Clinical experience with technetium-99m stannous polyphosphate for myocardial imaging

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Myocardial imaging with technetium-99m stannous polyphosphate was performed on 46 patients. Eleven patients had no cardiac disease, 22 had acute myocardial infarction, and 13 had stable arteriosclerotic heart disease.

Distinct patterns of myocardial activity were noted: (1) the patients with no obvious cardiac disease showed no cardiac activity; (2) stable arteriosclerotic heart disease showed faint, ill-defined cardiac activity, primarily in the anterior or inferior aspect of the left ventricle; (3) acute myocardial infarction showed intense, focal, well-defined activity, with a shape that characterized the location of the infarct.

Various centres are working to establish a method to estimate the size of a myocardial infarction. ST segment mapping (Maroko *et al.*, 1972) and determination of the isoenzymes of creatine phosphokinase (Sobel *et al.*, 1972) are two currently used investigative tools.

Recently, some workers have found that it is possible to use radioactive materials to detect the infarcted area (Gorten *et al.*, 1966; Hubner, 1970). Further a radio indicator sequestered by acute infarcted myocardium would also allow an estimation of the size of the infarction. Most of the techniques used in the past depended on failure of the ischaemic myocardium to take up the radionuclide, with a resultant negative image or a 'cold area'. Caesium-129 (Romhilt *et al.*, 1973), caesium-131 (Carr *et al.*, 1964), caesium-134 (Chandra *et al.*, 1973), rubidium-81 (Martin *et al.*, 1974), nitrogen-13 (Harper *et al.*, 1973), potassium-42 (Bennett *et al.*, 1972), potassium-43 (Zaret *et al.*, 1973), and radio-labelled fatty acids (Evans *et al.*, 1965), are radionuclides which provide this negative image. However, these materials cannot distinguish a recent from an old myocardial infarction and the physical and biological characteristics of these pharmaceuticals limit their clinical usefulness in detecting the infarcted tissue.

Bonte *et al.* (1974) have reported that technetium-99m stannous pyrophosphate can localize in the

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myocardium of dogs which have had experimentally produced myocardial infarction. Since the radionuclide accumulates in the necrotic area, it shows the lesion as an area of increased radioactivity, or as a hot spot.

In order to assess the clinical applicability of this new test, the following study was designed.

Subjects and methods

Forty-six patients were studied, 11 of whom had no cardiac disease. The patients presented with chest pain and scintigrams were performed to rule out a myocardial infarction. Twenty-two patients had an acute myocardial infarction with typical history, electrocardiogram, and enzyme changes. Seven had subendocardial infarction and the remaining 15 a transmural infarction. The age of these 22 patients ranged from 47 to 86 (mean 60) years. Fourteen of the patients were men. Seven of the patients with an acute myocardial infarction had repeat scintigrams performed.

All 13 patients with stable arteriosclerotic heart disease presented with chest pain and had pre-existent angina or an old myocardial infarction. A new myocardial infarction was subsequently not proven by serial electrocardiograms and enzyme studies. Their ages ranged from 36 to 87 (mean 63) years. Six patients were men.

Technetium-99m stannous polyphosphate, 15m

Ci, was administered intravenously to each patient. The polyphosphate is manufactured by New England Nuclear Corporation. Two chains are present in this product. This isotope has a half-life of 6 hours which allows repetition of the study every 24 hours. In acutely ill patients the radioactive material was transported to the patient's bedside in an appropriate lead-lined safe, designed for carrying syringes. Sixty minutes later, left anterior and left lateral scintiphotos of the upper thorax were obtained. A high resolution colimator, 140 Kev, was centred at the point of maximal cardiac pulsation for both views. There were 300 000 counts per scintiphoto with a 20 per cent window. A Nuclear Chicago gamma camera was used to obtain the images. The images were recorded both on a Polaroid format and a 35 mm format. The 35 mm format is favoured since the areas of increased activity are more dramatically portrayed.

The patients suspected of having an acute myocardial infarction were accompanied to the Nuclear Medicine Laboratory with appropriate resuscitators, life support equipment, monitors, and in the presence of a trained intensive care unit nurse, medical resident, and intern. No patient was examined if the clinical condition was not considered stable by the cardiology group. The patient was not transferred from the stretcher for the examination, and it was not necessary to move the patient's body. The only necessary movement was to allow the patient's left arm to be extended above shoulder level while he lay supine. The arm was supported in

this position for two minutes in order to obtain the left lateral scintiphoto. The total time necessary for the patient to remain in the Nuclear Medicine Laboratory for a complete examination, including positioning, recording, developing film, and provisional diagnosis, was approximately 12 minutes.

