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ORIGINAL PAPER

In-vivo assessment of normal T1 values of the right-ventricular myocardium by cardiac MRI

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Abstract To test feasibility of myocardial T1 mapping of the right ventricle (RV) at systole when myocardium is more compact and to determine the most appropriate imaging plane. 20 healthy volunteers (11 men; 33 ± 8 years) were imaged on a 1.5T scanner (MAGNETOM Avanto, Siemens AG, Erlangen, Germany). A modified look-locker inversion-recovery sequence was acquired at mid-ventricular short axis (SAX), as horizontal long-axis view and as transversal view at systole (mean trigger time 363 ± 37 ms). Myocardial T1 time of the left-ventricular and RV myocardium was measured within a region of interest (ROI) on generated T1-maps. The most appropriate imaging plane for the RV was determined by the ability to draw a ROI including the largest amount of myocardium without including adjacent tissue or blood. At systole, when myocardium is thicker, measurements of the RV myocardium were feasible in 18/20 subjects. Average size of the ROI was 0.42 ± 0.28 cm^2. In 10/18 subjects, short axis was the most appropriate imaging plane to obtain measurements ($p = 0.034$). Average T1 time of the RV myocardium was 1,016 ± 61 ms, and average T1 of the left-ventricular (LV) was 956 ± 25 ms ($p < 0.001$). T1 mapping of the RV myocardium is feasible during systole in the majority of healthy subjects but with a small ROI only. SAX plane was the optimal imaging plane in the majority of subjects. Native myocardial T1 time of the RV is significantly longer compared to the LV, which might be explained by the naturally higher collagen content of the RV.

Keywords T1 mapping · Right ventricle · Diffuse fibrosis

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Background

Several cardiac diseases are associated with an increase in myocardial collagen content (myocardial fibrosis), either focal or diffuse, which can be assessed by cardiac magnetic resonance (CMR) imaging by measuring the longitudinal relaxation time T1 of the myocardium [1]. This was made possible in the recent years by the development of the Modified Look-Locker Inversion Recovery (MOLLI) sequence, [2] composed of a single-shot balanced steady-state free-precession readout following an adiabatic magnetization inversion pulse.

By calculating the ratio of pre- and post-contrast reciprocal values of T1 measured in blood and myocardium corrected for the hematocrit, the extracellular volume fraction (ECV) can be estimated [ECV = ΔR1 myocardium/ΔR1 blood × (1 − hematocrit)], which is directly related to collagen content [3]. In several cardiac diseases associated with myocardial fibrosis, changes in myocardial T1 values and the ECV, compared to a normal control group could be demonstrated: for example, myocardial ECV has been shown to be increased in sarcomere mutation carriers of hypertrophic cardiomyopathy (HCM) even if left-ventricular hypertrophy was not present [4]. Also native T1 was significantly longer in patients with HCM and nonischemic dilated cardiomyopathy [5]. A strong correlation between ECV and histological fibrosis was

demonstrated in subjects with aortic stenosis [6]. Furthermore, myocardial T1 time has been shown to be altered in patients with diabetic cardiomyopathy [7, 8] and adult congenital heart disease [9]. These are just a few examples of what has been published related to detection and quantification of diffuse myocardial fibrosis in the near past.

All these publications have in common that myocardial fibrosis was measured in the left-ventricular (LV) myocardium. However, there are also diseases associated with fibrotic changes of the right-ventricular (RV) myocardium such as pulmonary artery hypertension [10] and arrhythmogenic right-ventricular dysplasia [11]. For this reason, T1 mapping of the right ventricle could be of clinical relevance in these patient groups.

To our knowledge there is a single publication where measurement of the T1 time of the right-ventricular myocardium was attempted. Plymen et al. [12] tried to obtain T1 values of the right-ventricular free wall in subjects with a transposition of the great arteries and with a systemic right ventricle after Senning or Mustard. But measurements showed a poor interobserver reproducibility and could therefore not be used for further analysis. In this study, the image acquisition was presumably performed in diastole, which is the usual acquisition modality for this kind of method, but, in the literature, image acquisition has been shown to be feasible also in systole with even better image quality due to the more compact and thicker myocardium [13].

The purpose of our study was to assess the feasibility of T1 mapping of the RV myocardium pre-contrast in healthy volunteers by acquiring during the systolic phase and to determine the most appropriate imaging plane, assessing the reliability of this method in terms of interobserver reproducibility and its precision as measured by the coefficient of variation of the acquired T1 values.

