

## Evaluation of the optimal administrated activity in gated myocardial perfusion SPECT

Noha G. Madian<sup>1</sup>, Islam Maamoun<sup>2</sup>, Hossam Yasin<sup>3</sup> and Reem H. El-Gebaly<sup>1</sup>

<sup>1</sup> Department of Biophysics, Faculty of Science, Cairo University, Giza, Egypt

<sup>2</sup> Nuclear Cardiology Department, Intensive Care Unit, Faculty of Medicine, Cairo University Hospitals, Giza, Egypt

<sup>3</sup> Nuclear Medicine Department, King Fahd Unit, Faculty of Medicine, Cairo University Hospitals, Giza, Egypt

**Abstract.** Prominence of radionuclide myocardial perfusion imaging (MPI) using single photon emission computed tomography (SPECT) has been investigated and shown to have high precision and predictive value. Improvement of the quality care for patients could be obtained by decreasing the radiation dose and increasing the image quality. The objective of this work is quantitative evaluation of the injected dose in MPI. 32 patients were categorized into 4 groups; each group received a different radiant dose. Image quality indices (Heart/Background (H/B), Heart/Lung (H/P) and Heart/Liver (H/L)) ratios and cardiac ejection fraction (EF%) were determined. It was observed from the images, that there is no substantial alteration in image quality among the groups. It was concluded that the most optimal dose providing the best image is the lowest one.

**Key words:** Myocardial perfusion imaging — Quantitative evaluation — Image quality — Image quality indices

### Introduction

Myocardial perfusion imaging (MPI) in combination with single photon emission computed tomography (SPECT) is a crucial technique used in knowing the performance of the heart in patients which are susceptible to coronary artery disease (CAD) (Doukky et al. 2016).

The American Society of Nuclear Cardiology (ASNC) achieved a radiation effective dose (ED) of 9 mSv in 50% by 2014 (equivalent to 3 years of US background radiation) for SPECT or photon emission computed tomography (PET) MPI patients (Cerqueira et al. 2010). It was found that the median radiation exposure for SPECT MPI to be 12.8 mSv (range, 2–41 mSv) *per* study. The outcomes of the ASCN were achieved by 2.6% of SPECT laboratories. The SPECT findings from 2015 do not substantially differ from the previous report by Jerome et al. from 2012 to 2013. In the United States, there was no significant change in overall radiation exposure for SPECT MPI. Imaging for stress-only remains underutilized, and thallium remains present in a substantial

amount of studies (8.4%). In contrast, cardiac PET MPI utilization has increased since 2012 and has resulted in significantly reduced radiation exposure in 2015. This reduction is likely because of increased use of 3-dimensional (3D) imaging systems (Desiderio et al. 2018). These radiation estimates from the IAC database are supported by studies from the International Atomic Energy Agency (IAEA) Nuclear Cardiology Protocols Study (INCAPS) investigators who report similar estimates of SPECT radiation exposure, but with an increased prevalence of stress-only imaging in 50 selected nuclear laboratories in the United States. Few of these investigators indicate SPECT MPI with low dose (Desiderio et al. 2018).

For cardiovascular imaging, radiation protection was recently improved by the American Heart Association which recommended a process through which patients were treated. The process includes radiation risks, expected benefits and clinical justification. This recommendation was designed as class I (beneficial) with level of evidence C (expert consensus) indicating the lack of data in this field (Fazel et al. 2014).

