informa
healthcare

Mechanism of Late Gadolinium Enhancement in Patients with Acute Myocardial Infarction

Christoph Klein, MD[1], Thaiz R. Schmal, MD[1], Stephan G. Nekolla, PhD[2], Bernhard Schnackenburg, PhD[3], Eckart Fleck, MD[1], and **Eike Nagel, MD[1]**

German Heart Institute Berlin, Berlin, Germany;[1] Nuklearmedizinische Klinik und Poliklinik der Technischen Universität München, Germany;[2] Philips Medical Systems, Hamburg, Germany[3]

ABSTRACT

Purpose: To investigate the mechanism of late gadolinium enhancement in irreversibly damaged myocardium in patients with acute myocardial infarct by determining kinetics of Gd-DTPA over time. ***Methods***: Twenty-nine patients (24 men; 64 $\pm$ 9 years) with acute myocardial infarction were imaged with functional and gadolinium enhanced cardiovascular magnetic resonance (CMR) 18 minutes post 0.2 mmol/kg Gd-DTPA. T1 of blood, remote and enhanced myocardium, as well as microvascular obstruction (MVO) was determined before and 5–40 minutes post contrast injection (Look-Locker), and the partition coefficient (λ) was calculated. ***Results***: T1 and λ were significantly different from 5–40 minutes post contrast in enhanced ($\lambda = 0.90 \pm 0.09$, p $<$ 0.001) compared to remote myocardium ($\lambda = 0.40 \pm 0.07$). λ achieved a steady state in remote but increased continuously in infarcted myocardium and to an even greater extent in MVO. T1 of enhanced myocardium was higher from 5–15 minutes, equal at 20 minutes and lower 25–40 minutes post contrast compared to blood, indicating a changing contrast between blood and late gadolinium enhancement over time. ***Conclusion:*** Enhancement in patients with acute infarction is mainly due to an increased λ, although reduced wash-in-wash-out adds to the effect. Differentiation between blood and enhanced myocardium may be difficult to achieve, if only little differences of T1 are available. Imaging at a later point will restore the contrast.

INTRODUCTION

In acute myocardial infarction the differentiation of stunned (viable) and necrotic (infarct) tissue of dysfunctional myocardium is possible with gadolinium enhanced cardiovascular magnetic resonance imaging (CMR) (1, 2) using an inversion recovery gradient echo technique (IR-G). Necrotic, compared to remote areas exhibit a higher signal intensity 5–20 minutes after the application of an extracellular contrast agent (enhancement). Due to the spatial resolution of CMR, the transmural extent of infarction can be determined and is a predictor of contractile recovery (3–6). Potential mechanisms of enhancement are an increased volume of distribution (7–10) and/or altered wash-in/wash-out kinetic (11) of gadolinium based extracellular contrast agents. While an excellent contrast between viable and necrotic tissue can be achieved, often the contrast between blood in the left ventricular (LV) cavity and necrotic tissue is less pronounced. This makes the detection and quantification of small subendocardial infarcts difficult, if not impossible. Aim of the present study was therefore to investigate the mechanism and degree of enhancement in patients with acute myocardial infarction, by measuring the longitudinal relaxation time (T1) over time of blood and myocardium and by calculating the partition coefficient of the contrast agent in remote and enhanced areas, a parameter independent of sequence parameters as with the standard inversion recovery gradient technique.

MATERIALS AND METHODS

Twenty-nine patients (24 men; 64 $\pm$ 9 years) with acute myocardial infarction and after successful interventional revascularization therapy (stenting) were included into the study after giving informed consent. Imaging was performed after normalization of cardiac enzymes (4 $\pm$ 2 days after the acute event).

Patients with atrial fibrillation, contraindications to CMR or unstable angina pectoris were excluded.