Methods

Image acquisition

Twenty healthy volunteers (11 men; 33 ± 8 years; age range 22–52 years) were scanned on a 1.5T clinical magnet (MAGNETOM Avanto, Siemens AG Healthcare Sector, Erlangen, Germany). A retrospectively gated cine steady-state free-precession (SSFP) sequence was acquired as horizontal long-axis view (HLA) with 40 reconstructed phases per heartbeat. Systole was determined visually by the smallest volume of the right ventricle and trigger time was noted. A MOLLI sequence was acquired at mid-ventricular short-axis (SAX), HLA view and as transversal view at systole by starting the data acquisition at the previously determined trigger time. The version of MOLLI that was used acquired 8 images over 11 heart beats resulting in a 3-3-5-pattern (3 heartbeats of image acquisition, 3 heartbeats recovery, 5 heartbeats acquisition) with a start inversion time (TI) of 120 ms and a TI increment of 80 ms. In the first 5 volunteers T1 maps were also acquired in diastole. Trigger time was determined by the largest volume of the right ventricle on cine SSFP images. The scan parameters used were the following: TE/TR 1.13 ms/2.7 ms; flip angle 35°; bandwidth 1,028 Hz/Px; resolution $1.4 \times 1.9 \times 7$ mm^3 (interpolated to $1.4 \times 1.4 \times 7$ mm^3), field-of-view 360×270 mm^2, partial Fourier factor 7/8, parallel imaging factor 2. The MOLLI sequence included automatic generation of T1 maps and motion correction. The T1 maps were checked for artefacts such as motion artefacts directly after acquisition. In cases where artefacts occurred, the sequence was immediately repeated ensuring good image quality of all images.

Image analysis

Images were transferred to a workstation (syngo Multi-Modality Work Place VE50A; Siemens AG Healthcare Sector, Erlangen, Germany). To measure T1 time of the RV and LV myocardium a ROI was drawn on the T1 maps by using the freehand ROI tool of the software. The most appropriate imaging plane for measuring T1 time of the RV myocardium was determined by the ability to draw a region of interest (ROI) on the corresponding T1 map without including adjacent blood or tissue. In cases where this was possible in more than one plane, the most appropriate plane was determined by the largest ROI. T1 time of the right- and left-ventricular myocardium (mean ± SD) were measured on the T1 map in the most appropriate imaging plane. In those subjects where measurement of RV T1 time was feasible in more than one plane, it was also obtained in the plane where the second largest ROI could be drawn. All measurements were performed on color-coded T1 maps as shown in Fig. 1. The window setting was individually adjusted for each T1 map aiming not at generating homogeneously colored myocardium that could hide partial-volume effects but to accentuate small differences in T1 time in order to display partial-volume effects and to avoid inclusion of adjacent blood or tissue.

Statistical analysis

Statistical analysis was performed using SPSS (IBM statistical software; version 21). A p value of <0.05 was considered to be statistically significant. The Chi square test with Williams correction was used to compare observed frequencies of the most appropriate imaging plane with the expected frequencies, which was equal distribution between the imaging planes. T1 time of left- and right-ventricular myocardium was compared with a

