Computed Tomography for Localization and Sizing of Experimental Acute Myocardial Infarcts

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SUMMARY Computed tomography (CT) has been used to quantitate acute myocardial infarct size in isolated, arrested canine hearts. Acute myocardial infarcts were produced in 20 hearts by either left anterior descending (13 dogs) or circumflex coronary artery ligation (seven dogs). Each animal was given iodinated contrast media intravenously immediately before sacrifice 24-72 hours postinfarction. All infarcts greater than 1 g and one of three infarcts 0.5 g or less were detected by CT imaging. Infarct volume determined by CT correlated with gross infarct weight (r = 0.83). CT imaging, however, consistently underestimated infarct volume; underestimation was largest in a group of patchy, predominantly subendocardial infarcts. As adequate equipment and techniques for in vivo studies are developed, CT imaging of the heart may become important in clinical evaluation of myocardial infarction.

BODY COMPUTED TOMOGRAPHY (CT) has stimulated interest in the possible use of CT in cardiac diagnosis. Early studies by several groups demonstrated the ability of CT to detect experimental myocardial ischemia and infarction in vivo. The very sensitive capacity of CT to resolve small differences in x-ray attenuation enables identification of areas of ischemia and infarction. However, it has not been clear whether CT is capable of accurate sizing of acute myocardial infarcts. This in vitro study was performed to assess the potential of CT to identify, localize, and quantitate experimental acute myocardial infarcts in isolated canine hearts and thus to help further establish the potential for CT cardiac imaging in vivo.

Materials and Methods

Twenty adult mongrel dogs weighing 15-25 kg were evaluated in this study. These animals were anesthetized with intravenous pentobarbital, intubated and ventilated on a Harvard respirator. Their chests were opened through a left thoracotomy, and either the proximal left anterior descending coronary artery (13 dogs) or the circumflex coronary artery (seven dogs) was permanently ligated. Their chests were closed and the animals were returned to their...
cages. Twenty-four to 72 hours after coronary artery ligation each animal was injected intravenously with heparin (1000 units) and iodinated vascular contrast medium (methylglucamine iothalamate, 600 mg/kg) 5 minutes before sacrifice. The animals then were killed with an overdose of intravenous pentobarbital. The chest of each animal was again opened, the great vessels were ligated, and the heart was removed and secured in a saline-filled plastic container.

The hearts were scanned in the Artronix CT head scanner which utilizes a pixel size of $1 \times 1 \times 3$ mm. The radiographic density scale of the scanner ranges from $-1024$ to $+1024$ units of attenuation with 0 equal to the density of water. Contiguous scans 3 mm thick were made from base to apex. The optimum display factors for visualizing myocardial infarcts were determined and remained constant throughout the experiment. Scans for these experiments distributed the grey scale from 38–70 units. An enlargement from each scan transparency was made, and the infarct was outlined on each 3 mm slice based on visual identification of density differences between infarcted and non-infarcted myocardium. A 1 cm reference grid was superimposed on at least one section from each heart. The area of infarction was determined by sonic planimetry, and the infarct volumes of the slices were summed to give an estimate of total infarct volume.

For determination of gross infarct weight, the hearts were sectioned at 1 cm intervals. The heart slices were then incubated in a solution of triphenyl tetrazolium chloride. The tetrazolium histochemical technique delineates infarcted tissue by intensely staining normal myocardium. Following staining the slices were fixed in formalin. The gross identification, dissection and weighing of the infarcted tissue were performed by a cardiac pathologist. With established myocardial infarcts the tetrazolium method has shown good correlation with histological necrosis and tissue enzyme depletion.

The infarct volume determined by CT was compared to the gross infarct weight determined by the tetrazolium method and evaluated statistically utilizing a simple linear regression (Pearson's) correlation coefficient. Gross infarct weight (g) divided by infarct volume ($\text{cm}^3$) determined by CT was calculated to obtain estimated infarct density, an evaluation of the accuracy of the technique.

