Effect of Coronary Occlusion and Myocardial Viability on Myocardial Activity of Technetium-99m-Sestamibi

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The timing effect of sestamibi administration with respect to the onset of myocardial ischemia and reperfusion was studied in swine. In different groups of animals sestamibi was administered prior to coronary artery occlusion, during occlusion, or ½ hour following reperfusion. Sestamibi administered prior to coronary occlusion resulted in an insignificant decrease in ^{99m}Tc activity in the ischemic zone. However, infarct zone activity was reduced to 62 ± 14% of the nonischemic zone. In contrast, administration during coronary occlusion resulted in similar significant reductions of both ischemic and infarct zone activity. Administration of sestamibi during reperfusion resulted in normal ischemic zone activity and markedly reduced activity in the infarct zone. Significantly reduced activity in the infarct zone was found to be independent of the timing of sestamibi administration with respect to the onset of myocardial ischemia and/or reperfusion. Thus, cell viability appears required for uptake and retention of isotope activity.

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Perfusion myocardial scintigraphy is increasingly employed as a noninvasive method for assessment of myocardial ischemia and infarction. Preliminary data suggest that technetium-99m-methoxyisobutyl isonitrile or sestamibi (^{99m}Tc-sestamibi), a new myocardial imaging agent, may be of value in detecting the extent of reperfusion and salvage following thrombolysis or mechanical recanalization for acute myocardial infarction (*1–3*). However, proper interpretation of myocardial perfusion scintiscans is dependent on an understanding of the relationship of uptake, tissue viability, and net clearance of the radiopharmaceutical.

The present study was undertaken to assess the significance of myocardial viability on the net accumulation of sestamibi and the resulting appearance of a static cardiac scan. To differentiate the role of blood flow (delivery) from tissue viability in the uptake of the radiopharmaceutical, the timing of administration of sestamibi was altered with respect to the onset of coronary hypoperfusion. A swine model of coronary occlusion and reperfusion was used to produce areas of transient myocardial ischemia and necrosis. Sestamibi was administered before, during, and after coronary occlusion in different groups of animals.

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MATERIALS AND METHODS

Animal Preparation

Twenty Hampshire pigs (weight 25–30 kg) were fasted for 12 hr prior to surgery. Anesthesia was induced with intramuscular ketamine 20 mg/kg, xylazine 2 mg/kg, atropine 1.0 mg, and maintained with morphine 2 mg/kg/hr. The swine were intubated and placed on a Harvard apparatus respirator set a rate of 16 respirations/minute and a tidal volume of 500 ml. Intravenous infusion with normal saline was established through a large ear vein. To ensure adequate skeletal muscle relaxation vecuronium bromide at 1 mg/kg/hr was infused continuously. A 7F multipurpose catheter (Cordis Corp.) was inserted in each femoral artery. One was advanced high in the descending thoracic aorta to monitor blood pressure and the other to the level of the diaphragm for simultaneous withdrawal of microsphere reference blood sampling.

Following median sternotomy, the heart was exposed and suspended in a pericardial cradle. A 0.5-cm segment of the left anterior descending artery (LAD) was dissected free of the myocardium immediately distal to the first diagonal branch. A small vascular clamp was employed to occlude the LAD artery at this point in order to produce ischemia in the myocardial zone subtended by this vessel.

An infant feeding tube was inserted into the left atrial appendage for injection of radiolabeled microspheres. Pressures were continuously recorded on an Electronics for Medicine recorder (Honeywell, Pleasantville, NY). Following completion of the surgery and instrumentation, the animals were anticoagulated with a bolus of heparin (5000 units). This was repeated each hour.

