Characterization of Acute and Chronic Myocardial Infarcts by Multidetector Computed Tomography
Comparison With Contrast-Enhanced Magnetic Resonance

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Background—We evaluated whether contrast-enhanced multidetector computed tomography (CE-MDCT) might characterize myocardial infarct (MI) with patterns similar to those obtained by contrast-enhanced magnetic resonance (CE-MR) and studied the underlying mechanisms.

Methods and Results—In vivo infarct characterization by CE-MDCT was shown to be feasible between 4 and 20 minutes after contrast injection in 7 pigs with MI. Subsequently, in 16 patients with acute MI and 21 patients with chronic MI, contrast patterns by CE-MDCT were related to CE-MR. Eighteen patients had hypoenhanced regions on early CE-MDCT images at the time of coronary imaging, and 34 patients had hyperenhanced regions on images acquired 10 minutes later. On a segmental basis, there was moderately good concordance of early hypoenhanced regions (92%, $\kappa=0.54$, $P<0.001$) and late hyperenhanced regions (82%, $\kappa=0.61$, $P<0.001$) between CE-MDCT and CE-MR.

Absolute sizes of early hypoenhanced (6±16 versus 7±16 g, $P=0.25$) and late hyperenhanced (36±34 versus 31±40 g, $P=0.14$) regions were similar on CE-MDCT and CE-MR and were highly correlated ($r=0.93$, $P<0.001$ and $r=0.89$, $P<0.001$ respectively). In 8 retrogradely perfused infarcted rabbit hearts, contrast kinetics of iomeprol were similar to gadodiamide, ie, slow wash in (8.7±6.7 versus 1.2±0.3 minutes, $P<0.001$) in infarct core and slow washout (20±12 versus 2.5±0.5 minutes, $P<0.001$) in both infarct core and rim compared with the remote region.

Conclusions—Because iodated contrast agents have similar kinetics in infarcted and noninfarcted myocardium as gadolinium DPTA, CE-MDCT can characterize acute and chronic MI with contrast patterns similar to CE-MR. CE-MDCT may thus provide important information on infarct size and viability at the time of noninvasive coronary imaging. (Circulation. 2006;113:823-833.)

Key Words: contrast media ■ imaging ■ magnetic resonance imaging ■ multigated computed tomography ■ myocardial infarction

Gadolinium DPTA contrast-enhanced MRI (CE-MR) can characterize both acute and chronic infarcts with specific time-dependent contrast patterns.1–4 In acute infarcts (myocardial infarction [MI]), images obtained shortly after contrast injection often demonstrate distinct areas of hypoenhancement within the infarct core, resulting from the reduced delivery of contrast to the infarcted regions, mostly as a consequence of microvascular obstruction.2,3 On the other hand, imaging performed late (10 to 15 minutes) after contrast injection generally shows the presence of hyperenhanced zones, the transmural extent of which exactly reflects that of the necrotic core.3 These delayed hyperenhancement areas have been observed in both acute and chronic MI and appear to result from increases in distribution volume3 and alterations of kinetics of extravascular contrast agents in necrotic areas.4
related to gadolinium in ex vivo isolated perfused rabbit hearts.

**Methods**

**Time Course of Contrast Enhancement in Pigs**
Seven anesthetized and intubated pigs (30 to 50 kg) underwent gated CE-MDCT 2 to 6 weeks after anterior MI created by surgical ligation of the mid left anterior descending coronary artery under general anesthesia. The care and treatment of all animals involved in this study were in accordance with the position of the American Heart Association on research animal use, adopted November 15, 1984. CE-MDCT images were acquired at baseline and every 2 minutes after bolus injection of iomeprol 2 mL/kg IV for a total of 24 minutes, during short breath holds obtained by stopping the mechanical ventilator for ~20 seconds. Two reviewers assessed signal intensity (SI) over time in the anterior (infarcted) and inferior (remote) region and in the LV cavity. Contrast-to-noise ratio (CNR) over time was computed as the difference in mean SI between the background noise in the LV cavity.

