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MYOCARDIAL VIABILITY

# Optimal Acquisition Parameters for Contrast Enhanced Magnetic Resonance Imaging After Chronic Myocardial Infarction

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## ABSTRACT

The aim of this study was to simplify the imaging of myocardial infarction based on theoretical aspects and patient variables and to define the optimal time for image acquisition. Thirteen patients with chronic myocardial infarction underwent magnetic resonance imaging. After injection of 0.2 mmol/kg body weight Gd-DTPA an inversion recovery turbo gradient echo sequence with different prepulse delays was applied every 3 to 5 minutes within an interval of 3 to 30 minutes. As parameters of investigation, the area of signal enhancement and the contrast between enhanced and nonenhanced myocardium were used. There was no influence of prepulse delay or time after contrast injection on the enhanced area. The contrast between enhanced and normal myocardium showed a peak at 6 minutes post Gd-DTPA injection and remained high. The contrast between blood and enhanced myocardium was best at 6 and 25 minutes with best intra- and interobserver variability. In conclusion, if a suitable contrast was achieved, the area of enhancement is independent of prepulse delay or imaging time. In most patients the highest contrast between blood, enhanced and normal myocardium is achieved 6 minutes and 25 minutes after contrast injection.

*Key Words*: Magnetic resonance; Myocardial infarction; Inversion recovery; Gd-DTPA.

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## INTRODUCTION

After myocardial infarction, the amount of necrotic tissue is an important predictor for the prognosis of the patient (Geltman et al., 1979; Sobel et al., 1972). Until recently, there was a lack of an accurate, noninvasive method for the assessment of infarct size in clinical practice. Methods used in clinical routine comprise evaluation of serum cardiac marker levels, the number of leads with alterations in electrocardiography, or radionuclide scintigraphy. These methods are limited by either poor spatial resolution and/or low accuracy. Echocardiographic assessment of wall motion abnormalities is influenced by hibernation and stunning, which can often not be differentiated from infarcted myocardium.

Recently, a new magnetic resonance imaging (MRI) technique using a prepulse to suppress the normal myocardial signal has been introduced (Simonetti et al., 2001). With this technique it is possible to image infarcted tissue after injection of Gd-DTPA (Judd et al., 1995; Kim et al., 1999; Lima et al., 1995; Wu et al., 1998). The method is based on the larger distribution volume of Gd-DTPA in irreversibly damaged myocardium (Arheden et al., 1999; Kim et al., 1999). Animal studies have shown a close correlation between the enhanced area in MR imaging and nonviable tissue in histological examinations both in acute (Judd et al., 1995; Wu et al., 1998) and chronic myocardial infarctions (Kim et al., 1999, 2000).

So far, the influence of the prepulse delay, the ideal delay between contrast injection and imaging on the area of enhancement, and the contrast between infarction and viable myocardium as well as left ventricular blood are currently under evaluation (Flacke et al., 2001; Oshinski et al., 2001) and are discussed controversially (Judd and Kim, 2002). A recently published study (Sandstede et al., 2001) examined the time course of contrast enhancement employing a conventional spin echo sequence. It is pointed out that a segmented k-space inversion recovery turbo gradient echo sequence that is used in the present study would be more suitable for a quantitative analysis and thus for the investigation of the image acquisition parameters.

The purpose of this study was to simplify the imaging of myocardial infarction based on theoretical aspects and patient variables and to define the optimal time for image acquisition.

## METHODS

Thirteen consecutive patients with coronary heart disease and chronic myocardial infarction (>3 months old) admitted for coronary angiography or a planned

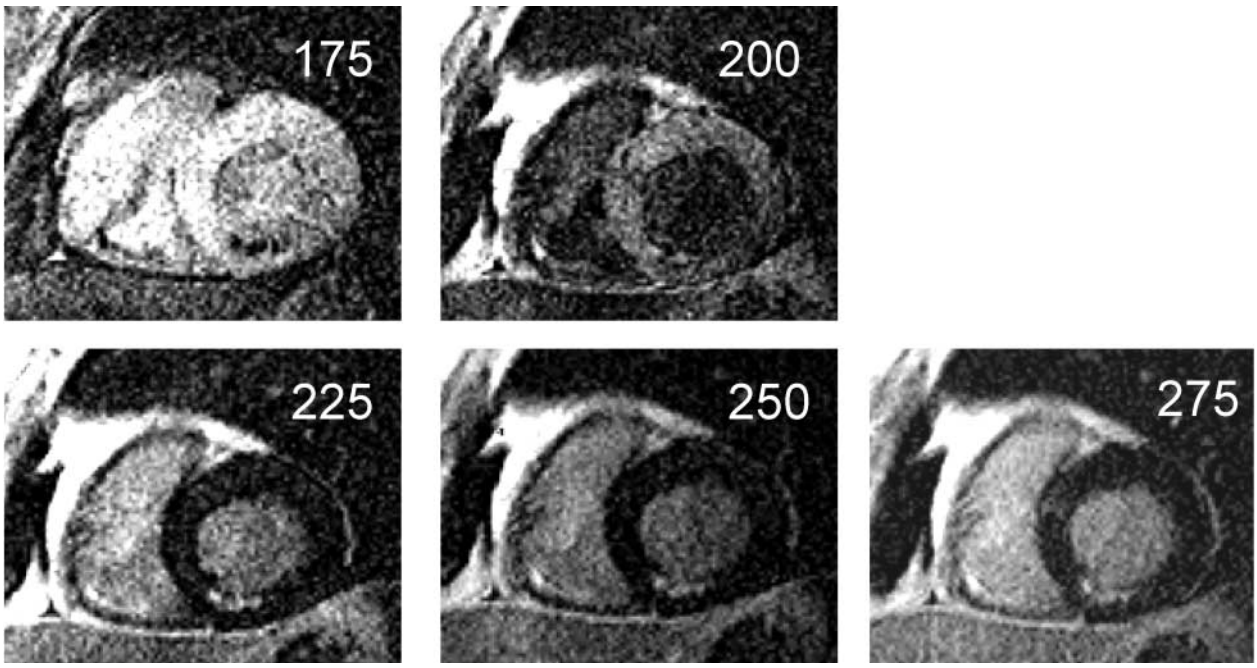


***Figure 1.*** Images for different prepulse delays for the same patient, measured 25 minutes postcontrast. A short prepulse delay (175 ms) may lead to an inversion of the contrast. In this case, with a prepulse delay of 200 ms the infarct cannot be discriminated from normal myocardium.



