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Myocardial Mapping in Systemic Sarcoidosis: A Comparison of Two Measurement Approaches

Myokardiales Mapping bei systemischer Sarkoidose: ein Vergleich zweier Messansätze

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ZUSAMMENFASSUNG

Ziel Untersuchung, ob T1- und T2-Mapping bei Patienten mit systemischer Sarkoidose zwischen krankem und gesundem Myokard unterscheidet. Vergleich der herkömmlichen Messmethode (Messung im gesamten mittventrikulären Myokard der kurzen Herzachse, SAX) mit einem standardisierteren Messansatz, bei dem die Relaxationszeiten ausschließlich im mittventrikulären Septum gemessen werden (ConSept).

Material und Methoden 24 Patienten mit bioptisch gesicherter extrakardialer Sarkoidose und 17 gesunde Probanden wurden prospektiv in diese Studie eingeschlossen und an einem 1,5-Tesla-Magneten unter anderem mittels nativem T1- und T2-Mapping untersucht. Patienten wurden im Rahmen der Auswertung unterteilt in Patienten mit (LGE+) und Patienten ohne späte myokardiale Kontrastmittelaufnahme (LGE–). Des Weiteren wurden die SAX- und die ConSept-Messmethode auf ihre Differenzierbarkeit zwischen gesundem und krankem Herzmuskelgewebe untersucht.

Ergebnisse Alle Patienten wiesen unabhängig von der gewählten Messmethode (ConSept bzw. SAX) signifikant längere T1- und T2-Relaxationszeiten im Vergleich zu den gesunden Probanden auf ($p < 0{,}05$). Jedoch zeigten sich keine signifikant unterschiedlichen Relaxationszeiten zwischen Patienten mit (LGE+) und ohne späte myokardiale Kontrastmittelaufnahme (LGE–), unabhängig von der gewählten Messmethode (ConSept/Sax) ($p > 0{,}05$). Der direkte Vergleich zwischen den Messmethoden ConSept und SAX zeigte beim T1-Mapping eine hohe Übereinstimmung in Bezug auf die Differenzierung zwischen krankem und gesundem Myokard (Kappa = 0,844).

Schlussfolgerung Mittels T1- und T2-Mapping ist es möglich, bei Patienten mit systemischer Sarkoidose zwischen krankem und gesundem Myokard zu unterscheiden. Darüber hinaus stellt das myokardiale Mapping einen möglichen Marker für die Früherkennung einer kardialen Beteiligung dar, was eine zeitgerechte Behandlung begünstigt. ConSept-T1-Mapping stellt einen gleichwertigen Messansatz zur SAX-Methode bei Sarkoidose-Patienten dar. Weitere Studien, inklusive Follow-up-Studien, sind notwendig, um diese vorläufigen Ergebnisse zu bestätigen.

Kernaussagen:

- Mapping kann zwischen krankem und gesundem Myokard bei Patienten mit systemischer Sarkoidose unterscheiden
- Mapping könnte zur Früherkennung einer kardialen Sarkoidose beitragen
- ConSept-T1-Mapping stellt einen alternativen Messansatz zur SAX-Methode bei Sarkoidose-Patienten dar

ABSTRACT

Purpose To investigate if T1 and T2 mapping is able to differentiate between diseased and healthy myocardium in patients with systemic sarcoidosis, and to compare the standard mapping measurement (measurement within the whole myocardium of the midventricular short axis slice, SAX) to a more standardized method measuring relaxation times within the midventricular septum (ConSept).

Materials and Methods 24 patients with biopsy-proven extracardiac sarcoidosis and 17 healthy control subjects were prospectively enrolled in this study and underwent CMR imaging at 1.5 T including native T1 and T2 mapping. Patients were divided into patients with (LGE+) and without (LGE–) cardiac sarcoidosis. T1 and T2 relaxation times were compared between patients and controls. Furthermore, the SAX and the ConSept approach were compared regarding differentiation between healthy and diseased myocardium.

Results T1 and T2 relaxation times were significantly longer in all patients compared with controls using both the SAX and the ConSept approach ($p < 0.05$). However, LGE+ and LGE– patients showed no significant differences in T1 and T2 relaxation times regardless of the measurement approach used (ConSept/SAX) ($p > 0.05$). Direct comparison of ConSept and SAX T1 mapping showed high conformity in the discrimination between healthy and diseased myocardium (Kappa = 0.844).

Conclusion T1 and T2 mapping may not only enable noninvasive recognition of cardiac involvement in patients with systemic sarcoidosis but may also serve as a marker for early cardiac involvement of the disease allowing for timely treatment. ConSept T1 mapping represents an equivalent method for tissue characterization in this population compared to the SAX approach. Further studies including follow-up examinations are necessary to confirm these preliminary results.

