

Comparative analysis of full-time, half-time, and quarter-time myocardial ECG-gated SPECT quantification in normal-weight and overweight patients

M. Lecchi, MS,^a I. Martinelli, MD,^a O. Zoccarato, MS,^b C. Maioli, MS,^a Giovanni Lucignani, MD,^a and A. Del Sole, MD^a

^a Nuclear Medicine Unit, Department of Health Sciences, University of Milan, San Paolo Hospital, Milan, Italy

^b Unit of Nuclear Medicine, S. Maugeri Foundation, IRCCS, Scientific Institute of Veruno, Veruno, NO, Italy

Received Oct 2, 2015; accepted Dec 10, 2015
doi:10.1007/s12350-015-0382-2

Background. The introduction of a camera-based dose-reduction strategy in myocardial perfusion imaging (MPI) clinical setting entails the definition of objective and reproducible criteria for establishing the amount of activity to be injected.

Aim. The aim is to evaluate the impact of count statistics on the estimation of summed-scores (SS), end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF).

Methods. Data rest/stress ECG-gated SPECT (2-day protocol and 8 MBq·kg⁻¹) were acquired with Bright View gamma camera and Astonish algorithm for 40 normal-weight and 40 overweight patients. Assuming that count statistics of shorter acquisition time may simulate that of lower injected activity, three simultaneous scans (full-time, half-time, and quarter-time scans) were started at the same time but with different acquisition time/projection (30, 15 and 8 seconds).

Results. A significant difference between SS values of half-time and quarter-time stress scans was found for overweight group ($P = .006$). Post hoc test showed significant differences for ESV ($P < .05$), EDV ($P < .01$) and EF ($P < .05$) between half-time and quarter-time scans for both patient groups.

Conclusions. The reduction of the count-statistics to a quarter of the MPI reference influenced negatively the quantification in overweight patients. The decrease of radiopharmaceutical activity to 25% of the reference seems practicable for normal-weight patients, while it is more appropriate an activity reduction limited to 50% for overweight and obese patients. (J Nucl Cardiol 2017;24:876–7.)

Key Words: Myocardial perfusion imaging • gated SPECT • iterative reconstruction • quarter-time scan • patient dose

Abbreviations

MPI	Myocardial perfusion imaging
SSS	Summed stress score
SRS	Summed rest score
EDV	End-diastolic volume
ESV	End-systolic volume

EF	Ejection fraction
GP	General purpose
IR	Iterative reconstruction
BMI	Body mass index

All editorial decisions for this article, including selection of reviewers and the final decision, were made by guest editor Jeroen J. Bax, MD, PhD
Reprint requests: Giovanni Lucignani, MD, Nuclear Medicine Unit, Department of Health Sciences, University of Milan, San Paolo

Hospital, Via Antonio di Rudini, 8, 20142 Milan, Italy;
giovanni.lucignani@unimi.it
1071-3581/\$34.00
Copyright © 2016 American Society of Nuclear Cardiology.

See related editorial, pp. 888–891

INTRODUCTION

Several scientific societies have produced recommendations aimed at reducing radiation exposure in myocardial perfusion imaging (MPI) studies with advanced software, dedicated detectors, and collimators, optimized specifically for MPI.^{1,2}

Among the various strategies to reduce the patients' dose, those that can be applied in studies with general-purpose (GP) gamma cameras are of particular interest as these cameras have the broadest diffusion.

The introduction of personalized radiopharmaceutical dosing in the clinical setting entails the definition of objective and reproducible criteria for establishing the amount of activity to be administered to each patient. Such criteria must be founded on the count statistics threshold of the MPI examination.³

As count statistics depends on both acquisition time and administered activity, a reduction of count statistics similar to that of low injected activities can be simulated by reducing the acquisition time. Based on this principle, several studies have been conducted with the aim of investigating potential dose-reduction strategies.⁴⁻⁶

The cardiac SPECT/CT guideline of the American Society of Nuclear Cardiology (ASNC), issued with the Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the Society of Cardiovascular Computed Tomography (SCCT), reports that the last generation of iterative reconstruction (IR) algorithms allows for half-time or quarter-time acquisition of the MPI scans performed with GP gamma cameras, while maintaining or enhancing cardiac image quality.^{7,8}

DePuy et al⁹ reported the clinical results of single-day MPI protocol with wide beam reconstruction (WBR) algorithm and 'quarter-time' SPECT on a GP gamma camera. The authors concluded that quarter-time WBR affords function assessment equivalent to those obtained with the full-time traditional reconstruction. However, these authors also highlighted some open issues when performing ECG-gated 'quarter-time' SPECT with GP gamma cameras in obese patients, as an excessive attenuation of photons by the soft tissues frequently produces artifactual myocardial perfusion defect.^{10,11}

In MPI, common clinical indicators of the diagnostic outcome are semi-quantitative indexes of left-

ventricular perfusion, like perfusion summed stress score (SSS) and summed rest score (SRS), and indexes of myocardial functional performance, like the left-ventricular ejection fraction (EF), the end-diastolic volume (EDV), and end-systolic volume (ESV).¹² The aim of the current study was to evaluate the impact of reducing count statistics by varying the acquisition time (from 100% to 50% and 25% of the time employed with traditional IR) on the quantification of the above clinical indicators, using a GP gamma-camera (Bright View, Philips) and a last generation IR algorithm (Astonish™ algorithm), in two populations, one of normal-weight patients and another of overweight or obese patients, defined as such on the basis of their body mass index (BMI). Statements for a camera-based dose-reduction strategy were also extrapolated.

PATIENTS AND METHODS

Study Design

Among the patients referred in 2014 for a diagnostic MPI examination to the Nuclear Medicine Unit of the 'San Paolo' Hospital, Milan, Italy, a dataset of exams was selected on the basis of the following inclusion criteria: patients had undergone both stress and rest ECG-gated SPECT with [^{99m}Tc]Tetrofosmin using a 2-day imaging protocol, both weight and height of the patient were recorded and the same expert operator had analyzed the full-time scan and wrote the medical report. Two groups of subjects were identified: the first group was formed by 40 consecutive patients with normal weight, defined as a body mass index (BMI) between 18.5 and 24.9 kg·m⁻² (*normal-weight group*). The second group included 40 consecutive patients with BMI ≥ 25 kg·m⁻² (*overweight group*). All patients signed an informed consent.

Radiopharmaceutical Injection and ECG-Gated SPECT Acquisition

In both rest and stress studies, the injected activity was 550 MBq (±10%) in patients weighing less than or equal to 70 kg, while in patients weighing more than 70 kg, the weight was multiplied by 8 to calculate the activity up to a maximum of 740 MBq (±10%), in accordance with the diagnostic reference level established by the Italian law.¹³

The stress test was performed with incremental loads of 25 W every 2 minutes. Patients exercised until they achieved >85% of their maximal age-predicted heart rate or they complained of exercise-limiting fatigue, chest pain, or dyspnea. [^{99m}Tc]Tetrofosmin was injected intravenously at peak exercise. Patients who were unable to achieve the targeted

heart rate or exercise were stressed pharmacologically. Dipyridamole was infused intravenously ($0.56 \text{ mg}\cdot\text{kg}^{-1}$ in 4 minutes) after an overnight fast, and [$^{99\text{m}}\text{Tc}$]Tetrofosmin was injected 3 minutes after the end of dipyridamole infusion. Aminophylline was given 3 minutes after the radiopharmaceutical injection. The time between radiopharmaceutical injection and stress/rest acquisition was 30 minutes or more in order to reduce the hepatobiliary uptake.

