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SHORT COMMUNICATION

Myocardial T1 values in healthy volunteers measured with saturation method using adaptive recovery times for T1 mapping (SMART1Map) at 1.5 T and 3 T

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Abstract
Myocardial T1 mapping is clinically valuable for assessing the myocardium, and modified look-locker inversion-recovery (MOLLI) approaches have been commonly used for measuring myocardial T1 values. To date, several other sequences have been developed for measuring myocardial T1 values, and saturation-recovery-based sequences have been shown to be less dependent on various factors, such as T2 times and magnetization transfer, than inversion-recovery techniques. Systematic differences in T1 values between different sequences have been reported; therefore, definition of the normal range of native T1 values is required before clinical usage can begin. The purpose of this study was to evaluate the reference range and sex dependency of native T1 values in the myocardium measured using one such saturation-recovery sequence, i.e., saturation method using adaptive recovery times for cardiac T1 mapping (SMART1Map). Myocardial T1 values were compared between SMART1Map and MOLLI in 24 young healthy volunteers at 1.5 T and 3 T, and differences in the T1 values between the sexes were assessed. The mean native T1 values in the myocardium were significantly longer with SMART1Map than MOLLI [1530.4 ± 49.2 vs 1222.1 ± 48.9 ms at 3 T ($p < 0.001$) and 1227.3 ± 41.9 ms vs 1014.8 ± 49.4 ms at 1.5 T ($p < 0.001$)]. A significant difference between the sexes was observed in the T1 values obtained using each sequence, excluding SMART-1Map at 3 T. The SMART1Map has a potential advantage to overcome the shortcoming of MOLLI, which underestimates T1 values; however, the sex-dependent difference remains obscure using SMART1Map.

Keywords Myocardium · Magnetic resonance imaging · T1 mapping · Saturation recovery

Introduction

Myocardial fibrosis is commonly observed in a variety of cardiac diseases and represents a major independent predictor of adverse cardiac outcomes, which are assessed using late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging (MRI) [1]. Recently, myocardial T1 mapping has been proposed as a means of characterizing tissue, and several sequences have been developed for T1 mapping. Modified lock-locker inversion recovery (MOLLI) has been widely used for measuring myocardial T1 values; however, it has drawbacks because it depends on the myocardial T2 values and the imaging parameters, leading to underestimated T1 values and the need for additional corrections to obtain results closer to the true values [2–5].

Saturation method using adaptive recovery times for cardiac T1 mapping (SMART1Map) is a sequence that uses a single-point saturation-recovery technique for myocardial T1 mapping; it is less sensitive to imaging parameters than MOLLI and does not require correction [6, 7]. In addition, the accuracy of the long delay times, which has previously been overlooked in cardiac imaging, is assured by measurement of the duration of every heartbeat. Myocardial T1 values depend on the sequence, and the normal range of myocardial T1 values obtained using SMART1Map has not been established. The purpose of this study was to evaluate the reference range and sex dependency of native myocardial

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T1 values measured by SMART1Map in comparison with MOLLI at 1.5 T and 3 T.

Materials and methods

Subjects

The institutional review board approved this study, and written informed consent was obtained from all participants. A total of 24 healthy volunteers were enrolled in this study. Healthy asymptomatic volunteers with no previous medical history were recruited through advertising in the community. No patients had symptoms of cardiovascular disease, hypertension or diabetes mellitus. All patients in this study showed normal cardiac morphology and function on MRI examination.

SMART1Map

The sequence design has been described in previous studies [6, 7]. In brief, this sequence is based on a saturation-recovery technique with single-point data acquisition. Image data without a saturation pulse are acquired during the first heartbeat to approximate an infinite saturation-delay time. Image data with four different shorter saturation-delay times are obtained over the next four heartbeats. Finally, image data with three longer saturation-delay times spanning two, three and four heartbeats (1,111,234) are obtained (Fig. 1).

