Technetium-99m sestamibi and tetrofosmin myocardial single-photon emission tomography: Can we use the same reference data base?

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Abstract. The aim of this study was to compare technetium-99m labelled tetrofosmin and sestamibi myocardial perfusion single-photon emission tomography (SPET) with one common sestamibi reference file for bull's eye imaging, with quantitation of the extent and severity of perfusion defects. Twenty patients suspected or known to have coronary artery disease participated in the study. Patients first underwent routine sestamibi myocardial SPET over 2 days, receiving doses of 400–600 MBq at stress and 600–800 MBq at rest. Then within the same week a 1-day tetrofosmin myocardial SPET study was performed, with a dose of 300 MBq at stress, followed 2.5 h later by a dose of 750 MBq at rest. Bull's eye images were generated for visual evaluation. Black-out defects according to the Cequal software analysis were only recorded if they comprised more than 10 pixels in men and 20 in women. According to the Cequal program, extent score and severity scores were expressed as number of pixels and deviations below reference limits. Five patients had normal myocardial SPET imaging with both radiotracers, while 15 had reversible, irreversible or partially reversible defects. The concordance of the results was high. The only two significant differences were that one patient had a reversible defect which appeared to be located in different myocardial regions (LAD vs RCA), and another patient had a defect that was partially reversible with sestamibi but irreversible with tetrofosmin. The results showed very high correlation coefficients for the extent and severity scores (linear correlation coefficient values of 0.99 and 0.94, respectively). In conclusion, it appears that changing between sestamibi and tetrofosmin has little influence on the interpretation of bull's eye images from the data file of a common reference population using one of the tracers.

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Introduction

Reference files of myocardial single-photon emission tomography (SPET) may be of support in discriminating between regional defects and normal variations in activity distribution. The files usually include a limited number of reference subjects and are often established with acquisition protocols that differ slightly from the routine acquisition protocols used in patient studies with regard to number of steps, collimators, matrix size, use of 1- or 2-day protocols etc. With the advent of technetium-99m sestamibi it was obvious that new reference files had to be established since both the kinetics of thallium-201 and sestamibi and the physical properties of the isotopes differed so markedly [1]. With new ^{99m}Tc-labelled tracers such as tetrofosmin and ^{99m}Tc-NOET the question of whether new reference data are needed has arisen again: although the isotope is the same, there are minor differences in the biodistribution and kinetics of the tracers [2–4].

The purpose of this investigation was to compare the interpretation of sestamibi and tetrofosmin SPET studies based solely on the visual appearance and quantitative analysis of defects as given by a sestamibi data base. This data base is included in the Cequal software program as distributed by the gamma camera production company (General Electric) for a sestamibi 1-day protocol.

Materials and methods

Patients. The population studied comprised 20 patients (17 men and 3 women; mean age 56.5 years, range 38–73) suspected or known to have coronary artery disease (CAD). None of the patients had unstable CAD, left bundle branch block, non-ischaemic

cardiomyopathy or significant valvular heart disease. One patient had had a heart transplant and was controlled for CAD. The study was approved by the Ethical Committee of Copenhagen [J. no. (KF) 01-272/94]. All patients received a careful oral and written explanation of the study and gave their written consent before participation.

Rest and stress studies. The patients first underwent routine sestamibi myocardial SPET over 2 days, receiving doses of 400–600 MBq at stress and 600–800 MBq at rest. Then a 1-day tetrofosmin myocardial SPET study within the same week was performed, with a stress study (dose 300 MBq) in the morning, followed by a rest study (dose 750 MBq) 2.5 h later. Care was taken that each patient underwent exactly the same stress protocol during the sestamibi and tetrofosmin studies. Twelve patients performed an upright bicycle test with the same increase in steps to the same maximum load on each occasion, and eight patients received a dipyridamole infusion with a dose of 0.14 mg/kg per minute given i.v. over 4 min. All methylxanthine medications and coffee, tea and cola consumption were discontinued for 18 h before dipyridamole infusion. In two patients theophylline was given (100–200 mg i.v.) 3 min after the termination of dipyridamole infusion.

Myocardial SPET imaging. Myocardial SPET was performed with a General Electric XR/T gamma camera and a high-resolution, parallel-hole, low-energy collimator with a 20% symmetrical window around 140 keV, employing 180° elliptical rotation beginning at the 45° right anterior oblique projection, with 64 projections and 20 s/projection. The image analysis was performed with a dedicated Starcam 3000 computer. Studies were reconstructed and processed with the Cequal software using decay correction from the start of image acquisition, a two-dimensional Butterworth filter (critical frequencies: 0.4 cycles/cm for rest and 0.52 cycles/cm for stress, with power factors of 10 and 5, respectively). After reorientation two 6.4-mm slices at a time were combined, giving a slice thickness of 12.8 mm. The final bull's eye images were used for comparison with the reference files of the Cequal 1-day ^{99m}Tc-sestamibi protocol. The sestamibi SPET studies were started 60 (stress) and 90 (rest) min after tracer injection, and the tetrofosmin studies 15 (stress) and 30 (rest) min after tracer injection.

