# Kirsten M. Becker\*, Jeanette Schulz-Menger, Tobias Schaeffter, Christoph Kolbitsch In vivo myocardial tissue characterization of all four chambers using high-resolution quantitative MRI

**Abstract:** Quantitative native  $T_1$  Mapping of the myocardium without the application of contrast agents can be used to detect fibrosis in the left ventricle. Spatial resolution of standard native T<sub>1</sub> mapping is limited by cardiac motion and hence is not sufficient to resolve small myocardial structures, such as the right ventricle and the atria. Here, we present a novel MR approach which provides cardiac motion information and native T<sub>1</sub> maps from the same data. Motion information is utilized to optimize data selection for T<sub>1</sub> mapping and a model-based iterative reconstruction scheme ensures high-resolution T<sub>1</sub> maps for the entire heart. Feasibility of the approach was demonstrated in three healthy volunteers. In the T<sub>1</sub> maps, the myocardium of all four chambers can be visualized and T1 values of the left atrium and right chambers were comparable to left ventricular T<sub>1</sub> values.

**Keywords:** T<sub>1</sub> mapping, myocardial tissue characterization, magnetic resonance imaging

https://doi.org/10.1515/cdbme-2018-0064

## 1 Introduction

Cardiovascular Magnetic resonance imaging (CMR) is an important modality for diagnosis of cardiovascular diseases. Fibrosis is considered to play a role in various cardiomyopathies, such as arrhythmias [1]. Qualitative CMR is used in clinical routine to detect fibrosis by late gadolinium enhancement imaging (LGE) in the ventricles and atria [2], but is limited to focal fibrosis. Recently, quantitative CMR ( $T_1$ ,  $T_2$  and  $T_2$ \* mapping) has become an important modality for myocardial tissue characterization [3,4]. Post-contract  $T_1$ mapping offers a method to assess focal and diffuse fibrotic tissue and post-contrast  $T_1$  times are suggested to be associated with atrial and ventricular fibrosis in arrhythmic patients [5-7]. However, contrast agents are required and observed  $T_1$  times are strongly depend on the contrast dose and delay time between contrast administration and measurement.

Native  $T_1$  mapping overcomes these limitations. Its main challenge is cardiac motion which strongly limits the achievable in-plane spatial resolution to approximately 2.0 x 2.0 mm<sup>2</sup> and therefore it is commonly only used in the left ventricle. For imaging of smaller structures, such as the right ventricle or the atria, with a thickness of less than 3 mm [8], spatial resolution is not sufficient.

In order to minimize cardiac motion, MR image acquisition is commonly restricted to the quiescent phase of the cardiac cycle (i.e. mid-diastole). The correct beginning and duration of data acquisition has to be set prior to the data acquisition and hence can only be estimated prospectively.

Here we demonstrate the feasibility of a high-resolution  $(1.0x1.0 \text{ mm}^2 \text{ in-plane resolution})$  native  $T_1$  mapping technique, that allows for mapping of all four chambers non-invasively. Cardiac motion information (cine images) is obtained from the same data prior to  $T_1$  reconstruction. The motion information is utilized to select only data with minimal cardiac motion for  $T_1$  mapping specifically for each subject and scan. This minimizes motion-induced blurring and optimizes the amount of data available for  $T_1$  mapping. A model-based iterative reconstruction technique is used to obtain accurate  $T_1$  maps obtained directly from the MR raw data. This ensures high quality  $T_1$  maps even from highly undersampled MR data.

<sup>\*</sup>Corresponding author: Kirsten M. Becker: Physikalisch-Technische Bundesanstalt (PTB), Abbestr. 2-12, Berlin, Germany, kirsten.becker@ptb.de

Jeanette Schulz-Menger: Charité Medical Faculty University Medicine, Working Group on Cardiovascular Magnetic Resonance, Experimental and Clinical Research Center (ECRC), DZHK partner site Berlin and Department of Cardiology and Nephrology, HELIOS Klinikum Berlin Buch, Berlin, Germany **Tobias Schaeffter, Christoph Kolbitsch**: Physikalisch-Technische Bundesanstalt (PTB), Braunschweig and Berlin, Germany and Division of Imaging Sciences and Biomedical Engineering, King's College London, London, United Kingdom



Figure 1: a) Data selection for T<sub>1</sub> mapping. b) Based on the cine image of the same acquisition, data for T<sub>1</sub> mapping within a window with minimal cardiac motion was selected.
c) T<sub>1</sub> was estimated using model-based iterative reconstruction.

## 2 Methods

#### 2.1 Data acquisition

2D data acquisition is performed continuously, with a spoiled gradient echo sequence. At constant time intervals, inversion pulses were applied (Figure 1a). Radial golden-ratio based data sampling with an angle increment of 111.25° between successive spokes allows for flexible reordering of the data. A recorded ECG signal was used for retrospective gating of the data to specific cardiac phases.

