

MYOCARDIAL INFARCT IMAGING USING ^{99m}Tc TECHNETIUM PYROPHOSPHATE AND ^{99m}Tc METHYLENE DIPHOSPHONATE: A CLINICAL EVALUATION

M. PARAMSOTHY K.T. SINGHAM

INTRODUCTION

THE use of radionuclides in elucidating ischaemic heart disease is a recent development. Since Bonte *et al.* (1974) first described the concentration of ^{99m}Tc Technetium labelled phosphates in acutely damaged myocardium numerous radio-pharmaceuticals, techniques, experience and data have accumulated in the non-invasive imaging methods for the direct visualisation of acute myocardial infarction. The radioisotopes may be used dynamically to provide information about the size of cardiac chambers, the ventricular ejection fraction, ventricular wall motion or regional perfusion of the myocardium. The radioisotope is injected rapidly as a bolus into a peripheral vein and its passage through the heart is recorded with a scintillation gamma camera interfaced with a data processor or computer system. Alternatively isotopes may be used for static imaging after equilibration and intracellular radioactive uptake occurs, displaying areas of normal, ischaemic or infarcted myocardium. Both techniques avoids cardiac catheterisation and are non-invasive, cheap, sensitive, safe, reproducible and repeatable. If a mobile gamma camera is available it can be done at the bedside and becomes extremely useful in the intensive care where the physician has to continuously monitor for changing cardiac physiology in ill cardiac patients. These techniques provide for the early diagnosis, sizing of the infarcted area, incrimination of the coronary arteries affected, follow-up studies, and monitoring effect of therapy.

Early diagnosis of myocardial infarction may be a problem. Various clinical conditions may obscure or mimic the clinical picture. Clinical, electrocardiographic and serum enzyme studies are sometimes insufficient to allow a definite appraisal; the characteristic pattern of chest pain may be absent (Papp, 1952) and atypical chest pain, so often present, only underlines the practical difficulties of differentiating the pain arising from acute myocardial infarction from other non-cardiac conditions. Situations known to give rise to uninterpretable electrocardiographic traces include the presence of previous myocardial damage caused by infarction or cardiac surgery, aberrant conduction, paced rhythms, or pre-excitation syndromes. In addition, serum enzyme measurement may be unreliable and false positive readings occur frequently (Savranoglu *et al.*, 1959; Sobel and Shell, 1972). Borderline results may maintain rather than eliminate the diagnostic problem. Doubts of myocardial infarction may also occur with ST segment changes or T-wave inversion without serum enzyme elevation or serum enzyme elevation without Q-waves especially after cardiac surgery when the serum enzyme concentrations are raised because of tissue trauma. The value of another specific and diagnostic technique which is safe, reproducible, repeatable and non-invasive is thus evident.

The two main approaches to acute myocardial infarct imaging consist of (1) the utilisation of potassium analogues, mainly ^{201}Tl Thallium (Tl) as thallos chloride and (2) the utilisation of ^{99m}Tc labelled radio-pharmaceuticals, mainly as ^{99m}Tc pyrophosphate.

^{201}Tl Thallium and the other potassium analogues are taken up by the normal myocardium, so that an infarct of any duration or a region of hypoperfusion is present as an area of absent or reduced radioactivity ("cold spot") whereas ^{99m}Tc labelled phosphates are taken up by damaged tissue so that an acute infarct is shown as a

M. Paramsothy M.B.B.S. (Mal), M.R.C.P. (UK)
Division of Nuclear Medicine
Department of Radiology
Faculty of Medicine, University of Malaya

K.T. Singham M.B.B.S. (Mal), M.Med (S'pore)
M.R.C.P. (UK), F.R.A.C.P.
Dept. of Medicine, University of Malaya

positive image ("hot spot"). The main advantage of ^{201}Tl imaging is that accurate diagnosis can be made within 6 hours of acute episode (Wackers *et al.*; 1976). Exercise ^{201}Tl myocardial scintigraphy is very sensitive and provides prognostically significant information about specific coronary lesions providing the ability to distinguish regions of myocardial ischaemia from fixed necrosis which is invaluable to surgeons planning myocardial revascularisation by coronary artery by-pass graft (CABG) surgery. However, it is extremely expensive and serial imaging of the patient is undesirable because of cost, dosimetry and long biological half-life characteristics. About one third of subendocardial lesions are not visualized (Pitt and Straus, 1976) and the negative ("cold area") rather than positive image ("hot area") of the infarct may provide some difficulties for interpretation.

With $^{99\text{m}}\text{Tc}$ -labelled pyrophosphate imaging accurate diagnosis can be made 24 hours after the acute episode with a false negative rate of less than 4 per cent (Parkey *et al.*; 1977).

Serial imaging of the same patient is possible, the radio-pharmaceutical being relatively cheap, and the dosimetry and biological half-life characteristics allow for daily images. Subendocardial infarcts can be diagnosed though small lesions may be missed and the positive ("hot area") rather than negative ("cold area") images makes interpretation less difficult: An old infarct can be differentiated from a recent one since only the latter will concentrate these radiopharmaceuticals. However, activity in the bony structures ($^{99\text{m}}\text{Tc}$ -labelled phosphates are bone imaging agents) may cause difficulties in interpretation and false positive images occur in about 10-15 per cent of patients.