**Patient Studies**
Two groups of patients were studied (Table 1). Group 1 consisted of 16 patients admitted with a first acute MI, diagnosed on the basis of elevated plasma cardiac enzymes, typical ECG changes, and the presence of an angiographically demonstrated partial or complete occlusion infarct-related artery. Patients were studied 11 ± 11 days (range 1–34 d) after anterior MI created by surgical ligation of the mid left anterior descending coronary artery under general anesthesia. The care and treatment of all animals involved in this study were in accordance with the position of the American Heart Association on research animal use, adopted November 15, 1984. CE-MDCT images were acquired at baseline and every 2 minutes after bolus injection of iomeprol 2 mL/kg IV for a total of 24 minutes, during short breath holds obtained by stopping the mechanical ventilator for ~20 seconds. Two reviewers assessed signal intensity (SI) over time in the anterior (infarcted) and inferior (remote) region and in the LV cavity. Contrast-to-noise ratio (CNR) over time was computed as the difference in mean SI between the background noise in the LV cavity.

**Contrast-Enhanced Multidetector Computed Tomography**
CE-MDCT was performed on a 16-slice system (Brilliance, Philips Medical Systems). A first set of images for both coronary imaging and analysis of early myocardial perfusion patterns was acquired immediately after intravenous injection of a bolus of 140 mL of iomeprol (Iomeron 400, Guerbet) at a rate of 4 mL/s. Images were acquired after automatic detection of the contrast bolus in the thoracic aorta during a 20- to 25-second breath hold. Tube rotation speed was 420 ms, detector collimation was 16×0.75 mm, pitch was 0.20 to 0.24, tube voltage was 140 kV, and effective tube current was 400 mAs. Dose modulation with reduction of tube current in systole was used to reduce dose exposure to the patient.

On the basis of results from the pig studies, a second series of gated breath-hold images was acquired for infarct visualization 10 minutes after contrast injection. To increase signal to noise and reduce dose, detector collimation was increased to 16×1.5 mm, and tube voltage was reduced to 90 kV.

Radiation exposure was ~7 mSv (dose-length product [DLP] 650 mGy·cm, irradiated volume [CTDvol] 38 mGy reduced by ±40% through ECG dose modulation) during first-pass imaging and 2.4 mSv (DLP 240 mGy·cm, CTDvol 12 mGy reduced by ±40% through dose modulation) during the late imaging sequence. Images were reconstructed at 75% of the RR interval with a retrospective multicycle ECG gating algorithm with half a tube rotation, and, depending on heart rate, information from 2 or 3 consecutive cardiac cycles. Temporal resolution varied according to the patient’s heart rate from 90 to 120 ms. Images were resliced into serial 10-mm-thick short-axis and 2- and 4-chamber–view long-axis slices.

**Contrast-Enhanced Magnetic Resonance**
CE-MR was performed with a 1.5T magnet (Philips Intera CV) equipped with a 5-element phased-array cardiac coil. After axial and
oblique localizer scout images were taken, an intravenous bolus of 0.05 mmol/kg gadodiamide (Omniscan, Nycomed) was injected at a rate of 3 mL/s. Simultaneously, a dynamic first-pass perfusion scan of 40 phases was acquired with an ECG-gated, saturation-recovery, interleaved, gradient echo pulse sequence with SENSE (sensitivity encoding), with a temporal resolution that covered 8 short-axis slices every other heart beat. Imaging parameters were as follows: repetition time 6.2 ms, echo time 1.2 ms, 128 × 128 image matrix interpolated to 256 × 256 pixels, 20° flip angle, 90° saturation pulse, 125-KHz bandwidth, and inversion time 90 ms. After completion of the first-pass images, a second bolus of 0.15 mmol/kg gadodiamide was given. Ten to 15 minutes later, short-axis images were acquired with a 3D inversion-recovery prepared fast gradient echo pulse sequence. Imaging parameters were as follows: repetition time 6 ms, echo time 2 ms, 256 × 192 × 10 image matrix, 20° flip angle, and 180° inversion pulse with inversion time 200 to 250 ms. Thereafter, 2- and 4-chamber-view long-axis images were acquired with a 2D inversion-recovery gradient echo pulse sequence.

