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Myocardial uptake characteristics of three ^{99m}Tc-labeled tracers for myocardial perfusion imaging one hour after rest injection

Agnieszka MANKA-WALUCH,* Holger PALMEDO,* Michael J. REINHARDT,* Alexius Y. JOE,* Christoph MANKA,** Stefan GUHLKE,* Hans-Jürgen BIERSACK* and Jan BUCERIUS*

*Department of Nuclear Medicine, University of Bonn, Bonn; Germany
**Department of Radiology, University of Bonn, Bonn; Germany

Objective: ^{99m}Tc-tetrofosmin and ^{99m}Tc-sestamibi are approved tracers for myocardial perfusion studies. Recently, a ^{99m}Tc-MIBI preparation from a different manufacturer (^{99m}Tc-cardiospect-MIBI) has been introduced to the market. Therefore, the aim of this study was the evaluation of ^{99m}Tc-tetrofosmin as well as of two different ^{99m}Tc-labeled MIBI tracers with regard to differences in imaging quality under resting conditions. ***Methods:*** Sixty patients (mean age 63.8 years ± 1.25) with known or suspected coronary artery disease but without evidence of rest-ischemia were included. Twenty patients in each group were examined by a two-day-rest-stress protocol using the three ^{99m}Tc-labeled tracers. Visual analysis of all images was performed by two experienced physicians blinded with regard to the applied tracer. Regions of interest (ROI) were defined over the heart, lung and whole body only in the rest imaging in order to calculate heart-to-lung, lung-to-whole body-, and heart-to-whole body-ratios. ***Results:*** The heart-to-lung ratio was statistically significant higher for ^{99m}Tc-cardiospect-MIBI as compared to ^{99m}Tc-sestamibi as well as to ^{99m}Tc-tetrofosmin. Furthermore, a significantly higher heart-to-lung ratio was found for ^{99m}Tc-sestamibi as compared to ^{99m}Tc-tetrofosmin. The heart-to-whole body-ratio and the lung-to-whole body-ratio were equivalent between all tracers. Visual analysis revealed only slight differences regarding image quality between all tracers. ***Conclusions:*** ROI analysis surprisingly revealed a significant higher myocardial uptake and consequently a higher heart-to-lung ratio for ^{99m}Tc-cardiospect-MIBI. Whether this leads to a better visual image quality has to be evaluated in future studies with larger study populations as well as semiquantitative segmental analysis of the myocardial perfusion images.

Key words: ^{99m}Tc-sestamibi, ^{99m}Tc-tetrofosmin, ^{99m}Tc-cardiospect-MIBI, myocardial uptake, pulmonary uptake

INTRODUCTION

^{99m}Tc-tetrofosmin (Myoview™, GE Healthcare Deutschland, Amersham Buchler GmbH & Co., Munich; Germany), and ^{99m}Tc-sestamibi (CARDIOLITE™, Bristol-Myers Squibb GmbH & Co. KGaA, Munich; Germany) are approved tracers for myocardial perfusion studies. Recently, ^{99m}Tc-cardiospect-MIBI (Cardio-SPECT™, Medi-Radiopharma Ltd., Budapest; Hungary) has been introduced as a generic compound to CARDIOLITE™ for myocardial perfusion imaging. For the two firstly named tracers previously published data regarding their diagnostic quality have been inconclusive.[1–6] However, no comparative data are to date available for ^{99m}Tc-cardiospect-MIBI. In contrast to thallium-201, which was the main tracer for assessment of myocardial perfusion for several decades, none of the presently investigated tracers show redistribution, so that a re-injection of the tracer is required for the rest acquisition. The uptake of both, tetrofosmin and MIBI tracers is known to be partly related to the Na^+/H^+ antiporter system within the cell membrane.[7] Only minor parts of the

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For reprint contact: Jan Bucerius, M.D., Department of Nuclear Medicine, University of Bonn, Sigmund-Freud-Str. 25, 53105 Bonn; GERMANY.
E-mail: jan.bucerius@ukb.uni-bonn.de

accumulated ^{99m}Tc-tetrofosmin inside the cells enter the mitochondria, whereas most of the accumulated ^{99m}Tc-sestamibi is related to mitochondrial uptake.[7] Previous biodistribution studies suggested more favorable heart-to-adjacent organ biokinetics for ^{99m}Tc-tetrofosmin as compared to ^{99m}Tc-sestamibi after exercise stress testing.[8] However, myocardial tracer uptake is closely related to the extent of ischemic disease as evaluated under stress conditions.[9,10] For the aim of evaluation of the myocardial tracer distribution analysis of only rest images therefore seems more appropriate.[11] A previously published study by Bangard et al. analyzing rest images of 21 patients without rest ischemia revealed a significantly better quality of imaging of ^{99m}Tc-sestamibi (due to a favorable biodistribution) as compared to ^{99m}Tc-furifosmin (Q12), another ^{99m}Tc-labeled tracer for myocardial perfusion imaging.[12] The aim of the present study was to evaluate the imaging quality of the applied ^{99m}Tc-labeled myocardial perfusion tracers with regard to myocardial, pulmonary, and whole-body-uptake under resting conditions.