A number of $^{99\text{m}}\text{Tc}$ -labelled radiopharmaceuticals are now available for acute infarct scanning e.g. $^{99\text{m}}\text{Tc}$ -tetracycline, $^{99\text{m}}\text{Tc}$ -glucoheptonate, $^{99\text{m}}\text{Tc}$ -dimercapto succinic-acid, $^{99\text{m}}\text{Tc}$ -pyrophosphate ($^{99\text{m}}\text{Tc}$ -PYP), $^{99\text{m}}\text{Tc}$ -methylene diphosphonate ($^{99\text{m}}\text{Tc}$ -MDP), $^{99\text{m}}\text{Tc}$ -ethyl-hydroxy-diphosphonate and $^{99\text{m}}\text{Tc}$ -imidodiphosphonate. $^{99\text{m}}\text{Tc}$ -pyrophosphate is the most commonly used agent but the new preparation $^{99\text{m}}\text{Tc}$ -imidodiphosphonate has now been used experimentally and clinically claimed to be superior and as the agent of choice (Ell *et al.*; 1978; Joseph *et al.*; 1978).

In addition to the traditional means of

diagnosis of acute myocardial infarction (clinical, electrocardiography and serum enzyme changes) the value of another specific and diagnostic technique in the early diagnosis of this condition is evident. This paper describes experience with $^{99\text{m}}\text{Tc}$ -stannous pyrophosphate ($^{99\text{m}}\text{Tc}$ -PYP) and $^{99\text{m}}\text{Tc}$ -methylene diphosphonate ($^{99\text{m}}\text{Tc}$ -MDP) myocardial imaging and its purpose is to clarify to what extent this investigation fulfils the above mentioned criteria.

MATERIALS AND METHODS

Patients admitted to the coronary care unit with suspected or proven myocardial infarction were imaged using an Ohio Nuclear Gamma Scintillation Camera Sigma 400 with a 10 inch diameter crystal detector and Differential Uniform Field Correction (DUFC). A low energy (140 Kev) high resolution 16,000 hole parallel hole collimator was used. The patients were brought to the Nuclear Medicine Unit for imaging when they were clinically stable. Each scintiscan was performed 1 hour after intravenous injection of 15 mCi of either $^{99\text{m}}\text{Tc}$ -PYP or $^{99\text{m}}\text{Tc}$ -MDP and routine anterior, left anterior oblique, and left lateral views were taken. Additional right anterior oblique view in some patients were obtained. For each image 400,000 counts were collected and took about 3 to 4 minutes. The imaging time for 3 views was approximately 15 minutes. Pictorial documentation was made on polaroid films. The images were rated 0 to 4 using the method of Parkey *et al.* (1974) and this depended on the activity produced by myocardial uptake of the radionuclides. 0 represents no activity; +1 questionable activity where cardiac activity cannot be distinguished from general tissue and blood background activity; +2 definite but faint activity over myocardium but less than uptake by bone; +3 and +4 represents increasing degrees of activity within the infarct, +3 being uptake equal to the uptake observed in sternum and ribs and +4 being greater than neighbouring bone activity (sternum and ribs). In this study 0 and +1 were considered as negative and grades +2 to +4 as positive for myocardial damage. No adverse reaction to the injection of the radiopharmaceutical or from the imaging process itself was noted in any patient. In addition every patient underwent daily 12 lead electrocardiograms and daily estimation of creatinine phosphokinase, aspartate transaminase and hydroxybutyric dehydrogenase.

TABLE I
PATIENT DATA

No.	Age/ Sex	Previous I.H.D.	E C G	Enzymes	Scan	Interval between onset and scan [days]	Complication
1.	53 M	Angina	Recent anterosep- tal MI	Raised	+ 4 positive anteroapical	3	—
2.	51 M	Yes with LVF	Unstable angina	Borderline rise	+ 3 positive lower anterior	3	Vent. ectopics C.C.F.
3.	62 F	Yes	Anterolateral sub- endocardial infarct	Borderline rise	+ 3 positive anterolateral	3	C.C.F. with A.F.
4.	46 M	MI	Anteroseptal MI	Borderline rise	+ 2 anteroseptal	1	—
5.	37 F	Primary arteritis unstable angina	Anteroseptal MI persistent S.T. elevation in V ₁ -V ₅	Raised	+ 4 anteroseptal persistent + 3 positive antero- septal activity	7	Ventricular aneurysm
6.	41 M	Angina	Anterior MI	Raised	+ 2 positive anterior	3	—
7.	76 M	—	Inferior MI	Raised	+ 3 positive inferior	4	—
8.	7 M	Hypercholesterol- emia MI	Inferior MI	Raised	+ 3 positive inferior	3	—
9.	68 M	—	Inferior MI	Raised	+ 4 positive inferior	2	Aberrant conduction transient bradycardia and nodal rhythm

