FULL PAPER

High-resolution myocardial $T_1$ mapping using single-shot inversion recovery fast low-angle shot MRI with radial undersampling and iterative reconstruction

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Objective: To develop a novel method for rapid myocardial $T_1$ mapping at high spatial resolution.

Methods: The proposed strategy represents a single-shot inversion recovery experiment triggered to early diastole during a brief breath-hold. The measurement combines an adiabatic inversion pulse with a real-time readout by highly undersampled radial FLASH, iterative image reconstruction and $T_1$ fitting with automatic deletion of systolic frames. The method was implemented on a 3-T MRI system using a graphics processing unit-equipped bypass computer for online application. Validations employed a $T_1$ reference phantom including analyses at simulated heart rates from 40 to 100 beats per minute. In vivo applications involved myocardial $T_1$ mapping in short-axis views of healthy young volunteers.

Results: At 1-mm in-plane resolution and 6-mm section thickness, the inversion recovery measurement could be shortened to 3 s without compromising $T_1$ quantitation. Phantom studies demonstrated $T_1$ accuracy and high precision for values ranging from 300 to 1500 ms and up to a heart rate of 100 beats per minute. Similar results were obtained in vivo yielding septal $T_1$ values of $1246 \pm 24$ ms (base), $1256 \pm 33$ ms (mid-ventricular) and $1288 \pm 30$ ms (apex), respectively (mean ± standard deviation, n = 6).

Conclusion: Diastolic myocardial $T_1$ mapping with use of single-shot inversion recovery FLASH offers high spatial resolution, $T_1$ accuracy and precision, and practical robustness and speed.

Advances in knowledge: The proposed method will be beneficial for clinical applications relying on native and post-contrast $T_1$ quantitation.

INTRODUCTION

Tissue characterization by native myocardial $T_1$ mapping as well as quantitation of perfusion and extracellular volume after contrast administration are essential ingredients of Cardiovascular magnetic resonance imaging (CMR) investigations and commonly performed by inversion recovery (IR) methods using Fast low-angle shot (FLASH),1,2 Echo planar imaging (EPI)3 or Steady-state free precession (SSFP) readouts4 according to the Look-Locker technique.5 To date, respective applications commonly rely on a modified Look-Locker inversion (MOLLI)6 or manifold derivatives therefrom (for a recent review of possibilities and limitations, see Kellman and Hansen7). In fact, despite widespread usage, most approaches still suffer from practical restrictions such as limited spatial resolution and/or compromised $T_1$ accuracy, so that further technical improvements are warranted.

Following the recommendations of the $T_1$ mapping Consensus Statement of the Society for Cardiovascular Magnetic Resonance and CMR Working Group of the European Society of Cardiology,8 the basic requirements and clinical needs for cardiac $T_1$ mapping comprise (i) speed, i.e. single-shot applications with measuring times of a few seconds only, (ii) $T_1$ accuracy, i.e. validated $T_1$ values with small standard deviations and without dependency on heart rate, (iii) sufficiently high spatial resolution, i.e. about 1-mm in-plane resolution and (iv) practical robustness, i.e. no motion sensitivity and no image artefacts due to susceptibility problems, SSFP bandings or radial streakings.

This work describes a novel method which effectively meets all aforementioned challenges. It is based on a single-slice acquisition during a brief breath-hold (typically 3 s only) which combines a single-shot IR-FLASH technique with pronounced radial undersampling of individual frames, iterative reconstruction by non-linear inversion (NLINV)9 and conjugate gradient methods as previously
described\textsuperscript{10,11} and fitting of a diastolic $T_1$ map after deletion of systolic (\textit{i.e.}, motion-affected) frames. The entire procedure is fully automatic and only requires triggering of the initial inversion pulse to early diastole. The results comprise both an image series representing the entire IR experiment and a colour-coded $T_1$ map where pixel intensities directly refer to $T_1$ values in milliseconds. The proposed $T_1$ mapping method complements previous real-time MRI acquisitions of cardiac function and flow\textsuperscript{12–15} which together bear the potential to develop a comprehensive real-time CMR examination.

