

In Vivo Estimation of Myocardial Infarct Size and Left Ventricular Function by Prospectively Gated Computerized Transmission Tomography

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SUMMARY We evaluated 11 dogs using computerized transmission tomography (CTT); eight were studied after coronary occlusion and three served as sham controls. Ungated scans (1 cm deep) of the left ventricle (LV) were obtained from LV apex to base to determine infarct size (IS). At the middle LV level, prospectively gated scans were obtained to determine LV function. In all infarct dogs, contrast medium enhancement of the entire infarct or the periphery of the infarct occurred. Autopsy IS was compared with the IS by CTT using either the inner (IM) or outer margin (OM) of the contrast-enhanced periphery of the infarcts as the border of the infarct. IS by both CTT techniques correlated well with autopsy IS (r = 0.89 for IM; r = 0.93 for OM). The estimate using OM (26.5 ± 12 g) gave IS sizes similar to autopsy values (25.5 ± 11.7 g), but IS derived using IM (14.1 ± 8.0 g) underestimated autopsy values by approximately 45% (p < 0.01). From the prospectively gated CTT images, we calculated mid-LV end-diastolic (EDA) and end-systolic areas (ESA) as well as percent area change before and after coronary occlusion. EDA increased from 17.0 ± 5.3 cm² to 23.7 ± 7.6 cm² (p < 0.05). ESA increased from 12.1 ± 4.1 cm² to 18.6 ± 7.2 cm² (p < 0.05), and percent area change decreased from 29.3 ± 5.0% to 21.7 ± 9.9% (p < 0.05). We conclude that CTT imaging can reliably estimate IS, particularly when the area of rim enhancement of the infarct is included within the presumed infarct region. Estimates of chamber function can be made from gated CTT scans. Anterior myocardial infarctions produce left ventricular dilatation with reduced chamber function, which can be detected by gated CTT scans.

QUANTITATION of myocardial infarct size is important in assessing clinical prognosis after infarction and in evaluating the effects of interventions designed to reduce the myocardial damage during ischemia.1–5 Ex vivo studies have shown that computerized transmission tomography (CTT) can be used to accurately quantify irreversibly damaged myocardial tissue.6–9 Recent reports have also shown the ability of CTT to quantify infarct size in vivo, though the method varied in each study.10, 11 The present study was designed to define the accuracy of CTT scans for quantitating infarct volume and to compare two CTT methods of assessing myocardial infarct size with autopsy values; we also used CTT to characterize middle left ventricular (LV) chamber dynamics before and after coronary occlusion by prospective ECG gating and evaluated the variability in estimates of cardiac function by prospective ECG gating of CTT images obtained on two different days.

Methods

Experimental Model

Eleven conditioned mongrel dogs (mean weight 28 ± 4 kg) constituted the study population. Each dog was given subcutaneous morphine sulfate, 3 mg/kg, and then anesthetized with i.v. pentobarbital, 25 mg/kg. Through a left thoracotomy, a hydraulic coronary occluder was placed around the proximal left anterior descending artery, and in four dogs an injection catheter was placed into the left atrial appendage. The catheters were burrowed subcutaneously and externalized. The wound was closed aseptically and the dogs were allowed to recover. Control CTT scans were ob-
tained in 10 of the 11 dogs. (One infarct dog did not have a control CTT study.)

Two to 3 days later, eight dogs were pretreated with subcutaneous morphine sulfate and intramuscular procarbazine and the hydraulic occluder was inflated. The dogs were again allowed to recover, and rescanned 4–7 days after the occlusion. The three control dogs were rescanned 5–8 days after the initial scan.

Postmortem Examination

Two to 3 days after the final scans were obtained (approximately 7–10 days after occlusion), each dog was anesthetized and killed with i.v. KCl. In four infarct dogs, approximately 1 million \( ^{111} \text{In} \)-labeled (420–460 \( \mu \text{Ci} \)) albumin microspheres (3M Co.) were injected through the atrial catheter before sacrifice. The microspheres were administered within 1–2 hours of labeling, and had been agitated for 5 minutes before injection. The diameter of the microspheres was 10–35 \( \mu \) (mean 20 \( \mu \)).

Each heart was removed and sectioned at 1-cm intervals from apex to base along the major axis of the LV and incubated in nitroblue tetrazolium dye, as described previously.\(^{12, 13} \) The endocardial and epicardial borders of the LV wall were traced onto clear film overlays. In the septal area, the right ventricular side of the septum was substituted for epicardial border. The area of grossly visible myocardial infarction was also traced onto the same overlays.

