Magn Reson Med Sci 2018; 17; 35–41
doi:10.2463/mrms.mp.2016-0092
Published Online: May 18, 2017

MAJOR PAPER

Saturation Recovery Myocardial T_1 Mapping with a Composite Radiofrequency Pulse on a 3T MR Imaging System

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Purpose: To evaluate the effect of a composite radiofrequency (RF) pulse on saturation recovery (SR) myocardial T_1 mapping using a 3T MR system.

Materials and Methods: Phantom and *in vivo* studies were performed with a clinical 3T MR scanner. Accuracy and reproducibility of the SR T_1 mapping using conventional and composite RF pulses were first compared in phantom experiments. An *in vivo* study was performed of 10 healthy volunteers who were imaged with conventional and composite RF pulse methods twice each. *In vivo* reproducibility of myocardial T_1 value and the inter-segment variability were assessed.

Results: The phantom study revealed significant differences in the mean T_1 values between the two methods, and the reproducibility for the composite RF pulse was significantly smaller than that for the conventional RF pulse. For both methods, the correlations of the reference and measured T_1 values were excellent (r^2 = 0.97 and 0.98 for conventional and composite RF pulses, respectively). The *in vivo* study showed that the mean T_1 value for composite RF pulse was slightly lower than that for conventional RF pulse, but this difference was not significant (P = 0.06). The inter-segment variability for the composite RF pulse was significantly smaller than that for conventional RF pulse ($P < 0.01$). Inter-scan correlations of T_1 measurements of the first and second scans were highly and weakly correlated to composite RF pulses (r = 0.83 and 0.29, respectively).

Conclusion: SR T_1 mapping using composite RF pulse provides accurate quantification of T_1 values and can lessen measurement variability and enable reproducible T_1 measurements.

Keywords: *myocardial T_1 mapping, saturation recovery, composite radio-frequency pulse, reproducibility, 3T magnetic resonance*

Introduction

Myocardial T_1 mapping has garnered increasing attention as a basic tool for cardiac MR imaging in the research and clinical settings, as it holds promise as a method for scanner-independent T_1 contrast and provides useful quantitative tissue information.[1] Measurement of myocardial T_1 relaxation times using T_1 mapping is potentially useful for the detection of interstitial expansion due to myocardial edema, fibrosis, and deposition of protein and other T_1-altering substances, such as lipids and iron (hemorrhage, siderosis).[2–4]

Late gadolinium enhancement imaging is an advancement of T_1-weighted imaging that allows the operator to select and nullify "normal" tissue to exaggerate the signal from any tissue with a different T_1 values, thus identifying focally abnormal regions of fibrosis, edema, and amyloid. Meanwhile, myocardial T_1 mapping requires quantification of the exact T_1 of the myocardium. Different tissues have specific ranges of T_1 signals (measured in ms) at a particular magnetic field strength that can be used to detect pathology.[5]

Several T_1 mapping techniques using different acquisition schemes have been proposed to sample T_1 recovery

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Received: August 30, 2016 | Accepted: March 29, 2017

signals. Multiple images with different T_1-weighting are generally acquired for quantitative T_1 estimates using a model of the T_1 recovery signal. Inversion recovery (IR) sequences using look-locker techniques, such as modified look-locker IR (MOLLI)[6,7] and related variants (e.g., shortened MOLLI [ShMOLLI]),[8,9] are commonly used for T_1 mapping and saturation recovery (SR) sequences are available.[10] The most assessed T_1-mapping sequences are MOLLI and ShMOLLI. Although IR T_1 mapping sequences are sensitive to extreme heart rate values and tends to underestimate the true T_1 value, these methods allow highly reproducible T_1 mapping of the heart with high levels of intra- and inter-observer agreement.[11,12] SR methods can overcome the limitations of IR sequences that underestimate myocardial T_1 values and yield high accuracy and reproducibility,[12–15] but require high performance saturation pulses, particularly with a high-field (e.g., 3T) MR system. Poor saturation performance results in errors in calculated myocardial T_1 values. Our group recently optimized the SR T_1 mapping technique using a composite radiofrequency (RF) pulse[16] to obtain high saturation efficiency and accurate myocardial T_1 values. The purpose of the present study was to evaluate the effect of a composite RF pulse on SR myocardial T_1 mapping using a 3T MR system.