#### 2.2 Image reconstruction

Due to the small thickness of the atrial wall, even small cardiac motion can strongly impair the reconstructed  $T_1$  maps. In order to be able to select data with minimal cardiac motion, dark blood functional cine images showing the changes of the heart during the cardiac cycle were reconstructed prior to  $T_1$  mapping from the same raw data (Figure 1b) [9]. Cine reconstruction was performed using an iterative kt-SENSE approach [10]. Based on the cine images, a time frame for  $T_1$  mapping was selected, where cardiac motion was minimal (Figure 1b). The length of this frame is flexible and can be optimized for each subject.  $T_1$  maps of the selected data were reconstructed by model-based iterative reconstruction (Figure 1c) [9,11]. The iterative process includes:

- 1. Image reconstruction for all selected time points.
- T<sub>1</sub> estimation by pixel-wise three-parameter fitting to a signal model. The signal model describes the behaviour of the spoiled gradient echo signal of the longitudinal magnetization during continuous data acquisition and multiple inversions.
- 3. Model prediction for all time points.
- 4. Substitution of the model predictions by the initial k-space data for data consistency.

The iterative process was stopped after a fixed number of iterations.

#### 2.3 In vivo imaging

The proposed approach was evaluated in three healthy volunteers (3 males, aged  $29.7 \pm 3.5$  years). Within a 25 s breath-hold, 2D slices were acquired with the following settings: in-plane resolution:  $1.0x1.0 \text{ mm}^2$ , FOV:  $320x320 \text{ mm}^2$  with 2-fold oversampling in radial direction, slice thickness: 8.0 mm, flip angle: 5°, TE/TR: 2.03/5.3 ms and a fixed interval between inversions of 2276 ms. Slices were oriented in four-chamber view (4ChV) and a short axis through both atria (ASAX).

Cine images were reconstructed with 15 cardiac phases. Data for  $T_1$  mapping were selected in a window between 300 and 360ms per cardiac cycle, depending on cardiac motion. For comparison purpose,  $T_1$  mapping was also performed by a common  $T_1$  mapping technique for mapping of the left ventricle, a 3(3)3(3)5 modified Look Locker inversion recovery (MOLLI) [12] in ASAX view in one of the subjects with the following settings: FOV: 360x307 mm<sup>2</sup>, slice thickness: 8.0 mm, in-plane resolution: 2.1x1.4 mm<sup>2</sup> and integrated motion compensation.  $T_1$  values were assessed in a manually drawn region-of-interest in the septum, left and right atria and right ventricle in 4ChV.



**Figure 2:** T<sub>1</sub> maps of two subjects in 4ChV. The myocardium of the right atrium can be visualized (a), as well as the myocardial wall of the right ventricle (b).



**Figure 3:** a) T<sub>1</sub> map in ASAX. In this orientation, the myocardium of the left atrium can be visualized. b) T<sub>1</sub> map of the same subject obtained by a MOLLI sequence. Here, the myocardium of the left atrium cannot be fully distinguished.

### 3 Results

High-resolution  $T_1$  maps of the four chambers could be reconstructed for all subjects. T1 maps obtained by our approach and the MOLLI sequence are presented in figure 2 and 3. The result of the voxel-wise fit is shown in figure 4. R<sup>2</sup> of the fit was larger than 0.9 in all voxels within the heart.  $T_1$ values in the three subjects are shown in table 1. In figure 5 a  $T_1$  map is shown in 4ChV, together with a qualitative anatomical image from the same raw data and same cardiac phase and the overlay of the two images.

**Table 1:**  $T_1$  values obtained by our approach in all chambers in the three subjects (mean  $\pm$  standard deviation within the region-of-interest).

Subject	T₁ septum [ms]	T₁ right ventricle [ms]	T₁ left atrium [ms]	T₁ right atrium [ms]
1	1230 ± 84	1288 ± 91	1263 ± 89	1272 ± 143
2	1287 ± 73	1258 ± 85	1281 ± 90	1234 ± 126
3	1260 ± 76	1287 ± 67	1290 ± 76	1291 ± 135

### 4 Discussion

Small structures, such as the myocardium of the right ventricle and both atria can be seen in the  $T_1$  maps. In ASAX orientation, myocardium of the left atrium can be visualized by our  $T_1$  mapping approach, whereas left atrial myocardium cannot be identified in the standard MOLLI  $T_1$  map (Figure 3b), which could possibly be explained by lower resolution and residual cardiac motion during data acquisition.  $T_1$  values of the chambers were in the range of septal  $T_1$  in the same subjects and high  $R^2$  values for all myocardial voxels suggest



Figure 4: Result of the voxel-wise T<sub>1</sub> fitting. a) The T<sub>1</sub> Map is masked by the R<sup>2</sup> map (b). Only T<sub>1</sub> values with a R<sup>2</sup> of larger than 0.9 are visualized. R<sup>2</sup> is larger than 0.9 in the entire heart.



