  mapping sequence ( $P = 0.65$  and  $0.36$  respectively). The accuracy and precision for individual vials are depicted in Figure 3.

## In Vivo Imaging

The myocardial  $T_1$  and  $T_2$  mapping sequences were successfully completed in all subjects without complications. Example  $T_1$  and  $T_2$  maps from two different subjects are shown in Figure 4, where the maps were of similar visual quality. In both cases there was good agreement of the myocardial  $T_1$  and  $T_2$  values. For subject A, the  $T_1$  and  $T_2$  values were:  $1211 \pm 82$  ms vs.  $1210 \pm 92$  ms for SASHA and proposed  $T_1$  respectively; and  $49.0 \pm 5.8$  ms vs.  $47.3 \pm 6.5$  ms for conventional and proposed  $T_2$  respectively. For subject B, the  $T_1$  and  $T_2$  values were:  $1217 \pm 90$  ms vs.  $1210 \pm 96$  ms for SASHA and proposed  $T_1$ ; and  $47.8 \pm 7.0$  ms vs.  $45.6 \pm 7.3$  ms for conventional and proposed  $T_2$ .

Across all the healthy adult subjects, the estimated ventricular septal  $T_1$  values were:  $1210 \pm 24$  ms and  $1191 \pm 29$  ms for SASHA and proposed  $T_1$  mapping respectively ( $P = 0.06$ ). The estimated  $T_2$  values were:  $48.2 \pm 2.8$  ms and  $47.3 \pm 2.3$  ms for conventional and proposed  $T_2$  mapping respectively ( $P = 0.23$ ). The measurements for  $T_1$  and  $T_2$  in individual subjects are depicted in Figure 5a. The precision in the septum was:  $133 \pm 31.0$  ms and  $121 \pm 20.7$  ms for SASHA and proposed  $T_1$  mapping respectively ( $P = 0.08$ ); and  $8.0 \pm 1.2$  ms and  $9.7 \pm 1.8$  ms for conventional and proposed  $T_2$  mapping respectively ( $P = 0.01$ ). The precision for  $T_1$  and  $T_2$  in individual subjects is depicted in Figure 5b. Bland-Altman analysis shows that the inter-observer variability was within the acceptable range ( $-9.6 \pm 42.3$  ms for  $T_1$ ;  $0.7 \pm 5.9$  ms for  $T_2$ ), as depicted in Figure 5c. The correlation coefficient between the two observers for all measurements was 0.99.

The estimated segment-based analysis showed that there was no difference between SASHA and proposed  $T_1$  mapping in terms of the segmental  $T_1$  values ( $P = N.S.$  for all), except for the inferolateral segment ( $1226 \pm 37.3$  ms vs.  $1198 \pm 37.6$  ms,  $P = 0.01$ ). There was no difference in terms of the segmental  $T_1$  precision between the two methods across all segments ( $P = N.S.$  for all). The results of the segment-based  $T_1$  analysis is depicted in Supporting Figure S2a. The segment-based  $T_2$  analysis revealed that there were no difference between the conventional and proposed  $T_2$  mapping across segments in terms of the  $T_2$  values and  $T_2$  precision ( $P = N.S.$  for all), except for the anteroseptal segment, where there was a difference for both the  $T_2$  values ( $46.9 \pm 2.9$  ms vs.  $46.0 \pm 2.9$  ms,  $P = 0.02$ ) and precision ( $7.7 \pm 1.6$  ms vs.  $9.1 \pm 1.9$  ms,  $P < 0.01$ ). The results of the segment-based  $T_2$  analysis is depicted in Supporting Figure S2b. Furthermore, for all methods, there was a loss of precision in the lateral segments compared to the septal segments ( $P < 0.01$  for all), consistent with previous studies (34).

## Discussion

In this study, we developed a sequence for simultaneously estimating co-registered myocardial  $T_1$  and  $T_2$  maps, based on a combination of saturation-recovery and  $T_2$ -preparation pulses. The proposed sequence was acquired in a single breath-hold over 13 heartbeats. In phantom studies, we established the accuracy of this sequence with respect to spin echo imaging, and also showed that the proposed sequence is heart-rate independent. We also showed that for in-vivo data, the quantified septal values were similar to existing methods for individual myocardial  $T_1$  or myocardial  $T_2$  mapping.

