

Validation of early image acquisitions following Tc-99 m sestamibi injection using a semiconductors camera of cadmium-zinc-telluride

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Background. Cadmium-zinc-telluride (CZT) cameras allow to decrease significantly the acquisition time of myocardial perfusion imaging (MPI), but the duration of the examination is still long. Therefore, this study was performed to test the feasibility of early imaging following injection of Tc-99 m sestamibi using a CZT camera.

Methods. Seventy patients underwent both an early and a delayed image acquisition after exercise stress test ($n = 30$), dipyridamole stress test ($n = 20$), and at rest ($n = 20$). After injection of Tc-99 m sestamibi, the early image acquisition started on average within 5 minutes for the exercise and rest groups, and 3 minutes 30 seconds for the dipyridamole group. Two independent observers evaluated image quality and extracardiac uptake on four-point scales. The difference between early and later images for each patient was scored on a five-point scale.

Results. The image quality and extracardiac uptake of early and delayed image acquisitions were not different for the three groups ($P > .05$). There was no significant difference between early and delayed image acquisitions in the exercise, dipyridamole, and rest groups, respectively, in 63%, 40%, and 80% of cases. In the exercise group and rest group, a defect was only present in early MPI, respectively, in 13% and 20% of cases. A defect was only present in delayed images in 10% of cases in the exercise group and in 45% of cases in the dipyridamole group.

Conclusions. There was no difference between early and later image acquisitions in terms of quality. This protocol reduces the length of the procedure for the patient. Beginning with early image acquisitions may help to overcome the artifacts that are observed at the delayed time. (*J Nucl Cardiol* 2017;24:1149–56.)

Key Words: Sestamibi • cadmium-zinc-telluride • myocardial perfusion imaging • SPECT • image quality

Abbreviations		MPI	Myocardial perfusion imaging
CZT	Cadmium-zinc-telluride	MLEM	Maximum-likelihood expectation maximization
LVEF	Left ventricular ejection fraction	SD	Standard deviation
ASNC	American Society of Nuclear Cardiology		
CAD	Coronary artery disease		
SPECT	Single photon emission computerized tomography		

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INTRODUCTION

A new generation of gamma cameras dedicated to cardiology was developed during the last decade using semiconductors of cadmium-zinc-telluride (CZT) and based on the principle of direct conversion. These CZT cameras demonstrated their superiority in terms of sensitivity, spatial resolution, energy resolution and image quality when compared to the Anger gamma camera.¹ This progress allowed to reduce significantly the acquisition time but also the injected activity without impairing image quality.^{1,2}

In addition to shorter image acquisition, reducing the delay between the injection of the radiopharmaceutical and the image acquisition would also allow a decrease of the total examination time; early image acquisition following stress would enable to get a closer assessment of post stress left ventricular ejection fraction (LVEF).

There is currently no recommendation for intervals between injection of the radiopharmaceutical and image acquisition for CZT cameras. The American Society of Nuclear Cardiology (ASNC) recommends an interval of at least 10-20 minutes for exercise, 30-60 minutes for rest, and 45-60 minutes for pharmacologic stress depending on the technetium 99 m agent used (Tc-99 m sestamibi and Tc-99 m tetrofosmin) and allowed a longer interval up to 2 hours,³ since redistribution is minimal with these agents.^{4,5}

A previous study using a CZT camera (Discovery NM 530c, General Electric) did not validate the early image acquisition (0 to 12 minutes following the rest injection) compared to delayed acquisition (45 to 60 minutes).⁶ Indeed, the images acquired within 8 minutes after rest injection were often uninterpretable due to excessive blood pool uptake, and the image quality was better on the rest images obtained later compared to images obtained at 8-12 minutes.