When processing the images, care was taken that the same axes of the left ventricle were obtained, as well as the same apex and base definitions, in the sestamibi and tetrofosmin studies. Bull's eye images were generated for visual evaluation, and defects exceeding the limits defined by the programme were quantitatively described by extent and severity scores (see below). Black-out defects were only recorded if they comprised more than 10 pixels in men and 20 pixels in women. A defect was regarded as reversible if it comprised more than 10/20 pixels (men/women) only during stress, as irreversible if it was unchanged from rest to stress, and as partially reversible if it was 10/20 pixels larger during stress.

Extent score was calculated according to the Cequal program. It represents the number of myocardial pixels below the reference limit for the particular myocardial region, as given by the Cequal program [5]. Severity scores were calculated from the extent scores by multiplying the figures with a factor reflecting the degree of deviation below the reference limit.

Statistics. Linear regression analysis was used for quantitative comparison of defects. $P < 0.05$ was considered significant.

Table 1. Classification of 20 patients referred for ischaemic heart disease by sestamibi (MIBI) and tetrofosmin bull's eye images as normal or abnormal

	MIBI	
	Normal	Abnormal
Tetrofosmin		
Normal	5	0
Abnormal	0	15

Table 2. Comparison of sestamibi (MIBI) and tetrofosmin defects according to reversibility

	MIBI		
	Rev.	Irrev.	Rev.+Irrev.
Tetrofosmin			
Rev.	6		
Irrev.		3	1[a]
Rev.+Irrev.			5

[a] One patient with an irreversible defect with tetrofosmin. With sestamibi it was predominantly reversible, cf. Fig. 1

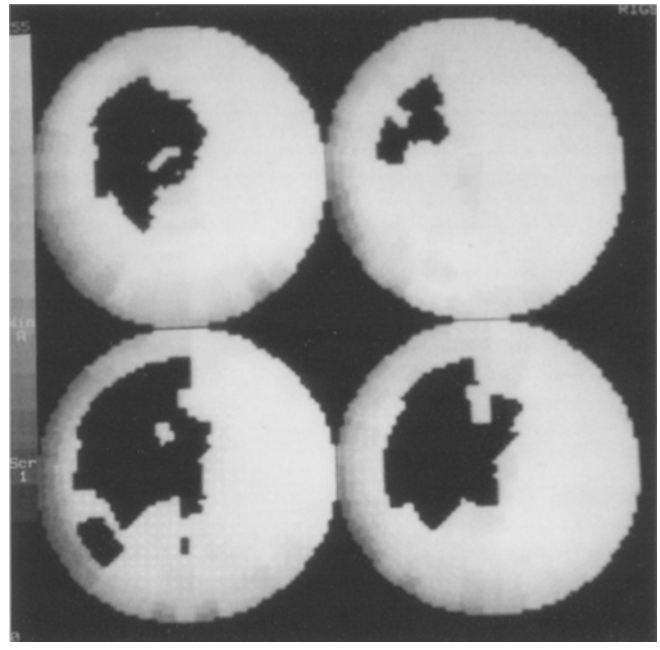


Fig. 1. ^{99m}Tc-sestamibi (*upper row*) and ^{99m}Tc-tetrofosmin (*lower row*) bull's eye images from the same patient at rest (*right*) and during stress (*left*). The sestamibi defect clearly increases from rest to stress (partially reversible), whereas the tetrofosmin defect is slightly larger during stress, i.e. is essentially unchanged (irreversible)

Results

The agreement between defects on the sestamibi and tetrofosmin bull's eye images is shown in Tables 1 and 2. Complete agreement was present when the bull's eye images were scored as normal or abnormal. Concerning reversibility, there was total agreement in all cases but one: a patient with a defect that was irreversible with tetrofosmin, but partially reversible with sestamibi (Fig. 1). The visual interpretation of the short-axis slices gave the same impression, but not so clearly as the bull's eye images.

When defect localisation was analysed according to the presumed coronary artery supply (Table 3), 45 out of 47 defects were located in the same region with the two tracers. Furthermore, there was a strong association between the extent and severity scores for sestamibi and tetrofosmin (Figs. 2, 3). The correlation was close to the line of identity, except for the highest value of the severity scores.