In terms of  $T_1$  quantification, the accuracy and precision associated with the proposed method were similar to those of the saturation-recovery based SASHA  $T_1$  mapping. It is understood that SASHA  $T_1$  mapping has better accuracy compared to Look-Locker based sequences, albeit with a degraded precision (23). Since our sequence utilizes a saturation-recovery approach for generating the  $T_1$  weighting of the individual images, the similarity in characteristics to SASHA sequence is warranted.

For  $T_2$  quantification, the accuracy of the proposed method was similar to a conventional  $T_2$  mapping sequence with 4  $T_2$ prep echoes, acquired over 12 seconds at 60 bpm. The correspondence between these sequences is not straightforward, since the  $T_2$  weighting in the proposed sequence is applied after a saturation recovery pulse (except for the image with no preparation), resulting in a diminished SNR for these images. This seeming disadvantage is mitigated by the ability to acquire an image at every heartbeat due to use of the saturation pulse to erase the magnetization history. On the other hand, the conventional sequence has a higher SNR, but requires multiple rest periods for magnetization re-growth, limiting the number of acquired images. Experimentally, this trade-off offsets the differences, and results in similar accuracy, albeit with a higher precision.

Previous joint  $T_1/T_2$  estimation techniques rely on combinations of inversion recovery and  $T_2$ prep (28-30). In (28), a sequence for the simultaneous estimation of  $T_1$  and  $T_2$  maps was proposed using interleaved inversion and  $T_2$ prep pulses. However, this sequence requires multiple relaxation cycles, necessitating a lengthy free-breathing scan, as opposed to a single breath-hold. In (29), an alternative joint estimation sequence was proposed based on the inversion-recovery balanced steady-state free-precession (bSSFP) curve. Due to the characteristics of this curve, the estimation is performed sequentially, by first estimating  $T_1$ , and using it to estimate  $T_2$ , as opposed to a simultaneous estimation procedure. Another approach acquires an image with no-preparation, followed by a  $T_2$ -prepared image, and an inversion pulse, after which 5 images are acquired using a triggered Look-Locker approach (30). These latter sequences can be acquired in a single breath-hold, and were shown to have accuracy similar to MOLLI, which was shown to have lower accuracy compared to saturation-recovery based  $T_1$  mapping sequences (23).

Nulling of the magnetization after the saturation pulse is essential for the performance of saturation recovery based mapping technique. Both composite and adiabatic saturation pulses have been shown to provide robust saturation in cardiac applications (31). Optimization of saturation pulses for myocardial mapping applications is an ongoing area of research (36), and these can be implemented into the current sequence in a straightforward manner. For saturation recovery techniques, it is important to note that in the low SNR regime, the noise in the images will be Rician, whereas the curve fitting process promotes a Gaussian noise model, which may lead to biases, although this was not observed in our study. The noise model mismatch may also be mitigated by multiple averages of the low SNR images.

A joint  $T_1/T_2$  mapping sequence provides complementary information through co-registered  $T_1$  and  $T_2$  maps in a single scan. The proposed sequence achieves this in the same time as an individual myocardial  $T_1$  or  $T_2$  mapping scan. Including the time for the patient to recover



between breath-holds for individual  $T_1$  and  $T_2$  mapping scans, this would lead to a scan time saving of more than 2-fold. Furthermore, the inherent co-registration may potentially facilitate distinguishing between fibrosis, acute or chronic myocardial infarction (30). However, since we are not aware of any clinical studies that use co-registered myocardial  $T_1$  and  $T_2$  maps, the incremental utility of this information is not known, and is beyond the scope of this work. Another benefit of simultaneously estimating the  $T_1$  and  $T_2$  maps, as opposed to a sequential estimation process, is that potential bias caused by one relaxation time in the fitting of the other is removed.

