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ORIGINAL PAPER

Cardiac T2 star mapping: standardized inline analysis of long and short axis at three identical 1.5 T MRI scanners

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Abstract

T2 star mapping can be applied for in vivo cardiac iron quantification. Current recommendations of imaging acquisition, post-processing and interpretation of normal values are based on old scanner types and in house software packages. A standardized comparison of short (SAX) and long axis (LAX) segments using commercially available software packages and modern scanners is lacking. To provide a standardized comparison of T2 star time values in SAX and LAX and to investigate intersegmental, interregional and inter-level comparison and the interscanner reproducibility. 84 cardiac MRIs in 28 healthy volunteers were performed with three structurally identical 1.5 T MRI scanners. A commercially available software package for T2 star mapping with automatic in-line motion correction was used for analysis. Regions of interest were manually placed in each of the 16 myocardial segments according to the AHA model in three SAX and three LAX. A total of 2856 ROIs were drawn and 102 segments per volunteer were analysed. Interscanner reproducibility was high (91%) and the mean myocardial T2 star time value for all evaluated segments was 34 ± 5.7 ms. No significant difference was found between all measurements in SAX (35 ± 5.5 ms) and LAX (34 ± 5.8 ms). T2 star time values varied significantly between heart segments in the same axis and in 44% between corresponding SAX and LAX segments. T2 star time values in SAX and LAX have a high interscanner reproducibility but can vary significantly between heart segments in the same axis. Comparability between corresponding SAX and LAX segments is limited. To get representative results T2 star time values should be obtained in more than one heart segment and for follow-up studies identical segments should be used to avoid a systematic bias.

Keywords Magnetic resonance imaging · Heart · Reproducibility of results · Cross-sectional study

Abbreviations

AHA	American Heart Association
bpm	Beats per minute
cMRI	Cardiovascular magnetic resonance imaging
ECG	Electrocardiography
FOV	Field of view
ICC	Intraclass correlation coefficient
LAX	Long axis view
LE	Late enhancement
MHz	Megahertz
MOLLI	Modified look-locker inversion recovery sequence
ms	Milliseconds
ROI	Region of interest
RR	RR-interval
SAX	Short axis view
T	Tesla
TE	Echo time
TI	Inversion time
TR	Repetition time

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Introduction

Cardiac MRI (cMRI) is widely used to investigate a variety of cardiac pathologies from depiction of myocardial infarction to other non-ischemic cardiomyopathies [1]. Cardiac iron overload is a serious condition, caused either by repeated blood transfusions for anemia (e.g. in thalassemia major) or increased intestinal iron absorption (e.g. hereditary hemochromatosis) [2]. Iron overload leads to severe heart failure and lethal arrhythmias but can be treated effectively if diagnosed early [1]. Parametric mapping techniques provide

a non-invasive tool for quantifying tissue alterations in myocardial disease and is capable of in vivo tissue characterization [1, 3, 4]. T2 star mapping is currently the only cardiac parametric mapping technique that is recommended in disease-specific clinical guidelines [1, 5] and seems to improve patient outcome in iron overload states [1, 4]. Besides iron overload T2 star relaxation times can be used to detect cardiac necrosis or intramyocardial hemorrhage and reperfusion injury post infarction [1, 6].

Current recommendations of imaging acquisition, post-processing and interpretation of physiologic values are mainly based on one publication in 2001 [7]. Anderson et al. correlated T2 star relaxation times with functional parameters such as left ventricular ejection fraction and left ventricular end-systolic volume in 106 patients with thalassaemia major. In this study one full thickness region of interest (ROI) was measured in the septal myocardium in one short axis (SAX) slice mid-cavity and a threshold of 20 ms was suggested to be pathologic for T2 star time values using an in-house software package [7]. However, a multitude of factors affect T2 star time values [1, 7], which limits comparability of published values between different sites [1]. Nowadays in clinical routine it is a widely accepted practice to place one ROI in the myocardial septum [1], although an inhomogenous myocardial iron deposition was described in iron overload patients [8–11] and reproducibility of global cardiac T2 star time values was demonstrated to be higher compared to mid-cavity septum measurements [12, 13].