Experimental Protocol

The experimental protocol is summarized in Figure 1. Following instrumentation, baseline hemodynamic measure-

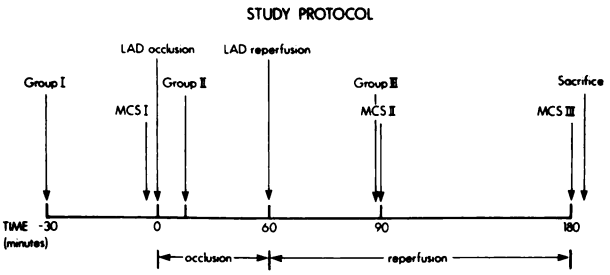

FIGURE 1
Study protocol (refer to text for details).

ments were recorded and the first set of microspheres was injected into the left atrium to ascertain control myocardial blood flow. A bolus of lidocaine 2 mg/kg was administered and supplementary doses were given throughout the experiment as needed. The LAD artery was occluded and ischemia was confirmed by the appearance of regional cyanosis, systolic bulging and accompanying ECG changes of ischemic injury. After 1 hr of coronary occlusion, the clamp was removed and reflow established. A second bolus of radiolabeled microspheres was injected 30 min after the initiation of reperfusion, and a third set 90 min later. Sestamibi (5 mCi) was injected intravenously 30 min prior to coronary occlusion in six swine (Group 1), 15 min after initiation of coronary occlusion in 6 swine (Group 2), and after 30 min of reperfusion in 8 swine (Group 3). Planar scintigrams in multiple views were performed during coronary occlusion and after 2 hr of reperfusion in 10 animals (4 in Group 1; 3 in Group 2; 3 in Group 3).

Following 2 hr of reperfusion, the vascular clamp was reapplied to the LAD artery and Evan's Blue, triphenyltetrazolium chloride (TTC) and euthanasia material were injected as described below. Myocardial samples from the unstained and TTC-stained zones within the region at risk as well as the Evan's Blue-stained samples from the nonischemic region were analyzed for blood flow, creatine kinase content, and ^{99m}Tc activity.

Measurement of Regional Myocardial Blood Flow

Serial measurements of regional myocardial blood flow were obtained by the radioactive microsphere technique as previously described (*4*) in two swine in Group 1, two in Group 2, and four in Group 3. Microspheres (10–12 microns) were labeled with scandium-46, rubidium-103, or tin-113 (New England Nuclear Corp., N. Billerica, MA), and each aliquot was calibrated to contain approximately 2 million microspheres. Each dose of microspheres was diluted to a volume of 5 ml with normal saline containing 0.01% polysorbate 80 (Tween 80) to prevent clumping. The bolus was agitated vigorously and infused into the left atrium over 10 sec followed by a flush of 10 ml saline. Dual-reference samples were withdrawn simultaneously from the thoracic and abdominal aorta at 4.2 ml/min over 2 min. Comparable counts in the arterial samples assured adequate dispersion of the microspheres.

Microspheres were injected at three times: prior to coronary occlusion, 30 min following initiation of reperfusion, and 90 min later. Following sacrifice and histochemical staining with Evan's Blue and TTC, the left ventricle and septum were dissected free of epicardial fat and vessels and divided into five or six (approximately 1 cm) slices from apex to base. Nine myocardial samples from each animal (0.25–0.40 g) were randomly taken from the middle of the pale, red, and blue zones in various slices of the trimmed left ventricle. Weighed tissue, duplicate blood reference samples, and pure isotope samples were analyzed for counts in a gamma well scintillation counter (Packer Autowell II). A multichannel analyzer was used with the following windows: scandium-46 = 740–1300 keV; rubidium-103 = 450–570 keV; tin-113 = 340–440 keV.

Myocardial blood flow was calculated by the equation:

$$Q_m = (C_m \cdot 100Q_r)C_r,$$

where Q_m is myocardial blood flow (ml/min), C_m is tissue radioactivity (counts/min), and C_r is the activity in the reference sample. Flow per gram of myocardium was calculated by dividing blood flow by the sample weight. Separation of isotopes and myocardial blood flow calculations were performed by the method of Heyman et al. (*4*). Myocardial blood flow ($ml \cdot min^{-1} \cdot g^{-1}$) was calculated for nonischemic, ischemic, and infarct zones prior to coronary occlusion, and at 30 and 120 min following initiation of reperfusion.

