

The radiation dose to overweighted patients undergoing myocardial perfusion SPECT can be significantly reduced: validation of a linear weight-adjusted activity administration protocol

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Background. Large body size can cause a higher proportion of emitted photons being attenuated within the patient. Therefore, clinical myocardial perfusion SPECT (MPS) protocols often include unproportionally higher radioisotope activity to obese patients. The aim was to evaluate if a linear weight-adjusted low-dose protocol can be applied to obese patients and thereby decrease radiation exposure.

Methods and result. Two hundred patients (>110 kg, BMI 18-41, [$n = 69$], ≤ 110 kg, BMI 31-58, [$n = 131$]) underwent ^{99m}Tc-tetrofosmin stress examination on a Cadmium Zinc Telluride or a conventional gamma camera using new generations of reconstruction algorithm (Resolution Recovery). Patients <110 kg were administered 2.5 MBq/kg, patients between 110 and 120 kg received 430 MBq and patients >120 kg received 570 MBq according to clinical routine. Patients >110 kg had 130% total number of counts in the images compared to patients <110 kg. Recalculating the counts to correspond to an administered activity of 2.5 MBq/kg resulted in similar number of counts across the groups. Image analyses in a subgroup with images corresponding to high activity and 2.5 MBq/kg showed no difference in image quality or ischemia quantification.

Conclusion. Linear low-dose weight-adjusted protocol of 2.5 MBq/kg in MPS can be applied over a large weight span without loss of counts or image quality, resulting in a significant reduction in radiation exposure to obese patients. (J Nucl Cardiol 2017;24:1912-21.)

Key Words: Myocardial perfusion imaging; SPECT • CZT detector • conventional gamma camera • image quality • radiation dose

INTRODUCTION

Ischemic heart disease (IHD) is one of the most common causes of death in the western world¹ and a major cause of heart failure.² Presence of stress-induced myocardial ischemia due to significant coronary stenosis has been shown to be of fundamental clinical importance for patient prognosis^{3,4} and need for revascularization therapy.⁵ Current ESC/EACTS (European Society of Cardiology/European Association for Cardio-thoracic Surgery) guidelines⁶ therefore strongly recommend having a stress examination performed in patients with suspected stable coronary artery disease

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(CAD) before decision for revascularization therapy is taken.

Myocardial perfusion single-photon emission computed tomography (MPS) is a well-established noninvasive imaging technique for detection of myocardial ischemia. Recently, a new generation of gamma camera systems was introduced based on a novel detector technology utilizing semiconductor detectors of Cadmium Zinc Telluride (CZT).^{7,8} Furthermore, a new generation of reconstruction methods for the conventional gamma cameras was recently introduced referred to as Ordered Subset Expectation Maximization with depth-dependent Resolution Recovery (OSEM-RR).⁹ Both CZT detectors and OSEM-RR can be used to reduce the radiation exposure to nonobese patients^{10–12} in accordance with ALARA (As Low As Reasonably Achievable).¹³

A large body size may cause a higher proportion of emitted photons being attenuated and scattered within the patient resulting in reduced number of primary photons reaching the detector. In order to compensate for this, clinical protocols often include administration of proportionally higher radioisotope activity to patients with higher body weight in accordance with American Society of Nuclear Cardiology (ASNC) guidelines,¹⁴ whereas others recommend a fixed dose to all patients regardless of weight.¹⁵ Both strategies result in a large variation in absorbed dose with potentially unnecessary high radiation exposure to patients with overweight/obesity and low body weight, respectively. Body mass index (BMI) is an index of weight-for-height that is commonly used to classify overweight and obesity in adults. The World Health Organization (WHO) definition is as follows: a BMI ≥ 25 is overweight and a BMI ≥ 30 is obesity.

We have previously demonstrated that the new CZT technology enables a radiation dose reduction in nonobese patients by implementing a low-dose protocol, 2.5 MBq/kg body weight.¹² Other studies have also demonstrated the possibility of low-dose protocol using new CZT technology or new generation of reconstruction algorithms OSEM-RR on conventional gamma cameras in nonobese patients.^{16–20} A recent study indicates the possibility of dose reduction also for obese patients with a fixed activity using the CZT technology.²¹

The aim of the present study was to evaluate whether a similar linear administration schedule can be extended to all adult patients, not only nonobese, on both CZT cameras and conventional gamma cameras using resolution recovery reconstruction, in order to enable a decrease in radiation exposure to obese patients.