Imaging protocol

All patients were examined in supine position using a 1.5 Tesla scanner (Intera, Philips Medical Systems, Best, The Netherlands) and a dedicated cardiac phased array surface coil. For regional function analysis, the left ventricle was imaged in short axis views, using a steady-state free precession sequence with retrospective gating (25 phases per cardiac cycle; TR 2.7 ms; TE 1.4 ms; flip angle 60°, spatial resolution $1.8 \times 1.8 \times 8$ mm^3). To evaluate myocardial necrosis, the left ventricle (LV) was imaged using short axis views approximately 18 minutes after injection of 0.2 mmol Gd-DTPA per kg body weight (bw) (Magnevist, Schering, Berlin, Germany) in mid-diastole. An inversion recovery 3D turbo gradient echo technique (IR-G) (TE/TR 2.3/4.8 ms, spatial resolution $1.4 \times 1.4 \times 5.0$ mm^3, flip angle 15°, acquisition time 215 ms, prepulse delay 225–300 ms) was used. For the evaluation of blood and myocardial T1 relaxation rate, a Look-Locker sequence (12, 13) was applied in three short axis views (apical, equatorial, basal) before and 5, 10, 15, 20, 25, 30, 35 and 40 minutes after the injection of the contrast agent. The Look-Locker sequence (TR/TE 12/5.1 ms, flip angle 6°, spatial resolution $1.4 \times 1.9 \times 8.0$ mm^3, phase interval 48 ms) consisted of a 180° inversion prepulse triggered by the R-peak of the electrocardiogram followed by 65 gradient-recalled echo images over several cardiac cycles with the patient holding his breath for 18 seconds. To ensure a maximal T1-relaxation, two 180° prepulses in this multi shot technique were separated by at least 3 seconds, depending on the heart rate.

Image analysis

Remote and infarcted myocardium and microvascular obstruction (MVO) were visually identified using enhanced images in one slice per patient. MVO was defined as a zone of hypo-enhancement surrounded by enhancement and located in the subendocardium. A similar slice in the Look-Locker technique was chosen. The size and insertion of the right ventricle and the papillary muscles served as landmarks. A region of interest (ROI) was placed in the left ventricular cavity (blood) and in remote (opposite to the infarct territory), enhanced and microvascular obstructed areas if present. These ROIs were of similar size and location in both imaging techniques. Signal intensities (SI) and the standard deviation (SD) in the representative IR-G slices were measured, and the relative differences to the remote myocardium and blood were calculated.

In the Look-Locker images myocardial motion was compensated for by adjusting the ROIs during the cardiac cycle if necessary. Signal intensity-time-curves were generated for each ROI (MASS by Medis, Leiden, The Netherlands). To determine T1, the curves were fit to the predicted longitudinal magnetization curves (12, 13).

An approximation of the partition coefficient λ, a parameter of volume of distribution can be calculated as follows:

