

MAJOR PAPER

Relationship between Measurement Errors in Myocardial T_1 Mapping and Heart Rate

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Purpose: Modified Look-Locker inversion recovery (MOLLI) using a 5s(3s)3s scheme is robust to tachycardia, but some errors are occasionally observed in myocardial T_1 mapping. We sought to evaluate the relationship between measurement errors in T_1 mapping and heart rate (HR) using a confidence map.

Methods: We enrolled 69 male patients with normal native T_1 values of the septal myocardium measured by a 5s(3s)3s MOLLI. The degree of measurement errors in the septal myocardium was assessed by two independent observers on a confidence map using a 4-point scale: 0, no errors; 1, errors located on the myocardial contour; 2, errors extended into the myocardial contour; and 3, errors extended into the midwall. We compared the scores of measurement errors and the average, maximum, minimum or variability of the HR indicated during the MOLLI scan (iHR), image phases of MOLLI or left ventricular ejection fraction (LVEF).

Results: Patients with score >1 for the septal myocardium had significantly lower minimum iHR than those with a score ≤ 1 ($P < 0.01$; 49.8 ± 10.1 vs. 59.6 ± 9.7 beat per min).

Conclusion: The confidence map shows more measurement errors in patients with lower minimum iHR. The myocardial T_1 values should be measured carefully in patients with bradycardia during MOLLI scanning.

Keywords: Myocardium, native T_1 mapping, modified Look-Locker inversion recovery (MOLLI), measurement error, hear rate

Introduction

Late gadolinium enhancement (LGE) magnetic resonance imaging (MRI) visualizes replacement fibrosis and is useful for differentiating various myocardial diseases and for their risk stratification.^{1–3} However, LGE does not detect interstitial fibrosis because of its results are binary based on the contrast between the reference myocardium and the scarred tissue. Extracellular volume fraction (ECV) or native T_1 value measurement is used to overcome this issue.^{4–8} These quantitative MRI methods identify diffuse interstitial fibrosis related to hospitalization caused by heart failure, interstitial expansion associated with amyloidosis, and myocardial

fibrosis associated with dilated cardiomyopathy.^{4–8} An important advantage of native T_1 mapping over LGE and ECV measurements is that no gadolinium-based contrast agents are needed.^{6,7}

Myocardial T_1 mapping is acquired using modified Look-Locker inversion recovery (MOLLI), saturation recovery, or a combination of these sequences.^{4–12} Each imaging sequence has its own merits and drawbacks regarding the signal-to-noise ratio, magnetization transfer, and R_1 homogeneity.^{11,12} The magnetic field strength and biological factors such as heart rate (HR) and respiratory and cardiac motion also affect the accuracy and precision of T_1 mapping.^{10–12} The use of 1.5T and a 5s(3s)3s MOLLI scheme may prevent interference from these biological factors noted above compared with the use of 3T or conventional MOLLI [i.e., a 3(3)3(3)5 scheme].^{11–13} Nonetheless, there are some controversies about the effects of arrhythmia and measurement errors in myocardial T_1 mapping.^{7,8,11,12,14–16}

A confidence map visualizes the measurement errors as black dots in myocardial T_1 mapping.¹² Using the map, we can estimate the overall image quality of the T_1 mapping and place the region of interest on the myocardium

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without errors, and the myocardial T_1 values are measured precisely.^{12,17} According to our experience it is difficult to measure the T_1 values in some patients with bradycardia, because the measurement errors involve the myocardium. We sought to evaluate the relationship between measurement errors in myocardial T_1 mapping and HR using a confidence map.

Materials and Methods

Patients

Between July 2017 and July 2019, we performed cardiac MRI, including 5s(3s)3s MOLLI T_1 mapping, in 160 patients with various myocardial diseases. We placed a circular region of interest on the septum of T_1 mapping as large as possible based on the ConSept study and excluded the patients with abnormal septal T_1 values, which were defined as two standard deviations (SD) below or above normal T_1 values acquired from 11 healthy male volunteers.^{14,18} Consequently, 69 male patients with normal native T_1 values of the septal myocardium were enrolled in this study. All included volunteers were men (ages 26–59 years) with a mean septal T_1 value of 1054.8 ms (SD, 28.2 ms; range, 998.4–1111.2 ms), and therefore only the male patients were included in the present study. Consequently, the ages of patients ranged from 17 to 86 years with the mean age of 60.6 years. Twenty-four patients had chronic kidney disease, 10 hypertrophic cardiomyopathy, six dilated cardiomyopathy, four angina pectoris, four mitral regurgitation, three chronic myocardial infarction, three hypertension, three suspected diabetic cardiomyopathy, three aortic regurgitation, two left ventricular non-compaction, two atrial fibrillation, and one each of cardiac sarcoidosis, myotonic dystrophy, ventricular premature contraction, atrioventricular block, and multiple valvular regurgitation. The diagnoses were based on the clinical presentations, laboratory data, cardiac MRI, and coronary angiography. The retrospective analysis of the data was approved by the Institutional Review Board. Informed consent for performing cardiac MR imaging examination including T_1 mapping was given by all patients.