TABLE 1
PATIENT DATA (Cont'd)

No.	Age/ Sex	Previous I.H.D.	E C G	Enzymes	Scan	Interval between onset and Scan [days]	Complications
10.	42 M	—	Unstable angina	Borderline rise	+3 positive anterior	3	—
11.	44 M	MI with LVF. Ventaneurysm with resection done. Persistent ST elevation in V leads	Previously abnor- mal? recent MI	Borderline rise	+3 anterior late- ral repeat scan 7 days later nega- tive	3	LVF
12.	54 M	—	Unstable angina	Borderline rise	+1 (negative)	14	—
13.	48 F	MI persistent ECG changes	Previous abnor- mal ECG? recent MI	Normal	+3 positive anteroseptal	9	CCF
14.	74 M	MI	Normal	Borderline rise	+1 (negative)	8	—
15.	54 F	MI	Unstable angina	Raised	0	3	—
16.	32 F	CHB	Anteroseptal MI CHB	Raised	0(MDP)	19	—
17.	53 M	Hypercholesterol- emia	Unstable angina	Raised	0	6	nodal rhythm with tachybrady arrhythmia. Sick sinus syndrome
18.	53 M	MI	Anteroseptal MI	Raised	+1 (negative)	—	—

Legend: MI = myocardial infarction
LVF = left ventricular failure

IHD = ischaemic heart disease
CCF = congestive cardiac failure

ECG = electrocardiogram
CHB = complete heart block

TABLE II
^{99m}Tc-PYP AND ^{99m}Tc-MDP SCAN RESULTS FROM
18 INVESTIGATED PATIENTS

Diagnosis	No. Cases	Positive Scan	Negative Scan	Sensitivity
Transmural infarction) PYP	7(39%)	6	1	85%
) MDP	2(11%)	1	50%
Subendocardial infarction) PYP	1 (6%)	1	0	100%
) MDP	0 (0%)	0	-
Unstable angina) PYP	3(16%)	2	1	66%
) MDP	2(11%)	0	-
Doubtful diagnosis) PYP	1 (6%)	1	0	-
) MDP	2(11%)	2	1
Patient total) PYP	12			
) MDP	6		

TABLE III
ANALYSIS OF ^{99m}Tc-PYP AND ^{99m}Tc-MDP SCANS AND
ENZYME RESULTS IN PATIENTS STUDIED

Diagnosis [ECG]	^{99m} Tc-PYP	^{99m} Tc-MDP	Total No. of Cases	Positive Enzymes	Borderline Enzymes	Negative Enzymes
Transmural infarction) +ve scan	6	1	7	6	1	0
) -ve scan	1	1	2	2	0
Subendocardial infarction) +ve scan	1	0	1	0	1	0
) -ve scan	0	0	0	0	0
Unstable angina (accelerated angina preinfarction syndrome)) +ve scan	2	0	2	0	2	0
) -ve scan	1	2	3	2	1
Previously abnormal electrocardiogram electrocardiogram) +ve scan	1	1	2	0	1	1
) -ve scan	0	0	0	0	0
Normal electrocardiogram) +ve scan	0	0	0	0	0	0
) -ve scan	0	1	1	0	1

To investigate the possibility of false positive myocardial imaging 50 patients referred for whole body bone scanning with a variety of non-cardiac conditions also underwent myocardial imaging 1 hour after intravenous injection of the same dose of the radionuclides. The patients' clinical data, serum enzyme result, electrocardiogram and the side and grading of radioactivity and interval between chest pain and imaging is summarized in Table I. Patient population consisted of 13 males and 5 females with age ranging from 27 to 76 years old. The mean time from onset of acute chest pain to imaging is 6 days (range = 1-19 days). In 12 patients ^{99m}Tc -PYP while in 6 patients ^{99m}Tc -MDP were used.

9 patients (50 per cent of all admissions) were diagnosed on the basis of the electrocardiogram to have transmural myocardial infarction (McConahay *et al*; 1970). Of these 7 patients had a positive scan and 2 patients had a negative scan: sensitivity of detection - 78 per cent (Table II). The 2 patients with negative scans were imaged at 17 and 19 days after infarction, and it is possible that earlier imaging would have been positive. 1 patient (6 per cent of admissions) was judged to have subendocardial infarction (Table I). She had a positive scan: sensitivity of detection - 100 per cent and borderline enzyme rise. Of the 9 patients with transmural infarction 8 had positive enzyme rises while 1 had borderline enzyme rise.

5 patients (28 per cent of admissions) were considered to have unstable angina (accelerated angina, preinfarction syndrome). Of these only 2 had positive scans with imaging done at 3 days after onset of acute chest pain: sensitivity of detection - 40 per cent. Both had borderline enzyme rises. Of the remainder 3 patients with negative scans, 2 had positive enzymes rises with

imaging done at 3 and 6 days from onset of chest pain; 1 patient had borderline enzyme rise with imaging done at 14 days from onset of chest pain.

