Detection of Remote Myocardial Infarction in Patients with Positron Emission Transaxial Tomography and Intravenous $^{11}$C-Palmitate

BURTON E. SOBEL, M.D., EDWARD S. WEISS, M.D., MICHAEL J. WELCH, PH.D., BARRY A. SIEGEL, M.D., AND MICHEL M. TER-POGOSSIAN, PH.D.

SUMMARY Ischemic myocardial injury has been detected recently in isolated perfused hearts and intact experimental animals with positron-emitting $^{11}$C-palmitate and reconstructive tomography providing cross-sectional images of the heart free from superimposed activity in overlying structures. To evaluate the applicability of positron emission transaxial tomography in detecting infarction in man, 10 normal human subjects and 12 patients who sustained documented acute myocardial infarction three to 12 months previously were studied. Tomograms were obtained after intravenous injection of 5 to 10 mCi of $^{11}$C-labeled palmitate, a physiological substrate of myocardium. Tomograms from all normal subjects exhibited homogeneous distribution of $^{11}$C-palmitate throughout each 1.5 cm thick cross section of the ventricle. Tomograms from all patients with remote anterior or inferior and posterior myocardial infarction exhibited diminished accumulation of $^{11}$C-palmitate delineating regions corresponding to the electrocardiographic locii of infarction. The distribution of $^{11}$C-palmitate detectable by positron emission transaxial tomography in a series of cross sections from apex to base in the same normal subject or patient with remote myocardial infarction was analogous to that observed in normal dogs and animals with experimentally induced myocardial infarction.

NONINVASIVE ASSESSMENT OF MYOCARDIAL ischemic injury is desirable since infarction in experimental animals appears to be a dynamic process, amenable to favorable modification, and infarct size appears to be an important determinant of prognosis in patients. However, generally available techniques entail some unavoidable limitations. Recently, ischemic injury in experimental animals has been evaluated with physiological substrates of myocardium, labeled with cyclotron-produced, positron-emitting radionuclides, an approach with several potential advantages. Interpretation of results obtained with physiological substrates of the heart labeled with positron-emitting radionuclides can be made in the context of extensive information already available regarding carbohydrate, lipid, and protein intermediary metabolism in normal and ischemic myocardium. Furthermore, the physical characteristics of positron-emitting radionuclides make these agents particularly suitable for quantitative assessment of their distribution in myocardium with computerized tomography avoiding some inherent limitations of conventional radionuclide imaging. Positron emission gives rise to pairs of photons, 180° apart, detectable by coincidence counting with paired scintillation detectors. These properties permit "electronic" collimation and detection of a constant count rate regardless of the position of the radiation source within the cylindrical field of view between the paired detectors. Thus, in contrast to detection of single photon emitters, detection of positron emission does not require correction for attenuation as a function of depth of the radiation source within the tissue.

Positron emission transaxial tomography employs computerized tomography to reconstruct transverse sectional tomographic images of an organ from a series of radiation profiles obtained at selected angles around the organ. With selection of an appropriate positron-emitting radionuclide and utilization of instrumentation exploiting the physical characteristics needed for computer reconstruction tomography, the resulting image is free from superimposed activity from overlying structures and accurately and quantitatively reflects the distribution of the radionuclide within a transverse section of the organ.

In our initial studies of positron-emitting radionuclides for assessment of ischemic myocardium, we observed decreased extraction of free fatty acid ($^{14}$C-palmitate) in isolated perfused hearts subjected to ischemia persisting for 30 minutes, although extraction remained normal after one minute of ischemia despite the low flow. Thus, decreased extraction was a characteristic of the metabolic alterations secondary to ischemia rather than simply reduction of perfusion and decreased delivery of tracer to the myocardium. Subsequently, myocardial infarction was detected, localized, and quantified in vivo with positron emission transaxial tomography in lightly anesthetized dogs subjected to coronary occlusion 48 hours earlier. After intravenous injection of $^{14}$C-palmitate in normal animals, the tracer was distributed homogeneously throughout each cross section of the left ventricle. However, in animals with myocardial infarction, diminished $^{14}$C-palmitate accumulation was readily apparent in transverse sections of the heart visualized tomographically and found to correlate closely ($r = 0.93$) with depletion of myocardial creatine kinase activity and necrosis assessed histologically in corresponding cross sections of the heart.

In the present study, we applied positron emission transaxial tomography to 10 normal human subjects and 12 patients with myocardial infarction to determine whether it was applicable to assessment of ischemic heart disease and its modification in man.