Magnetic resonance imaging

Cardiac MRI examinations were carried out with a 1.5T imager (Ingenia, Philips Healthcare, Best, The Netherlands) with a 28-channel torso array coil. Cine balanced steady-state free precession (SSFP) was performed using the following imaging parameters: repetition time (TR), 3.2 ms; echo time (TE), 1.6 ms; flip angle, 60°; in-plane resolution, 1.82 × 1.94 mm²; slice thickness, 8 mm; and sensitivity encoding with a reduction factor of 2. Thirty phases per cardiac cycle were acquired. A 5s(3s)3s MOLLI was used for T_1 mapping at the short-axis midventricular level. A single-shot balanced SSFP readout was used with an inversion time of

159.5 ms after the first inversion recovery (IR) pulse, followed by 5s data acquisition. Thereafter, a 3s interval was set, and the 3s data acquisition was done after an inversion time of 350.0 ms after the second IR pulse. This sequence in a 1.5T imager is used because of its robustness for higher HR,¹² and 7–12 MOLLI images were acquired during an approximately 11s breath-hold. The imaging parameters of balanced SSFP used for MOLLI were: TR, 2.8 ms; TE, 1.3 ms; k -space segmentation, 92; flip angle, 35°; in-plane resolution, 2.00 × 1.97 mm²; slice thickness, 10 mm; and sensitivity encoding with a reduction factor of 2.

Confidence map and T_1 mapping

Confidence map and T_1 mapping were acquired according to previously reported methods.^{12,17,18} Briefly, the pixel-wise parametric mapping was achieved by performing a curve fit to the multiple inversion time measurements. The Look-Locker correction was used for MOLLI.⁹ A fit residual was defined as the absolute value of difference between fitted myocardial T_1 values and measured myocardial T_1 values. After discarding the lowest and second lowest data points in order to avoid a possible bias induced by overfitting, the median absolute deviation δ was calculated from the median of the fit residuals/0.6745.¹² A measurement error on the confidence map was identified and shown as a black dot, when the δ was greater than 2.25 times the noise, which represented the noise estimated during scan preparation (Fig. 1a). T_1 mapping was generated based on the fitting to the pixel-wise multiple inversion time measurements (Fig. 1b). A nonrigid motion correction was not available in this study.

Imaging analysis

The degree of measurement errors in the septal myocardium on a confidence map was assessed by two independent radiologists with 2 and 5 years of experience, respectively, in cardiac MRI using Likert 4-point scoring: 0, no errors adjacent to the myocardium; 1, errors located on the myocardial contour; 2, errors extended into the myocardial contour; and 3, errors extended into the midwall (Figs. 1 and 2). Thus, the higher the score, the more the measurement errors were located in the myocardium. The HR indicated during MOLLI scanning were defined as iHR and the average, minimum, and maximum iHR were annotated using the information from data recorded in a Picture Archiving and Communication System (Centricity Universal Viewer, GE Healthcare, Milwaukee, WI, USA). LVEF was measured using a workstation (ViewForum, Philips Healthcare, Best, The Netherlands). First, the interobserver agreement was assessed using a kappa analysis. The agreement was defined as follows: excellent, $k > 0.8$; good, $k = 0.61–0.8$; moderate, $k = 0.41–0.6$; fair, $k = 0.21–0.4$; and slight, $k \leq 0.2$. Thereafter, the mean of the scores given by the readers was defined as the measurement errors in each patient. We divided the

