Quantification of Infarction in Cross Sections of Canine Myocardium In Vivo with Positron Emission Transaxial Tomography and $11^C$-Palmitate

EDWARD S. WEISS, M.D., SYED A. AHMED, M.D., MICHAEL J. WELCH, PH.D., JOSEPH R. WILLIAMSON, M.D., MICHEL M. TER-POGOSSIAN, PH.D., AND BURTON E. SOBEL, M.D.

SUMMARY To assess myocardial infarction quantitatively in 15 mm thick transverse sections of the canine heart in vivo we utilized a new technique, positron emission transaxial tomography (PETT) and cyclotron-produced $11^C$-palmitate ($11^C$-P) injected intravenously. Results were compared to regional myocardial creatine phosphokinase (CPK) depletion, diminished $11^C$-palmitate accumulation in tissue extracts, and infarction estimated morphometrically 48 hours after coronary occlusion. CPK activity and $11^C$-P content declined in parallel in transmural biopsies (N = 44) from normal and ischemic zones ($r = .92$) in six dogs; and infarct in 10 mm thick cross sections of the entire left ventricle estimated morphometrically (N = 26) in six other animals correlated with CPK depletion in contiguous 2.5 mm thick slices ($r = .92$). When the percentage of infarction in 15 mm thick cross sections was assessed tomographically in six other dogs 48 hours after coronary occlusion with $11^C$-P injected intravenously, results correlated with infarction in corresponding cross sections from the same hearts estimated morphometrically ($r = .97$, N = 9) and by analysis of CPK depletion ($r = .93$, N = 9). Thus, PETT permits estimation of infarction in cross sections of the left ventricle in vivo after intravenous injection of $11^C$-palmitate.

EVALUATION OF THE EXTENT OF MYOCARDIAL INFARCTION in vivo has become increasingly important because prognosis in patients appears to be influenced by infarct size" and because the extent of irreversible ischemic injury may be amenable to favorable modification" with interventions implemented during the early development of the insult. Although myocardial infarct scintigraphy is useful for detection and localization of infarction, quantification of ischemic injury with this technique may be limited because of the dependence of accumulation of tracer on the age of the infarct, and because of inherent limitations leading to disparities between the mass of injured tissue and its two-dimensional display." Precordial ST-segment elevations may reflect serial changes in the electrophysiological response of the heart to ischemia" but they do not provide a direct reflection of the absolute magnitude of infarction" and may be influenced by factors not directly related to ischemia such as drug effects, pericarditis, or changes in the concentration of electrolytes in extracellular fluid. Prediction or estimation of infarct size on the basis of time-activity curves of plasma enzymes such as creatine phosphokinase suffers from the prolonged interval required for acquisition of data prior to construction of projected portions of the curves." The present study was designed to develop and evaluate a method for quantitative estimation of the extent of myocardium undergoing infarction in vivo suitable for prompt, early, and sequential evaluation of the evolution of ischemic injury. Accordingly, we synthesized $11^C$-palmitate, a short-lived, positron-emitting, cyclotron-produced tracer of the predominant physiological substrate of myocardium," injected the material intravenously in closed chest dogs with myocardial infarction; and determined its distribution in ischemic myocardium with computer reconstructed images obtained by positron emission transaxial tomography in order to detect, localize, and quantify infarction in vivo. Results were compared to independent estimates of the extent of infarction based on biochemical and morphological analyses of hearts from the same animals.

This approach was predicated on several considerations. The positron-emitting tracer employed has a short half-life (20.4 min), permitting frequent sequential studies with a low total body radiation burden. Use of palmitate, a physiological substrate of the heart, permits interpretation of results in terms of the extensive information available characterizing myocardial intermediary metabolism and documenting diminished uptake and oxidation of free fatty...
acids in zones of ischemia and infarction.\textsuperscript{21-28} The distribution of positron-emitting isotopes in tissues can be quantified readily with coincidence counting, facilitating spatial resolution and delineation of the distribution of radioactivity in three-dimensional space.\textsuperscript{21} Furthermore, detection of radiation emitted from the heart is not distorted by the distance of the emitting source from each member of any pair of detectors. Quantification of infarction in a series of cross-sectional slices of myocardium by positron emission transaxial tomography should permit estimation of the entire mass of the infarct based on summation of the amount of infarct detected in each individual cross section.