Data Analysis

Early and late CE-MDCT and CE-MR images were transferred to a computer workstation (Mxview, Philips Medical Systems) and analyzed anonymously in duplicate by 2 blinded readers. To avoid recalling the patient’s images, the blinded readers analyzed CE-MDCT and CE-MR images in separate sessions, separated by at least 4 weeks. Presentation of CE-MDCT images was standardized with respect to window width (100) and center (100). The readers graded image quality of early and late CE-MDCT and CE-MR images on a 4-point scale (with 1 indicating nondiagnostic; 2, poor; 3, adequate; and 4, excellent). Early CE-MDCT and CE-MR images were visually examined for the presence of early hypoenhancement areas, defined as regions of decreased SI compared with normal myocardium. These regions had to persist for at least 4 frames on the cine CE-MR study. Late CE-MDCT and CE-MR images were examined for the presence of both hypoenhanced and hyperenhanced regions, the latter being defined as regions of increased SI compared with normal zones. On both CE-MDCT and CE-MR images, CNRs of early hypoenhanced and late hyperenhanced regions and percentage myocardial SI reduction (on early images) or increase (on late images) were calculated as follows:

\[
\text{1. Reduction} = \frac{S_{I_{\text{low-intensity region}}}-S_{I_{\text{normal region}}}}{S_{I_{\text{normal region}}}} \times 100
\]

\[
\text{2. Increase} = \frac{S_{I_{\text{high-intensity region}}}}{S_{I_{\text{normal region}}}} \times 100
\]

The extent of the early hypoenhanced and late hyperenhanced regions was analyzed both qualitatively and quantitatively. Qualitative analysis was performed in 16 segments per patient to evaluate whether hypoenhanced or hyperenhanced regions were present and whether their extent was subendocardial or transmural. The quantitative size of early hypoenhanced and late hyperenhanced regions was computed by a Simpson’s method: areas of hypoenhanced and hyperenhanced and LV endocardial and epicardial contours were visually traced on consecutive slices by the 2 observers. The extent of early hypoenhanced and late hyperenhanced regions was computed both in absolute terms (grams) and in percent of total LV mass, according to the Equations below:

\[
\text{3. LV mass (g)} = (\Sigma \text{LV epicardial area} - \Sigma \text{LV endocardial area}) \times \text{slice thickness} \times 1.06
\]

\[
\text{4. Hypeenhanced mass (g)} = \Sigma \text{Hypeenhanced area} \times \text{slice thickness} \times 1.06
\]

\[
\text{5. Hyperenhanced extent (\%)} = \frac{\text{Hyperenhanced mass (g)}}{\text{LV mass (g)}} \times 100
\]

Contrast Kinetics of Iomeprol Versus Gadodiamide in Isolated Rabbit Hearts

To compare contrast kinetics of iomeprol with gadodiamide, hearts from 8 rabbits that underwent MI by 60 minutes of snare occlusion of a left coronary artery branch followed by 30 minutes of reperfusion were excised and retrogradely perfused inside the CE-MDCT scanner. Perfusion was performed without recirculation at constant flow of 15 mL/min with heated and oxygenated Krebs-Henseleit buffer supplemented with 2% bovine albumin and 30 mmol/L 2,3-butanedione-monooxime to suppress myocardial contraction. By rapidly switching between different perfusate reservoirs, hearts were perfused respectively for 30 minutes with perfusate supplemented with 0.5 mmol/L gadodiamide (gadodiamide inflow), then without contrast agent (gadodiamide outflow), then with perfusate that contained 0.105 mmol/L iomeprol (iomeprol inflow), and finally again without contrast agent (iomeprol outflow). CE-MDCT images were acquired at baseline and at 1, 2, 3, 4, 5, 6, 7.5, 10, 12.5, 15, 20, 25, and 30 minutes during inflow and outflow of gadodiamide and iomeprol. At the end of the experiment, hearts were cut into ~5-mm-thick short-axis slices, and infarct size was measured after incubation in 2% TTC. CT images were resliced to 5-mm-thick short-axis slices, and time activity curves in the center and rim of the infarct and in a remote region were fitted monoexponentially to obtain regional wash-in and washout time constants (1/T2) for gadodiamide and iomeprol. Distribution volume of contrast agents was computed as the ratio of SI increase in the each region of interest to the SI increase in the LV cavity after 30 minutes of inflow. Size of iomeprol bright area was planimetered after 5 minutes of washout and compared with the TTC-negative area.