To our knowledge, a standardized comparison of SAX and LAX segments according to the AHA model using commercially available software packages and modern scanners is lacking. Aim of this study was to provide a standardized comparison of T2 star time values according to the AHA model in SAX and LAX and to investigate the intersegmental, interregional and inter-level comparison and the inter-scanner reproducibility of three 1.5 T MRI scanners from the same vendor with a dedicated commercially available software package.

Materials and methods

Population

A total of 28 healthy volunteers were included in this prospective, cross-sectional study. All subjects were recruited through advertising for research studies. None had evidence of cardiovascular disease or cardiac risk factors including hypertension, hyperlipidemia or diabetes, based on medical history. None was referred as patient for a clinical cMRI scan which then turned out to be normal. Volunteers older than 40 years of age, with known previous cardiac surgery and with contraindications to the cMRI examination (pacemaker, metal fragments, implants, arrhythmias or claustrophobia) were excluded. Institutional review board approval was obtained and all volunteers gave written informed consent.

MR acquisition parameters

All T2 star measurements were performed without the administration of any invasive agent using a commercially available software package with a 8-point gradient echo pulse sequence (MyoMaps, system software version E11, Siemens Healthineers, Erlangen, Germany) on three identical 1.5 T MRI systems (Magnetom Aera, Siemens Healthineers, Erlangen, Germany). All three scans in each volunteer were performed by the same technician on the same day using the same 16-channel phased array body coil. The volunteers were placed in a supine position, and images were acquired at endexpiratory breath hold with electrocardiogram gating. Initially scout images were acquired to localize the LAX and SAX of the heart. Three cinematic LAX (2-, 3- and 4-chamber view) and three SAX (base, mid-cavity and apex) were acquired with a retrospectively ECG-gated segmented k-space balanced steady state free-precession pulse sequence (trueFISP, Siemens Healthineers GmbH, Erlangen, Germany). Basal section was defined as a fixed distance of 2 cm to the mitral annulus in a diastolic four chamber view. Mid-cavity and apical were defined in the same four chamber view, each with a gap of 2 cm as shown in Fig. 1. Slice position and orientation were adopted from these acquisitions for T2 star time measurements. T2 star mapping parameters were selected as recommended by the vendor and were as follows: TR: 855 ms, TE: 2.08, flip angel: 20°, FOV read 400 mm, FOV phase: 81.3%, Phase resolution: 60%, slice thickness: 8 mm, base resolution: 256, voxel size: 1.6 × 1.6 × 8.0 mm. Optimal gating and breath-holding were ensured and raw images were assessed for potential image artefacts during scanning, to allow an immediate repeat of suboptimal measurements [14].

Image analysis and data processing

cMRI analysis was performed by two board certificated radiologist with each 8 years of experience in cardiovascular imaging (W.W., first observer; M.M., second observer). Both radiologists were blinded to all volunteer and other imaging data.

A ROI as large as possible carefully avoiding the adjacent blood pool or extracardiac structures was manually placed in each of the myocardial segments according to the AHA model in three SAX and three LAX with exception of heart segment 17 [15]. To assess inter- and intraobserver variability measurements were repeated in 7 randomly chosen volunteers (25%). A total of 16 T2 star time values in SAX and 18 T2 star values in LAX were measured per volunteer and scanner.

