Evaluation of Coronary Artery Disease Using Locally Prepared Myocardial Perfusion Agent99mTc-MIBI

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Abstract

Technitium (^{99m}Tc) labelled isonitrile complexes are recently introduced agents for imaging myocardial perfusion and viability. This study presents the first clinical experience with a locally prepared agent 99mTc methoxy iso butyl isonitrile (MIBI). Sixteen randomly selected cases (M:F 14:2, mean age 48 years) were included; clinically 4 patients were asymptomatic, 6 had history of Ml while remaining 6 had angina with no previous incidence of Ml. Separate injections were given for rest and stress studies either on the same day (9 cases) or on separate days (7 cases). All patients were stressed according to the Modified Bruce Protocol and 99mTc MlBl was injected at peak stress. Early blood pool and delayed static images showed reasonably good localization of MIBI in the viable myocardium and image quality was also comparable to what has been reported In literature. Scans were negative for any perfusion abnormality in 6 cases, positive for single vessel disease in 6 and for two vessels disease in 4 patients. We conclude that the locally prepared[9] 99mTc MlBl has optimal sensitivity and pharmacokinetic properties for myocardial imaging and detection of CAD. Moreover the local preparation would also entail considerable foreign exchange saving (JPMA 44:35, 1994).

Introduction

Imaging myocardial perfusion and viability is the primary objective of nuclear cardiology. Although that lium-201 has excellent physiological characteristics, its main limitations are high cost and the suboptimal physical properties. To circumvent these limitations, a new group of myocardial imaging agent consisting of 99mTc labelled isonitriles complexes like t-butyl isonitrile (TBI), carbory isopropyl isonitrile (CPI) and methqxy isobutyl isonitrile (MIBI) were produced. In various animal and human studies, the myocardial uptake of this agent was shown to be proportional to the regional myocardial blood flow[1]. In this study we present the clinical data of 99mTc..MIBI prepared by the Radioisotope Production Group of Pakistan Institute of Nuclear Sciences and Technology (PINSTECH), Islamabad.

Patients and Methods

Labelling of MIBI with 99mTc:

MIBI was labelled with Mo-Tc generator derived 99mTc pertechnetate according to the protocol specified by the manufacturer. The radiochemical purify and labelling efficiency were more than 96% when measured by paper chromatography.

Patient Population and Selection:

Sixteen patients were randomly selected which included 2 females and 14 males (mean age 48 years; range 40-60 years). Clinically these patients were classified as (a) patients with previous history of myocardial infarction (MI) (n=6), (b) patients with complaints of angina but no history of MI (n=6) and (c) clinically asymptomatic individuals having either deranged lipid profiles, hypertension or episodes of unexplained syncope (n=4). Amongst the 16 cases, 9 had hypertension, 3 had diabetes; history of

smoking and positive family history for IHD was elicited in 5 patients each. Lipid profiles were deranged in 2 of 6 cases in which they were available (Table I).

Table I. Associated risk factors.

Hyper-tension	Diabetes	Smoking	+ve family his.	Lipid profiles		
				High	Normal	Not done
9 (56%)	3 (19%)	5 (31%)	5 (31%)	2 (19%)	4 (25%)	10 (63%)

Clinical Protocols:

Three well recognised clinical protocols were followed[2,3]:

Protocol A: Stress and rest studies performed on separate days (n=7).

Protocol B: Rest images followed by the stress study on the same day (n= 2).

Protocol C: Stress study followed by rest images on the same day (n= 7).

Stress Study:

All patients were stressed according to Modified Bruce Protocol on bicycle ergometer. At peak stress 99mTc-MIBI was injected intravenously as a bolus of 20 mCi (740 MBq) in Protocol A and B and 7 mCi (259 MBq) in Protocol C.

Resting study:

Tc-99m MIBI was injected intravenously at rest as a bolus of 20 mCi (740 MBq) in Protocol A and C and 7 mCi (259 MBq) in Protocol B.