Two myocardial slices were selected where the infarcted area was largest; five tissue samples were cut from each of the two transverse slices (10 samples per dog). These tissue samples included the subendocardium and extended through approximately half the thickness of the myocardial wall, and varied with the amount of the myocardium infarcted. Each sample from within the infarcted area was taken near the center of the grossly visible damaged tissue. Additional samples were obtained from the periphery of the infarct, just inside the visible margin between infarcted (unstained) and normal (stained) myocardium. Tissue samples were also obtained from grossly normal myocardium adjacent to the infarct and from normal myocardium on the ventricular wall opposite the infarct. The volume of tissue samples varied from 0.21–1.06 ml. Blood was withdrawn during the injection of microspheres to enable calculation of regional flow.\(^{14} \)

The amount of the LV mass involved by myocardial infarction was measured by planimetry of the infarcted area and the area of the LV wall previously traced on the overlays. This was accomplished with an ultrasonic digitizer interfaced to a Hewlett-Packard Model 9825T desktop microprocessor and printer-plotter. The ventricular slices were each assumed to be cylindrical. Identical assumptions were made for the CTT scans. The variability of this technique in our laboratory is \( \pm 3.5\% \) when the slices are retracted and redigitized.

Computerized Transmission Tomographic Analysis

Ungated Scans

All studies were performed on a Technicare 2020 whole body scanner with a scan time of 2 seconds. The scanner had 720 stationary detectors and a 512 \( \times \) 512 image matrix. Each scan was 1 cm thick and obtained at 120 kVp.

During the scanning procedure each dog was preanesthetized with 2–5 mg/kg of morphine sulfate and anesthetized with 25 mg/kg of i.v. pentobarbital. The dogs were mechanically ventilated and placed in the scanner gantry. Each dog was paralyzed with i.v. succinylcholine. The dog was then allowed to stabilize for 20–30 minutes before the administration of contrast material. Meglumine diatrizoate (Renografin-76) was administered at a rate of 6 ml/minute for 5 minutes and then at 3 ml/minute for 5 minutes with a Harvard infusion pump, after which the infusion was halted. Between 6 and 8 minutes after initiation of the infusion, ungated scans were obtained from the apex to the base of the heart, reconstructed and reviewed to determine the scan through the middle of the LV. Exactly 10 minutes after the contrast infusion was stopped, a second series of ungated, 1-cm-thick images was obtained from the apex to the base of the LV. These scans were used to calculate infarct size. The first ungated scans (during infusion) were used to determine where the gated scans were to be performed.

The images were printed on transparent film along with spatial calibration markers. For each dog, we planimetered either the region of lower attenuation demarcated by the inner margin (IM) or outer margin (OM) of the area of contrast enhancement at the periphery of the infarction. In one dog, there was contrast enhancement of the entire area later shown to be infarcted (fig. 1). The images were digitized and planimetered identically to the postmortem slices, and similar geometric assumptions (cylindrical) were made for each slice. The volume of the CTT-calculated infarct size (either IM or OM) was obtained by summing the volume (each slice was 1 cm) of each slice from the base to the apex of the LV. Muscle specific gravity was assumed to be 1.05 g/cm\(^3\).

Each series of CTT images was replanimetered by two observers on a second occasion and variability for the IM method was \(< 4.7\% \) (mean 3.1\%), and for the OM technique \(< 5.2\% \) (mean 3.4\%).

Gated Scans

The ECG gating system uses the ECG signal to reference the data acquired from each of a series of standard scans obtained at the same anatomic level and to reconstruct a new series of gated images depicting 10% intervals of the cardiac cycle from one end-diastole to the next end-diastole.

To obtain a reconstructed image by standard CTT, a full complement of angular x-ray data is obtained over the scanning circle from 0 to 360\(^\circ\). Motion of the area of interest during the scanning period is the limiting factor in CTT imaging of the heart. Motion is minimized by the use of a paralytic agent and by holding respiration (at full inspiration) during the scanning period of 30–45 seconds.

Prospective gating assures the even distribution of the gating or biological window throughout the 360\(^\circ\).
scanning circle in the minimum number of scans and allows preselection of a fraction of the electrocardiographic RR interval width (gating or biologic window) to be monitored (fig. 2). We used a window encompassing 10% of the RR interval. Heart rates in the dogs in this study were 110–130 beats/min. Thus, the frame durations of the prospective ECG-gated images were 0.045–0.055 second. The prospective gating program builds in memory one angular data set for one of the biologic windows and updates this data set by adding the width and the angular position of each subsequent scan. In figure 2, if the system is monitoring portion 1 of the RR interval, only four angular segments will be obtained within the biological window during the current rotation of the x-ray tube. The remainder of the angular data acquired by the standard scan is not discarded, but contributes to the angular data sets of the nine other 10% portions of the RR interval (i.e., portions 2, 3, 4, etc.). To assure the even distribution of the R wave over the entire scanning circle, the prospective gating system examines the angular data sets obtained on prior scans for gaps in angular data and launches the x-ray tube at the appropriate time in relation to the ECG signal such that the windows will fall at the angular position where the largest gap exists (fig. 2). Six to eight scans were necessary to provide the images depicting the cardiac cycle from end-diastole to end-diastole (fig. 3).