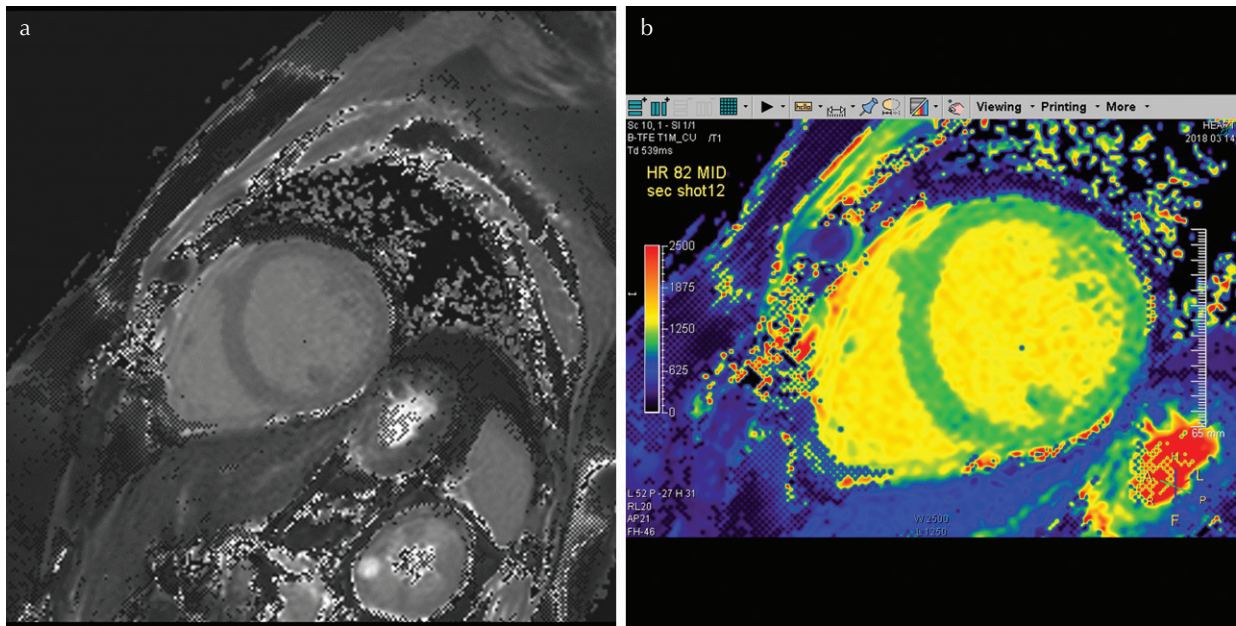


Fig. 1 Assessment of measurement errors on a confidence map. (a) In a 48-year-old patient with mitral regurgitation and a minimum heart rate of 82 beat per min indicated during the scan, no measurement errors were located adjacent to the septal myocardial contour (measurement error score = 0). (b) Color-scaled native T₁ mapping.

patients into two groups according to the scores of measurement errors in the septal myocardium: scores >1 represented the errors involving the myocardium and scores ≤1 represented the errors located outside the myocardium. The average, minimum, maximum iHR, or iHR variability defined as maximum iHR/minimum, image phases of MOLLI or left ventricular ejection fraction (LVEF) were compared between the two groups. A Mann–Whitney *U*-test was used for these comparisons. When significant differences were found, the correlation between the scores of the measurement errors in the septal myocardium and the variables (e.g., minimum iHR) was evaluated using a Spearman's test. StatView (SAS International, Cary, NC, USA) was used for the statistical analysis.

Results

Forty-eight of the 69 interventricular septum (70.0%) in 69 patients were given the same scores of measurement errors by the two readers, and the interobserver agreement was moderate ($k = 0.52$). Twenty-one of the 69 patients (30.4%) had scores >1 and the remaining 48 patients (69.6%) had scores ≤1. The septal myocardial T₁ values did not differ between the two groups ($P = 0.86$; 1058.6 ± 30.6 ms for the groups with scores >1 vs. 1057.4 ± 32.2 ms for the groups with scores ≤1).

The differences in iHR-based variables and LVEF between patients with scores of measurement errors >1 and those with the scores ≤1 are summarized in Table 1. The patient with scores of measurement errors >1 had significantly