Despite the low percentage of SPECT laboratories achieving ASNC goals, techniques are available to reduce radiation exposure and do not necessarily require purchase of new equipment. Reducing patient radiation exposure by protocol

**Correspondence to:** Noha G. Madian, Biophysics Department, Faculty of Science, Cairo University, Giza, Egypt  
E-mail: gamal\_noha@yahoo.com

selection could easily be addressed by tracer choice (neither thallium nor dual-isotope), doses dependent on the weight and the use of functional testing as stress-only approaches. The IAC database demonstrates that even in 2015, 8.4% of patient studies were using thallium in MPI protocols, despite ASNC recommendations against this practice. Data supporting the stress-first/stress-only concept demonstrate only 8% to 15% of all SPECT MPI studies are positive for ischemia, making stress-only imaging in a substantial percentage of patients feasible. Stress-only imaging has been recommended by professional societies for many years as a method of reducing radiation exposure by as much as 30 to 70%, but in 2015, < 0.5% of IAC laboratories used this practice (Desiderio et al. 2018).

In nuclear cardiology, it is important to reduce patient radiation exposure. Several trials were made in the last few years in order to increase photon sensitivity in nuclear cardiology scanner hardware, applying new software methods for SPECT reconstruction on conventional and enhance SPECT image quality with lower count statistics (Borges et al. 2007; DePuey et al. 2008, 2009, 2011, 2012; Vija et al. 2008; Maddahi et al. 2009; Venero et al. 2009; Druz et al. 2011; Duvall et al. 2018). Lately the SPECT regulations improve dose reduction by minimizing the use of Tl-201, adjusting the injected activity which is weight-dependent, using stress-only protocols, using new reconstruction algorithms and new cardiac camera technologies. All these parameters can reduce the radiation dose from a Tc99m-based study to  $\leq 5$  mSv if they are used individually and to 2.6 mSv or even less than 1 mSv if they are used in combinations (Wells 2020). Correspondingly, SPECT regulations praised to exploit the accuracy of the test by decreasing imaging artifacts like attenuation effects. These artifacts can be reduced by using ECG-gated acquisitions and taking images in two different patient positions. This recommendation gives an indirect and unclear solution with more information without any increasing in radiation exposure to the patient (Wells 2020).

SPECT MPI applying novel scanners and software for stress-only with low-radiotracer-dose protocols (half-dose or less than half-dose), had a small radiation dose compared to standard rest-stress MPI protocols (Dorbala et al. 2015). It was established that the MPI images of reduced dose by 19% protocol were considered equivalent to full dose protocol with high image quality (Melby et al. 2012). Increasing pitch decreases dose by reducing the time needed to cover a given axial field-of-view and thus decreases the duration of radiation exposure. Increased pitch also spreads out the distance between adjacent acquired slices and may lead to decreased resolution (Wells 2020).

It was found that MPI half time imaging method produce high quality diagnostic image in comparison with full time imaging (Ali et al. 2009). Evolution for MPI cardiac reconstruction method, there is no significant difference in image

quality between half dose and full dose images (Zafrir et al. 2012). This is true in case of obese patients by applying MPI half-dose reduction method. It was found that MPI procedure is feasible and can be performed in one day (Ali et al. 2009; Zafrir et al. 2012, 2013).

The diagnostic information increases by increasing the administered activity above a threshold point. The increase of the administered activity has no significance when an acceptable image quality has been reached. For each procedure, the administration activity increases to certain value known as optimum activity below which poor image quality and errors in diagnosis occur (Smith 1987). The indices of image quality (Heart/Background (H/B), Heart/Lung (H/P) and Heart/Liver (H/L) ratios) were used for evaluation of the image quality in nuclear cardiology (Ali et al. 2009). Automated 3D software is used for Left ventricle ejection fraction (LVEF), which need some geometrical change in LV cavity. The volume of LV cavity can be determined from this software in order to know the End diastolic volume (EDV) and the End systolic volume (ESV) (Zafrir et al. 2013).

The optimum injected dose of  $^{99m}\text{Tc}$ -MIBI for quantitative assessment of image quality in comparison to the standard injected dose was previously investigated (Melby et al. 2012). The purpose of the current study is to continue and to determine the optimum injected dose in SPECT MPI studies.