Table 3. Localisation of defects during stress/rest according to coronary artery supply regions in the Cequal program with sestamibi (MIBI) and tetrofosmin

	MIBI			
	No defect	LAD	LCX	RCA
Tetrofosmin				
No defect	–	1[a]/–		
LAD		10/7		
LCX			6/6	
RCA	1[a]/–			9/7

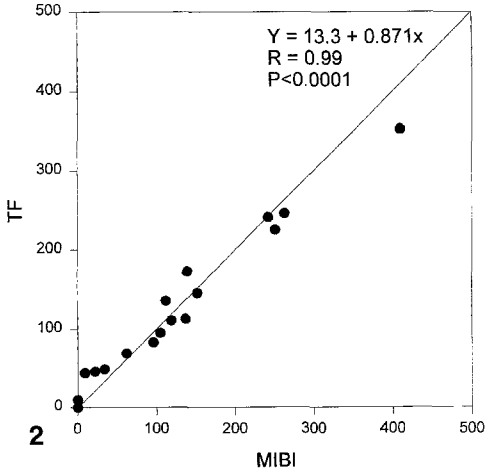
LAD, Left anterior descending artery; LCX, left circumflex artery; RCA, right coronary artery

[a] One patient with a stress defect localised differently with the two tracers

Discussion

The comparison of a 1-day tetrofosmin and a 2-day sestamibi myocardial SPET protocol with one common sestamibi reference data base for bull's eye imaging showed close agreement in the interpretation, based exclusively on the presence of significant defects. This agreement included the number of abnormal patient studies, the number of significant defects, and their localisation, reversibility, extent and severity in 20 patients suspected or known to have coronary artery disease, regardless of whether stress was induced by bicycle exercise or dipyridamole infusion. We did observe minor differences: In one patient the stress defect with tetrofosmin appeared mostly in the RCA region whereas with sestamibi it was localised mainly in the LAD region. In another patient an LAD defect was shown to be partially reversible with the 2-day sestamibi protocol but irreversible with the 1-day tetrofosmin protocol. We do not know whether the differences are due to the use of 2-day or 1-day acquisition studies, to different tracers or to biological variation. It has been shown that tetrofosmin administered by a 1- or 2-day protocol produces virtually identical SPET images [6] and yields the same sensitivities and specificity for the diagnosis and localisation of CAD [7]. It has also recently been reported that when sestamibi and tetrofosmin are applied using the same acquisition protocol, they yield nearly the same SPET data [8]. The present study confirmed that changing both the acquisition protocol and the tracer has limited consequences for the bull's eye appearance or for quantitative information.

It is always optimal to have exactly identical variables, including the same tracer, when a reference range is used. On the other hand it should be realised that when using a reference file with the same tracer from another department it is necessary to look at all the differences present between the acquisition protocols for the reference data and the routine procedure of the nuclear medicine department. If consideration is being given to establishing a data base within the department, it should be further remembered that the population of ref-



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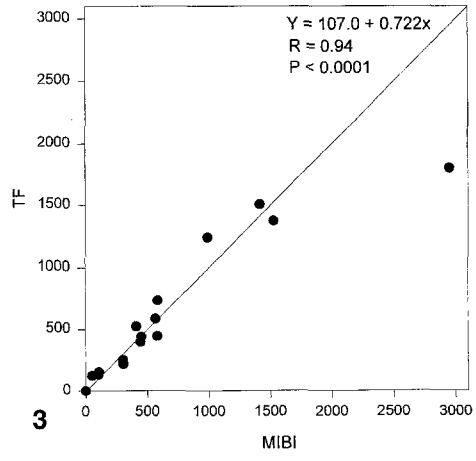

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Fig. 2. Close agreement between the extent scores of sestamibi (*MIBI*) and tetrofosmin (*TF*) stress defects, as calculated according to the Cequal program. The line of identity is shown

Fig. 3. Fairly close agreement between the severity scores of sestamibi (*MIBI*) and tetrofosmin (*TF*) stress defects, as calculated according to Cequal program. The line of identity is shown

erence subjects to be included should be sufficiently large and representative of the patients studied and that the normalcy rate should be adequate. One might easily introduce more errors than benefits if some of these demands were not satisfactorily fulfilled. Reference data bases must always be used with caution. If new acquisition variables are introduced, including a new radiopharmaceutical, it is recommended that at least a few subjects with a low likelihood of CAD and a number of patients with known disease are *systematically* tested against the old data base. The very limited differences between the sestamibi and tetrofosmin images in the present investigation seem to justify the use of an unchanged data base if changing the tracer from sestamibi to tetrofosmin or vice versa.

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