Effect of Coronary Blood Flow on Thallium-201 Uptake and Washout

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STEVEN J. LUKE, B.S., DEAN FRANKLIN, AND CRAIG C. WILLIAMS, R.P.H.

SUMMARY Myocardial uptake and washout of thallium-201 ($^{201}$TI) were studied in an experimental dog model in which regional blood flow to the posterior wall was varied by transient 2-minute occlusion of the circumflex coronary artery to produce transient ischemia and reactive hyperemia. Thallium-201 myocardial activity in a region of interest was determined continuously after i.v. administration by a gamma camera and computer program. Activity in the posterior wall was compared with that in the anterior wall in the same dog and the posterior wall of control dogs. Thallium-201 uptake was directly related to blood flow. With reactive hyperemia, there was a rapid and absolute increase in uptake followed by rapid washout; with ischemia, there was slow and decreased uptake followed by a slow washout. The calculated myocardial activity during washout in both ischemic and hyperemic areas approached values in control dogs long after blood flow had returned to baseline levels. Significant differences in washout slopes were found between the three groups of dogs ($-0.156\%/\text{min}$ in control dogs, $-0.244\%/\text{min}$ after reactive hyperemia, and $-0.076\%/\text{min}$ after transient ischemia, with half-washout times of 5.3 hours, 3.4 hours and 11.0 hours, respectively). These data suggest that both the initial decrease in activity in the ischemic area and the initial excess in the hyperemic area are corrected by different washout rates of ischemic and hyperemic cells during redistribution.

DESPITE extensive investigation of thallium-201 ($^{201}$TI) kinetics, the mechanisms responsible for a positive $^{201}$TI exercise test, i.e., an initial defect which disappears on delayed images, are not known. The test is useful in clinical assessment of coronary artery disease but, as with any test, an understanding of its limitations depends on knowledge of its basic mechanisms.

Differences in findings between experimental studies often result from differences in design. There is general agreement that myocardial uptake of $^{201}$TI is closely related to coronary flow at rest and exercise. Myocardial uptake is also increased by other interventions that increase coronary perfusion, including reactive hyperemia, adenosine or dipyridamole. The fraction of $^{201}$TI extracted by myocardial cells from blood is a potential variable, but apparently remains relatively constant under most conditions. One of the aims of this study was to investigate the time course of myocardial uptake after transient ischemia and reactive hyperemia.

Considerably less attention has been paid the role of myocardial washout of $^{201}$TI during the redistribution process which follows peak accumulation. The few studies of the myocardial washout phase have produced significant differences in results that could be explained by differences in experimental design. This study was designed to elucidate myocardial $^{201}$TI activity quantitatively and continuously during the uptake and washout phases in an experimental intact dog model in which regional coronary blood flow could be decreased during transient ischemia produced by 2-minute occlusion of the circumflex coronary artery and increased during reactive hyperemia.

Methods

Preparation

Five mongrel dogs that weighed 26–32 kg were anesthetized with sodium pentobarbital and respiration was controlled with a mechanical respirator. Through a left thoracotomy, a Konigsberg micro-manometer was inserted through the left ventricular apex to record pressure. To record dimensional changes, a pair of ultrasonic dimension crystals was implanted subendocardially, approximately 10 mm apart in the posterolateral wall (experimental area), and another pair was implanted in the anterior wall (control area). A Gould electromagnetic flow probe was placed around the circumflex coronary artery, immediately proximal to a hydraulic occluder. The ends of the occluder and wires were tunneled dorsally to the base of the neck. The dog was allowed to recover for 10 days. Use of ultrasonic dimension gauges to record shortening patterns of a myocardial segment has been reported. Three dogs without surgical intervention served as a control group. At the time of study, a catheter was placed in the superior vena cava for withdrawal of blood samples. Activity of $^{201}$TI was calibrated against a standardized Ge(Li) detector, and activities of 2–3 mCi were given intravenously in each study.