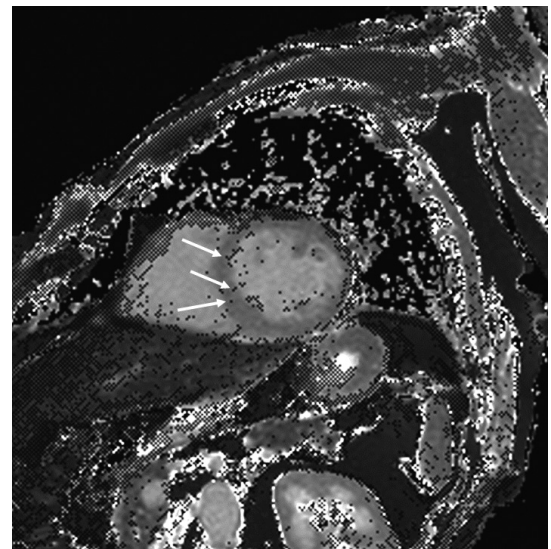


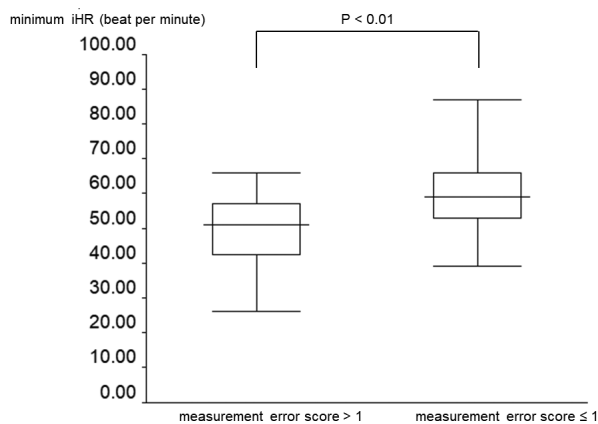
Fig. 2 Measurement errors on a confidence map in a patient with lower minimum heart rate indicated during the scan. In a 62-year-old patient with dilated cardiomyopathy, the measurement errors are visualized as black dots in the septal myocardium (arrows; measurement error score = 2.5). The average, maximum, and minimum heart rates during the scan are 67, 85, and 30 beat per min, respectively, and the image phases are 10.

lower values of minimum iHR than the patients with the scores ≤1 ($P < 0.01$; Fig. 3). The scores of measurement errors were significantly and inversely correlated with the minimum iHR ($r = -0.46$, $P < 0.01$; Fig. 4). Representative cases are shown in Figs. 1 and 2.

Table 1 Heart rate, image phase, and left ventricular ejection fraction between the patients with and without severe measurement errors

	scores ≤ 1	scores >1	<i>P</i>
Number	48	21	
iHR			
Average (bpm)	65.9 \pm 10.8	61.9 \pm 10.1	0.14
Maximum (bpm)	86.1 \pm 48.1	84.4 \pm 42.7	0.89
Minimum (bpm)	59.6 \pm 9.7	49.8 \pm 10.1	< 0.01
Variability	1.46 \pm 0.79	1.77 \pm 0.86	0.15
Image phases	9.71 \pm 1.40	9.19 \pm 1.50	0.17
LVEF (%)	50.5 \pm 13.4	46.0 \pm 12.2	0.19

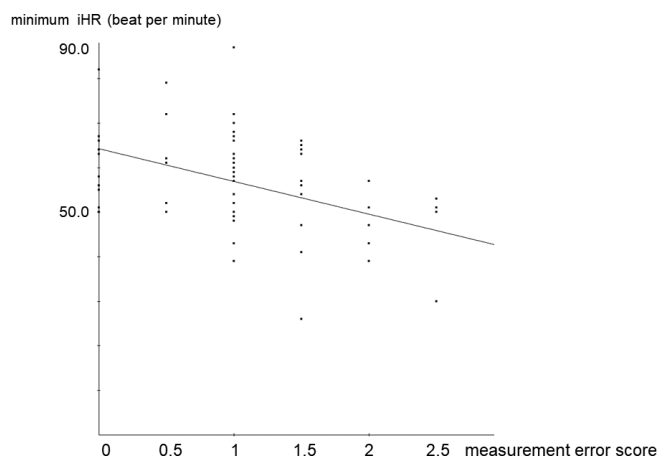
The scores of measurement errors >1 represent the errors involving the septal myocardium. The patients with the scores >1 significantly lower minimum indicated HR than the patients with the scores ≤ 1 . iHR, heart rate indicated on the monitor during MOLLI scan; bpm, beat per minute; LVEF, left ventricular ejection fraction.

**Fig. 3** Differences in the minimum heart rate indicated during the scan between the patients with and without severe measurement errors in the septum. Patients with the scores >1 have significantly lower values of minimum indicated heart rate (46.0 \pm 12.2 beat per min: bpm) than patients with the scores ≤ 1 (50.5 \pm 13.4 bpm; $P < 0.01$). iHR, heart rate indicated during MOLLI scan.

Discussion

This study, using a confidence map, demonstrated that the measurement errors involving the myocardium in T_1 mapping were observed in the septal myocardium of the patients who had lower minimum iHR. The scores of measurement errors inversely correlated with the minimum iHR. Therefore, the myocardial T_1 values should be estimated carefully in patients with bradycardia during MOLLI scanning.