In a preliminary qualitative evaluation of this approach, we verified the externally detectable diminution of myocardial accumulation of \textsuperscript{14}C-palmitate associated with reduction of coronary flow in isolated perfused rabbit hearts and demonstrated the feasibility of obtaining positron emission transaxial tomographic images of the heart in intact dogs.\textsuperscript{23} The present study was undertaken to extend these observations to permit quantitative estimation of infarction \textit{in vivo} and to define the quantitative relationships between computer reconstructed tomograms of infarcts and biochemical and morphological changes in the same tissue.

\section*{Materials and Methods}

\subsection*{Animal Preparations}

Myocardial infarction was produced in 22 dogs anesthetized with sodium pentobarbital, 30 mg/kg injected intravenously, by ligation of the left anterior descending coronary artery distal to the first septal branch. Immediately after ligation, the thoracotomy was closed. Eighteen animals survived this procedure and were included in the studies performed 48 hours after surgery.

Six animals were used to clarify the relationship between myocardial CPK depletion in a cross section of the entire left ventricle and morphometric estimation (see below) of infarction in an adjacent 10 mm thick cross section in the experimental preparation used. Total myocardial CPK activity was assayed in extracts of 2.5 mm thick cross sections. Results were compared to expected activity in the cross sections, calculated as the product of weight and CPK/g of histologically normal, nonischemic myocardium (averaged from four 0.5 g transmural biopsies in each heart). In each dog from this group, three or four pairs of cross sections were analyzed.

Six different animals were used to determine the relationship between myocardial CPK depletion 48 hours after coronary occlusion and diminution of regional \textsuperscript{14}C-palmitate accumulation in myocardium after intravenous injection of \textsuperscript{14}C-palmitate, five minutes before the animal was killed. Among the six animals studied with \textsuperscript{14}C-palmitate, myocardial CPK activity was assayed in five to eight 0.5 g transmural myocardial samples obtained with a precooled modified dental drill from ischemic and nonischemic regions of each heart. Results were compared to \textsuperscript{14}C-palmitate radioactivity in extracts of the same tissue used in a Packard liquid scintillation counter. This isotope was studied to facilitate interpretation of results of subsequent studies in other dogs in which tomography was performed after intravenous injection of \textsuperscript{14}C-palmitate 48 hours after coronary occlusion.

After relationships between \textsuperscript{14}C-palmitate, morphology, and CPK depletion had been examined, six additional animals were studied by positron emission tomography. In each of these, after tomography was completed, the animal was killed and infarction was verified and quantified by two procedures: myocardial CPK analysis and morphometric analysis. CPK analysis was performed in extracts of each of two 2.5 mm thick transverse sections of the entire left ventricle at the level corresponding to the tomographic image and adjacent to a central contiguous 10 mm thick cross section. Morphometric analysis was performed as described below on each central 10 mm thick cross section of the entire ventricle corresponding to the tomographic plane. In several animals more than one tomographic plane was studied with corresponding CPK and morphometric comparisons. For CPK and morphometric analyses, slices of the entire left ventricle were obtained from the rapidly frozen hearts of other animals. The transverse sections were obtained to correspond to tissue planes reflecting the field of view encompassed in each tomographic image based on the known 15 mm thickness of each tomographic section and the distance from the apex of the heart corresponding to each. The distributions of \textsuperscript{14}C-palmitate and myocardial CPK activity were determined by analysis of both in transmural punch biopsies of normal and ischemic tissue and transverse sections of the entire left ventricle.