Statistical Analysis

Values are reported as mean±1 SD. Statistical analysis was performed with SPSS version 11.5 software. Agreement in semiquantitative measurements between readers and between methods was compared with k-statistics. Discordant readings were resolved by consensus between the 2 readers. Interobserver reliability was assessed with 2-way random, single-measure intraclass correlation coefficient (ICC). Intraobserver and intrasubject reliability was assessed with 1-way random, 2-measure ICC. The average of the measurements of both readers was used for further analysis. CNRs and size of quantitatively measured early hypoenhanced and late hyperenhanced regions by CE-MDCT and CE-MR were compared with paired t test. Size of early hypoenhanced and late hyperenhanced regions by CE-MDCT and CE-MR was also compared with the Pearson’s correlation coefficient and by Bland-Altman plots. CNR of different regions in pigs and rabbits were compared over time with repeated-measurement ANOVA (the animal was considered a random factor, time and region of interest planned factors with repeated). Individual comparisons were made post hoc with the Tukey-Kramer test. All tests were 2-sided, and P<0.05 was considered statistically significant.

Results

Time Course of Contrast Enhancement in Pigs With Anterior Infarct

An example of serial CE-MDCT images in a pig with anterior infarct after bolus injection of iomeprol is shown in Figure 1a. The infarcted region demonstrated significantly higher SI than the remote region, starting 2 minutes and lasting until 24 minutes after contrast injection (Figure 1b). CNR (Figure 1c) was significantly higher than baseline starting at 4 minutes.
and remained stable until 20 minutes after contrast injection, after which it decreased rapidly.

**Patient Study**

All patients successfully underwent CE-MR and CE-MDCT without adverse reactions to contrast injection. Mean heart rate was not statistically different between the CE-MR and CE-MDCT studies (67±11 versus 66±13 bpm, *P*=0.52 by paired *t* test).

The clinical characteristics of the 2 groups of patients are shown in Table 1. Of the 16 patients with acute MI, 8 were treated by primary angioplasty and 1 by thrombolysis, whereas the remaining 7 did not receive reperfusion therapy because of late presentation. At the time of the CE-MDCT and CE-MR studies, the infarct-related artery was free of any residual coronary stenosis in 9 patients, showed a >50% luminal diameter stenosis in 2, and was totally occluded in 7. Among the patients with chronic LV ischemic dysfunction, 8 had undergone coronary revascularization before the CE-MDCT and CE-MR studies (4 by angioplasty and 4 by bypass surgery).

**Contrast-Enhancement Patterns on Early and Late CE-MDCT Images**

On the early images, CE-MDCT demonstrated the presence of dark or hypoenhanced regions in 18 of 37 patients (Figure 2). These dark areas were more prevalent in patients with acute MI (11 of 16) than in patients with chronic LV ischemic
dysfunction (7 of 21, \( P = 0.033 \) by \( \chi^2 \) test) and persisted on late images in 8 patients with acute MI. On late images, CE-MDCT identified delayed bright or hyperenhanced zones (Figure 3) in 34 of 37 patients (15 of 16 patients with acute MI and 19 of 21 patients with chronic LV ischemic dysfunction, \( P = 0.72 \) by \( \chi^2 \) test). Delayed hyperenhanced regions were observed in all 18 patients who exhibited early hypoenhanced areas but also in 15 patients without early hypoenhanced regions. Both early hypoenhanced and late hyperenhanced regions were located in the anatomic distribution of the infarct-related area and in an area that exhibited segmental dysfunction on cine-ventriculography and cine-MR.

**Comparison of CE-MDCT and CE-MR Contrast-Enhancement Patterns**

The presence of early hypoenhancement regions was confirmed in 20 patients by CE-MR (12 patients with acute MI and 8 patients with chronic LV ischemic dysfunction). There was a moderate concordance (92\%, \( \kappa = 0.54, P < 0.001 \)) in the identification of early hypoenhanced regions between CE-MDCT and CE-MR on a segmental basis. As indicated in Table 2, the concordance was slightly better in acute than in chronic infarcts.