Since a second type of CZT camera with different geometry and collimation is now available on the market, the D-SPECT camera (Spectrum Dynamics, Caesarea, Israel), we decided to assess the feasibility of early imaging following stress injection and rest injection using a CZT D-SPECT camera. The validation of such a protocol enabling a significant shortening of the procedure was awaited.⁷

METHODS

Study Population

Patients in our study were referred for the monitoring or detection of coronary artery disease (CAD) by myocardial

perfusion imaging (MPI) single-photon emission computerized tomography (SPECT) at European Georges Pompidou Hospital, University Paris Descartes and AP-HP, between November 2014 and April 2015. Seventy patients performed both an early and a delayed rest or stress acquisition depending on the availability of camera, doctors, and technicians. Thirty patients were included in the exercise stress test group, 20 in the dipyridamole stress test group, and 20 in the rest group.

Exercise Stress Test

Exercise stress test was performed according to international recommendations.⁸ Briefly, without contraindications, the patient underwent symptom limited bicycle exercise testing and continuous 12-lead ECG monitoring. At peak heart rate (at least 85% maximal predicted heart rate), Tc-99 m sestamibi was injected.

Dipyridamole Stress Test

Dipyridamole stress test was performed according to international recommendations.⁸ Patients were instructed to avoid caffeine-containing products for at least 12 hours. They were installed on the chair of the camera and received 0.76 mg/kg of dipyridamole over 4 minutes, the radiopharmaceutical (Tc-99 m sestamibi) being injected at the 7th minute.

Imaging Protocol

The administered doses of Tc-99 m sestamibi were 2.5 MBq/kg for exercise and dipyridamole groups and 5 MBq/kg for the rest group. The stress and rest images were acquired on a CZT D-SPECT camera whose characteristics have been described in previous studies.^{2,9} Each acquisition was preceded by the ingestion of a glass of cold sparkling water. The patient was seated as close as possible to the detectors, with left arm above the head of the camera. A 10-second pre-scan was performed at the beginning of each acquisition to identify the location of the heart and to set the angle limits of scanning for each detector. After the injection of the radiopharmaceutical (Tc-99 m sestamibi), the image acquisition started on average within 5 minutes for the patients of exercise stress test and rest group and 3 minutes 30 seconds for the patients of the dipyridamole stress test group. Each patient also underwent a delayed acquisition at least 45 minutes after radiopharmaceutical injection.

Image Reconstruction

Energy windows were set at 20% around the 140 keV photopeak for the Tc-99 m sestamibi. The total number of counts acquired was greater than 1000 Kcts at stress and 1500 Kcts at rest with an average duration of acquisition of 5 minutes at rest and 7 minutes at stress. The data were reconstructed using an iterative algorithm based on the maximum-likelihood expectation maximization (MLEM) method specifically designed for D-SPECT.^{9,10} All reconstructed images were reoriented according to short, vertical, and horizontal long-axis for visual comparison.

Image Analysis

Two independent observers, blind to acquisition parameters, performed a visual analysis. In the event of disagreement between the two observers, a consensus was reached through common reading. A comparison was performed between early and delayed perfusion images, the difference was scored on a five-point scale: 0 = no difference, 1 = mild on 1 territory, 2 = moderate on 1 territory or mild on 2 territories, 3 = important, and 4 = very important (a score ≥ 2 was considered significant). An evaluation of the inter-observer agreement rates on the visual analysis scores between early and delayed perfusion images was performed.

In addition, image quality was graded for both intervals on a subjective four-point scale: 1 = excellent, 2 = good, 3 = average, and 4 = poor. The quantification of extracardiac uptake was graded on a four-point scale: 1 = absent, 2 = mild, 3 = moderate, and 4 = important.

Ischemia was evaluated according to the 17-segment model for both time sequences and all patients.^{11,12} The images were classified into three categories: no ischemia, moderate ischemia (1-2 segments), and severe ischemia (>2 segments). If early or delayed acquisition was normal at stress, we did not perform a rest acquisition to avoid unnecessary reinjection.

Statistical Analysis

All continuous variables are expressed as mean \pm standard deviation (SD). A Fisher test was used to compare categorical variables. A *P* value $<.05$ was considered significant for all comparisons. The inter-observer variability was measured using percentage agreement and kappa with linear weighting value.