MATERIAL AND METHODS

Study population

Sixty patients (mean age 63.8 years ± 1.25) with known or suspected coronary artery disease but without any evidence of rest ischemia were examined using a ^{99m}Tc-sestamibi (n = 20), a ^{99m}Tc-tetrofosmin (n = 20) or a ^{99m}Tc-cardiospect-MIBI (n = 20) protocol, respectively. All the patients referred to our institution for routine myocardial imaging were eligible. Rest ischemia was excluded by a normal rest single photon emission computed tomography (SPECT-) study. The patient data of the sestamibi-, cardiospect-MIBI- and tetrofosmin-groups were compared concerning the patient's gender (sestamibi: males, n = 14; cardiospect-MIBI: males, n = 12; tetrofosmin: males, n = 10), age, body mass index (BMI), the severity of the coronary artery disease (CAD) as well as cardiac-related medication (Table 1). In patients with proven CAD, the number of affected major coronary vessels (LAD, RCA, RCX) was defined by a significant stenosis of >50% as revealed by coronary angiography which was performed in selected cases within a close time frame before or after myocardial perfusion imaging.

After giving informed consent to participate in this study each patient underwent a two day rest/stress protocol. ^{99m}Tc-cardiospect-MIBI was applied according to § 73 Abs. 1 Nr. 1 AMG (Gesetz über den Verkehr mit Arzneimitteln; German drug administration law) regularizing the application of drugs with authorization in the European Union. All protocols were performed according to the standard 2-day acquisition protocol applied at the Department of Nuclear Medicine, University of Bonn; Germany including stress acquisition on the first day of examination and rest acquisition on the day after. Approximately 370 MBq of each of the applied tracer was administered both for the exercise stress testing and rest acquisition. Before stress imaging, all patients were asked to cease cardiac related anti-ischemic medication for at least 24 h (β-receptors antagonists for at least 48 h). Furthermore, patients were instructed not to consume caffeine products for 24 h before myocardial perfusion imaging (MPI) and to fast on the day of MPI.

Fifty patients underwent stress testing with a symptom-limited upright bicycle ergometric test, the remaining 10 patients received pharmacological studies for several reasons [adenosine stress (Adenoscan™, Astellas Pharma US, Inc., Deerfield IL): 5 patients, and dipyridamole stress (Persantin™, Boehringer Ingelheim Austria GmbH, Vienna; Austria): 5 patients].

An intravenous dose of 370 MBq of one of the ^{99m}Tc-labeled tracers was administered approximately 1 min before termination of the stress test.

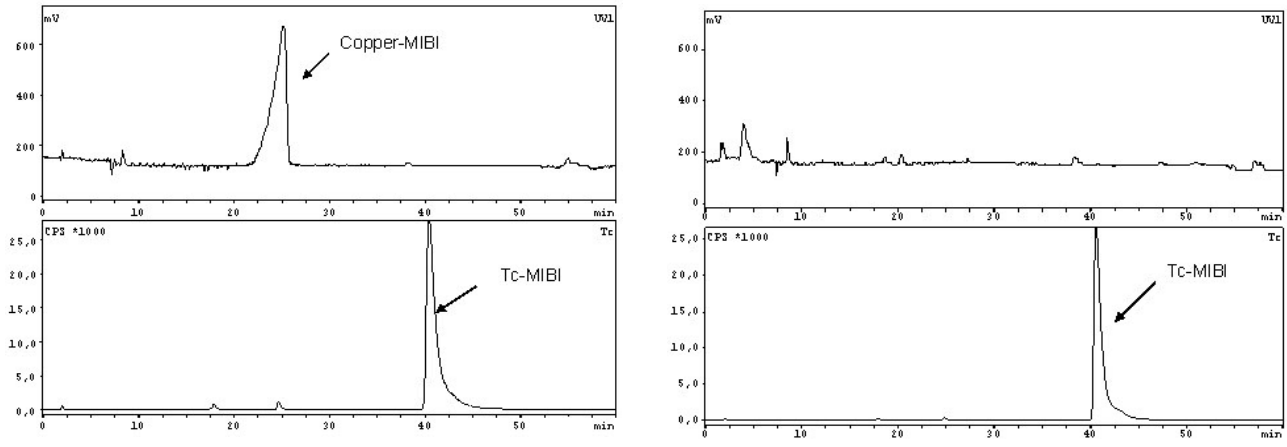
By intention, for the comparison of the biodistribution of the applied tracers, the study protocol was designed to analyze only images of the rest acquisition.