Delayed hyperenhanced regions were confirmed in 31 patients by CE-MR (14 patients with acute MI and 17 with chronic LV ischemic dysfunction). There was good agreement (82\%, \( \kappa = 0.61, P < 0.001 \)) in the identification of these hyperenhanced regions between both techniques on a segmental basis. Again, this concordance was slightly better for acute than for chronic patients (Table 3). Most (75 of 107) of the misclassified segments by CE-MDCT were located in border zones of infarcts according to CE-MR. Concordance for identification of infarct location was excellent (\( \kappa = 0.90, P < 0.001 \)) if performed on a patient basis (ie, anterior/inferior/no infarct).

**Signal Intensity, CNR, and Image Quality**

Mean SI of early hypoenhanced regions on early CE-MDCT images was reduced to 67 ± 19 Hounsfield units (HU) com-

**Figure 2.** Examples of hypoenhanced areas on early CE-MDCT and corresponding early CE-MR images. a, Anterior hypoenhancement in a patient 10 days after acute anterior MI. b, Inferior hypoenhancement in a patient 2 days after acute inferior MI.

**Figure 3.** Examples of hyperenhanced areas on late CE-MDCT and corresponding late CE-MR images. a, Anterior hyperenhancement in a patient with anterior MI 25 days ago. b, Inferior hyperenhancement in a patient with inferior MI 11 months earlier. c, Anterior hyperenhancement in a patient with anterior MI 6 months earlier. d, Complex late hyperenhancement pattern in a patient with chronic LV dysfunction, anterior infarction, and suspected hypertrophic cardiomyopathy.
pared with 100±26 HU in normal myocardium (P<0.001 by paired t test). Similarly, on early CE-MR images, SI in hypoenhanced regions was significantly reduced to 703±424 arbitrary units versus 1028±475 arbitrary units in normal myocardium (P<0.001 by paired t test). Thus, the percent SI reduction and the CNR in hypoenhanced regions were similar between early CE-MDCT and CE-MR (Figure 4). The 2 reviewers judged image quality of early images by CE-MDCT and CE-MR to be equally good (3.2±0.7 versus 2.9±0.7, P=0.08 by paired t test).

On late CE-MDCT images, SI of normal myocardium was 97±11 HU, and SI of hypoenhanced regions was increased to 131±16 HU (P<0.001 by paired t test). By CE-MR, SI of normal myocardium was 239±142 arbitrary units, and SI of hypoenhanced regions was increased to 1096±339 arbitrary units (P<0.001 by paired t test). Accordingly, the percent increase in SI and CNR for hypoenhanced regions was significantly higher on late CE-MR than on late CE-MDCT images (Figure 4). The subjectively graded image quality of late CE-MR images was also judged to be better than that of late CE-MDCT images (3.8±0.4 versus 3.1±0.8, P<0.001 by paired t test). There was poor correlation between quality of early or late CE-MDCT and corresponding CE-MR images in the individual patient (r=0.11, P=0.51 for early images, r=0.37, P=0.25 for late images).

Comparison of the Size of Hypoenhanced and Hyperenhanced Regions Between CE-MDCT and CE-MR

Tables 2 and 3 compare the size of the early hypoenhanced and late hyperenhanced areas measured by CE-MDCT and CE-MR. Measurements of size of early hypoenhanced area by CE-MDCT were highly correlated with size of early hypoenhanced area by CE-MR. Similarly, the size of late hyperenhanced area by CE-MDCT was highly correlated to the size of hypoenhanced area by CE-MR.

Table 4 compares the average measurements of early hypoenhanced and late hyperenhanced area between both techniques. Absolute sizes of early hypoenhanced (6±16 versus 7±16 g, respectively, P=0.25 by paired t test) and late hyperenhanced areas (in grams) were similar (36±34 versus 31±40 g, respectively, P=0.14 by paired t test) with both CE-MDCT and CE-MR. When expressed in percent LV mass, however, CE-MDCT overestimated the extent of hyperenhancement compared with CE-MR (20±15% versus 15±14%, P=0.002 by paired t test). This overestimation was present only in patients with acute infarcts (Table 4) and likely resulted from a tendency to underestimate total LV mass (172±56 versus 185±75 g, P=0.17 by paired t test) by CE-MDCT versus CE-MR in these patients.