MATERIALS AND METHODS

Study Population and Study Design

The study included 200 patients referred for MPS due to known or suspected coronary artery disease. All patients underwent a ^{99m}Tc-tetrofosmin stress examination, according to clinical routine. The stress was accomplished either by a bicycle ergometer test or pharmacologic stress. The amount of radioisotope was administered according to body weight for patients below 110 kg (2.5 MBq/kg). According to clinical routine, a fixed activity of 430 and 570 MBq \pm 10% was used for patients between 110 and 120 kg and above 120 kg, respectively. The syringe was measured before and after injection of ^{99m}Tc-tetrofosmin to calculate the specific administered activity. A subset of the included patients with a body weight over 110 kg were also scanned with a reduced acquisition time corresponding to an injected activity of 2.5 MBq/kg of body weight.

Rest examination was performed if the stress examination images were interpreted as abnormal. The rest examination was undertaken according to a predefined, in-house developed time schedule designed to meet the ASNC recommended guidelines of 3 times more activity in the rest examination in a 1-day protocol for patients <120 kg. Thus, individually adjusted activity was administered at rest depending on the duration between the two examinations, with a minimum of 2 hours, resulting in decreased activity with increased duration. Patients >120 kg was examined with a two-day protocol since the total activity otherwise would exceed what the Swedish regulations allow for MPS.

The number of counts in the left ventricle was analyzed on all images, and on a subset of images the perceived quality as well as a quantitative diagnostic analysis was performed. All patients provided written informed consent to participate in the study and the study was approved by the regional ethics committee.

Image Acquisition and Reconstruction

The scan was performed approximately 1 hour after the injection with either a CZT gamma camera (Discovery NM 530c, GE Healthcare) or a conventional gamma camera (Ventri, GE Healthcare) dedicated to cardiac imaging. Patients were scanned in supine position with the arms positioned over the head. Patients with high uptake of ^{99m}Tc-tetrofosmin in the abdomen were rescanned after intake of water and a walk to avoid activity in the abdomen in the images. ECG-gated images were acquired using 8 bins for both cameras. No correction for scatter or attenuation was performed. The images were reconstructed on a dedicated workstation (Xeleris, GE Healthcare). All images were reconstructed and reformatted into the standard axes (short axis, vertical long axis, horizontal long axis), and polar maps of the left ventricle were created.

CZT camera. Acquisition on the CZT camera after stress was made with a scan time of 475 seconds based on the study by Herzog et al.²² A 15% symmetrical energy window at

140 keV was used. The images were reconstructed with an iterative reconstruction algorithm. For gated stress images, Maximum Likelihood Estimation Method (MLEM) 30 iterations and Green OSL regularization alpha 0.4 and beta 0.4 were used and the images were postfiltered with a Butterworth filter with cut-off frequency of 0.4 and power 10. For the nongated stress images, MLEM 40 iterations and Green OSL regularization alpha parameter of 0.51 and a beta of 0.3 were used and the images were postfiltered with a Butterworth filter with a cut-off frequency of 0.37 and a power of 7. All reconstruction parameters used followed the recommendations from the manufacturer. The images on the CZT camera were acquired in list mode, which enables the images to be resampled into a shorter acquisition via the list mode tool Lister (Xeleris, GE Healthcare). Images for a subgroup of eight patients with a body weight over 110 kg (the patients administered with fixed activities) were resampled into an acquisition time that would correspond to an administered activity of 2.5 MBq/kg.

Conventional gamma camera. Acquisition on the conventional gamma camera after stress was performed with the detectors in L-mode using a 64×64 matrix and a 20% symmetrical energy window over the 140 keV photon peak. Sixty (60) projections were acquired in a total angular range of 180 degrees with a stop condition of 25 seconds per projection. The images acquired on the conventional gamma camera were reconstructed with a resolution recovery OSEM algorithm (Evolution, GE Healthcare) with 12 iterations and 10 subsets and postfiltered with a Butterworth filter with a cut-off frequency of 0.4 and a power of 10 in stress. A second acquisition with a shorter time per angle to correspond to an administered activity of 2.5 MBq/kg body weight was performed on a subgroup of eight patients with a body weight over 110 kg.