Radiopharmaceutical preparation and quality control

Tetrofosmin (Myoview™, GE Healthcare Deutschland, Amersham Buchler GmbH & Co., Munich; Germany), sestamibi (CARDIOLITE™, Bristol-Myers Squibb GmbH & Co. KGaA, Munich; Germany), and cardiospect-MIBI (Cardio-SPECT™, Medi-Radiopharma Ltd., Budapest; Hungary) are commercially available kits, which were labeled according to the manufacturers' guidelines. Routine quality control by thin-layer-chromatography (TLC) showed radiochemical purity of >95%. Tracers were injected within one hour after preparation.

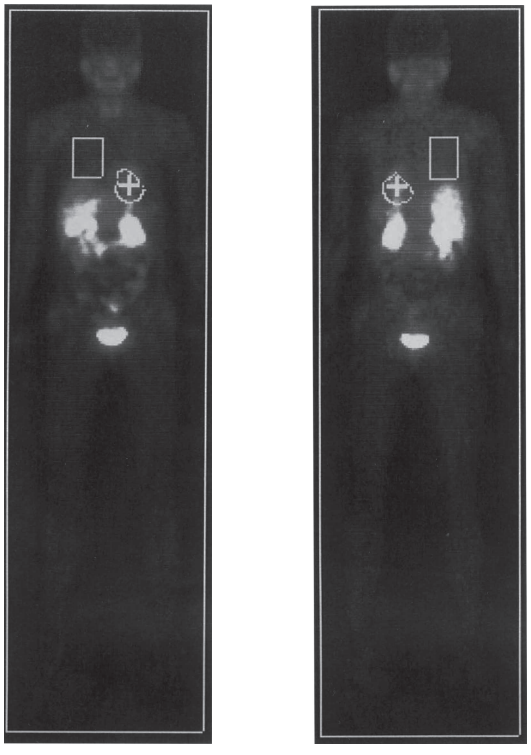
In the case of cardiospect-MIBI and sestamibi reversed phase high-performance liquid chromatography (HPLC) was performed in order to compare chemical and radiochemical profiles of both preparations. The respective kits were reconstituted by addition of 3 m*l* (~ 500 MBq) of the same ^{99m}Tc-generator eluate to each vial followed by heating at 100°C for 15 min. Samples of 30 μl were injected for HPLC analyses.

The HPLC-system consisted of a gradient pump (Kontron, Germany) and the effluent was monitored with an UV-detector at 254 nm. For radioactivity detection the outlet of the UV-detector was connected to a NaI(Tl) scintillation detector. The recorded data were processed on a Ramona software system (Raytest, Germany). The chromatography column used was a LiChrospher 100 RP-18 EC (250 × 4 mm) with a particle size of 5 μm (CS-Chromatograpie, Germany). For both radiopharmaceuticals a linear gradient was performed over 60 min starting from 100% aqueous solution (0.1% TFA) to 100% organic solution (acetonitrile) (see Figs. 1a and 1b). The radiochemical purity of both Tc-99m-MIBI-tracers (eluting at approximately 40 min) was very high with only minor differences in the radioactivity profiles. However, as already expected by comparison of the



a **b**

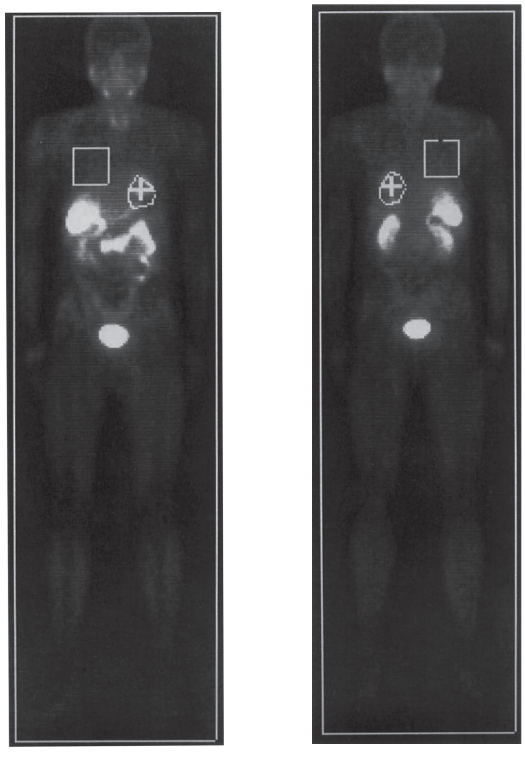
Fig. 1 HPLC chromatograms of sestamibi (a) and cardiospect-MIBI (b) showing identity with respect to the ^{99m}Tc-labeled compound (radioactivity channel in the lower chromatograms of each Figure) but major differences with respect to the copper MIBI portion as monitored in the UV-channel (upper chromatogram of each Figure). Details are given in the Method section. CPS: Counts per second.



a anterior **b** posterior

Distribution of ^{99m}Tc-MIBI.