RESULTS

Demographics

The clinical characteristics of patients studied are shown in Table 1. 57%, 75%, and 50% of the patients in

the exercise, dipyridamole, and rest groups, respectively, were referred for the detection of CAD.

Image Quality and Extracardiac Uptake

There was no significant difference in the image quality and extracardiac uptake between early and delayed image acquisitions for the three groups (Tables 2, 3).

All patients had images of quality suitable for the interpretation, graded good, or excellent in nearly all patients. Only one patient had an image quality considered as average in our study. He belonged to the rest group and the image quality was similar on early and delayed acquisitions.

No extracardiac uptake was observed in 83% of the early images acquisitions and 87% of delayed acquisitions in the exercise group. The score of extracardiac uptake tended to be higher in the early images acquisition for the dipyridamole and rest groups, but the difference was not significant (*P* = .1 and .09).

Visual Analysis

No significant difference was found between the early and delayed images in 19 acquisitions of the exercise group (63%), 8 of the dipyridamole group (40%), and 16 of the rest group (80%) (Figure 1).

In the exercise group, a significant difference was found in 37% of cases (11 patients) with a perfusion defect present or higher on early acquisition in 27% of cases (8 patients) and on delayed acquisition in 10% of cases (3 patients). A perfusion defect was observed in the inferior wall (2 patients) and the apex (2 patients) on the early images acquisition while perfusion at the later time was normal.

In the dipyridamole group, among the 12 cases in which a significant difference was found, perfusion defects were higher on the delayed images acquisition in 9 cases.

Table 1. Characteristics of patients

	Exercise group (n = 30)	Dipyridamole group (n = 20)	Rest group (n = 20)
Age, years (mean \pm SD)	66.1 \pm 9.3	70.7 \pm 11.9	66.1 \pm 12.1
Gender			
Male	20 (67%)	8 (40%)	15 (75%)
Female	10 (33%)	12 (60%)	5 (25%)
Weight, kg (mean \pm SD)	83.0 \pm 16.0	71.6 \pm 16.1	79.7 \pm 14.4
BMI, kg/m ² (mean \pm SD)	27.8 \pm 5.0	26.3 \pm 4.6	27.8 \pm 4.4
Detection CAD	17 (57%)	15 (75%)	10 (50%)
Monitoring CAD	13 (43%)	5 (25%)	10 (50%)

BMI, Body mass index; CAD, coronary artery disease

Table 2. Image quality

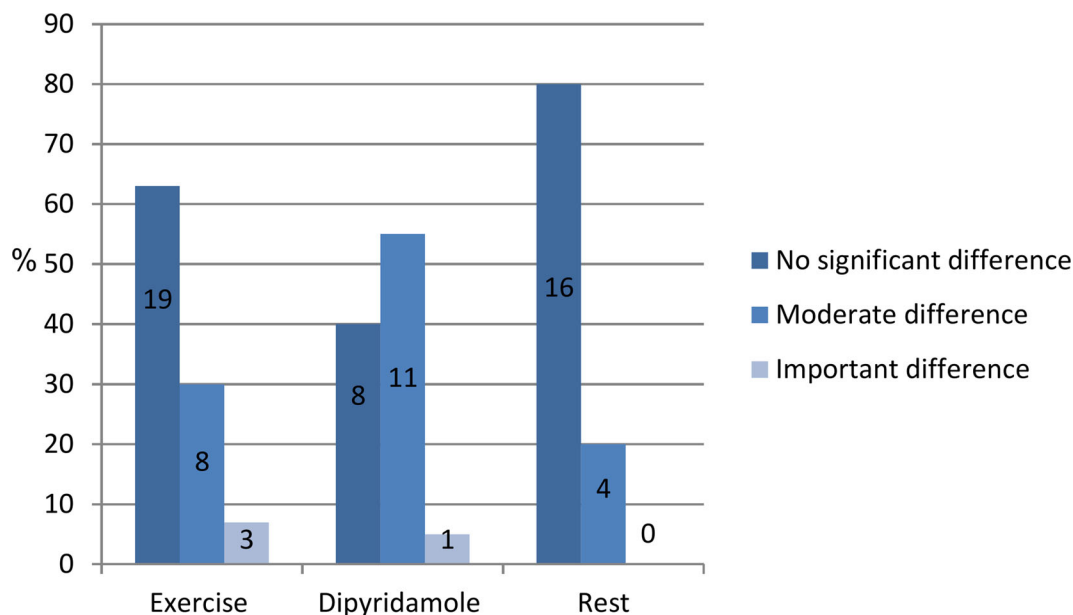
	Exercise group		Dipyridamole group		Rest group	
	Early	Delayed	Early	Delayed	Early	Delayed
1 = Excellent	29 (97%)	29 (97%)	16 (80%)	19 (95%)	15 (75%)	18 (90%)
2 = Good	1 (3%)	1 (3%)	4 (20%)	1 (5%)	4 (20%)	1 (5%)
3 = Average	0	0	0	0	1 (5%)	1 (5%)
4 = Poor	0	0	0	0	0	0