## Materials and Methods

Patients were prepared in fasting state before the test (6 hours at least) and stopped cardiac and hypertension medications before the test for 48 hours. 32 patients complaining from chest have performed MPI studies (Melby et al. 2012). All the patients were grouped into four groups, each receiving different dose (370, 555, 740 and 925 MBq). Tc-99m Sestamibi eluted from MON-TEK Generator  $^{99m}\text{Mo}/^{99m}\text{Tc}$  were administrated to each group with different values (El-Gebaly et al. 2014). Each group was injected intravenously and then scanned with dual head collimator LEHR gamma camera (Symbia one Siemens) (El-Gebaly et al. 2014).

The guidelines of the institution are required for all human experimental investigations.

### Administrated activity preparation

MON-TEK Generator  $^{99m}\text{Mo}/^{99m}\text{Tc}$  was used as a source for  $^{99m}\text{Tc}$ . After this elution process, 9250 MBq of  $^{99m}\text{Tc}$  was added to MIBI vial and heated 10 min in water bath. The administrated activity required was removed from the labeled vial and measured by the dose calibrator to get the required activity. The waste of the administrated activity in the syringe after patient injection was measured by the dose calibrator. The real injected activity was calculated by

subtraction the waste activity post injection from the total activity prepared before injection. Each group was administrated the injected dose of Tc-99m Sestamibi with stress study in nuclear cardiology and after 45 min, patient is scanned at high resolution by dual head collimator LEHR gamma camera (Symbia Siemens SPECT).

### Image processing

Data were stored in adequate computer Symbia (Germany), after 720 s time scan using matrix of 64×64. Nuclear medicine image expert assessed the image quality of each study. Filtered back projection method (FBP) reconstructs images in order of 4 and cut off 0.5.

### Image quality indices

Administered activity, matrix dimension, equipment, acquisition protocol, resting time after injection and acquisition time are all factors that affect the image quality. In the regions of interest (ROIs), the number of counts and the rate in the heart (H), liver (L), lungs (P) and background region (B) between the liver and the left ventricle were measured. After achieving all parameters, the optimum activity was determined due to high image quality which is equivalent to the standard group.

### Left ventricle ejection fraction (LVEF)

#### LVEF by echocardiography

Patients with left lateral recumbent perform quantitative echocardiographic studies. Apical four chamber view indicated LVEF images. Images were obtained from the apical two- and four-chamber views by knowing the abnormalities of the wall. The American Society of Echocardiography recommends that an irregular rhythm indicate five consecutive beats (El-Gebaly et al. 2014). The end-diastolic and end-systolic volume was accessed. LVEF was calculated as:  $LVEF = ((\text{end-diastolic volume} - \text{end-systolic volume}) \div \text{end-diastolic volume}) \times 100$ .

#### LVEF by SPECT

Data acquisition after 30 to 60 min administered dose of Tc-99m Sestamibi intravenously at stress study. SPECT data was acquired with high resolution dual-head gamma camera (Symbia one, Siemens). A total of 64 images were obtained with of 720 s total acquisition time.

Left ventricular epicardial and endocardial margins were performed by Cedars Sinai, computer-detection methods. Automated software was used to calculate the resting global LVEF from the gated SPECT images (El-Gebaly et al. 2015).

### Statistical analysis

ANOVA and Post-Hock tests Statistical Package for the Social Sciences SPSS were used to compare between groups and to evaluate the significant values of the image quality indices.

