Eur J Nucl Med (1986) 12:333–336

European Journal of Nuclear Medicine

The utilization of Tc-99m-TBI as a myocardial perfusion agent in exercise studies: Comparison with Tl-201 thallous chloride and examination of its biodistribution in humans

S.T. Benjamin Sia[1], B. Leonard Holman[1], Kenneth McKusick[2], Pierre Rigo[3], Fredric Gillis[3], Victor Sporn[4], Nestor Perez-Balino[4], Aldo Mitta[4], Henning Vosberg[5], Zsolt Szabo[5], Bodo Schwartzkopff[6], Jean-Luc Moretti[7], Alan Davison[8], John Lister-James[1], and Alun Jones[1]

[1] Department of Radiology, Division of Nuclear Medicine Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA
[2] Department of Radiology, Division of Nuclear Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA
[3] Hôpital de Bavière, Institut de Médicine, Université de Liege, Belgium
[4] Santatorio Guemes Medicina Nuclear, Buenos Aires, Argentina
[5] Nuclear Medizinische Klinik, der Universität, Düsseldorf, Federal Republic of Germany
[6] Kardiologische Klinik, Universität Düsseldorf, Federal Republic of Germany
[7] Service de Biophysique et de Médecine Nucleaire, Hôpital Henri Mondor, Créteil, France
[8] Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

Abstract. Twenty-four patients were studied with both ^{201}Tl-thallous chloride and ^{99m}Tc-TBI scintigraphy following exercise. Comparison of the two agents in detecting segmental myocardial ischemia and scar was made in 18 patients with evidence of coronary artery disease on ^{201}Tl-thallous chloride scintigraphy. Agreement between the two studies was observed in 77% (125 of 162) of left ventricular segments, suggesting that ^{99m}Tc-TBI can be used as a myocardial perfusion agent. Limitations were related to early high background activity from lungs and liver. The high lung activity and early myocardial redistribution within the 1st hour contributed to the failure of ^{99m}Tc-TBI to detect 16 segmental defects seen in the immediate post-exercise thallous chloride scan. Persistently high liver activity additionally affected accurate interpretation in the left ventricular segments close to the diaphragm. Improvement in the accuracy of ^{99m}Tc-TBI stress studies might be achieved with tomographic imaging to reduce the problem of background activity or by the development of ^{99m}Tc-labeled isonitrile analogues with rapid lung and liver clearance.

Key words: Myocardial perfusion scintigraphy – ^{99m}Tc t-butylisonitrile

^{201}Tl-thallous chloride has become established as a myocardial perfusion agent in the evaluation and management of patients with coronary artery disease (Holman 1984a). However, ^{201}Tl has physical characteristics that make it less than ideal for scintigraphy. For these reasons, there is a continuing interest in developing a ^{99m}Tc labeled myocardial perfusion agent (Deutsch et al. 1981; Eakins et al. 1982; Nishiyama et al. 1982a, b; Dudczak et al. 1983). In 1984, Holman et al. reported the usefulness of a new agent, ^{99m}Tc-hexakis (t-butylisonitrile)-technetium (I) (^{99m}Tc-TBI), for myocardial imaging in humans. We have undertaken a study to compare the accuracy of this agent with that of ^{201}Tl-thallous chloride for myocardial perfusion scintigraphy in patients undergoing exercise testing for the evaluation of coronary artery disease. We also studied the early biodistribution and clearance kinetics of ^{99m}Tc-TBI in humans following intravenous injection at peak exercise and at rest.

Offprint requests to: B. Leonard Holman, Department of Radiology, Division of Nuclear Medicine, 75 Francis Street, Boston, MA 02115, USA

Patients and methods

This was a multicenter study involving 24 patients referred to ^{201}Tl exercise testing for evaluation of coronary artery disease. Patients were studied during graded exercise using treadmill ergometry. At maximal obtainable exercise, 80 MBq ^{201}Tl-thallous chloride was injected intravenously, followed by 1 min of additional exercise. Imaging of the chest and upper abdomen, was performed in the anterior, 40° LAO and 60° LAO positions immediately and at 3 h after exercise.