Data acquisition

The images were obtained using 1.5-T and 3-T whole-body scanners (Discovery MR750 and Discovery MR450w, version 25 software, GE Healthcare, Waukesha, WI, USA) with 32-channel cardiac coils. The SMART1Map images of the apical, mid and basal regions of the short axis of the left ventricle (LV) were obtained following routine cine steady-state free precession (SSFP) in the vertical and horizontal long axes and the LV short axis. MOLLI images were acquired after performing SMART1Map in the same locations. The imaging parameters were as follows: for SMART1Map (14 heartbeats): TR/TE, 3.6/1.6 ms; flip angle, 60°; and matrix, 160 × 128; for MOLLI [3(3)3(3)5, 17 heartbeats]: TR/TE, 3.1/1.4 ms; flip angle, 35°; and matrix, 192 × 128. The following parameters were used for both techniques: field of view, 340–400 mm, depending on the patient's body size; slice thickness, 8 mm; number of excitations, 1; bandwidth, 166 kHz; and parallel imaging factor 2 (autocalibrating reconstruction for cartesian imaging; ARC). Pixelwise T1 maps were generated automatically from the T1-weighted series of source images.

Native myocardial T1 measurements

Native T1 values in the myocardium were measured on a picture archiving and communications system (PACS) viewer (RA1000, GE Healthcare, Waukesha, WI, USA). The T1 values acquired via MOLLI were corrected using Deichmann's method [2, 8]. The LV wall was divided using an American Heart Association (AHA)-17 segment model, which excluded the apex (segment 17). The T1 maps of the two methods were displayed in the same location on the PACS viewer. T1 values were measured in 384 segments using a region of interest (ROI), which was manually placed by two radiologists experienced in cardiovascular imaging in each segment to avoid the contamination of signals in the myocardium and cavity in the same ROI. One reader repeated the measurements after an interval of at least one month. Semiautomated segmentation was not used. The T1 values in all segments were averaged and are presented as the global T1 values in each person.

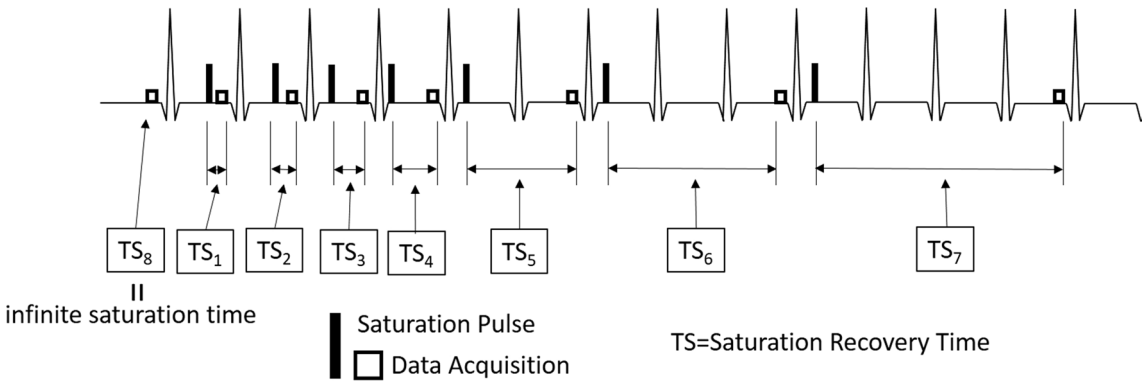

Fig. 1 Data acquisition pattern with the SMART1Map technique. This sequence was designed as a saturation-recovery technique

Statistical analysis

Values are reported as the mean ± standard deviation (SD). The characteristics of the male and female subjects were compared by Mann–Whitney *U* test. The myocardial T1 values of both methods were statistically compared by paired t-test. Sex-dependent differences in the myocardial T1 values were assessed by unpaired *t* test. A *p* value of <0.05 was considered statistically significant. Inter- and intra-observer variability in T1 values were evaluated using intraclass correlation coefficient (ICCs) with a two-way random model for SMART1Map and MOLLI on 1.5-T and 3-T scanners. The data were analyzed using the statistical packages in GraphPad Prism 7 (La Jolla, CA, USA) and SPSS version 25 (Chicago, IL, USA).