**METHODS AND MATERIALS**

All measurements were performed on a human MRI system operating at 3 T (Magnetom\textsuperscript{®} Prisma fit; Siemens Healthcare, Erlangen, Germany). Phantom measurements employed the 64-channel head coil, whereas human heart studies were performed using the 18-element thorax coil in combination with 12 elements of the 32-element spine coil. Six young subjects (two female, four male, age range 24–27 years) with no known illness (heart rate about 50–55 beats per minute (bpm)) were recruited among the students of the local university. Written informed consent, according to the recommendations of the local ethics committee, was obtained from all subjects prior to MRI.

According to the $T_1$ mapping Consensus Statement,\textsuperscript{8} experimental validations of the proposed technique were performed at different simulated heart rates with the use of a commercial reference phantom (Diagnostic Sonar Ltd, Scotland, UK) consisting of six compartments with defined $T_1$ values surrounded by water. As suggested, a long-repetition time (TR) IR fast spin echo (FSE) sequence with 13 logarithmically spaced inversion times between 50 and 2300 ms served for $T_1$ determination [TR = 7.2 s, echo time (TE) = 12 ms, 6 echoes and measuring time = 50 min].

The procedures for cardiac $T_1$ mapping described below (\textit{i.e.} data acquisition, image reconstruction and $T_1$ fitting) were implemented as an easy-to-use protocol on the MRI system by taking advantage of a bypass computer (sysGen/TYAN Octuple-GPU; Sysgen, Bremen, Germany) previously developed for real-time MRI\textsuperscript{9,15} and equipped with eight graphics processing units (NVIDIA\textsuperscript{®} GeForce\textsuperscript{®} GTX TITAN Black; NVIDIA, Santa Clara, CA). This bypass computer could be fully integrated into

Table 1. $T_1$ relaxation times for a reference phantom and simulated heart rates

| Heart rate\textsuperscript{c} | 0     | 40    | 60    | 80    | 100   |
|-------------------------------|-------|-------|-------|-------|-------|
| $T_1$, ms\textsuperscript{a}  | 331 ± 11 | 101 ± 2 | 315 ± 13 | 315 ± 13 | 314 ± 13 | 316 ± 13 | 317 ± 16 |
| $T_2$, ms\textsuperscript{b}  | 494 ± 22 | 46 ± 2  | 476 ± 18 | 475 ± 18 | 475 ± 18 | 476 ± 20 | 479 ± 23 |
|                               | 676 ± 19 | 81 ± 3  | 660 ± 25 | 659 ± 26 | 659 ± 26 | 661 ± 27 | 663 ± 29 |
|                               | 857 ± 25 | 132 ± 5 | 850 ± 28 | 850 ± 28 | 850 ± 28 | 852 ± 30 | 853 ± 30 |
|                               | 1225 ± 20 | 138 ± 4 | 1227 ± 34 | 1226 ± 34 | 1226 ± 34 | 1230 ± 36 | 1230 ± 37 |
|                               | 1501 ± 23 | 166 ± 5 | 1511 ± 42 | 1513 ± 43 | 1513 ± 44 | 1516 ± 46 | 1517 ± 50 |

\textsuperscript{a}$T_1$ values for a long-repetition time inversion recovery fast spin echo sequence.
\textsuperscript{b}$T_2$ values according to Sumpf et al.\textsuperscript{29}
\textsuperscript{c}Simulated heart rates (in beats per minute) correspond to the deletion of a 500-ms period ("systole") in each cardiac cycle. No images are deleted for zero heart rate.
the reconstruction pipeline of the commercial MRI system (Magnetom Prisma fit) by a single network connection. If the system software is compatible, the implementation takes less than an hour including installation of ready-to-use measuring protocols for cardiac $T_1$ mapping and other real-time CMR applications.