Fatty Meal:

As MIBI (sestamibi) is excreted mainly through the hepatobiliary tract, a fatty meal consisting of a glass of milk or chocolate was given about 10 mm after the injection of Tc-99m MIBI to accelerate hepato biliary clearance and to enhance resolution of the inferior wall of left ventricle.

Imaging:

Imaging was started about 60-90 minutes after injection of 9mTc- MIBI under a large field of view (LFOV) gamma camera with a LEAP collimator. Images were acquired in anterior, left anterior oblique 45° and 700 views (LAO 45 and 70). In first two clinically asymptomatic individuals, early dynamic blood images upto about 40 mins were also acquired anteriorly over chest, abdomen and neck.

Results

A) Image Quality

Dynamic Blood Pool Images:

These were acquired up to 45 mins after injection of Tc-99m MIBI in two clinically asymptomatic individuals. These images showed well outlined left ventricular muscle mass with better delineation of the ventricular cavity. As these images were acquired in the anterior projection right ventricle could not be seen. Early images also showed fair and diffuse tracer uptake over the liver and kidneys while mild and generalized pulmonary uptake was also noted in the immediate post-exercise images. With time there was progressive decline in the extra cardiac or background activity with the visualization of gall bladder and free activity in bowel loops. After fatty meal good contraction of gall bladder was also noted. Moderate tracer deposition over thyroid gland was also noted (Figure 1).