Assessment of In Vitro ^{99m}Tc-sestamibi Activity by Well Counting

The dose of sestamibi (5 mCi) administered to the swine was chosen to maximize image quality and counts seen on planar scintigraphy. All myocardial samples were counted 24–96 hr after sacrifice to minimize dead time of the gamma well counter. In each animal, sestamibi activity was determined in the nonischemic, ischemic, and infarct zones expressed as cts/g/min. Activity was not back-corrected to time zero. Averaged ^{99m}Tc counts in each animal from the ischemic and infarct zones were normalized to the nonischemic zone. Sestamibi activity in the region of risk (i.e., both the ischemic and infarct areas) in each animal was expressed as a percentage of that in the nonischemic region.

Evaluation of Region of Risk and Infarct Size by Histochemical Staining

Following the experimental protocol the area at risk was determined by reoccluding the LAD at the original site of occlusion and slowly infusing 50 ml of Evan's Blue solution into the left atrium. The area of the left ventricle that was not discolored blue was considered the area at risk. Simultaneous with the infusion of Evan's Blue, euthanasia material (15 ml) was administered. Following sacrifice, the heart was promptly excised and rinsed under cold tap water. Myocardial infarct size was determined by cannulating the LAD artery immediately distal to the site of occlusion and perfusing the vascular bed with 1.5% triphenyltetrazolium hydrochloride in 20 m*M* potassium phosphate buffer (pH 7.4; 37°C) (*5*). The stained heart was sliced transversely into five or six sections and the left ventricular walls were trimmed of the right ventricular free walls. The slices demonstrated three clearly defined zones. The nonischemic area stained blue. In contrast, myocardium within the area of risk either stained red (transiently ischemic) or appeared pale (infarct). Total left ventricular area at risk and infarct were separated by careful dissection and weighed. This gravimetric analysis of infarct size has been shown to correlate closely with planimetry (*6*).

Determination of Myocardial Tissue Creatine Kinase Activity

Myocardial samples weighing from 70 to 150 mg (blotted) were selected randomly from the middle of pale, red and blue zones in the various slices. On average, eight samples were obtained from each animal. The tissue was homogenized on ice in a 15-ml solution of tris 0.01 *M*, EDTA 0.001 *M*, and dithiothreitol 0.001 *M* at pH 8.0, and centrifuged for 30 min at 10,000 rpm at 4°C as described (*7*).

Supernatant samples were further diluted in a buffer containing 0.2% bovine serum albumin, and tris buffer 0.1 *M* at pH 7.4 (*8*). Total creatine kinase activity in the diluted supernatant was assayed at 37°C on a Technicon Ra-1000 instrument using the creatine kinase method of the German Society for clinical chemistry (*9*) with reagents prepared by Technicon (Tarrytown, NY). Results were calculated as IU/g myocardial tissue.

Planar Scintigraphy

Four animals injected with sestamibi before coronary occlusion (Group 1), three during occlusion (Group 2), and three after reperfusion (Group 3) underwent planar scintigraphy in multiple views using a portable, small field of view, single crystal camera with a dedicated minicomputer (Apex-215, Elscint). The camera was equipped with a low-energy, medium-resolution, parallel-hole collimator and the energy discriminator was set for the 140-keV photopeak of ^{99m}Tc with a 10% window. Image acquisition parameters were 128 × 128 matrix and 420 sec/image, which yielded at least 800,000 counts/frame. Images were obtained during occlusion in Groups 1 and 2, and following reperfusion in all three groups. Scintiscans were interpreted qualitatively independent of knowledge of the timing of sestamibi administration.