$$\lambda = \frac{\Delta R1_{myocardium}}{\Delta R1_{blood}}$$
$$= \frac{(1/T1_{postcontrast} - 1/T1_{precontrast})_{myocardium}}{(1/T1_{postcontrast} - 1/T1_{precontrast})_{blood}} \quad [1]$$
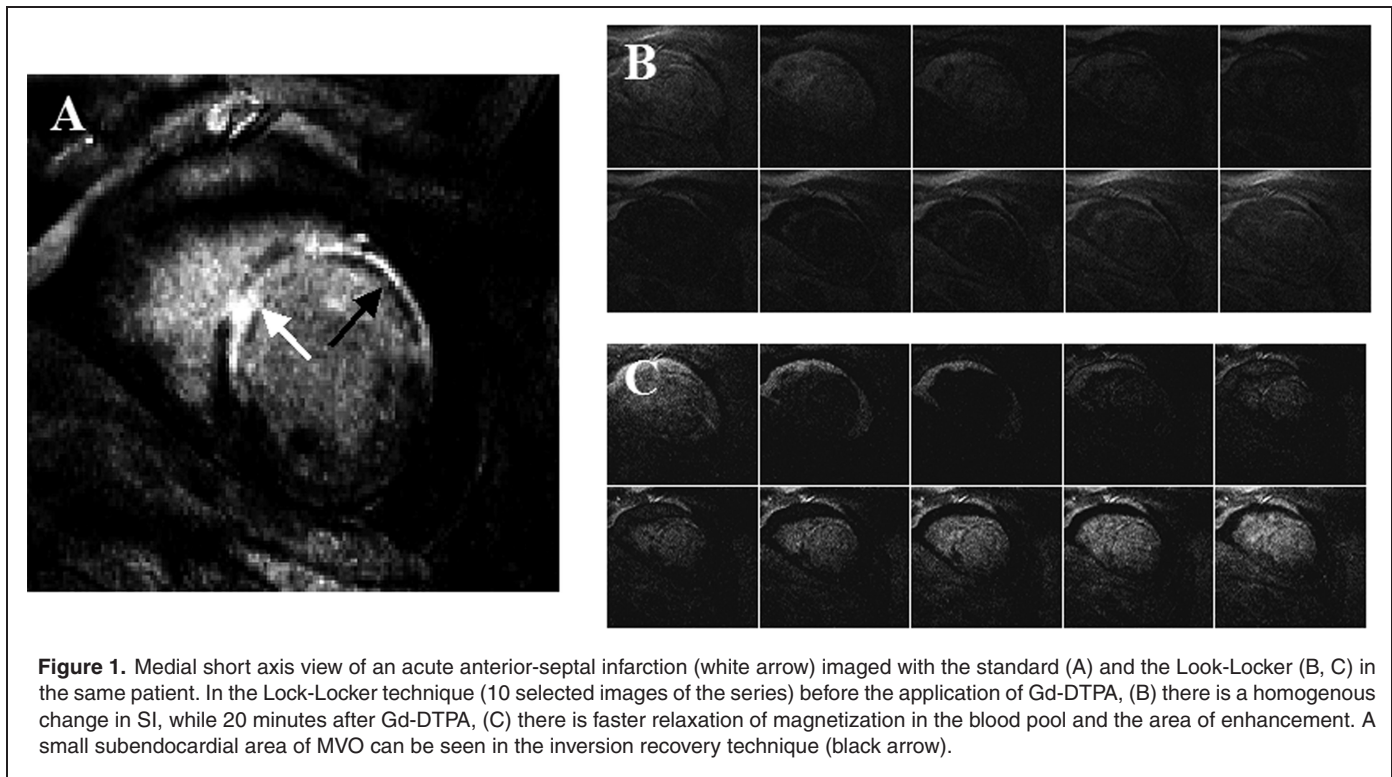
As Gd-DTPA is a freely diffusible tracer, change of concentration in the myocardium should follow the change of concentration in the blood. This is expressed by a steady state of λ without change over time. If, however, tissue perfusion is very low (reduced wash-in), Gd-DTPA concentration will not reach its maximum initially, and λ is, therefore, lower. When contrast concentration in the blood pool falls below tissue concentration, wash-out is also reduced due to the reduced perfusion. As a result, λ keeps artificially increasing. As the point in time when contrast concentration in blood falls below the concentration in tissue is unknown, the change from wash-in to wash-out can not be determined. Therefore, we defined potential reduced wash-in-wash-out by calculating the slope of λ over time (5–40 minutes).

Statistics

Mean and one SD are given for all continuous data. The significance of mean differences between remote, infarcted, microvascular obstructed myocardium and blood, as well as differences over time following contrast administration with the Look-Locker technique were evaluated by the Wilcoxon signed rank test, as no normal distribution was assumed. For the change of λ over time, a linear regression analysis was used. A value of $p < 0.05$ was considered significant.

RESULTS

In all 29 patients, an area of enhancement could be identified. MVO was found in 9 patients. Sixteen patients had an anterior, 10 an inferior and 3 a lateral infarction. The mean creatine kinase level was 1825 ± 1843 U/L (range 487–6552 U/L) with a MB-fraction of 220 ± 231 (range 37–855 U/L). In all patients, the infarct related artery as defined by invasive angiography represented the infarct site defined in CMR. Revascularization was successful with TIMI flow 3 (12.5 frames/s) in all patients. Fig. 1 shows an example of a patient with a large anterior acute infarction with enhancement in IR-G and the corresponding slice imaged with the Look-Locker technique before and 20 minutes after administration of contrast. The SI (IR-G) of infarcted myocardium was $45\% \pm 195\%$ ($p < 0.0001$) above the SI of remote myocardium. Contrast between enhanced myocardium and LV-blood was achieved ($122\% \pm 43\%$) but did not reach statistical significance ($p > 0.05$). SI of enhancement was below the SI of LV-blood in 7 patients. T1 values for blood, remote, microvascular obstructed and enhanced tissue are shown in Table 1 and visualized in Fig. 2. At baseline, T1 of necrotic

Figure 1. Medial short axis view of an acute anterior-septal infarction (white arrow) imaged with the standard (A) and the Look-Locker (B, C) in the same patient. In the Lock-Locker technique (10 selected images of the series) before the application of Gd-DTPA, (B) there is a homogenous change in SI, while 20 minutes after Gd-DTPA, (C) there is faster relaxation of magnetization in the blood pool and the area of enhancement. A small subendocardial area of MVO can be seen in the inversion recovery technique (black arrow).

