Measurement of infarct size and percentage myocardium infarcted in a dog preparation with single photon–emission computed tomography, thallium-201, and indium 111–monoclonal antimonyosin Fab

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ABSTRACT Single photon–emission tomography (SPECT) and indium 111–labeled monoclonal antimonyosin Fab fragments were used to measure myocardial infarct size in 12 dogs, six subjected to balloon catheter–induced coronary artery occlusion for 6 hr (late reperfusion) and six subjected to occlusion with reperfusion at 2 hr (early reperfusion). Tomographic imaging was performed 24 hr after the intravenous injection of labeled Fab fragments with the use of a dual-head SPECT camera with medium-energy collimators. Immediately after the first tomographic scan, thallium-201 was injected into nine of 12 dogs and imaging was repeated. Estimated infarct size in grams was calculated from transaxially reconstructed, normalized, and background-corrected indium SPECT images with the use of a threshold technique for edge detection. Estimated noninfarcted myocardium in grams was calculated from obliquely reconstructed thallium SPECT images by a similar method. The animals were killed and infarct size in grams and true infarct size as a percentage of total left ventricular myocardial volume were measured by triphenyl tetrazolium chloride staining. Estimated infarct size from indium SPECT images showed an excellent correlation with true infarct size (r = .95, SEE = 4.1 g). Estimated percentage myocardium infarcted was calculated by dividing estimated infarct size from indium images by the sum of estimated infarct size plus estimated noninfarcted myocardium obtained from thallium images. Correlation between the estimated percentage of myocardium infarcted and true percentage of myocardium infarcted was excellent (r = .93, SEE = 4.4%). We conclude that dual-isotope SPECT with indium 111–monoclonal antimonyosin antibodies and thallium-201 can accurately estimate infarct size and percentage myocardium infarcted.


AN ACCURATE and noninvasive radionuclide imaging technique to localize and size acute myocardial infarctions could provide valuable diagnostic and prognostic information for the care of patients and also prove useful in clinical research. With the advent of thrombolytic therapies and percutaneous transluminal angioplasty for acute myocardial infarction, a means to size the amount of myocardium that is irreversibly damaged would be particularly useful. Serial creatine kinase (CK)–MB in plasma, electrocardiographic ST segment maps, and gated blood pool measurements of regional left ventricular function have been used in the past to estimate the size of acute myocardial infarction.1–3 However, each of these techniques has limitations that have precluded widespread clinical use for this purpose. Technetium-99m (99mTc) stannous pyrophosphate is an infarct-avid imaging agent that is used clinically to diagnose myocardial infarction but that has been shown to be poorly delivered into highly avascular tissue in the central portions of infarcts,4 a property that theoretically would prevent it from being an ideal agent for sizing infarcts.

Khaw, Haber, and their colleagues5–9 developed
antibodies specific for cardiac myosin. They showed that polyclonal antcardiac myosin antibodies, F(ab')2, or antimyosin Fab fragments labeled with radioidine localized in myocardial cells irreversibly damaged by an ischemic insult and could be used to scintigraphically detect and localize myocardial infarcts in animals. More recently, hybridoma technology was used to produce monoclonal antibodies to human cardiac myosin. Conjugation of Fab fragments of these monoclonal antibodies to the bifunctional chelating agent, diethylene triamine pentaacetic acid (DTPA), facilitated radiolabeling with indium-111 (111In), a radiochemical that has good imaging characteristics. Although there is a recent report correlating infarct size in man measured with SPECT and 99mTc-labeled antimyosin with akinetic segments on contrast ventriculograms, there is no report on the results of infarct sizing using SPECT and antimyosin labeled with 111In. The first purpose of the present study was therefore to test whether the sizes of experimentally induced acute myocardial infarctions in a canine preparation quantified in vivo with 111In-monoclonal antimyosin Fab and SPECT imaging correlate with pathologic infarct size.