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coronary intervention underwent contrast-enhanced magnetic resonance (MR) imaging. The diagnosis of a previous myocardial infarction was confirmed for each patient by a history of elevated levels of serum creatine kinase, electrocardiographic criteria, or by coronary angiography. All patients gave informed written consent.

### MR Imaging Protocol

MR imaging was performed on a 1.5 T whole body scanner (ACS NT, Philips Medical Systems, Best, The Netherlands) with Power Track 6000 gradients (slew rate 105 T/m/s, amplitude 23 mT/m), cardiac software package INCA 2B, and a five-element phased-array cardiac coil. Two short survey scans to define the position and axis of the left ventricle were performed. Wall motion was then imaged during breath-holding with echo planar imaging in three short-axis views and two long-axis views using a steady-state free precession sequence. After obtaining the functional cardiac images, regional left ventricular function was visually analyzed online by a physician to determine regions with abnormal wall motion and wall thinning. This was the basis for planning the short-axis view for the contrast-enhanced imaging sequence.

A triggered RF spoiled segmented gradient echo sequence (echo time 3.6 ms, repetition time 8 ms, flip angle 15°) was used for infarct imaging. Slice thickness was 10 mm with a matrix of 256 × 256 pixels. The field of view was 380 mm. To obtain images with a low signal of normal myocardium intensity, a nonselective 180° inversion pulse was applied. Five different prepulse delays (175, 200, 225, 250, and 275 ms) were tested. Total imaging time for all five breath-holds was less than 30 seconds. A mid-diastolic trigger delay was chosen to minimize cardiac motion. Patients were instructed not to move during the study.

Five images with different prepulse delays were acquired at baseline. Then a standard double-dose of 0.2 mmol per kg body weight Gadolinium-diethylene-triamine pentaacetic acid (Gd-DTPA, Magnevist®, Schering, Berlin, Germany) was administered as a bolus with a power injector in a peripheral vein. The five images with different prepulse delays were then repeated after 3, 6, 9, 12, 15, 20, 25, and 30 minutes post contrast injection. Figure 1 shows sample images obtained at 25 minutes using different prepulse delays.

### MR Data Analysis

Image analysis was performed on a Sun Ultra Sparc 10 with the Easy Vision Software Rel. 4 (Philips, Best, The Netherlands). Regions of interest were placed in the left ventricular chamber to determine the signal intensity (SI) of blood and in an area anterior to the chest wall to determine the noise. Also, for each time point and prepulse delay, the enhanced area and unenhanced myocardium were manually delineated using closed contours. The following values were determined: mean, minimum, and maximum SI and the standard deviation within the region of interest in background noise, left ventricular blood, normal and enhanced myocardium as well as in the area of enhancement. The definition of enhanced myocardium was based on the visual perception of hyperintense areas within the myocardium as it is done in clinical routine.

Intraobserver variability was obtained by repeating the measurements by the same physician after 4 weeks. In addition, measurements at baseline, 6, 15, and 25 minutes were repeated by a different physician to determine the interobserver variability.

### Signal-to-Noise Ratio and Contrast Calculation

Signal-to-noise ratio (SNR) was calculated as the following signal intensities (SI) divided by the SI of the background noise:

$SI_1$ = blood.

$SI_2$ = normal myocardial signal intensity.

$SI_3$ = signal intensity of the enhanced myocardium.

The contrast was calculated as follows (Baierl et al., 1986):

$$C_{jk} = \frac{(SI_j - SI_k)}{\frac{1}{2}(SI_j + SI_k)} \quad \text{with } j \neq k \text{ and } j,\ k \in \{1,\ 2,\ 3\} \tag{1}$$

In order to visualize the contrast among all three structures (enhanced and normal myocardium as well as blood), a plot of the minimum contrast vs. the sum of all three contrast pairs (absolute values) was done:

$$\left(\arg\min_{jk}|C_{jk}|;\ \sum_{jk}|C_{jk}|\right) \quad \text{with } j > k;\ j;\ k \in \{1,\ 2,\ 3\} \tag{2}$$

### Calculation of the Inter- and Intraobserver Variability

Inter- and intraobserver variability were calculated according to Bland and Altman (1986):

$$\frac{|\text{observer1} - \text{observer2}|}{\frac{1}{2}(\text{observer1} + \text{observer2})} \quad (3)$$

### Statistics

Continuous data are presented as median with range. Comparison of the areas dependent on the prepulse-delay was performed with analysis of variance (ANOVA, Statistica 5, Statsoft). For the comparison of the areas dependent on the time after contrast injection, the Wilcoxon matched pairs test was used (Statistica 5, Statsoft). For analysis of differences of the baseline to post-contrast values and the inter- and intraobserver variability the two-tailed paired, Student's t-test was used. Categorical data were compared by the chi-square test. A statistical probability of $p < 0.05$ was considered to be significant.