Interobserver and Intraobserver Agreement

Interobserver and intraobserver agreement for identification of early hypoenhanced areas on segmental basis were, respectively, 90% (κ=0.43) and 92% (κ=0.55) on early CE-MDCT images and 87% (κ=0.34) and 90% (κ=0.55) on early CE-MR images. Interobserver and intraobserver agreement for identification of late hypoenhanced areas on segmental basis were, respectively, 76% (κ=0.54) and 88% (κ=0.62) on late CE-MDCT images and 81% (κ=0.63) and 80% (κ=0.62, P<0.001) on late CE-MR images.

Interobserver and intraobserver agreement for quantitative measurements of size of early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively. Interobserver and intraobserver agreement for early hypoenhanced area were ICC=0.88 and ICC=0.81 for measurement by CE-MDCT and ICC=0.54 and ICC=0.77 for measurements by CE-MR, respectively.
agreement for measurement of late hyperenhanced areas were ICC=0.89 and ICC=0.77 for measurements by CE-MDCT and ICC=0.87 and ICC=0.90 for measurements by CE-MR, respectively.

**Intrasubject Reproducibility**

In the 7 patients who underwent a second CE-MDCT scan within 6 months, infarct size assessed by CE-MDCT did not significantly change between the baseline and follow-up study either in absolute (36±34 versus 35±34 g, \( P=0.92 \) by paired \( t \) test) or relative terms (21±19% versus 18±17% LV mass, \( P=0.21 \) by paired \( t \) test). Intrasubject reproducibility of absolute infarct size by CE-MDCT was ICC=0.93. Intrasubject reproducibility on a segmental basis was 87% (κ=0.70). The average difference in infarct size between the baseline and follow-up scan was −0.6±14 g or −3±5%. The coefficient of repeatability for infarct size by CE-MDCT was ±4.2%.

**Contrast Kinetics of Gadodiamide and Iomeprol in Isolated Perfused Rabbit Hearts**

Figure 7a shows an example of serial LV short-axis CE-MDCT images obtained in an isolated rabbit heart before, during, and after infusion of gadodiamide and iomeprol. SI over time in infarct core, periphery, and noninfarcted remote region during gadodiamide and iomeprol wash-in and washout are shown in Figures 7b and 7c. Normal noninfarcted regions had similarly fast wash-in (1.2±0.3 versus 0.8±0.4 minutes, respectively, \( P=0.36 \)) and washout rates (2.5±0.5 versus 2.3±0.9 minutes, respectively, \( P=0.99 \)) for gadodia-
mide and iomeprol. In the peripheral rim of the infarct, the wash-in rates of both gadodiamide (1.8±0.9 minutes, P=0.74 versus remote) and iomeprol (1.2±0.2 minutes, P=0.64 versus remote) were similarly rapid as in noninfarcted regions, yet washout rates were significantly slower for both tracers (12±4 minutes for gadodiamide and 10±4 minutes for iomeprol, both P<0.001 versus remote) than in noninfarcted myocardium. The infarct core had significantly lower wash-in (8.7±6.7 and 6.9±3.5 minutes, respectively, both P<0.001 versus remote) and washout (20±12 and 15±15 minutes, respectively, both P<0.001 versus remote) rates for both gadodiamide and iomeprol than noninfarcted myocardium. There were no statistical differences in wash-in or washout rates of either tracer in either the rim or the core of the infarct (P=0.45, P=0.89, P=0.75, and P=0.71, respectively, by repeated-measures ANOVA and Tukey-Kramer post hoc test). Distribution volume measured 30 minutes after contrast injection was not significantly increased by either gadodiamide or iomeprol in the core (63±12% and 75±8%, respectively; P=0.97 and P=0.99 versus remote) or the rim of the infarct (74±13% and 80±7%, respectively; P=0.20 and P=0.27 versus remote by repeated-measures ANOVA) compared with remote region (67±12% and 73±11%, respectively). Size of bright area by iomeprol measured 5 minutes after outflow correlated well (r=0.95, P=0.001) with infarct size by TTC. There were no statistical differences in bright area by MDCT and TTC infarct size (13±12% versus 12±7% LV mass, P=0.72 by paired t test).