Fig. 2 Planar anterior and posterior whole-body acquisition approximately 60 min after intravenous injection of ^{99m}Tc-MIBI. ROIs around the left ventricle as well as within the right lung. ROI: Region of interest, +: ROI of the left cardiac ventricle, Chamber: ROI in the left lung.



a anterior **b** posterior

Distribution of ^{99m}Tc-Tetrofosmin.

Fig. 3 Planar anterior and posterior whole-body acquisition approximately 60 min after intravenous injection of ^{99m}Tc-Tetrofosmin. ROIs around the left ventricle as well as within the right lung. ROI: Region of interest, +: ROI of the left cardiac ventricle, Chamber: ROI in the left lung.

Table 1 Patient characteristics in both groups

	^{99m}Tc-sestamibi	^{99m}Tc-cardiospect-MIBI	^{99m}Tc-tetrofosmin
		Mean ± SD	
Age (years)	63 ± 13.8	64.8 ± 9.4	62.4 ± 10.2
Height (cm)	171.2 ± 8.8	170.6 ± 6.4	170.1 ± 10.1
Weight (kg)	77.7 ± 17.3	76.2 ± 14.4	79.1 ± 15.5
BMI	26.3 ± 4.6	26.4 ± 5.4	27.2 ± 4.3
		n (%)	
Gender			
Male	14 (70)	12 (60)	10 (50)
Female	6 (30)	8 (40)	10 (50)
CAD			
No CAD	13 (65)	15 (75)	11 (55)
1-CAD	3 (15)	2 (10)	3 (15)
2-CAD	2 (10)	2 (10)	5 (25)
3-CAD	2 (10)	1 (5)	1 (5)
Heart related medication			
β-blocker	6 (30)	9 (45)	12 (60)
ACE-inhibitors	4 (20)	5 (25)	9 (45)
Ca-inhibitors	3 (15)	2 (10)	2 (10)
Nitrates	5 (25)	5 (25)	5 (25)
Statins	7 (35)	8 (40)	4 (20)

SD: Standard deviation, CAD: Coronary artery disease, 1-CAD: 1-vessel coronary artery disease, 2-CAD: 2-vessel coronary artery disease, 3-CAD: 3-vessel coronary artery disease

formulation (package inserts) of the 2 different MIBI kits, differences could be observed in the UV-channel: While a sestamibi kit contains 1.0 mg of the copper-MIBI precursor (eluting at approx. 25 min), cardiospect-MIBI contains only 0.06 mg of the same compound (copper-MIBI) and thus did not exceed the detection limit.

Acquisition protocol

All patients were imaged according to our routine one-isotope protocol. The acquisition was done 60 min post injection. In all groups, data acquisition was performed by a whole body scan using a double-head gamma camera (Vertex^{TM}, Philips Nuclear Medicine-ADAC, Milpitas; CA) equipped with a low energy high resolution collimator (matrix 256 × 1024 × 16; speed 20 cm × min^{-1}). The whole procedure was part of a routine rest/stress study using a two day protocol.

Image analysis

The whole body activity was assessed by region of interest (ROI) measurements. The patients were not allowed to void the bladder before the whole body scan.

Visual analysis of all images was performed by two experienced physicians blinded with regard to the applied myocardial perfusion tracer.

Myocardial, pulmonary, and whole-body activities were assessed as previously described.[12] In short, the myocardial activity was measured using an individual circular ROI around the heart. Furthermore, individual ROIs were drawn around the whole-body in anterior and posterior projections. Heart-to-whole body-ratios were calculated for each patient. In addition, the lung-uptake was assessed by a fixed ROI measurement in the right lung, and a lung-to-whole body-ratio was calculated according to the heart-to-whole body-ratio as mentioned above. Finally, the heart-to-lung ratio was calculated for each patient and heart-to-lung and heart-to-whole body-ratios for each patient in a specific group are given according to the number of affected coronary vessels in order to elucidate a potential impact of extent of CAD on myocardial tracer uptake as reflected by both ratios (see Tables 2 and 3 as well as Figs. 2a, 2b, 3a, 3b, 4–6). Mean of all ratios in each group of patient according to the applied tracer was calculated and consecutively compared for significant differences between all tracers.