\subsection*{Preparation of Left Ventricular Biopsies for Analysis of \textsuperscript{14}C-Palmitate and Myocardial CPK Content}

All procedures were performed at 0 to 4° C. Myocardium was minced with scissors, suspended in 0.05 M Hepes-NaOH buffer, pH 7.4, 10 ml/g, and homogenized in a Virtis homogenizer for two 15 second bursts at half maximum speed. Aliquots of 0.4 ml of homogenate were removed for determination of \textsuperscript{14}C-palmitate radioactivity in a toluene based fluor after solubilization of protein with Protosol.

Myocardial CPK activity was assessed in extracts of whole homogenate of myocardium initially centrifuged for 20 minutes at 30,000 g at 0° C. The supernatant fraction was decanted, diluted with Hepes-NaOH buffer, pH 7.4, 0.05 M such that CPK activity was less than .2 IU/ml. CPK activity was assayed spectrophotometrically as previously described and protein was determined by the Biuret method.\textsuperscript{18}

CPK depletion per gram of wet weight was determined as follows: CPK activity was measured in four histologically normal regions from each heart, averaged, and designated as CPK\textsubscript{N}, expressed as IU/g. Total CPK activity in each 2.5 mm transverse section was measured directly and designated as CPK\textsubscript{T}, also expressed as IU/g. The percent CPK depletion was calculated from \([\text{CPK}_N - \text{CPK}_T]/\text{CPK}_N\) \times 100.

\subsection*{Morphometric Analysis of Infarction}

Frozen hearts were sliced into 10 mm thick sections for gross and histological examination. Alternating 2.5 mm thick sections were used for analysis of \textsuperscript{14}C-palmitate and CPK activity (fig. 1). Each 10 mm section was immersed rapidly in normal saline and photographed with a Graflex 4 \times 5" photcopy camera. Subsequently, the slice was fixed with 1.25% glutaraldehyde-1% formaldehyde buffered to pH 7.4 with Ringer's lactate solution and cut into blocks for
histology. Sections adjacent to regions analyzed biochemically were stained with hematoxylin and eosin. Each histological section was analyzed to detect infarction, projected, and combined to reconstruct an entire cross section of the heart with the area of necrotic tissue outlined by planimetry. The total area of each 10 mm thick transverse section and the area representing infarction were calculated with a Hewlett-Packard 9100 B calculator coupled to 9107 A digitizer. Calculations of the percentage of infarction in each region were made on the basis of the ratio of outlined infarct to normal myocardium in the entire cross section.

Preparation of 11C-Palmitate

11C-palmitate was produced by the reaction of pentadecyl magnesium bromide in diethyl-ether with 11CO2 produced in the Washington University Medical School cyclotron by the 10B(d,n) 11C nuclear reaction using boric oxide as the target material. After acidification with 3 ml of 1 N hydrochloric acid, the ether layer (4 ml) was separated and 2 ml of ethanol added. The ether/ethanol solution was boiled to remove the ether. At this stage of the preparation the ethanol contains both the labeled palmitate and pentadecane formed by the hydrolysis of the unreacted Grignard reagent. Eight ml of 4% albumin solution is then added and the solution maintained at 42° C for 5 minutes during which time the pentadecane precipitates. The precipitate is removed from the solution by millipore filtration prior to addition of the remaining 11C-palmitate.

Administration of 11C-Palmitate

For studies of the distribution of 11C-palmitate in myocardium after intravenous injection of the tracer, results were obtained by liquid scintillation counting of extracts prepared from biopsies. The tracer was prepared as follows: 250 μCi of palmitic-11C acid (labeled analogously to the 11C-palmitate preparation) in hexane was immersed in a water bath at 90° C until the hexane had been entirely evaporated. Subsequently, 1 ml of absolute ethanol was added to the radioactively labeled material, followed by 4% bovine serum albumin dissolved in 10 ml of 0.15 M NaCl warmed to 52° C. The solubilized 11C-palmitate was used for intravenous injection in the canine preparations. The use of 11C-palmitate permitted analysis of palmitate distribution in myocardial biopsies since the short half-life of 11C-palmitate (20.4 min) made destructive analysis of multiple samples for radioactivity impractical.