An ungated series of scans was obtained from apex to base of the heart during the infusion of contrast media. A midventricular area was selected for acquisition of the gated series. The skin of each dog was marked to ensure reproducible positioning for gated scans on subsequent studies. Gated images were then obtained for analysis of cardiac function immediately upon termination of contrast infusion.

All 10 frames were displayed (along with reference distance markers) and end-diastole (maximal chamber area) and end-systole (minimal chamber area) selected by visual inspection. End-diastolic (EDA) and end-systolic areas (ESA) were planimetered (fig. 4) and the percent changes in area determined ([EDA - ESA]/EDA) before and after coronary occlusion in seven dogs, and on two different occasions in the control dogs.

Statistics

All data are given as mean ± sd. Comparisons were made with a simple analysis of variance, and p values ≤ 0.05 were considered significant. Linear regression equations and correlations were performed with a least-squares fit.

Results

Analysis of Infarct Size

None of the three dogs who underwent operation but not occlusion had evidence by CTT scans or postmortem examination (gross inspection, myocardial staining or microscopic examination) of a myocardial infarction. In the four dogs studied with indium microspheres, residual blood flow was 0.3 ± 0.4% of normal blood flow in the center of the infarct, 5.2 ± 4.2% at the periphery of the infarct and 49.4 ± 21.2% at the margin of the infarct.

The individual values for morphometric, OM CTT and IM CTT infarct size estimates are given in table 1. The IM method significantly underestimated infarct size (14.1 ± 8.0 g) compared with the OM CTT method (26.5 ± 12.0 g, p < 0.01) and morphometric (25.5 ± 11.7 g, p < 0.01 values. The CTT estimate using the OM method was not significantly different from the morphometric value. Figures 5 and 6 show the relationship between morphometric infarct size and
the OM and IM CTT methods, respectively. The correlation coefficient for the linear relationship between the IM method and the morphometric was 0.89 ($y = 0.61x - 1.5 \, g; p < 0.01$, $\text{SEE} = 2.75 \, g$) and for the OM method was 0.93 ($y = 0.95x + 2.2 \, g; p < 0.001$, $\text{SEE} = 3.00 \, g$).

Variability of the LV Dimension and Function

The data for the control dogs are shown in table 2. The mean end-diastolic areas varied by an average of 6% (range 3–10%) and the mean end-systolic areas by an average of 6% (range 2–12%) between the two separate studies performed in these dogs. Although the mean percent area change did not differ between the two studies, the data from individual dogs varied by 3–10%.

Analysis of LV Dimensions in the Infarct Dogs

Individual data for EDA, ESA and percent area change are shown in table 3. One dog did not undergo gated CTT scanning before infarction. End-diastolic and end-systolic images for three of the dogs before and after coronary occlusion are displayed in figure 7. There was a consistent and significant increase in EDA and ESA and a reduction in percent area change. Heart rate did not differ between the two studies (122 ± 9 beats/min control vs 129 ± 12 beats/min after infarction).

Discussion

The present study demonstrates that in vivo quantitation of myocardial infarction size by CTT is feasible after contrast infusion. Including the contrast-enhanced region of the infarct, as well as the zone of reduced attenuation, provides infarct sizes that closely approximate the actual infarct volume.

Several previous studies have indicated that CTT scans of the heart demonstrate differential contrast enhancement of the periphery of the infarct.6, 11–13 This enhancement has been seen as early as 8 hours after coronary ligation11 and as late as 2 months after coronary occlusion.17 In our experience, the greatest differ-
ence (relative enhancement) between normal and infarcted myocardium occurs 10 minutes after i.v. administration of contrast medium, when the absolute x-ray attenuation is maximal.\(^6\)

In the present study, including the contrast-enhanced infarct zone did not significantly improve the correlation with the postmortem infarct size values in comparison with using CTT data excluding the enhanced zone (\(r = 0.93\) vs \(r = 0.89\)); however, the absolute infarct size was grossly underestimated when the enhanced segment was excluded. This finding is consistent with previous studies that show that the distributions of technetium-99m pyrophosphate and contrast medium are similar within the infarct, indicating that the contrast-enhanced zone occurs within the actual necrotic myocardium.\(^6\) Higgins and co-workers\(^6\) demonstrated that the distribution of iodinated contrast material in infarcted myocardium was similar to that of the infarct-avid scintigraphic agent technetium-99m pyrophosphate.\(^6\) The enhancement of the edge of the

![Figure 5. The correlation between computerized transmission tomography (CTT) infarct-size (inner margin technique) and the postmortem values.](image)

**Table 1.** Comparison of Infarct Size

<table>
<thead>
<tr>
<th>Dog</th>
<th>Morphometric size (g)</th>
<th>Outer margin size (g)</th>
<th>Inner margin size (g)</th>
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<td>10.7</td>
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<tr>
<td>7</td>
<td>24.6</td>
<td>23.1</td>
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</tr>
<tr>
<td>8</td>
<td>14.3</td>
<td>15.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Mean</td>
<td>25.5 ± 11.7</td>
<td>26.5 ± 12.0</td>
<td>14.1 ± 8.0</td>
</tr>
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</table>

\(^*p < 0.01\) vs morphometric and outer margin results.