The remaining 3 patients (16 per cent of admissions) presented with doubtful diagnosis and 2 had abnormal electrocardiograms resulting from conduction defects or previous ischaemic damage rendering electrocardiographic diagnosis impossible. These two had positive scans with negative or borderline enzyme rises and repeat scans 7 days later were negative; one of them had previous massive infarction and resection of ventricular aneurysm 3 years previously presented with mild left ventricular failure but had no chest pain. The remaining 1 patient who had angina pectoris for past 18 years and myocardial infarction 8 years ago presented with chest pain but had a normal ECG and borderline enzyme rise. The scan was negative but was done at 8 days after the onset of chest pain and it is possible that an earlier imaging would have been positive. Further analysis of these results is presented in Table III.

One of the patients with acute transmural infarction had primary arteritis for the past 10 years, angina pectoris for the past 5 months and accelerated angina for 1 month prior to admission. She presented with severe retrosternal pain, and electrocardiogram indicated acute anteroseptal infarction. Positive enzyme rise and +4 positive scan were obtained. Repeat electrocardiograms 6 months later showed persistence of ST elevation in V1-V5 leads and a repeat scan at this time still showed +3 positive anteroseptal activity indicating a ventricular aneurysm.

Table IV shows the results of myocardial images obtained with the group of 50 patients

TABLE IV
50 PATIENTS WITH NON CARDIAC PATHOLOGY REFERRED FOR WHOLE BODY BONE SCANNING

Isotope	No. of Patients	+4 activity image	+3 activity image	+2 activity image	+1 activity image	0 activity
^{99m}Tc -PYP	25	0	0	0	2	23
^{99m}Tc -MDP	25	0	0	0	1	24

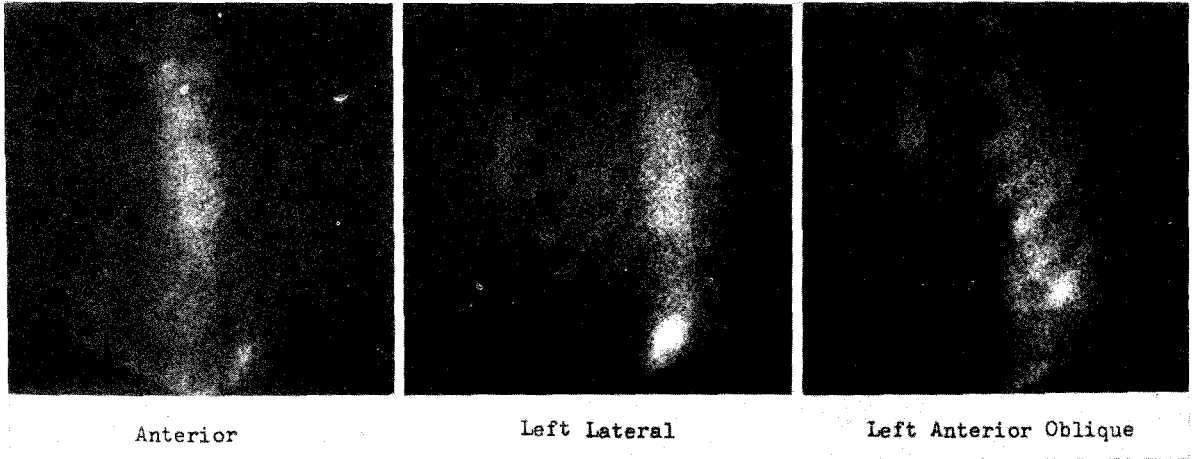


Figure 1. M. Paramsothy et al. Normal ^{99m}Tc -PYP Scan.