At a later date, at least 24 h after the initial scan (mean 32 days, range 1–128 days), the patients were re-exercised to the same level. At 1 min prior to cessation of exercise, 370 MBq of ^{99m}Tc-TBI was injected intravenously. Within 15 min of injection, 5-min sequential images of the chest and upper abdomen were obtained in the anterior or 40° LAO position for the 1st h. Images in the anterior, 40° LAO and 60° LAO positions were then obtained at 1, 2, 3, and up to 24 h postinjection.

In all patients, a further injection of 370 MBq ^{99m}Tc-TBI was given intravenously at rest at least 24 h after the previous ^{99m}Tc-TBI injection (mean 9 days, range 1–21 days). Images of the chest and upper abdomen were obtained in a manner similar to that described for the exercise study.

Analogue and 128 × 128 digital images were collected using the same type of scintigraphic camera in all cases.

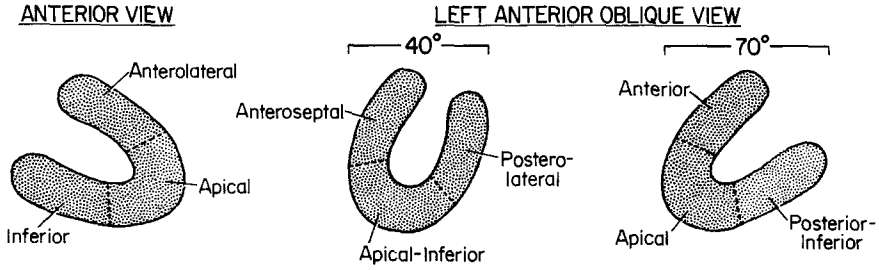

Fig. 1. Schematic representation of segmental division of the left ventricle in three projections

Table 1. Comparison of exercise performances for the ^{201}Tl and ^{99m}Tc-TBI studies in 18 patients with acceptable studies and coronary artery disease

	^{201}Tl	^{99m}Tc
Heart rate (beat/min)	129± 14	134± 14
Peak systolic blood pressure (mm Hg)	187± 28	187± 30
Double product (beat × mm Hg/min)	24,000±4,600	25,000±5,200

Table 2. Reasons for stopping exercise during ^{201}Tl exercise study in 18 patients with acceptable studies and coronary artery disease

Reasons for stopping exercise	Number of patients
ST depression	2
Angina	6
Fatigue	5
Maximum double product achieved	5

Table 3. Comparison of ^{201}Tl and ^{99m}Tc-TBI myocardial perfusion scintigraphy in detecting left ventricular segmental abnormalities

	^{99m}Tc-TBI		
	Normal	Transcient ischemia	Fixed defect
^{201}Tl Normal	82	7	4
Transcient ischemia	13	26	3
fixed defect	3	7	17

Total number of segments = 162

The cameras were equipped with all purpose parallel hole collimators and were interfaced to one of several computers: GE Star, Elscint Dycomet, Krupp EPR1100 or Sopha Medical. Data were reviewed on a digital display by the principal investigator of each institute and two other investigators (KAM, STBS) independently without prior clinical knowledge of the patients.

The 1-h ^{99m}Tc-TBI exercise and rest images were compared with the ^{201}Tl exercise and 3-h delayed images. The left ventricle was divided into three segments in each image as shown in Fig. 1. Each segment was graded as normal, ischemic, or scarred on the basis of a transient or permanent defect.

Utilizing the sequential images obtained during the 1st h of the ^{99m}Tc-TBI exercise and rest studies, regions of interest were placed over the heart, lung, liver, and spleen to obtain in vivo biodistribution and clearance kinetics.