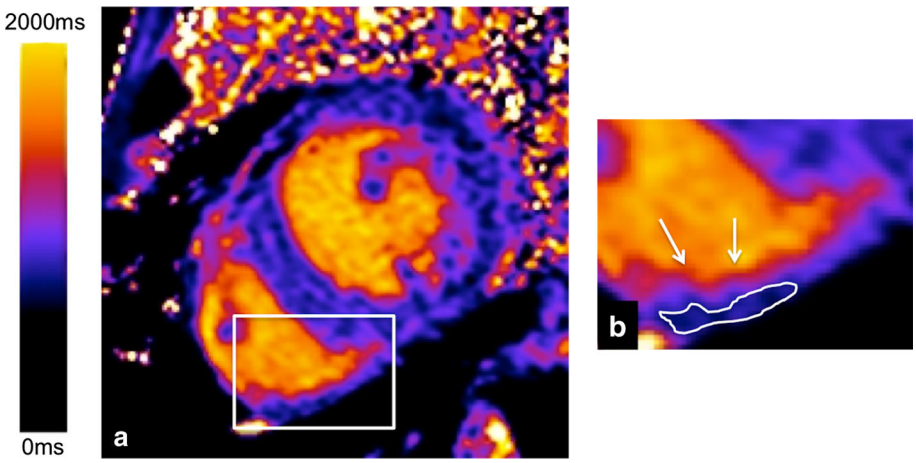

Fig. 1 T1 map acquired in systole in the short-axis view. In (**b**) the enlarged detail outlined with a *white square* in (**a**) is shown. A small ROI was placed on a compact homogenous part of the RV myocardium (**b**). The border zone that appears at the border between myocardium and blood related to partial-volume effects (*arrows* in b) was excluded to avoid inclusion of blood

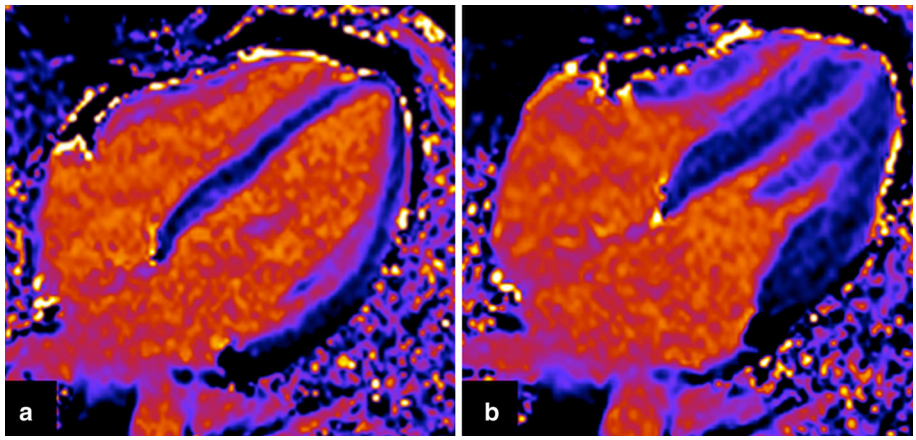

Fig. 2 T1 map acquired in the horizontal long axis view during diastole (**a**) and systole (**b**). During diastole the myocardium is very thin making placement of a region of interest without inclusion of adjacent tissue or blood pool impossible. During systole right-ventricular myocardium is more compact enabling measurement of myocardial T1 time

paired *t* test. To assess agreement between measurements of the RV myocardium within subjects, a Bland-Atman plot was generated. The coefficient of variation (standard deviation across the ROI divided by the average over the same ROI), intended as a measure of method precision, was calculated for each measurement of the right- and left-ventricular myocardium and compared with a paired *t* test. To assess interobserver agreement, the concordance correlation coefficient (CCC) was calculated and Bland–Altman plots were generated.

Results

In the first 5 volunteers, T1 maps were acquired during systole and diastole. On none of the T1 maps acquired at diastole (average trigger time 624 ± 74 ms) it was possible to draw a ROI on the RV myocardium without inclusion of adjacent blood or tissue due to the thinness and trabeculated structure of the RV myocardium (Fig. 2). Therefore in the following 15 volunteers acquisitions were performed in systole only.

Average trigger time to obtain images in systole was 363 ± 37 ms. In 18 of 20 volunteers, a ROI could be placed on the RV myocardium without obvious inclusion of adjacent blood or tissue to measure T1 time in at least one of the three imaging planes. In the other two volunteers (both women with a BMI of 16.6 and 20.1, respectively), it was impossible to draw a ROI without including adjacent blood due to the thinness of the myocardium in any plane. In 10/18 subjects SAX was the most appropriate imaging plane to obtain measurements, in 7/18 it was the transverse plane and in only one subject it was the HLA view, making the preference for the SAX plane statistically significant ($p = 0.034$). In 5/18 subjects it was possible to place a ROI to obtain measurements of the RV T1 time without obvious inclusion of blood in all three planes, in 7/18 subjects measurements could be obtained on two of the three planes and in 6/18 subjects measurements could be obtained on only one of the three planes. In 15 of all 20 volunteers a ROI could be placed on the short-axis plane to measure RV myocardial T1 time without obvious inclusion of blood, in 12/20 on the transverse plane and in only 8/20 in the HLA view.

