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MYOCARDIAL INFARCTION AND SCAR

T_1 Mapping in Patients with Acute Myocardial Infarction

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ABSTRACT

Pixel-by-pixel calculation of T_1 values (T_1 mapping) has been used in different tissues to focus on T_1 changes in a quantitative fashion. The aim of this study was to establish T_1 mapping of human myocardium on a 1.5 Tesla system and to examine its diagnostic potential in patients with acute myocardial infarction (AMI). 8 patients with reperfused AMI (day 3 ± 1) underwent multi-breath-hold MRI in a 1.5 Tesla system. Sets of five images with varying T_1 weighting were acquired prior to and after the administration of contrast agent to generate images from calculated T_1 values (T_1 mapping). Prior to the contrast agent administration, all patients showed T_1 prolongation in the area of infarction, which was identified in separate measurements using the delayed enhancement approach. Compared to noninfarcted areas, T_1 values in the infarcted areas were increased by $18 \pm 7\%$ (SE, $p < 0.05$). The spatial extent of the area of T_1 prolongation was larger than that of the hyper-enhanced areas in conventional contrast-enhanced images. T_1 maps obtained after the application of Gadolinium-DTPA revealed a T_1 reduction of $27 \pm 4\%$ in infarcted tissue compared to noninfarcted areas ($p < 0.05$). The areas showing T_1 reduction were in agreement with the hyper-enhanced regions in conventional T_1-weighted images. T_1 mapping visualizes changes in the longitudinal relaxation time induced by AMI. T_1 mapping can detect myocardial necrosis without the use of contrast media. Information that can be extracted from a combination of pre- and postcontrast T_1 maps exceeds that from conventional contrast studies.

Key Words: Magnetic resonance; T_1 mapping; Myocardial infarction; Contrast media.

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Assessing infarct size and adjacent cardiac function is important for clinical decision-making. The electrocardiogram (ECG) and techniques for the detection of wall motion abnormalities are inexact in this regard (Birnbaum et al., 2001; Christian et al., 1990). Eichstaedt et al. applied magnetic resonance imaging (MRI) to assess acute myocardial infarction (AMI) by determining signal intensity changes after Gd-DTPA administration (Eichstaedt et al., 1989). Judd et al. extended these observations by introducing a pulse sequence with heavy T_1 weighting (Judd et al., 1995). Using this technique, Kim et al. found delayed enhancement in MR images 30 min after Gd-DTPA that spatially matched the infarcted area as determined with direct tissue staining in an animal model (Kim et al., 1999). Animal data also showed an increase of the longitudinal relaxation time T_1 in myocardial tissue within hours after the onset of infarction (Johnston et al., 1985). In humans, T_1 calculations from images low-field MR systems were used to assess graft rejection in patients after cardiac transplantation (Wisenberg et al., 1987). Wacker et al. adapted quantitative T_1 measurements to analyze myocardial perfusion using a 1.5 Tesla system (Wacker et al., 1999).

T_1 mapping is an imaging technique that has mainly been employed for the characterization of brain tissue (Deichmann et al., 1999; Henderson et al., 1999). Waller et al. showed that T_1 mapping based on a spin-labeling technique can be used for the quantification of perfusion and regional blood flow in rat hearts (Waller et al., 2000; 2001). T_1 mapping uses multiple scans with varying T_1 weighting in order to calculate T_1 values on a pixel-by-pixel basis, from which a parametric image can be reconstructed. Pixel intensities in these images correspond to T_1 values. The purpose of this study was to implement T_1 mapping of human myocardium on a clinical MR system and to examine its diagnostic potential in patients with acute myocardial infarction.

METHODS

Patients

Eight patients (seven male, one female) underwent MRI on day 3 ± 1 after a first myocardial infarction as defined by ST-segment elevation in at least two adjacent ECG leads, serologic evidence for myocardial necrosis (peak creatine kinase 1398 ± 384 U/l, range 424–3262 U/l), and typical clinical symptoms. All patients underwent coronary angiography and angioplasty at 8.5 ± 1.1 h after the onset of symptoms as summarized in Table 1. Stents were placed in seven of eight patients. Three patients showed anterior and five revealed inferior infarction. None of the patients had clinical symptoms of myocardial ischemia at the time of MRI.