### TABLE 4. Size of Hypoenhanced Area on Early CE-MDCT and CE-MR Images and of Hyperenhanced Area on Late CE-MDCT and CE-MR Images

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<thead>
<tr>
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<th>Acute Infarcts (n=16)</th>
<th>Chronic Infarcts (n=21)</th>
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<td>CE-MDCT</td>
<td>CE-MR</td>
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<td>Size of hypoenhanced area on early images</td>
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<tr>
<td>In grams</td>
<td>10±23</td>
<td>12±23</td>
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<td>In % LV mass</td>
<td>5±10</td>
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<td>Size of hyperenhanced area on late images</td>
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<td>In grams</td>
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<td>45±53</td>
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<tr>
<td>In % LV mass</td>
<td>26±15</td>
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Statistical comparisons were performed with paired t test.

**Discussion**

**Infarct Characterization by CE-MDCT**

Few studies have reported on the use of CE-MDCT for infarct characterization. Most of these previous studies solely described hypoenhancement areas on early images in acutely infarcted myocardium.10–17 By contrast, presence of delayed hyperenhancement in infarcted myocardium by CE-MDCT has been described only inconsistently by some experimental studies,16,18–22 and only recently has been shown to be present in humans.23 The present study confirmed that CE-MDCT can provide infarct characterization in vivo both in pigs with experimental infarcts and in humans. We confirmed that, similar to CE-MR,1–4 CE-MDCT can identify 2 distinct contrast-enhancement patterns in MI, ie, early hypoenhancement, observed on images of tissue perfusion obtained shortly after contrast injection, and delayed hyperenhancement, seen on images acquired 10 minutes after contrast injection. We found that the location and extent of these 2 contrast-enhancement patterns on CE-MDCT images are in good agreement with those seen on CE-MR images and that patterns have good interobserver, intraobserver, and intrasubject reproducibility.

**Underlying Mechanisms of Contrast-Enhancement Patterns by CE-MDCT**

The underlying mechanisms for contrast-enhancement patterns are well understood for gadolinium CE-MR. Indeed, hypoenhancement by CE-MR results from the reduced delivery of contrast in the subendocardium of acute MI with
microvascular obstruction, the so-called “no-reflow” phenomenon. Hyperenhancement occurs at later imaging times in both acute and chronic infarcts and results from both increased distribution volume and reduced inflow and outflow velocity to the extravascular contrast agent in infarcted myocardium. In the present study, we investigated the underlying mechanisms of contrast enhancement of iodated contrast agents by comparing their contrast kinetics and distribution volume to gadodiamide in isolated perfused infarcted rabbit hearts. Our study demonstrated that similar mechanisms underlie contrast enhancement of infarcts by iomeprol and gadodiamide. Indeed, similar to gadolinium-DTPA, the infarct core demonstrates reduced inflow rates to iomeprol, which results in early hypoenhancement during contrast inflow. Hyperenhancement of the infarct core and rim results from reduced outflow rates to both gadodiamide and iomeprol relative to normal myocardium. In fact, we observed that the inflow and outflow kinetics of iomeprol and gadodiamide in different regions of the heart were similar. This probably reflects the fact that despite different molecular structures, the molecular weight and extracellular volume of distribution of both contrast agents are almost identical. In agreement with a study assessing contrast kinetics in isolated rabbit hearts using CE-MR, but in contrast to in vivo CE-MR studies, we did not observe increased distribution volume of gadolinium or iomeprol in infarcted versus remote myocardium. A possible explanation might be development of edema in both infarcted and remote myocardium in these isolated perfused rabbit hearts, which occurs despite supplementation of perfusate with albumin to increase oncotic pressure.