In this study, all in vivo datasets were acquired using a breath-hold approach. Respiratory drift may occur in patients that have problems breath-holding, which may corrupt the estimated  $T_1$  maps and their homogeneity, although this was not observed in the healthy subjects. Registration of the individual images using advanced techniques may be beneficial in patients (37).

This study has several limitations. Only a small number of healthy subjects were recruited. Further clinical evaluations on larger cohorts are warranted to quantify changes in  $T_1$  and  $T_2$  relaxation times in different populations using the proposed method. No validation of the  $T_1$  or  $T_2$  values has been performed in vivo, since a reference time cannot be assessed in the myocardium in a reasonable scan time. Only a single mid-ventricular short-axis slice was imaged in this study. In the proposed approach, a saturation recovery pulse is used at every heartbeat, leading to lower SNR in the individual images, which translates to signal inhomogeneity and spatial variability in the  $T_1$  and  $T_2$  maps. The manual segmentation for the measurements in this study avoided high levels of signal inhomogeneity and contamination. This approach might not be adequate in patients with truly inhomogeneous myocardium, which may limit the application of this technique to diverse patient populations.

## Conclusion

The proposed sequence allows for simultaneous estimation of accurate and co-registered quantitative myocardial  $T_1$  and  $T_2$  maps, without exhibiting heart-rate dependence. It has similar accuracy compared to existing  $T_1$  and  $T_2$  maps sequences of the same duration, and has similar precision for  $T_1$  mapping, albeit having reduced precision for  $T_2$  mapping. Hence, the proposed method enables accurate simultaneous  $T_1$  and  $T_2$  quantification in half the scan time.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgements

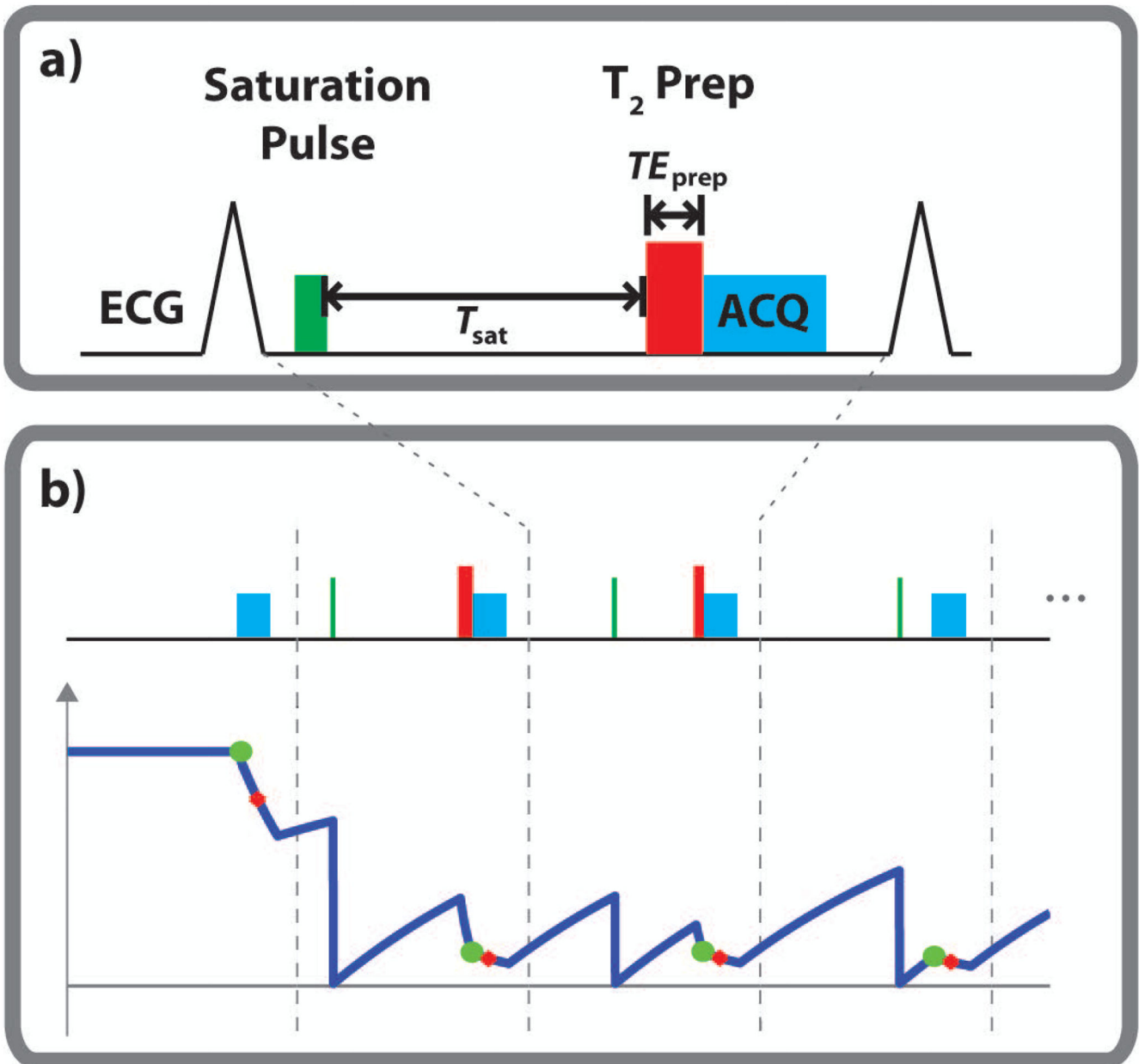
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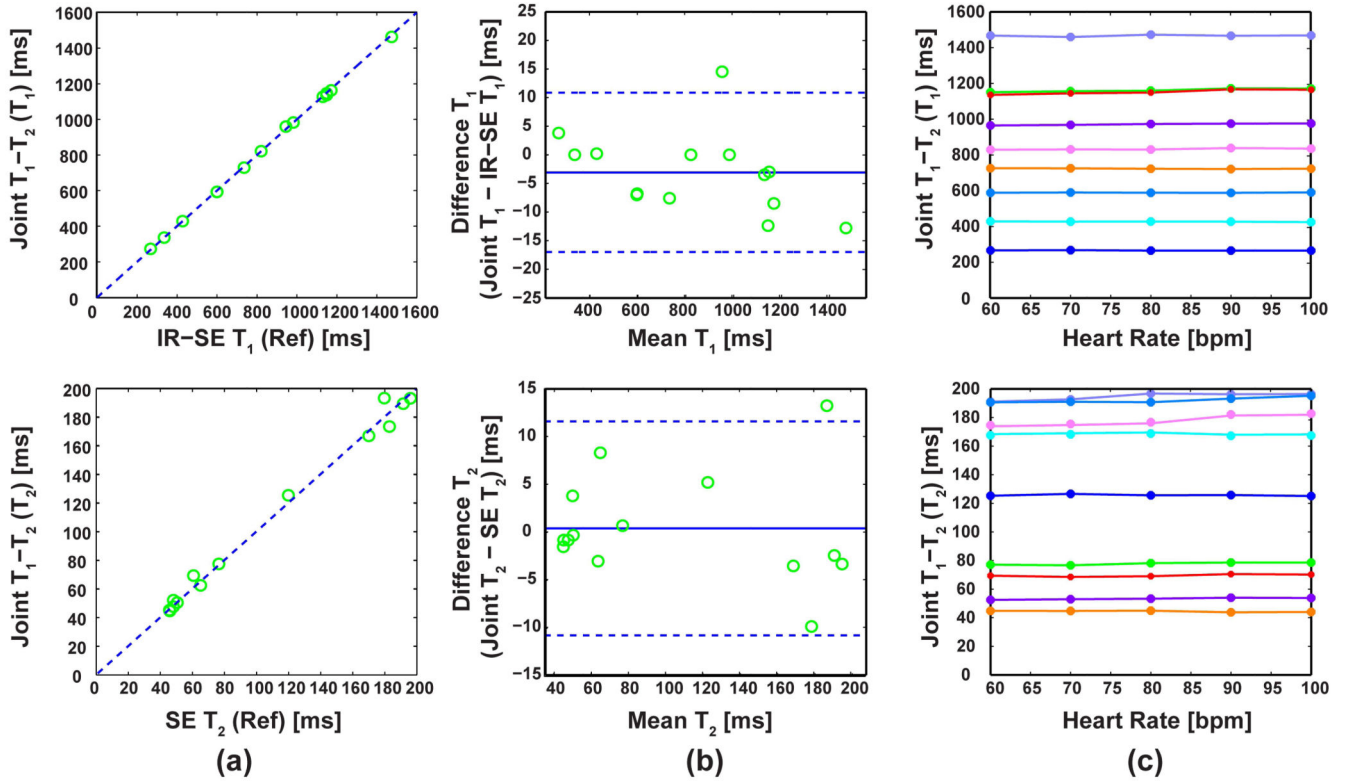