MRI acquisition and reconstruction
The chosen acquisition scheme for cardiac $T_1$ mapping is illustrated in Figure 1. In order to achieve maximum robustness and $T_1$ accuracy, a previously developed IR FLASH sequence\cite{10} was applied as a single-slice technique using a non-selective adiabatic 180° inversion pulse triggered to early diastole. The present study employed a simple and robust finger pulse trigger and a 100-ms delay to inversion. Although the method yields similar accuracy for a slice-selective inversion pulse when applied to stationary tissue (data not shown), cardiac $T_1$ mapping exclusively used a non-selective inversion pulse to minimize the effects of through-plane motion and myocardial perfusion.

Continuous image readout after inversion was based on a radial FLASH sequence with pronounced undersampling. Time-efficient spoiling of residual transverse magnetizations was accomplished by random radiofrequency (RF) phases.\cite{16} Cardiac $T_1$ maps were then acquired at a nominal in-plane resolution of $1.0 \times 1.0 \text{mm}^2$ and 6-mm section thickness using a field of view $= 256 \times 256 \text{mm}^2$ in combination with a resolution of 512 complex data points per radial spoke (using two-fold oversampling). All spokes were homogeneously distributed over 360°, whereas five successive frames used complementary sets of spokes in sequential order. Other parameters were $\text{TR} = 2.26 \text{ms}$, $\text{TE} = 1.47 \text{ms}$ and flip angle of 4°.

The number of spokes per frame varied from 27 to 23 and finally 19 spokes yielding a temporal resolution of 61, 52 and 43 ms, respectively. The total acquisition time was initially chosen to be 8 s but later reduced to 4 and 3 s.

Image reconstruction has previously been described for the case of non-cardiac $T_1$ mapping\cite{10,11} and employs the same iteratively regularized NLINV algorithm as developed for real-time MRI; for details, see Uecker et al.\cite{9} Apart from an advanced gradient-delay correction\cite{14} and data compression to 10 virtual channels based on a principal component analysis, the method takes advantage of some degree of spatial smoothness of coil sensitivities as well as of temporal regularization to the preceding frame. However, this latter term of the underlying cost function is downsized relative to the data consistency term by a factor of two during each iteration. The reconstruction ensures high temporal fidelity as demonstrated for a motion phantom rotating at defined speed\cite{17} and therefore does not compromise the resolution of contrast changes during inversion recovery.

The actual reconstruction process starts immediately after the end of data acquisition, first by a reverse NLINV reconstruction of the last 10 frames to obtain high-quality coil sensitivity maps using 6 iterations. Subsequently, the entire image series was reconstructed in the reverse order by fixing the coil sensitivities to those obtained by NLINV. The resulting linear inverse problem was solved by the iteratively regularized conjugate gradient method, again using six iterations.

Prior to $T_1$ fitting, the images were spatially filtered by a recently developed modified non-local means algorithm.\cite{18} The filter
preserves small isolated details and efficiently removes background noise [corresponding to a 60% signal-to-noise (SNR) improvement] without introducing blur, smearing or patch artefacts. This is accomplished by extending the conventional non-local means algorithm to adapt the influence of the original pixel value according to a simple measure for patch regularity. Detail preservation is improved by a compactly supported weighting kernel which closely approximates the commonly used exponential weight.

Temporal median filtering was only used for the purpose of displaying image series, whereas no temporal filter was used for $T_1$ mapping. The median filter extended over five frames to match the number of frames with different sets of spokes, e.g. in the studies of Uecker et al. and Frahm et al. As illustrated in Figure 1, the influence of systolic motion on the fitting of a diastolic $T_1$ map was minimized by automatically deleting images over a period of 500 ms starting from 400 ms prior to each finger pulse trigger signal.