Fifty-three myocardial scans were obtained in the 46 subjects. Informed consent was obtained from all the patients.

Results

Tables 1 to 3 tabulate the clinical information and the scan results on the 46 patients. No myocardial activity was found in the 11 patients without obvious heart disease (Fig. 1).

The patients with stable arteriosclerotic heart disease were studied 2 to 20 days after the onset of symptoms (mean 8.6 days). All but one of these patients had studies which showed faint, ill-defined activity, primarily in the anterior or inferior aspect of the left ventricle (Fig. 2). The acute myocardial infarction patients had images obtained 2 to 18 days after the onset of the infarct (mean 6.1 days). All these patients had intense, focal, well-defined increased activity in the region corresponding to the electrocardiographic localization of the infarction. A typical 'C' shaped zone of intense activity was seen in the anterior wall myocardial infarctions (Fig. 3) and a plate-like zone of increased activity was seen in the inferior wall myocardial infarction (Fig. 4).

Seven of the patients with an acute myocardial

TABLE 1 *Patients without arteriosclerotic heart disease*

Patient	Age	Sex	Chest pain	Discharge diagnosis	ECG	Highest AST	CK	LDH	Scan	Scan days after admission
FD	69	M	+	Carcinoma of prostate	Normal	20	85	245	No activity	21
RA	41	F	+	Carcinoma of tonsillar fossa	Normal	15	50	280	No activity	4
CC	69	M	+	Carcinoma of bladder	Normal	20	60	100	No activity	5
JM	50	M	+	Hypertension	Non-spec. ST-T wave changes	20	35	240	No activity	4
JD	62	M	+	Carcinoma of lung	Normal	20	140	275	No activity	9
CA	42	F	+	Metastatic carcinoma	Normal	10	70	200	No activity	5
EP	63	M	+	Rheumatic heart disease; mitral insuff.	Non-spec. ST-T wave changes	20	35	245	No activity	5
LP	48	M	+	Acute pericarditis	Non-spec. ST-T wave changes	30	110	300	No activity	4
CG	53	M	+	Carcinoma of lung	Normal	9	65	255	No activity	5
AR	18	M	+	Duodenal ulcer	Normal	15	70	250	No activity	6
AS	65	M	+	Syncope	Non-spec. ST-T wave changes	23	220	245	No activity	5

Normal enzyme values=AST 7-40 units, LDH 150-400 units, CK 0-130 units.

Note: AST=aspartate aminotransferase; CK=creatin kinase; LDH=lactic dehydrogenase.

TABLE 2 Patients with arteriosclerotic heart disease

Patient	Age	Sex	Chest pain	Condition	ECG	Highest AST	CK	LDH	Scan	Scan days after admission
AG	62	M	+	Angina	Old anterior wall myocardial infarction	30	55	305	Faint activity	14
NS	36	M	+	Angina	Non-spec. ST-T wave changes	15	75	220	Faint ill defined activity	3
WS	56	M	+	Angina	Non-spec. ST-T wave changes	22	55	250	Faint activity	3
MC	72	F	+	—	Old inferior wall MI	20	60	200	Faint activity	3
BC	87	M	+	Angina	Non-spec. interventricular conduction defect	33	60	185	Faint activity	3
FW	60	M	+	—	Old antero-septal	23	115	390	Faint activity	5
EL	75	F	+	Angina	Non-spec. ST-T wave changes	34	60	350	Faint activity	14
VW	59	F	+	—	Left bundle-branch block	56	110	390	Faint activity	20
CM	71	F	+	Angina	Right bundle-branch block	40	140	295	Faint activity	9
NL	48	M	+	—	Old anterior wall	14	70	260	Faint activity	2
HR	58	F	+	Angina	Non-spec. ST-T wave changes	24	95	240	Faint activity	16
MB	81	F	+	Congestive heart failure	Left ventricular hyper.	27	165	290	No activity	15
RF	54	F	+	—	Old antero-septal MI	24	65	340	Faint activity	5

For abbreviations, see Table 1.