myocardium, but not of MVO was slightly, but significantly ($p < 0.05$) increased compared to remote myocardium. Five minutes after contrast, T1 values differed significantly between the different states of tissue. This could be appreciated for as long as 40 minutes post contrast administration. Twenty minutes after contrast application, however, no significant difference between T1 of blood and enhanced myocardium was appreciated while T1 of blood was always significantly lower compared to remote myocardium. Fig. 3 shows λ of Gd-DTPA for remote, enhanced and microvascular obstructed myocardium over time. A

significant ($p < 0.001$) difference between remote and enhanced myocardium could always be appreciate. While there is steady state in remote myocardium, infarction shows an altered pattern with a continuous increase of λ, even more distinct in MVO. Fig. 4 demonstrates the box plot with the median, quartiles, and extreme values of the slope (5–40 minutes) of the partition coefficient of remote, infarcted and MVO myocardium. A wide variety in the slopes of enhanced myocardium and MVO can be appreciated, indicating an individual alteration of λ over time. However, in 25 of the 29 patients (86%), the slope of infarcted tissue was larger than in remote, indicating altered wash-in and wash-out in most of acute myocardial infarctions.

Table 1. T1 values in milliseconds of LV-blood, remote, infarcted myocardium and MVO.

Time (minutes)	LV-blood	remote	infarct	MVO
Baseline[⊗, §]	1270 ± 80	880 ± 60	950 ± 50	870 ± 70
Post contrast (minutes)				
5[§, ⊗]	210 ± 30	370 ± 60	240 ± 30	630 ± 130
10[§, ⊗]	260 ± 40	430 ± 60	270 ± 30	560 ± 110
15[§, ⊗]	290 ± 50	460 ± 50	300 ± 40	540 ± 120
20[⊗]	320 ± 50	480 ± 60	320 ± 40	530 ± 100
25[§, ⊗]	340 ± 60	500 ± 50	330 ± 40	510 ± 100
30[§, ⊗]	360 ± 60	520 ± 50	340 ± 40	500 ± 90
35[§, ⊗]	380 ± 70	530 ± 60	360 ± 40	500 ± 80
40[§, ⊗]	400 ± 70	550 ± 60	360 ± 40	500 ± 90

After contrast application LV-blood was always significantly different from remote myocardium and MVO. MVO = microvascular obstruction, LV = left ventricular.
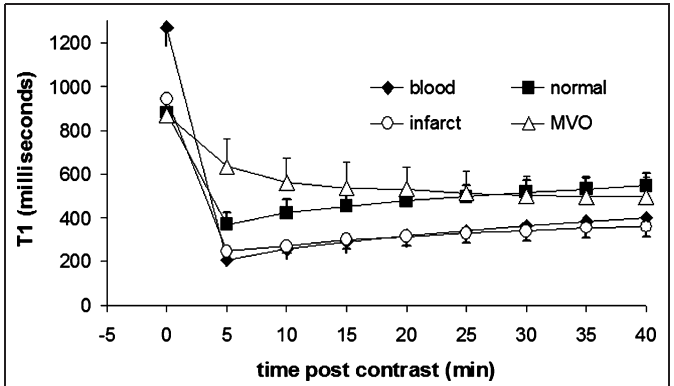[⊗]remote vs. infarct ($p < 0.05$).
[§]LV-blood vs. infarct ($p < 0.05$),

