Emission computed tomography with technetium-99m pyrophosphate for delineating location and size of acute myocardial infarction in man

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SUMMARY Emission computed tomography with technetium-99m pyrophosphate was used to delineate the location and estimate the size of myocardial infarcts in 20 patients with documented acute myocardial infarction. Tomography was performed after planar imaging within 2–5 days after the onset of infarction. A series of transaxial, frontal, and sagittal tomograms were reconstructed from 32 views imaged from the left side of the patient’s chest with a rotating gammacamera. Infarct volume was measured from the tomographic images by computerised planimetry and was compared with the cumulative release of creatine kinase MB isoenzyme. The planar images showed discrete myocardial uptake in 13 of the 20 patients and diffuse uptake throughout the cardiac region in the remaining seven. In contrast, the tomographic images clearly delineated discrete myocardial uptake by avoiding confusion of myocardial activity with that of surrounding structures, particularly bones, in all patients. For the 10 patients whose infarct size was assessed by analysis of the creatine kinase MB curve there was a close correlation between infarct volume estimated by tomography and by cumulative creatine kinase MB release. Thus emission computed tomography can provide a three dimensional map of technetium-99m pyrophosphate distribution within the heart and is thus able accurately to localise and estimate the size of myocardial infarcts in man.

Since its introduction into clinical medicine in 1974¹² myocardial scintigraphy with technetium-99m pyrophosphate has been widely used for detecting, localising, and estimating the size of acute myocardial infarcts. Standard planar imaging has, however, some limitations that restrict its clinical application because of the geometric constraints of a two dimensional display. The recent introduction of emission computed tomography provides a complete three dimensional image of the distribution of the tracer.³⁵ This technique has already been applied to thallium-201 myocardial imaging, and some interesting clinical results have been reported.⁶⁸ Furthermore, accurate sizing of acute myocardial infarcts has been carried out with this technique and technetium-99m pyrophosphate in animal models.⁹¹⁰ Nevertheless, there have been few attempts to apply this technique to technetium-99m pyrophosphate imaging in man.¹¹ We therefore report our experience of using emission computed tomography for technetium-99m pyrophosphate myocardial imaging to delineate the location and size of acute myocardial infarcts in man.

Patients and methods

We studied 20 patients (17 men, three women; mean age 60 (range 31–77) years) admitted to our coronary care unit with acute myocardial infarction between January 1982 and February 1983. Acute myocardial infarction was diagnosed if the following three criteria were met: (a) a history of typical chest pain lasting one hour or more; (b) the presence of a characteristic pattern of increase in the serum creatine kinase MB activ-
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Myocardial scintigraphy with technetium-99m pyrophosphate was performed 2–5 days (mean 3.2 days) after the onset of symptoms of myocardial infarction. Images were obtained approximately three hours after an intravenous injection of 15–20 mCi (540–720 MBq) of technetium-99m pyrophosphate using a large field of view gammacamera (Hitachi: Gamma View) equipped with a low energy high resolution parallel hole collimator. Planar views included the anterior, 45° left anterior oblique, and left lateral projections, collecting 600 000 counts for each image. Scintigrams were interpreted by two observers who were unaware of the clinical diagnosis. Radioactivity in the cardiac region was graded on a scale of 0 to 4+ according to the classification described by Parkey et al.² Scintigrams graded 2+ or higher were considered to be positive. In addition, radionuclide uptake was classified as either discrete—if it was localised to one or more myocardial regions not including the left ventricular cavity—or diffuse—if it was present throughout the region of the heart including the left ventricle.¹³

After planar imaging, tomography was performed using a rotating gammacamera with a high resolution parallel hole collimator supported by a gantry (General Electric: Maxi-400 T) interfaced to a digital computer (DEC: PDP 11/60). The camera rotated from a 45° left posterior oblique to a 45° right anterior oblique position of the patient so that data from only the anterior half of the heart were collected. A total of 32 discrete view images—that is, one image every 5.8°—were acquired over 180°.⁵ Each image was acquired for 20 s for a total acquisition time of 11 minutes. Contiguous transaxial tomograms were reconstructed into 12 mm thick multiple slices by a filtered back projection method using a convolution algorithm⁵⁷ without attenuation correction. Each transaxial tomogram was rotated perpendicular to the long axis of the left ventricle. Thereafter, frontal and sagittal tomograms were reorganised from the set of transaxial tomograms so that the frontal and sagittal tomograms nearly corresponded to the short axis and long axis sections of the heart respectively.⁵⁷ The reconstructed images were displayed in a 64 × 64 matrix (Fig. 1).