All patients performed an 8 bin/cycle ECG-gated SPECT acquisition with a GP 2-headed SPECT, BrightView (Philips), equipped with low-energy high-resolution collimators, on a 64×64 matrix with a pixel size of 6.39 mm and over a 180° arc (64 projections, zoom = 1.46). Scan time per projection was set to 30 seconds (100% time scan). For each projection, two other views were acquired concurrently (added views) lasting 15 and 8 seconds, respectively, allowing the recording of two additional ECG-gated SPECT studies, i.e., 50% and 25% time scans. The whole acquisition time for the ECG-gated SPECT was 16 minutes. The two added scans were ECG-gated SPEC SPECT of 8 and 4.3 minutes, respectively.

SPECT Image Reconstruction and Quantification

ECG-gated and summed projections were reconstructed using AstonishTM algorithm with default parameters (3 iterations, 8 subsets, 2 cut-off frequency and 4 it., 8 sub., 1 c.f., respectively). No attenuation or scatter correction was applied.

Using AutoquantTM software (ver. 7.0), an expert operator evaluated SS, EDV, ESV, and EF for each image set, rest and stress scans independently considered (17-segment polar map). As a method to highlight differences in count rate distribution, the same full-time database of normality was used for the images obtained by the three scans with different acquisition time.

The same expert operator analyzed the full-time SPECT and wrote the medical report. A reversible defect was established in case of reduced/lack of perfusion in a part of the left ventricle on stress images that was no more noticeable on rest images. A fixed defect was defined as a reduced perfusion on stress images that was evident even on rest images.

Statistical Analysis

The impact of different scan times was assessed by ANOVA analysis for both the normal-weight and the overweight group. A post hoc test (Tukey pairwise for multiple contrasts) was also performed to identify differences among the perfusion and functional parameters derived from the acquisitions with 100, 50, and 25% scan times.

The degree of agreement between 100% and 50% time scans and between 50% and 25% time scans were evaluated for SS and EF according to Bland and Altman as the mean of the differences (bias) $\pm 1.96 \times$ standard deviation (SD) of the differences (95% limits of agreement between scans). Statistical analysis was performed using the software R (Version 3.0.2, R Foundation for Statistical Computing, Vienna, Austria). Differences were considered significant when *P* value was $\leq .05$.

When not mentioned, values are shown as mean \pm standard error of the mean.

Patients' Effective Dose Estimation

Patients' effective dose was estimated according to International Commission on Radiological Protection (ICRP) as follows: $0.008 \text{ mSv}\cdot\text{MBq}^{-1}$ for a rest study¹⁴ and $0.0069 \text{ mSv}\cdot\text{MBq}^{-1}$ for a stress study.¹⁵ An injected activity equal to 740 MBq corresponds to 5.92 mSv for the rest exam and 5.11 mSv for a stress study ($\sim 11 \text{ mSv}$ for both exams).

RESULTS

Study Population

Baseline characteristics of the 80 patients included in the study are summarized in Table 1. The average BMI was 23.4 ± 0.2 and $29.4 \pm 0.6 \text{ kg}\cdot\text{m}^{-2}$ for normal-weight and overweight groups, respectively. Two patients belonged to the class-III obese group ($\text{BMI} \geq 40 \text{ kg}\cdot\text{m}^{-2}$). In 56 patients, medications were withheld at least 24 hours before the test for nitrates and 48 hours for calcium antagonists and beta blockers.

In 38 normal-weight patients and 33 overweight and obese patients, an exercise test was performed. The remaining nine patients underwent a pharmacological stress test with dipyridamole.

In the normal-weight group, the mean [$^{99\text{m}}\text{Tc}$]Tetrofosmin administered activity was $591 \pm 7 \text{ MBq}$ and $588 \pm 8 \text{ MBq}$ for stress and rest exams, respectively. In 29 patients of this group, a radiopharmaceutical activity equal to 550 MBq ($\pm 10\%$) was injected.

In the overweight group, the mean [$^{99\text{m}}\text{Tc}$]Tetrofosmin administered activity was 659 ± 12 and $659 \pm 13 \text{ MBq}$ for stress and rest exams, respectively. In nine patients of this group, 740 ($\pm 10\%$) MBq was administered.

The mean effective dose for stress plus rest studies was 8.8 mSv (range 8.1-11.0 mSv) for normal-weight patients and 9.8 mSv (range 7.8-11.9 mSv) for overweight and obese patients.

Perfusion defects were not observed in 10 normal-weight and 15 overweight or obese patients. One or more fixed myocardial perfusion defects were found in 10 normal-weight patients and in 6 subjects in the overweight group, while one or more reversible defects were found in 17 normal-weight patients and in 15 overweight subjects.

Perfusion Quantification

In the rest studies, no significant differences were found between the summed rest scores calculated by using the full-time, half-time, and quarter-time scan

Table 1. Description of the patient groups

Characteristics	Normal-weight group (n. 40)	Overweight group (n. 40)
Age (years)	65.2 (SD 12.8)	64.1 (SD 11.4)
Male (n)	28	26
Weight (kg)	66.2 (SD 6.7)	82.9 (SD 14.2)
BMI (kg·m ⁻²)	23.4 (SD 1.4)	29.4 (SD 4.0)
Stress type (n)		
Exercise	38	33
Pharmacologic	2	7
Activity (MBq)		
Rest	588 (SD 50)	659 (SD 80)
Stress	591 (SD 47)	659 (SD 74)
Effective dose (mSv)		
Rest	4.7 [4.3-6.1]	5.3 [4.1-6.5]
Stress	4.1 [3.7-5.0]	4.5 [3.7-5.8]
Medical report		
Negative	10	15
1 reversible defect	13	12
1 fixed defect	9	6
1 rev. defect + 1 fix. defect	3	4
≥2 reversible defects	4	3
≥2 fixed defects	1	0

data, for both the normal-weight group and the overweight group of patients (Table 2).

In the stress exams, no significant differences were found between summed stress scores calculated by using the full-time, half-time, and quarter-time scan data only in the normal-weight patients. On the contrary, the SSS values of the overweight and obese patients were significantly different between full-time, half-time, and quarter-time scans data ($P = .006$, ANOVA). The post hoc test demonstrated significantly higher summed stress scores calculated using 25% time scans compared to those with 50% time scans (4.3 ± 0.7 vs. 4.9 ± 0.8 , $P = .022$), whereas no significant difference was found between the SSS values calculated using 100% time and 50% time scans (Table 2; Figure 1). Among the 40 overweight or obese patients, 4 patients (10%) with normal risk on the basis of SSS% value from full-time scans ($SSS\% \leq 5\%$) showed a worsening of their risk classification after 75% reduction of acquisition time ($SSS\% > 5\%$). Only one patient of these had already SSS% above 5% at 50% time reduction.