To account for variations in left ventricular weight, infarct size may best be expressed as a percentage of total left ventricular myocardial mass. To estimate infarct size as a percentage of the total mass of the left ventricle, it is necessary to measure the mass of the noninfarcted myocardium with a marker of myocardial perfusion. Therefore, the second purpose of our study was to test whether the percent of left ventricle that is infarcted could be measured in a dog preparation with thallium-201 (201Tl) and 111In-antimyosin Fab and SPECT imaging.

Methods

Method of induction of infarction. Twenty-six male mongrel dogs weighing 35 to 65 pounds were anesthetized, intubated with cuffed endotracheal tubes, and ventilated with room air via a volume-cycled respirator. The left external jugular vein and carotid artery were isolated via a cutdown. Acute myocardial infarctions were created by a balloon catheter technique. A modified No. 8F right coronary Judkins angiographic catheter was inserted via the left carotid artery and positioned in the left coronary ostia. A No. 2F Fogarty embolectomy catheter was then passed through the Judkins catheter, and the balloon was inflated in the proximal left anterior descending coronary artery of 24 dogs and in the left circumflex of two dogs. Occlusion of the vessel was verified by angiography. The balloon was left inflated for either 2 hr (14 dogs, early reperfusion group) or 6 hr (12 dogs, late reperfusion group). Early and late occlusion times were selected to create infarct sizes varying as widely in magnitude as possible and to compare radiopharmaceutical delivery into larger vs smaller infarctions. One hour after deflation of the balloon and removal of the Fogarty catheter all of the animals were injected intravenously with 2 to 3 mCi of 111In-labeled murine antimyosin Fab monoclonal antibodies (Centocor, Malvern, PA). Paper chromatography, which was performed on all of the 111In-labeled antibodies before injection, showed greater than 95% binding of the isotope to the antibody. All catheters were removed, a central venous line was left in the left internal jugular vein, and the dogs were allowed to wake up, extubated, and transferred to metabolic cages.

Venous blood samples were taken every 12 hr for 48 hr from four dogs to determine serum clearance of 111In-labeled Fab. One ml of each venous blood sample was counted in a Picker Spectroscale R4W well counter for 1 min with a PHA window setting from 225 to 275 keV. Serum clearance curves showed that by 24 hr blood activity (cpm/g) had decreased to 15% of initial activity and fell further to 5% by 48 hr, similar to the results of Bell et al. Ten dogs died either during balloon inflation or within 48 hr after balloon deflation. Three dogs were found not to have infarctions and all three had negative scans. Of the remaining 13 dogs, one was never scanned for technical reasons, leaving 12 dogs that survived with infarctions and were scanned and killed. Of these 12 animals, six were reperfused at 2 hr and six at 6 hr. Twenty-four hours after balloon occlusion of a coronary artery, the animals were anesthetized with sodium pentobarbital (30 mg/kg iv), intubated to maintain an airway, and placed in the right lateral decubitus position on the pallet of the SPECT camera.

Imaging. Imaging was performed with a rotating dual-head digital gamma camera (Picker International, Northford, CT) equipped with medium-energy parallel-hole collimators. Spatial resolution (full width at half maximum) at 10 cm for 111In on this system is 2 cm. Two 15% windows were used centered over the 171 and 245 keV photopeaks characteristic of 111In. Data acquisition was not gated to the electrocardiogram. The dogs were allowed to breathe spontaneously during scanning. Data were acquired by each head from 30 equally spaced stops over a 180 degree circular arc, yielding a 360 degree acquisition with 60 total projection images. Each image was acquired over 1 min and yielded 12,000 to 20,000 counts/image. On average, 7% of these counts or 1658 counts per pixel were within the myocardial region with indium activity. Tomographic data were acquired in a 64 × 64 word matrix with a 1.33 × software zoom factor and commercial software (MIPS, Ann Arbor). Planar 111In images were next acquired for 5 min in the anterior and 90 degree left lateral views. Then, without moving the animals, a 2.0 mCi 201Tl dose was injected into nine of the dogs. After a 10 min equilibration time, 5 min anterior and left lateral acquisitions were obtained with the use of only the 70 keV photopeak of 201Tl. A repeat tomographic dual-head acquisition via this energy window was then performed. Approximately 9000 to 15,000 counts per image were obtained for each of the 60 201Tl images. In one animal, after completion of the indium tomographic scan and before injection of 201Tl, a series of five 5 min planar images was obtained every 30 degree between a right anterior oblique and left lateral projection with use of a 15% window centered on the 70 keV photopeak of 201Tl. The thallium dose was then injected and this imaging sequence was repeated. The average percentage of total counts over the left ventricular region of interest on the thallium scans that represent downsscatter from the indium activity into the thallium window equaled 12%.