Methods

Positron emission transaxial tomograms were obtained after injection of 5 to 10 mCi of $^{14}$C-palmitate in 4% albumin...
intravenously in a 10 ml bolus at a rate of 1 ml/sec in 10 normal subjects and 12 patients who had recovered from acute myocardial infarction three months to one year prior to study. Patients were selected consecutively according to the following criteria: acute myocardial infarction documented at the time of the initial episode with characteristic serial changes in plasma creatine kinase (CK) activity, elevated plasma MB CK activity, transmural ECG changes including evolution of Q waves, and willingness to participate in the study. Although positive tomograms were obtained from three additional patients with subendocardial infarction, without Q waves, these patients were not included in this initial report. Among the 12 patients with transmural myocardial infarction, six exhibited anterior, four lateral, and two posteroinferior infarcts according to conventional electrocardiographic criteria. Three minutes after injection of $^{11}$C-palmitate, an interval selected to permit clearance of tracer from the blood pool, the distribution of $^{11}$C-palmitate in myocardium was determined within six minutes, an interval providing recording of 0.5 to 1 $\times$ 10$^6$ counts. Computer reconstructed images of the distribution of $^{11}$C-palmitate were obtained with a positron emission transaxial tomograph designed at Washington University$^7$, $^{16}$, $^{17}$ in the same fashion as in previous studies with experimental animals,$^{18}$ with each image requiring acquisition of data for at least six minutes; hence, reconstruction of the entire left ventricle, necessitating at least four cross-sectional images, required substantially more time (30 to 60 minutes) with current instrumentation. The time required for acquisition of data used for each serial reconstruction increases because of the rapid decay of the radionuclides used (for example the 20.4 minute half-life of $^{11}$C-palmitate). However, instrumentation currently being tested permits simultaneous acquisition of data needed for reconstructive tomography at four levels, thereby reducing substantially the overall time required for tomographic reconstruction of the entire heart to six to 12 minutes after intravenous injection of $^{11}$C-palmitate. In the present studies in human subjects, electrocardiographic gating was not employed. The current resolution of the instrumentation can be varied from 1 cm full width at half maximum to 2 cm full width at half maximum of the line spread function. Images shown in this report were obtained with a resolution of 15 mm full width at half maximum.

Results

Tomograms obtained from all normal subjects exhibited a characteristic distribution of $^{11}$C-palmitate dependent upon the level, from apex to base of the heart, at which the tomogram was obtained. Each image reflects the distribution of $^{11}$C-palmitate in a 1.5 cm thick cross section of the heart. As can be seen in figure 1, at the level of the A-V valve, the distribution of $^{11}$C-palmitate in left ventricular myocardium conforms to a horseshoe pattern, similar to

![Figure 1](http://circ.ahajournals.org/)

**Figure 1.** Transmission and emission tomograms obtained in a normal subject at the level of the atrioventricular valves are shown in the upper two panels. The transmission image was obtained by placing a positron-emitter, $^{44}$Cu, around the subject at a selected level of the thorax, and was used for calculations of attenuation coefficients employed in reconstruction of the emission tomograms. The right-hand panel illustrates a $^{11}$C-palmitate emission tomogram from a normal subject. The horseshoe-shaped image of the left ventricular myocardial distribution of $^{11}$C-palmitate can be compared with a photograph of a cross section of a cadaver at a corresponding level in the lower right panel. The slight accumulation of tracer in the right-hand portion of the emission tomogram is in the dome of the liver. In the lower left panel, a digital printout of the emission tomogram is shown, obtained by encompassing within the dashed line all values of counts exceeding 50% of the maximum value obtained in any region of the tomogram.
that seen at the corresponding level of the heart in intact dogs. This pattern of the distribution parallels the anatomy of the left ventricular free wall, anterior surface, and interventricular septum evident in the photograph of the transcoracic cross section at the same level in a cadaver specimen shown in figure 1 for purposes of comparison.

In patients with anterior myocardial infarction, diminution of accumulation of $^{11}$C-palmitate was evident corresponding to the electrocardiographic locus of infarction. As seen in figure 2, this diminution appeared in the image as a defect in the anterior left ventricular free wall. In two patients with anterior infarcts, anterior transmural defects were evident in tomograms despite considerable regression of Q waves present within several days after myocardial infarction.

As can be seen in figure 3, positron emission transaxial tomography permitted detection of acute myocardial infarction in the inferior and posterior regions of the heart at this level. The tomogram shown was obtained from a patient with Q waves in leads II, III, and aV_{F} who had sustained an inferior myocardial infarction four months prior to evaluation with positron emission transaxial tomography. The transmural, posteroinferior diminution of accumulation of palmitate, in a wedge-shaped pattern with the base on the endocardial surface, is apparent.

As shown in figure 4, positron emission transaxial tomography permits acquisition of a series of images representing a sequence of transverse sections of the heart from apex to base after a single injection of $^{11}$C-palmitate intravenously. As was the case in the intact dog preparations studied previously, the distribution of $^{11}$C-palmitate is concentric near the apex of the heart but conforms to a horseshoe pattern in sections including the atrioventricular or atrial myocardium at the posterior border of the heart, since the amount of tracer accumulated by these structures is not visualized under the conditions used. As can be seen in the figure, infarction may be visualized in tomograms at several levels of the heart from apex to base. In some cross sections, $^{11}$C-palmitate is detectable in abdominal viscera, but tracer visualized in the thorax is confined exclusively to myocardium.