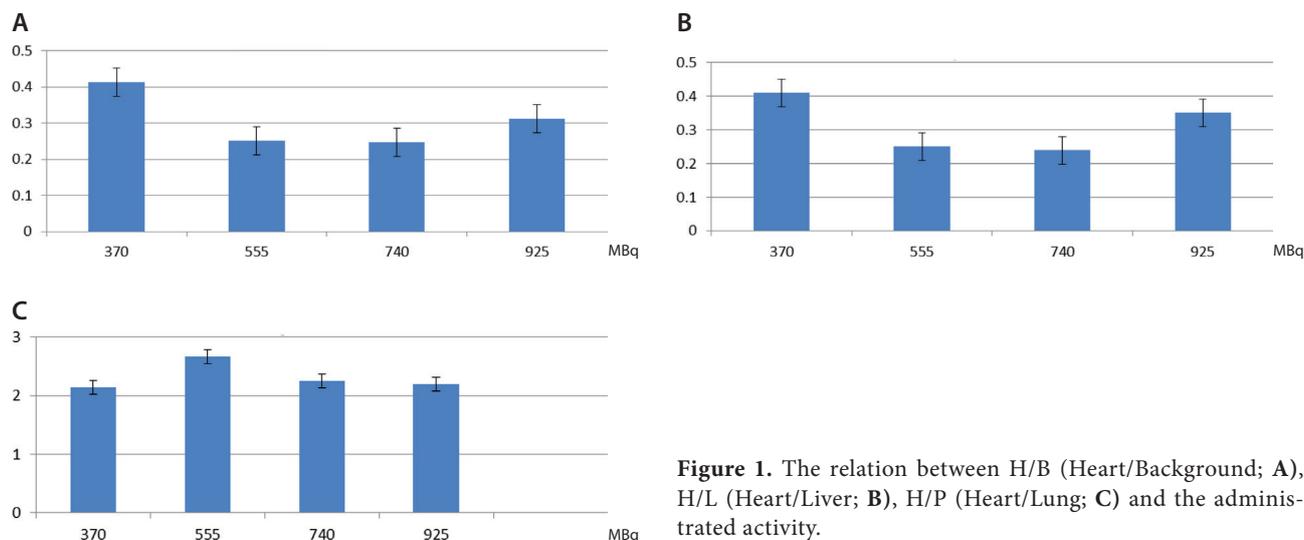
### Results

The image quality of the four groups showed no significant difference as was reported in a previous study (Smith 1987). The variation between image quality indices and administrated activity was evaluated (Tables 1 and 2).

**Table 1.** Relation between the image quality indices and the administrated activity

Dose(MBq)	H/B	H/L	H/P
370	2.1	1.3	2.6
	2.9	2.2	3
	1.2	1.01	1.9
	2	0.7	1.7
	2.6	1.1	2.6
	2	1.3	2.4
	2.1	1.4	2.3
	2.2	0.9	2.3
555	2.9	1.07	2.2
	2.5	1.02	2.5
	2.4	1.4	2.6
	2.4	0.7	2.1
	2.6	1.4	2.5
	3.6	1.2	2
	2.4	0.8	2
	2.5	1.8	2.2
740	2.7	0.9	2.6
	2.4	1.2	2.7
	2.1	1	2.3
	2	1.1	2.2
	2.1	1	2
	2	1.1	2.2
	2	1.02	2.2
	2.7	1.8	2.5
925	2.5	0.9	2.2
	2.7	1.07	2.5
	2.5	1.9	2.3
	2.1	1.9	2.4
	2	1.2	2
	2.1	0.9	2.3
	1.6	0.8	1.6
	2.1	1.0	1.8

H/B, Heart/Background; H/P, Heart/Lung; H/L Heart/Liver (ratios of image quality). For more detail information, see section "Materials and Methods".



**Figure 1.** The relation between H/B (Heart/Background; **A**), H/L (Heart/Liver; **B**), H/P (Heart/Lung; **C**) and the administered activity.

There is no significance difference between image quality indices (H/B, H/P and H/L ratios) for different groups ( $p > 0.05$ ) as shown in Figure 1. Since the gated MPI is used for calculation of ejection fraction statistically, no significant difference was found between the ejection fraction calculated by SPECT at different administered activities and the ejection fraction calculated by echocardiography where  $p > 0.05$  (Table 3) for each group in Figure 2. The mean value of the ejection fraction for all studies was  $60 \pm 15\%$ .