Data analysis — indium. Projection images from the indium scans were reconstructed into 2 pixel thick (1 cm) transaxial slices by filtered backprojection with a 0.25 Butterworth filter (figure 1). All slices in which myocardium could be distinguished were selected for analysis. All slices were normalized to the myocardial pixel containing the greatest number of counts in the entire study. Background was defined as the average of all counts within the thorax and away from the infarct. This area was determined by use of an isocount contour including all

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pixels with less than 30% of the maximum counts. This background value was subtracted from all pixels and compared with the maximum myocardial count to obtain the target-to-background ratio. The edge of the infarct was defined by a threshold isocount contour representing 70% of the normalized background-subtracted counts in each slice. The total number of voxels in these contiguous slices was determined and multiplied by voxel volume to yield total infarct size in milliliters. Infarct volume was converted to size in grams by multiplying by the specific weight of myocardial tissue (1.05 g/ml).

The threshold value used for determining the infarct edge was derived from phantom experiments in which three spheres of varying sizes (12 to 60 ml) were filled with indium and suspended equidistant from the center of a 6.5 liter circular tub containing background indium activity; these spheres were imaged with dual-head SPECT acquisition. The justification for use of a single threshold value for both early and late reperfusion experiments was based on another phantom experiment. Three identical 30 ml cylinders were filled with differing concentrations of $^{111}$In to vary the target-to-background ratio from 2.85 to 12.24, and were then imaged with SPECT. Volumes were calculated from reconstructions that were normalized to the maximum pixel value, and then were recalculated from the same reconstruction after normalization and background subtraction. For target-to-background ratios above 5, volumes measured from the normalized studies accurately estimated the true volumes. The use of the same threshold for phantoms with target-to-background ratios below 5 overestimated the true volumes. Subtracting background counts did not change the accuracy of volume calculations for the high target-to-background phantom, but did improve the accuracy of volume calculations for phantoms with low target-to-background ratios.

Data analysis — thallium. Projection images from the thallium scans were reconstructed into 2 pixel thick oblique long- and short-axis slices by filtered backprojection with a 0.25 Butterworth filter. Efforts were made to exclude the liver from the reconstruction. All slices containing myocardial $^{201}$TI activity were normalized to the myocardial pixel containing the greatest number of counts, and background counts determined by an isocount method were subtracted from every pixel. The edges of noninfarcted myocardium were defined by a threshold isocount contour representing 65% of the normalized, background-subtracted counts in each slice. This threshold value was determined from the thallium scans of two animals that were found on pathologic examination to have no infarct. The total volume of myocardium containing $^{201}$TI activity was determined in contiguous slices, summed to yield total size of noninfarcted myocardium, and converted to grams by multiplying by the specific weight of myocardial tissue.

The percentage of the left ventricle infarcted for each animal was calculated as infarct size from the indium scan divided by the sum of infarct size (indium) plus noninfarcted myocardium (thallium) times 100.

Pathology. At 24 to 48 hr after imaging, the dogs were killed, hearts were excised, and the pathologic infarct size was determined. The left ventricle was sliced into 3 mm thick transverse sections and stained with triphenyl tetrazolium chloride (TTC). The border of each slice and the border of the infarcted zone of each slice then were traced on a sheet of transparent plastic. The cross-sectional area of infarct in each slice was measured with a computer-assisted planimeter, and infarct size was expressed as the sum of total infarct cross-sectional area over the sum of total left ventricular cross-sectional area (percentage of left ventricle). This value was converted to grams by multiplying the percent infarct by total left ventricular weight.