## RESULTS

### Patient Characteristics

Baseline characteristics of the patients are shown in Table 1. Myocardial infarctions were at least 6 months old, with one exception as the patient underwent MR imaging 89 days after myocardial infarction during a hospital stay for planned coronary angioplasty (Table 1). Median heart rate at examination was 63, range 59 to 77 bpm.

All patients completed the study protocol, and no complications during MR imaging occurred.

***Table 1.*** Baseline data of the patients.

| | |
|---|---|
| Male | 92% ($n = 9$) |
| Age, median years | 65.0 (48–70) |
| Amount of contrast medium, mL | 32.0 (24–45) |
| Left ventricular ejection fraction | 48% (31–70%) |
| Age of myocardial infarction, mean days | 2847 (58–5390) |
| Q-wave infarction | 69.2% ($n = 9$) |
| Multiple infarctions | 15.4% ($n = 2$) |
| anterior infarction | 38.5% ($n = 5$) |
| posterior infarction | 61.5% ($n = 8$) |
| Conservative management | 38.5% ($n = 5$) |
| Thrombolysis | 15.4% ($n = 2$) |
| Multi vessel disease, % | 84.6% ($n = 11$) |
| Percutaneous angioplasty, % | 38.5% ($n = 5$) |
| Coronary artery bypass, % | 23.1% ($n = 3$) |
| Target vessel revasculated prior to imaging, % | 38.5% ($n = 5$) |
| Enhanced area, % of slice | 14 (2–29) |

### Time-Intensity Curves

All patients showed visible contrast enhancement; however, in two patients only a very small area (60–70 $mm^2$) was seen. The localization of the enhanced areas correlated well with wall motion abnormalities and electrocardiographic changes.

Precontrast baseline images revealed no demarcation of the infarction. After contrast agent administration the following alterations in signal intensity (SI) could be observed:

There was a strong and significant increase in blood SI immediately after contrast agent injection for all prepulse delays with a gradual decrease over time (Fig. 2a). With the three longer prepulse delays there was a similar, but less pronounced increase of SI in normal myocardium with a maximum of 3 minutes and a following gradual decrease. With the two short prepulse delays, SI of normal myocardium was low at 3 minutes with a gradual increase over time (Fig. 2b). The enhanced myocardium showed an intermediate effect; there was a significant increase in SI after contrast agent injection for all but the shortest (175 ms) prepulse delays (Fig. 2c).

Figure 3 shows the contrast between enhanced and nonenhanced areas as well as between enhanced myocardium and blood for the different prepulses and imaging times. The contrast between the normal and enhanced myocardium for prepulse delays longer than 200 ms did not increase after 9 minutes. The contrast between scar and blood (broken line) showed a maximum at 3 minutes with a phase of near-isointensity between the enhanced infarct area and the LV blood between 9 and 20 minutes after contrast administration. At 25 minutes and 30 minutes, contrast for both scar and normal myocardium as well as for scar and blood was high for the prepulse delays of 225 ms and 250 ms. At this time, blood was darker than scar tissue.

In order to judge the contrast relationships of all three structures (blood, enhancement area, and normal myocardium) a plot of the minimum contrast vs. the sum of all three contrast pairs is shown in Fig. 4. It shows a decrease of the total contrast with time. In addition, a period of low minimum contrast can be found.



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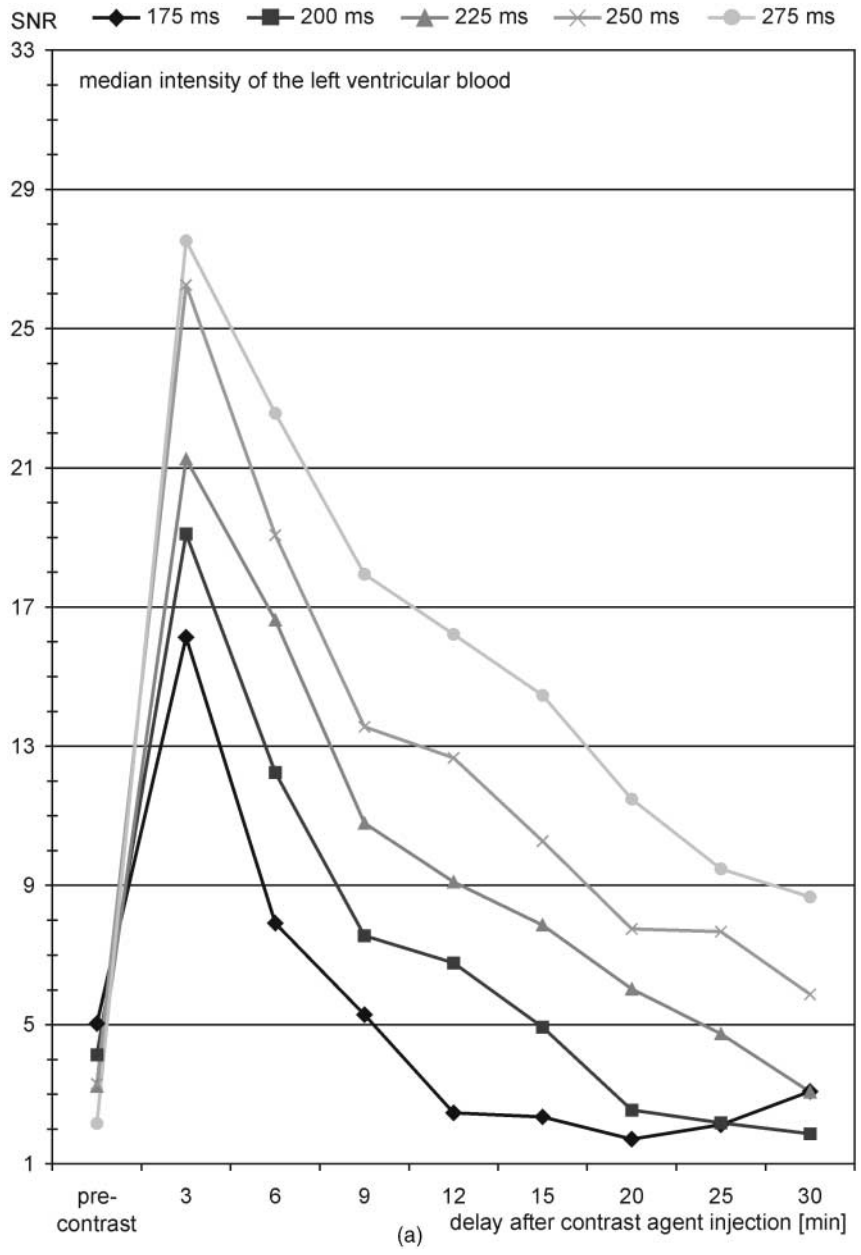