Data Analysis

All data were analyzed using analysis of variance. Values are given as mean ± s.d. A p value <0.05 was considered the lower level of significance.

RESULTS

Hemodynamics

Hemodynamic data including heart rate and mean arterial blood pressure throughout the experimental period are summarized in Table 1. There were no significant differences among the groups at baseline, during coronary occlusion, 30 or 120 min after reperfusion.

Transient Ischemic Area and Infarct Size Quantification by TTC

The weights of the left ventricles, the ischemic areas and infarct zones are listed in Table 2. Left ventricular weight was 67.0 ± 10.0 g in Group 1, 69 ± 4.1 g in Group 2, and 70.9 ± 6.8 g in Group 3 swine. The myocardial transiently ischemic regions were not significantly different between the three groups. Furthermore, the infarct zone weights as determined by unstained tissue in the regions infused with TTC were similar.

Myocardial Creatine Kinase Content

The creatine kinase content in myocardial samples in all three groups taken from nonischemic, ischemic, and infarct regions as defined by histochemical staining is seen in Table 3. Nonischemic zone CK content was similar in all three groups of swine as was the case with ischemic and infarct regions. However, the CK content in the ischemic zones was significantly reduced in all groups when compared to the nonischemic region. There was a further significant decrease in the infarct zone compared to the ischemic zone.

Regional Myocardial Blood Flow

The regional myocardial blood flow in the nonischemic, ischemic and infarct zones for the three groups prior to coronary occlusion, and 30 and 120 minutes after reperfusion is summarized in Table 4. All three groups demonstrate homogeneous regional blood flow during the experiment. In the three groups, blood flow values were not significantly different from baseline conditions throughout the entire experiment, confirming complete reperfusion.

Myocardial ^{99m}Tc Activity

The relative activity of sestamibi in nonischemic, ischemic, and infarct regions in all the groups of swine is noted in Table 5. When the radiopharmaceutical was administered prior to occlusion (Group 1 swine), the nonischemic zone exhibited the highest activity. An insignificant reduction to 92% ± 11% in the ischemic region was seen, while the activity in infarct zones was significantly reduced to 62% ± 14% ($p < 0.01$) of that determined in the nonischemic region.

Following administration of sestamibi during coronary occlusion (Group 2 swine), the relative activity in the ischemic and infarct zones was significantly reduced to 33% ± 2% and 37% ± 3% respectively of that in the nonischemic region ($p < 0.01$). There was no significant difference between the activity in the ischemic and infarct zones.

In Group 3 swine, where sestamibi was administered 30 min after initiation of reperfusion, the highest activity was seen in the ischemic zone. The relative activity in the infarct zone was 38% ± 10% of that seen in the nonischemic zone.

Planar Scintigraphy

Planar scintigrams were performed in four of six swine in Group 1. Scans were obtained at the end of the occlusion period and the end of the reperfusion period. All scintigrams demonstrated a homogeneous distribution of the radiopharmaceutical and no defects were noted in either the initial or late scintigrams (Fig. 2).

Planar scintigraphy was performed in three of eight swine in Group 2 during coronary occlusion as well as

TABLE 1
Hemodynamic Data

		Control	Occlusion	Reperfusion 30′	Reperfusion 120′
HR	Group 1 (before oc)	81.2 ± 7.2	81.2 ± 14	95.3 ± 18	89.6 ± 8.5
	Group 2 (during oc)	86.8 ± 12	90.2 ± 15	94.8 ± 18	92.7 ± 12
	Group 3 (in rep)	85.8 ± 11	93.1 ± 12	95.6 ± 14	91.0 ± 15
MAP	Group 1 (before oc)	88.8 ± 13	78.0 ± 10	74.4 ± 12	80.8 ± 12
	Group 2 (during oc)	96.3 ± 8.8	75.2 ± 13	75.8 ± 12	84.1 ± 8.2
	Group 3 (in rep)	86.4 ± 12	79.2 ± 14	74.1 ± 12	78.2 ± 8.0

Hemodynamic changes throughout the experimental period. No significant differences are present. HR = beats per minute; MAP = mean arterial pressure mmHg; oc = occlusion; and rep = reperfusion.

during reperfusion. All three animals exhibited a large defect during occlusion that persisted unchanged throughout the period of reperfusion (Fig. 3).