Figure 5: Qualitative anatomical scan, anatomical scan overlaid with the T1 map of the same acquisition and the T1 map (left to right).

a robust fit. The standard deviation of  $T_1$  values within the atrial region-of interest is higher than in the septum. This could be explained by the smaller number of voxels in the right atrial region-of-interest.

The overlay of  $T_1$  Map and structural image allows to immediately relate the  $T_1$  values to its underlying anatomy without any misregistration errors due to varying breath-hold positions and could be used for further analysis of the  $T_1$ map.

So far, cine images have only been used to select the quiescent phase of the heart but they could also be utilized to obtain motion information to correct for cardiac motion. This would allow for more data to be used for  $T_1$  mapping in each cardiac cycle and achieve a clinically feasible scan time.

Evaluation in patients with atrial and ventricular fibrosis has to be performed in future research.

### 5 Conclusion

The feasibility of native  $T_1$  mapping in both ventricle and atria was demonstrated for the first time. In the future, we will investigate the extension of the technique to 3D in order to further improve the accuracy of  $T_1$  maps especially in regions with complex geometry, such as the atria. This will ensure native  $T_1$  mapping can be used as non-invasive biomarker for diffuse and focal fibrosis in the whole heart in patients with arrhythmias.

#### **Author Statement**

Research funding: The authors state no funding involved. Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent has been obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

#### References

- Boldt A, Wetzel U, Lauschke J, et al. Fibrosis in left atrial tissue of patients with atrial fibrillation with and without underlying mitral valve disease.Heart. 2004;90(4):400-405.
- [2] McGann CJ, Kholmovski EG, Oakes RS, et al. New Magnetic Resonance Imaging-Based Method for Defining the Extent of Left Atrial Wall Injury After the Ablation of Atrial Fibrillation. J Am Coll Cardiol. 2008;52(15):1263-71.
- [3] Schelbert EB, Messroghli DR. State of the Art: Clinical Applications of Cardiac T1 Mapping. Radiology. 2016;278(3):658–76.
- [4] Messroghli DR, Moon JC, Ferreira VM, et al. Clinical recommendations for cardiovascular magnetic resonance mapping of T1, T2, T2 \* and extracellular volume : A consensus statement by the Society for Cardiovascular Magnetic Resonance (SCMR) endorsed by the European Association for Cardiovascular. J Cardiovasc Magn Reson. Journal of Cardiovascular Magnetic Resonance; 2017;19:75:1–24.
- [5] Beinart R, Khurram IM, Liu S, et al. Cardiac magnetic resonance T1 mapping of the left atrial myocardium, Heart Rhythm. 2013;10(9):1325-1331
- [6] McLellan AJ, Ling LH, Azzopardi S. Diffuse ventricular fibrosis measured by T<sub>1</sub> mapping on cardiac MRI predicts success of catheter ablation for atrial fibrillation. Circ Arrhythm Electrophysiol. 2014:7(5):834-840.
- [7] Chen Z, Sohal M, Voigt T, et al. Myocardial tissue characterization by cardiac magnetic resonance imaging using T1 mapping predicts ventricular arrhythmia in ischemic and non-ischemic cardiomyopathy patients with implantable cardioverter-defibrillators.Heart Rhythm. 2015;12(4):792-801.
- [8] Varela M, Kolbitsch C, Theron A, et al. 3D high-resolution atrial wall thickness maps using black-blood PSIR. Journal of Cardiovascular Magnetic Resonance. 2015;17(Suppl 1):P239.
- [9] Becker KM, Schulz-Menger J, Schaeffter T, Kolbitsch C. Multi-parametric cardiac MRI for T1 mapping and cine imaging using iterative model-based image reconstruction. Proc. Intl. Soc. Mag. Reson. Med 25. 2017.
- [10] Tsao J, Boesiger P, Pruessmann KP. k-t BLAST and k-t SENSE: dynamic MRI with high frame rate exploiting spatiotemporal correlations. Magn Reson Imaging. 2003;50:1031–1042.
- [11] Tran-Gia J, Stäb D, Wech T, et al. Model-based Acceleration of Parameter mapping (MAP) for saturation prepared radially acquired data. Magn Reson Med. 2013;70(1992):1524-1534.
- [12] Messroghli DR, Radjenovic A, Kozerke S, Higgins DM, Sivananthan MU, Ridgway JP. Modified look-locker inversion recovery (MOLLI) for high-resolution T 1 mapping of the heart. Magn Reson Med. 2004;52:141–6.