Materials and Methods

MR experiments

All studies were performed with a clinical 3T MR scanner (Achieva 3.0T X-series TX, Koninklijke Philips N.V., Amsterdam, the Netherlands) equipped with a 32-channel torso cardiac coil using a conventional multishot SR method. The SR T_1 mapping sequence in this study was based on two image acquisitions (short- and long-saturation time delay [TD] images), as described previously.[15] Scanning parameters of 2D turbo field echo using the SR method with conventional and composite RF pulses were as follows: repetition time/echo time = shortest/shortest; slice thickness = 8.0 mm; number of slices = 1, field-of-view = 36 × 36 cm^2; acquisition matrix = 128 × 128 (reconstruction matrix = 256 × 256); number of signal averages = 1; SENSE factor = 2.0; and saturation TD = approximately 5000 and 500 ms, with an electrocardiogram trigger and breath holding (only *in vivo* studies). T_1 can be calculated pixel-wise by dividing the short saturation TD image ($I_{TD\ short}$) by the long saturation TD image ($I_{TD\ long}$) to correct for the unknown longitudinal magnetization (M_0) and then solving the Bloch equation governing T_1 relaxation describing the ideal SR experiment, as follows:

$$[I_{TD\ short} = M_0\,(1 - e^{-TD/T_1})] \,/\, (I_{TD\ long} = M_0)$$

$$= (1 - e^{-TD/T_1})\,T_1 = -\,TD \,/\, log$$

$$(1 - I_{TD\ short} \,/\, I_{TD\ long})$$

Conventional and composite RF pulse schemes are shown in Figs. 1 and 2. Composite RF pulse-designed water suppression was enhanced through T_1 effects (WET). The WET presaturation pulse used in this study applied a four-pulse saturation train that was modified from the WET saturation scheme originally used for spectroscopy.[17] Previous articles demonstrated that this four-pulse scheme achieved better water suppression than conventional three-pulse chemical shift selective (CHESS) saturation schemes over a wide range of T_1 values and B_1 inhomogeneities.[18] To obtain optimal water suppression over a wide range of B_1 fields, a series of numerical simulations of the WET sequence were performed using the following description to minimize residual magnetization (M_R) under large B_1 and T_1 ranges:

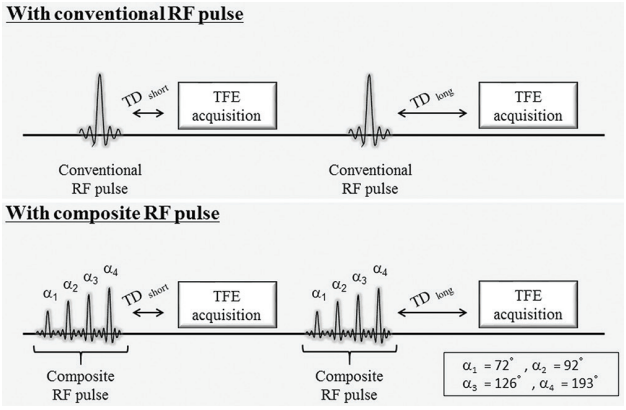

Fig. 1 Saturation recovery T_1 mapping sequence with conventional and composite radiofrequency (RF) pulses. Short and long saturation time delay images using a 2D turbo field echo readout. A composite RF pulse applied a four-pulse train to saturate magnetization uniformly and yielded more accurate and reproducible T_1 measurements on a high-field 3T MRI system. TD, time delay; TFE, turbo field echo.