In Group 3 animals, which received sestamibi during the reperfusion period, scans were performed in three of six swine after two hours of reperfusion. Two swine demonstrated small defects at the apex and one had a normal scan. (Fig. 4,5)

DISCUSSION

The present study examined the myocardial distribution of sestamibi injected intravenously before, during coronary occlusion, or during reperfusion. As seen in Table 5, the myocardial activity depended significantly both on the timing of injection and myocardial integrity.

In vitro studies suggest that the initial uptake of the isonitriles and their cellular distribution depend on diffusion across the cell membrane. Using differential centrifugation, Mousa et al. (*10*) demonstrated that under normal conditions 70%–80% of sestamibi is in the cytosol and is bound with high affinity to a small molecular weight myocardial protein at the cystosolic site. The remainder of the sestamibi is bound mainly to the different cell membranes including the mitochondria. Mousa (*10*) using isolated heart strips and Maublant et al. (*11*) using cultured myocardial cells also showed that hypoxia reduced the uptake of sestamibi. In addition, hypoxia alters the subcellular distribution such that the cytosol content drops to about 42% while the membrane content increases to 53% from 13% under normal conditions (*10*).

Studies using other members of the isonitrile group have also suggested that nonspecific binding of the agent to the cell membrane or other components of the cell is a significant factor in the net myocardial accumulation of these radiopharmaceutical agents. Piwnica-Worms et al. studied Tc-CPI in cultured chick hearts using cell fractionation techniques and showed tight binding to the cell membranes (*12*). They attributed this phenomenon to the lipophilic properties of the isonitrile group. Similarly, Sands et al., using human erythrocytes and neonatal myocytes, demonstrated that a large portion of another isonitrile (TBI) is nonspecifically bound to the membrane and suggested a lipophilic mechanism (*13*).

These reports help explain our results and also indicate the expected findings in the clinical setting. In Group 1, sestamibi injected prior to coronary occlusion is distributed according to myocardial blood flow and is taken up by the cell by passive or facilitated diffusion. The technetium labeled compound is then bound in

TABLE 2
Comparison of Left Ventricular Area of Risk and Infarct Zone Weights in the Three Groups

	Left Ventricle (g)	Area of Risk (g)	Infarct (g)
Group 1 (before oc)	67.0 ± 10	12.9 ± 3.1	3.9 ± 1.1
Group 2 (during oc)	69.0 ± 4.1	15.2 ± 3.3	3.1 ± 1.4
Group 3 (in rep)	70.9 ± 6.8	15.3 ± 1.8	4.4 ± 2.3

Values are shown in grams and represent mean ± s.d. The three groups do not show any significant difference in the different zones. Rep = reperfusion and oc = occlusion.

TABLE 3
Myocardial Creatine Kinase Content (IU/g) Following 60-min LAD Occlusion and 120-min Reperfusion in the Three Groups

	Nonischemic	Ischemic	Infarct
Group 1 (before oc)	2276 ± 83.0	1713 ± 272*	975 ± 452*
Group 2 (during oc)	2373 ± 160	1614 ± 269*	611 ± 226*
Group 3 (in rep)	2290 ± 156	1832 ± 258*	736 ± 411*

Results are expressed as mean ± s.d.

* $p < 0.01$ represents a significant difference compared to left. The groups did not show significant differences for CK content within the same zone.