Data Collection

Each dog was anesthetized with 30 mg/kg of sodium pentobarbital and placed in the right decubitus position under an Ohio Nuclear (series 100) gamma camera with a parallel-hole, high-sensitivity collimator (to maximize count statistics), which was angled at a 45° left anterior oblique view to visualize the anteroseptal wall (control area: anterior wall) and the posterolateral wall (ischemic area: posterior wall).

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Measurements of left ventricular performance included left ventricular pressure, left ventricular dP/dt and segment length changes. These measurements were made to verify ischemia and return to control conditions. In addition, coronary blood flow, heart rate and lead 2 of the ECG were recorded. Arterial blood pH was maintained at 7.40 ± 0.05 and PCO2 at 30 ± 5 mm Hg throughout the experiment.

The left circumflex coronary artery was occluded for 2 minutes in the dogs with implanted occluders. For the ischemia study, 201TI was administered as an i.v. bolus at the onset of the occlusion. For the reactive hyperemia study, 201TI was administered 30 seconds after release of the occlusion at a time which coincided with peak coronary blood flow. Residual 201TI activity in the syringe was measured for later correction of the total activity given. Time 0 was designated as the time of 201TI administration in each study group. The dynamic 201TI activity from the entire field of view, including the left ventricle, were stored continuously in a 64 × 64 matrix and accumulated for each 30-second frame in the computer (Modemed System, MDS) during the initial 30 minutes and then for two successive 1-minute frames at 10-minute intervals thereafter. The studies in control dogs and in the ischemia group were terminated after 3 hours and after 4 hours in the reactive hyperemia group. Each dog served as its own control and was studied for both ischemia and reactive hyperemia at intervals of 1 week.

Blood samples were obtained through an indwelling catheter at 1, 3 and 5 minutes after 201TI administration and at 10–20-minute intervals. Activity in each sample was counted in a well scintillation counter, corrected for decay at the time each sample was withdrawn and expressed as activity per milliliter of whole blood. The blood volume was determined using 51Cr-labeled red blood cells and 185I-labeled human serum albumin after residual 201TI had decayed sufficiently.

Data Analysis

To determine the blood clearance of 201TI, expressed as percent activity remaining in the blood pool, a value for 100% 201TI activity per milliliter blood at a time 0 was calculated. The calculation assumed that an even distribution of 201TI within the blood pool had occurred and was based on the activity of administered 201TI and the blood volume. Each measured activity of a given blood sample was expressed as percent activity relative to the time 0 value and the mean value ± SD was calculated at each data point in three groups of dogs (table 1).

Upon completion of the myocardial imaging data collection, 7–10 mCi of technetium-99m pertechnetate was given as a bolus to define the region of the background, and regions of interest from the anterior and posterior walls were defined (fig. 1). Counts obtained over the anterior and posterior walls and the background area were normalized and the background counts were subtracted from the counts obtained over the anterior and posterior walls at each data point (net counts in anterior and posterior walls). Finally, the net counts derived from two adjacent 30-second frames were totaled for each plotted point during the initial 30 minutes; thereafter, two 1-minute frames were averaged to derive the counts per minute at each plotted data point.

The region of the left anterior descending coronary artery received no direct mechanical intervention; therefore, the anterior wall was considered to be a control region in each dog. The peak myocardial activity of 201TI in the anterior wall was designated as 100% activity and the rest of the activities in the anterior and posterior walls were expressed relative to this value. Then, the mean value ± SD was calculated at each data point in three groups of dogs to express percent changes of 201TI in the myocardium. Similarly, the background activity was expressed relative to the peak activity in the anterior wall. Therefore, the time-activity curves in the anterior and posterior walls and the background were directly comparable. Decay correction was not made for these calculations.