Key Points:
- Mapping may enable noninvasive recognition of cardiac involvement in patients with systemic sarcoidosis
- Mapping may serve as a marker for early cardiac involvement in patients with systemic sarcoidosis
- The ConSept approach can be used as an alternative measuring method in sarcoidosis patients

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Introduction

Sarcoidosis is a chronic inflammatory disease which can affect multiple organs but mostly affects the lungs. Histologically, the disease is characterized by non-caseating granulomas [1]. Cardiac involvement in the context of this disease is considered a life-threatening situation [2]. At the same time, the diagnosis of cardiac sarcoidosis (CS) is difficult since the symptoms are rare and usually only occur in advanced stages of disease with AV-conduction block, heart failure, or sudden death [3]. In order to facilitate diagnosis of cardiac involvement in patients with systemic sarcoidosis, two guidelines have been proposed: The Japanese Ministry of Health and Welfare (JMHW) guidelines (originated in 1993 and revised in 2006) and the 2014 Heart Rhythm Society (HRS) expert consensus criteria [1, 4]. Apart from histological proof of disease by endomyocardial biopsy, which is known to have a low sensitivity, both guidelines rely on clinical confirmation (the latter is based on diagnostic algorithms, i. e. combinations of major and minor criteria allowing for diagnosis). Cardiac magnetic resonance imaging (CMR) is a reliable noninvasive diagnostic tool not only for the diagnosis of ischemic cardiomyopathies, but also non-ischemic cardiomyopathies such as CS [5–8]. Furthermore, T1 mapping and T2 mapping are novel and robust tools for the noninvasive assessment of diffuse myocardial fibrosis and edema, respectively [9, 10]. Myocardial mapping is commonly performed in the short axis orientation including the entire tissue of a whole midventricular short axis slice (SAX). Recently, a new measurement approach, where the region of interest (ROI) is placed conservatively within the midventricular septum (ConSept), has been proposed as a more standardized method for the assessment of native and post-contrast T1 values in diffuse myocardial disease [11]. Excellent inter- and intraobserver correlations for both the SAX and the ConSept approach have been proven in several previous studies [11–13].

The aim of this study was first to test the feasibility of native T1 and T2 mapping to differentiate between healthy and diseased myocardium in patients with systemic sarcoidosis and second to compare the SAX and the ConSept approach regarding their diagnostic performance.