Moreover, for the overweight and obese patients, a significant increase in the upper limit of agreement was found in the Bland and Altman plot of the SSS values between 50% and 25% time scans (3.52 points with a 95% confidence interval, CI, of 2.71-4.34) compared to

Table 2. Statistical results for SS for normal-weight and overweight groups of patients in relation to scan acquisition time

Patient group	Acquisition time (% of the reference)	SS	
		Rest	Stress
Normal-weight	100%	4.3 ± 0.8	7.1 ± 1.1
	50%	4.5 ± 0.9	7.3 ± 1.1
	25%	4.5 ± 0.9	7.4 ± 1.0
	ANOVA:	ns	ns
Overweight	100%	2.0 ± 0.6	4.2 ± 0.7
	50%	2.2 ± 0.7	4.3 ± 0.7
	25%	2.4 ± 0.7	4.9 ± 0.8
	ANOVA:	ns	$P = .0056$

Reference acquisition time = 16 minutes.
SS, Summed score; P, probability.

that (2.45 points with a 95% CI of 1.80-3.16) between 100% and 50% time scans (Figure 2).

For both groups of patients, a trend in the differences among the SSS values was not found and the variability remained consistent across the average SSS values.

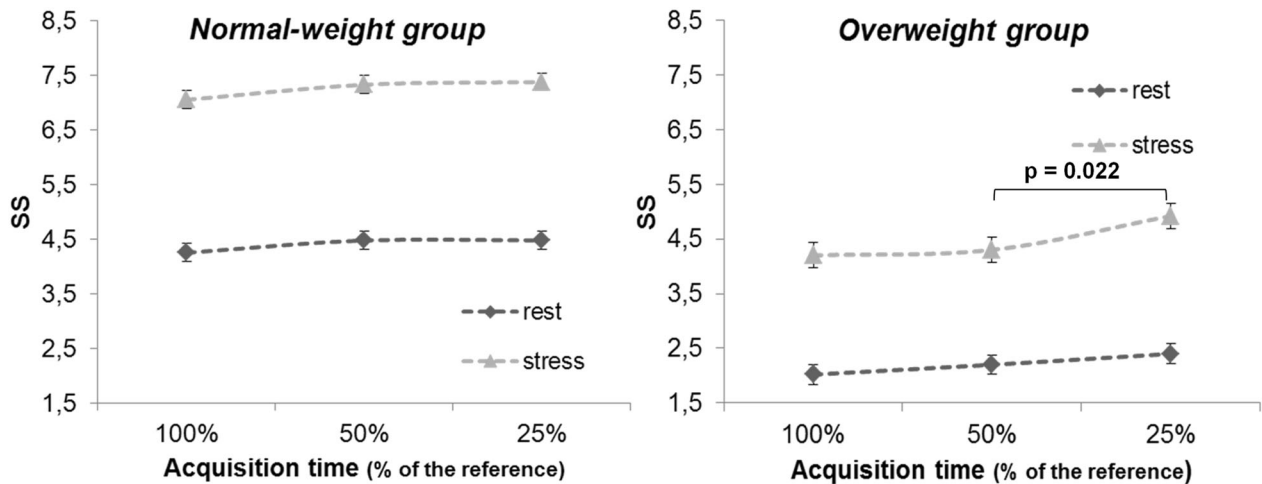


Figure 1. Summed score (SS) for rest (SRS) and stress (SSS) studies, as a function of acquisition time (reference = 16 minutes) for normal-weight and overweight groups. Points represent means and vertical bars represent Fisher's least significant differences (P = probability from the post hoc test).

Function Quantification

For normal-weight patients, the results of statistical analysis showed significant differences among the scans with different acquisition times for all the myocardial functional indicators considered in this study ($P < .01$, ANOVA), except for EDV values of stress studies and ESV values of rest studies (Table 3). Post hoc test showed that all the significant differences were between half-time scan and quarter-time scan ($P < .05$).

Similarly, for the overweight group, the statistical analysis showed significant differences among the scans with different acquisition times for all the myocardial functional indicators ($P < .01$), except for EDV values of stress studies. Post hoc test showed that all the significant differences were between 50% time scan and 25% time scan ($P < .05$), except for ESV values of rest exam that showed a significant difference between 100% time scan and 25% time scan ($P = .045$). The left-ventricular EF values of the overweight group showed the most significant difference ($P < .001$) between half-time scan and quarter-time scan, both for rest and stress studies.

The myocardial functional indicators considered in this study showed peculiar trends in relation to the acquisition time of the ECG-gated SPECT scans. Both for normal-weight and overweight groups, the calculated value of end-diastolic volume decreased with the reduction of acquisition time, while the end-systolic volume slightly increased (Figure 3). Left-ventricular ejection-fraction, which derives from the EDV and ESV values found, decreased with lowering of scan duration,

with a very marked trend for the overweight group of patients (Figure 4).

Bland and Altman plots of EF values between 100% and 50% time scans and between 50% and 25% time scans, for normal-weight and overweight groups, are shown in Figures 5 (rest) and 6 (stress). A trend in the differences between the EF values obtained from the different scans was not found, and the variability remained consistent across the average EF values. The lower limit of agreement between EF quantifications significantly decreased among the comparisons. Moreover, for the rest studies of the overweight group, also the upper limit of agreement significantly increased from 2.90% (95% CI 1.86%-3.93%) between 100% and 50% time scans, to 4.05% (95% CI 2.48%-5.62%) between 50% and 25% time scans. Consequently, for the overweight and obese patients, the agreement interval between EF values obtained from half-time scan and quarter-time scan was wider than that between full-time scan and half-time scan.

DISCUSSION

Myocardial perfusion imaging is a well-established, highly standardized test to detect significant coronary artery disease and to risk-stratify patients with regard to cardiac event-free survival.¹⁶ From a diagnostic standpoint, the reduction of the injected activity into the patient would be especially critical for stress studies where the presence, extent, and severity of one or more perfusion defects could influence the classification of the patient in a groups of risk for cardiac death and myocardial infarction.^{17,18}