Statistical analysis

For statistical analysis of the calculated ratios between all groups analysis of variance (ANOVA) with appropriate correction for multiple comparisons was performed. Patient related variables were compared using a χ^2 analysis for categorical variables, whereas an ANOVA was applied for continuous variables. Differences with a two-tailed $p < 0.05$ were considered to be statistically significant. All statistical analyses were performed using SPSS^{TM} statistical package 10.0 (SPSS Inc., Chicago, ILL).

RESULTS

The analysis of the patient records did not show significant differences in gender, age, BMI, or the severity of the coronary disease. Furthermore, no significant differences

Table 2 Heart-, whole body-, and lung-uptake (counts) in all patients according to the applied tracer

# Pts.	^{99m}Tc-tetrofosmin			^{99m}Tc-sestamibi			^{99m}Tc-cardiospect-MIBI		
	Heart	WB	Lung	Heart	WB	Lung	Heart	WB	Lung
1	21730	853949	21806	18922	869051	13907	16562	612228	13379
2	11892	708050	11846	11063	703329	11879	33870	1067815	12511
3	12674	674332	12759	13617	643302	11317	37068	1288913	15339
4	12947	695832	10351	7283	531674	9472	49831	1554671	14839
5	13768	577460	10182	10838	671412	11109	59847	1188042	21955
6	33126	406253	20958	15848	621287	14995	22641	912770	8234
7	23250	959782	18552	13354	669235	11558	24948	950966	9999
8	25291	835615	14886	13519	563656	7952	21724	740134	9370
9	22699	833366	18210	13088	489574	6614	19420	368299	5084
10	19011	738946	12481	13501	585087	6719	14931	603585	4357
11	10537	523355	10749	10566	321789	5492	11656	455867	9137
12	14031	772336	12151	10459	335746	5090	12977	531679	8717
13	10118	610749	13077	13966	5907006	7295	15409	607066	8367
14	14524	733499	14723	13454	536427	9422	25702	1095736	9605
15	13328	680456	8984	10993	637955	9443	38495	1378751	13176
16	19017	780005	15582	18574	678936	14289	35162	1141629	15333
17	8316	613441	11287	23551	652509	13013	28758	949076	9154
18	7881	622639	9136	15565	624617	8334	24945	1019800	16624
19	12345	567222	10126	18557	717153	9077	28079	1159960	81975
20	12872	789643	12311	15594	825810	14734	38050	1354118	14659
Mean	15967.6	698846.2	13507.6	14115.4	879277.6	10085.4	28003.5	949055.0	15090.4
SD	6472.6	130252.6	3783.7	3731.5	1190866.6	3091.6	12543.0	337150.2	16293.7

Pts.: Patients, #: all uptake values are given as total counts, WB: Whole body, SD: Standard deviation

Table 3 Heart to lung-, heart to whole body-, and lung to whole body-ratio in all patients according to the applied tracer

Pts.	^{99m}Tc-tetrofosmin			^{99m}Tc-sestamibi			^{99m}Tc-cardiospect-MIBI		
	H/WB	H/L	L/WB	H/WB	H/L	L/WB	H/WB	H/L	L/WB
1	0.025	0.996	0.026	0.021	1.36	0.016	0.027	1.238	0.022
2	0.017	1.004	0.017	0.016	0.93	0.017	0.032	2.707	0.012
3	0.019	0.993	0.019	0.021	1.2	0.018	0.029	2.417	0.012
4	0.019	1.251	0.015	0.014	0.77	0.078	0.032	3.358	0.010
5	0.024	1.352	0.018	0.016	0.98	0.017	0.050	2.726	0.018
6	0.082	1.581	0.052	0.026	1.06	0.024	0.025	2.750	0.009
7	0.024	1.253	0.019	0.02	1.16	0.017	0.026	2.495	0.011
8	0.030	1.699	0.018	0.023	1.7	0.014	0.029	2.318	0.013
9	0.027	1.247	0.022	0.027	1.98	0.014	0.053	3.820	0.014
10	0.026	1.523	0.017	0.023	2.01	0.011	0.025	3.427	0.007
11	0.020	0.980	0.021	0.032	1.57	0.017	0.026	1.276	0.020
12	0.018	1.155	0.016	0.031	2.06	0.015	0.024	1.489	0.016
13	0.017	0.774	0.021	0.024	1.91	0.001	0.025	1.842	0.014
14	0.020	0.987	0.020	0.025	1.42	0.017	0.023	2.676	0.009
15	0.020	1.483	0.013	0.017	1.16	0.015	0.028	2.922	0.010
16	0.024	1.220	0.020	0.03	1.29	0.021	0.031	2.293	0.013
17	0.014	0.737	0.018	0.036	1.81	0.019	0.030	3.142	0.010
18	0.013	0.863	0.015	0.025	1.87	0.013	0.024	1.501	0.016
19	0.022	1.219	0.018	0.025	2.04	0.013	0.024	0.343	0.071
20	0.016	1.046	0.016	0.018	1.06	0.018	0.028	2.596	0.011
Mean	0.02	1.17	0.02	0.02	1.49	0.02	0.03	2.37	0.02
SD	0.01	0.27	0.01	0.01	0.44	0.005	0.01	0.86	0.01