TABLE 3 Patients with acute myocardial infarction

Patient	Age	Sex	ECG location	Highest AST	CK	LDH	Scan	Days after infarct
WN	64	M	Right bundle-branch block; anterior subendocardial MI	66	635	315	Focal increased activity—anterior	9
MJ	43	M	Anterior subendocardial MI	50	300	445	Focal increased activity—anterior	7
CV	63	F	Anterior wall MI	225	1425	1000	Focal increased activity—anterior	2
MM	61	F	Anterior subendocardial MI	108	800	470	Focal increased activity—anterior	9
MG	62	M	Inferior subendocardial MI	62	435	410	Focal increased activity—inferior	3
WD	63	M	Old inferior wall; new anterior subendocardial MI	35	175	330	Broad area activity, anterior and inferior	7
JL	68	M	Old inferior wall; new antero-septal	70	400	375	Focal increased activity—anterior	2
CD	86	F	Anterior wall MI	56	290	495	Focal increased activity—anterior	3
US	73	M	Inferior wall MI	60	340	425	Focal increased activity—inferior	3
PT	62	M	Inferior wall MI	286	2575	650	Focal increased activity—inferior	18
RF	63	F	Anterior wall MI	156	1470	950	Focal increased activity—anterior	9
WJ	47	M	Anterolateral wall MI	510	4700	1170	Focal increased activity—anterior	11
GS	48	F	Anterolateral subendocardial MI	33	270	335	Focal increased activity—anterolateral	5
MG	68	F	Anterior wall MI	45	480	395	Focal increased activity—anterior	10
EV	74	F	Old inferior wall MI; new inferior wall MI	60	200	400	Focal increased activity—inferior	4
DN	72	M	Anterior wall MI	50	180	425	Focal increased activity—anterior	3
LS	55	M	Anterior wall MI	37	305	320	Focal increased activity—anterior	6
SD	64	M	Old inferior wall; new anterior wall MI	198	1440	640	Focal increased activity— anterior	3
HR	69	M	Inferior MI	125	860	570	Focal increased activity—inferior	5
JB	56	M	Anterior—subendocardial MI	24	610	270	Focal increased activity—anterior	9
CM	62	F	Anterior wall MI	50	200	375	Focal increased activity—anterior	3
LH	60	M	Inferior wall MI	60	330	450	Focal increased activity—inferior	4

infarction (Table 4) had repeat scintigrams performed 14 to 32 days after the initial onset of symptoms (mean 22 days). Four of these follow-up studies showed less activity in the myocardium than the initial scintigrams. In these patients the enzymes had returned to normal values and the electrocardiogram had stabilized.

Three patients showed an increase in activity and a larger area of involvement. These patients also had clinical evidence of extension based on a new bout of chest pain, an increase in enzymes, and characteristic electrocardiographic abnormalities (Fig. 5 and 6).

FIG. 1 Anterior and left lateral scintiphotos of patient AR, with no cardiac disease. The ribs and sternum are well seen. There is no cardiac activity.

FIG. 2 Anterior and left lateral scintiphotos in patient FW, with stable arteriosclerotic heart disease. Note the faint ill-defined activity.

Discussion

Bonte *et al.* (1974) determined that ^{99m}Tc -stannous pyrophosphate can localize in the hearts of dogs with experimentally produced myocardial infarction. These authors suggested that with myocardial cell death there was a cellular influx of calcium ions which localized within the mitochondria in the crystalline structure hydroxyapatite. Since ^{99m}Tc -stannous pyrophosphate labels hydroxyapatite for bone scanning, this isotope can also image fresh myocardial infarctions on the basis of the hydroxyapatite content. Other possible mechanisms in-

clude binding of phosphate to damaged cell membranes, uptake in other cytoplasmic or nuclear organelles, or binding to leucocytes invading the infarcted area.

Subsequently the same group performed myocardial scans on 15 patients with acute myocardial infarction (Parkey *et al.*, 1974). Thirteen patients had scans 3 to 7 days after the infarction and these were strongly positive in the regions corresponding to the electrocardiographic localization of the infarction. The remaining 2 patients were scanned more than 9 days after the infarction and their scans were negative. They also studied 2 patients with

FIG. 3 Anterior and left lateral scintiphotos in patient WN, with an acute anterior wall myocardial infarction. Note the 'C' shaped zone of intense activity in the lateral view.

FIG. 4 Anterior and left lateral scintiphotos in patient US, with an inferior wall myocardial infarction. Note the plate like zone of increased activity.

stable arteriosclerotic heart disease and found questionable activity in their scintigrams.

Our present study supports and extends these observations. An acute myocardial infarction can be detected as early as 2 days and as late as 10 days after the infarction. Two patients in our study had positive scans 11 and 18 days after the onset of symptoms. However, they also had the highest CK values, which may explain the persistent activity. The myocardial activity is localized in the areas corresponding to the electrocardiographic abnormalities. Further, a characteristic 'C' shape zone of intensive activity was found in the anterior wall

myocardial infarction while a plate-like zone of activity was found in the inferior wall myocardial infarction. Normal individuals show no cardiac activity. However, patients with stable arteriosclerotic heart disease do show faint ill-defined cardiac activity in the anterior or inferior aspect of the left ventricle. The exact reason that these scintigrams were faintly positive in these patients is uncertain, but several possibilities deserve mention. The positive scintigrams might indicate that there is a continual loss of small diffuse amounts of myocardial tissue caused by repeated bouts of myocardial ischaemia, or there may have been a

FIG. 5 Anterior and left lateral scintiphotos in patient SD obtained 3 days after his anterior wall infarction. These photos are copies of the polaroids. Thus, the area of isotope uptake is white on a black background.