P value >.05 for all groups

Table 3. Extracardiac uptake

	Exercise group		Dipyridamole group		Rest group	
	Early	Delayed	Early	Delayed	Early	Delayed
0 = Absent	25 (83%)	26 (87%)	8 (40%)	14 (70%)	5 (25%)	10 (50%)
1 = Mild	5 (17%)	3 (10%)	6 (30%)	5 (25%)	8 (40%)	5 (25%)
2 = Moderate	0	1 (3%)	4 (20%)	0	0	2 (10%)
3 = Important	0	0	2 (10%)	1 (5%)	7 (35%)	3 (15%)

P value >.05 for all groups

**Figure 1.** Difference between early and delayed image acquisitions according visual analysis.

In the rest group, there were more perfusion defects on the early acquisition in 20% of cases (four patients).

The inter-observer variability on the visual analysis scores between early and delayed images was 87% (kappa 0.84, 95% CI 0.76-0.94%).

Ischemia findings for exercise and dipyridamole groups are shown in Table 4.

In the exercise group, five patients had stress acquisition only and two patients in the dipyridamole group.

DISCUSSION

Nuclear cardiology plays a key role in CAD patient management. However, SPECT MPI is the longest time-consuming imaging technique when compared to other

Table 4. MPI interpretation

	Exercise stress test group		Dipyridamole stress test group	
	Early	Later	Early	Later
No ischemia	16	15	13	10
Moderate ischemia	7	9	4	6
Severe ischemia	2	1	1	2

modalities. No other imaging modality necessitates the patient to wait several hours between two image acquisitions. Any technical solution enabling to shorten the procedure would be welcome.

Improved performances of CZT camera allow a significant reduction of the image recording times. To reduce further the duration of the examination, we studied the feasibility of early image acquisition following stress and rest injection of Tc-99 m sestamibi. Several studies have already investigated early acquisition following injection of technetium 99 m agents. Giorgetti and al.¹³ demonstrated that early stress and rest Tc-99 m tetrofosmin imaging at 15 minutes following injection are feasible on Anger camera. A study of 30 patients using a CZT camera (Discovery NM 530c, General Electric) did not validate early rest acquisition.⁶ Early images were often uninterpretable because of a too high extracardiac uptake. Another study showed a superior quality of early rest images with technetium 99 m agents on a CZT D-SPECT camera with a double isotope acquisition.¹⁴ The extracardiac uptake was less frequent when rest acquisition began 2 minutes after the rest injection. To the best of our knowledge, no study has been performed evaluating the feasibility of early acquisition on both rest and stress images on CZT camera.

Our study demonstrates that early and delayed image acquisitions with CZT D-SPECT camera are equivalent in terms of image quality. Extracardiac uptake, even when marked, did not interfere with the image quality (Figure 2).

When differences were found, we considered that a perfusion defect appearing on early images only had an artifactual origin since early redistribution of Tc-99 m sestamibi has not been reported.^{4,5} Taillefer¹⁵ did not show redistribution of sestamibi between 15 and 60 minutes. Studies that reported redistribution were performed between 1 and 3 hours^{16,17}.