![Figure 6. The correlation between the computerized transmission tomography (CTT) infarct size (outer margin technique) and the morphometric infarct estimates.](image)

Table 2. Mid-Ventricular Function Analysis Control Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>EDAA (cm(^2))</th>
<th>ESA (cm(^2))</th>
<th>(%) AA</th>
<th>EDAA (cm(^2))</th>
<th>ESA (cm(^2))</th>
<th>(%) AA</th>
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<td>0.34</td>
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<tr>
<td>Mean</td>
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<td>0.27</td>
<td>14.3</td>
<td>10.5</td>
<td>0.27</td>
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<tr>
<td>±SD</td>
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<td>±1.4</td>
<td>±0.07</td>
<td>±1.2</td>
<td>±1.7</td>
<td>±0.06</td>
</tr>
</tbody>
</table>

Abbreviations: EDAA = end-diastolic area; ESA = end-systolic area; \(\%\) AA = percent area change.

Table 3. Mid-Ventricular Function Analysis

<table>
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<th>Dog</th>
<th>Preocclusion</th>
<th>Postocclusion</th>
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<tbody>
<tr>
<td></td>
<td>EDAA (cm(^2))</td>
<td>ESA (cm(^2))</td>
</tr>
<tr>
<td>1</td>
<td>8.4</td>
<td>5.9</td>
</tr>
<tr>
<td>2</td>
<td>18.8</td>
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<td>7</td>
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<td>12.0</td>
</tr>
<tr>
<td>Mean</td>
<td>17.0</td>
<td>12.0</td>
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<tr>
<td>±SD</td>
<td>±5.2</td>
<td>±4.1</td>
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</table>
thallium-201 and technetium-99m pyrophosphate concentrations were all low. Additionally, Abraham et al. demonstrated substantial iodine concentrations in myocardial cells within the infarct zone, but no iodine in normal myocardium. They postulated that intracellular iodine accumulation was a marker of the loss of cellular membrane integrity and presumptive evidence of irreversible cellular damage. Newell and co-workers studied dogs and 2-day-old and 30-day-old myocardial infarctions to evaluate the uptake of iodinated contrast material with the presence and severity of ischemically damaged myocardial cells. They found that contrast entered the ischemically damaged cell (or attached itself to the membrane of the damaged cell), and was excluded from the normal myocardial cell. Cellular uptake of iodine was observed in both the acute and more mature myocardial infarctions. Consequently, they felt that iodine accumulation might not necessarily indicate the presence of a fresh myocardial infarct, but was compatible with recent or acute damage. The accumulation of iodine in chronic infarctions has not yet been tested.

During acute ischemia, LV function deteriorates in conjunction with LV dilatation. After myocardial infarctions, we found a reduction in LV global function (percent area change) and an increase in end-diastolic and end-systolic dimensions. The limitation of using a single cross-sectional slice, similar to using a single two-dimensional echocardiographic cross section, is that regions of the ventricle may be noncontractile or hypercontractile and not be well visualized. Accordingly, additional views of the LV could be obtained if desired and this limitation minimized. An additional limitation of the present study was the restriction of the infarct to the distribution of the left anterior descending artery. The anatomy of the human coronary system and the myocardium jeopardized by certain lesions may differ significantly from those in our limited experiment in dogs. Thus, the value of this technique in man needs to be clarified.

Others have proposed the use of retrospective ECG gating of computerized transmission tomograms of the heart. Gated reconstructions using this technique are obtained at appropriate portions of the cardiac cycle from a series of scans. Unlike prospective gating where the x-ray tube is launched at the appropriate time by the ECG gate, this approach retrospectively selects data from simultaneously acquired ECG and radiographic data. Thus, retrospective gating is limited by variable window gating, missing blocks of angular data and longer acquisition times. Full cardiac cycles are more difficult to evaluate, and sections of the cardiac cycle may not be available for analysis.

We conclude that myocardial infarct size and chamber function can be obtained from CTT scans in dogs. This technique may be useful for assessing infarcts in humans and, in particular, interventions intended to modify infarct size.

References
6. Higgins C, Hagen P, Newell J, Schmidt W, Haigler F: Contrast enhancement of myocardial infarction: dependence on necrosis and
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