**Results**

When iodinated contrast is given intravenously just before CT imaging, a myocardial infarct is delineated as an area of decreased X-ray attenuation due to the lack of contrast medium in the infarct. The ventric-
Table 1. Myocardial Infarct Sizing by Computerized Tomography in 20 Dogs

<table>
<thead>
<tr>
<th>Dog</th>
<th>Hours post-infarct</th>
<th>Location</th>
<th>Involvement</th>
<th>Volume by CT (cm³)</th>
<th>Gross weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>48</td>
<td>Anterior</td>
<td>T</td>
<td>24.2</td>
<td>24.8</td>
</tr>
<tr>
<td>B</td>
<td>48</td>
<td>Anterior</td>
<td>SE</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>C</td>
<td>24</td>
<td>Anterior</td>
<td>SE</td>
<td>9.3</td>
<td>11.7</td>
</tr>
<tr>
<td>D</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>17.6</td>
<td>27.7</td>
</tr>
<tr>
<td>E</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>22.2</td>
<td>26.2</td>
</tr>
<tr>
<td>F</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>6.3</td>
<td>14.1</td>
</tr>
<tr>
<td>G</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>7.9</td>
<td>11</td>
</tr>
<tr>
<td>H</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>14.1</td>
<td>20.4</td>
</tr>
<tr>
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<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>8.6</td>
<td>18.8</td>
</tr>
<tr>
<td>J</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>7</td>
<td>9.8</td>
</tr>
<tr>
<td>K</td>
<td>24</td>
<td>Anterior</td>
<td>T</td>
<td>4.3</td>
<td>7.2</td>
</tr>
<tr>
<td>L</td>
<td>24</td>
<td>Anterior</td>
<td>SE</td>
<td>0</td>
<td>0.5</td>
</tr>
<tr>
<td>M</td>
<td>24</td>
<td>Anterior</td>
<td>SE</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>N*</td>
<td>72</td>
<td>Posterior</td>
<td>SE</td>
<td>1.1</td>
<td>28.7</td>
</tr>
<tr>
<td>O</td>
<td>24</td>
<td>Posterior</td>
<td>T</td>
<td>16.4</td>
<td>31.7</td>
</tr>
<tr>
<td>P</td>
<td>24</td>
<td>Posterior</td>
<td>SE</td>
<td>7.4</td>
<td>26.3</td>
</tr>
<tr>
<td>Q</td>
<td>24</td>
<td>Posterior</td>
<td>T</td>
<td>9.8</td>
<td>24</td>
</tr>
<tr>
<td>R</td>
<td>24</td>
<td>Posterior</td>
<td>SE</td>
<td>7</td>
<td>13.2</td>
</tr>
<tr>
<td>S</td>
<td>24</td>
<td>Posterior</td>
<td>SE</td>
<td>3.4</td>
<td>12.9</td>
</tr>
<tr>
<td>T</td>
<td>24</td>
<td>Posterior</td>
<td>SE</td>
<td>9.2</td>
<td>17.1</td>
</tr>
</tbody>
</table>

* N, the only 72-hour infarct, was excluded from the final sizing statistics; although it was quite large, the infarct was extremely patchy.

Abbreviations: CT = computed tomography; SE = patchy, predominantly subendocardial; T = homogeneous, transmural.

The combined sizing results in the anterior and posterior infarcts are presented in table 1 and illustrated in figure 4. Dog N was excluded from the sizing statistics since this dog had a large but predominantly patchy subendocardial infarct and since CT had misjudged infarct size in this heart by a margin considerably out of proportion to findings in the other hearts (table 1). Infarct weights ranged from 0.3–31.7 g. Experimental infarct volumes determined by CT ranged from 0.5–24.2 cm³. The density of normal myocardium is approximately 1.06 g/cm³. With the edema of acute infarction, density is expected to decrease slightly. The determined density (weight divided by volume determined by CT) of infarcted myocardium in this study was, however, 1.15 g/cm³, indicating that CT underestimated infarct volume (table 2). Infarct volume determined by CT did correlate, however, with actual infarct weight (r = 0.83, n = 19).

A more detailed evaluation of the correlations between CT and postmortem infarct size is shown in figures 5–8. There was an excellent correlation between CT and postmortem estimates of infarct size in the 13 anterior infarcts (fig. 5). The correlation between the two techniques for sizing the six posterior infarcts was not as close (fig. 6), with CT clearly underestimating actual infarct size. When transmural anterior and posterior infarcts were analyzed, the two techniques correlated moderately well (fig. 7). The correlation between CT imaging and postmortem estimates of infarct size in the eight canine hearts that had patchy, predominantly subendocardial infarcts was r = 0.81 (fig. 8).