Figure 2. T1 values in milliseconds over time of blood, remote and infarcted myocardium and MVO before and after the application of 0.2 mmol/Gd-DTPA/kg (values see Table 1). At 20 minutes there is a T1 crossing of enhanced myocardium and LV-blood.
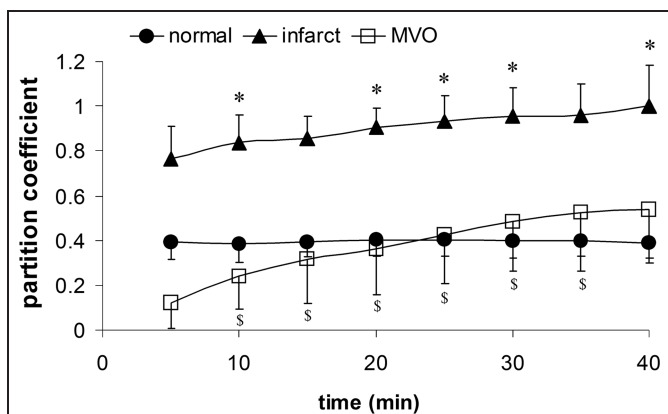
Figure 3. Time course of the partition coefficient in remote and infarcted myocardium and MVO 5–40 minutes after the application of 0.2 mmol Gd-DTPA/kg bw. While there is steady state in remote, wash-in-wash-out kinetics in infarcted myocardium and MVO is altered. *$p < 0.05$ compared to the λ before in enhanced myocardium. $^{\$}p < 0.05$ compared to the λ before in MVO.

DISCUSSION

This study investigates the partition coefficient and "late" contrast kinetics of Gd-DTPA in patients with acute myocardial infarction. It demonstrates that an increased volume of distribution is the main mechanism for increased SI of necrosis as the partition coefficient is elevated compared to remote myocardium
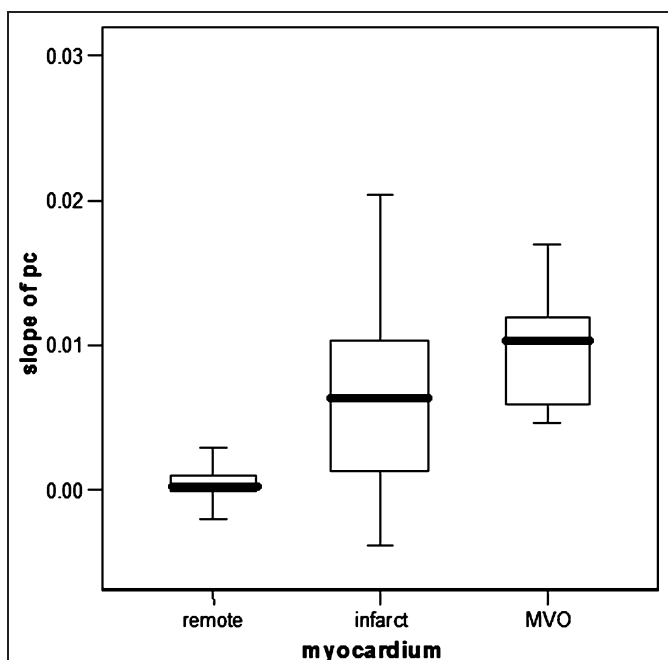

Figure 4. Boxplot showing the median, quartiles, and extreme values of the slope (5–40 minutes) of the partition coefficient of remote, infarcted and microvascular obstructed myocardium. There is a statistical significant difference between remote, infarct and MVO tissue ($p < 0.01$). pc = partition coefficient.

as early as 5 minutes post Gd-DTPA injection, a time when the so called "late enhancement" can be started to be imaged. Additionally, an altered wash-in and wash-out kinetic contributes to the high contrast as demonstrated by an increased slope of λ in the enhanced, but not the remote areas. A different wash-in wash-out kinetic of Gd-DTPA in enhanced myocardium also contributes to the differences of T1 between blood and infarct over time, resulting in a "contrast crossing" and a point where the SI of blood and enhancement are similar.

Partition coefficient in infarcted and remote myocardium

Gadolinium enhanced cardiovascular magnetic resonance is increasingly used for the detection and assessment of acute myocardial infarction, as it enables the quantification of the extent and transmurality of the infarct, a predictor of functional recovery after restoration of blood flow (3, 4) in patients. The quantification of Gd-DTPA content in the tissue by using the signal intensity is problematic as signal intensity is not proportional to contrast concentration (14) and the IR-G technique is additionally dependent on the inversion prepulse delay. However, by using T1 measurements and calculating ΔR1 ratio of myocardium and blood the quantification of bulk tissue content of Gd-DTPA, a freely diffusible extracellular tracer can be achieved (15). Several animal studies (16, 17) and one human study (8) have demonstrated that the partition coefficient and, thus, the volume of distribution in areas of infarction is increased. This is in concordance with scintigraphic (18) that describe intracellular diffusion of DTPA and histological data (7, 19) using TTC staining, an indicator of necrosis. As λ was increased as early as 5 minutes after contrast application and stayed elevated up to 40 minutes, the end of our data acquisition, an increased volume of distribution can be assumed as the main mechanism for enhancement over the whole period of image acquisition in the clinical setting. This is in agreement with the above mentioned studies. Ideally, the direct calculation of the volume of distribution would be desirable. However, steady state needs to be accomplished and that was not the case in the enhanced regions of our study population, indicating altered wash-in wash-out kinetics. To overcome this problem, a bolus with an additional continuous infusion to achieve a constant concentration of contrast in the blood pool could be used. With this technique, differences in perfusion of different tissue can be overcome (9, 17). This was not performed in the present study, as the aim was the evaluation of contrast behavior with the technique used clinically by most centers and with most of the experience. Thornhill et al (16), however, found a good correlation of λ after bolus application, constant infusion approach and CMR in a canine model at an imaging time more than 8 minutes after bolus application.