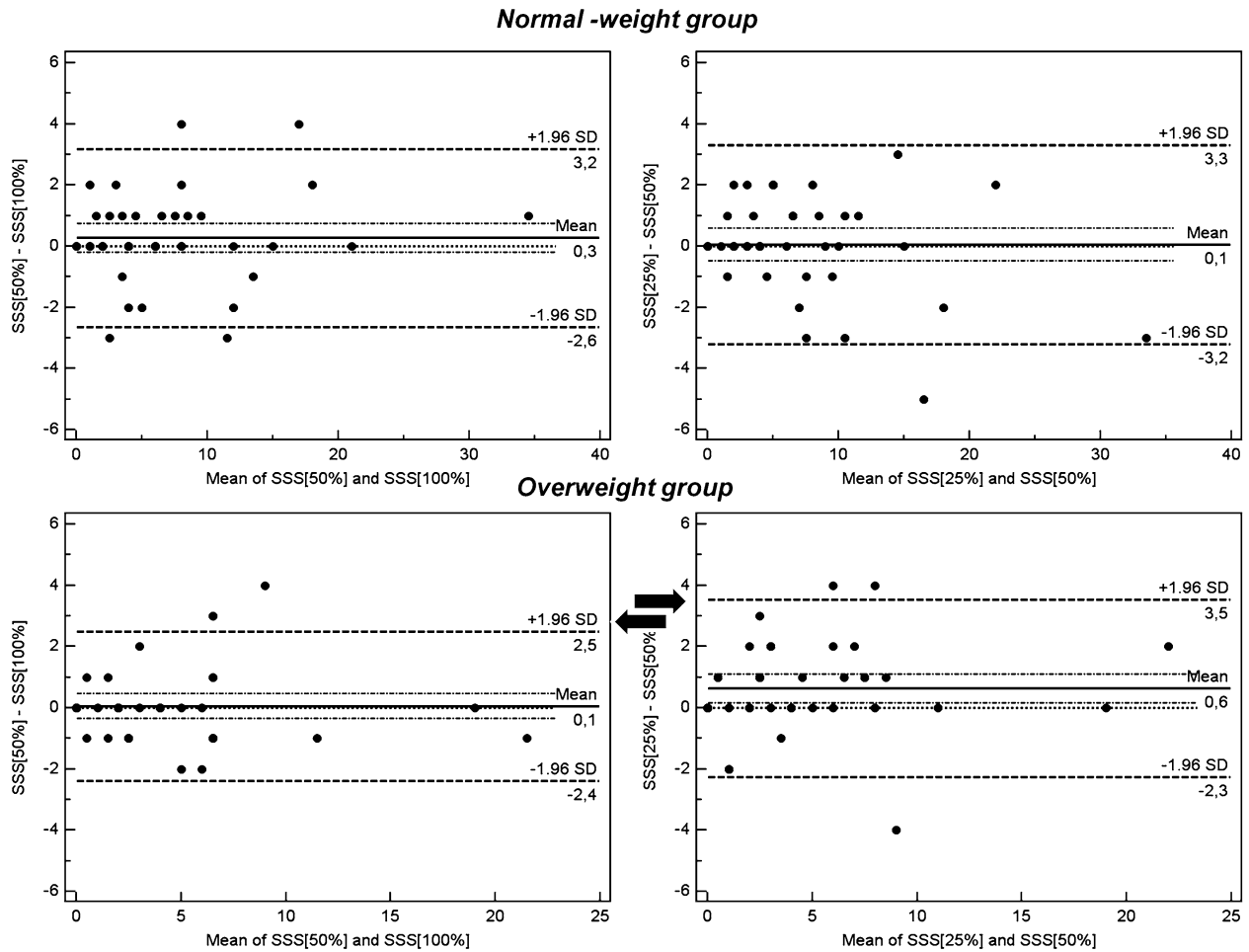


Figure 2. Bland and Altman plots of summed stress score (SSS) values obtained from 100% and 50% time scans (*left*) and 50% and 25% time scans (*right*) for normal-weight (*above*) and overweight (*below*) groups. Bias (mean) and limits of agreement ($\pm 1.96 \times \text{SD}$) between the scans are shown. For the overweight group of patients, the upper limit of agreement (*arrows*) significantly increased from 2.45 points between 100% and 50% time scans to 3.52 points between 50% and 25% time scans.

Several strategies can be adopted to contain patients' dose in MPI. Stress-first or stress-only MPI, as well as low-radiotracer-dose protocols (half-dose or less than half-dose) using novel scanners, collimators or software, can significantly reduce patients' dose compared with standard-dose rest-stress MPI protocol.¹⁹ The use of dedicated cameras equipped with cadmium-zinc-telluride detectors allows to obtain high diagnostic performance²⁰ with significant reduction in patients' dose,²¹ but the availability of such equipment is still limited.

This is the first study, to our knowledge, that reports the results of ECG-gated SPECT quantification down to a quarter of the reference acquisition time taking into account the patient weight in the radiopharmaceutical dosing protocol ($8 \text{ MBq} \cdot \text{kg}^{-1}$ up to 740 MBq) with a

general-purpose gamma-camera (Bright View, Philips) and a last generation of IR algorithm (AstonishTM algorithm). It has been demonstrated that there is no additional improvement in image quality with increasing activity above 750 MBq .²² Although soft tissue attenuation and scatter indeed increase proportional to weight, BMI, chest circumference, and bra cup size are better parameters to predict count rate loss.

We previously demonstrated, in an anthropomorphic phantom study, that the application of IR algorithms with resolution recovery and noise reduction to general-purpose gamma cameras hold the promise of significantly reducing patient dose until 75% of the Ref. 23. However, some open issues remain in relation to the quantification of cardiac perfusion and functional indicators with such low doses, mostly in the presence of

Table 3. Statistical results for EDV, ESV, and EF for normal-weight and overweight groups in relation to scan acquisition time

Patient group	Acquisition time (% of the reference)	EDV (mL)		ESV (mL)		EF (%)	
		Rest	Stress	Rest	Stress	Rest	Stress
Normal-weight	100%	92.9 ± 5.6	92.3 ± 6.7	40.8 ± 5.0	42.1 ± 6.0	60.3 ± 2.1	59.6 ± 2.2
	50%	92.7 ± 5.6	91.8 ± 6.6	40.8 ± 5.0	42.3 ± 6.0	60.0 ± 2.0	59.1 ± 2.2
	25%	91.6 ± 5.5	91.6 ± 6.8	41.2 ± 4.9	43.1 ± 6.1	59.1 ± 2.0	58.3 ± 2.2
	ANOVA:	$P = .0004$	ns	ns	$P = .0056$	$P = .0040$	$P = .0007$
Overweight	100%	88.5 ± 5.2	85.2 ± 5.1	34.4 ± 4.1	33.5 ± 4.0	64.6 ± 1.8	64.4 ± 1.8
	50%	87.6 ± 5.2	84.7 ± 5.1	34.8 ± 4.2	33.9 ± 4.1	64.1 ± 1.9	63.8 ± 1.9
	25%	85.6 ± 5.1	84.0 ± 5.2	35.3 ± 4.1	34.7 ± 4.1	62.6 ± 1.9	62.4 ± 1.8
	ANOVA:	$P < 10^{-5}$	ns	$P = .0024$	$P = .0014$	$P < 10^{-5}$	$P < 10^{-5}$

Reference acquisition time = 16 minutes.

ESV, End-systolic volume; EDV, end-diastolic volume; EF, ejection fraction; P, probability.