Results

The characteristics of the volunteers are shown in Table 1. Females had significantly lower mean age and shorter height than males, but no significant differences were observed in the other characteristics. In this study, T1 mapping was successful in all cases on both the 1.5-T and 3-T scanners. Representative images acquired at 1.5 T and 3 T are shown in Fig. 2.

The mean native T1 value in the myocardium was 1227.3 ± 41.9 ms at 1.5 T and 1530.4 ± 49.2 ms at 3 T with SMART1Map and 1014.8 ± 49.4 ms at 1.5 T and 1222.1 ± 48.9 ms at 3 T with MOLLI. The results of the myocardial T1 measurements and sex-based T1 values are shown in Table 2, and significant differences were observed between the sexes for all sequences except SMART1Map at 3 T (Fig. 3). The inter- and intra-observer variability were excellent for measuring global myocardial T1 values using data obtained by both sequences, with ICCs ranging from 0.917 to 0.996 (Table 3).

Discussion

We have demonstrated the feasibility of SMART1Map and the normal range of native myocardial T1 values using SMART1Map at 1.5 and 3T. A significant difference was observed between the results of SMART1Map and MOLLI. A significant difference in native T1 values between men and women was also detected with these methods except SMART1Map at 3T. Myocardial T1 values have been reported to be dependent on the measurement technique. Currently, MOLLI is widely used and considered to be a standard method for measuring myocardial T1 values. The normal range of myocardial T1 values with MOLLI was previously demonstrated to be 940–1050 ms at 1.5 T and

Table 1 Characteristics of the healthy volunteers

	Women ($N=12$)	Men ($N=12$)	*p* value
Age (years)	29.3 ± 4.0 (22–35)	25.8 ± 4.2 (20–35)	0.049
Height (cm)	159.8 ± 5.2 (153–168)	172.5 ± 4.4 (162–178)	<0.001
Weight (kg)	59.4 (43–83)	66.2 ± 6.7 (57–77)	0.49
BMI (kg/m^2)	23.3 ± 4.6 (18.4–35.5)	22.2 ± 1.7 (19.3–24.6)	0.62
Heart rate (beats/min)	62.5 ± 6.0 (52–72)	59.9 ± 10.5 (48–81)	0.15

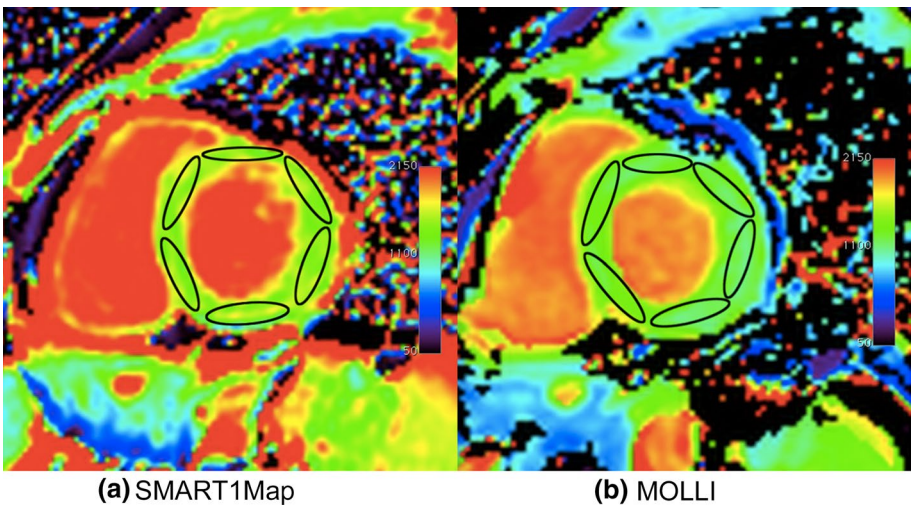

Fig. 2 T1 map obtained by **a** SMART1Map and **b** MOLLI in the short axis of the LV in a healthy 29-year-old woman at 3 T. The ROIs used for measuring T1 values in each segment are shown