Statistical analysis. The relationship between measured in-
Infarct size determined with $^{111}$In and true infarct size as assessed ty TTC staining was analyzed by linear regression. Differences in the regression lines for infarcts reperfused early and those reperfused late was assessed by analysis of variance. A similar analysis was performed for the percent of left ventricle that was infarcted.

**Results**

**Infarct size by indium vs TTC staining.** Figure 2, *top*, shows planar images from a dog with an acute myocardial infarction produced by 2 hr of left anterior descending occlusion and reperfusion. Uptake of $^{111}$In in the region of the infarction and complimentary $^{203}$Tl uptake in noninfarcted myocardial tissue are seen. The target-to-background ratio for this infarct was 14.0. The infarct size by SPECT was 7 g and that by TTC staining was 11 g. Figure 2, *bottom*, shows the planar scintigraphic images of a dog with an acute myocardial infarction produced by 6 hr of left anterior descending.

**FIGURE 2.** *Top left,* The left lateral indium planar scans of dog 7 with an infarct from a 2 hr left anterior descending occlusion. There is intense indium uptake in the anteroapical region of the heart and uptake in the liver and the kidney. *Top right,* The complementary left lateral $^{203}$Tl scan, which shows an anteroapical defect corresponding to the region of the indium uptake. *Bottom left,* The left lateral planar scans of dog 6 with an infarct from a 6 hr left anterior descending occlusion. There is mildly intense indium uptake in the anteroapical region of the heart. The activity in the liver is greater than that in the infarct. *Bottom right,* The complementary left lateral $^{203}$Tl scan.
occlusion. In comparison with figure 2, *top*, there was only mildly intense $^{111}$In uptake in the anteroapical region of the heart and greater activity in the liver. The target-to-background ratio for this infarct was 4.4. The size of the acute myocardial infarction by SPECT $^{111}$In imaging was 31 g; the size obtained by TTC was 35 g.

Table 1 lists the individual values for the measurement of myocardial infarct size by SPECT $^{111}$In-antimyosin imaging and by TTC staining for all 12 dogs. Infarct weight by TTC ranged from 2 to 41 g. Five infarcts were below 11 g (dogs 1, 3, 7, 10, and 12). All five of these small infarcts were detected by the SPECT indium scan. The correlation between infarct size measured by $^{111}$In-antimyosin imaging and that measured by TTC staining was excellent ($r = .95$, $p < .01$; figure 3). The regression equation was: $I_S^{est} = 0.96 I_W^{true} - 0.07$, with a standard error of 4.1 g, where $I_S^{est}$ is estimated size of infarction and $I_W^{true}$ is true size of infarction. Along with the regression equation a 95% confidence interval was determined for individual values. All data from dogs undergoing early and late reperfusion fell within this limit. Table 1 also lists the $^{111}$In target-to-background ratios for all 12 dogs, which ranged from 4.4 to 16.0. The mean value in animals undergoing reperfusion at 2 hr (early) was $10.9 \pm 3.3$, and that for those reperfused at 6 hr (late) was $6.6 \pm 1.7$ ($p < .05$). The mean size of the infarcts of dogs in the late reperfusion group estimated from

![Graph showing regression for relationship between estimated infarct mass from the $^{111}$In reconstruction and true infarct weight by TTC staining. The 95% confidence limits are shown. IM = infarct mass; IW = infarct weight; solid circles = reperfused infarcts; open triangles = nonreperfused infarcts.]
the $^{111}$In scans was larger than that in the animals in the early reperfusion group (26.2 ± 14.2 vs 10.7 ± 4.6 g; $p < .05$). Separate regression equations relating infarct size determined by $^{111}$In imaging and TTC staining were fit to the data obtained after early and late reperfusion and no significant differences were detected by analysis of variance.

**Percentage of myocardium infarcted.** Figure 4 shows SPECT tomographic reconstructions from dog 11 with an acute myocardial infarction produced by a 2 hr occlusion of the left anterior descending artery. The top two images are reconstructions parallel to the long axis of the heart — $^{201}$TI on the left and $^{111}$In on the right. The bottom two images are reconstructions perpendicular to the long axis of the heart. The amount and location of uptake of indium-labeled antimyosin in the reconstructions correspond to the size and location of the defects seen on the thallium reconstructions.