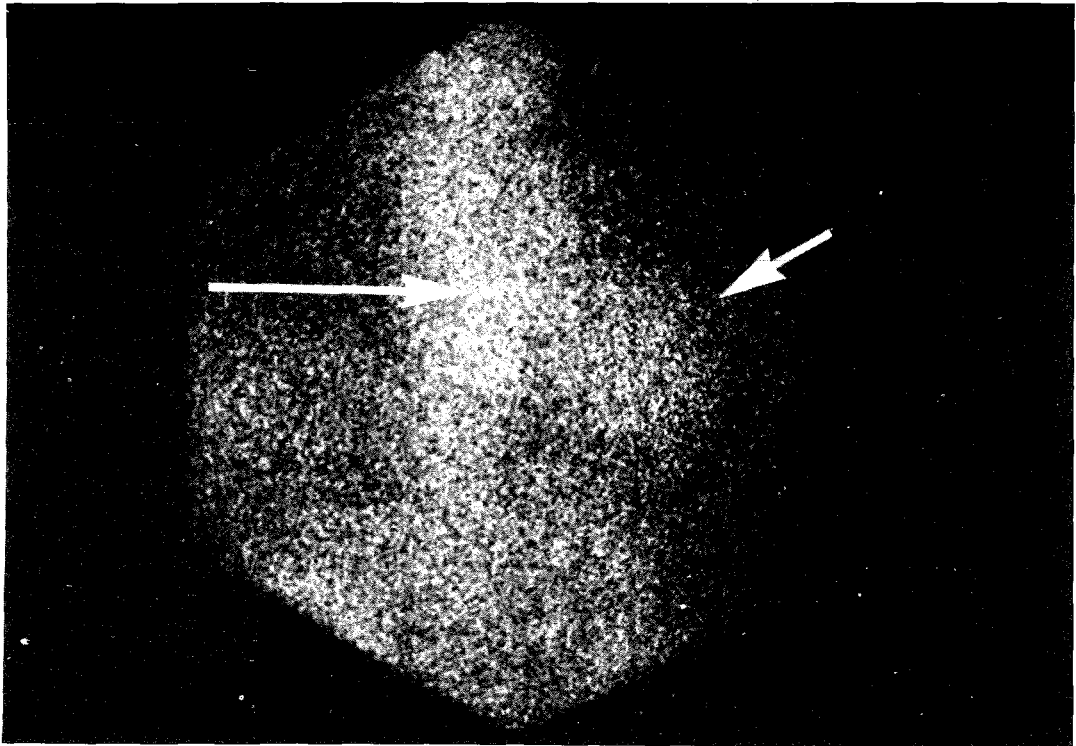


Figure 2. M. Paramsothy et al. ^{99m}Tc -MDP Scintigram [anterior view] of anteroseptal infarct.

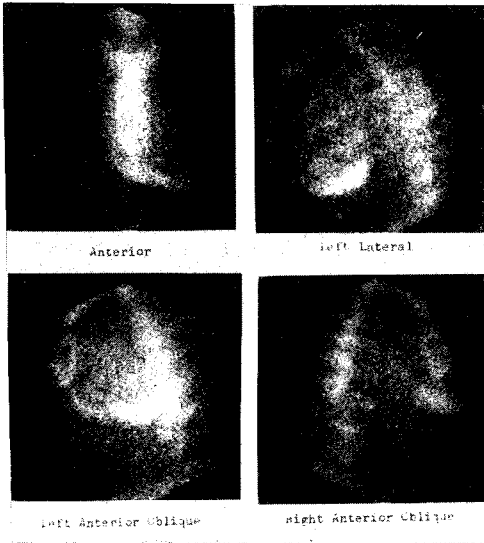


Figure 3. M. Paramsothy et al. A typical ^{99m}Tc -PYP Scan of a patient with an inferior myocardial infarction.

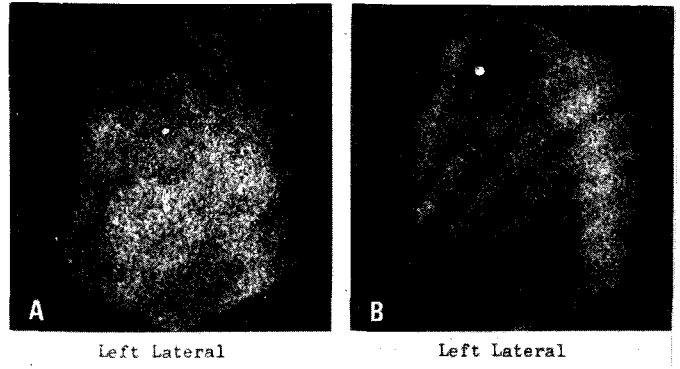


Figure 4. M. Paramsothy et al. Serial ^{99m}Tc -PYP Scan.



Figure 5. M. Paramsothy et al. Typical Scan of a subendocardial infarct.

with no history of heart disease referred for whole body scanning for a variety of reasons but mainly for the detection of bony metastasis.

In our study with ^{99m}Tc -PYP and ^{99m}Tc -MDP the apparent low sensitivity of detection with ^{99m}Tc -MDP is probably due to the fact that most of the patients imaged with this radiopharmaceutical had a long interval time between chest pain and imaging (varied from 3 to 19 days). In relation to quality of images both radiopharmaceutical appeared to be similar in their ability.

Fig. 1 to 5 represents the spectrum of scintiscans obtained with this technique in this series of patients.

DISCUSSION

Imaging of acute myocardial infarct can be performed both with radiopharmaceuticals that visualize the normal myocardium (42K, 43K, 81Rb, 86Rb, 129Cs, 131Cs, 201Tl) and with those that visualize the abnormal myocardium (^{99m}Tc -tetracycline, ^{99m}Tc -glucoheptonate, ^{99m}Tc -phosphates). Each group of radiopharmaceuticals has advantages and disadvantages and has been discussed previously.

^{201}Tl (^{201}Tl) with its 74-hr half life and 81-Kev x-ray and high myocardial extraction efficiency (greater than 80 per cent) and more suitable imaging properties has now become established as the imaging agent of choice in the evaluation of patients with ischaemic heart disease. Exercise ^{201}Tl myocardial scintigraphy provides prognostically significant information about specific coronary lesions and the necessary functional equivalent to coronary arteriogram and is probably the most sensitive method for the detection of myocardial ischaemia. It is more sensitive than S-T segment depression on the exercise ECG (Wainwright and Maisey, 1978).

