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. 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).

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.

Several $T_1$ mapping techniques using different acquisition schemes have been proposed to sample $T_1$ recovery information.
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.\(^\text{10}\) 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 tend 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.\(^\text{11-12}\) SR methods can overcome the limitations of IR sequences that underestimate myocardial $T_1$ values and yield high accuracy and reproducibility,\(^\text{12-15}\) 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\(^\text{16}\) 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.\(^\text{15}\) 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 ($I_{TD\text{ short}}$) by the long saturation TD image ($I_{TD\text{ long}}$) 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:

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

$$= (I - e^{-TD/T_1}) T_1 = -TD / \log (I - I_{TD\text{ short}} / I_{TD\text{ long}})$$

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 pre-saturation pulse used in this study applied a four-pulse saturation train that was modified from the WET saturation scheme originally used for spectroscopy.\(^\text{17}\) 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.\(^\text{18}\) 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 ($M_0$) 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, $a_1$, $a_2$, $a_3$, and $a_4$ are used 72, 92, 126, and 193 degrees, respectively.
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\[ M_R(n) = M_0 \left\{ (1 - e^{-\frac{TR}{T_1}})e^{-\frac{t}{T_1}} \cos \theta_1 \cos \theta_2 \ldots \cos \theta_n + \right. \\
\left. (1 - e^{-\frac{t}{T_1}})(e^{-(n-1)\frac{t}{T_1}} \cos \theta_2 \cos \theta_3 \ldots \cos \theta_n + \right. \\
\left. \ldots + e^{-\frac{t}{T_1}} \cos \theta_n + 1)^{19} \right\} \\
\]

where \( M_0 \) is the equilibrium magnetization, \( n \) is the number of applied suppression pulses, \( \theta_n \) 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 T1 maps were created with an automated image registration technique.

**Phantom study**

A phantom that contained eight cylindrical phantoms with different T1 and T2 values (\( T_1 = 230–1900 \) ms; \( T_2 = 40–110 \) ms) was used for comparisons of the T1 mapping methods. T1 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 = \( 20 \times 20 \) cm\(^2\); acquisition matrix = \( 192 \times 192 \); and inversion time = 100, 200, 400, 800, 1000, 1500, and 2000 ms. T1 value was determined three times, and the average value of the three measurements was taken as the T1 reference value. Each of the SR T1 maps with conventional and composite RF pulses was acquired 10 times. Mean T1 values were measured in the regions of interest (ROI) on each T1 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 T1 mapping methods with conventional and composite RF pulses were performed two times each for all volunteers. On mid-ventricular short-axis T1 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 T1 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 T1, 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 T1 measurements, SD between the T1 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).

**Results**

**Phantom study**

The mean T1 values and SD of the measured T1 values for conventional and composite RF pulses are shown in Table 1. There were significant differences in the mean T1 values of the vials except for vial no. 1 (reference T1 value = 290 ms). SD of the measured T1 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 T1 value = 290 ms) (Fig. 4). SD of the measured T1 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 T1 values. SD was more than 140 ms.
in vial number 6 (reference T<sub>1</sub> value = 1180 ms), 7 (1333 ms), and 8 (1797 ms). For both methods, the correlations of the reference and measured T<sub>1</sub> values were excellent (r<sup>2</sup> = 0.97, P < 0.01 [conventional RF pulse], and r<sup>2</sup> = 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<sub>1</sub> 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 ms 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 (ρc) 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<sub>1</sub> mapping with the SR method using composite RF pulses yielded more accurate and less variable measurements for a wide range of T<sub>1</sub> values as compared with the conventional RF pulse method. Meanwhile, the results of our *in-vivo* study...
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![Fig. 6 Bland–Altman analysis of the T<sub>1</sub> 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.](image)

showed that use of composite RF pulses significantly reduce inter-segment variability of T<sub>1</sub> values with excellent inter-scan correlations.

Myocardial T<sub>1</sub> values are altered in various disease states due to increased water content or other changes to the local molecular environment. Changes in myocardial T<sub>1</sub> values are considered important biomarkers. Characterization of the T<sub>1</sub> values of myocardial tissue may be used to detect and assess various cardiac diseases and have been shown to convey important prognostic significance.\(^1,2\) Furthermore, T<sub>1</sub> mapping has the potential to detect and quantify various cardiac diseases at early stages of disease.\(^1,2\)

Multiple approaches are currently available to obtain myocardial T<sub>1</sub> 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.\(^2\) 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<sub>1</sub> mapping, and reported that SASHA and SAPPHIRE yielded higher accuracy, lower precision, and similar reproducibility as MOLLI and ShMOLLI for T<sub>1</sub> measurements. They also found that MOLLI and ShMOLLI led to an underestimation of myocardial, particularly with higher T<sub>1</sub> values. Other studies identified several factors affecting MOLLI measurements, including T<sub>2</sub>-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<sub>1</sub> 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<sub>1</sub> mapping. Using composite RF pulses as pre-saturation pulses, saturated magnetization is uniform and yields more accurate and reproducible T<sub>1</sub> measurements with a high-field 3T MR system. Our SR T<sub>1</sub> 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<sub>1</sub> map images caused by breathing, patient movement, and mistriggering. Furthermore, while MOLLI and SASHA are a commercial or research application, our SR T<sub>1</sub> 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<sub>0</sub> and B<sub>1</sub> scale factors. For instance, enhanced water suppression has been achieved over narrow ranges of B<sub>0</sub> and B<sub>1</sub> for MR spectroscopy at 1.5-T\(^17\) and optimized composite pulses have been employed for wide B<sub>0</sub>/B<sub>1</sub> ranges at 7.0-T system.\(^24\) Composite saturation pulses with flip angles optimized for high performance over B<sub>0</sub> and B<sub>1</sub> 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<sub>1</sub> 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<sub>1</sub> imaging. In accordance with our findings, they concluded that optimized composite saturation pulses can minimize errors in quantitative SR T<sub>1</sub> mapping. In our phantom results, T<sub>1</sub> measurement variability for composite RF pulse was significantly smaller than that for conventional RF pulses except for short T<sub>1</sub> value object (vial no. 1, reference T<sub>1</sub> 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<sub>1</sub> objects. Meanwhile, the signals can vary during signal recovery process in long T<sub>1</sub> 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<sub>1</sub> 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\textsuperscript{27} and provide interesting insights into various cardiac diseases,\textsuperscript{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.\textsuperscript{28} $B_0$ 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 $B_0$ 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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