MR Imaging

MRI studies were performed on a 1.5 Tesla Signa CV/*i*® whole body system (GE Medical Systems, Milwaukee, Wisconsin), using a standard 4-element cardiac phased array coil. The region of infarct-related edema was localized by a T_2-weighted triple inversion recovery sequence including blood suppression and short TI preparation for fat suppression (STIR) using long axis views (Simonetti et al., 1996). A short-axis slice was placed into the central region of edema-induced high signal intensity. For the T_1 mapping, a set of five images employing varying inversion times (TI: 50 to 1000 ms) was acquired using an inversion recovery (IR)-prepared

Table 1. Baseline characteristics of patients.

Patient	Age [y]	Sex	Day of MRI post-AMI	Time to cath [h]	Peak CK [U/l]	Vessel
1	43	m	4	5.3	420	RCA
2	38	m	3	8	3260	LCX
3	65	m	3	12	630	LCX
4	71	m	2	5.25	990	LAD
5	80	m	1	6.5	510	RCA
6	65	m	3	7.75	2820	LAD
7	67	f	1	14.15	1610	LCX
8	73	m	3	9.15	930	LAD

Time to cath = time from onset of symptoms until catheterization. CK = creatinekinase. Vessel = infarct-related coronary vessel as assessed by coronary angiography.

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fast gradient echo sequence (TE: 1.1 ms; slice thickness 15 mm; matrix 128 × 64 or 128 × 128; FOV 32–36 cm; number of averages 1). Each image was taken within one breath hold (mean acquisition time: 17 s). TR was kept high by acquiring data only every third heartbeat (resulting in an effective TR of 3 × R-R interval) in order to minimize saturation effects. The ECG trigger delay was individually adapted to the different TI and the heart rate of the patient in order to guarantee the acquisition of all images at the same time point within the cardiac cycle (Fig. 1). Gadolinium-DTPA (Magnevist®, Schering AG, Berlin, Germany) was administered via peripheral intravenous access in a dose of 0.2 mmol/kg body weight. Ten minutes after the contrast bolus application, another set of five images was obtained using identical parameters. Finally, one image was acquired with a fast gradient echo inversion recovery sequence (TE 1.4 ms; TR: 1 × R-R; TI: 200 to 300 ms; slice thickness 10 mm; matrix 256 × 192; identical slice position) for the detection of delayed enhancement.

Image Reconstruction and T_1 Analysis

Each set of IR-prepared images was computed and transformed into a parametric T_1 map with pixel intensity reflecting T_1 values (FuncTool™, GE Medical Systems, Milwaukee, Wisconsin). Areas of high-signal intensity in postcontrast IR-prepared images were classified as myocardial infarction due to the pattern of delayed hyper-enhancement and were declared as reference areas ("reference"). In all cases, the localization was in agreement with the angiographically determined territory of the infarct-related vessel. In pre- and in postcontrast T_1 maps, T_1 values within the reference areas were obtained by defining regions of interest using the intensity tool of a standard MRI viewing software. Mean T_1 values of the entire cross-section of the left ventricle ("global") and T_1 values within a remote myocardial area ("remote") were registered. In precontrast T_1 maps, areas of increased T_1 values exceeding the spatial extent of the reference areas as assessed visually were classified as "peripheral."

Statistical Analysis

Statistical analysis was performed on an Apple G3 PowerPC using standard software (StatView™ Version 4.5, Abacus Concepts, Berkeley), applying