Materials and Methods

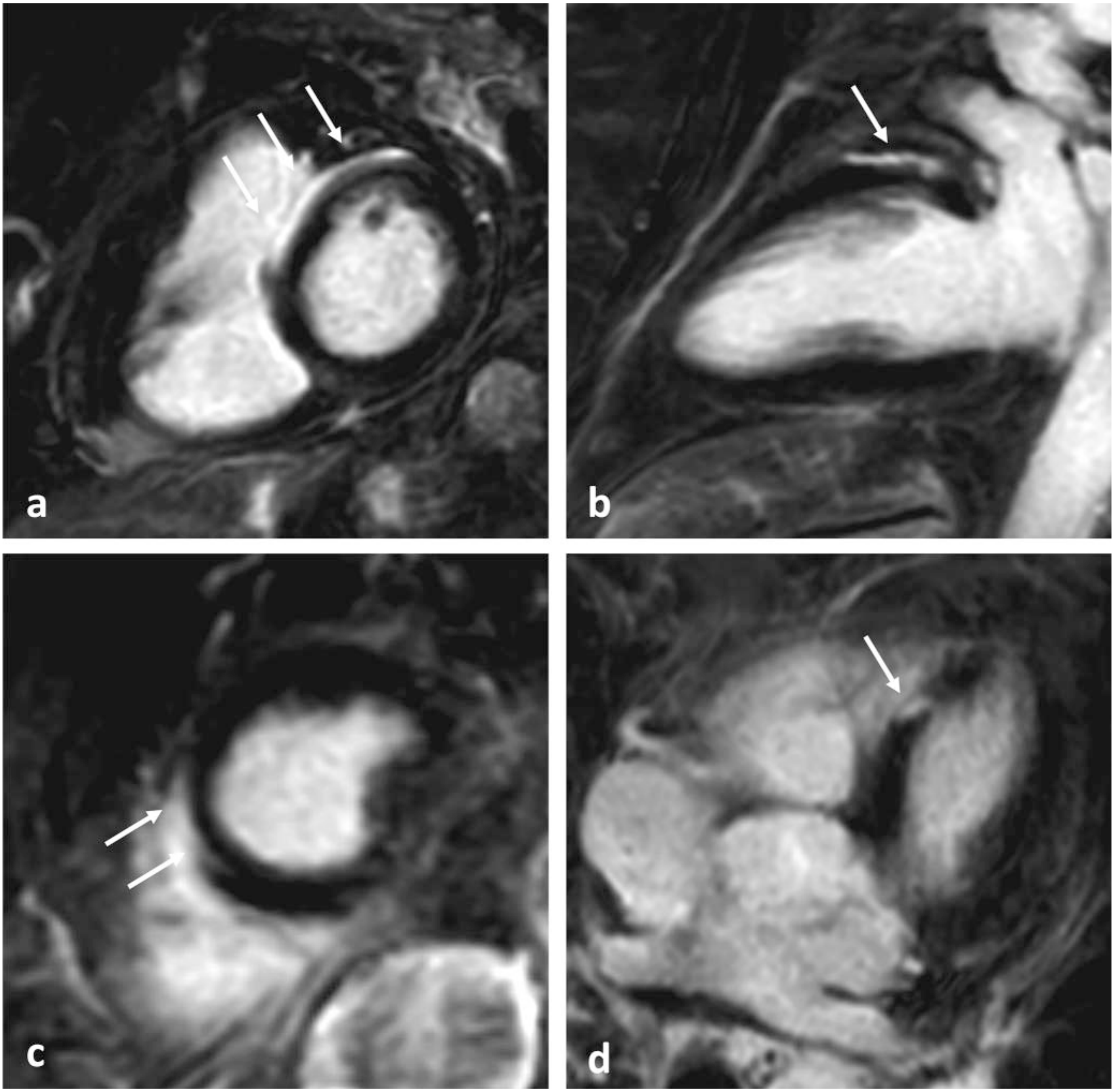
Study protocol and study population

The study was approved by the local ethics committee. 24 patients with biopsy-proven extracardiac sarcoidosis and 17 healthy controls underwent cardiovascular magnetic resonance (CMR) imaging at 1.5 T (Ingenia, Philips Healthcare, Best, The Netherlands). The control group consisted of volunteers and normotensive outpatients referred for clinical CMR due to nonspecific thoracic pain with subsequently normal CMR findings – as previously described [13, 14]. The majority of patients (21/24) presented with pulmonary manifestation. 8 patients suffered from arterial hypertension. However, none of the included patients had a history of distinct cardiac disease (e. g., coronary artery disease with coronary stenosis > 50 % according to angiography results, myocardial infarction, myocarditis, or cardiomyopathy).

For CMR examination an imaging protocol for the assessment of inflammatory heart disease was used. Based on the HRS expert consensus criteria, according to which the clinical diagnosis of CS can be made from a combination of extracardiac histologic confirmation of sarcoidosis and detection of LGE by CMR, CS was diagnosed in patients with the presence of LGE in a non-ischemic pattern (epicardial or midmyocardial) [4]. Based on the CMR results, patients were subdivided into patients presenting with LGE (LGE+; ▶ **Fig. 1**) and patients without evidence of LGE (LGE–).

CMR imaging

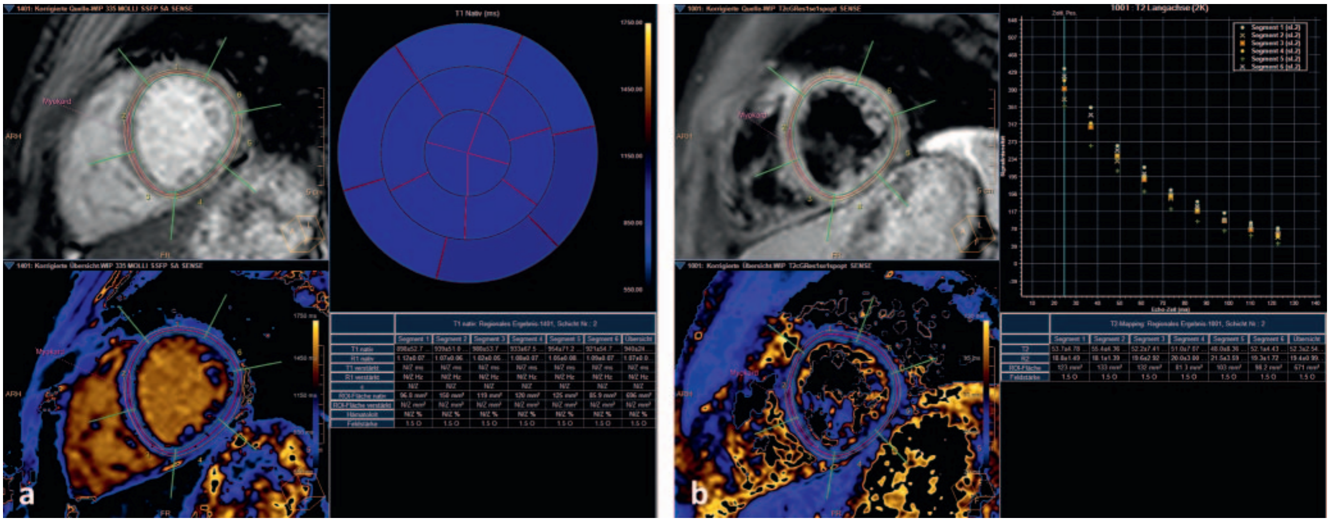
CMR imaging was performed at 1.5 T (Ingenia Philips Healthcare, Best, Netherlands) using a 32-channel torso coil with a digital interface for signal reception. Left ventricular (LV) wall motion and