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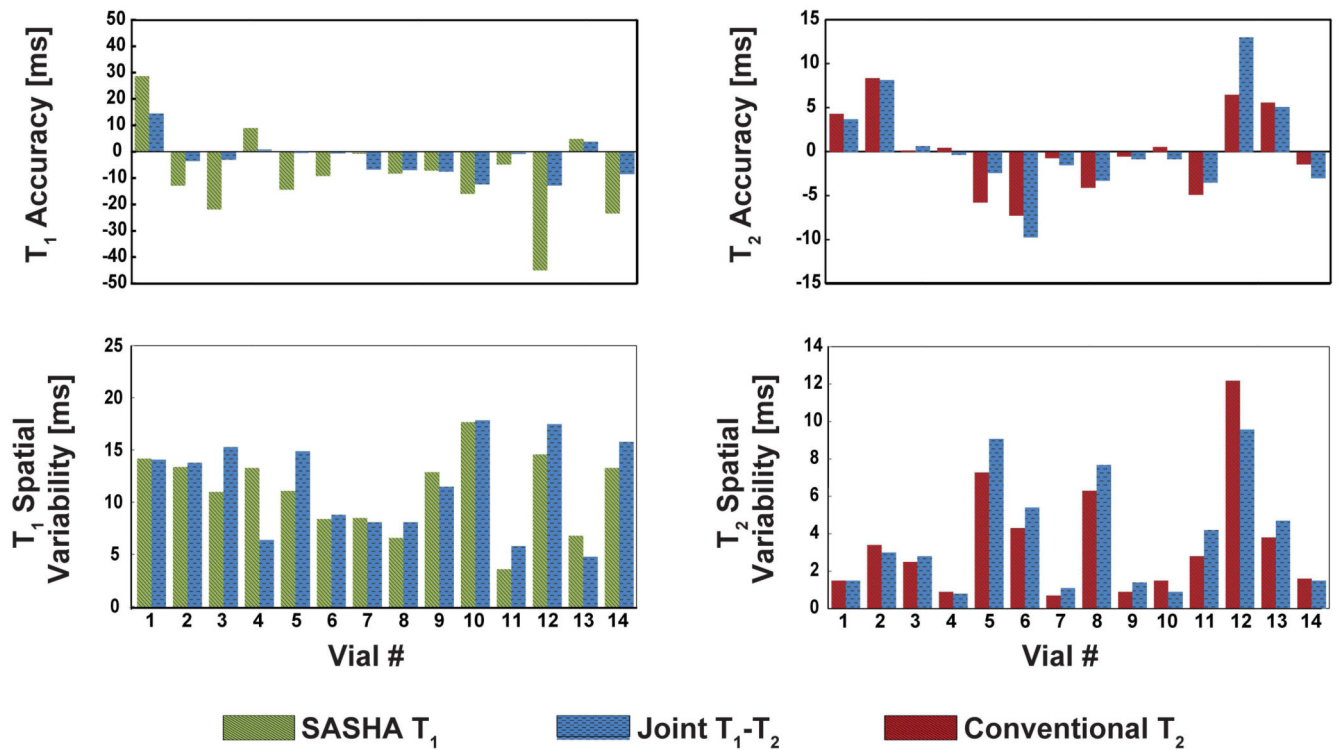
**Figure 1.**