$T_1$ quantitation

After reconstruction, spatial filtering and systolic deletion, the remaining complex images were fitted to the complex signal model:

$$M(t) = M_{ini} \left[ \gamma - (1 + \gamma) \exp \left( -\frac{t}{T_1^*} \right) \right]$$

(1)

where $M_{ini}$ is the initial complex signal after inversion; $t$ is the central time point (i.e. radial spoke) of each frame during inversion recovery; $\gamma$ is the ratio between the steady-state signal $M_{ss}$ and $M_{ini}$; and $T_1^*$ is the shortened apparent $T_1$ due to multiple low flip-angle RF excitations. The same phase is assumed for $M_{ss}$ and $M_{ini}$, which leads to four unknown real-valued parameters: $\text{Re}\{M_{ini}\}$, $\text{Im}\{M_{ini}\}$, $\gamma$ and $T_1^*$. A pixelwise estimation was performed using the Trust-Region algorithm (Chapters 4.1 and 4.3 in the study of Nocedal and Wright) based on the Dlib C++ library. The algorithm performs an unconstrained minimization of the cost function defined by

$$\frac{1}{2} \sum_i ((\text{Re}\{M(t) - Y(t)\})^2 + (\text{Im}\{M(t) - Y(t)\})^2)$$

(2)

where $Y$ corresponds to the vector of pixel intensities during inversion recovery. The iterative optimization was stopped if the relative difference of the objective function values between successive iterations was <10$^{-5}$. $T_1$ was then calculated according to:

$$T_1 = \frac{T_1^*}{\gamma} + 2\delta t$$

(3)
with $\delta t$ the delay between inversion and the start of data acquisition. In the present implementation, this period covered half of the inversion pulse (5 ms) and a following spoiler gradient (10 ms). For the assessment of myocardial $T_1$ values, the regions of interest were carefully selected to exclude contributions from the blood pool. These analyses were accomplished using the arrayShow tool in MATLAB® (MathWorks®, Natick, MA).

RESULTS
Table 1 summarizes $T_1$ relaxation times for a reference phantom. The data were acquired with the radial IR-FLASH method proposed for cardiac $T_1$ mapping (43-ms resolution and 3-s duration) at different simulated heart rates ranging from 40 to 100 bpm. Zero heart rate refers to $T_1$ fitting without deletion of any frames. A comparison with $T_1$ relaxation times obtained by a long-TR IR-FSE technique reveals excellent agreement for most (long) values, whereas two tubes with shorter values are slightly underestimated (maximum deviation 5%).

Figures 2 and 3 demonstrate cardiac $T_1$ maps for different numbers of spokes per frame, i.e. different temporal resolution, and different durations of the IR-FLASH measurement, respectively. In all cases, visual inspection reveals no detectable difference. This qualitative finding is confirmed by the quantitative analysis in Table 2.

The effect of filtering prior to $T_1$ fitting is demonstrated in Figure 4 comparing raw images and $T_1$ maps with and without application of a spatial filter. Figure 5 shows three $T_1$ maps for a single subject in a basal, mid-ventricular and apical short-axis section, whereas Figure 6 summarizes the mid-ventricular $T_1$ maps of all six subjects. A full cardiac image series which corresponds to the $T_1$ map in the mid-ventricular section of Figure 5 is available as Supplementary Video A. The quantitative results for all six subjects are summarized in Table 3 (septal $T_1$ values in a basal, mid-ventricular and apical section) and Table 4 (segmental $T_1$ values in a mid-ventricular section), respectively.

DISCUSSION
This work describes a novel method for myocardial $T_1$ mapping which offers accuracy, high spatial resolution, practical robustness and speed. The results indicate that myocardial $T_1$ mapping by IR-FLASH may be performed at a nominal resolution of 1.0 mm, a temporal resolution of 43 ms per frame and within a measuring time of only 3 s. $T_1$ accuracy was confirmed in a phantom study providing reference $T_1$ values for a long-TR IR-FSE sequence. A slight

Figure 5. Myocardial $T_1$ maps of a basal, mid-ventricular and apical section. Single-shot inversion recovery FLASH was performed at 43 ms resolution (19 spokes) for a duration of 3 s.