***Figure 2.*** Mean signal-to-noise ratios (SNR) of left ventricular blood (a), normal myocardium (b), and the enhanced area (c). The five different prepulse delays (black for 175 ms to light grey for 275 ms) produced similar intensity-curves at differerent levels of absolute signal intensity. Note that the x-axis is not linear.

*(continued)*

### Enhancement Area

Concerning the post-contrast delay, a tendency towards a smaller area of enhancement was only found at 3 minutes in comparison to later time points. This was significant for all time points except for 6 and 15 minutes (Table 2). After 3 minutes there was no significant change of the enhancement area. In general, the mean area of the enhanced myocardium was not significantly influenced by the prepulse delay (each individual compared over time to itself with ANOVA ($p = 0.997$)).

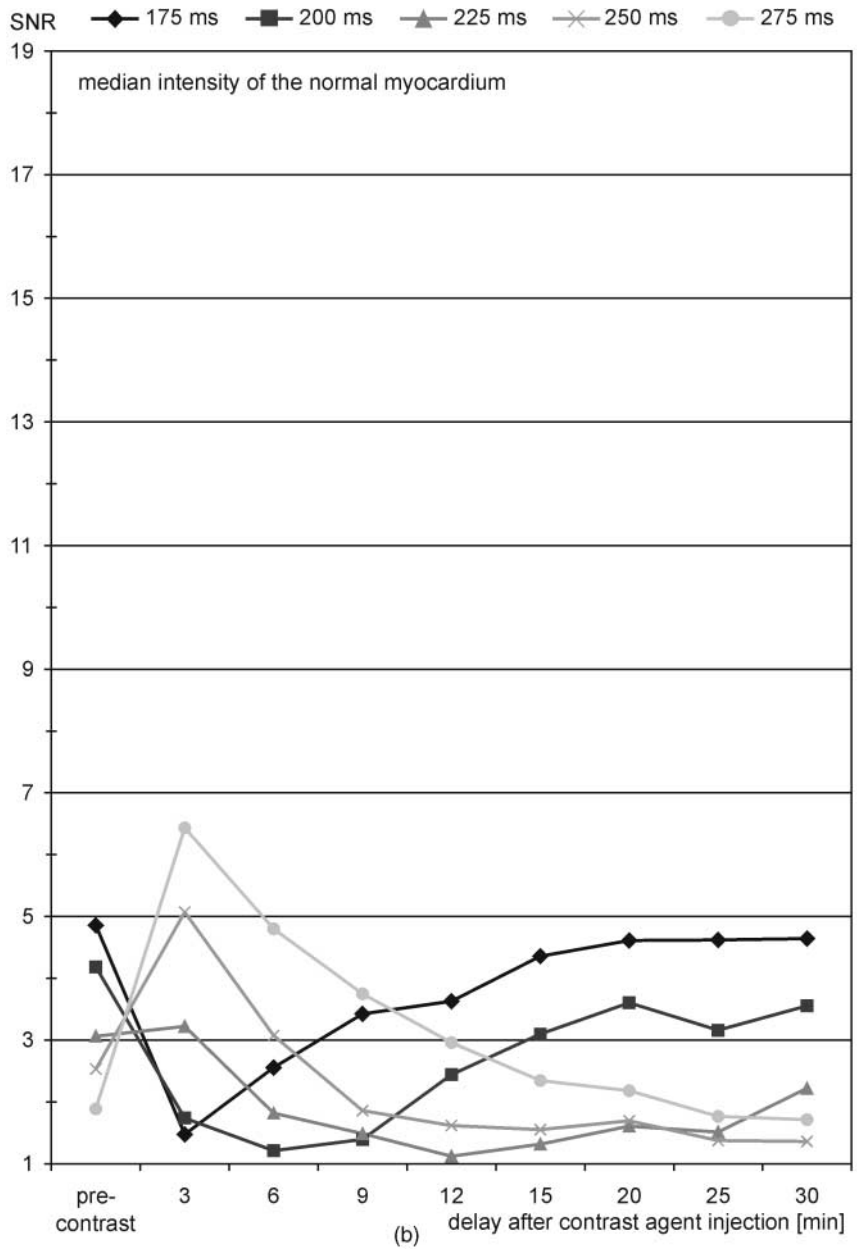


***Figure 2.*** Continued.

### Intra- and Interobserver Variability

Intra- and interobserver variability for measuring the signal-to-noise were 4.3% (Fig. 5) and 6.2%, respectively. Regarding the postcontrast injection time, variability of the signal-to-noise measurement was lowest at 6 and 25 minutes. The intraobserver variability for the determination of the enhanced area is shown in Fig. 6. For prepulse delays of 225–275 ms, variability was best at 6 and worst at 15 and 20 minutes ($p = 0.035$). The mean interobserver variability for the determination of the enhanced area was not significantly different for the selected time points: 9.5% at 6, 11.2% at 15, and 10.0% at 25 minutes.