Results

Patient population

Twenty-four patients completed the entire study and had complete data for all parts of the study for analysis. One of these patients was treated between the ^{201}Tl and ^{99m}Tc-TBI studies and one had very poor quality ^{99m}Tc-TBI studies due to high liver activity overlapping the myocardial images. These two patients were excluded from further analysis.

Comparison of ^{201}Tl with ^{99m}Tc-TBI myocardial perfusion scintigraphy

Of the 22 patients with acceptable studies, 18 demonstrated scintigraphic evidence of coronary artery disease. They consisted of 17 men and 1 woman, with ages ranging from 41 to 72 years. Chronic stable angina was experienced by 12 patients, 5 patients had stable angina following myocardial infarction, and 1 patient had a recent myocardial infarction with no subsequent angina. Six patients were on

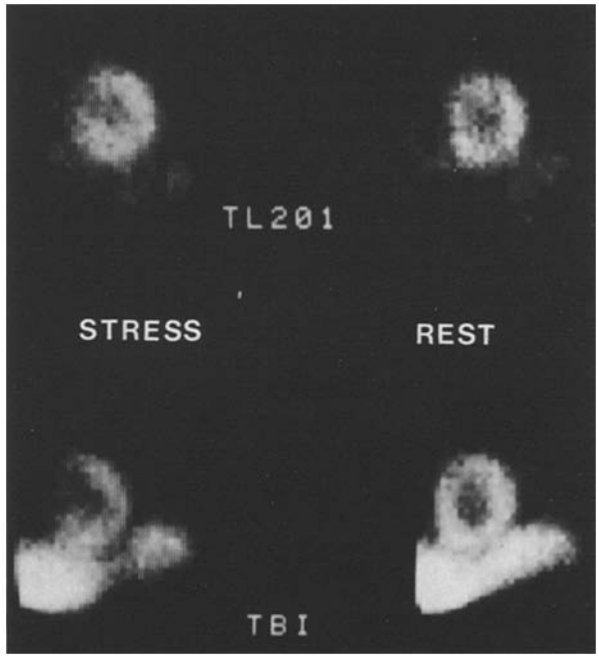

Fig. 2. Comparison of ^{201}Tl and ^{99m}Tc-TBI myocardial scintigraphy in LAO 40° projection, demonstrating transient ischemia in the septum. Images on the *left* are stress studies and images on the *right* are rest studies

Table 4. ^{99m}Tc-TBI activity ratio in the heart, lung, and liver, during the 1st h

	Rest study (min)			Exercise study (min)		
	5	30	60	5	30	60
Heart/lung	0.9	1.1	1.3	0.9	1.2	1.3
Heart/liver	0.6	0.5	0.4	0.7	0.5	0.5

Table 5. ^{99m}Tc-TBI activity in the heart, lung, liver and spleen at 30 and 60 min after injection compared to the activity at 5 min (normalized for area and decay)

	Rest study		Exercise study	
	30 min	60 min	30 min	60 min
Heart	88.1%	85.1%	88.5%	83.3%
Lung	66.7%	57.7%	70.5%	58.5%
Liver	125.1%	126.7%	127.8%	129.7%
Spleen	96.6%	79.8%	103.4%	92.7%

beta-blockers. Comparison of the ^{201}Tl and ^{99m}Tc-TBI studies was made in these 18 patients.

The exercise parameters for both stress tests were comparable (Table 1). The reasons for stopping exercise in the ^{201}Tl study are listed in Table 2.

Comparison of ^{201}Tl with ^{99m}Tc-TBI in detecting myocardial ischemia and scar in the 162 left ventricle segments is summarized in Table 3. In all, there was agreement between the two studies in 125 segments (77%) (Fig. 2). There was agreement in 88% of segments which were normal with ^{201}Tl.

The area of greatest disagreement was in the failure of ^{99m}Tc-TBI to detect 16 segmental defects seen in the immediate postexercise ^{201}Tl scan. ^{99m}Tc-TBI studies also failed to detect ten fixed defects seen on redistribution ^{201}Tl imaging.