## Discussion

The target of the work is to study the relation between the diagnostic image quality and patient radiation protection. In 2014, a total radiation exposure of  $\leq 9$  mSv stated by ASNC should be achieved in 50% of SPECT or PET MPI studies (Schiller et al. 1989). The diagnostic value increases with increasing administered activity. The results of image quality are independent on the administered activity. Optimum activity should be improved for each procedure below which poor quality images and possible errors occurs (Cerqueira et al. 2010).

**Table 2.** Image quality indices for the different injected activities

Dose (MBq)	H/L	H/B	H/P
370	$2.3500 \pm 0.410$	$1.23875 \pm 0.4137$	$2.1375 \pm 0.452$
555	$2.2625 \pm 0.250$	$1.084286 \pm 0.250$	$2.6625 \pm 0.338156$
740	$2.3375 \pm 0.23867$	$1.14000 \pm 0.247$	$2.2500 \pm 0.28122$
925	$2.1375 \pm 0.35054$	$1.20875 \pm 0.311$	$2.2000 \pm 0.44341$

Data are means  $\pm$  SD. For abbreviations see Table 1.

In the myocardial perfusion imaging SPECT, 1100 MBq administered activity, 11.4 mSv effected dose and 70-kg patients standard doses were taken. We can increase the dose by increasing the patient weight by 1.48 MBq/kg for  $^{99m}\text{Tc}$ -MIBI (Holly et al. 2010; Cheng and Xiaohong 2019). Based on the protocol used and by increasing the acquisition time and changing the software, hardware and the standard doses, dosage can be reduced (Acampa et al. 2016; Cheng and Xiaohong 2019).

There are two points of view; one is the qualitative view, in which an expert proves that all image qualities are accepted. Second is the quantitative view, in which there is no significance difference in image quality indices between groups.

The ratios between the counts in the heart and background, lung and liver in different groups were not significantly different, because in stress study the heart injected dose is 1.5% while, the injected dose of other organs is 98.5% (ICRP 1998).

The indices of image quality are better instead of their higher values. It means that the number of counts in the heart is higher than in other organs considered as background (Diaz et al. 2003). The image quality indices shown in Figure 1 had no significant difference between the four groups in which  $p$  value  $> 0.05$ , so stress study in myocardial perfusion SPECT is feasible with 370 MBq.

As a result, it was observed that the dose delivered to the organs was increased by increasing the injected dose, while the opposite was true for a low injection dose. Rest and stress imaging undergo tissue attenuation artifacts due to anatomic structures leading to perfusion abnormalities mimicking ischemia. These abnormalities resulted in incorrect diagnosis of myocardial scar/infarction (Fleischmann et al. 1998; Picano et al. 2000; Beller 2019).