Intraobserver variability of all measured data was significantly ($p < 0.01$) higher for the two short prepulse delays (175 and 200 ms) as compared with the three longer delays (225–275 ms).



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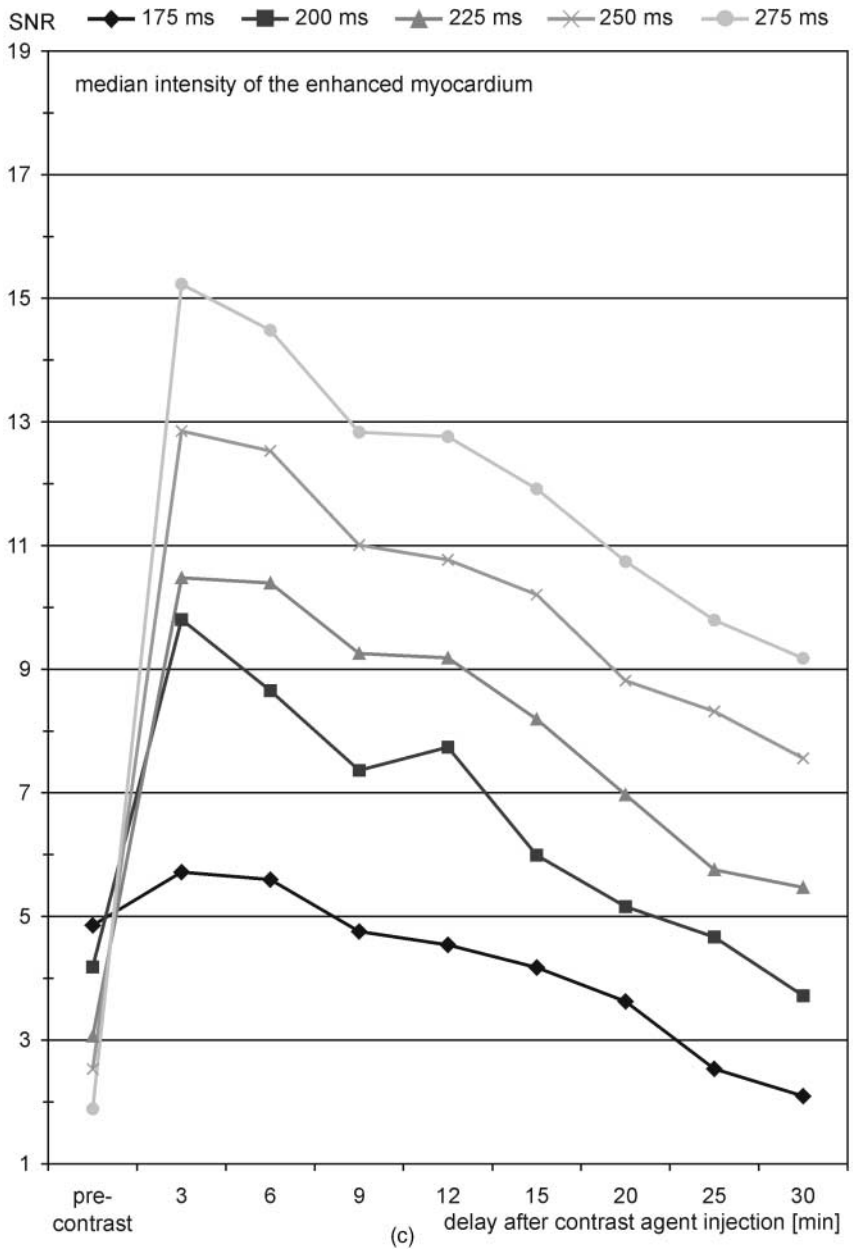


***Figure 2.*** Continued.

The intraobserver variability for the determination of the enhanced area correlated significantly ($r = 0.61$; $p < 0.01$) with the combined contrast ratio of scar to blood and normal myocardium. To find a more objective parameter for the discrimination of left ventricular blood and enhanced myocardium, an additional correlation of the contrast between blood and enhanced myocardium with a measurement of the wall thickness of the enhanced myocardium was done: Low intra-observer variability correlated significantly ($r = 0.77$; $p < 0.01$) with a high contrast.

## DISCUSSION

This study shows that contrast-enhanced MR imaging of chronic myocardial infarction can be performed with excellent reproducibility. An adequate