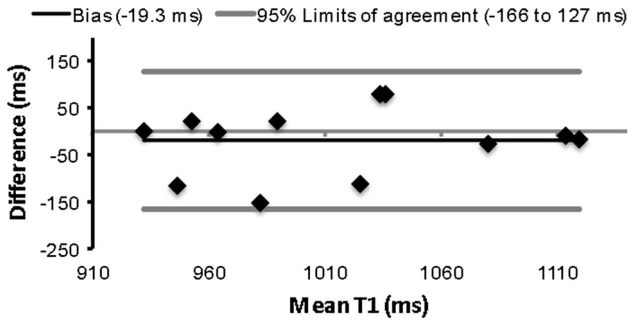

Fig. 3 Bland-Altman plots comparing measurements of right-ventricular myocardial T1 time of two imaging planes in the same subject (n = 12)

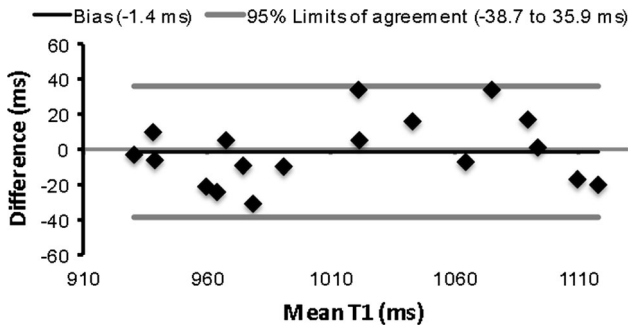

Fig. 4 Bland-Altman plots comparing measurements of right-ventricular myocardial T1 time of the two readers

The average size of the ROI used for measurements of the T1 time of the RV myocardium that could be placed on the best imaging plane without including adjacent blood was 0.42 ± 0.28 cm^2 (21.4 ± 14.3 voxels).

In the 12 subjects where measurements of RV T1 time could be obtained in at least two planes, the Bland–Altman plot shows a good agreement of the measurements within subjects with a mean bias of −19.3 ms and 95 % limits of agreement of −166 to 127 ms (Fig. 3).

The average myocardial T1 time of the left and right ventricle was 956 ± 25 and 1,016 ± 61 ms ($p < 0.001$), respectively. The average coefficient of variation of measurements obtained of the LV myocardium was 5.0 %, whereas the one for the RV myocardium was 4.7 % ($p = 0.15$).

The interobserver agreement was high with a CCC of 0.96. There was good agreement according to the Bland–Altman method with a mean bias of −1.4 ms and 95 % limits of agreement of −38.7–35.9 ms (Fig. 4).

Discussion

In the current study we demonstrated feasibility to measure T1 time of the RV myocardium by placing a ROI on T1 maps obtained at systole in the majority of healthy volunteers with a high interobserver agreement. In a previous publication measurement of RV myocardial T1 time obtained on T1 maps presumably acquired at diastole was not feasible [12]. In our study, T1 maps were acquired in systole, when RV myocardium is more compact and thicker. However, the average size of the ROI was small (0.42 ± 0.28 cm^2) in our cohort of healthy subjects (Fig. 1). In patients with hypertrophied right-ventricular myocardium, the size of the ROI might be larger. In two women of our cohort with a low BMI and low left and right ventricular myocardial thickness, it was impossible to draw a ROI encompassing a sufficiently homogeneous area of tissue on T1 maps in all three imaging planes. This can be explained because linear correlation between the BMI and RV myocardial mass has been shown in adjusted models [14]. Therefore, in some healthy subjects with a low BMI it might be impossible to draw a ROI without inclusion of adjacent blood. However, in other volunteers of our cohort measurements could be obtained despite a low BMI.

The most appropriate imaging planes were short axis and the transverse plane while the HLA view was determined as the best imaging plane in only one subject. Even in those cases where the SAX view was not considered the most appropriate plane, frequently it was still possible to measure T1 time of the RV myocardium on T1 maps acquired as SAX view (15 out of 20 subjects). This finding implies that in future studies and clinical applications, T1 mapping of the RV myocardium should be acquired in SAX first. If it is impossible to draw a ROI on the SAX maps, the transverse plane could be tried next. This approach should be the most time-efficient when trying to identify the most suitable imaging plane (Fig. 5).