Differences in wash-in and wash-out kinetics

Additionally to an increased volume of distribution, an altered wash-in and wash-out kinetic, where Gd-DTPA becomes "trapped" in the infarcted tissue due to the severely reduced

wash-out is another possible mechanism for enhancement of infarcted tissue. Using an in-situ rabbit heart model, Kim et al (11) demonstrated that enhancement was not present after 30 minutes of constant infusion of Gd-DTPA indicating a similar volume of distribution. After stopping the infusion, areas of infarct enhanced possibly due to severely reduced wash-out kinetic. They concluded that a reduction of functional capillary density due to intravascular neutrophil accumulation and red blood cell stasis leads to the severely reduced blood flow of the enhanced areas. Our protocol with a single bolus can not distinguish between wash-in and wash-out. A constant infusion approach would be necessary to determine wash-in, and when a steady state is achieved, the ending of the infusion to determine wash-out. We did not use a constant infusion protocol to determine exactly when wash-in and wash-out occurs, and we started imaging 5 minutes after contrast application, a period when the bolus has been equally diluted in the blood pool and renal excretion has already begun. Therefore, we use the term "altered wash-in wash-out" for a constant increase of λ without reaching a steady-state. The tissue that showed severely reduced wash-in wash-out patterns in our study is MVO, and it seems likely that in areas with MVO this mechanism may be more dominant. Possibly, additional to the very different experimental setting by Kim and colleagues, MVO may have been present in most of their infarcted tissue as demonstrated by the high percentage of clotted capillaries.

Most other investigators found no different wash-in wash-out kinetic of Gd-based extracellular contrast agents in infarcted compared to remote myocardium. They showed a steady state situation of λ in animal models of reperfused myocardial infarction (7, 10, 20). One study using a canine model also demonstrated an altered wash-in wash-out as λ reached a steady state 8 minutes after contrast application but not before (16). In our patient population, steady state in the enhanced regions compared to remote myocardium was not reached in most areas as demonstrated by the slope of λ (Figs. 3 and 4). Possible explanations would be the differences in the pathophysiology of experimental and atherosclerotic infarctions with either still reduced flow at the microvascular level in general or islet of MVO in areas of enhancement, which were too small to be detected individually. This is in agreement with the findings of Taylor et al (21) who demonstrated reduced myocardial perfusion in enhanced areas in patients with successfully reperfused (TIMI III) myocardial infarction. In patients with chronic infarction using a similar study design as this study, it was shown that the increase of λ was dependent on reduced myocardial flow, measured by positron emission tomography and an increased volume of distribution (22). It, thus, seems plausible that in acute myocardial infarction, a similar mechanism may be responsible, although myocardial flow was not determined in our patient population. As we defined MVO in images 18 minutes post contrast, we can not rule out small areas of MVO which went undetected at point in time and were therefore included in enhancement. They would have altered the contrast kinetic in enhanced regions.