To estimate infarct volume, we analysed the tomogram in the most appropriate section that showed the uptake transversely, selecting transaxial tomograms in anterior infarcts and frontal tomograms in inferior infarcts. To define the boundary, the mean count

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**Fig. 1 Emission computed tomograms with technetium-99m pyrophosphate in a patient with acute anterior myocardial infarction:** (a) transaxial sections (viewed from below with anterior surface up) imaged from the cranial (left) to the caudal region (right); (b) frontal sections (viewed from left anterior oblique projection) from the apical (left) to the basal region (right); and (c) sagittal sections (viewed from right anterior oblique projection) from the septal (left) to the lateral region (right). Discrete uptake in the anterior myocardial wall is shown by arrows. In the schematic drawings the solid areas represent the damaged regions: r, ribs; s, sternum; v, vertebrae.

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[1] Myocardial emission tomography with technetium-99m pyrophosphate
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density was plotted along 5 to 10 horizontal profiles selected as passing through the infarct edge in each tomogram (Fig. 2a). The mean count at the points of the steepest change in counts across the edges was calculated and subtracted from each image (Fig. 2b). In the resulting image the area of increased tracer uptake was outlined with a light pen and measured by computerised planimetry (Fig. 2c). The total number of pixels in all slices showing increased tracer uptake were added together and multiplied by a size factor (0.432 ml per one pixel) to determine infarct volume. Infarct volume thus obtained was expressed in millilitres. The tomographic images were interpreted independently by two observers without knowledge of the patient’s clinical and laboratory findings. The site of the image abnormality was the same in all cases. The interobserver variation in measuring infarct volume was within 7% and the intraobserver variation within 5%.

A biochemical estimate of the extent of myocardial tissue damage was obtained in 10 patients who were admitted within six hours after the onset of infarction. Serum samples were collected for creatine kinase MB analysis at four hour intervals for 48 hours from the time of admission and every 12 hours for the following 48 hours. Creatine kinase MB isoenzyme activity was separated from sera by diethylaminoethyl-Sephalose column chromatography using minicolumns. Enzyme activity of the column eluate was determined according to Rosalki. A computer was used to generate each serum creatine kinase MB time-activity curve to fit an exponential to the downslope of the curve by the least squares method and to derive an individual disappearance constant of creatine kinase MB from serum for each patient. The cumulative release of creatine kinase MB was calculated using a modification of the original formula of Shell et al., Sobel et al., and Roberts et al. and represents the total amount of creatine kinase MB that would appear in the serum in the absence of enzyme disappearance. Enzyme curves were analysed only in patients whose creatine kinase MB concentrations at the onset of the serum sampling period were within normal limits.

Infarct volume estimated by tomography with technetium-99m pyrophosphate in each patient was compared with the cumulative release of creatine kinase MB by linear regression, and a correlation coefficient was obtained.

Results
The results are summarised in the Table. Of the 20 patients studied, the electrocardiographic site of transmural infarction was anteroseptal in seven, anterolateral in three, anteroseptal with lateral wall involvement in two, and inferior in seven. In the seven patients with an inferior infarct, electrocardiography indicated additional transmural lateral wall involvement in one and posterior wall involvement in two. One patient had a subendocardial infarct. Two had a documented previous myocardial infarct.

The planar images showed uptake of technetium-99m pyrophosphate graded 2+ or higher in the cardiac region in all patients. Thirteen patients had discrete myocardial uptake localised to regions which corresponded anatomically with the electrocardiographic localisation of the infarct on their planar images. The remaining seven patients (five with
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Table  Scintigraphic and enzymatic data

<table>
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<tr>
<th>Case No</th>
<th>Age (sex)</th>
<th>ECG location of MI</th>
<th>Planar uptake pattern</th>
<th>Emission computed tomography</th>
<th>Cumulative CKMB release (IU/l)</th>
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Ant, anterior wall; Sep, septum; Lat, lateral wall; Inf, inferior wall; Post, posterior wall; CKMB, creatine kinase MB isoenzyme.

Infarct volume measured from tomographic images ranged from 10 ml to 108 ml (Table). For the 10 patients in whom enzymatic infarct size was obtained by integration of the completed creatine kinase MB curve there was a close correlation between infarct volume measured by tomography and by the cumulative release of creatine kinase MB (r=0.91, p<0.001, Fig. 5). Five of these 10 patients had inferior infarct and the remaining five had anterior infarct.