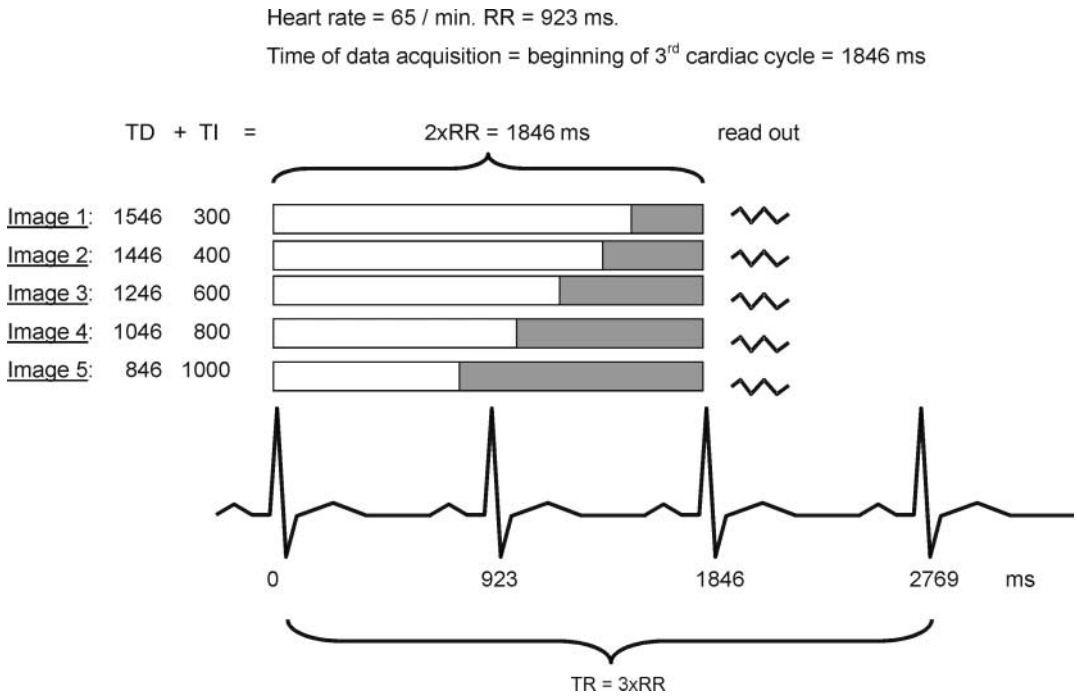

Figure 1. Basic time scheme for the acquisition of a set of T_1-weighted images using varying inversion times, which serves as a data source for the T_1 mapping. The sum of inversion time (TI) and trigger delay (TD) was held constant at 2× R-R to assure data acquisition at the beginning of the 3rd cardiac cycle.

the nonparametric Wilcoxon Signed Rank test. All values are expressed as mean ± standard error.

RESULTS

T_1 maps were obtained for all patients before and after contrast agent application; a representative example is shown in Fig. 2. Prior to contrast agent application, areas of infarction ("reference") showed an increase in the longitudinal relaxation time T_1 for all patients. After the application of contrast media, a T_1 decrease was found for infarcted tissue. Under precontrast conditions, T_1 was significantly longer in infarct areas ($T_1 = 849 \pm 60$ ms), compared to T_1 of remote ($T_1 = 721 \pm 37$ ms, $p < 0.05$) and global myocardium ($T_1 = 771 \pm 49$ ms; $p < 0.05$). For the postcontrast situation, T_1 was found to be significantly shorter in