Results

Transient Ischemia

Figure 2 shows typical changes in one dog indicative of regional ischemia and return of these measures of left ventricular performance to control values after recovery. During the occlusion, heart rate increased about 40% (p = 0.05). The left ventricular

<table>
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<th>Reactive hyperemia (n = 5)</th>
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Values are mean ± SD.
systolic pressure tended to be slightly lower during the occlusion. The left ventricular end-diastolic pressure increased significantly ($p < 0.005$). Left ventricular dP/dt did not change significantly. A typical ECG change during the occlusion was an elevation of the ST segment, but depression was also observed in two of 10 experiments.

During ischemia, segment length shortening in the control region of the anterior wall remained within 10% of the baseline segment length. The ultrasonic crystals in the ischemic region of the posterior wall showed diminished systolic shortening or even passive elongation (fig. 2).27, 28 No abnormal changes in shortening pattern were seen in the anterior wall.

**Figure 1.** (upper) The blood pool image of the left ventricular cavity and the great vessels in the left anterior oblique view (LAO) after i.v. technetium-99m and (lower) upon completion of the data collection of thallium-201. This allowed definition of a region of background (Bkg) between the aorta and left atrium, and regions of interest in the anterior and posterior walls (ROI). At each data point after normalization, the background activity was subtracted from the region of interest to calculate the net counts from the myocardium.

**Figure 2.** Measurements of left ventricular performance before, during and after occlusion of the circumflex coronary artery. The ischemic changes (see text) have disappeared within a few minutes after release of the occlusion.
Immediately after release of the occlusion, an increase in segmental shortening was found in the ischemic area. These functional changes returned to near-baseline levels within a few minutes.

**Reactive Hyperemia**

Blood flow in the circumflex coronary artery reached its peak within 15 seconds after release of the occlusion, and peak flow was about three times greater than baseline flow in all dogs (fig. 3). The peak flow continued for more than 1 minute and returned to the approximate baseline level in 3–4 minutes.

**Time Activity Changes of $^{201}$TI**

The changing $^{201}$TI myocardial activity in the anterior and posterior walls in the control group is shown in figure 4. The peak $^{201}$TI activity from the anterior wall was seen 40 minutes after administration. Thallium-201 activity was consistently higher in the posterior wall than in the anterior wall ($p < 0.001$) (figs. 4 and 5), as more muscle tissue was included in the posterior wall because the right decubitus position was used.

The time-activity curves in the ischemia studies are shown in figure 6. The peak $^{201}$TI activity in the anterior wall occurred 50 minutes after administration, while activity in the posterior wall peaked at 80 minutes and, on the average, equaled that in the anterior wall at 120 minutes; the two time-activity curves tended to cross over with time. Because of a large variability of activities in the posterior walls of the small number of dogs studied, only a marginally significant statistical difference in uptake was found ($p \approx 0.05$). The left ventricular scintigrams in a given dog, however, clearly demonstrated decreased activity in the posterior wall relative to the anterior wall during the first hour after release of the occlusion (fig. 5).

Data from the reactive hyperemia studies are shown in figure 7. The peak $^{201}$TI uptake in the anterior wall occurred 50 minutes after time 0, whereas the peak uptake in the posterior wall was found in 10 minutes. The peak activity in the posterior wall was 1.8–3.0 times higher than the peak value in the anterior wall. When uptake values in the posterior and anterior walls were compared at 10 minutes the posterior wall showed 2.3–3.7-fold higher $^{201}$TI activity. That is, the increase in $^{201}$TI activity in the posterior wall was approximately proportional to the increase in circumflex coronary flow induced by reactive hyperemia, and significantly higher than that in the anterior wall, where coronary flow presumably was little changed ($p < 0.001$). However, the peak flow and the peak $^{201}$TI uptake did not coincide in time. Peak $^{201}$TI uptake followed peak flow by approximately 10 minutes in all dogs. These changes in myocardial $^{201}$TI activity were confirmed visually (fig. 5).