As indicated in figures 1 and 2, under the conditions used to obtain tomograms in the present study, the right ventricle is not visualized. By adjustment of the window such that low count rates are displayed rather than suppressed, the right ventricle can be detected. However, since our purpose was to illustrate changes associated with myocardial infarction, and on the basis of previous studies in experimental animals, we arbitrarily selected a count rate of 50% of maximum or less to define the ventricular chambers and the tissues surrounding the heart. Accordingly, regions with count rates this low were not visualized in the images photographed for figures 1 and 2. The absolute magnitude of counts in right ventricular myocardium is low for several reasons including...
the low metabolic rate of the right ventricle compared to the left ventricle, a consequence of the lower intraventricular pressure and energy requirements of the tissue. In addition, because the right ventricular wall is so thin compared to the left, the overall count rate within a 15 mm² region will be lower when that region encompasses a cross section of right ventricular compared to left ventricular myocardium.

Discussion

This study was undertaken to determine whether positron emission transaxial tomography permits detection of remote myocardial infarction in patients. Results in experimental animals, previously reported, indicate that this technique provides quantitative estimation of the distribution and extent of acute myocardial infarction, 48 hours after occlusion, verified by biochemical and morphological analysis of the heart. Verification of quantitative relationships between tomographic images and the extent of infarction in patients will require extensive clinical investigation of patients evaluated at selected intervals soon after the onset of acute myocardial infarction, since it is well recognized that contraction of evolving scars occurs during the reparative phase. In addition, it will be necessary to analyze complete reconstructions of the entire ventricle from apex to base for purposes of comparison with independent indices of the overall extent of infarction such as plasma creatine kinase time-activity curves or histochemical analyses of the heart at necropsy in patients who succumb.

The use of [11C]-palmitate for positron emission transaxial tomography requires an on-site cyclotron because of the short half-life of the radionuclide. Although current instruments are expensive, extensive efforts are underway, including those stimulated by a recent National Cancer Institute program, to develop low cost cyclotrons suitable for use in medical centers. On the other hand, it appears likely that positron emission transaxial tomography can be performed under certain conditions with radionuclides such as gallium 68 or rubidium 82 that can be synthesized with generators and therefore do not require cyclotron on site. However, interpretation of tomograms obtained with such agents will not necessarily be the same as interpretation of those obtained with [11C]-palmitate since the different imaging agents are subject to markedly different metabolic disposition. Accordingly, the basis for clinical utility of each agent must rest on evaluation under controlled conditions, often requiring studies in experimental animals to identify relationships between changes detectable tomographically, altered regional perfusion, altered metabolism, and irreversible injury.

Progress made in modifying evolving infarction in experimental animals and clinical findings relating infarct size to prognosis have stimulated efforts for estimation of the distribution of ischemia and infarction with the use of radionuclides administered intravenously. Conventionally, imaging of myocardium is performed with a scintillation camera. This device is well suited for many clinical applications, but unfortunately it exhibits some limitations.
in studies concerned with imaging the heart including: 1) representation of three-dimensional space in the twodimensional plane of the image with superimposition of myocardium limiting image contrast and impairing quantitative evaluation of the distribution of tracer within the heart; and 2) attenuation of gamma radiation by tissue interposed between the tracer and the detector making quantitative assessment of the distribution of radionuclide within the heart difficult.

Despite these limitations, considerable progress has been made in detecting heterogeneity of perfusion with radionuclides such as thallium-201 and other analogs of potassium injected intravenously.

Positron emission transaxial tomography appears to provide a means for quantitative detection of alterations in metabolism in the heart induced by ischemia of brief duration with externally detectable changes in isolated perfused hearts and intact dogs observed within 30 minutes. Results of sequential studies or comparisons of tomograms obtained with metabolic substrates and vascular markers should permit differentiation between changes secondary to ischemia and changes indicative of infarction even during the early evolution of ischemic insults to the heart. However, precise interpretations of single tomograms will require a great deal of information to characterize the size and variation of lipid pools in normal and ischemic myocardium, and effects of neural and endocrine stimulation of the heart on tomograms obtained by positron emission transaxial tomography. Nevertheless, promising results in experimental animal preparations and patients suggest that positron emission transaxial tomography will provide a useful means for evaluating myocardial ischemia and its sequelae in man.

Acknowledgment

We appreciate the support provided by H. Dieter Ambos, Ms. Barbara Asberry, Mrs. Carol Higgins, and Nizar Mullani, and preparation of the manuscript by Ms. Carolyn Lohman.

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Detection of remote myocardial infarction in patients with positron emission transaxial tomography and intravenous 11C-palmitate.
B E Sobel, E S Weiss, M J Welch, B A Siegel and M M Ter-Pogossian

doi: 10.1161/01.CIR.55.6.853

_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

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