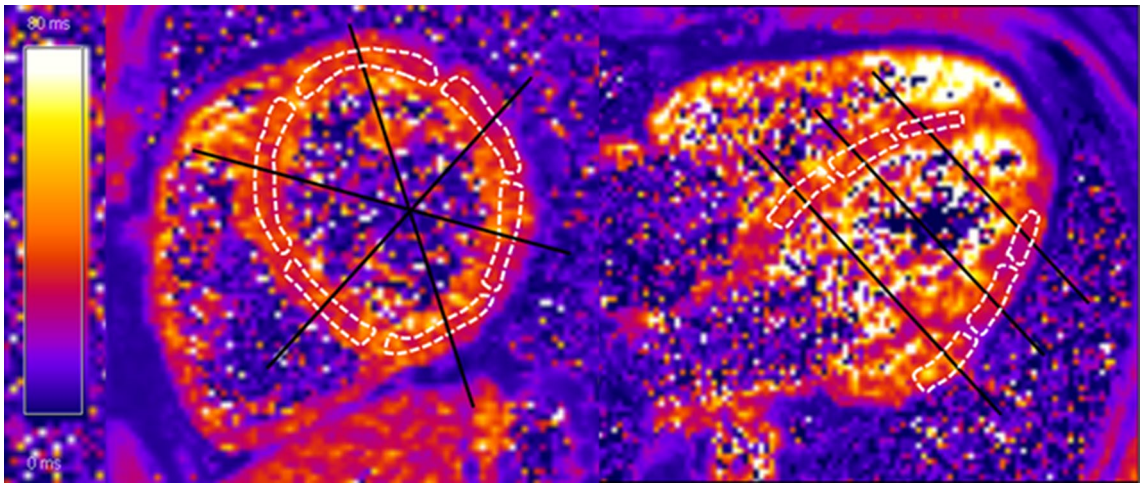

Fig. 1 Segmental ROIs (dashed white lines) in basal short axis and four-chamber view of the same volunteer. Measurement levels of short (basal, mid-cavity and apical) and long axis (four, three and two chamber view) are marked with black lines

The image quality for all segments was visually rated by two observers (M.M. and W.W.) in consensus by using a three point scale: 3—good image quality with no artifacts; 2—satisfactory with minor artifacts; 1—nonevaluable with major artifacts [16].

For interscanner reproducibility T2 star time values in SAX and LAX were compared between all three MRI scanners. For intersegmental reproducibility corresponding heart segment pairs in SAX and LAX were compared. Segment 14 and 16 in SAX were compared to its corresponding segment in three chamber and four chamber view resulting in a total of 18 matching pairs. For interregional differences heart segments in SAX and LAX were arranged in six groups (in the manuscript referred to as vertically grouped segments). The classification is exemplarily color-coded in Fig. 2: anterior (yellow, segment 1, 7, and 13), anteroseptal (blue, segment 2, 8, and 14), inferoseptal (red, segment 3, 9, and 14), inferior (orange, segment 4, 10, and 15), inferolateral (green, segment 5, 11, and 16) and

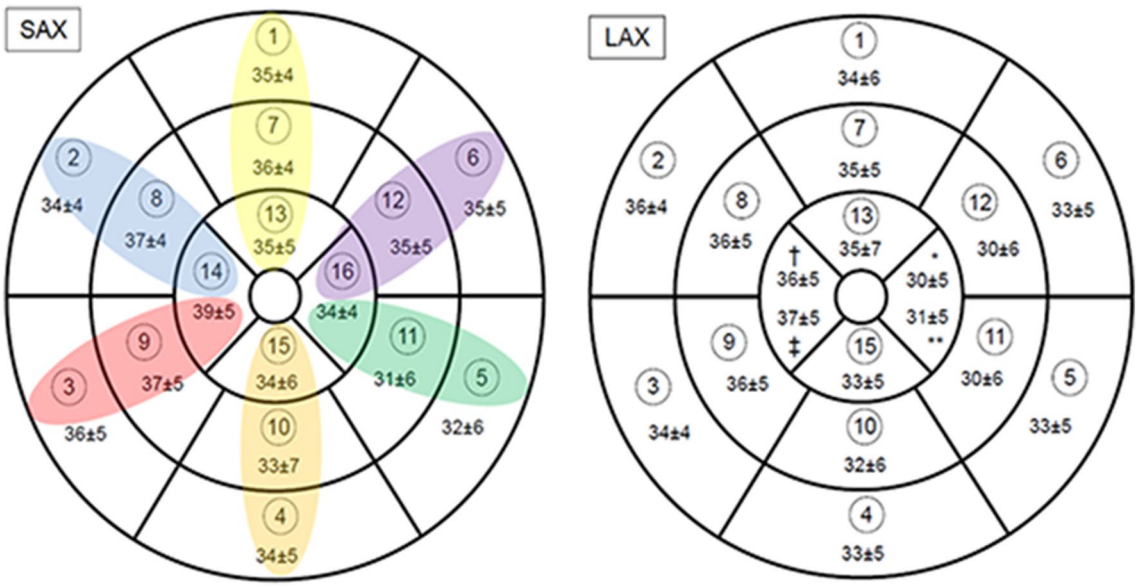

Fig. 2 Mean T2 star time values and single standard deviation for all measured heart segments in short axis (SAX) and long axis (LAX). Color markings symbolize the segmental classifications for the interregional analysis. Heart segments were arranged in six groups: anterior (yellow, segment 1, 7, and 13), anteroseptal (blue, segment 2, 8, and 14), inferoseptal (red, segment 3, 9, and 14), inferior (orange, segment 4, 10, and 15), inferolateral (green, segment 5, 11, and 16) and anterolateral (purple, segment 6, 12,and 16). Single asterisk (*) indicates apical septal (segment 14) in three chamber view. Double asterisk (**) indicates apical septal (segment 14) in four chamber view. Single cross (†) indicates apical lateral (segment 16) in four chamber view. Double cross (‡) indicates apical lateral (segment 16) in three chamber view

anterolateral (purple, segment 6, 12, and 16). These groups were compared to each other (in total 15 pairs).