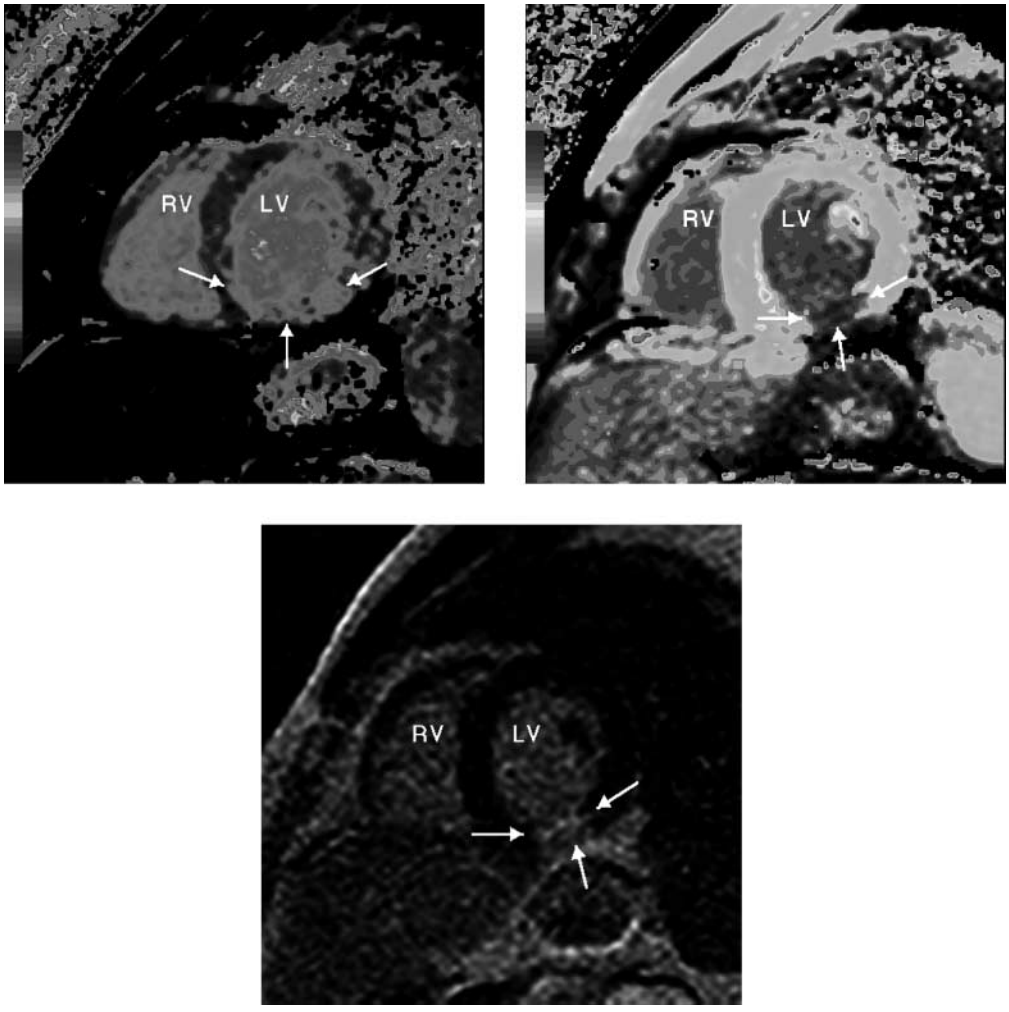

Figure 2. Single-slice short-axis view obtained from a patient three days after inferior myocardial infarction. *Upper left and upper right panels:* Calculated color coded parameter maps that illustrate the quantitative changes in T_1 prior to the (Upper left) and after (Upper right) the contrast agent application. The infarcted area is marked by arrows. The color bar reflects the range of T_1 values. Prior to the contrast application, a T_1 increase was observed for infarcted tissue (Upper left). The middle image represents the situation after the contrast agent application. The contrast agent was accumulated in the necrotic infarcted area leading to a T_1 decrease as reflected by the quantitative T_1 map. Differences exist betweeen the spatial extent of the infarcted area obtained under pre- and postcontrast conditions as illustrated by the different positions of the arrows. Lower panel: Conventional postcontrast T_1-weighed image showing the area of necrosis as delayed hyper-enhancement surrounded by signal-suppressed myocardium (TI = 300 ms). The area corresponds to the postcontrast T_1 map. (RV: right ventricular cavity; LV: left ventricular cavity).

infarcted areas ($T_1 = 262 \pm 19$ ms) as compared to remote ($T_1 = 362 \pm 27$ ms; $p < 0.05$) and global myocardium ($T_1 = 331 \pm 23$ ms; $p < 0.05$). In conclusion, the observed percentage T_1 change for infarcted tissue was $+18 \pm 7\%$ in precontrast maps and $-27 \pm 4\%$ in postcontrast maps. Fig. 3 shows the differences in T_1 values between infarcted and remote areas.

At closer examination, the spatial extent of the areas of increased T_1 values exceeded that of the infarcted areas as defined by delayed hyper-enhancement. The areas of T_1 prolongation covered $269 \pm 40\%$ of the reference area size. T_1 values in peripheral layers of the infarction were not significantly lower, compared to areas in the center of the infarction ($T_1 = 842 \pm 46$ ms vs. 849 ± 60 ms, respectively; $p = 0.16$). As in the center of the infarction, peripheral T_1 values were significantly higher compared to nonaffected areas ($T_1 = 842 \pm 46$ ms vs. 721 ± 37 ms; $p < 0.05$).

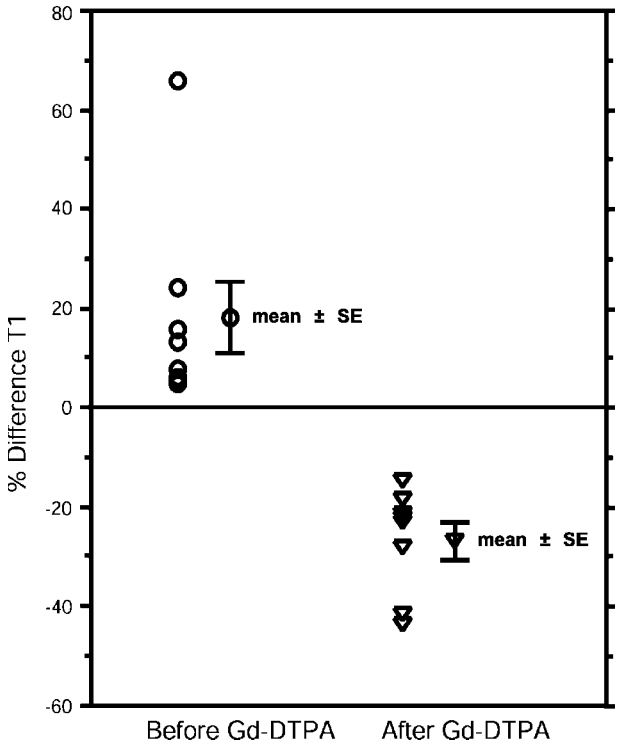

Figure 3. Differences between infarcted and remote areas normalized to the individual remote areas. Prior to the application of contrast agent, T_1 in infarcted areas is always longer than T_1 in remote areas. After the administration of Gd-DTPA, T_1 in infarcted areas is shorter than T_1 in remote areas.