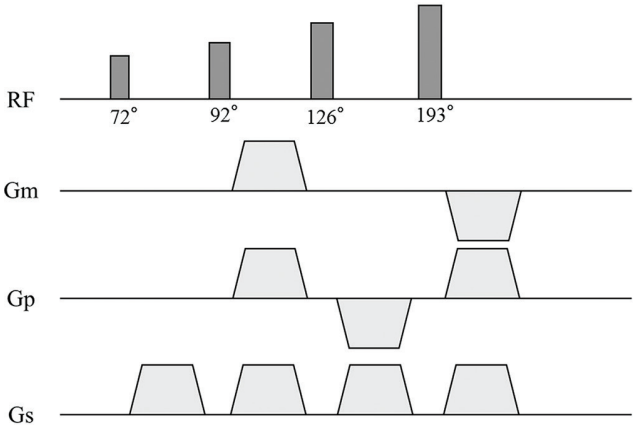

Fig. 2 Pulse sequence diagrams for the saturation recovery T_1 mapping sequence with composite radiofrequency (RF) pulse. The composite RF pulse consists of specified non-selective four hard pulses. The angles of these four pulses, α1, α2, α3, and α4 are used 72, 92, 126, and 193 degrees, respectively.

$$M_R(n) = M_0\{(1 - e^{TR/T_1})e^{-\tau/T_1}\cos\theta_1\cos\theta_2...\cos\theta_n + (1 - e^{-\tau/T_1})[e^{-(n-1)\tau/T_1}\cos\theta_2\cos\theta_3...\cos\theta_n + ... + e^{-\tau/T_1}\cos\theta_n + 1]\},^{19}$$

where M_0 is the equilibrium magnetization, n is the number of applied suppression pulses, θ_n is the flip angle of the *n*th RF pulse, and *TR* is the overall repetition time. This approximation of the residual magnetization assumes complete dephasing of the spins between pulses and localized instantaneous RF pulses.[20] Using a proprietary software program (PRIDE software, Philips Healthcare, Eindhoven, the Netherlands), myocardial T_1 maps were created with an automated image registration technique.

Phantom study

A phantom that contained eight cylindrical phantoms with different T_1 and T_2 values (T_1 = 230–1900 ms; T_2 = 40–110 ms) was used for comparisons of the T_1 mapping methods. T_1 reference values for the phantoms were determined using the gold standard IR spin echo sequence. Scanning parameters of IR spin echo sequence were as follows: repetition time/echo time = 10000/13 ms; slice thickness = 5.0 mm; number of slices = 1; field-of-view = 20 × 20 cm^2; acquisition matrix = 192 × 192; and inversion time = 100, 200, 400, 800, 1000, 1500, and 2000 ms. T_1 value was determined three times, and the average value of the three measurements was taken as the T_1 reference value. Each of the SR T_1 maps with conventional and composite RF pulses was acquired 10 times. Mean T_1 values were measured in the regions of interest (ROI) on each T_1 map. A ROI of at least 80% of the whole area was drawn on the center of the cylindrical phantoms.

In vivo study

Ten healthy volunteers (eight men and two women, age, 31.4 ± 7.9 years; range, 25–52 years) with no prior cardiac history or symptoms of cardiovascular disease or known cardiac risk factors, and not taking cardiovascular medications and with normal electrocardiography findings were enrolled in this study. Informed consent was obtained from all volunteers and the study protocol was approved by our institutional review board. Both SR T_1 mapping methods with conventional and composite RF pulses were performed two times each for all volunteers. On mid-ventricular short-axis T_1 map images, the myocardium in each segment (anterior, septal, lateral, and inferior segments) was manually contoured (Fig. 3).