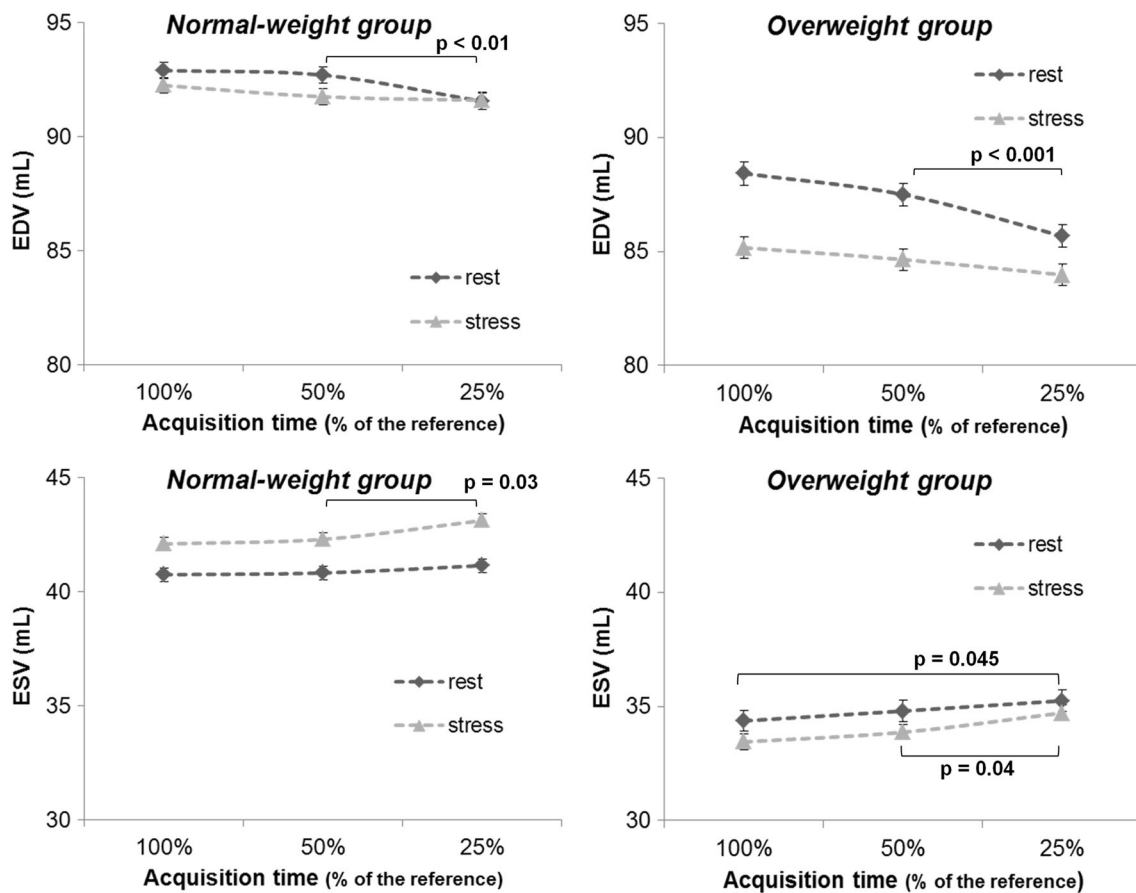


Figure 3. End-diastolic volume (EDV) and end-systolic volume (ESV) for rest and stress studies, as a function of acquisition time (reference = 16 minutes) for normal-weight and overweight groups. Points represent means and vertical bars represent Fisher's least significant differences (P = probability from the post hoc test).

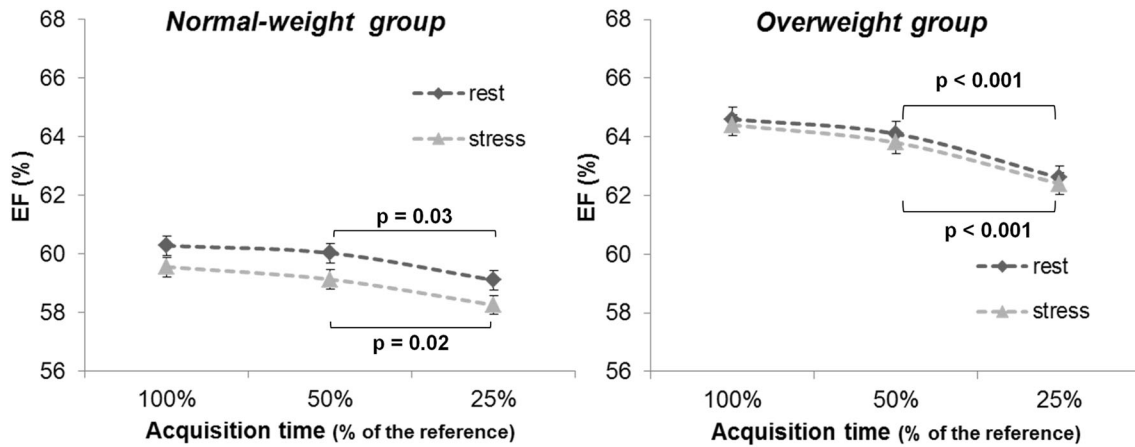


Figure 4. Left-ventricular ejection fraction (EF) for rest and stress studies, as a function of acquisition time (reference = 16 minutes) for normal-weight and overweight groups. Points represent means and vertical bars represent Fisher's least significant differences (P = probability from the post hoc test).