DISCUSSION

This study demonstrates that quantitative T_1 mapping can be used to visualize myocardial T_1 changes that occur in patients with acute myocardial infarction. T_1 mapping offers a diagnostic tool for the detection of AMI without the application of contrast media.

T_1-weighted contrast media-enhanced MRI is becoming more and more accepted as an established approach to visualize myocardial infarction (Wu et al., 1999). This technique uses the contrast enhancement of infracted tissue for its differentiation from noninfarcted areas. It has been shown that best contrast between infarcted and noninfarcted tissue is achieved by the suppression of signal contributions from healthy myocardium using an inversion recovery preparation experiment (Simonetti et al., 2001). This T_1-weighted technique yields variable results because image contrast is influenced by other tissue properties such as T_2 effects or proton density. In addition, the contrast-to-noise-ratio is given by the inversion time and the contrast agent concentration used. In conclusion, signal intensities or signal intensity changes after contrast agent application are not comparable among images or patients.

In contrast, T_1 mapping, which results in quantitative images calculated from multiple T_1-weighted images, is a promising tool to overcome these difficulties by the advantage of providing absolute T_1 values rather than relative signal intensities. This results in improved comparability and reproducibility.

The experimental results demonstrate that T_1 mapping of acute myocardial infarction is clinically feasible using a 1.5 Tesla system. The infarcted area was correctly identified in all cases. Precontrast T_1 maps showed that the area of necrosis (as identified by a delayed hyper-enhancement pattern in conventional, contrast-enhanced images) was related to a prolonged T_1. This T_1 prolongation was also detectable in the areas surrounding the pure necrosis. The reason for T_1 changes in these peripheral zones of the infarction is still under discussion. One hypothesis is that increased water content of the tissue from infarct-related edema might be responsible for the alterations in T_1. Water accumulation in tissues leads to T_1 prolongation (Williams et al., 1980). However, it is still unclear whether or not these changes in magnetic properties also reflect transient structural changes associated with myocardial stunning. In practice, precontrast T_1 maps offer a potential screening tool for acutely infarcted myocardium but do not allow quantification of necrosis size. Postcontrast T_1 maps showed a T_1 reduction limited to the central areas of the injury. Thus, it seems to be

plausible that noncontrast T_1 changes reflect pathophysiological changes that are not exclusively due to myocardial necrosis. The differences in the spatial extent of pre- and postcontrast T_1 map alterations might be useful for further tissue characterization.

The intention of this study was to show that T_1 mapping is feasible on a 1.5 Tesla MR system and to examine if it is sensitive enough to detect relaxation changes in AMI in a pilot study. The pulse sequence used allowed the reconstruction of basic T_1 maps but bears the potential for improvements in the spatial and temporal resolution. Although incomplete relaxation was corrected for by keeping TR long (i.e., three R-R intervals), there were still saturation effects depending on heart rate that might result in different T_1 levels for patients showing differences in heart rate. This renders interpatient comparisons of absolute T_1 values unsuitable. In the literature, T_1 values for healthy myocardium at 1.5 Tesla approximate 1000 ms (Flacke et al., 2001; Wacker et al., 1999). For future studies, modified pulse sequences should be used in order to address these issues. One way to enhance the temporal resolution would be the Look-Locker approach (Gowland and Mansfield, 1993; Look and Locker, 1970), which applies multiple readouts within one relaxation experiment. Since a readout over the full cardiac cycle would lead to motion artifacts, ECG triggering in this technique is challenging (Waller et al., 2000). A solution to avoid T_1 underestimation from incomplete relaxation would be the application of a saturation-recovery instead of an inversion-recovery preparation pulse (Tsekos et al., 1995).

Noncontrast T_1 mapping detects necrotic areas with high sensitivity in patients with acute myocardial infarction and overcomes several limitations of established T_1-weighted imaging techniques. The combination of pre- and postcontrast T_1 mapping may deliver information on tissue surrounding the necrosis, which is supplemental to conventional MR approaches and which requires further investigation.

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