Statistical analysis

All numeric values are reported as the mean ± standard deviation (SD). Differences in the mean values between the two methods with normally and non-normally distributed data were determined with the two-tailed independent *t*-test and the Mann–Whitney *U*-test, respectively. Correlations between the reference and measured T_1 values in the phantom study, and inter-scan correlations determined in the *in-vivo* study were assessed using the Pearson correlation or Spearman coefficient. The concordance correlation coefficient was used to explore the inter-scan agreement of the two methods. The root mean square error (RMSE) among reference T_1, composite RF pulse, and conventional RF pulse was calculated to evaluate the accuracy of each method. A Bland–Altman analysis was also used to compare the agreement of the first and second measurements for each method in the *in-vivo* study. To assess the inter-scan variability of the T_1 measurements, SD between the T_1 values over each myocardial segment for the conventional and composite RF pulse methods for *in-vivo* study were compared using the Levene test. A difference with a probability (*P*) value of < 0.05 was considered statistically significant. We used softwares for statistical analyses (MedCalc, MedCalc Software, Mariakerke, Belgium, JMP software, SAS Institute, Cary, NC, USA).

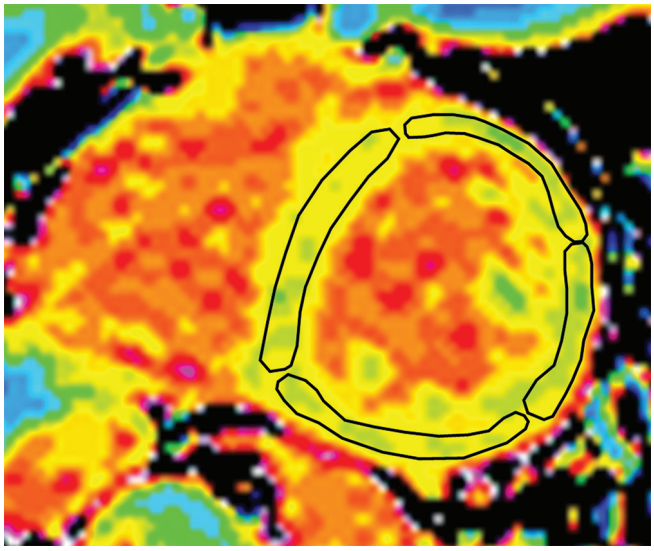

Fig. 3 For the *in vivo* study, we manually contoured the myocardium in each segment (anterior, septal, lateral, and inferior segments) on the mid-ventricular short-axis T_1 map image.

Results

Phantom study

The mean T_1 values and SD of the measured T_1 values for conventional and composite RF pulses are shown in Table 1. There were significant differences in the mean T_1 values of the vials except for vial no. 1 (reference T_1 value = 290 ms). SD of the measured T_1 values for the each vial of the composite RF pulse was statistically significantly smaller than that for conventional RF pulses except for vial no. 1 (reference T_1 value = 290 ms) (Fig. 4). SD of the measured T_1 values for the composite RF pulse was less than 10 ms. On the other hand, that of the conventional RF pulses was larger, particularly with higher T_1 values. SD was more than 140 ms

Table 1. The mean and standard deviation (SD) of the measured T_1 values for conventional and composite radiofrequency (RF) pulses in the phantom study

Vial no.	T_1 reference value (ms)	Mean measured T_1 values (ms)			SD of the measured T_1 values (ms)		
		Conventional RF pulse	Composite RF pulse	*P* value	Conventional RF pulse	Composite RF pulse	*P* value
1	290	320.6	325.2	0.27	12.2	7.3	0.17
2	570	561.3	579.3	<0.01	11.6	5.3	0.04
3	630	623.9	645.1	<0.01	16.8	6.7	0.02
4	810	768.9	863.4	0.03	99.7	9.7	<0.01
5	910	840.3	923	0.03	86.6	9.2	<0.01
6	1180	1095.2	1211	0.04	140.9	9.6	<0.01
7	1333	1242.6	1396.2	0.04	179.9	4.4	<0.01
8	1797	1543	1730.8	<0.01	164.4	1.2	<0.01