Impact on image acquisition

We demonstrated that differences in T1 between remote and enhanced areas exist between 5–40 minutes after contrast application. This suggests the ability of IR-G imaging to differentiate between viable and infarcted tissue during this time period. However, when looking at Table 1 and Fig. 2, T1 of blood is smaller than T1 of enhanced areas between 5 and 15 minutes, similar at 20 minutes and larger after 20 minutes, suggesting that the contrast between blood and infarction in T1 weighted images changes from negative to positive. At approximately 18 minutes post contrast, no significant difference between SI of infarct and blood could be achieved. If hardly any contrast exists, detection of small subendocardial infarcts and absolute quantification may be difficult to achieve, and additional image acquisition at a later stage, when T1 values are again "drifting apart" may be necessary (23). The different contrast kinetics in different patients as shown by the varying up slopes of λ make an universal applicable timing of image acquisition difficult. Adequate contrast between the different tissues must be confirmed in each patient individually. A resent study by Hombach et al (24) postulated that MVO was, in addition to infarct size, predictive of LV adverse remodeling. In that study MVO was defined 6–12 minutes after contrast application. Our results suggest a high T1 dynamic over time. Beek et al (3) demonstrated a significant change of the size of MVO over time in acute myocardial infarction. Therefore, for future studies, a definition of MVO in terms of timing of image acquisition and/or imaging techniques (late gadolinium enhancement vs. first pass perfusion) needs to be established in order to draw valid clinical conclusions.

There are, however, several limitations of this study. The Look-Locker technique acquires images after an inversion prepulse during several cardiac cycles. Therefore, SI-changes do not represent the exact same tissue due to in- and through-plane motion. However, care was taken by the placement of the ROIs in each phase that only infarcted or remote myocardium was included, therefore, minimizing a mixture of different tissues. It would have been interesting to know, if the size of enhancement or MVO decreases or increases over time as this was suggested by Beek et al and Oshinski et al (3, 25). We did not evaluate infarct size at different time points after contrast application as first, spatial resolution of the Look-Locker technique is not sufficient to evaluate possible small changes in size and second, in plane motion made such analysis impossible. A newer technique for T1 mapping (26) was not available at the beginning of the study and was, therefore, not used. Also, it would have been preferable if another method of defining infarction and remote myocardium had been available. There is, however, a large body of evidence that enhancement correlates well with infarction defined by histology and scintigraphy and is meanwhile accepted as an appropriate imaging tool.

In conclusion this study may shed some light into the mechanism of contrast enhanced CMR in reperfused acute myocardial infarction in patients. We demonstrated that the volume of distribution of Gd-DTPA in enhanced tissue is significantly increased

compared to viable tissue. This seems to be the main mechanism of the late enhancement effect, although delayed wash-in wash-out kinetic of contrast has a contributory role.