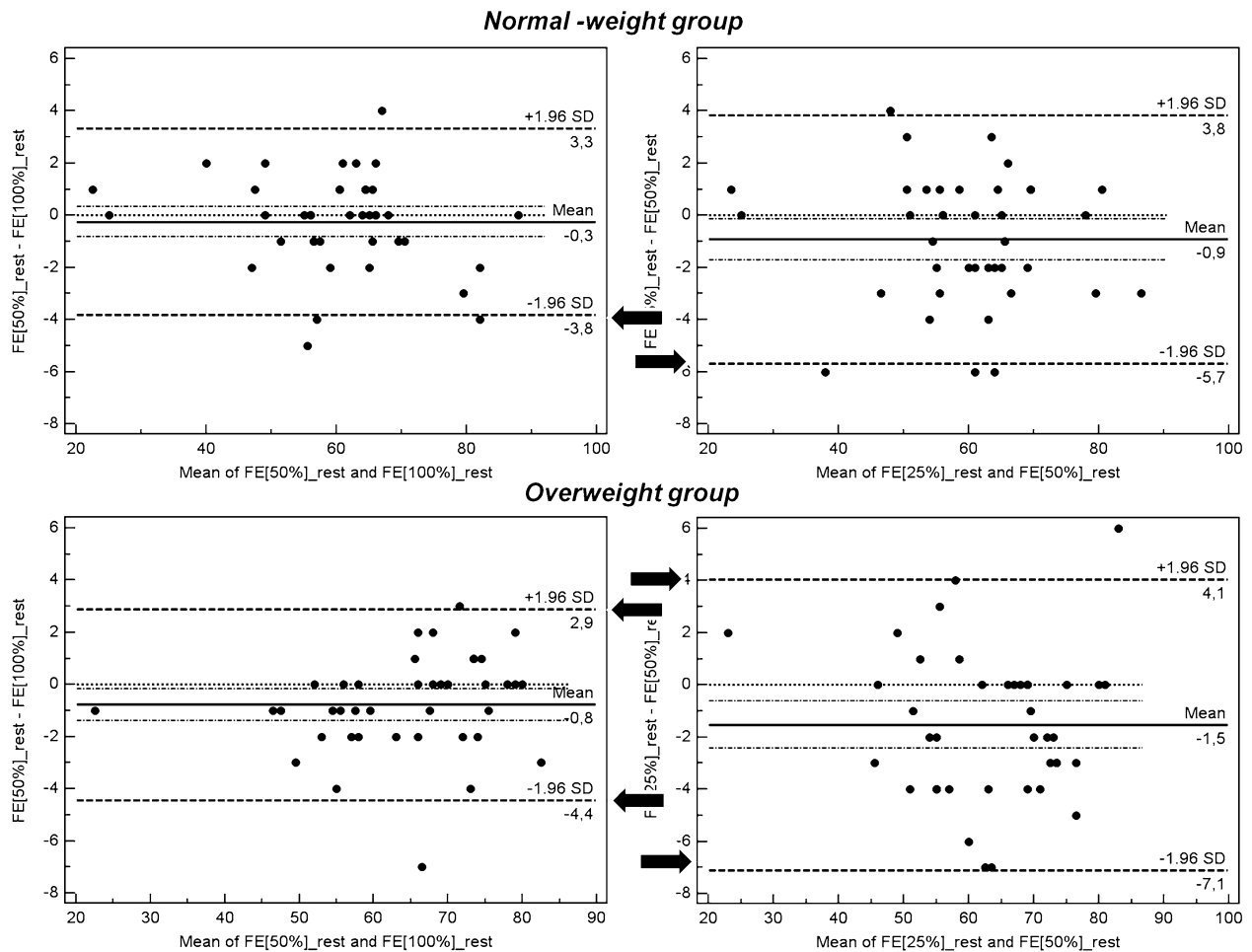


Figure 5. Bland and Altman plots of left-ventricular ejection fraction (EF) values for rest studies obtained from 100% and 50% time scans (left) and 50% and 25% time scans (right) for normal-weight (above) and overweight (below) groups. Bias (mean) and limits of agreement ($\pm 1.96 \times SD$) between the scans are shown. The upper and lower limits of agreement indicated by arrows represent values that are significantly different between the plots.

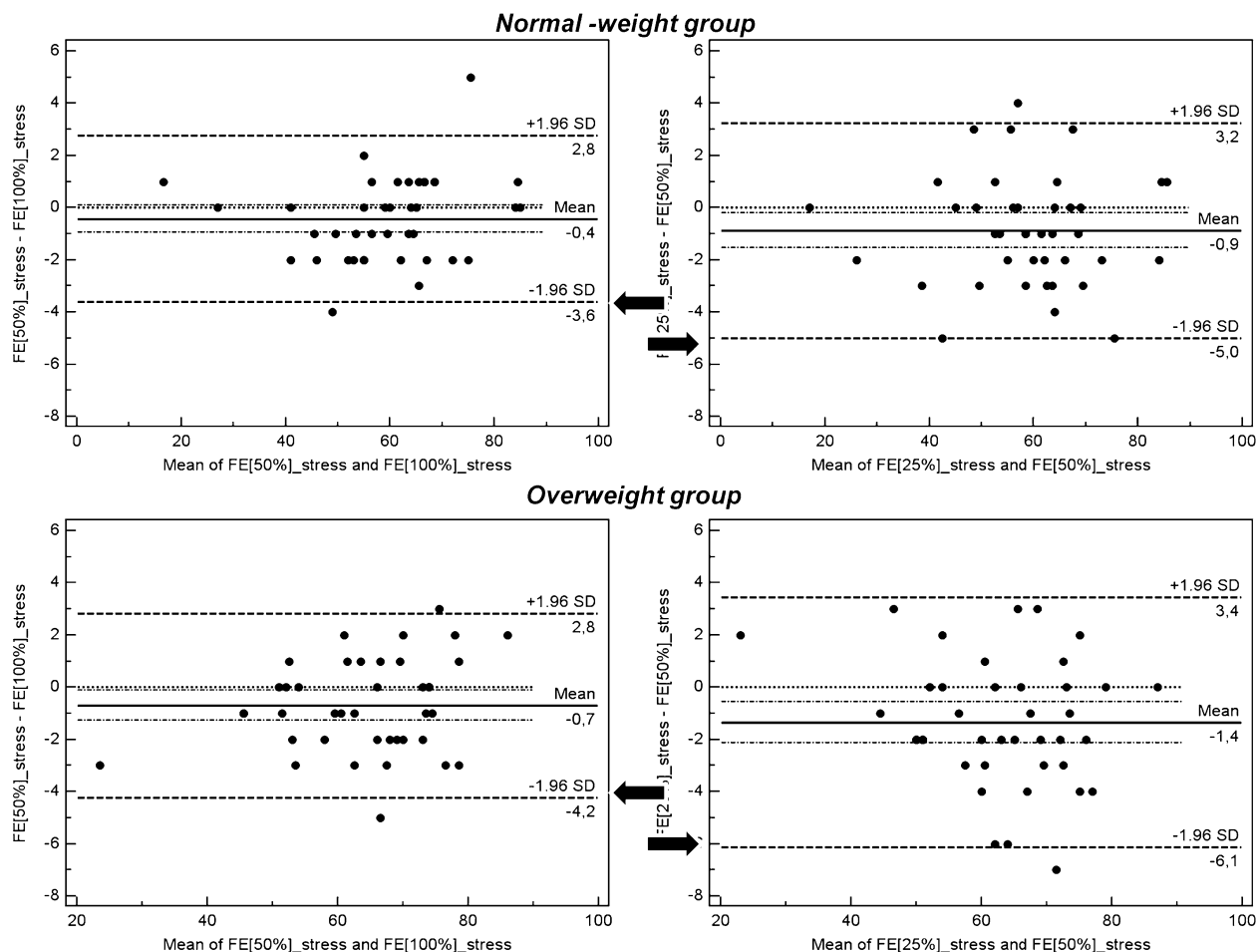


Figure 6. Bland and Altman plots of left-ventricular ejection fraction (EF) values for stress studies obtained from 100% and 50% time scans (*left*) and 50% and 25% time scans (*right*) for normal-weight (*above*) and overweight (*below*) groups. Bias (mean) and limits of agreement ($\pm 1.96 \times \text{SD}$) between the scans are shown. The lower limits of agreement indicated by arrows represent values that significantly change between the plots.

overweight and obese patients,⁹ which are very frequent in stress/rest ECG-gated SPECT.

We chose to evaluate only the fully automated quantitative analysis of MPI studies using the results of 100% time scans as gold-standard for the perfusion and functional indicators. Quantitative analysis eliminates observer variability and bias, it is useful for comparing sequential MPI studies. This approach is generalizable to other centers, as it not dependent on the physician expertise.

The results of this study show that both the SSSs and SRSs are overestimated following the reduction of acquisition time, i.e., with lower count statistics, in particular in overweight group (Figure 1). In fact, a significant overestimation, on average 14%, of the SSS values from half-time scan to quarter-time scan was found for this group of patients. This appears related to

an incorrect quantification of perfusion defects when the acquisition time drops below 50% of the reference (see Figure 7 for an example). Defects were more extent, more severe, or both. These results are not unexpected. It is well recognized that reduced count density, noisy scans result in perfusion artifacts. However, as discussed in the introduction, re-emphasis of this potential limitation with newer reduced count-density techniques is timely and appropriate.

This is particularly interesting if the diagnostic outcomes of the two patient groups are compared (Table 1), as the overweight group presented a lower number of reversible and fixed perfusion defects than the normal-weight group (Table 1). Moreover, the perfusion SSS and SRS values of normal-weight patients resulted higher than those of overweight and obese patients (Table 2).