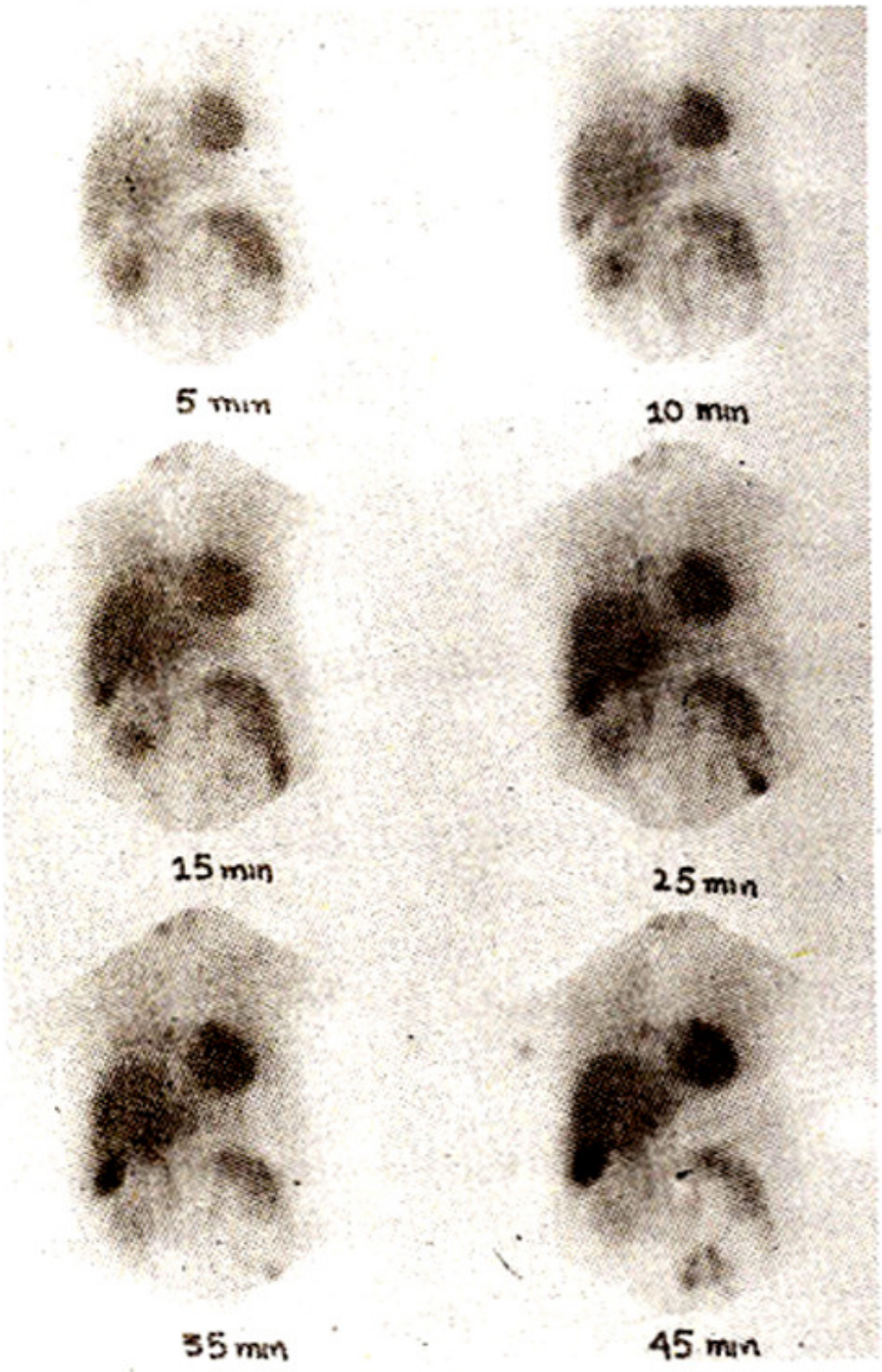

Figure 1. Sequential images upto 45 minute post-injection showing MIBI's localization in the heart and liver followed by clearance through biliary tract.

Static Images:

Static images acquired 60-90 mm after injection showed reasonably good resolution with better delineation of ventricular cavity and viable myocardium segment as compared with thallium- 201

images which have rather limited resolution. There was also good contrast between normal and "mal-perfused" myocardial segment. In female patients no attenuation of anterior wall by breast was seen which is a common problem with thallium-201 imaging (Figure 2).