▶ **Fig. 1** Late enhancement images of two patients with cardiac sarcoidosis. SA **a** and VLA **b** views of a 71-year-old patient with subepicardial LGE within the midventricular and basal antero-septal wall (arrows). SA **c** and HLA **d** views of a 61-year-old patient with subepicardial LGE within the midventricular antero-septal wall (arrows).

▶ **Abb. 1** Late-Enhancement-Bilder zweier Patienten mit kardialer Sarkoidose-Beteiligung. Kurze **a** und vertikale lange Achse **b** eines 71-jährigen Patienten mit subepikardialer Narbe mittventrikulär und basal anteroseptal (Pfeile). Kurze **c** und horizontale lange Achse **d** eines 61-jährigen Patienten mit subepikardialer Narbe mittventrikulär anteroseptal (Pfeile).

functional analysis were assessed during breath hold using electrocardiographically gated steady-state free precession cine images in the standard cardiac axes. Black-blood T2-weighted short tau inversion recovery sequences acquired in vertical long axis (VLA), short axis (SA), and transverse orientation were used for the assessment of myocardial edema. Prior to and < 1 min after intravenous injection of a single dose (0.1 mmol per kilogram of bodyweight) of extracellular contrast agent (Gadovist, Bayer Healthcare, Leverkusen, Germany), T1-weighted images in transverse orientation were acquired to assess inflammation-associated myocardial hyperemia (early gadolinium enhancement ratio (EGEr) > 4), as previously described [15]. As soon as the EGE images were acquired, an additional single dose of contrast agent was administered for the assessment of late gadolinium enhancement



▶ **Fig. 2** T1 **a** and T2 **b** mapping images of a midventricular SA slice with raw images in the upper left hand corner and corresponding color-coded maps in the lower left hand corner. Relaxation times are represented in the form of a color-coded grid **a** and in a diagram **b** in the upper right hand corner; absolute values are listed in a spreadsheet below. Images represent both the SAX and the ConSept approach.

▶ **Abb. 2** T1- **a** und T2- **b** Mapping-Bilder in mittventrikulärer kurzer Herzachse mit Rohbildern in der linken oberen Ecke und dazugehörigen farbkodierten Maps in der unteren linken Ecke. Die Relaxationszeiten werden in Form eines farbkodierten 16-Segment-Modells **a** bzw. in Diagrammform **b** in der jeweils rechten oberen Ecke angezeigt, die absoluten Relaxationszeiten in der darunter angezeigten Tabelle. Die Abbildungen zeigen sowohl den ConSept- als auch den SAX-Messansatz.

(LGE), which allows for the detection of myocardial scar and fibrosis. LGE imaging using segmented inversion-recovery gradient echo sequences was performed 10–15 minutes after injecting the second bolus of contrast agent in HLA, SA, and VLA. The employed inversion time was determined using the Look-Locker technique.

Native T1 maps were obtained in end-diastole in a single midventricular short axis slice using the 3-3-5 modified Look-Locker inversion recovery scheme [16]. T2 relaxation times were also assessed in a single midventricular short axis slice using a hybrid gradient and spin-echo sequence (GraSE), as previously described [17].

Image analysis

Cardiac function and interventricular septal thickness (IVST) were analyzed offline using appropriate software (ViewForum, Philips Healthcare). Left ventricular end-diastolic volume (LVEDV) and ejection fraction (LVEF) were measured manually by tracing the left ventricular endocardial borders. Quantitative assessment of LGE was executed using the N-standard deviation method, where a signal intensity 4 standard deviations above the signal intensity of remote myocardium was considered LGE-positive [18].