(a) The sequence diagram. A saturation pulse is applied in every R-R interval to eliminate the magnetization history. Following  $T_1$ -based recovery for a duration of  $T_{sat}$ , a  $T_2$ -prep with echo length  $TE_{prep}$  is applied to generate the additional  $T_2$  weighting, after which a single-shot bSSFP image is acquired. (b) The mapping sequence acquires the first image with no magnetization preparation (corresponding to  $T_{sat} = \infty$  and  $TE_{prep} = 0$ ), followed by 12 images (3 are shown) acquired with different  $T_{sat}$  and  $TE_{prep}$  values. The major characteristics of the longitudinal magnetization signal curve are depicted under the pulse sequence diagram. The green circles indicate the magnetization at the end of the preparation pulses, whereas the red circles depict the magnetization when the k-space center is acquired, showing the effect of the bSSFP imaging pulses.



**Figure 2.**

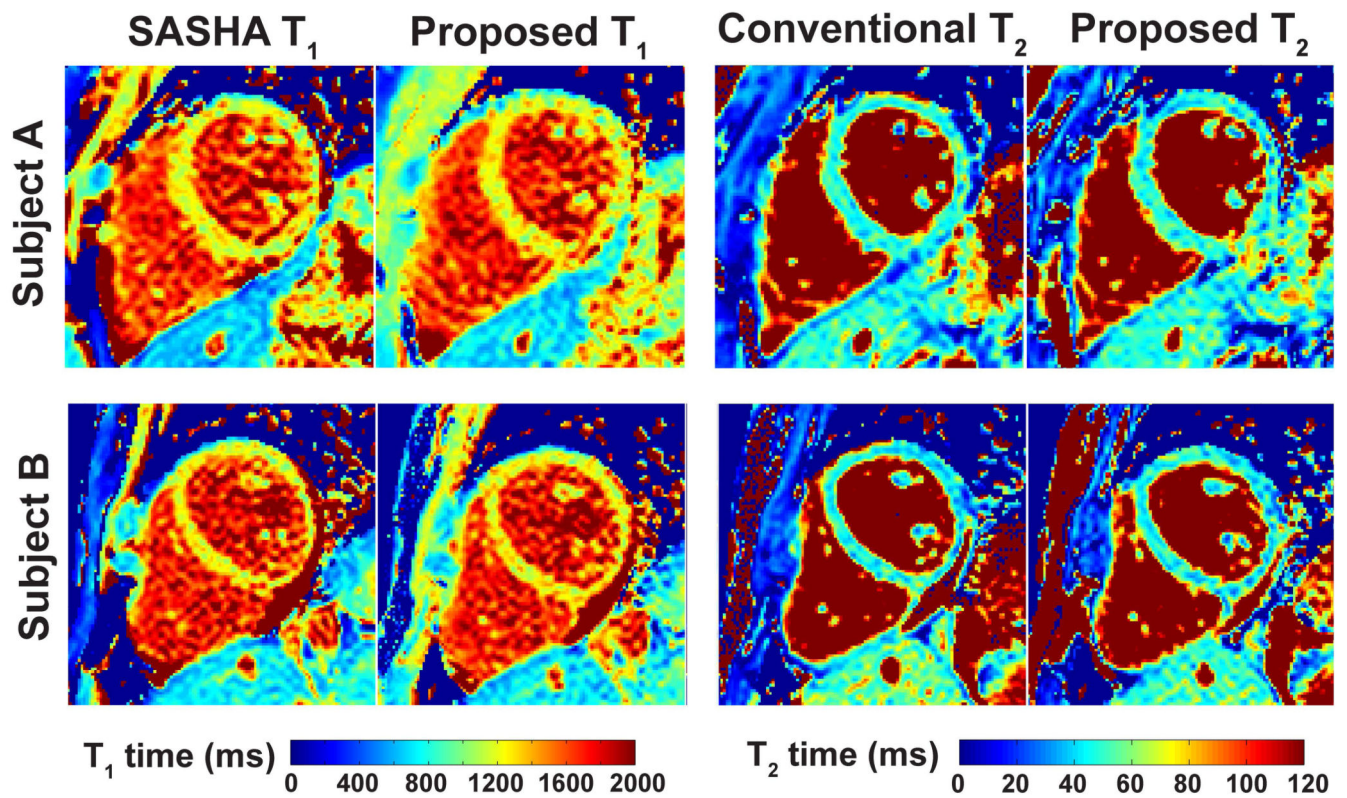
Phantom results comparing the proposed method to the reference values, as well as showing the heart-rate independence of the method. **(a)**  $T_1$  and  $T_2$  (top and bottom rows respectively) values from the proposed method versus the reference values from the spin echo sequences. The  $T_1$  and  $T_2$  values calculated using the proposed sequence were not different than the reference values ( $P = 0.49$  in both cases). **(b)** Bland-Altman plots comparing the proposed method and reference values, where the variation is within the acceptable range. **(c)** The  $T_1$  and  $T_2$  values (top and bottom rows respectively) in several vials using the proposed sequence for different heart rates, showing no correlation. The vials are color-coded consistently for the  $T_1$  and  $T_2$  graphs.