Positron Emission Transaxial Tomography

Five to ten millicuries of 11C-palmitate in a solution of 4% albumin was injected intravenously in an 8 ml bolus at a rate of 1–2 ml/sec 48 hours after coronary occlusion in lightly anesthetized dogs. Three minutes later, an interval selected to permit clearance of the tracer from the blood pool, the distribution of 11C-palmitate in myocardium was determined by detection of positron emission during an 8 to 16 minute interval providing detection of 0.5 to 1.0 × 106 counts. At least one and as many as seven tomograms were obtained from each animal corresponding to one or more 15 mm thick cross sections of myocardium. Immediately after completion of the tomograms, 250 μCi of 11C-palmitate in 4% albumin were injected intravenously. The animals were killed five minutes later with an overdose of anesthesia. 11C-palmitate was administered in order to permit subsequent analysis of the distribution of this tracer based on liquid scintillation counting of extracts obtained from transmural punch biopsies and transverse sections of the excised heart.

Quantitative assessment of the organ distribution of 11C-palmitate in myocardium in the studies in vivo was based on a computer reconstructed image of positron emission (511 keV gamma rays) from 15 mm thick cross sections of the heart. Correction factors for attenuation were first obtained with the use of a ring containing 11C-Cu in a solution of concentrated nitric acid placed within the empty tomograph and then within the same field of view but around the experimental canine preparation. Positron emission from 11C-palmitate accumulated in myocardium after intravenous injection was detected and quantified with a positron emission transaxial tomograph designed at Washington University. This instrumentation employs six banks of 8 Nal crystals to detect positron emission. The detectors are rotated with a programmed pattern of motion around the experimental animal at the level of the heart. Data are analyzed by computer to produce reconstructed cross-sectional images from data profiles from each pair of detectors.

The percentage of infarct in each 15 mm thick cross section of the left ventricle in vivo was estimated by analysis of the digital printout of the 2,500 data points utilized for computer reconstruction of the entire left ventricular cross-sectional tomographic image. In order to define the epicardial and endocardial margins of the ventricular image on the digital printout, a horizontal profile of the image gray scale was obtained on a Tektronix Type 524 wave form monitor. In this profile the region of the ventricular myocardium was defined by inclusion of all data points with values exceeding 50% of the maximum value detected. A Versatec plotter was used to obtain digital printouts of the distribution of 11C-palmitate radioactivity in each image of normal canine ventricles at the midventricular and A-V valvar levels. The region corresponding to myocardium was delineated with a hand drawn line surrounding those digital values conforming to the count rate criterion. This area correlated well with the oscilloscopic display of the image of myocardium, typically approximately circular, obtained at the midventricular level and with the typically horseshoe-shaped image, obtained at the level of the A-V valves (fig. 2).
Tomographic images obtained 48 hours after coronary occlusion revealed appearance of a large anterior defect, which interrupted the circular image noted in animals without coronary occlusion (fig. 3). The determination of percentage of infarction represented by these defects was calculated by planimetric measurement of the image area defined in the digital printout. This area was then quantitatively compared to the calculated area between the two circles derived from the minimal diameters across the inner and outer perimeters of the tomogram (fig. 4).

A proportionality constant was used for calculation of percentage of infarction at the level of the A-V valves since these tomograms are horseshoe-shaped because of the nonvisualized posterior left atrial border. The area of ventricular myocardium in this region was estimated in ten images from normal dogs and found to average 60% (range = 54 to 67%) of the total area between the two concentric circles at midventricular level. Thus, at this level, the percentage of infarction was estimated by subtracting the planimetered area of the infarct from 0.6 times the area between these concentric circles.