Analysis of T1 and T2 relaxation times

Analysis was performed using dedicated software (Philips IntelliSpace 9, Philips Healthcare, Best, Netherlands). Prior to analysis, automatic motion correction was performed in all maps. T1 and T2 relaxation times were measured using two different approaches: (I) including the whole midventricular short axis slice (SAX) and (II) placing the region of interest (ROI) within the midventricular septum (ConSept) as previously described (▶ **Fig. 2**) [11]. To compare both methods (SAX vs. ConSept) regarding their diagnostic performance in differentiating between healthy and diseased myocardium, in-house-defined sequence-specific cut-off values (T1 > 1000 ms, T2 > 55.9 ms) for an abnormal myocardium in patients with acute myocarditis were previously used [19].

Statistical analysis

SPSS Software Version 25 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Data are shown using means and their standard deviations (SD) for continuous variables and frequency distributions. Categorical variables are listed in percentages. Univariate ANOVA by the application of Turkey-HSD post-hoc tests was used to compare mean differences between groups. The spearman's rank correlation coefficient was used to evaluate statistical dependence between rankings of two variables. $P < 0.05$ indicated a significant difference. Comparison of diagnostic performance between groups was performed using the Cohen's kappa coefficient (K).

Results

All individuals were scanned successfully. T1 and T2 maps were checked for artifacts by a radiologist on the scanner and repeated in case of motion and/or breathing artifacts, thus, no image drop out was recorded. Patient characteristics are presented in ▶ **Table 1**. The LVEF in LGE+ patients (57.4 ± 5 %) was significantly lower than in LGE– patients (63.8 ± 7 %; p = 0.038). On average, LGE accounted for 2.3 % (1–7 %) of the left ventricular mass.

▸ **Table 1** Patient characteristics.

▸ **Tab. 1** Patientencharakteristiken.

	all patients	LGE+	LGE–	controls	significance: patients/controls
n	24	8	16	17	
age (y)	53.9 ± 12	52.9 ± 15	54.4 ± 11	39.8 ± 14	p = 0.005
male	11 (46 %)	4 (50 %)	7 (44 %)	13 (77 %)	p = 0.661
BMI	27.5 ± 6	26.5 ± 5	27.9 ± 6	26 ± 4	p = 0.521
heart rate	70.4 ± 10	68 ± 9	71.6 ± 10	69.9 ± 16	p = 0.916
left ventricular functional parameters					
LVEDV/BSA (ml/m^2)	63.4 ± 12	63.8 ± 14	63.2 ± 13	75.8 ± 10	p = 0.009
LVEF (%)	61.7 ± 2	57.4 ± 5	63.8 ± 7	61.5 ± 2	p = 0.029
IVST (mm)	9.5 ± 1	8.8 ± 1	9.9 ± 1	9.6 ± 1	p = 0.092
cardiovascular risk factors					
diabetes	4 (17 %)	1 (13 %)	3 (19 %)		
hypertension	8 (33 %)	2 (25 %)	6 (38 %)		
smoking	4 (17 %)	1 (13 %)	3 (19 %)		
hyperlipidemia	2 (8 %)	1 (13 %)	1 (6 %)		
obesity	2 (8 %)	1 (13 %)	1 (6 %)		
symptoms					
angina	1 (4 %)	0	1 (6 %)		
dyspnea	8 (33 %)	4 (50 %)	4 (25 %)		
fatigue	5 (21 %)	2 (25 %)	3 (19 %)		
pertussis	3 (13 %)	0	3 (19 %)		
musculoskeletal pain	1 (4 %)	1 (13 %)	0		
ECG abnormalities					
VES		0	1 (6 %)		
LBBB		0	1 (6 %)		
sarcoidosis manifestations					
lung	21 (88 %)	7 (88 %)	14 (88 %)		
lymph node	3 (13 %)	1 (13 %)	2 (13 %)		
liver	6 (25 %)	1 (13 %)	5 (31 %)		
skin	4 (17 %)	1 (13 %)	3 (19 %)		
spleen	1 (4 %)	0	1 (6 %)		
bone	3 (13 %)	0	3 (19 %)		
eye	4 (17 %)	0	4 (25 %)		
cns	1 (4 %)	0	1 (6 %)		
years since diagnosis					
duration of disease (y)	11.2	10.9	11.3		
< 1	0	0	0		
1–4	7 (29 %)	2 (25 %)	5 (31 %)		
5–9	7 (29 %)	3 (38 %)	4 (25 %)		
≥ 10	10 (42 %)	3 (38 %)	7 (44 %)		