Vial #	1	2	3	4	5	6	7	8	9	10	11	12	13	14
T <sub>1</sub> (ms)	945	1131	1149	336	983	821	600	599	736	1149	428	1476	268	1172
T <sub>2</sub> (ms)	48	61	77	51	192	183	46	196	46	48	170	180	120	65

**Figure 3.**

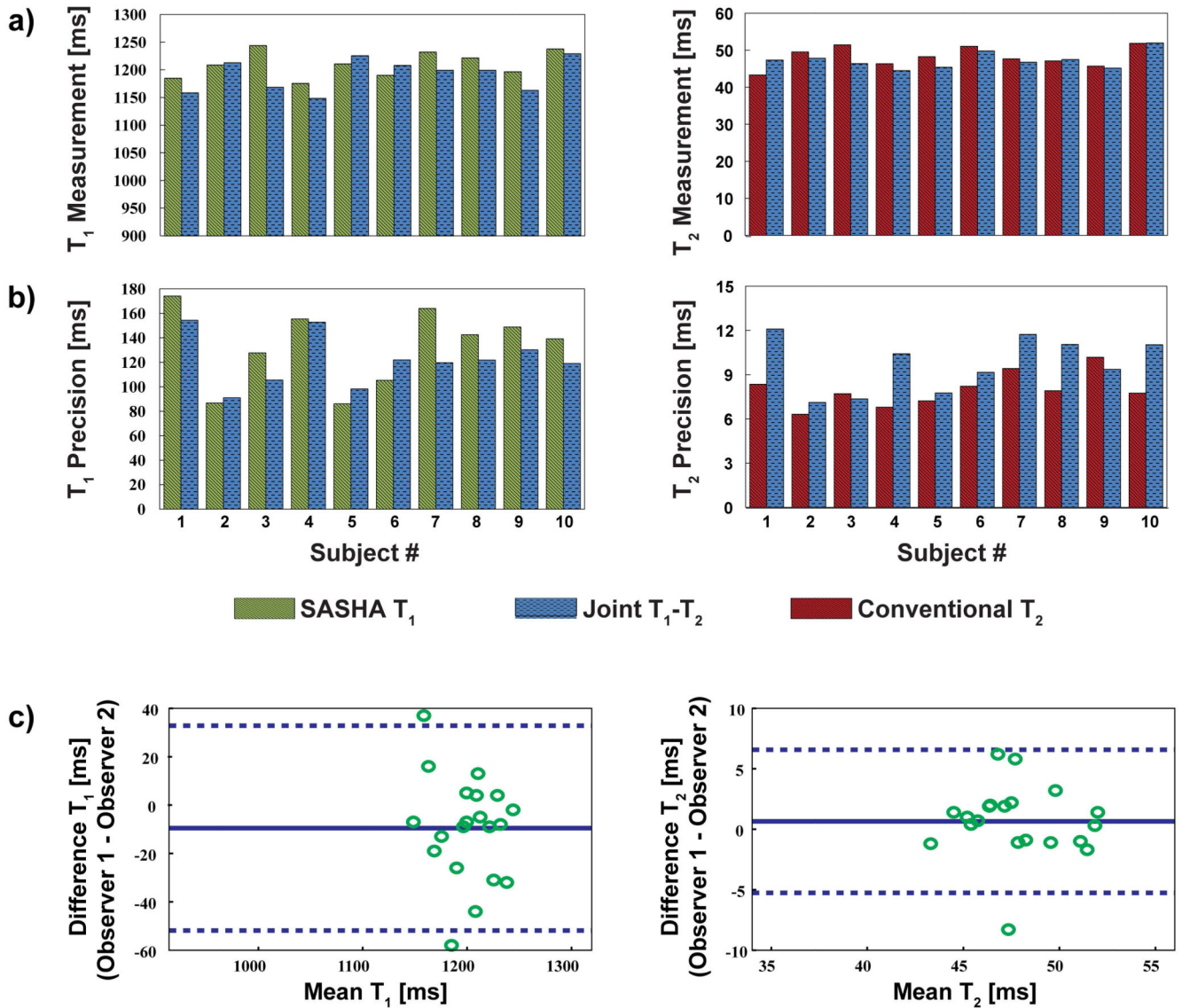
Phantom results comparing the proposed method with SASHA T<sub>1</sub> mapping and conventional T<sub>2</sub> mapping of same duration. There was no difference among the corresponding methods in terms of accuracy ( $P=0.11$  for T<sub>1</sub> and  $P=0.65$  for T<sub>2</sub>) or precision ( $P=0.34$  for T<sub>1</sub> and  $P=0.36$  for T<sub>2</sub>). The reference T<sub>1</sub> and T<sub>2</sub> values of the vials from the spin echo sequences are depicted as well.