Figure 2. This figure shows the smallest infarct detected (dog M). This homogeneous infarct is located in the anterior papillary muscle (white arrow). It was readily visualized on computed tomography scan (B, black arrow). Orientation of the slices accounts for the absence of right ventricle in the gross section.
Discussion

Interest in infarct sizing has increased as investigators have reported relationships between infarct size and complications such as refractory ventricular arrhythmias, refractory congestive heart failure and cardiogenic shock. Infarct sizing also is potentially useful in the evaluation of therapeutic interventions. For these reasons, myocardial infarct sizing has become an important thrust of myocardial evaluation techniques.

![Graph](https://example.com/graph.png)

**Figure 4.** This graph illustrates the combined results of 19 infarcts. Gross infarct weight in grams is plotted against infarct volume in cubic centimeters as determined by computed tomography. The dashed line represents the density of water which is approximately 1. The density of normal myocardium is 1.06. With the edema of acute infarction, density is expected to decrease slightly.
Several methods of infarct sizing have recently been developed, including precordial ST mapping and measurement of R wave loss, the measurement of serum creatine kinase levels, technetium-99m stannous pyrophosphate myocardial infarct scintigraphy, thallium-201 myocardial infarct scintigraphy, and ¹¹C-palmitate emission tomography. Each technique has limitations.

The sensitive capacity of CT to resolve small differences in x-ray attenuation makes CT imaging potentially an attractive means of imaging the heart. The primary barrier to successful in vivo imaging is that even the currently available relatively short scan time of 3 seconds per slice is too long to image the heart without marked degradation of the reconstructed image due to cardiac motion. To obtain high resolution reconstruction, each point in the matrix must remain in a fixed position during the rotation of the scanner. Without this fixed reference image, quality has been demonstrated to deteriorate significantly. To enable studies of the beating heart, three approaches have been suggested: 1) reducing the data collection time per slice to milliseconds; 2) synchronizing (gating) data collection to occur only during selected segments of the cardiac cycle; 3) synchronizing the data with the cardiac cycle following data acquisition. The last of these three methods has undergone the most recent development and holds the greatest promise for CT imaging of the heart. In vivo CT scanning of the heart will require some solution to the motion problem before scans with adequate resolution for the quantitation of infarcts can be obtained. In the present study, however, arrested hearts were used to provide the optimal situation for CT sizing of acute myocardial infarcts so that its advantages and disadvantages for this purpose could be readily evaluated.

The data obtained in this investigation demonstrate that CT imaging is potentially capable of identifying experimental myocardial infarcts of 1 g and larger. This imaging technique even correctly identified the presence of one of three infarcts less than 1 g in weight (0.5 g).

The small infarct which was visualized was homogeneous and sharply defined. The other two infarcts less than 1 gram in weight which were not visualized were less homogeneous. This suggests that this imaging technique has a high sensitivity for the detection of small subendocardial myocardial infarcts which may exceed the sensitivity of other current infarct imaging techniques. The sensitivity of the technique for infarct detection appears promising and certainly merits further evaluation.

A statistically significant correlation between in-

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**Table 2. Correlation of Infarct Volume Determined by CT with Gross Infarct Weight**

<table>
<thead>
<tr>
<th>Infarct Type</th>
<th>N</th>
<th>r</th>
<th>P</th>
<th>Density (g/cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All infarcts</td>
<td>19</td>
<td>0.83</td>
<td>&lt;0.001</td>
<td>1.15</td>
</tr>
<tr>
<td>Anterior infarcts</td>
<td>13</td>
<td>0.94</td>
<td>&lt;0.001</td>
<td>1.14</td>
</tr>
<tr>
<td>Posterior infarcts</td>
<td>6</td>
<td>0.81</td>
<td>&lt;0.05</td>
<td>1.42</td>
</tr>
<tr>
<td>Homogeneous transmural infarcts</td>
<td>11</td>
<td>0.80</td>
<td>&lt;0.01</td>
<td>0.96</td>
</tr>
<tr>
<td>Patchy predominantly subendocardial infarcts</td>
<td>8</td>
<td>0.81</td>
<td>&lt;0.02</td>
<td>1.86</td>
</tr>
</tbody>
</table>

N = number of hearts represented.

Density of normal myocardium is approximately 1.06. The density of infarcted myocardium would be expected to decrease due to edema formation. The calculated densities reflect the accuracy of correlation with infarct mass.