▸ **Table 1** (Continuation)

	all patients	LGE+	LGE–	controls	significance: patients/controls
medication					
ß-blockers	10 (42 %)	4 (50 %)	6 (38 %)		
ARB/ACE inhibitors	10 (42 %)	4 (50 %)	6 (38 %)		
ASS	0	0	0		
CCB	2 (8 %)	0	2 (13 %)		
statins	2 (8 %)	1 (13 %)	1 (6 %)		
diuretics	5 (21 %)	3 (38 %)	2 (13 %)		
steroids	12 (50 %)	4 (50 %)	8 (50 %)		
azathioprine	2 (8 %)	0	2 (13 %)		

LGE = late gadolinium enhancement, LVEDV = left ventricular end-diastolic volume, BSA = body surface area, LVEF = left ventricular ejection fraction, IVST = interventricular septal thickness, ECG = electrocardiogram, VES = ventricular extrasystoles, LBBB = left bundle branch block, CNS = central nervous system, ARB = angiotensin receptor blocker, ACE = angiotensin converting enzyme, ASS = acetylsalicylic acid, CCB = calcium channel blocker.
LGE = Late Gadolinium Enhancement; LVEDV = linksventrikuläres enddiastolisches Volumen; BSA = Körperoberfläche; LVEF = linksventrikuläre Ejektionsfraktion; IVST = interventrikuläre Septumdicke; ECG = Elektrokardiogram; VES = ventrikuläre Extrasystolen; LBBB = Linksschenkelblock; CNS = zentrales Nervensystem; ARB = Angiotensin-Rezeptor-Blocker; ACE = Angiotensin-converting Enzyme; ASS = Acetylsalicylsäure; CCB = Kalziumkanalblocker.

None of the ConSept measurements included LGE. Both measurement techniques (ConSept and SAX) showed significantly longer T1 and T2 relaxation times in patients (LGE+, LGE–) compared to controls ($p < 0.001$ for T1 ConSept and SAX; $p = 0.001$ for T2 ConSept and SAX), whereas no significant differences could be shown between patient groups ($p > 0.05$; ▸ **Fig. 3**). Overall, ConSept T1 relaxation times were longer than SAX T1 relaxation times (controls: 954 ± 34 ms vs. 941 ± 37ms; all: 1000 ± 45 ms vs. 988 ± 47ms; LGE–: 997 ± 34 ms vs. 984 ± 41ms; LGE+: 998 ± 31 ms vs. 992 ± 17 ms), but did not reach statistical significance ($p > 0.05$ for all parameters). There were also no significant differences between ConSept and SAX with regard to the T2 relaxation times ($p > 0.05$; ▸ **Table 2**). No significant correlation could be detected between T1 and T2 relaxation times and duration of disease, irrespective of the measurement approach used ($p > 0.05$ for all parameters). This was neither the case when comparing T1 and T2 relaxation times of patients undergoing cortisone treatment vs. patients who did not ($p > 0.05$ for all parameters). Using previously defined cut-off values for diseased myocardium, the ConSept and the SAX approach showed high conformity in discrimination between healthy and diseased myocardium regarding T1 relaxation times (K = 0.844), compared to T2 mapping (K = 0.150).

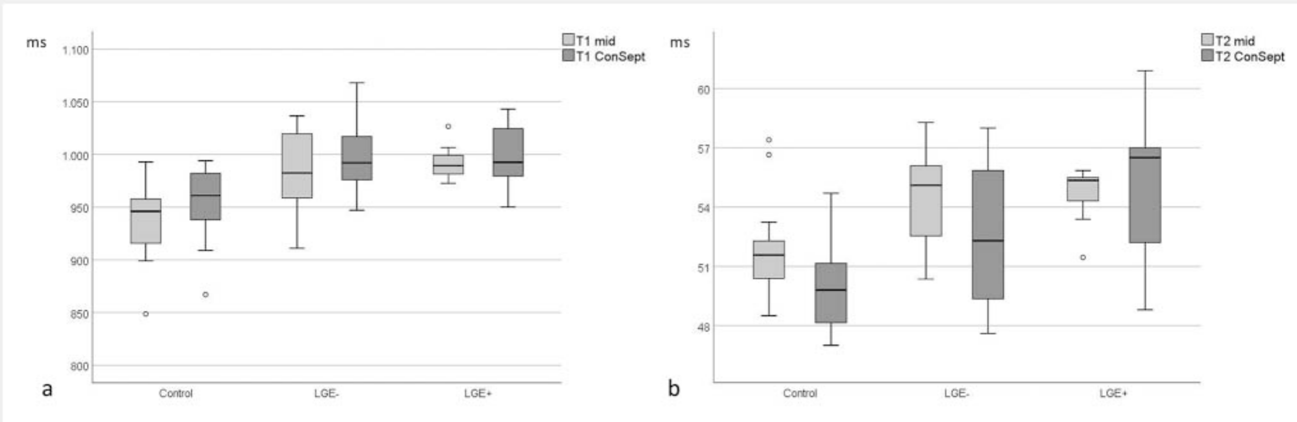
9 patients (38 %) showed T1 relaxation times above the cut-off value of 1000 ms (LGE+: ConSept + SAX 2 (25 %), ConSept 1 (13 %), SAX 0; LGE–: ConSept + SAX 5 (31 %), ConSept 0, SAX 1 (6 %)), whereas 13 patients (54 %) showed T2 relaxation times above the cut-off value of 55.9 ms (LGE+: ConSept + SAX 2 (25 %), ConSept 2 (25 %), SAX 1 (13 %); LGE–: ConSept + SAX 0, ConSept 4 (6 %), SAX 4 (6 %)).