If redistribution happens, it should be delayed (more than 1 hours after injection).

If early redistribution of Sestamibi should be of clinical relevance, it is very improbable that the numerous clinical studies published during the last two decades, where image acquisitions were performed 45-60 minutes after injection at stress, would have found similar diagnosis performances than thallium 201 SPECT.

In our interpretation process, a defect appearing on delayed image only is an artifact. Thus we considered that a defect present at one time only (early or late) was an artifact.

In our comparison study, we decided to not use a computerized quantification on a 17-segment model.^{11,12} Indeed this technique highlights defects that are not visible or not considered significant by visual analysis of a trained observer. This model is a potential source of error in such study: for an example, it would not identify patient with similar difference score but with a change in location of defects. This type of methodology has already been used in previous studies.¹⁸ Visual semi-quantitative analysis is used by most of nuclear medicine centers in common practice.

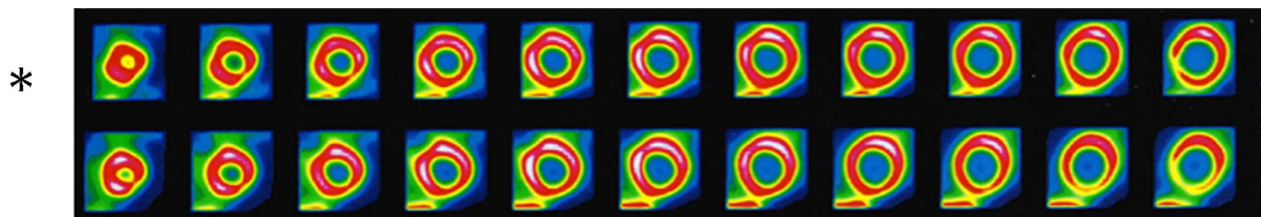


Figure 2. Rest acquisition. There is no difference between early and delayed images (*). The extracardiac uptake is important but has no influence on the image quality, which remains good.

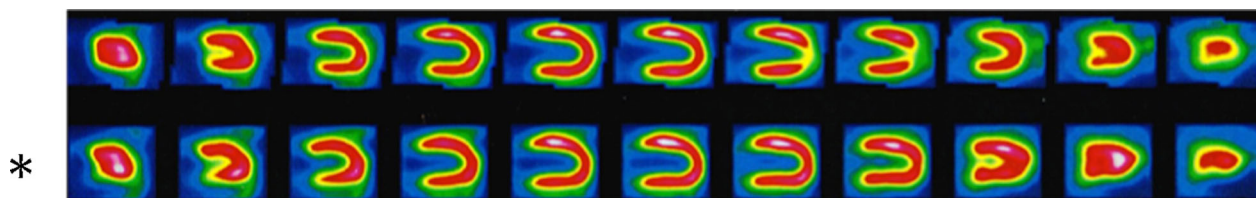


Figure 3. Exercise acquisition. A perfusion defect is observed on apex on the early images although delayed images (*) are normal on this region.

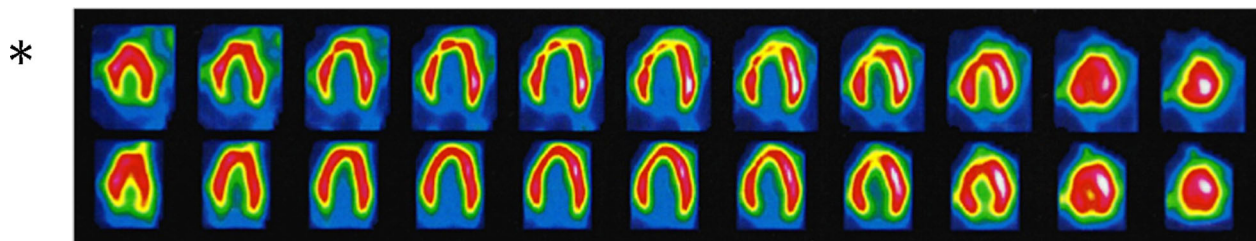


Figure 4. Exercise acquisition. On delayed images (*) a perfusion defect appears on the apex although this region is normal on early images.