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**Figure 5.** This graph of 13 anterior infarcts includes both transmural and subendocardial infarcts.
The four experimental infarct groups analyzed (anterior, posterior, transmural, and predominantly subendocardial), the 13 anterior infarcts showed the best correlation of infarct volume determined by CT and gross infarct weight. Contributing at least in part to the relatively better correlation of anterior infarcts were the wide range of infarct sizes (0.3–27.7 g) and the larger number of infarcts included in this group. The poorer correlation found in experimental posterior infarcts ($r = 0.81$) is not fully understood, but deserves further study in a larger series. The second division of infarcts into homogeneous transmural

![Figure 6](image)

**Figure 6.** This graph separates the transmural posterior infarcts from the patchy, predominantly subendocardial posterior infarcts. In this group infarct size was greatly underestimated.

![Figure 7](image)

**Figure 7.** This graph includes the homogeneous, transmural infarcts, both anterior and posterior. This group provided the most accurate overall infarct density.
infarcts and patchy, predominantly subendocardial infarcts did not show improved correlation in either group \(r = 0.80\) and \(r = 0.81\), respectively. The grouping did, however, emphasize a marked difference in CT infarct density (transmural 0.96 g/cm\(^3\) and subendocardials 1.86 g/cm\(^3\)), indicating a marked underestimation of infarct size in patchy, predominantly subendocardial infarcts. Calculations of infarct density indicated that the transmural infarcts showed an anticipated decreased density (0.96 g/cm\(^3\)) associated with the edema accompanying acute infarcts compared to the density of normal myocardium (1.06 g/cm\(^3\))\(^8\) (table 2). The extreme case of underestimation occurred with dog N, which had a gross infarct weight of 28.7 g and a disproportionately small infarct volume determined by CT of 1.1 cm\(^3\) (table 1). This was the only infarct 72 hours old studied in the present series, and its inclusion in the sizing statistics would have decreased the overall correlation remarkably \(r = 0.69\). Although this posterior infarct was the second largest in this series, the infarct was extremely patchy and predominantly subendocardial. This sizing discrepancy between the CT estimate and infarct weight seems likely to be related to the presence of collateral reperfusion of the infarcted area, as well as the patchy character of the infarct.

The perfusion dependence of this CT imaging technique for quantitative sizing purposes is obvious. Infarcted nonperfused myocardium is easily differentiated on CT scans from the surrounding myocardium which is perfused with iodinated contrast medium. The underestimation of infarct volume in this study seems to be related to collateral flow of contrast into the infarcted tissue. Patchy infarcts also present some problem to the technique, since small foci of necrosis may be easily hidden by surrounding normally perfused myocardium. That this almost certainly occurred in the present study is suggested by the marked underestimation of infarct volume in the patchy, predominantly subendocardial infarcts.

Carlsson and coworkers\(^8\) have recently suggested that iodinated contrast media administered intravenously undergoes three phases of accumulation in regions of myocardial infarction: 1) in the first 5 minutes there is decreased contrast in the infarct relative to the normal myocardium; 2) in the second phase there is marked increased accumulation of contrast ("contrast entrapment") in the infarct relative to the surrounding normal myocardium; 3) within 45 minutes contrast medium in the infarct has washed out. It is possible that improved results could be obtained utilizing the second phase of contrast entrapment rather than the first phase of decreased contrast which was utilized in this study. The data of Carlsson, et al.,\(^8\) Powell and associates\(^8\) and Higgins, et al.,\(^8\) also suggest that infarcts may be visualized adequately without iodinated contrast due to the edema associated with acute infarction. Underestimation of infarct volume, however, may be an inherent problem in these approaches. Additional testing of these approaches will be necessary to allow determination as to whether contrast medium aids or hinders quantitation of infarct size using CT imaging.

In summary, our findings suggest that CT could represent an extremely sensitive technique for myocardial infarct detection. CT readily visualized all

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**Figure 8.** The graph illustrates the correlation of volume determined by computed tomography in the patchy, predominantly subendocardial infarcts.
infarcts greater than 0.5 g in size, and one of three infarcts weighing 0.5 g or less was accurately sized. CT tended to underestimate infarct volume, but statistically significant correlation of infarct volume determined by CT with actual infarct weight was found. It is likely that the underestimation of infarct volume is due at least partly to the perfusion dependence of this technique. CT cardiac imaging should allow accurate measurements of ventricular dimensions and be a noninvasive means to detect various regional myocardial abnormalities. The practical utilization of this technique now awaits the development of adequate gating methodology to reduce the detrimental effect of cardiac motion on CT reconstruction. The rapid development of CT imaging systems for cardiac work is anticipated and certainly will be the focus of much attention in the immediate future.

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References

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