TABLE 4
Myocardial Blood Flow (cc/min/g)

		Control	Reperfusion 30′	Reperfusion 120′
Group 1 (n = 2)	Nonischemic	1.15 ± 0.34	1.31 ± 0.56	1.55 ± 0.54
	Ischemic	1.17 ± 0.20	1.37 ± 0.48	1.54 ± 0.39
	Infarct	1.09 ± 0.13	0.95 ± 0.46	1.07 ± 0.32
Group 2 (n = 2)	Nonischemic	1.27 ± 0.36	1.73 ± 0.71	1.41 ± 0.48
	Ischemic	1.54 ± 0.52	1.46 ± 0.47	1.33 ± 0.44
	Infarct	1.48 ± 0.62	1.60 ± 0.72	1.36 ± 0.74
Group 3 (n = 4)	Nonischemic	1.16 ± 0.28	1.40 ± 0.49	1.25 ± 0.20
	Ischemic	1.21 ± 0.23	1.50 ± 0.60	1.62 ± 0.40
	Infarct	1.12 ± 0.30	1.36 ± 0.26	1.40 ± 0.44

Myocardial blood flow did not change significantly between control and reperfusion for the different zones nor was there a significant difference in flow between the three groups throughout the experiment.

the cytosol or to the membrane. Thus, images obtained after injection show uniform uptake. After coronary occlusion and the resultant area of infarction, the damage to the membrane is sufficient to cause a loss of sestamibi from the irreversibly damaged tissue. This is seen as decreased activity of sestamibi in the infarct area with a slight but insignificant decrease in the transiently ischemic zone. In the absence of a major loss of myocardial cell integrity as confirmed by the relatively small loss of CK from the ischemic region, technetium-labeled sestamibi is held within the cell and myocardial activity remains high. Due to the relatively small infarct size, the scintigraphic images obtained after reperfusion fail to detect any defect.

In contrast, administration of sestamibi during occlusion results in very low net accumulation of the technetium labeled compound within the area at risk. This is consistent with the large area of hypoperfusion seen on the planar images. Even in a model of brief coronary occlusion, precluding irreversible myocardial damage, administration of sestamibi during the occlusion period is associated with decreased myocardial activity and a perfusion defect on imaging (*14*). In the absence of any active process promoting cellular uptake, any increase

TABLE 5
Technetium-99m Myocardial Activity

	Non-ischemic	Ischemic	Infarct
Group 1 (before oc)	1.00	0.92 ± 0.11	0.62 ± 0.14*
Group 2 (during oc)	1.00	0.33 ± 0.02*	0.37 ± 0.03†
Group 3 (in rep)	1.00	1.16 ± 0.14	0.38 ± 0.10*

Ischemic and infarct values are normalized to nonischemic zone.

* $p < 0.01$ compared to left.

† $p < 0.01$ compared to above.

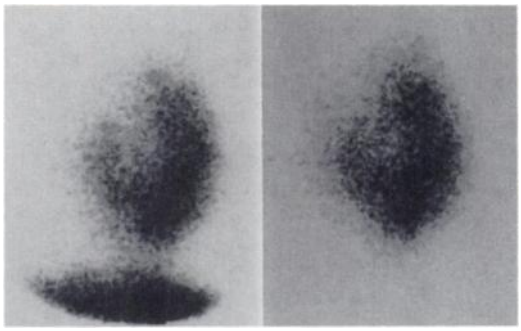

FIGURE 2
In this Group 1 animal, images were obtained in the 10° RAO projection during coronary occlusion (left) and during reperfusion prior to sacrifice (right). No area of hypoperfusion is seen.

in technetium activity in the reversibly injured zone would depend on additional delivery of sestamibi. The blood level of sestamibi falls rapidly following intravenous injection. Furthermore, as this radiopharmaceutical is bound within the cell and does not circulate, there is little available sestamibi to be taken up by reperfused viable tissue following transient coronary occlusion unless the blood level is increased by a second injection (*15*). Thus, in spite of reperfusion of ischemic and infarcted myocardium, the activity of the technetium-labeled agent remains low in both zones consistent with a recently reported study in man (*1*). The technetium activity in the region of risk was greater than 30% of that noted in the nonischemic zone. In a swine model as the coronary blood flow to the region subtended by an occluded artery approaches zero (*16*), this relatively high activity would appear to be an overestimation of perfusion. In a similar manner, two other groups of investigators (*17,18*) have recently demonstrated that at very low flow rates within the central ischemic zone, technetium activity is higher than expected. This over-