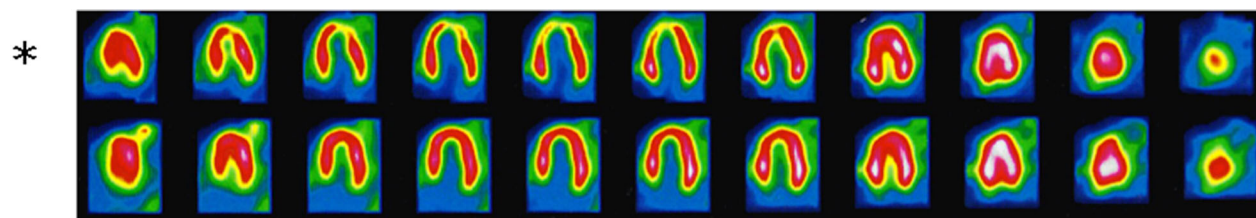


Figure 5. Dipyridamole acquisition. A defect is observed on the apex on delayed images (*) although early images are normal on this region.

In the exercise group, no difference was observed in nearly 60% of cases. When there was a disagreement, we found more severe perfusion defects on the early images (Figure 3) but in 10% of the cases, the abnormalities were only present on delayed images (Figure 4). In most cases, the largest perfusion defects that appeared in early images were on the inferior wall or on the apex corresponding to artifact. Therefore, it seems useful to begin SPECT acquisition with early images following the injection and to perform a second acquisition later when perfusion abnormalities are located at the inferior wall or the apex. In the majority of cases with this protocol, we can overcome the artifactual perfusion defects present in early and/or delayed images, and avoid unnecessary rest reinjection.

In the dipyridamole group, we found a higher difference between images at the two different times. In 45% of cases, perfusion defects were recorded on delayed image acquisitions only (Figure 5), without preferential location. In vasodilator test, early image

acquisition seems therefore more appropriate to avoid unnecessary rest reinjection.

At rest, there was a very good agreement between the two examination times. In 80% of cases, no significant differences were found. In 20% of cases, a perfusion defect was present on inferior wall or the apex, more severe in 10% of cases in early images. If stress images show normal perfusion on these segments, these defects present only on rest images can be easily assessed as of artifactual origin. Our findings confirm the results of a previous study.¹⁴ However, the study using the Discovery NM camera found that early rest images were not feasible.⁶ This difference could be at least explained by a different geometry of collimation between Discovery NM camera and D-SPECT cameras. Indeed the orientation of the collimators situated on both sides of the heart makes Discovery NM camera more sensitive to extracardiac uptake.

Myocardial perfusion defects of artifactual origin due to a extracardiac uptake have been described,¹⁹ even

though extracardiac uptake may be non-visible on images. Liver, gall bladder, and spleen uptake rapidly rise following Tc-99 m sestamibi injection.^{5,20} According to our experience, these artifacts seem to be more frequently visible on CZT cameras. Algorithms used for image reconstruction and attenuation artifacts that were hidden by scatter on Anger cameras could be a part of the explanation.

LIMITATIONS

A subjective semi-quantitative visual analysis was performed for the interpretation of the images. Since this is a feasibility study, we did not compare the results of image acquisition at the different delay with the result of coronary angiography, and there was no clinical follow-up.

NEW KNOWLEDGE GAINED

This study allows a significant reduction of delay between the injection of the radiopharmaceutical and image acquisitions using a CZT D-SPECT camera and Tc-99 m sestamibi.

CONCLUSIONS

This study validates the early image acquisition protocol using a CZT D-SPECT camera and Tc-99 m sestamibi after exercise test, dipyridamole test, and rest. Early and delayed image acquisitions were equivalent in terms of quality. Starting with early image acquisitions may help to overcome the artifacts that are observed at the delayed time, particularly after dipyridamole stress. This protocol reduces the length of the procedure enabling to increase the throughput of patients and may avoid unnecessary reinjection.

Disclosures

There is no conflict of interest to declare.

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