Pts.: Patients, H/WB: Heart-to-whole body ratio, H/L: Heart-to-lung ratio, L/WB: Lung-to-whole body ratio, SD: Standard deviation

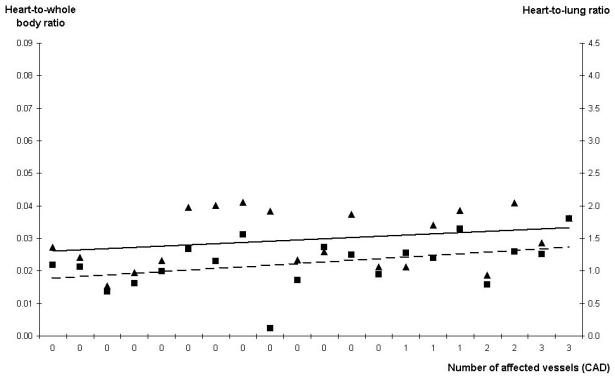


Fig. 4 Heart-to-whole body- and heart-to-lung ratios are shown for each patient in the ^{99m}Tc-sestamibi group in relation to the degree (i.e. numbers of affected vessels) of coronary artery disease. CAD: Coronary artery disease, Square: Heart-to-whole body ratio (*dotted line*), Triangle: Heart-to-lung ratios (*uninterrupted line*).

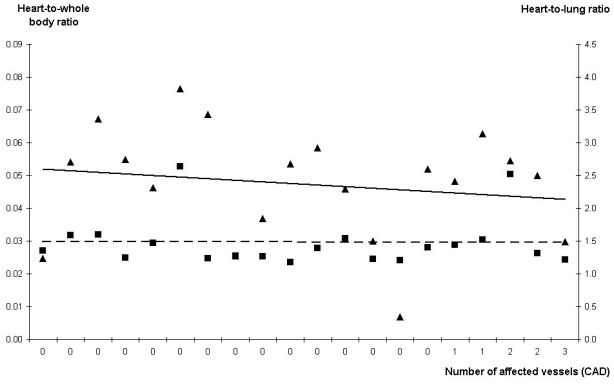


Fig. 5 Heart-to-whole body- and heart-to-lung ratios are shown for each patient in the ^{99m}Tc-cardiospect-MIBI group in relation to the degree (i.e. numbers of affected vessels) of coronary artery disease. CAD: Coronary artery disease, Square: Heart-to-whole body ratio (*dotted line*), Triangle: Heart-to-lung ratios (*uninterrupted line*).

between any groups could be found with regard to the administered cardiac-related medication (Table 1).

Visual analysis of the rest images revealed a good image quality in each case and only slight differences between the tracers.

Counts of ROI analysis of myocardial-, lung, and whole body-uptake in each patient as well as mean and standard deviation of all patients according to the applied tracer are given in Table 2.

Heart-to-whole body-, heart-to-lung, and lung-to-whole body ratio of each patient as well as mean and standard deviation of all patients according to the applied tracer are shown in Table 3. The heart-to-lung ratio was significantly higher for cardiospect-MIBI as compared to tetrofosmin (cardiospect-MIBI: 2.37 ± 0.86; tetrofosmin: 1.17 ± 0.27; $p < 0.0001$) as well as compared to MIBI

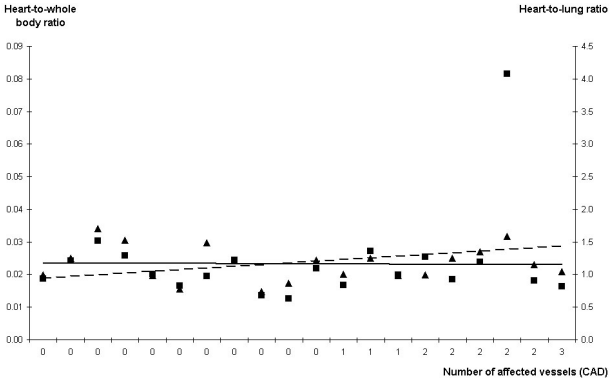


Fig. 6 Heart-to-whole body- and heart-to-lung ratios are shown for each patient in the ^{99m}Tc-tetrofosmin group in relation to the degree (i.e. numbers of affected vessels) of coronary artery disease. CAD: Coronary artery disease, Square: Heart-to-whole body ratio (*dotted line*), Triangle: Heart-to-lung ratios (*uninterrupted line*).