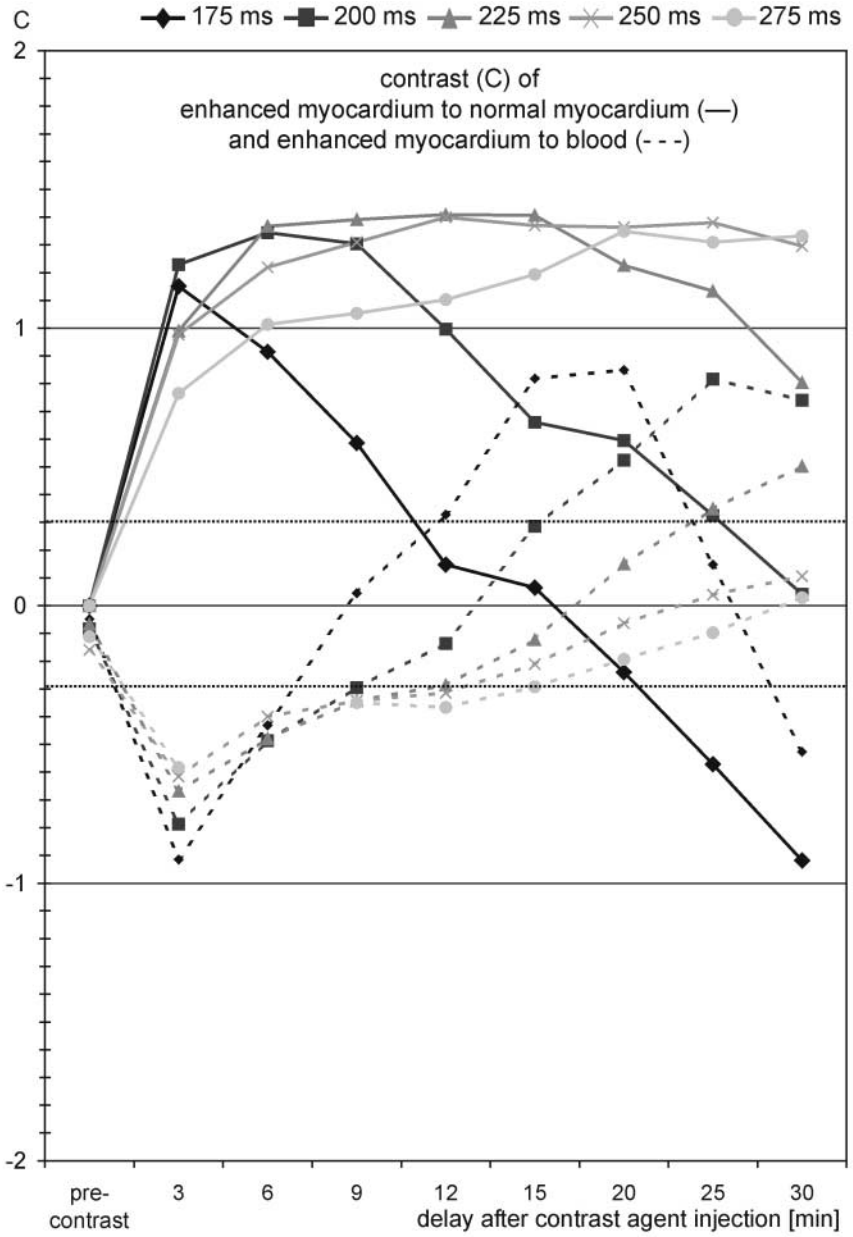


***Figure 3.*** The mean contrast between enhanced and normal myocardium (solid line) as well as enhanced myocardium and left ventricular blood (broken line) for the five prepulse (black for 175 ms to light grey for 275 ms). The dotted line indicates the area of contrast of less than 30%. Such contrast cannot be visually appreciated.

prepulse delay and an adequate time for image acquisition is required, though. The results give rise to the following conclusions:

1. According to the nature of the inversion recovery sequence, there will be a time point after bolus injection for a fixed prepulse delay in which the signal of the normal myocardium is the same amount below the zero crossing point (which means "nulling" of the signal), as the signal from scar tissue is above the zero crossing point. This leads to no discernible contrast between these two tissues, thus the prepulse delay has to be adjusted to "null" the myocardial signal, or at least have a higher signal for scar tissue than for normal myocardium, which is true for all prepulse delays longer than the "ideal" delay leading to a "nulling" of the normal myocardium.



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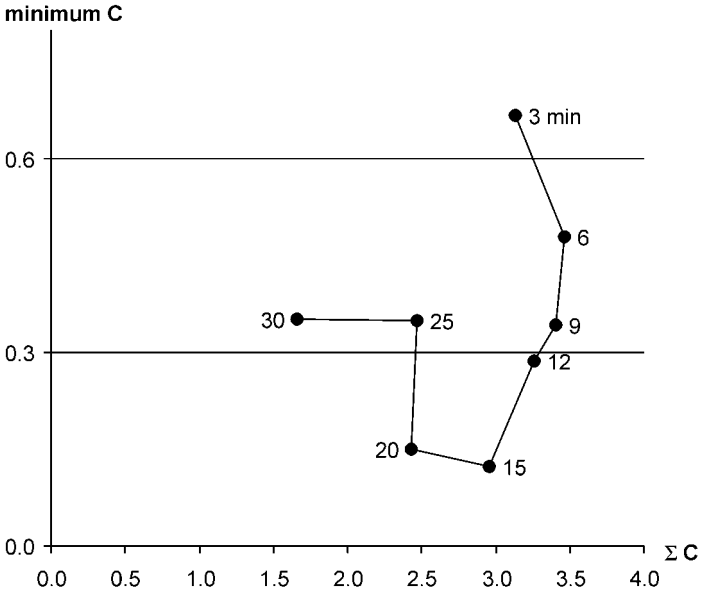


***Figure 4.*** Plot of the minimum contrast vs. the sum of all contrast pairs (enhanced to normal myocardium, normal myocardium to blood, blood to enhanced myocardium) for a prepulse delay of 225 ms. Dots (named with time postcontrast) in the right upper corner represent a favorable discrimination of the three structures. A continuous decrease of the maximum contrast with time and a period with a low minimum contrast can be found. This figure is showing a combination of the contrast of all three tissues and supports the assumption that can be made from Fig. 3 that there is a time point of weak contrast (12 to 20 minutes).