**Clinical Implications**

The ability of CE-MDCT to characterize ischemic myocardium at the time of noninvasive coronary imaging has important clinical implications, both in terms of risk stratification and decision making. In patients with acute MI, both the extent of early hypoenhanced region, which reflects the extent of microvascular obstruction, and the extent of delayed hyperenhanced region, which reflects infarct size, have indeed been associated with an increased risk of complications during follow-up, including the development of adverse LV remodeling. When combined with the assessment of re-

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**Figure 7.** Example (a) and contrast kinetics of gadodiamide (b) and iomeprol (c) in isolated perfused rabbit hearts. *P*<0.05 vs remote region at the same time (repeated-measures ANOVA with Tukey-Kramer post hoc comparison). BL indicates baseline.
gional function, analysis of the early and late contrast-enhancement patterns also provides valuable information on tissue viability, and hence on the likelihood of functional recovery after revascularization.\textsuperscript{7,25}

The present study suggests that CE-MDCT has similar tissue characterization capabilities to CE-MR. Similar to CE-MR, CE-MDCT could thus also allow for risk stratification of acute MI and for the identification of viable myocardium in patients with coronary artery disease and reduced LV function; however, at present, the image quality of late CE-MDCT images is not quite as good as that of late CE-MR images. In addition, visually determined infarct size by CE-MDCT slightly overestimated infarct size by CE-MR, although this was only true in relative terms, likely due to overestimation of total LV mass. Further refinements in technique are expected to overcome this limitation and improve image quality in near future. Another limitation of CE-MDCT is exposure of patients to x-rays and to potentially toxic contrast agents. This limits the ability to serially repeat studies in the same patient. Because of these limitations, CE-MDCT will likely not become a first-line test to assess myocardial viability if CE-MR is available. Yet, the information on tissue characterization it provides can be obtained almost for free when CE-MDCT is performed for the purpose of noninvasive coronary imaging. Indeed, once coronary imaging has been performed, tissue characterization only requires a second, delayed acquisition to be performed, with no additional contrast injection and very little additional radiation exposure. If combined with the reconstruction of the systolic phases to measure LV volumes and ejection fraction, CE-MDCT might offer the opportunity to assess coronary anatomy, cardiac function, and tissue characterization in one single imaging session that lasts less than 15 minutes.

Study Limitations
A 16-segment model was used to compare perfusion patterns between CE-MR and CE-MDCT on a regional basis. A potential limitation of this approach is that segments within the same coronary distribution might not be truly independent. This might have increased the concordance between CE-MDCT and CE-MR on a segmental basis.

Conclusions
The present study demonstrates that CE-MDCT imaging of infarcted myocardium allows for the identification of the same contrast-enhancement patterns as CE-MR, i.e., an early hypoenhancement pattern, which probably reflects microvascular obstruction in acute infarcts, and a delayed hyperenhancement pattern, which reflects the infarct extension of both acute and chronic infarcts. This places CE-MDCT in a favorable position relative to other technologies for the assessment of myocardial viability in patients with coronary artery disease.

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Disclosures
None.

References
CLINICAL PERSPECTIVE

Multidetector gated computed tomography (MDCT) has recently emerged as a promising technique for noninvasive coronary imaging. In the present study, we demonstrated that contrast-enhanced MDCT can characterize acute and chronic infarcts with contrast patterns similar to contrast-enhanced cardiac magnetic resonance (CMR) imaging, based on the similar kinetics of iodinated contrast agents in infarcted and noninfarcted myocardium as gadolinium DTPA. We report that (1) hypoenhanced regions are present on early images of tissue perfusion obtained shortly after contrast injection, likely reflecting the presence of microvascular obstruction, the so-called “no-reflow phenomenon,” and (2) delayed hyperenhancement on images acquired 10 minutes later is seen, analogous to hyperenhancement CMR imaging, corresponding to the extent of myocardial necrosis. This ability of MDCT to characterize myocardial tissue at the time of noninvasive coronary imaging has important clinical implications. Indeed, it suggests that MDCT can, much like contrast-enhanced CMR, measure the extent of microvascular obstruction (the so-called “no-reflow phenomenon”) and estimate infarct size in patients after acute infarction. It might thus allow for risk stratification of such patients. It might also be useful for the identification of viable and nonviable myocardium in patients with chronic left ventricular dysfunction. Finally, it might help to distinguish whether heart failure is of ischemic or nonischemic origin. Because such tissue characterization by MDCT can be performed within 15 minutes in combination with assessment of coronary anatomy and cardiac function imaging, this places MDCT in a favorable position for the comprehensive assessment of patients with coronary artery disease.
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