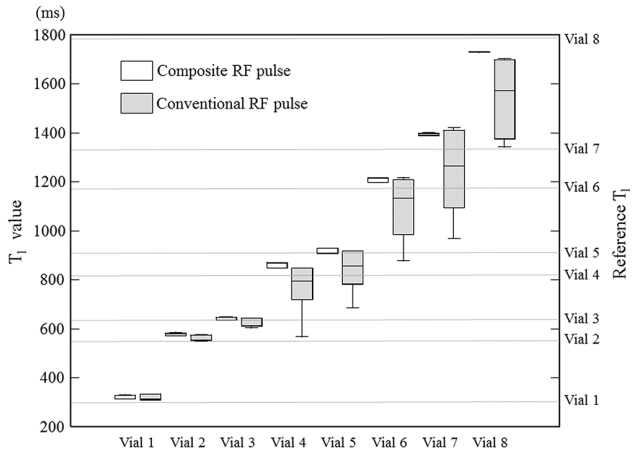

Fig. 4 Box plot showing the mean T_1 values of eight cylindrical phantoms (reference T_1 value = 290–1797 ms). There were significant differences in the mean T_1 values of the vials except for vial no. 1 (reference T_1 value = 290 ms). standard deviation (SD) of the measured T_1 values for the composite radiofrequency (RF) pulse was significantly smaller than that for conventional RF pulse except for vial no. 1. SD of the measured T_1 values for composite RF pulse was >10 ms.

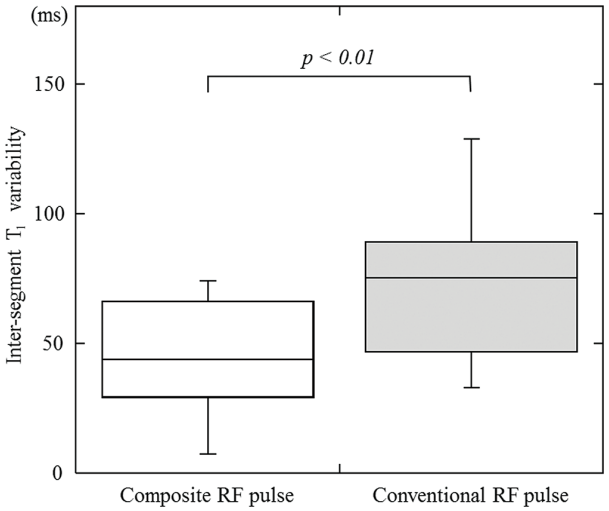

Fig. 5 Box plot showing the inter-segment variability for the composite radiofrequency (RF) pulse of the *in vivo* study. The inter-segment variability for the composite radiofrequency (RF) pulse was significantly smaller than that for the conventional RF pulse (44.5 ± 21.4 vs. 72.8 ± 29.2 ms, $P < 0.01$).

in vial number 6 (reference T_1 value = 1180 ms), 7 (1333 ms), and 8 (1797 ms). For both methods, the correlations of the reference and measured T_1 values were excellent ($r^2 = 0.97$, $P < 0.01$ [conventional RF pulse], and $r^2 = 0.98$, $P < 0.01$ [composite RF pulse]). The composite RF pulse method showed the smaller values of RMSE than those of conventional RF pulse method (41.9 ms vs. 146.9 ms).

In vivo study

The mean T_1 value for the composite RF pulses was slightly lower than that for the conventional RF pulses, but this difference was not significant (1415 ± 35.6 vs. 1456 ± 51.6 ms, $P = 0.06$). The inter-segment variability for the composite RF pulses was significantly smaller than that for conventional RF pulses (44.5 ± 21.4 vs. 72.8 ± 29.2 ms, $P < 0.01$) (Fig. 5). Correlation coefficients (r) and concordance correlation coefficient (ρ_c) for the inter-scan agreement were 0.29 ($P = 0.41$) and 0.28, respectively, for the conventional RF pulse and 0.83 ($P < 0.01$) and 0.64, respectively, for composite RF pulse. Inter-scan comparisons showed a lower Bland–Altman limit of agreement with the composite RF pulse (mean difference, −26.5 ms; 95% limit of agreement, −70.0–17.0 ms; coefficient of repeatability, 66.3) than with the conventional RF pulse (9.9 ms; –140.9–160.7 ms; 144.3) (Fig. 6).