Thallium-201 washout was approximately linear after peak uptake (figs. 4, 6 and 7). Thus, washout data were fitted by least-squares analysis to a straight line, $y = a + bx$. A normalized rate of change, $b/a$, was calculated for each dog and this was designated as the washout slope, and expressed as a percent of loss of activity per minute ($%/\text{min}$). The washout slopes were expressed as the mean $\pm$ SD in the anterior wall of the control, ischemia, and reactive hyperemia groups, and were $-(0.105 \pm 0.040)$%/min, $-(0.122 \pm 0.032)$%/min, and $-(0.138 \pm 0.063)$%/min, respectively. Washout slope in the posterior wall in the control group was $-(0.156 \pm 0.030)$%/min, compared with $-(0.076 \pm 0.020)$%/min in the ischemia group and $-(0.244 \pm 0.034)$%/min in the reactive hyperemia group. The washout slopes of the anterior wall were significantly lower than in the posterior wall.
wall in the three groups and the posterior wall in the control group showed no significant difference when compared to each other. However, significantly different washout slopes were observed between anterior and posterior walls of both the ischemia group ($p < 0.05$) and the reactive hyperemia group ($p < 0.02$). Furthermore, comparison of the washout slope in the posterior wall (fig. 8) of any of the study groups with the posterior wall of either of the other two groups showed a significant difference in all comparisons (control vs ischemia, $p < 0.005$; control vs reactive hyperemia, $p < 0.02$; ischemia vs reactive hyperemia, $p < 0.001$). These findings indicate a significantly slower $^{201}$TI washout when it was preceded by a slow uptake in the case of ischemia and a significantly accelerated washout when it was preceded by rapid and increased $^{201}$TI uptake as a consequence of increased coronary blood flow in the case of reactive hyperemia. These significantly different washout rates in the three groups indicate that coronary blood flow at the time of $^{201}$TI administration determines the subsequent $^{201}$TI myocardial kinetics.

Figure 6. Time-activity curves in the anterior and posterior walls were obtained in the ischemia group of five dogs by the same method as described in figure 4. The ischemic posterior wall had a significantly slower uptake and reached its peak 80 minutes after thallium-201. This was followed by slower washout slope, $-(0.076 \pm 0.020)$ %/min, compared to the anterior wall, $-(0.122 \pm 0.032)$ %/min. There was a tendency for activity crossover between anterior and posterior walls after 120-140 minutes, suggesting that the similar activity ratio between anterior and posterior walls (fig. 4) will follow with time.

Figure 7. Time-activity curves in the anterior and posterior walls obtained from the same group of dogs shown in figure 6. A significantly increased uptake in the posterior wall was found, which peaked 10 minutes after maximal blood flow induced by reactive hyperemia. The peak activity was followed by rapid washout in the posterior wall $-(0.244 \pm 0.034)$ %/min, compared with a relatively slow washout in the anterior wall $-(0.138 \pm 0.063)$ %/min.
The mean half-washout time from the posterior wall was 5.3 hours in the control group, 3.4 hours in the reactive hyperemia and 11.0 hours in the ischemia group.

Uptake and Washout of $^{201}$TI

In contrast to the significant differences in the time-activity curves in the posterior walls of the three study groups, the range of average time activities from the anterior walls was small in the three groups (fig. 9). The percent activity in the anterior wall and in background approximated each other soon after the peak uptake in the anterior wall was realized, and the approximate myocardium to background ratio of 1:1 persisted thereafter. This has been observed previously in humans24, 11 and experimental animals.29 The highest background activity was seen in the ischemia group in the initial several minutes, but a significant difference was found only at 1 minute ($p < 0.005$). Although the blood pool activity is not the same as the background activity, it is largely responsible for background counts soon after administration, and this is noted in the significantly delayed $^{201}$TI clearance at 1 minute in the ischemia group ($p < 0.01$) (table 1). The residual percent $^{201}$TI activity in blood was nearly identical in the three groups at 3 minutes and thereafter. Background counts during the first several minutes shift rapidly from the blood pool to other tissues (table 1). In addition, percent activity in the anterior wall in the three groups at each data point showed no significant difference. These findings of nearly equal activity in anterior wall, background and residual blood pool activity in three groups provide a basis for comparing activity in the posterior wall. The activities in the posterior walls in three groups were all significantly different from each other at each data point, except at 160 and 180 minutes in the comparison between control and reactive hyperemia groups. These findings emphasize the differences in $^{201}$TI kinetics in the uptake and washout phases as a result of altered coronary blood flow and the timing of $^{201}$TI administration. Further, a rapid washout of $^{201}$TI after its rapid and increased uptake in the reactive hyperemia group corrected its initial excess to about the same level as the control group at 160 minutes. Thus, the activity in the posterior wall was absolutely increased with reactive hyperemia and absolutely decreased with ischemia.