**Figure 4.**

Example in vivo  $T_1$  and  $T_2$  maps from two different subjects. The maps are visualized with similar quality, and in both cases there was a good agreement of the myocardial  $T_1$  and  $T_2$  values (Subject A:  $1211 \pm 82$  ms vs.  $1210 \pm 92$  ms for SASHA and proposed  $T_1$  respectively;  $49.0 \pm 5.8$  ms and  $47.3 \pm 6.5$  ms for conventional and proposed  $T_2$  respectively. Subject B, the  $T_1$  and  $T_2$  values were:  $1217 \pm 90$  ms vs.  $1210 \pm 96$  ms for SASHA and proposed  $T_1$ ;  $47.8 \pm 7.0$  ms and  $45.6 \pm 7.3$  ms for conventional and proposed  $T_2$ ).





**Figure 5.**

Summary of the left ventricular septal T<sub>1</sub> and T<sub>2</sub> measurements for all healthy adult subjects, comparing the proposed joint T<sub>1</sub>/T<sub>2</sub> method with SASHA T<sub>1</sub> mapping and conventional T<sub>2</sub> mapping of same duration. **(a)** The estimated septal T<sub>1</sub> values were:  $1210 \pm 24$  ms and  $1191 \pm 29$  ms for SASHA and proposed T<sub>1</sub> mapping respectively ( $P = 0.06$ ). The estimated T<sub>2</sub> values were:  $48.2 \pm 2.8$  ms and  $47.3 \pm 2.3$  ms for conventional and proposed T<sub>2</sub> mapping respectively ( $P = 0.23$ ). **(b)** The precision in the septum was:  $133 \pm 31.0$  ms and  $121 \pm 20.7$  ms for SASHA and proposed T<sub>1</sub> mapping ( $P = 0.08$ ); and  $8.0 \pm 1.2$  ms and  $9.7 \pm 1.8$  ms for conventional and proposed T<sub>2</sub> mapping respectively ( $P = 0.01$ ). **(c)** The inter-observer variability was within the acceptable range ( $-9.6 \pm 42.3$  ms for T<sub>1</sub>;  $0.7 \pm 5.9$  ms for T<sub>2</sub>).