Figure 5 shows similar reconstructions for an acute myocardial infarction produced by 6 hr of occlusion of the left circumflex artery (dog 9). In the long-axis reconstruction (top), the uptake of $^{111}$In in the infero-posterior myocardium corresponds to the same region of the heart in which $^{201}$TI uptake is absent. The same correspondence between $^{111}$In uptake and the $^{201}$TI defect is seen in the short-axis reconstructions shown at the bottom.

The regression for the relationship between mass of noninfarcted myocardium estimated from the $^{201}$TI reconstructions and the pathologic weight of noninfarcted myocardium calculated from the TTC-stained cardiac slices is shown in figure 6, top. The correlation coefficient for these data was .83. The regression equation was: $\text{NIM}_{\text{est}} = 0.85 \text{NIM}_{\text{true}} + 20.8$, with a standard error of 12.5 g, where $\text{NIM}_{\text{est}}$ and $\text{NIM}_{\text{true}}$ are estimated and true noninfarcted myocardium.

The relationship between the percent of the left ventricle infarcted estimated from the SPECT images of both $^{111}$In and $^{201}$TI and the TTC staining of pathologic sections was also highly significant, with an $r$ value of .93 (figure 6, bottom). The regression equation was: $\text{PMI}_{\text{est}} = 0.79 \text{PMI}_{\text{true}} + 1.9$, with a standard error of 4.4%, where $\text{PMI}_{\text{est}}$ and $\text{PMI}_{\text{true}}$ are estimated and true percent myocardium infarcted.

**Discussion**

The data from the present study show that acute myocardial infarcts can be sized accurately in dogs by use of $^{111}$In-labeled monoclonal antimyosin Fab and SPECT imaging. In addition, the data show that dual-isotope imaging with $^{111}$In and $^{201}$TI is feasible, yielding complementary images of the regions of infarcted and noninfarcted myocardium, respectively. The percentage of the left ventricle infarcted calculated from the dual-isotope SPECT reconstructions correlated closely
with percentage infarct measured pathologically from TTC staining. There were no significant differences in the estimates of sizes of infarctions in dogs in the early vs late reperfusion group relative to the true size determined by TTC staining.

**Previous techniques.** Clinically available methods to estimate infarct size in man have not proven completely accurate. Infarct size estimated from the area under the CK curve has been shown to correlate with infarct size by myocardial CK depletion in animals and changes in the curve have been shown to occur after interventions to alter infarct size in man. However, the accuracy of individual CK determinations is dependent on the assay technique used. In addition, variations in the washout rate of the enzyme from the infarcted area into the blood and the presence of right ventricular infarction can also affect the size and shape of the curve and the accuracy of estimates of infarct size by analysis of CK curves. Analysis of the 12-lead electrocardiogram to size myocardial infarctions from changes in R wave voltage have not been proven to be quantitative. Wall motion analysis from gated blood pool scintigraphy is widely performed. However, abnormal wall motion can be produced in noninfarcted myocardium by the effect of “tethering” on myocardium at the border between normal and dyskinetic regions and also by “stunning” of ischemic but not infarcted myocardial tissue. In addition, old infarcts cannot be distinguished from acute infarcts solely by analysis of normal wall motion.

Several radionuclide techniques have been used to estimate infarct size in animals and in man. $^{201}$TI and

**FIGURE 6.** Top, The regression between mass of noninfarcted myocardium estimated from the thallium reconstructions and the true noninfarct weight calculated from the TTC-stained cardiac slices. Solid circles = reperfused infarcts; open triangle = nonreperfused infarcts. Bottom, The regression for relationship between percent of the left ventricular myocardium infarcted (PMI) estimated from the SPECT images of $^{111}$In and $^{201}$TI and true PMI from TTC staining.
SPECT have been used to measure infarct size in dogs by the measurement of perfused myocardial mass. There are, however, several limitations to this technique. First, it is difficult to size a perfusion defect when the epicardial boundaries of the defect are unknown. Second, the $^{201}$TI technique cannot distinguish between infarction and ischemia and is not applicable in the clinical setting of prior transmural infarction.