**Results**

The Relation between Myocardial CPK Depletion, Diminution of 14C-Palmitate Accumulation, and Morphologically Evident Infarction

Results of analyses of CPK activity and 14C-palmitate radioactivity in 44 transmural samples of myocardium from normal and ischemic zones from six dogs are shown in figure 5. As can be seen, regions with low 14C-palmitate accumulation were characterized by marked depletion of CPK activity. The correlation between the percentage of CPK depletion and the percentage of diminution of 14C-palmitate accumulation was 0.92. As can be seen in table 1, depletion of CPK in transverse sections of the entire left ventricle correlated closely with necrosis estimated morphologically in adjacent sections. Since 14C-palmitate accumulation was diminished in proportion to myocardial CPK depletion

---

**Figure 2.** Representative images obtained by positron emission transaxial tomography after intravenous injection of 14C-palmitate in a lightly anesthetized dog. As can be seen, the characteristic distribution of 14C-palmitate is circular at the midventricular level, but conforms to a horseshoe-shaped pattern at the level of the A-V valves because the posterior portion of the heart in this region comprises left atrial rather than ventricular myocardium. A, P, R, L refer to anterior, posterior, right, and left, respectively. The central areas within the circle and horseshoe patterns correspond to the left ventricular cavity. The endocardial margin is somewhat blurred because these images were obtained without electrocardiographic gating.

**Figure 3.** Positron emission transaxial tomograms (top panels) obtained at the midventricular level in a normal dog (left) and a dog with an anterior myocardial infarction induced by coronary occlusion 48 hours earlier (right). Printouts of the digital data with lines encompassing normal myocardium drawn as indicated in the text are shown in the bottom two panels. The midventricular image from the dog with the myocardial infarct shows diminution of 14C-palmitate uptake with a defect in the anterior portion of the cross-sectional image (top) and conforming to results apparent on the printout of the digital data shown below.
throughout ischemic zones (fig. 5), these results suggested that necrosis could be estimated by analysis of myocardial accumulation of palmitate estimated externally. Furthermore, since palmitate-$^{13}$C and palmitate-$^{14}$C are likely to be equivalent metabolically, it appeared that necrosis could be estimated by external assessment of $^{13}$C-palmitate uptake.

In six dogs subjected to coronary occlusion but not studied tomographically, myocardial CPK depletion in 2.5 mm thick transverse sections of the left ventricle at multiple levels from apex to base correlated closely with morphometric estimates of infarction in the adjacent 10 mm thick cross section (fig. 6) ($r = .92$, $N = 26$ pairs of sections). Thus, the depletion of myocardial CPK activity and $^{13}$C-palmitate accumulation correlated closely with morphometric estimates of infarction in the adjacent transverse section.

**Estimation of Infarction in Cross Sections of the Left Ventricle**

*In Vivo* Based on Analysis of Positron Emission Transaxial Tomograms

Areas of myocardial infarction were estimated in 15 mm serial sections of myocardium represented by tomograms obtained sequentially from apex to base in closed chest dogs.

**Table 1. Analyses in Transverse Sections of the Entire Left Ventricle Obtained from Three Dogs**

<table>
<thead>
<tr>
<th>Dog number</th>
<th>$A$ CPK activity % decrease from normal sample</th>
<th>$B$ $^{13}$C-palmitate uptake % decrease from normal sample</th>
<th>Morphological determination of infarct size (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.0</td>
<td>5.9</td>
<td>0.0</td>
</tr>
<tr>
<td>1</td>
<td>2.5</td>
<td>8.8</td>
<td>2.0</td>
</tr>
<tr>
<td>3</td>
<td>9.1</td>
<td>12.2</td>
<td>9.2</td>
</tr>
<tr>
<td>2</td>
<td>10.9</td>
<td>14.4</td>
<td>16.8</td>
</tr>
<tr>
<td>3</td>
<td>19.0</td>
<td>12.3</td>
<td>14.3</td>
</tr>
<tr>
<td>1</td>
<td>23.3</td>
<td>26.1</td>
<td>29.0</td>
</tr>
<tr>
<td>2</td>
<td>26.0</td>
<td>20.0</td>
<td>18.7</td>
</tr>
<tr>
<td>2</td>
<td>29.6</td>
<td>14.8</td>
<td>15.5</td>
</tr>
<tr>
<td>3</td>
<td>31.5</td>
<td>32.7</td>
<td>31.6</td>
</tr>
</tbody>
</table>

The correlation coefficient between results in columns $A$ and $C$ (linear regression, least squares method) was .94, and that between results in columns $B$ and $C$ was .94.
The relationship between infarct size estimated morphologically and infarct size estimated from myocardial CPK depletion in an adjacent transverse section of the entire left ventricle is indicated here. Results obtained 48 hours after coronary occlusion with these two methods correlated closely.