To analyse interlevel variations all T2 star time values in SAX and LAX were divided in three groups (in the manuscript referred to as horizontally grouped segments) and compared to each other: basal (segment 1–6), mid-cavity (segment 7–12) and apical (segment 13–16).

Statistical analysis

Kolmogorov–Smirnov test with Lilliefort correction was used to evaluate the data for normal distribution. Descriptive statistical data analysis was provided as mean values, range and single standard distribution. Non-parametric Friedman test was performed for evaluation of T2 star values between the three different MRI acquisition time points as normal distribution was not assumed by Kolmogorov–Smirnov test. Post hoc analysis was performed by using Dunn–Bonferroni pairwise comparison test. Bland–Altman plots were used for visual comparison between T2 star time values of each measurement time point. Furthermore non-parametric Wilcoxon rank sum test was used for comparison between corresponding heart segments in short and long axis and for comparison of vertically and horizontally grouped heart segments in SAX and LAX respectively. For assessment of reproducibility, the agreement of measurements performed by two different observers was determined by using the Pearson correlation. Intraobserver reliability of the first observer was evaluated additionally by using intraclass correlation coefficient (ICC). Significance was accepted for p values < 0.05. Statistical analysis was performed using the software package SPSS Statistics Version 21 (SPSS Inc./IBM, Chicago, Illinois).

Results

The study population consisted of 14 female and 14 male volunteers, mean age was 25 ± 7 years (range 19–31 years). The average heart rate during the examination was 65 ± 4 bpm (range 54–78 bpm).

The MRI examination of all 28 volunteers was of good quality (score of 3 in 100%) in all assessed segments. There were no notable artifacts.

Overview T2 star time values

A total of 102 segments per volunteer were analysed consisting of 16 segments in SAX and 18 segments in LAX at three different examination time points. A total of 2856 ROIs were drawn and the mean myocardial T2 star time value for all evaluated segments in all subjects including all scans was 34 ± 5.7 ms (women: 35 ± 5.6 ms; men: 33 ± 5.7 ms). Means for each scanner were as follows: scanner 1: 33.9 ± 5.9 ms, scanner 2: 33.8 ± 5.6 ms and scanner 3: 34.5 ± 5.6 ms. T2 star time value for all segments in SAX was 35 ± 5.5 ms (range 13.9–83.4 ms) and 34 ± 5.8 ms (range 9.6–93.3 ms) in LAX. Mean T2 star time values for horizontally grouped heart segments (basal, mid-cavity, apical) in SAX and LAX vary from 33.1 ± 5.9 (LAX mid-cavity) to 35.5 ± 5.4 (SAX apical). T2 star time value of all assessed heart segments ranged between 9.6 and 93.3 ms (Table 1). In total 82 segments (3.3%) showed values < 20 ms distributed across all heart segments in SAX and LAX with a standard deviation of 4.0. Mean T2 star time values and single standard deviation for every measured heart segment in SAX and LAX are provided as an overview in Fig. 2.

Interobserver and intraobserver reliability

Interobserver and intraobserver variability for the three different examination time points were low with an intraclass correlation coefficient of 0.83 and 0.99.

Interscanner comparison of T2 star time values

T2 star time value was not significantly different in 31/34 (91%) segments between different examination time points. Mid-cavity inferior (segment 10, $p = 0.014$) and apical anterior (segment 14, $p = 0.002$) in short axis and mid-cavity anterolateral (segment 12, $p = 0.002$) in four chamber view showed a significant difference between the three different examination time points. Bland–Altman plots showed a good agreement between the measurements of each scanner. Further, no systematic difference between the measurements could be identified (Fig. 3a–c).