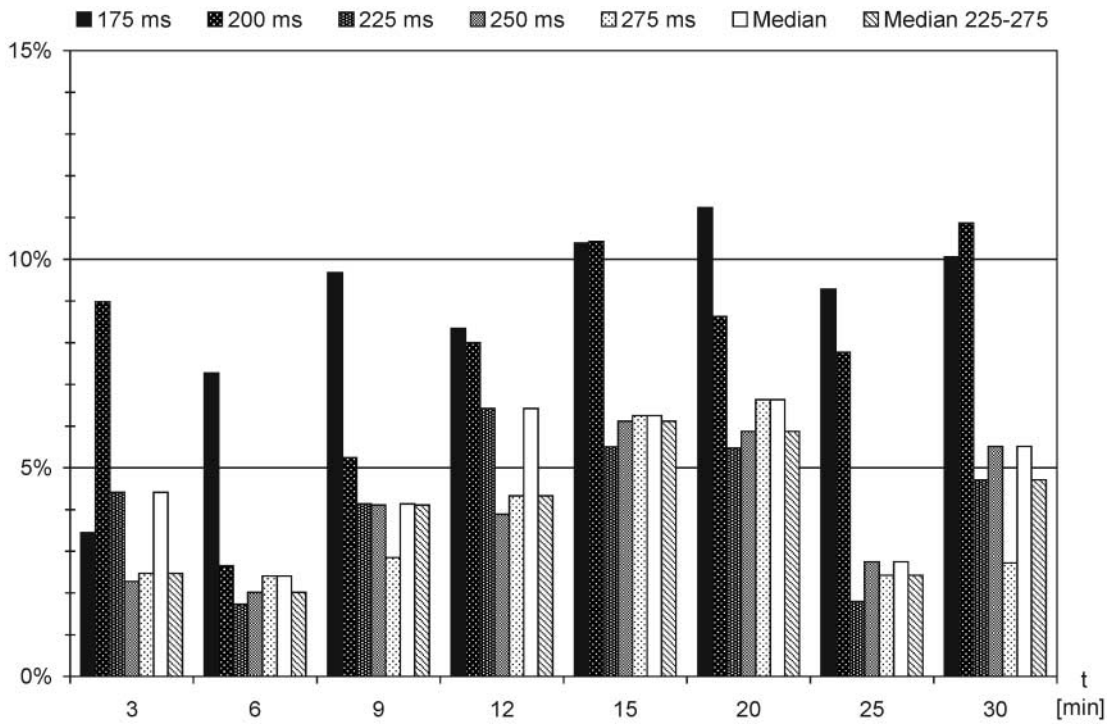


***Figure 5.*** Intraobserver variability of the signal-to-noise ratios of the enhanced myocardium for the five prepulse delays (black for 175 ms to light grey for 275 ms). The white bar represents the mean of all delays, the hatched bar shows the mean only for 225, 250, and 275 ms.

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***Table 2.*** Mean area ($mm^2$) of the enhanced myocardium at different delays after contrast agent injection. No general significant influence of the prepulse delay on the mean area was observed. There was a tendency towards smaller areas measured only at 3 minutes as compared to later time points. Beyond 3 minutes, there was no significant change of the enhanced area.

| | Mean area at different delays after contrast agent injection | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Prepulse delay | 3 | 6 | 9 | 12 | 15 | 20 | 25 | 30 |
| 175 | 220 (45–752) | 220 (44–733) | 233 (55–815) | 203 (51–745) | 215 (57–756) | 258 (64–625) | 241 (72–694) | 296 (49–654) |
| 200 | 236 (40–706) | 270 (70–766) | 223 (59–797) | 246 (62–787) | 233 (67–673) | 215 (53–678) | 213 (62–688) | 307 (59–637) |
| 225 | 285 (41–681) | 315 (69–753) | 269 (59–768) | 263 (54–743) | 259 (46–692) | 250 (75–809) | 237 (74–703) | 256 (55–708) |
| 250 | 243 (48–731) | 278 (78–734) | 287 (69–726) | 297 (53–752) | 228 (78–694) | 245 (77–793) | 253 (72–783) | 252 (59–825) |
| 275 | 238 (58–809) | 247 (79–744) | 295 (68–748) | 291 (55–680) | 237 (67–737) | 230 (76–791) | 249 (75–715) | 223 (57–769) |
| Median | 238 | 270 | 269 | 263 | 233 | 245 | 241 | 256 |
| p–value to 3 minutes | | 0.054 | 0.025 | 0.016 | 0.131 | 0.022 | 0.048 | 0.019 |