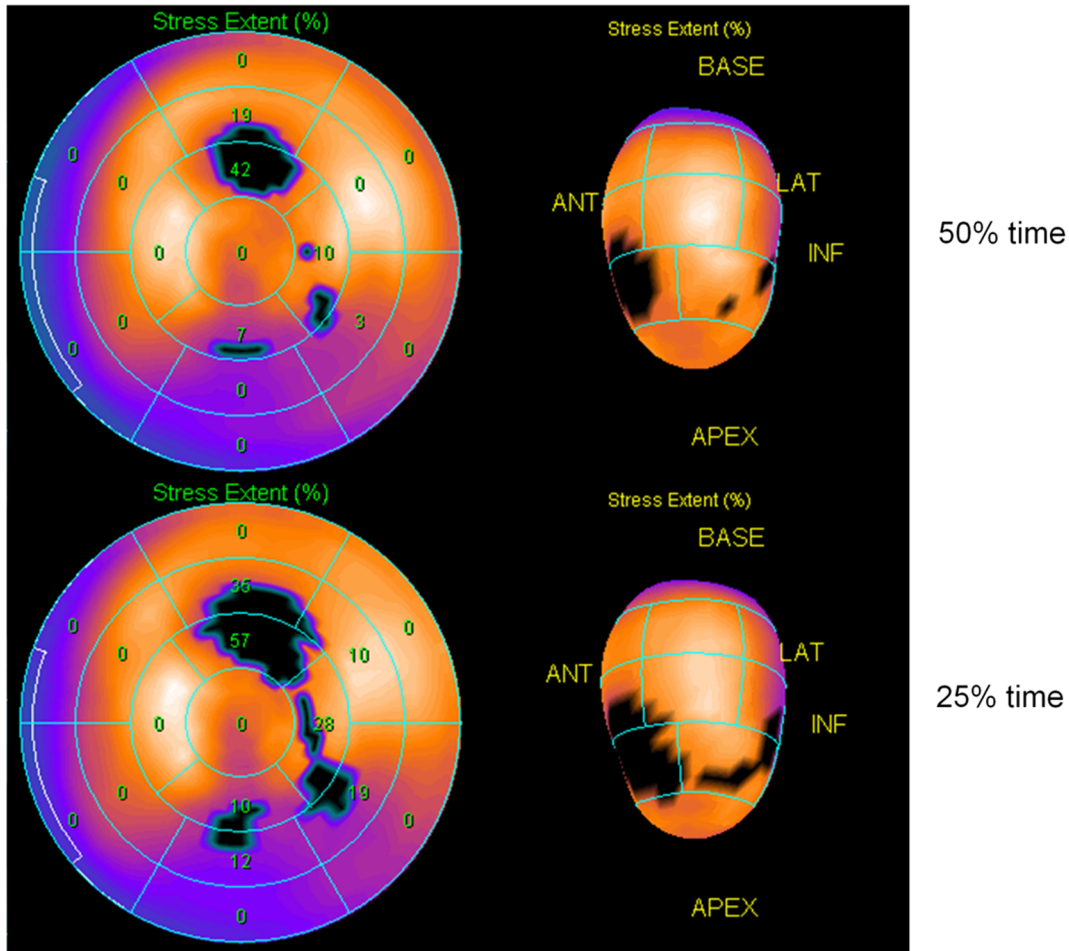


Figure 7. Polar maps (stress study) of a patient of overweight group (male, 91 kg and $27.5 \text{ kg}\cdot\text{m}^{-2}$) with a SSS difference of 4 points between 50% and 25% time scans (4 vs. 8 points, respectively).

It is important to underline that a summed score for the stress exam higher than the real one could produce the worsening of the diagnostic judgment of the MPI examination with a subsequent wrong risk-stratification of the patient with regard to cardiac event-free survival.

We found also an upper limit of agreement between half-time and quarter-time scan quantification of 3.52 points for SSS (5.2% if we consider SSS% for 17-segment polar map). We believe that this limit of agreement is not clinically acceptable as 5.2% is higher than the width of the groups of risk defined using SSS% (<5% is considered normal or nearly normal and scores from 5% to 9% are mildly abnormal, 10%-14% moderately abnormal, and >14% severely abnormal).²⁴ As a consequence, the quantification results of ECG-gated SPECT with a quarter of the reference acquisition time could allocate an overweight or obese patient in a worse group of risk than the 100% time scan. In fact, 4 overweight patients with normal risk on the basis of

SSS% value from full-time scans ($\text{SSS}\% \leq 5\%$) showed a worsening of their risk classification after 75% reduction of acquisition time ($\text{SSS}\% > 5\%$).

Finally, we found also a wider agreement interval for EF of the rest studies between 50% and 25% time scans respect to 100% and 50% time scans (Figure 5). Thus, for the overweight and obese patients, the reduction of count statistics to the quarter of the reference seems to be inappropriate as it could cause an overall worsening of the diagnostic judgment of the MPI investigation.

The confidence in the results of the present study is based on the fact that the results found for the perfusion and functional parameters for full-time vs. half-time comparison are consistent with those previously published by other authors using 2-day imaging protocols.^{13,25,26}

The design of scan protocol used (three simultaneous scans with different scan time/projection) permitted

to extrapolate the results to low-radiotracer-dose protocols, as it maintains the same lost-time due to camera movement and settling in the resulted three scans. In fact, it has been demonstrated that this lost-time could create a discrepancy between acquisition time and injected activities, as reducing acquisition time appears to have a more dramatic effect on image quality than a comparable reduction of injected activity.²⁷

NEW KNOWLEDGE GAINED

The results of our study showed that the decrease of injected activity up to 25% of the reference may not influence the perfusion quantification in normal-weight patients (patients' effective dose about 3 mSv for 2-day imaging protocol), while it is more appropriate an activity reduction limited to 50% for overweight and obese patients (patients' effective dose about 6 mSv). The adoption of a dose-reduction strategy based also on the patient BMI may be more suitable than the weight-based dosing protocol-alone.

LIMITATIONS

In the last generation of IR algorithms, the image quality is strictly dependent on the specific combination of gamma-camera and collimators used. Therefore, for systems other than the one used in the current study, validations with other clinical studies are necessary.

Moreover, in the current study, attenuation and scatter corrections were not applied as routinely done in our center. The application of scatter and attenuation corrections could lead better image quality performance,²³ but a nuclear medicine center should be taking into account that the use of a CT in SPECT/TC scanners can be associated with a small, but additional radiation dose to the patients.

Finally, to avoid the introduction of misleading factors, we used the manufacturers' recommendations for IR parameters and the same perfusion databases of normality for the scans with different count statistics. The optimization of reconstruction parameters with count density could provide better diagnostic image quality for ECG-gated SPECT, while the use of low-dose perfusion database could provide less perfusion overestimation.²⁸

CONCLUSION

The last generation of IR algorithm considered in this study (AstonishTM) allows to decrease the acquisition time of the MPI stress/rest exams (Bright View gamma camera, Philips) up to a quarter of the reference for normal-weight patients (BMI < 25 kg·m⁻²). On the

contrary, in overweight and obese patients, the reduction of acquisition time to a quarter of the MPI reference influences negatively the perfusion quantification of the stress studies (worsening of the diagnostic judgment), even if a weight-based dosing protocol is used. These results could be applied directly (half/quarter strategy) or by adopting a proportional relationship between the injected activity and the BMI of the patient (BMI modulated strategy) to overcome problem of borderline patients between the two groups. Further clinical studies on patients are needed to confirm the full portability of this BMI-based dosing protocol to the clinical ground.

Disclosures

The authors declare that they have no conflict of interest.