(cardiospect-MIBI: 2.37 ± 0.86; sestamibi: 1.49 ± 0.44; $p < 0.0001$). Furthermore, a significantly higher heart-to-lung ratio was found for MIBI as compared to tetrofosmin ($p = 0.027$). In contrast to these findings, the heart-to-whole body ratio (tetrofosmin vs. MIBI: $p = 1.0$; tetrofosmin vs. cardiospect-MIBI: $p = 0.27$, and MIBI vs. cardiospect-MIBI: $p = 0.112$) and the lung-to-whole body ratios (tetrofosmin vs. MIBI: $p = 0.499$; tetrofosmin vs. cardiospect-MIBI: $p = 0.514$, and MIBI vs. cardiospect-MIBI: $p = 1.0$) were almost equal for all three tracers.

Heart-to-whole body- and heart-to-lung ratios for each patient according to the number of affected coronary vessels in one of the three groups are given in Figures 4–6. No trend towards a reduced myocardial tracer uptake, as reflected by a lower heart-to-whole body- and/or heart-to-lung ratio, in relation to a higher degree (i.e. multivessel disease) of CAD could be observed in the ^{99m}Tc-sestamibi- or ^{99m}Tc-tetrofosmin group. In contrast, in the ^{99m}Tc-cardiospect-MIBI group both ratios tended to be slightly decreased with a higher number of affected coronary vessels (Figs. 4–6).

DISCUSSION

Radionuclide myocardial perfusion imaging is a well established method for clinical evaluation of patients with suspected or known ischemic heart disease. Although several ^{99m}Tc-labeled agents have been developed, today ^{99m}Tc-sestamibi and ^{99m}Tc-tetrofosmin are mostly utilized in clinical practice.[13–15] However, recently published comparative studies have shown variable results for the lung uptake of the both tracers.[1–6,8,16] Furthermore, for ^{99m}Tc-cardiospect-MIBI comparative data regarding kinetics and biodistribution are not yet available.

Since the contrast of two neighboring tissues or organs is a measure of image quality, especially the heart-to-

lung-ratio is important in order to evaluate the diagnostic value of myocardial perfusion tracers. The differences in previously published results[3–6] may be explained by technical and methodical differences, e.g. time of imaging or placement of the regions of interest. All studies published so far examined tracer-uptake in the heart and in neighboring organs (e.g. lung, liver, etc.) only during stress conditions.[3–6] Münch et al. studied the time course of uptake by various organs after the stress injection: myocardial uptake was at least 45% higher at 1 h with tetrofosmin than with sestamibi.[4] The aim of our study was to examine the uptake of the three tracers (mainly in the lung and the heart) in resting conditions. This was intended, as myocardial tracer uptake is closely related to the extent of ischemic disease as evaluated under stress conditions. Therefore, evaluation of resting imaging with regard to myocardial tracer distribution seems to be more appropriate. For this reason in our study only rest images were evaluated in contrast to previously published studies.[4,5]

Patients, who were included in our study, did not vary statistically significant regarding gender, age, body mass index or the severity of the coronary artery disease between the three groups of tracer applied. Since there was no significant difference in the patient population, the influence on the image quality of intra-individual variations could be minimized. This is important as, by intention, we have not compared tetrofosmin- as well as both MIBI-tracers within the same individual for radiation safety and ethical reasons. This is in accordance with several previously published studies using the same approach of data acquisition.[4,6,10]

It is well-known that the specificity of myocardial SPECT is reduced for over-weight patients, particularly for the exclusion of the coronary artery disease due to attenuation artifacts. Furthermore, use of cardiac-related medication, especially anti-ischemic drugs, can bias the results of myocardial perfusion imaging. In the present study, no statistically significant differences were found between any groups with regard to cardiac-related medication. Additionally, a potential impact of cardiac-related medication could be further minimized, as all of those medications had been discontinued several days before rest imaging with all tracers in the present study.