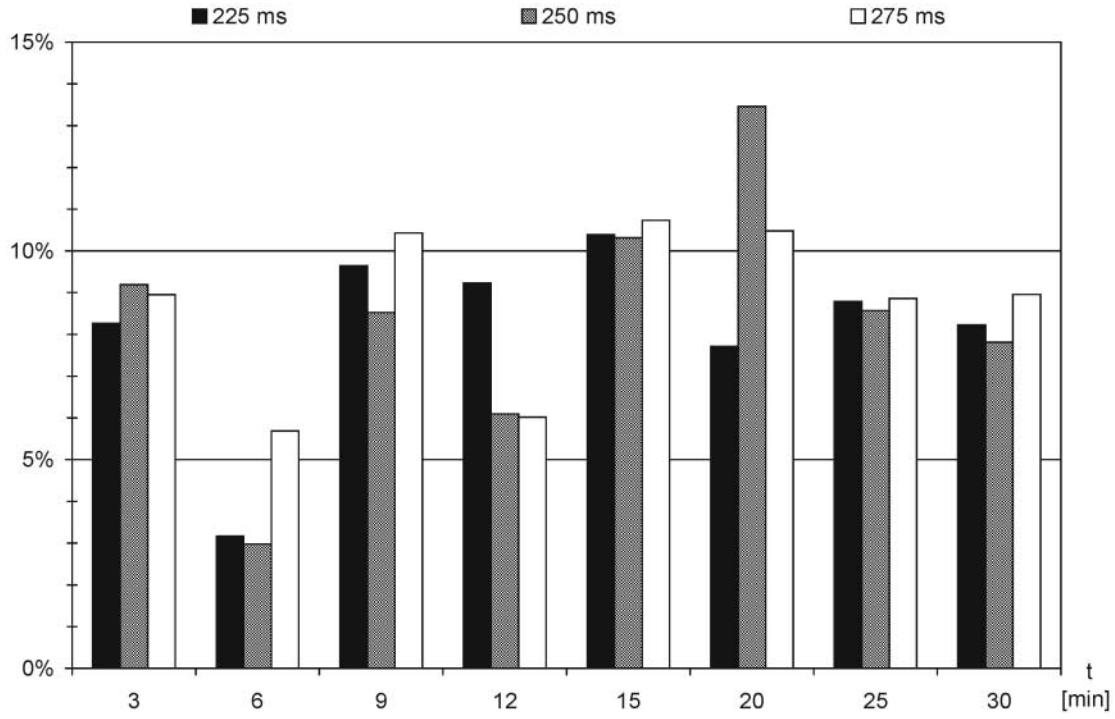


***Figure 6.*** Intraobserver variability of the area of the enhanced myocardium for three prepulse delays (dark grey for 225 ms to light grey for 275 ms).

2. If a sufficient contrast is achieved, the area of the enhanced myocardium is independent of the prepulse delay.
3. The area of enhanced myocardium is independent of the interval between contrast injection and image acquisition after 6 minutes postinjection.
4. Strong contrast between scar tissue and normal myocardium can be found as early as 3 minutes after contrast agent injection. For prepulse delays of $\geq 225$ ms, contrast remains high for 30 minutes; for prepulse delays of $< 225$ ms, contrast drops rapidly within 9–20 minutes.
5. Strong contrast between scar tissue and blood can be found early (3 minutes postinjection), and attenuated, late (25 to 30 minutes). The longer the prepulse delay the longer the time after injection before contrast recovers. At 9 to 20 minutes postinjection, a period of lower contrast between blood, enhanced, and normal myocardium was observed.
6. Inter- and intraobserver variability are lowest when contrast between scar and blood as well as scar and normal myocardium are high; however, the correlation is not very strong.

This means that since the area of enhancement is independent of the prepulse delay and the time point postinjection (after 3 minutes), both parameters should be chosen to optimize contrast between scar to normal myocardium and scar to blood. Furthermore, optimal contrast yields minimal inter- and intraobserver variability.

In the present study blood was brighter than scar during the first few minutes after bolus injection, followed by a phase with low contrast. After 15 to 30 minutes, the contrast between scar and blood returned; however, scar was now brighter than blood. At two time points optimal demarcation of myocardial infarction was found: 6 to 9 minutes (bright blood and dark normal myocardium) and 25 to 30 minutes (bright scar and dark normal myocardium). This was supported by the low intra- and interobserver variability.

In previous studies infarct imaging was performed 10 (Kim et al., 1996; Lima et al., 1995; Ramani et al., 1998; Wu et al., 1998) to 20 minutes (van Dijkman et al., 1989) after contrast medium injection, and, thus, suboptimal demarcation of the infarct may have been achieved.

Interestingly, intraobserver variability was also low at 12 minutes, a time point where contrast between blood and enhanced area is very low. In addition, overall inter- and intraobserver variability was remarkably low. This might be explained by the fact that a priori knowledge can successfully be applied to determine the endocardial

border. In comparison to the area measurement, a better correlation was found for the wall thickness measurement. From this could be inferred that for wall thickness measurements a good discrimination of the blood and the enhanced myocardium is crucial, while this may not be so important for the determination of the infarct volume.

The prepulse delay (together with other parameters, such as heart rate, TR, flip angle, and prepulse angulation) influences the contrast between infarcted and noninfarcted myocardium as well as between scar and blood. However, the area of enhancement was not influenced by the duration of the prepulse delay. With the parameters used in the current study optimal results were achieved for prepulse delays between 200 and 275 ms. Shorter prepulse delays had a significantly higher inter- and intraobserver variability.

The results from this study can only be applied for chronic myocardial infarction, as no patients with acute or subacute infarctions were included since there might be differences in the kinetics of Gd-DTPA (Flacke et al., 2001; Oshinski et al., 2001). In addition, the use of different or fractionated dosages may influence the observed time points.

Other contrast agents may have different kinetics. However, Sandstede et al. (2001) showed a similar time course of the signal intensities measured in acute myocardial infarctions using a Gd-BOPTA and a conventional spin-echo-sequence without a prepulse. A recently presented observation showed similar contrast kinetics in patients with ischemic cardiomyopathy (Klein et al., 2002) with two comparable time points when the highest difference of the T1 value of normal and infarcted myocardium is measured. Thus, it can be assumed that the general finding for the contrast kinetics with a time span of unfavorable contrast can be applied to various settings, with adjustment of the absolute time points for best contrast.

The following recommendation for scar imaging of chronic infarctions with an inversion recovery sequence and a bolus of 0.2 mmol Gd-DTPA per kg body weight can be made: Images should be obtained either early (6 to 9 minutes) or late (>25 minutes). For the sequence used in the study in most cases a prepulse delay about 225 ms (>200 to 275) results in optimal contrast.

## ABBREVIATIONS

| | |
|---|---|
| BMI | body mass index |
| Gd-DTPA | Gadolinium-diethylene-triamine pentaacetic acid |
| MR | magnetic resonance |
| SD | standard deviation |
| SI | signal intensity |
| C | contrast |

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