Discussion

Our phantom study demonstrated that myocardial T_1 mapping with the SR method using composite RF pulses yielded more accurate and less variable measurements for a wide range of T_1 values as compared with the conventional RF pulse method. Meanwhile, the results of our *in-vivo* study

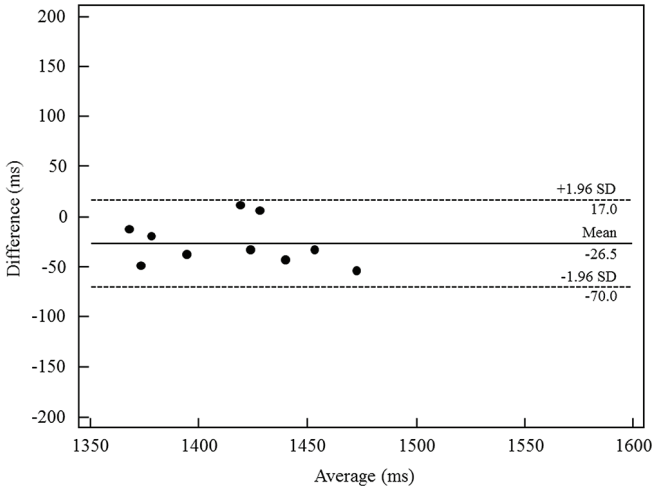

Fig. 6 Bland–Altman analysis of the T_1 measurements for the composite radiofrequency (RF) pulse methods. The lower Bland–Altman limit of agreement was with the composite RF pulse method. SD, standard deviation.

showed that use of composite RF pulses significantly reduce inter-segment variability of T_1 values with excellent inter-scan correlations.

Myocardial T_1 values are altered in various disease states due to increased water content or other changes to the local molecular environment. Changes in myocardial T_1 values are considered important biomarkers. Characterization of the T_1 values of myocardial tissue may be used to detect and assess various cardiac diseases and have been shown to convey important prognostic significance.[1,21] Furthermore, T_1 mapping has the potential to detect and quantify various cardiac diseases at early stages of disease.[1,21]

Multiple approaches are currently available to obtain myocardial T_1 values, including IR and SR sequences. However, the collection of further information regarding the accuracy, precision, and reproducibility of the different approaches is crucial to reach consensus.[22] Roujol et al.[12] compared the accuracy, precision, and reproducibility of IR methods (MOLLI and ShMOLLI), the SR method (saturation recovery single-shot acquisition [SASHA]), and a combined method (saturation pulse prepared heart rate independent IR [SAPPHIRE]) for myocardial T_1 mapping, and reported that SASHA and SAPPHIRE yielded higher accuracy, lower precision, and similar reproducibility as MOLLI and ShMOLLI for T_1 measurements. They also found that MOLLI and ShMOLLI led to an underestimation of myocardial, particularly with higher T_1 values. Other studies identified several factors affecting MOLLI measurements, including T_2-dependence, the magnetization transfer effect, flow, motion, and dependence on the inversion efficiency.[12,13,23] SR sequences yielded excellent accuracy for a wide range of T_1 values that are less sensitive to the magnetization transfer effect as well as other factors.[12] SR techniques are, however, noisier and somewhat more artifact prone because of non-ideal saturation efficiency at this point in time. The SR sequence with composite RF pulse applied in our study is a newly developed SR acquisition method for T_1 mapping. Using composite RF pulses as pre-saturation pulses, saturated magnetization is uniform and yields more accurate and reproducible T_1 measurements with a high-field 3T MR system. Our SR T_1 mapping sequence with a composite RF pulse is based on only two images, short and long TD images, whereas MOLLI acquires 11 images with different inversion times during 17 heartbeats and requires a relatively long breath-hold duration. SASHA also consists of 10 images acquired over consecutive heartbeats.[10] Unlike MOLLI and SASHA, our method is inherently insensitive to heart rate and rhythm conditions[15] and has less misregistration of post-processed T_1 map images caused by breathing, patient movement, and mistriggering. Furthermore, while MOLLI and SASHA are a commercial or research application, our SR T_1 mapping sequence consist of commonly-used pulse sequences that do not require a commercial application.