Figure 6. Myocardial $T_1$ maps of all six subjects (mid-ventricular section, magnified view). Single-shot inversion recovery FLASH was performed at 43 ms resolution (19 spokes) for a duration of 3 s.
therefore be due to a partial failure of the image of compounds and tissues with short acquisition which extends to a maximum TE of 72 ms and thus

This advantageous behaviour refers to the independence of relaxation times. Similar effects are to be expected for IR methods with a SSFP readout module, because such sequences require relatively long T2 relaxation times to build up sufficiently strong transverse coherences.

Apart from T1 accuracy, the results in Table 1 confirm the independence of T1 quantitation on the heart rate up to 100 bpm which effectively refers to the independence of T1 on the number of fitted images after elimination of “systolic” frames. This advantageous behaviour reflects the fact that the highly undersampled radial FLASH readout ensures a sufficiently large number of frames for a proper sampling of the IR signal time course. T1 precision was also demonstrated to be high both in vitro and in vivo. It is characterized by small standard deviation values of 3–5% of the mean for phantom measurements and 4–8% for septal T1 values (compare Tables 1–4). Moreover, the achieved T1 mapping quality not necessarily depends on the use of filtering as shown by the comparison in Figure 4. Nevertheless, although high-quality T1 maps may be obtained by fitting unfiltered images, the use of a new modified non-local means filter further improves the SNR of T1 maps without the expense of blurring.

Although myocardial T1 relaxation times found here were in general agreement with literature values, comparisons to previous results are compromised by numerous technical differences or even inadequacies. As an example, the present values are in the range of those reported in the study by Kawel et al but slightly higher than in that by Lee et al, and lower than in the study by Lee et al, who all used similar MOLLI sequences. Of course, all techniques including the one proposed here suffer from some general limitations of the Lock-Locker approach which often are due to

### Table 3. T1 relaxation times of the septal wall

| Subject | Basal T1, #frames | Mid-ventricular T1, #frames | Apical T1, #frames |
|---------|-------------------|-----------------------------|-------------------|
| #1      | 1250 ± 69/48      | 1266 ± 64/48                | 1298 ± 72/58      |
| #2      | 1237 ± 60/48      | 1263 ± 54/47                | 1291 ± 58/47      |
| #3      | 1270 ± 74/35      | 1287 ± 69/35                | 1332 ± 60/38      |
| #4      | 1277 ± 71/47      | 1295 ± 61/49                | 1298 ± 50/47      |
| #5      | 1215 ± 68/49      | 1209 ± 51/47                | 1256 ± 48/47      |
| #6      | 1227 ± 61/49      | 1227 ± 51/47                | 1253 ± 46/48      |
| Mean    | 1246 ± 24         | 1256 ± 33                   | 1288 ± 30         |
| von Knobelsdorff-Brenkenhoff et al | 1286 | 1157 | 1159 | 1181 |
| Lee et al | 1315 | 1157 | 1159 | 1181 |

*T1 (in milliseconds, mean ± standard deviation in a region of interest covering most of the septal wall) for single-shot inversion recovery-FLASH at 43 ms resolution (19 spokes) and 3 s duration. #Frames refers to the number of images retained after deletion of systolic frames.

### Table 4. Regional myocardial T1 relaxation times

| Subject | Anterior T1, ms | Septal T1, ms | Inferior T1, ms | Lateral T1, ms |
|---------|----------------|--------------|---------------|--------------|
| #1      | 1295 ± 70      | 1261 ± 70    | 1223 ± 95     | 1218 ± 70    |
| #2      | 1191 ± 60      | 1259 ± 56    | 1245 ± 91     | 1157 ± 64    |
| #3      | 1212 ± 62      | 1291 ± 68    | 1270 ± 89     | 1238 ± 69    |
| #4      | 1224 ± 64      | 1304 ± 64    | 1230 ± 92     | 1217 ± 68    |
| #5      | 1169 ± 56      | 1206 ± 59    | 1155 ± 79     | 1166 ± 57    |
| #6      | 1173 ± 56      | 1234 ± 58    | 1171 ± 66     | 1156 ± 69    |
| Mean    | 1211 ± 47      | 1259 ± 56    | 1216 ± 44     | 1192 ± 36    |

*T1 (in milliseconds, mean ± standard deviation per standardized region of interest in a mid-ventricular section) for single-shot inversion recovery-FLASH at 43-ms resolution (19 spokes) and 3-s duration.