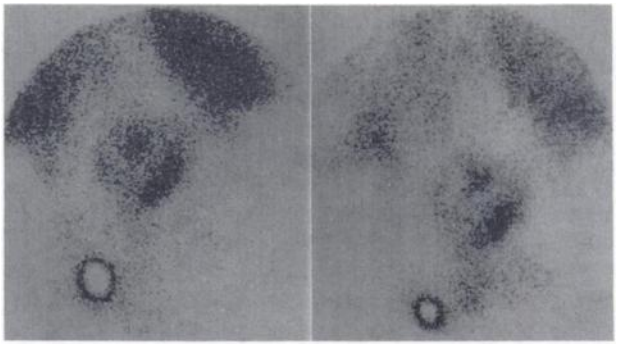

FIGURE 3
In this Group 2 animal, images were obtained in the 20° LAO projection prior to reperfusion and 2 hr after reperfusion prior to sacrifice. A large area of hypoperfusion is seen involving the anterior and apical segments in the initial images. No change is seen on the delayed images.

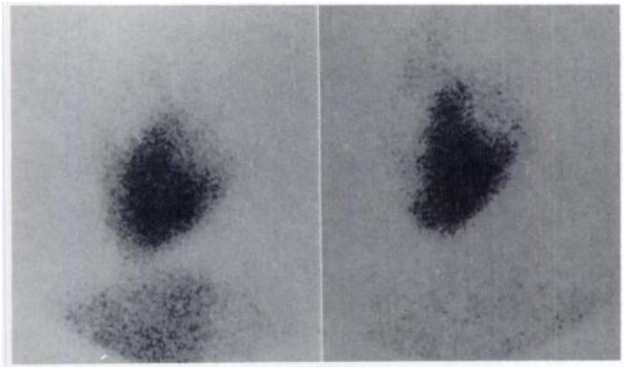

FIGURE 4
In this Group 3 animal, images were obtained in the 20° LAO projection early and late during reperfusion. No defect is seen.

estimation of hypoperfusion may be due to the fact that sestamibi is a diffusable tracer.

In Group 3, sestamibi was injected after re-establishing myocardial blood flow. As previously reported and confirmed in the present study, (Table 4) myocardial blood flow after 30 min of reperfusion is similar to baseline in a swine model after 60 min of coronary occlusion (*16*). Thus, delivery of the agent to both injured and noninjured cells is equal. Based on the results of TTC staining and measurement of CK content, the ischemic area is comprised primarily of viable myocardium with a significant but small number of cells demonstrating a loss of membrane integrity as measured by tissue CK depletion (Table 3).

This blend of viable and nonviable myocardium in the ischemic zone is consistent with the variable finding on imaging. Thus, small defects were seen in two of the studies. In contrast, the infarct zone, characterized by significant CK depletion and lack of colored precipitant formation following TTC infusion, exhibited markedly diminished sestamibi activity in spite of adequate delivery of the agent. Myocardial infarct zones in all three groups of swine demonstrated low levels of the technetium-labeled radiopharmaceutical. Thus, irrespective of the timing or adequacy of the delivery of this agent to the cellular milieu, there is relatively little net accumulation in nonviable tissue (Table 5). Indeed a recent study employing tomographic scintigraphic analysis of infarct size showed a close correlation with actual infarct volume (*19*).