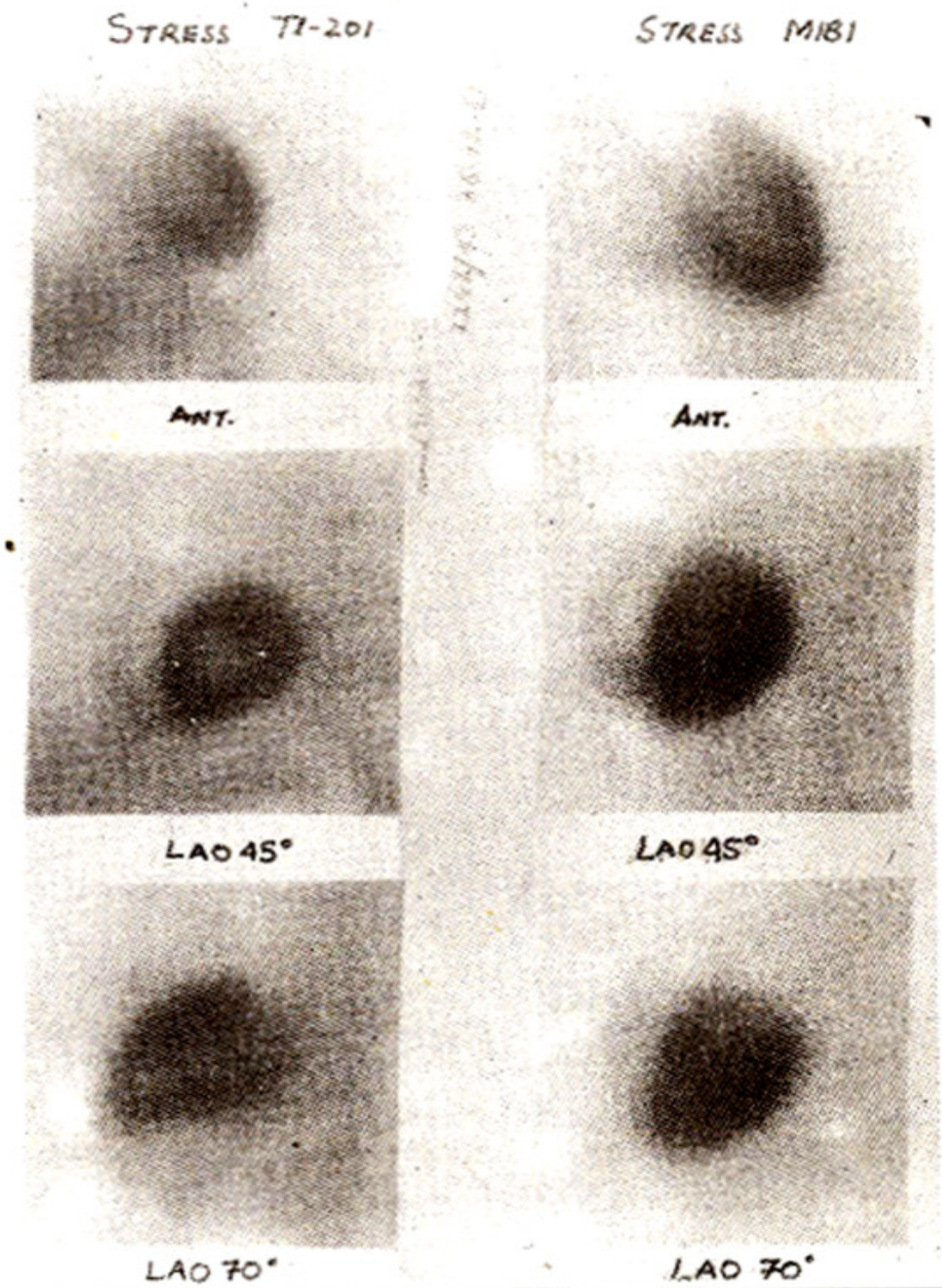

Figure 2. Comparison of quality of stress ^{201}T1 and ^{99m}Tc-MIBI images in a normal individual.

B) Clinical Results:

Stress test was maximal in 7, sub maximal in 6 while remaining 3 individuals could not perform adequate stress. Stress test was positive for exercise induced is chaemic in 5 patients and remained inconclusive due to complete left bundle branch block (LBBB) in 2 others. A negative stress test was obtained in remaining 9 patients (Table II).

Table II. Brief clinical data.

No.	Age (yrs.)	Sex	Diagnosis	Protocol	Stress test	Scan interpre-tation
1	42	M	Asymptomatic	A	max. (-ve)	Negative
2	44	M	Asymptomatic	A	max. (-ve)	Negative
3	52	M	MI	C	Submax. (-ve)	SVD
4	40	M	Angina	A	max. (inconcl.)	Negative
5	50	F	Angina	A	Submax. (+ve)	SVD
6	46	F	Asymptomatic	A	submax. (-ve)	Negative
7	55	M	MI	C	max. (-ve)	2VD
8	46	M	Angina	C	submax. (+ve)	2VD
9	46	M	Angina	B	Inadeq. (+ve)	SVD
10	52	M	MI	B	max. (-ve)	SVD
11	60	M	Angina	C	submax. (-ve)	Negative
12	58	M	MI	C	inadeq. (+ve)	2VD
13	53	M	MI	A	max. (-ve)	SVD
14	50	M	Angina	A	inadeq.(inconl)	2VD
15	44	M	Asymptomatic	C	max. (-ve)	Negative
16	40	M	MI	C	submax. (+ve)	SVD

Protocol A = Separate day
Protocol B = Same day rest/stress
Protocol C = Same day stress/rest

Negative = Normal
SVD = One vessel disease
2VD = Two vessel disease

Out of sixteen individuals, perfusion study was negative for any perfusion abnormality in 6 while it was positive for well defined perfusion defects in 10 cases. In 6 patients perfusion defects were localized to a single vessel territory while in remaining 4 two vessels were involved. Left anterior descending artery (LAD) was the niost common artery involved in 6 cases followed by left circumflex artery (LCX) in 5 and right coronary artery (RCA) in three (Figure 3).