Although Soman et al. found a significant difference with regard to quantification of defect severity between tetrofosmin and sestamibi in patients with mild to moderate coronary artery disease in a recently published study, most published papers showed no substantial differences between the two tracers regarding the detection of coronary artery disease.[5] Furthermore, in the ROBUST study with 2,560 patients randomized to either tetrofosmin, thallium, or MIBI, in a subset of 137 patients without myocardial infarction, angiography, or revascularization no significant differences between any of the evaluated tracers with regard to sensitivity or specificity were observed.[6] In contrast, our results could not confirm these findings as we did observe a statistically significant higher heart-to-lung ratio for ^{99m}Tc-sestamibi as compared to tetrofosmin which was previously reported by Flamen et al.[8] Furthermore, we also found significant differences in the calculated heart-to-lung ratio of ^{99m}Tc-cardiospect-MIBI as compared to both ^{99m}Tc-tetrofosmin as well as ^{99m}Tc-sestamibi indicating a higher myocardial uptake of ^{99m}Tc-cardiospect-MIBI. This was surprising, as we did not expect any significant difference with regard to body-distribution between the two MIBI-tracers. One potential explanation could be related to the different amounts of the Cu-MIBI-complex serving as a ^{99m}Tc-MIBI-precursor within both MIBI-preparations (sestamibi: 1 mg Cu-MIBI; cardiospect-MIBI: 0.06 mg Cu-MIBI). We have to speculate that this difference could result in a higher competition for myocardial uptake between Cu-MIBI and ^{99m}Tc-MIBI in the sestamibi-compound. Cu-MIBI as well as ^{99m}Tc-MIBI are mono-cationic species mimicking potassium cations as the principal mechanism of myocardial cell uptake. However, the reasons for the different myocardial uptake of the MIBI-tracers remain to be analyzed in detail. Whether the observed higher myocardial uptake of ^{99m}Tc-cardiospect-MIBI leads to an expectable better visualization of these MIBI-images as compared to tetrofosmin- and sestamibi-tracers has to be evaluated in future studies with larger study populations as well as semiquantitative segmental analysis of the myocardial perfusion images.

Study limitations

The small study population as well as the absence of an attenuation correction and of gated SPECT are limitations of the present study. Although we have taken no account of the desirability of acquiring ECG gated images or the increasing availability of attenuation and scatter correction, all of which can improve image quality and reduce artifacts, the findings of the present study are important for assessing the contributions that can be made by these developments. Furthermore, we did not calculate precise time intervals between injection of the tracers and the onset of data acquisition. However, data acquisition was started exactly 60 min after injection of the tracer in each patient. Another limitation of the present study is related to the heterogeneity of the study population with regard to the extent of atherosclerotic altered coronary vessels and to missing information about left ventricular function of each patient in our study population. One has to postulate that with a higher degree of CAD, i.e. multi-vessel disease, the myocardial tracer uptake should be significantly reduced, especially as compared to patients with no evidence of CAD. This would bias the results of our study as the number of patients with no suspected or with proven CAD differed between the three groups. However, as the differences with regard to the degree of CAD failed to be statistically significant between the three groups and a trend to even higher heart-to-whole body- and heart-to-

lung ratios, reflecting a higher myocardial tracer uptake, with an increasing degree of CAD could be observed in the ^{99m}Tc-sestamibi as well as the ^{99m}Tc-tetrofosmin group this limitation should not significantly bias our results. This is further supported by the fact that in the ^{99m}Tc-cardiospect-MIBI group, in which patients could be shown to have significantly higher heart-to-lung ratios as compared to those in both other groups, both heart-to-lung- and heart-to-whole body ratios tended to decrease with a higher degree of CAD. With regard to an impaired left ventricular function, potentially leading to lung congestion and consecutively to an increased lung uptake of the three tracers, the potential bias of our results should be minimal as no significant differences could be found between the lung-to-whole body ratios of any groups. As such, significant differences observed between the heart-to-lung ratios of all groups in the present study should not be impacted by an altered lung uptake in one group but should be closely related to a different myocardial uptake of the three tracers. These noted limitations as well as the observed differences with regard to the myocardial uptake of both MIBI-tracers have to be addressed in a future study with a greater study population.

CONCLUSION

As compared to ^{99m}Tc-tetrofosmin as well as ^{99m}Tc-sestamibi, the significantly higher myocardial uptake of ^{99m}Tc-cardiospect-MIBI led to a significantly higher heart-to-lung ratio. Although the resulting higher contrast should lead to better visualization of myocardial perfusion defects, future studies have to be performed in order to evaluate potential benefits of the new ^{99m}Tc-MIBI tracer with regard to image quality. Above that, it seems desirable to obtain similar data during stress. However, here, differences of perfusion due to coronary artery disease related ischemia have to be considered so that it will not be easy to define comparable groups.

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