The typical tomograms obtained at the midventricular (circular) and A-V valvular level (horseshoe-shaped pattern) are shown in figure 2. At least four images were obtained from each dog, but many did not encompass regions of infarction. As can be seen in figure 3, the presence of infarction 48 hours after left anterior descending coronary occlusion in a tomogram corresponding to a 15 mm thick section of the left ventricle at the midventricular level is readily apparent in the image and the digital printout of the data. The anterior defect contrasts with an image from the same level obtained from a normal dog. The percentage of infarction in cross sections from each of six dogs studied tomographically estimated from the area in the tomogram correlated closely with the extent of infarction in the corresponding slice analyzed morphometrically (fig. 7) by an observer unaware of the results obtained tomographically ($r = .97, N = 9$ pairs of slices) and with infarction estimated from CPK depletion in the adjacent 2.5 mm thick slice analyzed by another observer, also unaware of the tomographic results ($r = .93, N = 9$ pairs of slices from six dogs). As can be seen, CPK depletion and morphological estimates of infarction correlated closely in sections corresponding to those imaged ($r = .92, N = 9$ pairs of slices). These results indicate that estimates of infarction in cross sections of the left ventricle obtained by analysis of positron emission transaxial tomograms in vivo correspond closely to estimates of infarction based on analysis of myocardial CPK depletion and to morphometric estimates of infarct size in the corresponding transverse section.

Application of the tomographic approach to estimating the entire mass of an infarct is illustrated in figure 8. As can be seen, sequential tomograms corresponding to 15 mm thick cross sections of the heart delineate a volume of infarction that can be calculated from the cross-sectional area representing diminished $^{13}$C-palmitate uptake in each cross section multiplied by the thickness of each. Improved results should be available with instrumentation now being developed that will permit 1) simultaneous accumulation and differentiation of data from four sections from each heart, and 2) electrocardiographic gating with reduction of impairment of resolution due to movement of the heart throughout the cardiac cycle.

**Discussion**

The use of radioisotopes to detect myocardial injury or ischemia externally has employed intravenous administration of inorganic ions such as $^{41}$K, $^{133}$Cs, $^{85}$Rb, $^{87}$Rb, $^{201}$TI, $^{67}$Ga; $^{11}$N labeled NH$_4$$_2$ and intracoronary injection of radioisotopes of inert gases such as $^{86}$Kr and $^{133}$Xe. These moieties were selected because of advantages in physical or biological properties but none is a physiological substrate of myocardium. Efforts to utilize organic substrates of the heart as agents for imaging myocardium have involved fatty acid analogs labeled with $^{18}$F and $^{187}$Te. Unfortunately, these derivatives are metabolically altered substrates exhibiting less uptake than the corresponding $^{13}$C-labeled congeners. Furthermore, quantification of their distribution has been difficult.

In the present study we utilized a physiological substrate of the heart by synthesizing radionuclides incorporating positron-emitting $^{13}$C. Previously, we demonstrated that
showed that the diminished extraction of $^{11}$C-palmitate was a function of the duration of low flow and an index of metabolic manifestation of ischemia rather than a reflection simply of decreased delivery of the tracer to myocardium. The present results indicate a similar relationship between decreased palmitate accumulation demonstrated by PETT in areas exhibiting diminished CPK content in myocardium. The two correlations 1) between CPK depletion and histologic necrosis, and 2) between decreased accumulation of both $^{14}$C- and $^{11}$C-palmitate and CPK depletion, support the interpretation that under the conditions selected (48 hours after coronary occlusion), diminished $^{11}$C-palmitate accumulation detectable tomographically reflects infarction. Thus, although CPK content and $^{11}$C-palmitate accumulation are independently regulated, both are affected under these particular conditions as a result of infarction.