REFERENCES

1. Kim RJ, Fieno DS, Parrish TB, Harris K, Chen EL, Simonetti O, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. Circulation 1999;100:1992–2002.
2. Wu E, Judd RM, Vargas JD, Klocke FJ, Bonow RO, Kim RJ. Visualization of presence, location, and transmural extent of healed Q-wave and non-Q-wave myocardial infarction. Lancet 2001;357:21–28.
3. Beek AM, Kuhl HP, Bondarenko O, Twisk JW, Hofman MB, van Dockum WG, et al. Delayed contrast-enhanced magnetic resonance imaging for the prediction of regional functional improvement after acute myocardial infarction. J Am Coll Cardiol 2003;42:895–901.
4. Choi KM, Kim RJ, Gubernikoff G, Vargas JD, Parker M, Judd RM. Transmural extent of acute myocardial infarction predicts long-term improvement in contractile function. Circulation 2001;104:1101–07.
5. Gerber BL, Garot J, Bluemke DA, Wu KC, Lima JA. Accuracy of contrast-enhanced magnetic resonance imaging in predicting improvement of regional myocardial function in patients after acute myocardial infarction. Circulation 2002;106:1083–9.
6. Hillenbrand HB, Kim RJ, Parker MA, Fieno DS, Judd RM. Early assessment of myocardial salvage by contrast-enhanced magnetic resonance imaging. Circulation 2000; 102:1678–83.
7. Arheden H, Saeed M, Higgins CB, Gao DW, Bremerich J, Wyttenbach R, et al. Measurement of the distribution volume of gadopentetate dimeglumine at echo-planar MR imaging to quantify myocardial infarction: comparison with 99mTc-DTPA autoradiography in rats. Radiology 1999;211:698–708.
8. Flacke SJ, Fischer SE, Lorenz CH. Measurement of the gadopentetate dimeglumine partition coefficient in human myocardium in vivo: normal distribution and elevation in acute and chronic infarction. Radiology 2001;218:703–10.
9. Pereira RS, Prato FS, Sykes J, Wisenberg G. Assessment of myocardial viability using MRI during a constant infusion of Gd-DTPA: further studies at early and late periods of reperfusion. Magn Reson Med 1999;42:60–68.
10. Saeed M, Higgins CB, Geschwind JF, Wendland MF. T1-relaxation kinetics of extracellular, intracellular and intravascular MR contrast agents in normal and acutely reperfused infarcted myocardium using echo-planar MR imaging. Eur Radiol 2000;10:310–18.
11. Kim RJ, Chen EL, Lima JA, Judd RM. Myocardial Gd-DTPA kinetics determine MRI contrast enhancement and reflect the extent and severity of myocardial injury after acute reperfused infarction. Circulation 1996;94:3318–26.
12. Brix G, Schad LR, Deimling M, Lorenz WJ. Fast and precise T1 imaging using a TOMROP sequence. Magn Reson Imaging 1990;8:351–56.
13. Look DC, Locker DL. Time saving measurement of NMR and EPR relaxation times. Rev Sci Instrum 1970;41:250–51.
14. Tweedle MF, Wedeking P, Telser J, Sotak CH, Chang CA, Kumar K, et al. Dependence of MR signal intensity on Gd tissue concentration over a broad dose range. Magn Reson Med 1991;22:191–94.
15. Donahue KM, Burstein D, Manning WJ, Gray ML. Studies of Gd-DTPA relaxivity and proton exchange rates in tissue. Magn Reson Med 1994;32:66–76.
16. Thornhill RE, Prato FS, Wisenberg G, Moran GR Sykes J. Determining the extent to which delayed-enhancement images reflect the partition-coefficient of Gd-DTPA in canine studies of reperfused and unreperfused myocardial infarction. Magn Reson Med 2004;52:1069–79.
17. Tong CY, Prato FS, Wisenberg G, Lee TY, Carroll E, Sandler D, et al. Measurement of the extraction efficiency and distribution volume for Gd-DTPA in normal and diseased canine myocardium. Magn Reson Med 1993;30:337–46.
18. Pereira RS, Prato FS, Wisenberg G, Sykes J. The determination of myocardial viability using Gd-DTPA in a canine model of acute myocardial ischemia and reperfusion. Magn Reson Med 1996;36:684–93.
19. Rehwald WG, Fieno DS, Chen EL, Kim RJ, Judd RM. Myocardial magnetic resonance imaging contrast agent concentrations after reversible and irreversible ischemic injury. Circulation 2002;105:224–29.
20. Arheden H, Saeed M, Higgins CB, Gao DW, Ursell PC, Bremerich J, et al. Reperfused rat myocardium subjected to various durations of ischemia: estimation of the distribution volume of contrast material with echo-planar MR imaging. Radiology 2000;215:520–28.
21. Taylor AJ, Al-Saadi N, Abdel-Aty H, Schulz-Menger J, Messroghli DR. Friedrich MG. Detection of acutely impaired microvascular reperfusion after infarct angioplasty with magnetic resonance imaging. Circulation 2004;109:2080–85.
22. Klein C, Nekolla SG, Balbach T, Schnackenburg B, Nagel E, Fleck E, Schwaiger M. The influence of myocardial blood flow and volume of distribution on late Gd-DTPA kinetics in ischemic heart failure. J Magn Reson Imaging 2004;20:588–93.
23. Grebe O, Paetsch I, Kestler HA, Herkommer B, Schnackenburg B, Hombach V, et al. Optimal acquisition parameters for contrast enhanced magnetic resonance imaging after chronic myocardial infarction. J Cardiovasc Magn Reson 2003;5:575–87.
24. Hombach V, Grebe O, Merkle N, Waldenmaier S, Hoher M, Kochs M, et al. Sequelae of acute myocardial infarction regarding cardiac structure and function and their prognostic significance as assessed by magnetic resonance imaging. Eur Heart J 2005;26:549–57.
25. Oshinski JN, Yang Z, Jones JR, Mata JF, French BA. Imaging time after Gd-DTPA injection is critical in using delayed enhancement to determine infarct size accurately with magnetic resonance imaging. Circulation 2001;104:2838–42.
26. Messroghli DR, Plein S, Higgins DM, Walters K, Jones TR, Ridgway JP, et al. Human Myocardium: Single-Breath-hold MR T1 Mapping with High Spatial Resolution–Reproducibility Study. Radiology 2006; in press.