Discussion

A better understanding of $^{201}$TI kinetics during and after regional myocardial ischemia requires careful interpretation of reported findings in relation to experimental design. Our findings are applicable to a situation in which $^{201}$TI is given during transient ischemia or during the peak flow of reactive hyperemia. Thallium uptake by myocardial cells depends on both myocardial perfusion and extraction by myocardial cells. Our findings strongly suggest that a major determinant of $^{201}$TI uptake during transient ischemia is the magnitude of coronary blood flow at the time of $^{201}$TI administration. During total occlusion of the circumflex coronary artery, uptake occurs but is markedly diminished. That any uptake occurs at all is presumably attributable to collateral circulation, which is ex-
tensive in the dog. Immediately after release of the 2-minute occlusion, uptake may have been enhanced transiently by reactive hyperemia. Thereafter, myocardial perfusion was normal. Peak myocardial activity in the ischemic area was not reached until 80 minutes, presumably because of a very low concentration of $^{201}$TI in circulating blood and, hence, a low concentration gradient between blood and ischemic cells. Diminished extraction seems unlikely. Ultrasonic measurements of left ventricular performance, which have been shown to be a reliable indicator of ischemia, was returned to normal within a few minutes after release of the occlusion. During reactive hyperemia, uptake appeared to be directly proportional to coronary blood flow.

The rapid and large net gain of $^{201}$TI in reactive hyperemia was followed by rapid net loss. The slow gain after transient ischemia was followed by a slow loss. These induced abnormal states slowly approached the normal resting state over time by correcting initial excess or deficit after flow returned to baseline levels. The observed differences in $^{201}$TI uptake and washout are absolute, not relative, differences that reflect the magnitude of coronary blood flow. Thus, redistribution is likely a dual phenomenon in which the initial excess or deficit is corrected by differential clearance of $^{201}$TI from the normal or hyperemic tissue compared with the ischemic area and an absolute increase in activity in the ischemic area. The latter process probably predominates during first hour; differences in regional myocardial washout predominate thereafter.

Apparent differences between our results and those of others may be explained by differences in experimental design. The timing and frequency of observations may be critical in explaining widely divergent results when coronary blood flow in dogs was experimentally increased. An increase in $^{201}$TI uptake was found when coronary blood flow was increased by adenosine or dipyridamole and myocardial activity was evaluated by either serial imaging or tissue samples. On the other hand, Weich and co-workers found a logarithmic decrease in $^{201}$TI uptake where coronary blood flow was increased in excess of demands by drugs, including adenosine. These investigators counted blood samples from the coronary sinus during hyperemia for only 25 seconds. We have shown that when $^{201}$TI was given during peak flow of reactive hyperemia, peak myocardial activity occurred 10 minutes after administration, by which time flow had already returned to the baseline level. Failure to appreciate the time lag between peak flow and peak myocardial activity may also explain the lack of correlation between regional blood flow measured by the labeled-microsphere technique and tissue activity. In one such study, microspheres and $^{201}$TI were given simultaneously during reactive hyperemia and the dog was sacrificed 1 minute later, well before the expected peak activity. Our experimental design required collections of counts every 30 seconds and relatively high activities were given. The delay in accumulating counts was no more than 30 seconds. Wharton et al performed a study with many design characteristics similar to ours. They only examined the uptake phase of $^{201}$TI kinetics, however, after transient regional ischemia or reactive hyperemia. Dogs were sacrificed and samples counted 6–10 minutes after circumflex occlusion. They concluded that the perfusion defect observed on the initial scintigram was influenced by the duration of ischemia. As in our experiments, if $^{201}$TI was given during maximum reactive hyperemia, the defect was almost entirely obliterated.