References

1. Cerqueira MD, Allman KC, Ficaro EP, Hansen CL, Nichols KJ, Thompson RC, et al. Recommendations for reducing radiation exposure in myocardial perfusion imaging. *J Nucl Cardiol* 2010;17:709-18.
2. Flotats A, Knutti J, Gutberlet M, Marcassa C, Bengel FM, Kaufmann PA, et al. Cardiovascular Committee of the EANM, the ESCR and the ECNC. Hybrid cardiac imaging: SPECT/CT and PET/CT. A joint position statement by the European Association of Nuclear Medicine (EANM), the European Society of Cardiac Radiology (ESCR) and the European Council of Nuclear Cardiology (ECNC). *Eur J Nucl Med Mol Imaging* 2011;38:201-12.
3. Slomka PJ, Dey D, Duvall WL, Henzlova MJ, Berman DS, Germano G. Advances in nuclear cardiac instrumentation with a view towards reduced radiation exposure. *Curr Cardiol Rep* 2012;14:208-16.
4. Valenta I, Treyer V, Husmann L, Gaemperli O, Schindler MJ, Herzog BA, et al. New reconstruction algorithm allows shortened acquisition time for myocardial perfusion SPECT. *Eur J Nucl Med Mol Imaging* 2010;37:750-7.
5. Aldridge MD, Waddington WW, Dickson JC, Prakash V, Ell PJ, Bomanji JB. Clinical evaluation of reducing acquisition time on single-photon emission computed tomography image quality using proprietary resolution recovery software. *Nucl Med Commun* 2013;34:1116-23.
6. Enevoldsen LH, Menashi CA, Andersen UB, Jensen LT, Henriksen OM. Effects of acquisition time and reconstruction algorithm on image quality, quantitative parameters, and clinical interpretation of myocardial perfusion imaging. *J Nucl Cardiol* 2013;20:1086-92.
7. Dorbala S, Di Carli MF, Delbeke D, Abbara S, DePuey EG, Dilsizian V, et al. SNMMI/ASNC/SCCT guideline for cardiac SPECT/CT and PET/CT 1.0. *J Nucl Med* 2013;54:1485-507.
8. Zoccarato O. Innovative reconstruction algorithms in cardiac SPECT scintigraphy. *Q J Nucl Med Mol Imaging* 2012;56:230-46.
9. DePuey EG, Bommireddipalli S, Clark J, Thompson L, Srour Y. Wide beam reconstruction "quarter-time" gated myocardial perfusion SPECT functional imaging: A comparison to "full-time" ordered subset expectation maximum. *J Nucl Cardiol* 2009;16:736-52.
10. Nakazato R, Slomka PJ, Fish M, Schwartz RG, Hayes SW, Thomson LE, et al. Quantitative high-efficiency cadmium-zinc-

- telluride SPECT with dedicated parallel-hole collimation system in obese patients: Results of a multi-center study. *J Nucl Cardiol* 2015;22:266-75.
11. Notghi A, Williams N, Smith N, Goyle S, Harding LK. Relationship between myocardial counts and patient weight: Adjusting the injected activity in myocardial perfusion scans. *Nucl Med Commun* 2003;24:55-9.
 12. Xu Y, Hayes S, Ali I, Ruddy TD, Wells RG, Berman DS, Germano G, Slomka PJ. Automatic and visual reproducibility of perfusion and function measures for myocardial perfusion SPECT. *J Nucl Cardiol* 2010;17:1050-7.
 13. Marcassa C, Zoccarato O, Calza P, Campini R. Temporal evolution of administered activity in cardiac gated SPECT and patients' effective dose: Analysis of an historical series. *Eur J Nucl Med Mol Imaging* 2013;40:325-30.
 14. ICRP. Radiation dose to patients from radiopharmaceuticals. A fourth addendum to ICRP Publication 53. <http://www.icrp.org>.
 15. Publication ICRP. 106. Radiation dose to patients from radiopharmaceuticals. Addendum 3 to ICRP Publication 53. *Ann ICRP* 2008;38:126.
 16. Hage FG, AlJaroudi WA. Review of cardiovascular imaging in *The Journal of Nuclear Cardiology* in 2014: Part 2 of 2: Myocardial perfusion imaging. *J Nucl Cardiol* 2015;22:714-9.
 17. Hachamovitch R, Hayes S, Friedman JD, Cohen I, Shaw LJ, Germano G, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: What is the warranty period of a normal scan? *J Am Coll Cardiol* 2003;41:1329-40.
 18. Matsuo S, Nakajima K, Horie M, Nakae I, Nishimura T. J-ACCESS Investigators. Prognostic value of normal stress myocardial perfusion imaging in Japanese population. *Circ J* 2008;72:611-7.
 19. Dorbala S, Blankstein R, Skali H, Park MA, Fantony J, Mauceri C, et al. Approaches to reducing radiation dose from radionuclide myocardial perfusion imaging. *J Nucl Med* 2015;56:592-9.
 20. Zoccarato O, Lizio D, Savi A, Indovina L, Scabbio C, Leva L, et al. Comparative analysis of cadmium-zinc-telluride cameras dedicated to myocardial perfusion SPECT: A phantom study. *J Nucl Cardiol* 2015.
 21. Perrin M, Djaballah W, Moulin F, Claudin M, Veran N, Imbert L, et al. Stress-first protocol for myocardial perfusion SPECT imaging with semiconductor cameras: High diagnostic performances with significant reduction in patient radiation doses. *Eur J Nucl Med Mol Imaging* 2015;42:1004-11.
 22. Robinson CN, van Aswegen A, Julious SA, Nunan TO, Thomson WH, Tindale WB, et al. The relationship between administered radiopharmaceutical activity in myocardial perfusion scintigraphy and imaging outcome. *Eur J Nucl Med Mol Imaging* 2008;35:329-35.
 23. Zoccarato O, Scabbio C, De Ponti E, Matheoud R, Leva L, Morzenti S, et al. Comparative analysis of iterative reconstruction algorithms with resolution recovery for cardiac SPECT studies. A multi-center phantom study. *J Nucl Cardiol* 2014;21:135-48.
 24. Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: Differential stratification for risk of cardiac death and myocardial infarction. *Circulation* 1998;97:535-43.
 25. Leva L, Brambilla M, Matheoud R, Vigna L, Marino P, Inglese E. The relationship between quantitative perfusion and functional results and acquisition time with reduced administered activity for ^{99m}Tc tetrofosmin myocardial gated-SPECT. *Clin Nucl Med* 2012;37:e162-9.
 26. Sun XX, Tian YQ, Wang DY, He ZX. Shortened acquisition time or reduced-activity dose for gated myocardial perfusion SPECT with new reconstruction algorithm. *Int J Cardiovasc Imaging* 2013;29:1287-93.
 27. Caobelli F, Kaiser SR, Thackeray JT, Bengel FM, Chieragato M, Soffientini A, et al. Q SPECT allows a significant reduction in administered dose and acquisition time for myocardial perfusion imaging: Evidence from a phantom study. *J Nucl Med* 2014;55:2064-70.
 28. Nakazato R, Berman DS, Hayes SW, Fish M, Padgett R, Xu Y, et al. Myocardial perfusion imaging with a solid-state camera: Simulation of a very low dose imaging protocol. *J Nucl Med* 2013;54:373-9.