Table 1 Descriptive data for horizontally grouped heart segments in short (SAX) and long axis (LAX)

	Number of items	Mean	Standard deviation	Range
SAX				
Basal	504	34.2	5.2	13.9–83.4
Mid-cavity	504	34.6	5.7	10.5–60.8
Apical	336	35.5	5.4	17.8–78.3
LAX				
Basal	504	33.9	5.1	15.3–54.5
Mid-cavity	504	33.1	5.9	12.8–87.3
Apical	504	33.7	6.3	9.6–93.3

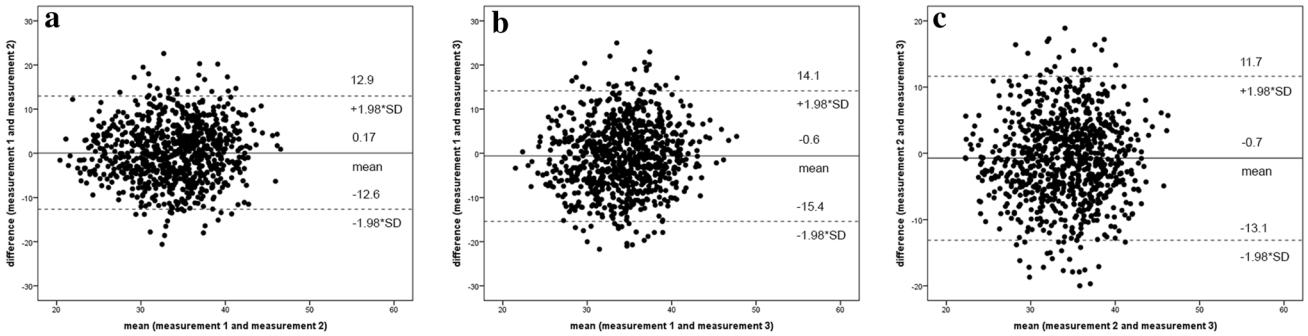

Fig. 3 **a–c** Bland–Altman plots of all three measurement time points. Horizontal lines indicate mean difference (center line) and the upper and lower border of agreement (mean difference ± 1.96 × standard deviation)

Intersegmental comparison of T2 star time values

10/18 (56%) corresponding myocardial segment pairs (SAX vs. LAX) showed no statistically significant difference. Consistent results could be shown in basal, med-cavity and in apical segments. Basal anteroseptal (segment 2), basal inferoseptal (segment 3), basal anterolateral (segment 6), mid-cavity anterolateral (segment 12), apical anterior (segment 14) and apical lateral (segment 16) differed significantly. None of the anterior or inferior segment pairs varied significantly. A detailed statistical overview is provided in Table 2.

Table 2 Comparison of corresponding heart segments in short and long axes

Short axis (SAX)	Long axis (LAX)	*p* values
Segment 1	Segment 1 two chamber	0.302
Segment 2	Segment 2 three chamber	**0.001***
Segment 3	Segment 3 four chamber	**0.006***
Segment 4	Segment 4 two chamber	0.427
Segment 5	Segment 5 three chamber	0.418
Segment 6	Segment 6 four chamber	**0.030***
Segment 7	Segment 7 two chamber	0.087
Segment 8	Segment 8 three chamber	0.071
Segment 9	Segment 9 four chamber	0.214
Segment 10	Segment 10 two chamber	0.637
Segment 11	Segment 11 three chamber	0.412
Segment 12	Segment 12 four chamber	**0.000***
Segment 13	Segment 13 two chamber	0.893
Segment 14	Segment 14 four chamber	**0.035***
Segment 14	Segment 14 three chamber	**0.010***
Segment 15	Segment 15 two chamber	0.101
Segment 16	Segment 16 four chamber	**0.000***
Segment 16	Segment 16 three chamber	**0.001***

*Significant p-values are bolded

Interregional comparison of T2 star time values

For interregional differences heart segments in SAX and LAX were arranged in six groups. These groups were compared to each other (in total 15 pairs).

SAX

In 7% (1/15) no significant difference was found between vertically grouped SAX heart segments. Only anterolateral (segment 6, 12 and 16) and inferior (segment 4, 10 and 15) grouped segments ($p = 0.14$) were comparable. All other segment pairs differed significantly (Table 3).