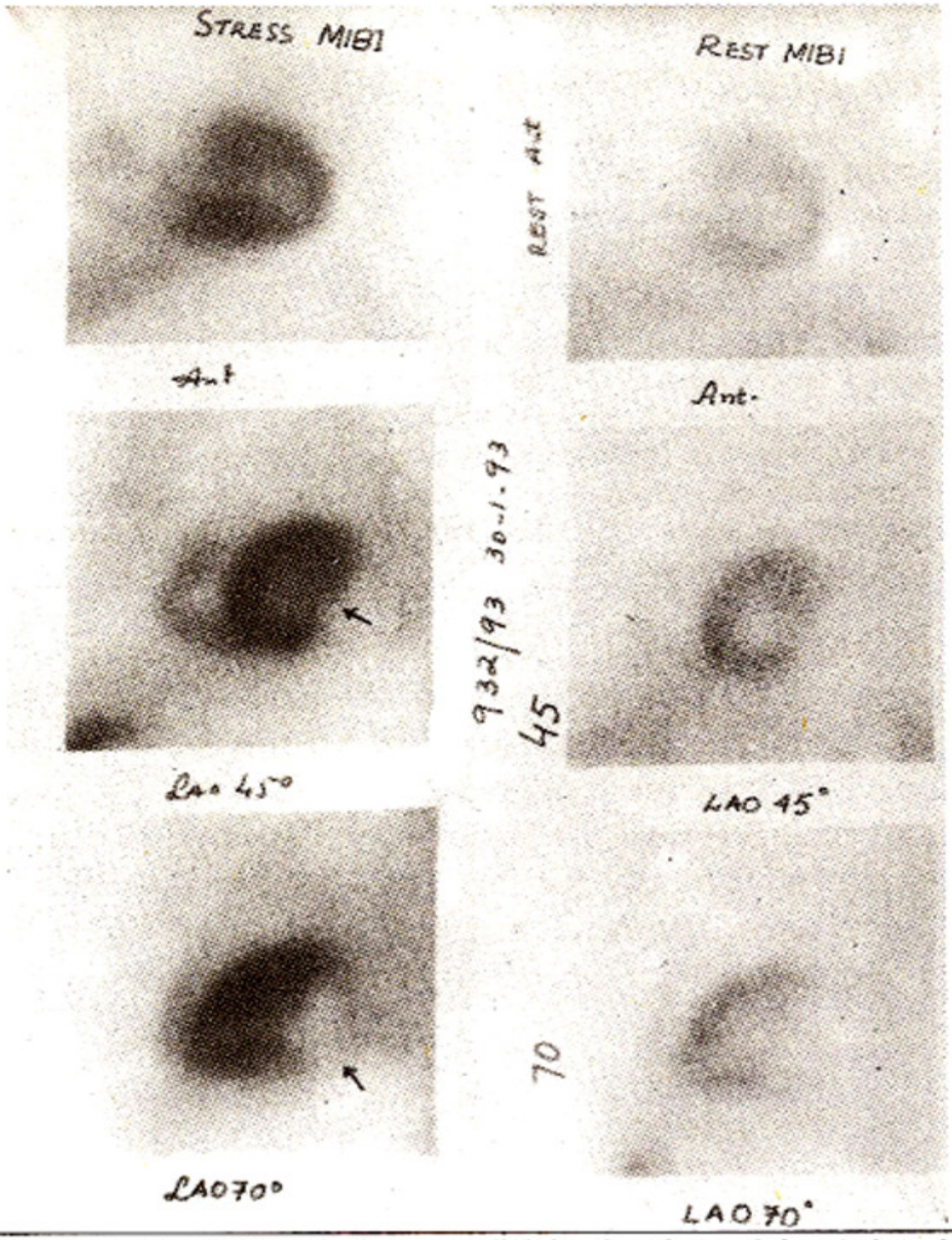

Figure 3. Stress-Rest MIBI study showing well defined perfusion defects in lateral wall and posterobasal segment in LAO 45° and 70° views respectively. Partial reversibility of perfusion (viable myocardium) seen in the lateral wall defect in resting LAO 45° view.