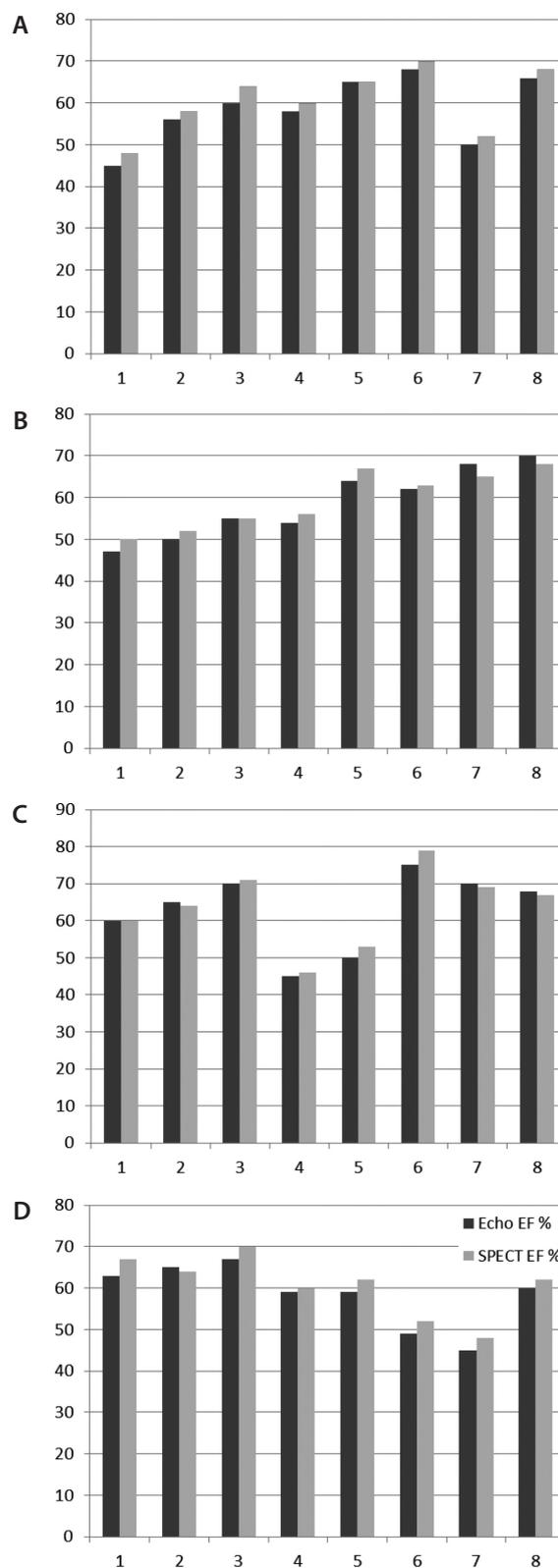
The relation between the Echocardiography Ejection Fraction (EF%) and SPECT EF% was not significant for all groups, so the quantitative functions as EDV, end systolic volume (ES) and EF% can be measured accurately with low administrated activity (370 MBq). The optimum activity was 370 MBq Tc-99m-MIBI for stress study in which optimum image quality was achieved and this agrees with ALARA (as low as possible reasonable achievable) concept.

This research supports following the recommendations of ASNC, as follows (Cerqueira et al. 2010):

- (1) Use radionuclide with small  $T_{1/2}$  such as Tc-99 m and PET tracers.

**Table 3.** Represents the relation between the echocardiography ejection fraction and the ejection fraction of different groups calculated by myocardial perfusion SPECT

Dose (MBq)	Echo (EF%)	SPECT (EF%)	
370	45	48	
	56	58	
	60	64	
	58	60	
	65	65	
	68	70	
	50	52	
	66	68	
555	47	50	
	50	52	
	55	55	
	54	56	
	64	67	
	62	63	
	68	65	
	70	68	
740	60	60	
	65	64	
	70	71	
	45	46	
	50	53	
	75	79	
	70	69	
	68	67	
	925	63	67
		65	64
67		70	
59		60	
59		62	
49		52	
45		48	
60		62	



**Figure 2.** The relation between the echocardiography ejection fraction and the ejection fraction of 370 MBq (A), 555 MBq (B), 740 MBq (C) and 925 MBq (D) group calculated by myocardial perfusion SPECT.

- (2) Study the stress test only.
- (3) Using dosage dependent on weight.
- (4) Iterative reconstruction should be used for the processing of SPECT and PET MPI.
- (5) Two acquisition detectors (180°) in Anger camera MPI studies.
- (6) The geometry of SPECT imaging should be of high sensitivity.
- (7) Using of high sensitivity collimators can reduce the injected radiation.
- (8) Widening the energy window requires further validation prior to clinical practice.
- (9) Continuous acquisition, and count consistency methods require further validation before implementation into clinical practice.

## Conclusion

370 MBq administrated dose gives the optimum results in image quality in comparison with high dose 925 MBq. This is in agreement with ALARA.

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