A total of 17 patients showed T1 and/or T2 relaxation times above cut-off value, 5 (29 %) of them with evidence of LGE. 11 of these 17 patients (65 %) showed clinical symptoms such as fatigue, dyspnea (NYHA I-III) and/or angina pectoris, whereas only 3 (43 %) of the 7 remaining patients showed clinical symptoms, however without statistical significance ($p > 0.05$). The proportion of individuals above cut-off receiving cortisone therapy (53 %) was slightly higher compared to the whole patient population (42 %) ($p > 0.05$).

Discussion

Cardiac involvement in sarcoidosis, which leads to myocardial inflammation and subsequent fibrosis, may result in life-threatening complications. Thus, early diagnosis is desirable. While LGE has become an established marker of myocardial involvement, it is not quantitative and may miss early as well as diffuse myocardial involvement. It has been shown that both T1 mapping and T2 mapping are reliable methods to detect diffuse inflammatory processes and myocardial fibrosis in patients with inflammatory heart disease [14, 20–22]. Native T1 is nonspecific regarding the underlying pathophysiologic substrate of disease as it may reflect both myocardial edema and fibrosis. T2 mapping on the other hand is more water-sensitive. Therefore, a combination of both is favorable to distinguish between fibrotic or edematous changes within the myocardium [23].

In the current study, we successfully performed myocardial T1 and T2 mapping in patients with biopsy-proven systemic sarcoidosis and overall normal LVEF using two different methods: the conventional approach measuring relaxation times within the whole midventricular SA slice of the left ventricle (SAX) and by placing a ROI conservatively within the midventricular septum (ConSept). Both methods revealed higher native T1 as well as



▶ **Fig. 3** Box-plots showing T1 **a** and T2 **b** mapping results of both the SAX (shaded in light grey) and the ConSept approach (shaded in dark grey).

▶ **Abb. 3** Box Plots mit den Ergebnissen des T1- **a** und T2- **b** Mappings der SAX- (hellgrau) und der ConSept-Messmethode (dunkelgrau).

▶ **Table 2** Results for T1 and T2 measurements regarding the SAX and the ConSept approach.

▶ **Tab. 2** Mittels SAX und ConSept erhobene T1- und T2-Relaxationszeiten.

	controls	**all patients**	**p-value**	**LGE–**	**LGE+**	**p-value**
SAX						
T1 (ms)	941 ± 37	988 ± 47	0.004	984 ± 41	992 ± 17	0.599
T2 (ms)	52 ± 2	54 ± 3	0.010	54 ± 3	55 ± 2	0.881
ConSept						
T1 (ms)	954 ± 34	998 ± 32	0.001	997 ± 34	998 ± 31	0.950
T2 (ms)	50 ± 2	54 ± 4	< 0.001	53 ± 3	55 ± 4	0.284

LGE = late gadolinium enhancement.
LGE = Late Gadolinium Enhancement.

T2 relaxation times in patients – irrespective of the prevalence of LGE – compared to controls.

Studies investigating the diagnostic value of T1 and T2 mapping in sarcoidosis patients at a field strength of both 1.5 T and 3 T have been published in the past, either using the SAX or the ConSept approach exclusively [23, 24]. Greulich et al., for example, investigated T1 and T2 relaxation times using the current gold standard, the SAX approach, in sarcoidosis patients with no or nonspecific symptoms at 1.5 T. Patient characteristics including age, sex, LVEF, percentage of patients undergoing steroid treatment and percentage of LGE-positive patients were similar to those of our presented patient population. In agreement with the aforementioned study, native T1 and T2 relaxation times were significantly higher in patients compared to controls independent of the presence of LGE. Also, T1 and T2 relaxation times in LGE+ patients in the present study were higher compared to LGE– patients, however, without statistical significance.