Discussion

MIBI or RP-30 is a lipophilic, monovalent cation that localizes in the myocardial cells by simple

diffusion without active transport and is reported to bind strongly to a small molecular weight cytosolic protein[4]. Unlike thallium it does not redistribute over time and, therefore, separate injections have to be given for resting and stress studies[5]. Hepatic uptake is also present but since MIBI is excreted by the biliary tract, myocardium to liver ratio increases overtime. Most of the comparative studies have shown that ^{99m}Tc-BIMI has better sensitiviivity and specificity for coronary artery disease (CAD) as compared with ^{201}T1[6-8] In this brief clinical trial, the myocardial perfusion agent MIBI manufactured by the Radio Isotope Production Group at PINSTECH, Islamabad shows reasonably good localization of the tracer in the viable myocardium. The pharmacokinetics and image quality are also comparable to what is mentioned in current literature. In this, study, four individuals were clinically asymptomatic but study was advised due to either resting ECG changes or deranged lipid profiles. They had negative stress test and normal perfusion scans. In these individuals with low pre-test probability, a negative perfusion study almost rules out the possibility of CAD. In such cases the reported incidences of a false negative study is less than 1%[7]. Similarly, in symptomatic patients either with or without a previous MI, the findings of perfusion scans correlate well with clinical history and stress EGGs. None of these patients have had angiography yet. However, it is an ongoing clinical trial and a comprehensive protocol being worked upon. The initial clinical data presented in this study validates the utility of locally produced. In summary, locally prepared ^{99m}Tc-MIBI has optimal pharmacokinetic properties and sensitivity for the detection of existence and severity of CAD. Moreover, the local preparation would also save considerable foreign exchange.

References

1. Rama, K.N., Nunn, AD. and Kucaynsti, B.L. A neutral 99mTc complexfor myocardial imaging. J.Nucl.Med., 1989;30:1830-34.
2. Borges-Neto, S., Coleman, RE. and Jones, RH. Comparison of one and two day rest and treadmill cardiolite test. J.Nucl.Med., 1988;29:790-94.
3. Tallifer, R., Gagnon, A, La Flamme, L et al. Same day injection of MIBI for SPECT imaging. Comparison between rest-stress and stress-rest aequence. Eur. J.Nucl.Med., 1989;15:113-17.
4. Mousa, S.A. and Mains, M. Retention of RP-30 in the heart maybe due to binding to a cytoaolic protein (abstract). J.Nucl.Med., 1987;28:619:
5. Mouss, S.A. and Cooney, J.M. Regional myocardial distribution of RP-30 in clinical model of myocardial iechaemia and reperfusion (abstract). J.Nucl.Med., 1987;28:620.
6. Watson D.D., Smith, W.H., Campbell, N.P. etal. Quantitative myocardial imagingwitb mTe MIBI: comparison with Th-201 (abstract). J.Nucl.Med., 1987;28:653.
7. Maddabi,J., Ganzi, W., Ninomiys, K etal. mTcMIBIand T1-201 myocardial perfusion imaging in patients with CAD: quantitative comparison of planar and SPECT J.Nucl.Med., 1987;28:654-60.
8. Karcher, 0., Rutherford, J.D., Keiss, M.C. etat Quantitative and qualitativecomparison of T1-201 and Tc-99m MIBI by SPECT in CAD. J.Nucl.Med., 1987;28:856-60.