Biodistribution and clearance kinetics of ^{99m}Tc-TBI

The relative distribution of ^{99m}Tc-TBI in the heart, lung and liver at 5, 30, and 60 min after intravenous injection at rest and at peak exercise is shown in Table 4. The clearance kinetics of these organs during the 1st h are shown in Table 5.

At 5 min there was significant background activity in the lung and liver for both the rest and exercise studies. There was a gradual improvement in heart-to-lung ratio over the next hour due mainly to washout from the lungs where the activity has decreased by more than 40% by 1 h after injection (Fig. 3). However, background activity from liver and spleen remained high with liver activity increasing over the 1st h after injection. This led to obscuring of the diaphragmatic aspects of the left ventricle (Fig. 4) in four patients while making interpretation of the ^{99m}Tc-TBI scan impossible in one patient. The spleen caused similar problems in two patients.

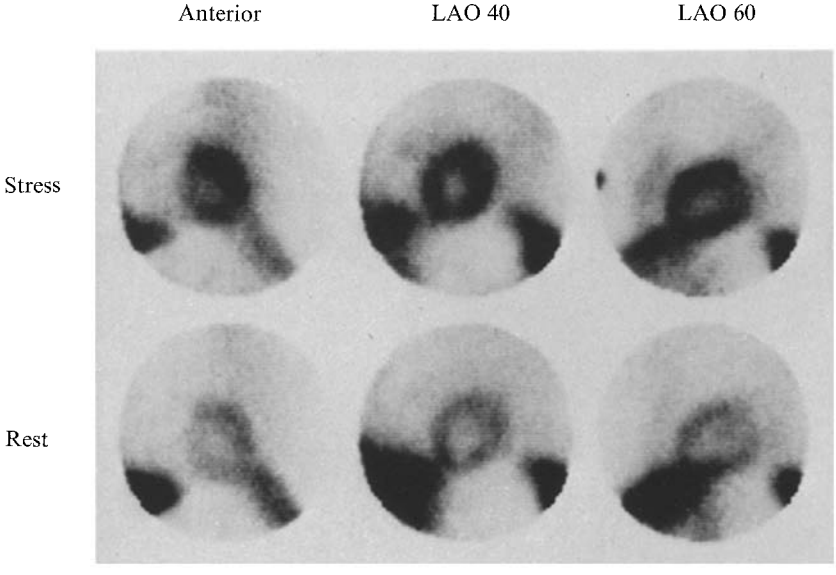

Fig. 3. ^{99m}Tc-TBI myocardial scintigraphy demonstrating normal perfusion in three projections

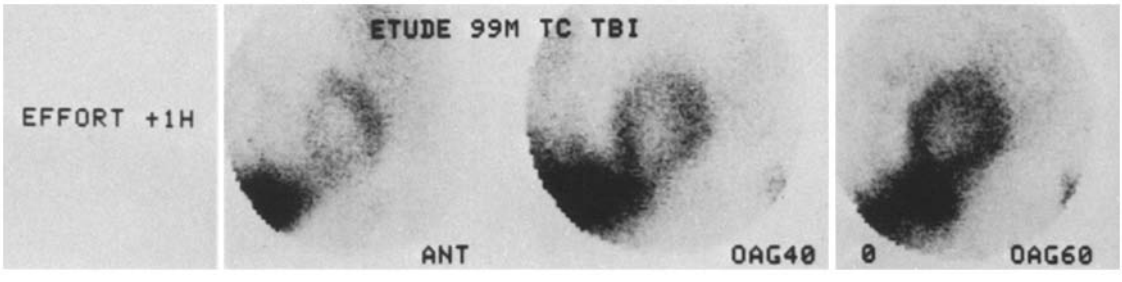

Fig. 4. ^{99m}Tc-TBI myocardial scintigraphy in three projections at 1 h after injection, demonstrating high liver activity obscuring a possible apical-inferior defect

Discussion

Our study confirms the earlier finding that myocardial uptake of ^{99m}Tc-TBI in the human is substantial (Holman et al. 1984). The good correlation between ^{201}Tl and ^{99m}Tc-TBI in detecting normal, ischemic or scarred myocardium suggests that ^{99m}Tc-TBI can be used as a myocardial perfusion agent in humans and supports animal data which showed excellent correlation between its uptake and blood flow in normal and ischemic myocardium (Holman et al. 1986).