*Mean ± standard deviation across subjects.
the presence of residual motion both in plane and through plane. For example, diastolic circulation of blood within the ventricles leads to image intensities which violate the expected IR signal model and preclude a reliable fitting of blood \( T_1 \) relaxation times. Even myocardial movements may play a role during early diastolic phases. However, this mainly becomes a problem for motion-sensitive readouts such as SSFP sequences, whereas short-TE FLASH sequences as used here and recently proposed by others\textsuperscript{26,27} are much less affected. This is because SSFP sequences inherently rely on the establishment of phase coherence over multiple repetition intervals which is commonly precluded (i.e. spoiled) in the presence of motion, whereas FLASH sequences interrogate a pool of longitudinal magnetization with independent low-flip angle excitations that give rise to spin-density weighted images for the low flip angles used for \( T_1 \) mapping. In fact, when exploiting the additional motion robustness of radial encodings in the present implementation, preliminary trials of myocardial \( T_1 \) mapping during free breathing showed little if any qualitative and quantitative difference to breath-hold scans (data not shown). Thus, the proposed method seems to be robust enough to even work in patients who are unable to perform any breathing protocol.

Another factor contributing to myocardial \( T_1 \) values is the different access to high spatial resolution and the concomitant consideration of partial volume effects. Such problems have been reported for thin myocardial walls\textsuperscript{7} including the assessment of fibrosis in the peri-infarct zone as well as for the right ventricle.\textsuperscript{28} These \( T_1 \) mapping studies using MOLLI techniques were performed at 1.4 $\times$ 1.9 $\times$ 8.0 mm\(^3\) for low heart rates and 1.9 $\times$ 2.3 $\times$ 8.0 mm\(^3\) at high heart rates.\textsuperscript{7} A higher resolution of 1.2 $\times$ 1.2 $\times$ 4 mm\(^3\) was only achieved with the use of a segmented readout module after inversion which therefore required repetitive acquisitions and very long measuring times of 2.5 min per \( T_1 \) map.\textsuperscript{28} Another recent work using IR-FLASH employed a sliding-window reconstruction\textsuperscript{27} at 1.17 $\times$ 1.17 $\times$ 8.0 mm\(^3\) resolution, which was achieved by twofold zero-padding, i.e. an interpolation of the acquired resolution. To the best of our knowledge, the method proposed here is the first technique for myocardial \( T_1 \) mapping which offers 1.0 $\times$ 1.0 $\times$ 6.0 mm\(^3\) resolution within a measuring time of only 3 s.

The most important limitation of this study is the small sample size. This is because the work represents a new technical development which requires basic validation with use of a \( T_1 \) reference phantom and a group of normal subjects. Obviously, this precedes any evaluation of the clinical utility of the proposed \( T_1 \) mapping in a large cohort of patients. Moreover, at this stage, widespread clinical applications are hampered by the fact that the technical solution requires dedicated software and hardware which so far is only available for MRI systems of the same manufacturer as used here. A remaining temporary restriction is the computational time needed for image reconstruction and \( T_1 \) fitting which currently takes about 13 s per \( T_1 \) map. Nevertheless, this may not necessarily block the clinical workflow, because a delayed reconstruction does not interfere with continuous acquisitions.

**CONCLUSION**

Myocardial \( T_1 \) mapping based on single-shot IR-FLASH with radial undersampling and iterative reconstruction as well as \( T_1 \) fitting with automated deletion of systolic frames meets most current clinical challenges. The proposed method warrants extensive clinical trials as it promises significant advantages for CMR studies which rely on native or post-contrast \( T_1 \) quantitation.

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