The measurement errors in a confidence map are caused by uncompensated heart motion due to variation in the cardiac cycle.^{12,18} The iHR variability could correspond to the variation in the cardiac cycle and was not related to the scores of measurement errors in a confidence map in the

**Fig. 4** The scores of measurement errors on a confidence map are significantly and inversely correlated to the minimum heart rate indicated during the scan ($r = -0.46$, $P < 0.01$). iHR, heart rate indicated during MOLLI scan.

present study. This result might be due to less motion of the interventricular septum. The septum may be an appropriate region for measuring myocardial native T_1 values even in patients with high iHR variability. Otherwise, T_1 mapping during systole can delineate the myocardial contour more clearly, whereas the normal native T_1 at systole should be determined.^{10,13} So far, attention has been paid to tachycardia because of insufficient longitudinal recovery in patients with tachycardia,^{10,11,18,19} but not to bradycardia in myocardial T_1 mapping. In the present study, the measurement errors involving the myocardium in T_1 mapping were observed substantially in patients who had lower minimum iHR. We found a significant relationship between the measurement errors and the minimum iHR. When a low minimum iHR occurs earlier after the IR pulse, the data during a shorter inversion time from an IR pulse when the change in myocardial signals is large can be missed (Fig. 5). Especially, when there are the lower minimum iHR and average iHR, the image phases acquired by the 5s(3s)3s MOLLI decrease (Fig. 5), and therefore the median absolute deviation \acute{o} can be larger after discarding the data points with the lowest and second lowest \acute{o} . Therefore, the minimum iHR could contribute to the degree of measurement errors in myocardial T_1 mapping. These possible drawbacks of 5s(3s)3s MOLLI can be overcome by shortening the inversion time, increasing data acquisition time [e.g., 6s(3s)4s], or changing to the HR-fixed MOLLI [e.g., 5(HR)3(HR)3(HR)]. These sequences could be used firstly for the patients with known bradycardia.

This study has several limitations. First, the study population was biased toward patients with chronic kidney disease. They are good candidates for native T_1 mapping because of their contraindication to gadolinium-based contrast agents. Second, in the cases of severe measurement errors at the septal region (e.g., score ≥ 2), the

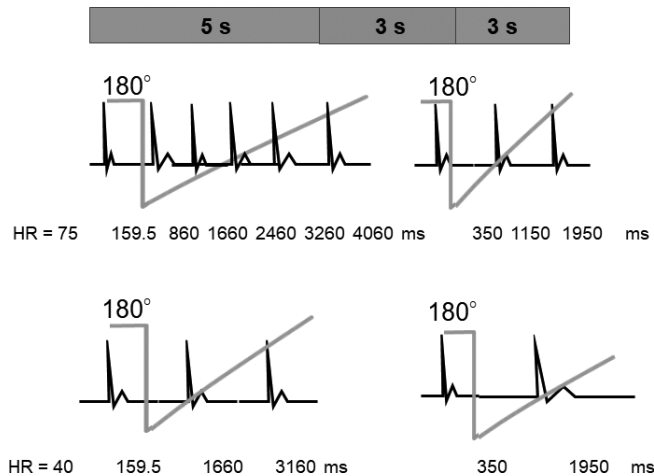


Fig. 5 5s(3s)3s MOLLI in cases of higher heart rate (i.e., 75 beat per min: bpm) and lower heart rate (i.e., 40 bpm). Some image phases with lower or close to the normal myocardial T₁ value (e.g., 1060 ms) are acquired in the case of 75 bpm, while only 5 or 6 phases were acquired and just two phases have the delay time lower or close to the normal myocardial T₁ in the case of 45 bpm.

“normal” native T₁ values was just within the limited region of interest. Third, our results can only be applied to other patient populations if a 1.5T imager and 5s(3s)3s MOLLI are used, and the subjects are men with normal septal T₁ values. Fourth, we did not use a nonrigid motion correction to compensate for the cardiac motion. This might not significantly impact the present results because the electric noise is estimated during the preparation scan and the minimum iHR and image phase are independent of the correction. Fifth, we did not know when and how often bradycardia occurred during MOLLI scanning in each patient. Indeed, there was an overlap of the minimum iHR of patients with the scores >1 and those with the scores ≤1. We speculate that the timing of bradycardia is related to degree of the measurement errors in the confidence map.

Conclusion

The confidence map shows more measurement errors in patients with lower minimum iHR. The minimum iHR was inversely correlated with the degree of errors. The myocardial T₁ values should be estimated carefully and may only be accurate within limited regions in patients with bradycardia during MOLLI scanning.

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Conflicts of Interest

Naoya Matsumoto has received lecture fee from Nihon Medi-Physics and Fujifilm Toyama Chemical Co., and research funding from Fujifilm Toyama Chemical Co. These fee and funding are related to nuclear cardiology but not to the topic of this study. The other authors declare no conflict of interest related to this study.

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