The clinical implications of this experimental study are of particular interest in the patient who presents with a prolonged episode of chest pain and is suspected of being in the process of a first acute myocardial infarction. If sestamibi is administered and no defect is seen, then this strongly suggests that the vessel is patent. Moreover, any infarct would in fact be quite small and thus aggressive invasive procedures would not be warranted. In contrast, if a defect is seen, its size and extent can be used to reflect patency of the vessel. A small area not reflecting the expected size of the infarction based on the electrocardiogram would likely indicate reperfusion with a relatively small area of infarction. In contrast, a large defect seen on the sestamibi images in the acute setting would strongly suggest that the vessel is totally occluded and that additional aggressive measures may be warranted (*20*).

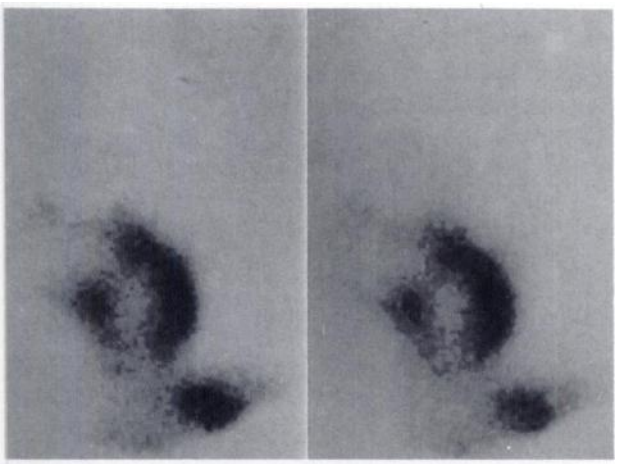

FIGURE 5
In this Group 3 animal, images were obtained in the 20° RAO projection early and late during reperfusion. A small area of hypoperfusion is seen in the apical area, which appears unchanged in the delayed images.

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EDITORIAL

Technetium-99m-Sestamibi: Another Window on Myocardial Viability?

The ability to assess myocardial viability following ischemic injury has been the central quest of many imaging modalities, including nuclear, ultrasound, magnetic resonance, and angiographic techniques. In this issue, Freeman et al. have offered further evidence to support the concept that the new myocardial perfusion tracer technetium-99m- (^{99m}Tc) sestamibi reflects not only blood flow but also cell viability is particularly welcome and exciting (*1*).

Of the currently available imaging modalities, the ultimate gold standard of the presence of viable but ischemic myocardium is the return of myocardial function following revascularization (*2*) or evidence of persistent glucose metabolism in an area of ischemia on positron emission tomography (PET) (*3*). Unfortunately, the former is only valid in retrospect, while the latter is not available in the usual clinical settings. The myocardial perfusion agents used for SPECT imaging are much less ideal for this purpose. It has been well known that the traditional stress and redistribution thallium scans may underestimate the extent of viable myocardium due to inadequate redistribution on the standard 4-hr delay studies (*4,5*). The ability to obtain a 24-hr delayed scan (*5*) or to reinject a second dose of thallium prior to the redistribution study can improve the detection significantly (*6*). The potential of imaging myocardial perfusion while obtaining information on myocardial viability using ^{99m}Tc-sestamibi opens an entirely new prospect in the study of myocardial viability.

In this study, Freeman et al. by using an occlusion/reperfusion swine model, administered ^{99m}Tc-sestamibi prior to or during coronary occlusion or at 30 min following reperfusion. The authors have found that if sestamibi was given during coronary occlusion, there was a significant reduction of myocardial sestamibi activity in both the ischemic and infarcted hypoperfused zones. On the other hand, if sestamibi was given during reperfusion, it demonstrated a relatively normal activity in the ischemic zone, while there was a marked reduction in activity in the infarct zone. This suggested that myocardial cell viability was indeed important for the uptake and retention of the isotope. Furthermore, if sestamibi was given prior to occlusion, there was also decreased sestamibi activity in the infarct zone subsequent to reperfusion. This can be interpreted as faster clearance of the

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