Table 2 Native T1 in the myocardium for the entire group and for the male and female groups with SMART1Map and MOLLI at 1.5 T and 3 T

	Overall	Women	Men	*p* value between women and men
1.5 T				
SMART1Map (ms)	1227.3 ± 41.9	1244.9 ± 46.7	1209.7 ± 28.7	0.037
MOLLI (ms)	1014.8 ± 49.4	1046.9 ± 45.1	982.7 ± 28.5	< 0.001
p value	< 0.001	< 0.001	< 0.001	
3 T				
SMART1Map (ms)	1530.4 ± 49.2	1534.3 ± 24.7	1526.6 ± 33.7	0.53
MOLLI (ms)	1222.1 ± 48.9	1259.1 ± 29.7	1185.0 ± 33.6	< 0.001
p value	< 0.001	< 0.001	< 0.001	

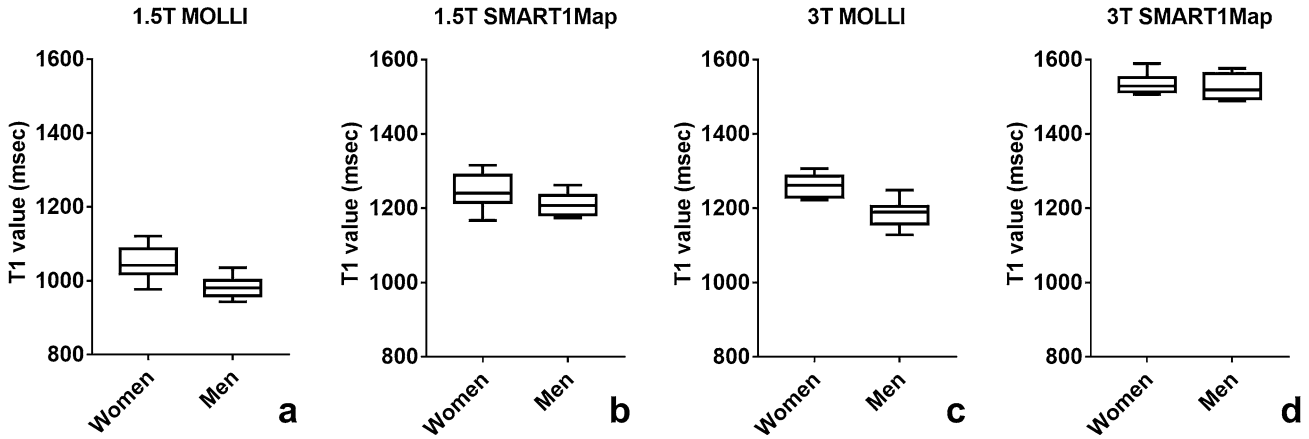

Fig. 3 Box-and-whisker plots of myocardial T1 values for each sex obtained by **a** MOLLI and **b** SMART1Map at 1.5 T and **c** MOLLI and **d** SMART1Map at 3 T. A significant difference was observed for all sequences but SMART1Map at 3 T

Table 3 Intra- and inter-observer variability in T1 values obtained by SMART1Map and MOLLI

ICC	Intra-observer	Inter-observer
SMART1Map		
1.5 T	0.927	0.937
3 T	0.947	0.995
MOLLI		
1.5 T	0.978	0.917
3 T	0.996	0.994

1052–1286 ms at 3 T [5, 9–14], and the mean T1 values in the current study were within these ranges. However, the evaluation of T1 values obtained by MOLLI requires a large local database of normal results against which to compare individual values, and comparing T1 values between scanners and sites is difficult. Especially at 3 T, T1 recovery might be incomplete in MOLLI sequences due to longer T1 times, especially in people with high heart rates. Revised MOLLI sequence have been proposed to increase accuracy and precision, such as in the scenario of 5(3)3 [15–19].