Discussion

Because technetium-99m pyrophosphate myocardial scintigraphy directly visualises the acutely infarcted myocardium it has been used to aid in the detection and localisation of acute myocardial infarcts. This technique is of particular value when other clinical and laboratory evidence is inconclusive. In addition to its diagnostic potential, scintigraphy provides prognostic information as well. Many previous studies using conventional two dimensional imaging have shown that well localised radionuclide images of cardiac activity have been consistently correlated with documented regions of acute myocardial infarction. Because of diffuse uptake throughout the left ventricular region the clinical application of this technique is, however, limited when two dimensional imaging is used. Initially, the diffuse pattern of radionuclide uptake was identified in patients with subendocardial myocardial infarction. But this pattern was also noted in significant proportions of
patients with unstable angina,29 30 myocarditis,31 cardiomyopathy,29 32 and even in some patients without apparent heart disease.13 33 In some cases this diffuse pattern may be due to persistent blood pool activity,13 33 which may be mistaken for a positive image with planar imaging. Furthermore, the planar images cannot localise the site of the infarct when they show diffuse uptake.

In the present study tomography improved visualisation of the infarct by clearly separating myocardial activity from that of overlying or underlying structures, particularly bones, and by increasing contrast between infarct and background (Figs. 1, 3, and 4). The tomographic images showed discrete myocardial uptake corresponding to the electrocardiographic site of the infarct in all patients with acute myocardial infarction, including seven with diffuse uptake on the planar images (Fig. 3). Our equipment can reorganise not only transaxial tomograms but also frontal and sagittal tomograms, which greatly assisted the accurate assessment of radionuclide distribution. Thus, emission computed tomography can provide more
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Fig. 4 (a) Planar images and (b) frontal tomograms in a patient with acute inferior myocardial infarction. In the schematic drawing the solid area represents the infarct. The tomograms provided more detailed information on the anatomical extension of the infarct (arrows). r, ribs; s, sternum.

Fig. 5 Correlation between infarct volume estimated by emission computed tomography with technetium-99m pyrophosphate and the cumulative release of creatine kinase MB isoenzyme in 10 patients with acute anterior (●) and inferior (○) myocardial infarction.

detailed three dimensional information on the anatomical location of infarcts. It may also improve the specificity of the diffuse pattern of uptake, although this subject requires further study. Technetium-99m pyrophosphate myocardial imaging has also been valuable in estimating infarct size. Previous studies in animals have shown excellent correlations between scintigraphic estimates of infarct size and histological infarct weight. Several problems are, however, encountered in estimating infarct size with planar myocardial imaging in man. Probably the most fundamental problem results from the two dimensional representation of a three dimensional structure. Nevertheless, good correlations have been reported between the area of radionuclide uptake and peak creatine kinase activity, and cumulative creatine kinase release, and precordial electrocardiographic mapping measurement in patients with anterior infarcts. On the other hand, a weaker correlation has been found in patients with inferior infarcts because the entire area of the inferior infarct cannot be viewed from in front in the standard planar projections. These limitations can be overcome with tomographic imaging techniques. Initial animal studies using a rotating gammacamera system reported an excellent result in all locations of experimental infarcts. Lewis et al used rotating slanthole tomography for three dimensional sizing of experimental infarcts and obtained satisfactory results. Recently, Holman et al have applied emission computed tomography with a multiple scanning detector system to radionuclide imaging in man and reported a
significant relation between infarct size estimated by this tomographic technique and the patient's prognosis.\textsuperscript{11}

In the present study we used emission computed tomography with a rotating gammacamera to measure infarct volume in patients with acute myocardial infarction and obtained a close correlation between infarct volume measured from tomographic images and cumulative creatine kinase MB release (Fig. 5). Since the images are effectively three dimensional inferior infarcts could be equally accurately sized by this technique. Thus emission computed tomography can extend the infarct sizing capability of radionuclide imaging to include inferior infarcts as well as anterior infarcts in man.

With single photon emission computed tomography, another problem is the inability to correct fully for attenuation, which may produce image distortion. It has been pointed out, however, that correction for attenuation is much less of a problem when the volume occupied by the radioactivity rather than the absolute amount of activity present in that volume is measured.\textsuperscript{4,11} In addition, the extent of infarction is more strongly related to the distribution of technetium-99m pyrophosphate than to the concentration of the tracer because its concentration in necrotic myocardium is dependent on flow.\textsuperscript{25,42,43} This fact may be an advantage in emission computed tomography in sizing infarcts. We, therefore, analysed the distribution of radionuclide uptake to measure the extent of infarction. We believe that emission computed tomography can provide geometrically reliable three dimensional sections of radionuclide uptake distribution.

In summary, this preliminary clinical study of patients with acute myocardial infarction indicated the feasibility of emission computed tomography for assessing technetium-99m pyrophosphate myocardial uptake in man. The multiaxial tomograms were of good quality and were acquired quickly enough for clinical purposes. This technique can lead to accurate quantification as well as improved localisation of acute myocardial infarction. Since it uses commercially available tracers it appears to be promising for widespread clinical application.

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References


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