LAX

In 13% (2/15) no significant difference was found between vertically grouped LAX heart segments. Anteroseptal (segment 2, 8 and 14) was comparable to inferoseptal (segment 3, 9 and 14) ($p = 0.40$) and inferolateral (segment 5, 11 and 16) to anterolateral (segment 6, 12 and 16) ($p = 0.10$). All other segment pairs differed significantly (Table 3).

Interlevel comparison of T2 star time values

For interlevel differences heart segments in SAX and LAX were arranged in 3 groups (basal, mid-cavity and apical).

Table 3 Interregional comparison for short (SAX) and long axes segments (LAX)

Region	Region	SAX p-value	LAX p-value
Anterior	Anteroseptal	**< 0.01***	**< 0.01***
Anteroseptal	Inferoseptal	**0.02***	0.40
Anteroseptal	Inferior	**< 0.01***	**< 0.01***
Anteroseptal	Inferolateral	**< 0.01***	**< 0.01***
Anteroseptal	Anterolateral	**< 0.01***	**< 0.01***
Inferoseptal	Anterior	**< 0.01***	**0.02***
Inferoseptal	Inferior	**< 0.01***	**< 0.01***
Inferoseptal	Inferolateral	**< 0.01***	**< 0.01***
Inferoseptal	Anterolateral	**< 0.01***	**< 0.01***
Inferior	Anterior	**< 0.01***	**< 0.01***
Inferior	Inferolateral	**< 0.01***	**< 0.01***
Inferior	Anterolateral	0.14	**< 0.01***
Anterior	Inferolateral	**< 0.01***	**< 0.01***
Anterior	Anterolateral	**0.02***	**< 0.01***
Anterolateral	Inferolateral	**< 0.01***	0.10

For interregional differences heart segments in SAX and LAX were arranged in six groups: anterior (segment 1, 7 and 13), anteroseptal (segment 2, 8 and 14), inferoseptal (segment 3, 9 and 14), inferior (segment 4, 10 and 15), inferolateral (segment 5, 11 and 16) and anterolateral (segment 6, 12 and 16)

*Significant p-values are bolded

SAX

No significant difference was found for T2 star time values between basal, mid-cavity and apical level (Table 1).

LAX

Basal values were significantly higher than mid-cavity T2 star time values ($p = 0.004$), whereas no significant difference could be found between basal and apical and between apical and mid-cavity (Table 1).

Discussion

T2 star time value assessed with commercially available software with in line motion correction on three identical 1.5 T MRI scanners from the same vendor is highly reproducible with no significant difference of 91% of heart segments. Mean overall T2 star time value was 34 ± 5.7 ms. Results were comparable for SAX and LAX measurements but with significant segmental variations.

T2 star mapping represents a non-invasive biomarker for characterizing pathologies and is in contrast to endomyocardial biopsy ideal for serial monitoring [1, 17]. According to the recently published consensus paper by Messroghli et al. T2 star mapping for iron overload should be performed at 1.5 T by analyzing an interventricular septal ROI. For the stratification of cardiac iron overload, a 3-tier risk model (low risk, > 20 ms; intermediate risk, 10–20 ms; and high risk, < 10 ms) should be used if images are acquired at 1.5 T with ≥ 8-point gradient echo pulse sequences [1]. Otherwise no standard of procedure concerning comparable quantification of T2 star time values between different sites has been established at the moment. For therapy monitoring and patients' outcome reliable follow-up examinations are essential [2, 18] and transferability of the T2 star technique among different MRI sites is mandatory, which is not established for current hard- and software packages [12].

Reproducibility is a key issue prior to any dissemination of this technique, especially across Asia and the Mediterranean, where iron overload is most prevalent, as well as in immigrant populations [7]. In literature T2 star time values differ significantly between scanners from different vendors and transferability between MRI sites is not established for current hard- and soft-ware packages [12]. The variability could be modelled as the sum of two independent stages: acquisition stage (involving scanner, MR sequence, MR operator variability) and image analysis stage (involving image analysis software, software operator variability) [12]. If image analysis is performed at different sites, an additional slight increase of variability should be expected due to the fact that measurement reproducibility will be affected by interobserver instead of intraobserver variability [12]. These technical prerequisites of T2 star mapping make it difficult in the clinical routine for patients and clinicians to follow their measurements over time, especially if they move out of the area or the scanner changes. Against this background we have performed our investigation with one of the most frequently sold MRI scanners worldwide (more than 3000). In our study interscanner reproducibility for these three 1.5 MRIs from the same vendor was high using a commercially available software package. This proof of principle has been demanded by Abdel-Gadir et al. who used the same soft- and hardware for ultrafast cMRI for iron quantification in thalassemia patients in the developing world [19].