The ability to distinguish regions of myocardial ischaemia from fixed necrosis using ^{201}Tl -scintigraphy is invaluable to surgeon planning myocardial revascularization by CABG surgery and this can be accomplished more economically by abandoning separate rest and stress injections and instead re-imaging the myocardium several hours after initial administration of ^{201}Tl when significant intramyocardial redistribution of tracer has occurred. At present the three most

clinically relevant uses of this technique are (1) Detection of specific coronary artery disease e.g. left anterior descending (LAD) disease; especially in public transport personnel such as airline pilots and in patients without symptoms but strongly positive exercise electrocardiograms. (2) Distinction of myocardial necrosis from myocardial ischaemia e.g. in the preoperative assessment of CABG patients. (3) Follow up of CABG patients - non-invasive detection of graft closure. There are other valuable and potential applications but remain to be completely explored.

^{201}Tl myocardial scintigraphy should be the initial method of choice in the assessment of ischaemic heart disease if this technique is available. It can be suitably combined with ^{99m}Tc -multiple gated acquisition (MUGA) scintigraphy as one sequential procedure in individual patients. The information obtained by both methods is complimentary as perfusion defects cause ventricular wall motion and resulting pump function abnormalities. It is invaluable in the coronary care unit where the cardiologist need to monitor patient's cardiac function continuously and evaluate therapy instituted. The chief disadvantages of ^{201}Tl are its cost and its restricted availability. (^{201}Tl) is cyclotron produced and has a half life of 74-hrs). Daily serial imaging of the same patient is undesirable because of high cost, dosimetry and long biological half-life characteristics. An old infarct cannot be distinguished from a recent one.

The advantage of ^{99m}Tc -labelled phosphates imaging are accurate diagnosis can be made 24 hours after the acute episode with a false negative rate of less than 4 per cent (Parkey *et al*, 1977). Serial daily imaging of the same patient is eminently possible as the radiopharmaceutical is relatively cheap, and the dosimetry and biological half-life characteristics allow for daily images (70 mRad for ^{201}Tl against 15mRad/mCi, for ^{99m}Tc whole body). An old infarct can be distinguished from a recent one since only the latter will concentrate these radiopharmaceuticals. These substances are thought to be bound with the calcium ion of hydroxyapatite crystals in or near the mitochondria of damaged cells and accumulate mainly in the tissue at the edge of the infarct. However, the sub-cellular distribution experiments by Dewanjee and Kahn (1976) did not substantiate this theory and suggested that the uptake of technetium chelates in myocardial infarcts may be due to the formation of

polynuclear complexes with denatured macromolecules rather than to the deposition of calcium in mitochondria. This would also explain why other technetium chelates such as ^{99m}Tc -labeled tetracycline and glucoheptonate have some ability to concentrate in myocardial infarct although they are in no way considered bone scanning agents. The uptake of these radiopharmaceuticals by damaged myocardial tissue produce a positive image ("hot spot") without interference from the normal myocardium. Images of high technical quality are obtained by using radiopharmaceuticals of high signal to noise ratio (uptake in infarcted myocardium/uptake in normal myocardium). The signal to noise ratio for ^{99m}Tc -pyrophosphate and ^{99m}Tc -methylene diphosphonate is 5:1. Recently a new bone imaging agent ^{99m}Tc -imidodiphosphonate (^{99m}Tc -IDP) with a signal to noise ratio of 20:1 has been used experimentally and clinically and claimed as the agent of choice (Ell *et al*, 1978 and Joseph *et al*, 1978). Minimum interference from the blood pool background activity is important in producing high quality images, and this is dependent on the blood clearance rates of the radiopharmaceuticals. The percentage of 5-minute post-injection sample at 1 hr for ^{99m}Tc -MDP = 25%; ^{99m}Tc -PYP = 39%; and ^{99m}Tc -IDP = 30% (Ell *et al*, 1978). Activity in the bony structures is minimized if imaging is performed 1 hr after intravenous injection. Contrast enhancement by computer processing with background and rib subtraction techniques make the image even better seen. This may be necessary in about 10% of cases especially of infarctions in the posterior wall which have superimposed rib structure seen. However uptake in normal bone is not considered a disadvantage for it allows exact location of the sternum and xyphoid and the rib arches, this being an excellent anatomical reference system for the interpreting observer. Throughout this investigation it was consistently felt that both for the nuclear medicine physician and the cardiologist the interpretation of these images is much easier and perhaps, therefore, more accurate.