T1 time of the right-ventricular myocardium was significantly longer compared to the left-ventricular myocardium (1,016 ± 61 vs. 956 ± 25 ms; $p < 0.001$). We hypothesize that this finding is due to the fact that the collagen content of the normal RV myocardium is naturally 30 % higher compared to the LV myocardium meaning that the non-contrast T1 time of the former is expected to be longer compared to the latter [15, 16].

The main strength of the study is that it was performed in human subjects, thus providing values that can be used as reference for future studies. However, it is a limitation of the study that histological samples could not be collected for analysis and correlation, since the study was performed on healthy human subjects. For this reason, a direct proof that the difference in relaxation times is not caused by accidental inclusion of adjacent blood cannot be obtained. However, when placing the ROI we carefully avoided inclusion of blood by avoiding the border zone around the myocardium (see Fig. 1) as suggested in [17] for the LV. Measurements in trabeculated parts of the RV myocardium

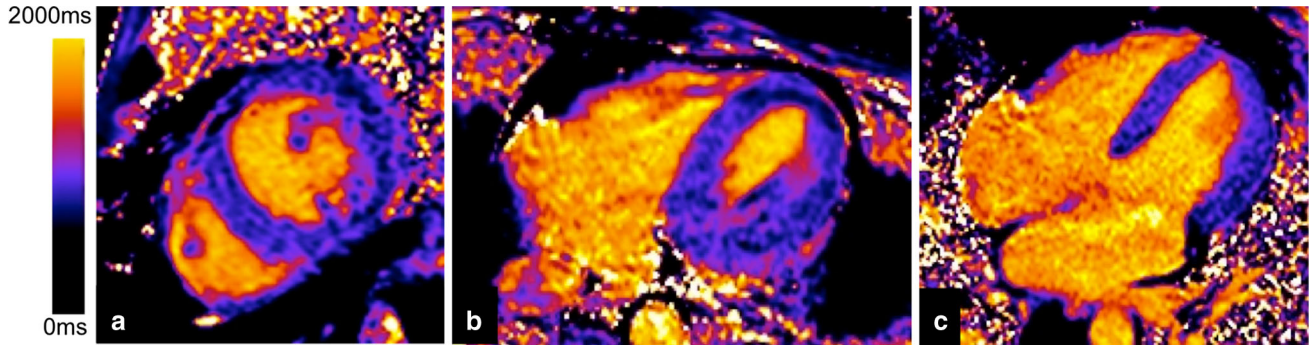

Fig. 5 T1 maps of the same volunteer of Fig. 1 acquired at systole in the short-axis view (**a**), the transverse plane (**b**) and in the HLA view (**c**). RV myocardial T1 time could only be measured in short axis (shown in Fig. 2) while in the transverse plane and the HLA view a ROI could not be placed without inclusion of blood since RV myocardium was too thin and trabeculated

can be avoided by placing the ROI in areas with homogeneous color on the color T1 maps. Using these guidelines, measurements of the LV and RV myocardium achieved similar precision, thus indicating that the ROIs encompassed regions of similarly homogeneous histological composition, and corroborating the hypothesis that blood with substantially longer T1 time was excluded. Further, we could demonstrate a good agreement between measurements of RV T1 time obtained in the same subject in two different imaging planes. However, for this study we were using the current standard version of the MOLLI sequence that is used for the left ventricle provided by the scanner vendor. Parameters of the sequence including spatial and temporal resolution remained unchanged. This was chosen as an acceptable tradeoff to avoid sacrificing one parameter in favor of the other, as lower temporal resolution bring the danger of motion artifacts, especially in systole, while lower spatial resolution give rise to higher partial volume effects. However, due to the characteristics of the studied area, higher resolution would be advisable, and this is a limitation of the current study. A MOLLI sequence with improved spatial resolution might be advantageous for T1 mapping of the right ventricle but would require a more advanced sequence implementation, which is not currently available. This could enable placement of a larger ROI and reduce partial volume effects.

In conclusion, in the present study we were able to demonstrate that T1 mapping of the RV myocardium was feasible in healthy subjects when images were obtained at systole. However, both the imaging plane and the region of measurement have to be chosen carefully and the ROI that could be placed without inclusion of blood was small. For this reason, this approach is useful when investigating diffuse myocardial effects of the RV rather than focal lesions. For a time-efficient approach, the SAX plane should be tried first followed by the transverse plane.

Conflict of interest None.

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