The ConSept approach was initially proposed by Rogers et al. in 2013 [11]. It was based on previous 1.5 T and 3 T data revealing distinct regional variation of left ventricular T1 relaxation times with septal values being highest and showing a smaller spread of values than lateral [25] owing to confounding factors (e. g. inclusion of voxels outside the usually thin free left ventricular wall or partial volume effects, and a signal gradient, declining towards the lateral wall, due to an increasing distance from the receiver coil). While the SAX approach includes the aforementioned susceptible segments, the idea was to develop a robust method for the assessment of left ventricular T1 relaxation times by placing the ROI conservatively within the midventricular septum (ConSept). ConSept proved to be robust with excellent reproducibility for native and post-contrast T1 values as well as partition coefficient measurements [11]. ConSept was further employed in T2 mapping and, together with ConSept T1 mapping, proved to be a reliable method to differentiate patients from healthy volunteers in inflammatory heart diseases [26, 27]. Septal sampling allowing for differentiation between health and disease reinforced the assumption that also primarily focal inflammatory diseases have a high burden of subclinical (without visible LGE) myocardial involvement. Puntmann et al. investigated T1 and T2 mapping in 53 patients with biopsy-proven extracardiac sarcoidosis and preserved LVEF (56 %) at 3 Tesla using the ConSept approach, revealing higher native T1 and T2 relaxation times in patients compared to controls [23]. Again, these results match results of the underlying study with the slight, but interesting difference that the mean LVEF of patients in the present study was within normal range (61.7 %). The fact that LGE– patients in the present study – except for one individual with a remote increase in EGEr – showed otherwise inconspicuous CMR exams, underlines the abovementioned assumption that myocardial mapping may actually detect subclinical cardiac involvement in cardiac sarcoidosis.

This is the first study to perform both the ConSept and the SAX method in the same cohort of sarcoidosis patients, thus allowing for a direct comparison of both methods. ConSept and SAX showed high conformity with respect to discriminating healthy from diseased myocardium regarding T1 mapping (84 %). This corroborates the assumption that despite the fact that sarcoidosis is characterized by patchy involvement of the myocardium, diffuse subclinical cardiac involvement may be present and detected by septal sampling only. Conformity between the ConSept and the SAX approach using T2 mapping on the other hand was rather low. The inadequacy of T2 mapping results might be explained by taking account of STIR and EGEr results: patients and controls both had T2 ratios within normal range and only one LGE– patient revealed a remote increase in EGEr implying that, except for one patient, none of the individuals who underwent CMR showed signs of active myocardial inflammation. In conclusion, bearing in mind that T2 mapping is water-sensitive and alterations in myocardial structure, if present, are mainly due to post-inflammatory fibrosis, this might explain disconformity between T1 and T2 mapping results.

A few limitations apply to this study. Endomyocardial biopsy was not performed in this study due to its invasiveness and known sampling error. Controls examined in this study were not age-matched to the patient group. While T1 relaxation times have been shown to not be age- or gender-related [13], Boenner et al. revealed age-related differences in myocardial T2 relaxation times [12]. Thus, although patients were of a similar age (averages of 40 and 54 years, respectively), age-related differences in T2 relaxation times cannot be fully excluded as a potential limiting factor in this study. Previous studies investigated the inter- and intra-observer variability of both the SAX and the ConSept approach in inflammatory and also diffuse myocardial diseases with excellent results [11, 14, 28]. Therefore, these criteria were not examined in the current study. A recent study has shown that pulmonary arterial hypertension (PAH) causes elevation of left ventricular T1 relaxation times [29]. Two patients in the underlying study showed mild echocardiographic signs of PAH. Manifest chronic PAH may constitute a confounding factor in this study. However, no signs of relevant PAH were noted in the respective CMR studies. ROC analyses for assessment of diagnostic performance were not performed in this study due to a comparably small patient cohort, underlining the need for further larger scale studies.

Conclusion

T1 mapping and T2 mapping may not only enable noninvasive recognition of cardiac involvement, but may also have the potential to serve as markers for early cardiac involvement of disease allowing for timely treatment. ConSept T1 mapping represents an equivalent method for tissue characterization compared to the SAX approach. Further studies including follow-up examinations are necessary to confirm these preliminary results.

CLINICAL RELEVANCE

- Myocardial mapping may enable noninvasive recognition of cardiac involvement in patients with sarcoidosis and should therefore be considered for CMR imaging
- The use of myocardial mapping may contribute to early detection of the disease and thus may enable timely treatment
- ConSept T1 mapping represents a faster and easier-to-use method for myocardial tissue characterization in patients with systemic sarcoidosis compared to the SAX approach

Conflict of Interest

The authors declare that they have no conflict of interest.

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