Nielsen and co-workers evaluated initial $^{201}$TI uptake in exercising dogs in which circumflex coronary flow was restricted with a mechanical snare. Thallium-201 and radioactive labeled microspheres were administered during exercise. Dogs were sacrificed after 5 minutes and tissue samples were counted in vitro. They found a close linear relationship (correlation coefficient 0.98 or greater) between $^{201}$TI uptake and regional coronary blood flow. Blood flow increased three- to sevenfold in the region with unrestricted blood flow, compared with a blood flow of less than 0.1 ml/min/g of tissue in a region with restricted flow. Differences between their findings and ours may be explained by differences in experimental design. We found similar directional changes in coronary flow and $^{201}$TI uptake, but of somewhat lesser magnitude, in the posterior walls of dogs with either reactive hyperemia or ischemia. There are several reasons for these apparent differences. Increases in flow to normally perfused tissue are probably greater with exercise than with reactive hyperemia. Decreases in $^{201}$TI uptake in our ischemic preparation were partially neutralized by the transitory nature of the occlusion, which was followed by reactive hyperemia. A major limitation is in vivo measurements of myocardial activity; that is, the inherent resolution of the gamma camera results in averaged regional differences in activity, which is not a problem with in vitro counting of small samples. In addition, the gamma camera requires a longer period of time to collect enough counts to ensure accurate imaging. A major difference between Nielsen’s study and ours is that they evaluated only initial $^{201}$TI uptake, whereas we examined the washout phase as well.

Few critical and quantitative data are available relative to the washout phase of myocardial activity after $^{201}$TI administration. Some of these studies were performed in humans after an episode of unstable angina pectoris or during exercise-induced ischemia with and without prior myocardial infarction by serial imaging in which the anterior and posterior walls were compared by qualitative criteria. Results of myocardial washout from ischemic myocardium during continuous occlusion of a coronary vessel are probably inapplicable to results derived from transiently ischemic myocardium. In dog studies, Gewirtz and co-workers administered $^{201}$TI 10 minutes before occlusion of a coronary artery. Myocardial activity in the persistently ischemic region was followed by sequential drill biopsy specimens. They found no significant differences in myocardial clearance between control and ischemic areas at 15 minutes and at 2 hours.
In accord with our findings, Pohost and co-workers, using nonquantitative serial scintigraphy in dogs, showed that the apparent difference in activity between a transiently ischemic region and a normal myocardium gradually lessened over a 100-minute period. Schelbert and co-workers studied washout by analyzing myocardial activity in tissue samples of sacrificed dogs in whom $^{201}$TI was given during transient ischemia. During the initial 30 minutes after release of the occlusion, the percent increase in myocardial uptake in the ischemic area exceeded the percent decrease in activity in normal myocardium. At 4 hours, the percent decrease in activity in normal myocardium exceeded the decrease in the previously ischemic myocardium. These results are in general agreement with ours, although the time course of myocardial activity was limited by the infrequent samples.