If high sensitivity of detection of myocardial infarction is to be achieved with this technique serial scanning is mandatory. Two patients had clinical and electrocardiographic evidence of transmural infarction and positive enzymes rises but negative scans. Both patients, however were

scanned at 17 days and 19 days after the acute event, clearly too late and these two cases should not be counted as true false negatives. The optimal time for imaging is between 24 and 48 hrs after the acute event. A positive result with a technetium scan may usually be obtained up to 6 days after acute episode; after this the image begins to fade and this is a most useful feature of positive myocardial infarct imaging as it allows the differentiation of an old infarct from a recent one (Ell *et al*, 1978). In our series one patient had previous myocardial infarction with aneurysm from anterolateral wall resected and presented with mild left ventricular failure but no chest pain; and another patient with previous infarction presented with chest pain. Both patients had persistent electrocardiographic changes since the previous episode and negative or borderline enzyme rise in this episode and electrocardiographic diagnosis of recent infarction was problematic. Both patients had +3 positive scans and repeat scans 7 days later were negative, confirming recent reinfarction. (Fig. 4). Infrequently the positive image persists for weeks or months and could be a problem in interpreting subsequent scintiscans in these patients who are at risk of reinfarction. (Parkey *et al*, 1977). Persistent S-T elevation in V1-V5 electrocardiographic leads and persistent positive scans could suggest ventricular aneurysm. One patient in our series who had a 10 year history of primary arteritis, 5 months history of angina pectoris, and 1 month history of accelerated angine had an acute antero-septal infarction with ECG changes and a +4 positive scintiscan. Repeat studies 6 months later showed persistent ST elevation on V1-V5 leads and +3 positive antero-septal activity scintiscans indicating an antero-septal ventricular aneurysm. Thus meaningful interpretation is possible by correlation with the clinical status and comparison with previous scintiscans. Baseline myocardial scans should be considered for patients with symptomatic coronary artery disease.

Assessing the image is subjective and the grading 0 to +4 using the method of Parkey *et al* (1974) refers to visibility of the image and not to its size. Assessing the size of an infarct by technetium scans is not reliable as uptake depends on blood flow and is not proportional to the volume of the infarct. Recent work indicate increased localization of the phosphate com-

pounds in areas of reduced coronary flow implying that some perfusion is required for the tracer to be extracted and positive uptake does not necessarily mean cell death or irreversible injury. In our series out of the 5 patients diagnosed to have unstable or accelerated angina 2 had +3 positive scintiscans at 3 days after the onset of acute chest pain. Of the remaining 3 patients with negative scans 2 had initial scans done at 6 and 14 days after onset of acute chest pain and this delay could possibly have affected the imaging. Radioactive uptake in unstable angina has been also documented elsewhere (Donsky *et al*, 1976). Myocardial uptake has also been observed in patients with stable angina, valve calcification, cardiomyopathy, after direct current transthoracic shock therapy and on dialysis with secondary hyperparathyroidism and uremic pericarditis.

Unequivocally positive scans are present in about 90-95% of ECG proved transmural infarcts; where a localised area of uptake is seen (Fig. 2, 3); in subendocardial infarction the images are less intense and usually diffuse (Fig. 5), so that necrosis can seldom be localised anatomically. In our series positive scans in ECG proved transmural infarcts were obtained in 78% of cases. However this does not reflect the true sensitivity of detection as in both patients with negative scans the imaging were done at 17 and 19 days after the acute event. Fewer than 4% false negative results occur with optimal timing of imaging (1-3 days after the onset of infarction) and performance of serial imaging (Parkey *et al*, 1977). A localised zone of intense activity in the anterior wall is seen on anterior infarction (Fig. 2) and plate-like or band-shaped activity along the inferior or diaphragmatic wall of myocardium occurs in inferior wall infarction (Fig. 3). In our series the lower rate of positive scans using ^{99m}Tc -MDP as compared to ^{99m}Tc -PYP does not reflect its true sensitivity of detection as many of the patients imaged with this radiopharmaceutical had long time intervals between onset of event and time of imaging; in addition lesser number of patients were scanned with ^{99m}Tc -MDP than ^{99m}Tc -PYP. Both the imaging agents have similar signal to noise ratio (5:1) though ^{99m}Tc -MDP images at 1 hr have significantly less background activity. In majority of patients, the diagnosis of myocardial infarction could be made on the basis of well established criteria. A high sensitivity (85%) was achieved with ^{99m}Tc -PYP

scanning in patients considered to have transmural infarction. The one patient with subendocardial infarction (100%) had positive scan. 2 of the 9 patients with transmural infarction and the 1 patient with subendocardial necrosis had only borderline enzyme increases and may represent the hinterland between infarction, and ischaemia without infarction, and illustrates the use of technetium scans being sufficiently sensitive to show myocardial damage undetected by enzyme elevation. In these 3 cases the technetium scans were considered to be of special diagnostic value.

3 patients (16%) presented with a doubtful diagnosis either because of previous abnormal and uninterpretable electrocardiograms or because of normal electrocardiogram (Table III). The 2 patients with previous abnormal electrocardiograms had positive scans with normal or borderline enzyme levels. Repeat scans 7 days later were negative and it was considered justifiable to classify these patients as infarcted or having severe ischaemia. In the 1 patient with normal electrocardiogram and borderline enzyme levels the negative scintiscan was of value in excluding infarction. Thus in all these 3 cases the ^{99m}Tc -phosphates scans were of considerable diagnostic value. False positive images occur in about 10-15% of patients and may be secondary to delayed clearance of radiotracer from cardiac blood pool e.g. in renal diseases; breast tumours; functioning breast parenchyma in premenopausal females; healing rib fractures or other rib abnormalities, and carcinoma. In our group of 50 patients with noncardiac pathology none had positive myocardial images (Table IV).