In contrast, saturation-recovery techniques are expected to provide more accurate measurements, which is expected to enable the direct comparison of myocardial T1 values between patients, scanners, sites, and vendors [20]. Meanwhile, the T1 values obtained using saturation-recovery single-shot acquisition (SASHA) and the hybrid saturation-pulse-prepared heart-rate independent inversion-recovery (SAPPHIRE) technique ranged from 1170–1220 ms at 1.5 T. A few studies have estimated the reference range of myocardial T1 values with saturation-recovery techniques at 3 T, which was reported to be 1432–1578 ms [13, 14, 21, 22]. The saturation recovery technique is utilized in either SMART1Map or SASHA. In SMART1Map, the data are characteristically acquired at a single-point across several heart beats for longer saturation recover time. During the post-processing, recorded 'real' saturation time is used for T1 curve fitting to reduce the influence of irregular heart beat. Despite the different sequence design, the native T1 values obtained with SMART1Map are in the same range of previously-reported T1 values using SASHA.

The current study identified sex-based differences between the T1 values obtained using the different methods

except for SMART1Map at 3 T. Myocardial T1 values have been reported to be slightly higher in females than in males for both inversion and saturation recovery techniques [11, 23–26]. However, in several studies, no significant differences in the myocardial T1 values were observed between the sexes [12, 27]. A significant difference in myocardial T1 values between sexes was observed with MOLLI and SASHA ($p < 0.0001$) in a previous study that enrolled 94 healthy volunteers and used 1.5 T scanners [25]. This study demonstrated a physiological variation in the myocardium between sexes. However, the sex difference was not detected using ShMOLLI in the same groups, which revealed that the detectability of sex differences depends on the MRI sequence. In addition, no significant difference in native myocardial T1 between sexes was detected with SASHA at 3 T [28]. A saturation recovery sequence can have errors when the magnetization preparation pulse does not fully saturate magnetization, especially for a 3 T scanner, due to the inhomogeneous B1 field [29]. The measured T1 values with error might obscure the difference between sexes. Inhomogeneous B1 fields and incomplete saturated magnetization may be reasons for the lack of significant difference in T1 values between men and women. Improvements in the homogeneity of the magnetic field and saturation pulse design are expected to clarify these differences.

Several previous studies have suggested that myocardial T1 values obtained by MOLLI in females decrease with increasing age; when a group of subjects has a wide age range, this difference might be less obvious. However, myocardial T1 values were reported to be independent of age in a previous study using SASHA at 1.5 T [26]. In the current study, the difference between the sexes could be observed because all subjects were of a similar age. Currently, the number of studies using saturation-recovery techniques is limited. Future studies are expected to discuss the clinical value of saturation-recovery myocardial T1 measurements.

Study limitations

Our study has several limitations. The first limitation is the small size of the study population; further studies are necessary to confirm the clinical value of SMART1Map. The second limitation is that data were obtained only from people of a young age. As previously described, the relationship between age and native T1 values remains controversial; while increased native T1 values have been reported in older people, other studies have found that T1 values remained comparable or decreased with age [11, 28, 30]. Further studies on the age dependency of native T1 values are expected. The third limitation is a lack of data regarding the extracellular volume (ECV). In this study, the ECV was not discussed because contrast material was not administered to the healthy volunteers. Revised MOLLI sequences have recently become available, which may achieve a different result in T1 measurements. For the scanners used in this study, the revised MOLLI sequence was not available, and therefore, it could not be compared with the SMART1Map results.

Conclusion

Myocardial T1 measurements were successfully obtained using the SMART1Map sequence at 1.5 T and 3 T for evaluation of the reference range of myocardial T1. Native myocardial T1 values were significantly longer for SMART1Map than MOLLI. Sex dependency was observed for all sequences except SMART1Map at 3 T. The SMART1Map has a potential advantage to overcome the shortcoming of MOLLI, which underestimates T1 values; however, the sex-dependent difference remains obscure using SMART1Map.

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Compliance with ethical standards

Conflict of interest GE Healthcare provided a grant for conducting the volunteer study. One author (AN) is an employee of GEHC Japan. His role in this study was limited to preparing the sequence. The funder had no role in the study design, data collection, data analysis, decision to publish, or preparation of the manuscript.

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