**Clinical Implications**

Patients who have a positive $^{201}$TI exercise test generally have underlying coronary occlusive disease, and reactive hyperemia in the ischemic area is probably not important. Rather, reactive hyperemia is a model for understanding the increased perfusion of normal myocardium. The maximum difference in myocardial activity between overperfused normal myocardium and ischemic myocardium occurs within 10 minutes after administration of the radionuclide (fig. 8), emphasizing the need for early imaging. Thereafter, activity falls rapidly in the normal myocardium (probably reflecting an excessive concentration gradient) while it is still increasing in the ischemic area. The difference in activity is probably related to the degree of exercise. Appreciation of the different washout characteristics of hyperemic normal tissue and ischemic tissue gives the clinician insight into the need for delayed images to differentiate ischemic from infarcted tissue. The delayed washout of $^{201}$TI from ischemic myocardium long after coronary blood flow has returned to normal is best explained by a decrease in the concentration gradient between the previously ischemic area and blood. Slow washout from an ischemic area should accelerate the redistribution process, which in some patients may be completed within 1 hour. Additional factors that we did not evaluate but that undoubtedly influence the development and persistence of an initial scintigraphic defect and perhaps the new appearance of a delayed defect include the duration of the ischemic episode, the presence of underlying critical stenosis of one or more coronary arteries, the extent and distribution of collateral flow, and the presence of underlying infarcted cells that share the same area as the ischemic cells.

The recognition of an ischemic defect in clinical practice, considering the limitations of gamma camera resolution of small differences in activity, depends on relative differences between ischemic and nonischemic myocardium. Flow can increase in a narrowed coronary artery, but if the increase is much greater in the fully patent vessels, a defect may be observed. Identification of a regional scintigraphic defect during rest angina or after inadequate exercise is made more difficult by the absence of significantly increased uptake in normal myocardium as is seen with high-level exercise.

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**Gamma Camera Quantitation of Thallium-201 Redistribution at Rest in A Dog Model**

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**SUMMARY** Defects seen at rest on thallium-201 (201TI) scintigraphy can disappear over time. We obtained sequential 5-minute scans over 127 ± 9.4 minutes in seven open-chest dogs with fixed, stable regional flow reductions (normal zone flow 0.76 ± 0.09 ml g−1 min, ischemic zone flow 0.49 ± 0.04 ml g−1 min [mean ± SEM], p < 0.05) as determined by microsphere injection. Sequential 5-minute scans were obtained after i.v. injection of 1.5 mCi of 201TI. Data were stored in a 64 × 64 pixel computer matrix. Qualitatively, defects that showed redistribution were seen in all dogs. Quantitatively, greater count loss from peak activity distinguished the normal zone, but overlap was great. Alternate quantitative methods using background subtraction altered the characteristics of the time-activity curves, but did not enhance the separation of ischemic from normal zones. Patterns of 201TI redistribution from gamma camera imaging are profoundly influenced by the method of quantitation. No single method of quantitative analysis separated ischemic from normal zones in all dogs. The clinical significance of patterns at rest requires redefinition.

IN PATIENTS with severe angiographic coronary artery disease, defects at rest on thallium-201 (201TI) scintigraphy can disappear over time.4,8 Quantitative analysis of the scans in these patients suggested that 201TI uptake in hypoperfused, but presumably viable, regions played the dominant role in 201TI redistribution.5,4 If correct, the concept of delayed uptake of 201TI into myocardial regions with subnormal coronary flow is important for two reasons. First, it would aid in identifying ischemic zones in patients with qualitatively normal scans6,8 and help separate infarct from ischemia. Second, it could lead to a quantitative method of blood flow determination from time-activity curves, because preliminary data indicate that the rate of uptake is related to the degree of flow reduction.7,8

However, Leppo et al.9 presented data showing that washout rather than washin dominates the process of redistribution when flow is segmentally enhanced. If the animal model of Schelbert et al.8 applies, delayed uptake will occur only when resting flow has been reduced by 80% of normal. Patients reported to show areas of myocardium with delayed 201TI uptake were asymptomatic and showed no ECG evidence of acute ischemia at the time of 201TI injection.8 Catheterization at another time revealed no wall motion abnormalities in many of these patients.

Thus, the mechanism and significance of scintigraphic patterns of redistribution are controversial. Our study was designed to explore methods of quantitating gamma camera scans and to use these methods to characterize patterns of 201TI redistribu-
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