FIG. 6 A repeat scintiphoto obtained 18 days after the infarction now shows a larger area of involvement.

myocardial infarction in the distant past. However, it is very easy to separate the acute myocardial infarction with the focal intense activity from the minimal, non-focal cardiac activity seen in the stable arteriosclerotic patients.

Willerson *et al.* (1975) also administered technetium-99m stannous pyrophosphate to 17 patients with electrocardiographic and enzymatic evidence of an acute subendocardial myocardial infarction. In each patient the scintigrams were positive. However, it was not possible accurately to localize the area of myocardial damage in many of their patients. This is in contrast to the ability to localize fairly precisely the area of damage in transmural myocardial infarctions.

Botvinick *et al.* (1975) produced infarctions in 6 closed chest dogs. Scintiphotographs were taken 48 hours after the occlusion using technetium-99m pyrophosphate. Clear images of the infarction were obtained which correlated well with electrocardiographic localization. The animals were sacrificed and significant radioactivity was found only in regions of histologically confirmed infarction. Further the isotope localized specifically in areas of infarcted myocardium in amounts proportional to the degree of CK depletion. The authors concluded that these data provide strong support for the clinical application of this technique in the detection and quantification of acute myocardial infarction.

Willerson *et al.* (1975) have also subsequently reported in a larger series of patients that infarct size can be estimated from technetium-99m stannous pyrophosphate scintigrams. These authors are still not certain that some ischaemic but not necessarily

irreversibly damaged cells may also label with technetium-99m pyrophosphate.

Bonte and his associates used technetium-99m stannous pyrophosphate for their studies. This agent is now limited to investigational use, while the ^{99m}Tc -stannous polyphosphate is widely available. Both agents appear to give diagnostic scintigrams 60 minutes after the injection of the radionuclide. Further studies will be required to assess the relative merits of these two agents.

This new imaging technique can help to distinguish between an acute myocardial infarction and other conditions that cause chest pain. It may assist the surgeon by delineating precisely the area of damaged myocardium that may require operative intervention. It can detect an extension of the myocardial infarction. Most importantly, these tests can be carried out without danger or discomfort to the critically ill patient. Particularly if the institution is equipped with mobile scintillation cameras. The tracer is safe, inexpensive, and almost universally available.

Tetracycline labelled with ^{99m}Tc can also detect a myocardial infarction as a 'hot' spot (Holman *et al.*, 1974). However, the optimal time for the scintiscan study using tetracycline labelled radionuclide is one to three days after the onset of chest pain. After three days little or no cardiac activity is observed. This contrasts with the ^{99m}Tc polyphosphate studies. Positive scans can be obtained more than two weeks after the infarction. Further, the tetracycline labelled radionuclide produces a high uptake in the liver, resulting in difficulty in sizing diaphragmatic infarcts. Other radionuclides are currently being investigated. Technetium-99m

TABLE 4 Myocardial infarction patients with follow-up scintigrams

Patient	First scan	Days after infarction	Second scan	Days after infarction	Comment
HR	Focal increased activity—inferior	5	Less activity—inferior	14	
LS	Focal increased activity—anterior	6	Less activity—anterior	26	
GS	Focal increased activity—anterolateral	5	No activity	25	
JM	Focal increased activity—anterior	7	Increased activity larger area	14	8 days after infarction—chest pain, enzyme rise, anterior transmural MI
SD	Focal increased activity—anterior	3	Increased activity larger area—anterior	18	15 days after infarction—chest pain, enzyme rise, T-wave inversion in precordial lead
CV	Focal increased activity—anterior	2	More extensive involvement—anterior	26	10 days after infarction—chest pain, enzyme rise, T-wave inversion in precordial leads
MM	Focal increased activity—anterior	9	Minimal persistent activity	32	

glucoheptonate has been found to be localized in areas of acutely infarcted myocardium in animals as well as in humans. Strauss *et al.* (1975) found that there was a good correlation between peak CK values and the percentage of the left ventricular area accumulating this isotope. Kramer *et al.* (1974) have reported that gallium-67 citrate can accumulate selectively in recently infarcted canine myocardium: the infarction appears as a hot zone. Gallium enters or is retained within the infarcted region as a result of the inflammatory cell response to the ischaemic cell damage.

Myocardial scanning appears to be a valuable technique for establishing the presence or absence of a myocardial infarction. These studies should be extended to gain more information about this new and promising test.

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