Image Analysis

The total number of counts in the left ventricle was derived for all studies by delineating the ventricle by automatic segmentation. The number of counts in the acquired images, C_{acq} , for both cameras was recalculated to correspond to the number of counts that would have been acquired if the administered activity would have been 2.5 MBq/kg, $C_{2.5MBq/kg}$ (Eq. 1). $m_{patient}$ is the patient's body weight and A_0 is the administered activity to the patient.

$$C_{2.5MBq/kg} = C_{acquired} \cdot \frac{2.5 \cdot m_{patient}}{A_0}. \quad (1)$$

For a subgroup of 16 patients (8 examined on CZT and 8 examined on conventional gamma camera), the image quality (qualitative and quantitative) for the images of the current administration schedule and for images corresponding to an administered activity of 2.5 MBq/kg was evaluated. Two experienced observers reviewed the images in a randomized order. The readers were blinded to each other and all patient data as well as to if the data set were current administration schedule with fixed activities or 2.5 MBq/kg. The image quality was visually graded according to a four-point scale

(1 = poor, 2 = adequate, 3 = good, 4 = excellent). The following variables were considered when grading the image quality: noise level, the homogeneity of uptake as seen on both the tomographic short- and long-axis slices and on the polar plot representation. For quantification of ischemia, summed stress score was manually determined. The analysis was performed based on the 17-segment model of the left ventricle²³ using the myocardial perfusion SPECT module in the software Segment as previously described.²⁴

The total number of counts in the left ventricle was derived also for the rest images. The counts from the stress examination were decay-corrected and subtracted from the rest image. In the same way as for the stress image, the counts from the rest images were recalculated to correspond to the number of counts that would have been acquired if the administered activity would have been 3.1 MBq/kg, (Eq. 1). 3.1 MBq/kg is clinically used for rest examination since the uptake in the ventricle is lower in rest than in stress. For the patients examined with a two-day protocol was the number of counts recalculated to correspond to an injected activity of 3.1 MBq/kg.

Dosimetry

The mean absorbed dose to whole body (\bar{D}) as a function of body weight was calculated for our current clinical administration schedule, administered activity according to body weight (2.5 MBq/kg), the activity recommended by the ASNC (444 MBq for patients below 70 kg, 444 MBq + 11.5 MBq/kg body weight for patients over 70 kg)²⁵ and by the European Association of Nuclear Medicine (EANM) (500 MBq)¹⁵ (Eq. 2). The residence time (τ , the number of decays in whole body per administered activity) for ^{99m}Tc-tetrofosmin was taken from the International Commission on Radiological Protection (ICRP) publication 106.²⁶ The S value (absorbed dose to whole body per decay in the whole body) was scaled according to body weight ($m_{patient}$). The administered activity to the patient is denoted A_0 . The mass of the phantom for which the original S value was determined ($m_{phantom}$) equals to 73 kg.

$$D = A_0 \cdot \tau \cdot S \cdot \frac{m_{phantom}}{m_{patient}}. \quad (2)$$

Statistical Analysis

The data are presented as mean \pm SD. To test for differences in number of counts between 4 and 2.5 MBq/kg, a paired *t* test was used. To test for differences with regards to image quality and summed stress score, the Wilcoxon signed-rank test was used. Statistical significance was defined as $p < 0.05$.

RESULTS

All 200 patients successfully underwent a stress examination, 82 by exercise and 118 by pharmacologic. Thirty-three (33) of the patients had a body weight over 120 kg (BMI 31-58), 36 patients had a body weight

Table 1. The table shows the number of patients in the three different weight groups and on which camera their images were acquired [body mass index (BMI)]. In total were 200 patients included in this study

| | <110 kg | 110–120 kg | >120 kg | Total |
|---------------------------------|----------------------|---------------------|---------------------|----------------------|
| Conventional gamma camera (BMI) | 50 (18–41, mean 29) | 19 (32–42, mean 37) | 29 (31–58, mean 42) | 98 (18–58, mean 34) |
| CZT camera (BMI) | 81 (21–36, mean 29) | 17 (31–43, mean 36) | 4 (31–37, mean 34) | 102 (21–36, mean 30) |
| Total BMI | 131 (18–41, mean 29) | 36 (31–43, mean 36) | 33 (31–58, mean 41) | 200 (18–58, mean 32) |

Table 2. Baseline characteristics of all included patients (N or mean ± SD)

| | Exercise stress (n = 82) | Pharmacological stress (n = 118) |
|--------------------------|--------------------------|----------------------------------|
| Age (years) | 64 ± 10 | 66 ± 10 |
| Male | 56 (68%) | 87 (74%) |
| Female | 26 (32%) | 31 (26%) |
| BMI (kg/m ²) | 31 ± 7 (21–52) | 33 ± 7 (18–58) |
| Body weight (kg) | 94 ± 22 (55–156) | 102 ± 23 (51–193) |
| Diabetes | 16 (20%) | 42 (36%) |
| Hyperlipidemia | 38 (46%) | 60 (51%) |
| Hypertension | 46 (56%) | 79 (67%) |
| Smoking | 55 (67%) | 88 (75%) |
| Family history of CAD | 28 (34%) | 45 (38%) |
| History of MI | 21 (26%) | 35 (30%) |
| PCI | 21 (26%) | 37 (31%) |
| CABG | 9 (2%) | 23 (19%) |