In clinical routine it is a widely accepted practice for diffuse cardiac disease to place a septal ROI in a single mid-cavity SAX [1], although Positano et al. stated a true heterogeneity in the iron overload distribution in 230 thalassemia major patients by ruling out artefactual effects in the analyzed cMRIs [10]. They suggested using a segmental cardiac analysis in the early detection of myocardial iron overload in borderline thalassemia major patients [10]. We systematically evaluated T2 star time values in healthy volunteers for every single segment according to the AHA segment model in SAX and LAX. Only 56% of corresponding heart segments were comparable between both axes but mean T2 star time values were almost identical (35 ± 5.5 ms SAX

and 34 ± 5.8 ms LAX). Our detailed analysis additionally found significant interregional variations for the majority of regions, even within the septum itself.

In addition a wide range of T2 star time values was found (9.6–93.3 ms) in our healthy population; in 3.3% of all assessed segments even < 20 ms. A wide range of standard values was also reported by Ramazzotti et al. They scanned five healthy subjects at six different sights using two different MRI scanners [12]. T2 star time values of 16 myocardial segments were assessed with a custom-written software and ranged from 20 to 60 ms (mean 36.2 ± 4.0 ms) [12]. In addition Westwood et al. have also described a wide range of T2 star time values comparing scanners of different vendors (27.1 ± 5.0 ms vs. 47.5 ± 10.3 ms) by scanning ten volunteers (mean age 34.9 ± 5.0) and using an in-house designed software [7].

The allegedly pathological segments in our study did not show a systematic distribution pattern or an elevated standard deviation as an indirect hint for underlying susceptibility artefacts, which could explain our findings. There was no systematic difference in the standard deviation between the septum or other regions of the heart indicating a higher occurrence of artifacts in any heart segment.

The exact underlying mechanisms of interregional, intersegmental and interlevel variations in T2 star time values between corresponding or different heart segments in our study and in previously published studies in the context of other cardiac parametric approaches are not fully assignable. According to Rogers et al. and Kawel et al., who have assessed regional variations, it is unlikely that differences between heart segments or within the same heart segment (short vs. long axis) represent a true regional disparity in longitudinal relaxation [20–22]. Rather they are likely related to a number of confounding factors including magnetic susceptibility artefacts, issues pertaining to receiver coil sensitivity and signal gradient between heart segments due to different distances from the receiver coil elements [20, 21]. But also the structure of myocardial muscle itself may lead to segmental variations.

Limitations

Our study has several limitations. First the number of volunteers included is rather small. Intercenter studies with a large number of volunteers and patients are needed to confirm our results for this specific type of scanner.

Second, only one sequence was used and the effect of different imaging pulse sequences on our results remains unclear.

Third, only one mapping sequence, one dedicated commercially software and one specific MRI scanner from only one vendor were evaluated. Our results cannot be translated or compared to other vendors or different field strengths as T2 star time values are not directly comparable between 1.5 T and 3 T [1]. Further, T2 star time values can be affected significantly by the performed sequence, basically by every scan parameter (slice thickness, flip angles etc.), by the used coil or by the used post-processing software [1]. As a consequence, our results should only be compared to other parameter values if they are obtained under similar conditions [1].

Conclusion

Cardiac T2 star mapping with identical hardware and commercially available software is highly reproducible in SAX and LAX which allows comparability of examinations between different sites. T2 star values vary between heart segments and even between corresponding SAX and LAX segments in healthy people, which demands a cautious interpretation of single segmental values. The wide range of T2 star values between heart segments and published interscanner differences question a fixed threshold for pathological values, in particular as a device-specific calibration for cardiac T1 and T2 mapping is mandatory, and whether the placement of a single septal ROI in a mid-cavity SAX can be representative [1]. In our opinion, measurement of relaxation times should be done in multiple segments and for follow-ups same segments in identical planes should be measured to obtain consistent and reliable results.

Compliance with ethical standards

Conflict of interests The authors declare that they have no competing interests.

Ethical approval Institutional review board approval was obtained and all volunteers gave written informed consent.

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