Composite saturation pulses composed of trains of shaped RF pulses with mathematically optimized flip angles have been designed for several different ranges of B_0 and B_1 scale factors. For instance, enhanced water suppression has been achieved over narrow ranges of B_0 and B_1 for MR spectroscopy at 1.5-T[17] and optimized composite pulses have been employed for wide B_0/B_1 ranges at 7.0-T system.[24] Composite saturation pulses with flip angles optimized for high performance over B_0 and B_1 ranges expected at 3T systems have also been investigated *in-vivo*.[25,26] However, the maximum residual longitudinal magnetization of more than 8% of this design may be a significant cause of error when applied to quantitative imaging sequences. Chow et al.[14] optimized composite saturation pulses for quantitative SR T_1 mapping for 1.5-T and 3T systems, and achieved absolute residual longitudinal magnetization of less than 1% in phantom experiments, enabling greater accuracy in quantitative SR T_1 imaging. In accordance with our findings, they concluded that optimized composite saturation pulses can minimize errors in quantitative SR T_1 mapping. In our phantom results, T_1 measurement variability for composite RF pulse was significantly smaller than that for conventional RF pulses except for short T_1 value object (vial no. 1, reference T_1 value = 290 ms). It can be assumed that the signals fully recover with short delay time regardless of the type of saturation pulse in short T_1 objects. Meanwhile, the signals can vary during signal recovery process in long T_1 objects unless they are high performance saturation pulses.

There were some limitations to our study that should be addressed. First, the study cohort included a small number of volunteers; thus, our proposed techniques must be rigorously evaluated in large-scale clinical investigations. Second, the volunteers were limited to relatively young healthy adults, while in actual clinical practice, patients demonstrate a wide range of pathologic myocardial T_1 values and greater variability in body size, heart rates, and motion artifacts, as

compared with healthy volunteers, which may affect the results. Third, while post-contrast T_1 mapping and extracellular volume (ECV) measurements are useful for the detection of diffuse interstitial fibrosis[27] and provide interesting insights into various cardiac diseases,[1,21] we did not perform post-contrast T_1 mapping and did not assess the ECV. To address these issues, studies are underway to determine whether SR T_1 mapping with composite RF pulses convey additional advantages for ECV measurements. Fourth, although the composite RF pulse method lessens the measurement variability, a possibility cannot be denied that the real T_1 variability becomes obscure. Regional differences in native myocardial T_1 values for healthy adult in MOLLI sequences have been previously reported; the native T_1 values were longer in the left ventricular septum vs. lateral wall.[28] B_1 inhomogeneities and motion artifacts in the lateral wall may affect the regional differences in native myocardial T_1 values. Although SR T_1 mapping using composite RF pulse may lessen the regional differences in native myocardial T_1 values by the better B_1 inhomogeneities and higher temporal resolution, further investigations are needed to confirm this issue. Fifth, we did not compare our SR T_1 mapping method to the MOLLI method, which is the most common T_1 mapping sequence. Therefore, further studies comparing these T_1 mapping methods are required. Finally, different results may be obtained if different MR systems are used because myocardial T_1 values are variable between the systems and sequences.

In conclusion, the proposed T_1 mapping with the SR method using composite RF pulse provides accurate quantification of myocardial T_1 values and can lessen measurement variability and enable reproducible myocardial T_1 measurements when compared to the use of conventional RF pulse.

Conflicts of Interest

Tomoyuki Okuaki is an employee of Philips Ltd. The other authors declare no conflicts of interest in regard to the products under investigation or the subject matter discussed in this manuscript.

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