As expected from the physical characteristics of ^{99m}Tc, these images consistently appeared to have better resolution than those of ^{201}Tl. However, there are limitations to the use of ^{99m}Tc-TBI for perfusion imaging after stress. The early high activity in the lungs resulted in unacceptably high background activity on images obtained immediately after exercise. We found that by 15 min after injection, the 40° LAO image of the heart was often technically acceptable. For other projections, it was necessary to wait at least 1 h in order to obtain technically acceptable images. It is likely that in some cases redistribution will have occurred in the 1st h after stress; this was, in fact, observed in two of our patients. The methodology we employed, therefore, reduces the sensitivity for detecting myocardial ischemia. Early redistribution, within the 1st h, is likely to have contributed significantly to the failure of ^{99m}Tc-TBI to detect the 16 segmental defects seen in the immediate postexercise ^{201}Tl scan.

In addition, interpretation of the left ventricular segments close to the diaphragm is less reliable due to the persistently high liver activity. This may have contributed further to the decreased sensitivity of ^{99m}Tc-TBI to detect defects seen by ^{201}Tl in both the immediate postexercise and the redistribution studies.

It is expected that tomographic imaging, which was not employed in this study, could significantly reduce the problem of background activity. Furthermore, the development of ^{99m}Tc-labeled isonitrile analogues that clear rapidly from the lung and liver should overcome the technical problems of ^{99m}Tc-TBI imaging.

Acknowledgements. Dr. S.T. Benjamin Sia is a current recipient of an Overseas Fellowship of the National Heart Foundation of Australia.

References

Deutsch E, Glavan KA, Sodd VJ, Nishiyama H, Ferguson DL, Lukes SJ (1981) Cationic Tc-99m complexes as potential myocardial imaging agents. J Nucl Med 22:897–907

Dudczak R, Angelberger P, Homan R (1983) Evaluation of 99m-Tc-dichloro bis (1,2-dimethylphosphino) ethane (99m-Tc-DMPE) for myocardial scintigraphy in man. Eur J Nucl Med 8:513–515

Eakins MN, Glavan KA, Kronague JF (1982) The myocardial uptake and biodistribution of kit formulated 99m-Tc-labeled cationic complex, $Tc(dmpe)_2cl_2^+$. J Label Comp 19:1457–1459

Holman BL (1984) Nuclear cardiology. In: Braunwald E (ed) Heart disease, 2nd edn. W.B. Saunders, Philadelphia, pp 351–399

Holman BL, Jones AG, Lister-James J, Davison A, Abrams MJ, Kirshenbaum JM, Tumeh SS, English RJ (1984) A new Tc-99m-labeled myocardial imaging agent, hexakis (t-butylisonitrile)-technetium(i) [Tc-99m TBI]: initial experience in the human. J Nucl Med 25:1350–1355

Holman BL, Campbell CA, Lister-James J, Jones AG, Davison A, Kloner RA (1986) The effect of reperfusion and hyperemia on the myocardial distribution of Tc-99m-TBI. J Nucl Med 27:1172–1177

Nishiyama H, Deutsch E, Adolph RJ, Sodd VJ, Libson K, et al. (1982a) Basal kinetic studies of Tc-99m DMPE as a myocardial imaging agent in the dog. J Nucl Med 23:1093–1101

Nishiyama H, Adolph RJ, Deutsch E, Sodd VJ, Libson K, et al. (1982b) Effect of coronary blood flow on uptake and washout of Tc-99m-DMPE and Tl-201. J Nucl Med 23:1102–1110

Received March 8, 1986 / June 7, 1986