Infarct size and location have also been estimated with the infarct-avid imaging agent $^{99m}$Tc stannous pyrophosphate. The uptake of this agent on a cellular level is related to high intracellular and intramitochondrial accumulation of calcium. There is conflicting evidence as to whether or not this agent also accumulates in ischemic but not irreversibly damaged myocardial cells. It has been shown in several animal studies that uptake of $^{99m}$Tc in infarcted tissue is not inversely related to regional blood flow measured by microspheres. Maximal uptake was observed at the periphery of the infarcted area where blood flow was only moderately reduced. Despite these potential limitations, it was recently reported that $^{99m}$Tc stannous pyrophosphate and SPECT estimated infarct size correlated well with pathologic infarct weight in dogs.

Evidence from several different kinds of studies supports the premise that uptake of antimyosin antibody is specific for cell death. Anticardiac antibody is taken up only by myocardial cells with altered membrane permeability. The uptake of antimyosin in infarcted tissue has been shown to be inversely related to regional myocardial blood flow, with the greatest uptake of antimyosin observed in the subendocardium of the center of the infarct. In addition, antimyosin localizes only in regions of myocytes identified as necrotic by hemotoxylin and eosin staining. Using cell-sorting techniques, Khaw et al. have shown that injured myocardial cells that take up radiolabeled antimyosin do not grow in tissue culture.

Percentage of left ventricle infarcted. To account for variations in left ventricular weight among patients, it is useful to express infarct size as a percent of total left ventricular myocardial mass. Recently Wolfe et al. demonstrated in dogs that the percent of the left ventricle infarcted, called the “infarction fraction,” could be estimated by combining SPECT imaging of $^{201}$TI and $^{99m}$Tc pyrophosphate. A dual-isotope study with these two agents is cumbersome, however, because scatter from the larger $^{99m}$Tc dose interferes with the $^{201}$TI image acquisition. Thallium must be given and imaged first. Several hours must then elapse before technetium pyrophosphate is given so that blood pool clearance of $^{201}$TI can occur before imaging is repeated. During this waiting period the subject cannot move, making the protocol potentially difficult to achieve in awake patients.

A dose of only 3 mCi of $^{111}$In was used in the present study. At this dose there is significantly less downscatter in the region of the heart from the $^{111}$In photopeaks into the 70 keV window set for $^{201}$TI (12%) than downscatter from the usual $^{99m}$Tc stannous pyrophosphate dose. These differences in dosages and physical properties allow thallium imaging to be performed after indium has been administered or simultaneous imaging of both isotopes. A single 30 min dual-isotope acquisition after administration of $^{201}$TI makes this technique feasible in patients with acute infarction.

Early vs late reperfusion. Since we did not study animals with permanent occlusions, we did not evaluate the delivery of radiopharmaceutical into areas of infarct supplied by permanently occluded arteries. It has been shown in dogs that infarcts produced by 6 hr of occlusion are very similar pathologically to infarcts due to permanent occlusions and that only about 16% of the total amount of myocardium at jeopardy can be salvaged by reperfusion after 6 hr. However, when reperfusion occurs after 6 hr of occlusion, reperfusion injury and hemorrhage occur within the injured areas, resulting in histopathologic changes different from those seen with permanent occlusion. Because reactive hyperemia may occur before no reflow and because the infarct reperfused after 6 hr is hemorrhagic, radiopharmaceutical delivery may be greater to this area than to an infarcted area supplied by a permanently occluded artery. In this study, based on target-to-background ratios, less $^{111}$In was taken up into the areas of infarction of dogs in the late than in the early reperfusion group. It would not be surprising therefore if infarcts from permanent occlusions have even lower target-to-background ratios than those reperfused after 6 hr, but this hypothesis at present is unproven.