Reconstructive tomography offers several advantages in spatial resolution. For example, the technique delineates and separates the display of anterior and posterior regions and provides a cross-sectional representation avoiding the superimposition encountered with conventional imaging techniques. This facilitates quantification of the distribution of tracer and hence assessment of metabolism in a cylindrical volume of tissue. It also permits quantitative assessment of reduced accumulation of tracer and representation of a cold zone in three-dimensional space.

In the present study quantification of the percentage of myocardial infarction in 15 mm thick cross sections of the heart was determined by analysis of the digital printout of the data points obtained by computer reconstruction. A close correlation was obtained between the percentage of infarction estimated by analysis of each tomogram and histologic estimates of infarction in the corresponding transverse section of the left ventricle.

Determination of the total mass of ischemic ventricular myocardium by positron emission transaxial tomography with $^{11}$C-palmitate depends on imaging geometrically contiguous regions of the heart without overlap. This presently requires movement of the experimental animal in 15 mm increments in a cephalad direction to obtain sequential images of the entire left ventricle. The rapid decay of activity encountered with the short-lived $^{11}$C-nuclide requires progressively longer sampling intervals to obtain sufficient counts for computer reconstruction with sequential images. Accordingly, in this study, ungated images were used to permit the acquisition of the maximal amount of counts after a single injection of $^{11}$C-palmitate even though the use of ungated images resulted in diminished resolution.

The myocardial infarctions studied in this investigation resulted from coronary occlusion of 48 hours’ duration. This interval was chosen because histological indices of infarction and CPK depletion are well established within 48 hours after occlusion. Well circumscribed areas of ischemia can be detected as soon as 20 minutes after coronary occlusion by positron emission transaxial tomography with $^{11}$C-palmitate but unlike the case in which the occlusion is maintained for longer intervals, diminished uptake of $^{11}$C-palmitate is completely reversible with reperfusion. Thus, the capability for early recognition of ischemia after experimental coronary occlusion may presage significant potential for early clinical detection of jeopardized myocardium. In addition, the short half-life of $^{11}$C (20.4 min) permits se-
sequent studies in an individual organism facilitating repeated examinations during the early evolution of acute myocardial ischemic injury. The differentiation of ischemia from infarction should be possible by analysis of results of sequential studies in the same experimental animal or patient, once the duration of ischemia sufficient to abolish $^{13}$C-palmitate accumulation and required to produce infarction has been defined. Results in this study suggest that positron emission transaxial tomography utilizing cyclotron-produced, short-lived, positron-emitting radionuclides of physiological substrates of myocardium will facilitate objective evaluation of the efficacy of potentially therapeutic interventions on the extent of infarction ultimately sustained after an ischemic insult.

Acknowledgment

We appreciate the assistance of Mrs. Carol Higgins, Mr. Nizar Mullani, Ms. Duell Robison, and Ms. Maria Straatma in biochemical, radiochemical, and tomographic procedures and Ms. Carolyn Lohman in preparing this manuscript.

References

23. Scheuer J, Brachfeld N: Myocardial uptake and fractional distribution of palmitate-1-C$^14$ by the ischemic dog heart. Metabolism 15: 945, 1966
42. Poe ND, Robinson GD, MacDonald NS: Myocardial extraction of variously labeled fatty acids and carbohydrates. (abstr) J Nucl Med 14: 440, 1973
Quantification of infarction in cross sections of canine myocardium in vivo with positron emission transaxial tomography and 11C-palmitate.
E S Weiss, S A Ahmed, M J Welch, J R Williamson, M M Ter-Pogossian and B E Sobel

Circulation. 1977;55:66-73
doi: 10.1161/01.CIR.55.1.66
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
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/55/1/66

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/