CONCLUSION

In assessing the role of technetium-labelled phosphates myocardial scanning the conventional methods of diagnosis of infarction has to be considered. Doubt whether infarction has occurred arises most often in patients with old infarction with persistent ECG changes, left bundle branch block, subendocardial infarction and after cardiac operation when the serum enzymes concentration are raised because of tissue trauma. It will be in these cases the physicians could find the scintigram useful in establishing myocardial ischaemic necrosis. It is a safe, simple, cheap, reproducible, repeatable, non-invasive, and sensitive test (95% sensitivity of detection). Gamma cameras are expensive and

few medical units have them. For reliable results care in technique and caution in interpretation should be exercised. ^{201}Tl myocardial perfusion scintigraphy is probably the most sensitive test for ischaemic heart disease and when combined with $^{99\text{m}}\text{Tc}$ -MUGA scintigraphy which provides information about wall motion, cardiac chambers, ejection fraction is invaluable in coronary care unit. However, $^{99\text{m}}\text{Tc}$ -labelled phosphates myocardial scintigraphy is still the more widely used method.

SUMMARY

Radioisotope detection and localisation of myocardial infarction is discussed. Its clinical value and pitfalls are also discussed. The clinical application of this safe, simple, sensitive, repeatable, reproducible and non-invasive method in Malaysian patients performed during the period October 1978 to April 1979 at the University Hospital is reviewed. The main value of $^{99\text{m}}\text{Tc}$ -labelled phosphate scan is in the demonstration and localisation of recent myocardial infarctions in patients where the electrocardiogram or serum enzymes changes are unhelpful.

REFERENCES:

- Bonte, F.J., Parkley, R.W., Grahm, K.d., Moore, J., and Stokely, E.M. (1974). A new method for radionuclide imaging of myocardial infarcts. *Radiology*, **110**, 473-474.
- Dewanjee, M.K., Kahn, P.C. (1976). Mechanism of localization of $^{99\text{m}}\text{Tc}$ -labeled pyrophosphate and tetracycline in infarcted myocardium *J. Nucl. Med.*, **17**, 639-646.
- Ell, P.J., Langford, R., Pearce, P., Lui, D., Elliott, A.T., Woolf, N., and Williams, E.S. (1978). $^{99\text{m}}\text{Tc}$ -Imidodiphosphate: A superior radiopharmaceutical for in vivo positive myocardial infarct imaging. I: Experiment data. *Br. Heart J.*, **40**, 226-233.
- Joseph, S.P., Ell, P.J., Ross, P., Donaldson, R., Elliott, A.T., Brown, N.J.G., Williams, E.S. (1978). $^{99\text{m}}\text{Tc}$ -Imidodiphosphate: a superior radiopharmaceutical for in vivo positive myocardial infarct imaging. II: Clinical data. *Br. Heart J.*, **40**, 234-241.
- McConahay, D.R., McCallister, B.D., Hallermann, F.J., and Smith, R.E. (1970). Comparative quantitative analysis of the electrocardiogram and the vectocardiogram; correlations with the coronary arteriogram. *Circulation*, **42**, 245-259.
- Papp, C. (1952). Acute cardiac infarction without pain. *Br. Heart J.*, **14**, 250-259.
- Parkey, R.W., Bonte, F.J. and Meyer, S.L. (1974). A new method of radionuclide imaging of acute myocardial infarction in humans. *Circulation*, **50**, 540-546.
- Parkey, R.W., Bonte, F.J., Buja, L.M., Stokely, E.M., and Willerson, J.T. (1977). Myocardial infarct imaging with technetium-99m phosphates. *Seminars Nucl. Med.*, **7**, 15-28.
- Pi, H.B., and Strauss, H.W. (1976). Myocardial imaging in the non-invasive evaluation of patients with suspected ischaemic heart disease. *Am. J. Cardiology*, **37**, 797-806.
- Savranoglu, N., Boucek, R.J., and Casten, G.G. (1959). The extent and reversibility of myocardial ischaemia in dogs. *Am. Heart J.*, **58**, 726-731.
- Sobel, B.E., and Shell, W.E. (1972). Serum enzyme determinations in the diagnosis and assessment of myocardial infarction. *Circulation*, **45**, 471-482.
- Wackers, F.J. Th., Sokole, E.B., Samson, G., Schoot, J.B. van der, Lie, K.I., Liem, K.L., and Wellens, H.J.J. (1976). Value and Limitations of Thallium-201 scintigraphy in the acute phases of myocardial infarction. *New England J. Med.*, **295**, 1-5.
- Wainwright, R.J., Maisey, M.N. (1978). Cardiac imaging, Part 1, Myocardial perfusion scintigraphy. *Hospital Update*, **4**, 623-639.