Small vs large infarcts. There were five dogs with small (<11g) infarcts. The correlation coefficient calculated for these five data points was lower (.71) than for the remainder of measurements (.91). Errors from partial volume effect or respiratory and/or cardiac motion are magnified for smaller infarcts. In addition to partial volume, limits of resolution also affect measurement of small infarcts. If the 10 g infarct were spherical, the calculated diameter would be 3.3 cm, close to the intrinsic resolution of the camera at a typical imaging distance. Although these limitations exist, all infarcts were detected by the method.

Technical considerations. In the present study, the raw tomographic data were not corrected for scatter or at-
tenuation. Scatter represents a fairly uniform component of an image and background correction acts roughly as a first-order scatter correction. Methods for scatter correction are under active investigation at present. We chose not to perform attenuation correction because the methods commercially available, which assume uniform distribution of activity within a medium of uniform density, are inadequate for the thorax and the more complex iterative techniques are not presently available. In addition, Lewis et al. showed that for target-to-background ratios above 5 and with the use of a threshold technique, disregarding attenuation correction altogether gave better accuracy for sizing experimental infarcts labeled with \(^{99m}\)Tc stannous pyrophosphate than either first-order or iterative methods.

Threshold definitions are critical to the estimation of infarct size. From the work of Holman et al., in which perfused myocardial mass was quantitated from tomographic \(^{201}\)Tl reconstructions, increasing the threshold level by only 5% led to a 20% underestimation of infarct size. In addition, for any given threshold, the estimated size of an object with a low target-to-background ratio will be larger than the estimated size of the same object with a high target-to-background ratio. This latter factor is more critical for clinical application since background activity will vary among patients. We found from phantom studies that by subtracting background before applying a threshold, the effect of varying target-to-background ratio on estimated size was decreased significantly even for ratios below 5. Finally, as the data in this study showed, despite target-to-background ratios varying from 4.4 to 16.0, use of a single 70% threshold value yielded an excellent correlation to true infarct size.

Clinical application and potential limitations. The advantages of \(^{111}\)In-antimyosin for localizing and potentially sizing myocardial infarction in man include specificity for irreversibly damaged myocytes and doses and imaging properties that allow dual-isotope imaging with \(^{201}\)Tl. Limitations include the slow clearance of the antimyosin from the blood pool, which delays imaging 24 to 48 hr after injection, making this technique suboptimal for diagnosing or sizing infarcts within the first 24 hr, and introduces the potential error of misinterpreting blood pool activity if the scan is read too early. Another potential technical limitation of the technique is hepatic \(^{111}\)In-antimyosin uptake, which may be difficult to separate from cardiac activity in patients with inferior infarcts.

A recent clinical study in man using \(^{99m}\)Tc-labeled antimyosin Fab SPECT imaging, and a threshold technique for edge detection, reported a good correlation with percentage akinetic segment on the contrast ventriculogram and infarct size by \(^{99m}\)Tc stannous pyrophosphate, although infarct size by pyrophosphate SPECT was 1.7 times larger than that by antimyosin SPECT. A clinical trial evaluating the safety and usefulness of \(^{111}\)In-monoclonal antimyosin in patients with acute transmural myocardial infarctions is now underway. In a preliminary report on 51 patients, the location of antimyosin uptake agreed with the electrocardiographic infarct site in 47 of 51. The four patients with equivocal \(^{111}\)In-antimyosin scans had normal ejection fractions and therefore probably very small infarcts.

In summary, \(^{111}\)In-labeled monoclonal antimyosin antibodies specifically localized in infarcted myocardium in dogs and the infarcts were well visualized on SPECT images. Infarct size estimated from transaxial reconstructions with the use of a threshold method for edge detection correlated well with infarct size by TTC. In these 12 animals, there was no difference in the ability of the technique to size infarctions reperfused early and late when compared with size by TTC staining. The estimated percent of the left ventricle infarcted from \(^{201}\)Tl and \(^{111}\)In-antimyosin SPECT images correlated well with the percentage of the left ventricle infarcted.

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_Circulation_. 1987;76:181-190
doi: 10.1161/01.CIR.76.1.181

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/76/1/181