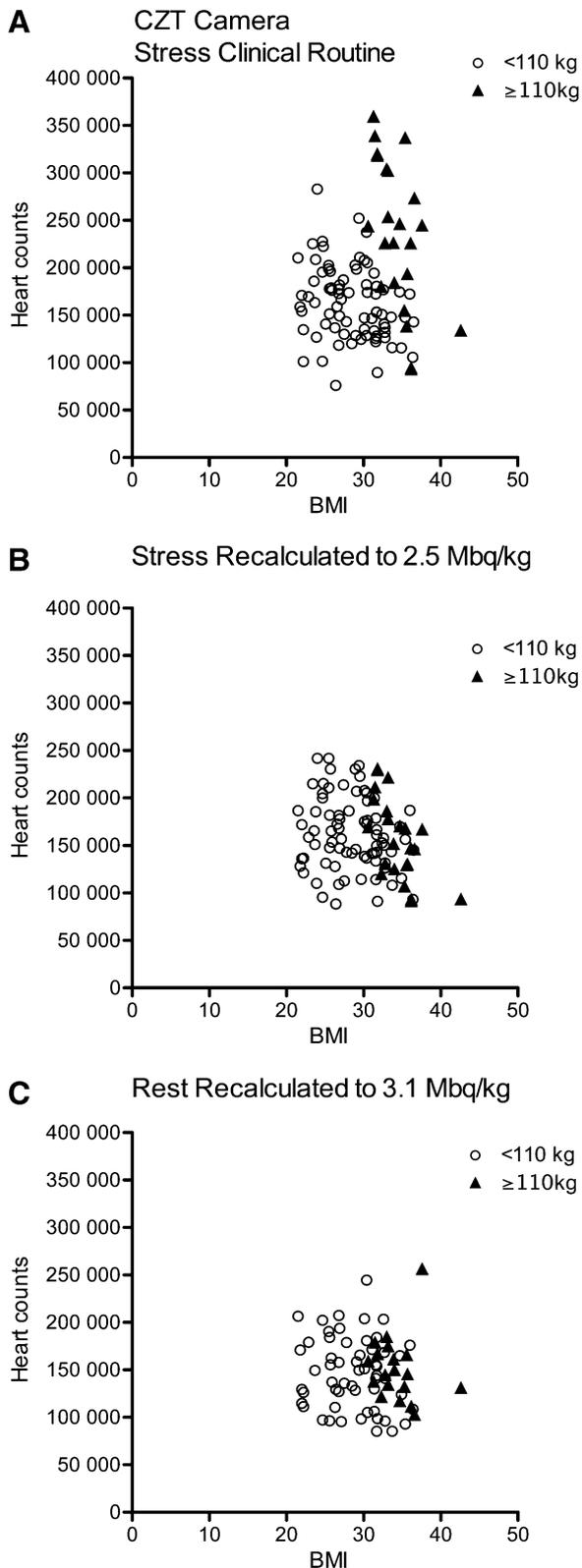
between 110 and 120 kg (BMI 32–42), and 131 patients had a body weight below 110 kg (BMI 18–41). The injected activities were (mean ± SD) 2.57 ± 0.21 MBq/kg, 413 ± 29 MBq and 583 ± 53 MBq at stress for the three weight protocols <110, 110–120, and >120 kg, respectively. Ninety-eight (98) of the patients (50 patients with a body weight <110 kg (BMI mean 29), 19 between 110 and 120 kg (BMI mean 37), and 29 with a weight >120 kg (BMI mean 42) were examined on the conventional gamma camera and 102 patients (81 patients with a body weight <110 kg (BMI mean 29), 17 between 110 and 120 kg (BMI mean 36), and 4 with a weight >120 kg (BMI mean 34) on the CZT camera (Table 1). Patient characteristics are shown in Table 2.

NUMBER OF COUNTS

The total numbers of reconstructed counts in the left ventricle for the stress examination on the CZT camera were 1.63E5 ± 0.37E5, 2.21E5 ± 0.76E5, and 2.99E5 ± 0.61E5 for patients <110 kg, 110–120 kg, and >120 kg, respectively (Figure 1A). The

recalculation of the total number of counts to correspond to an injected activity of 2.5 MBq/kg for two patient groups >110 kg administered with fixed activities was 1.58E5 ± 0.43E5 for the CZT camera, which did not differ significantly from the number of counts in patients <110 kg (*p* = 0.63; Figure 1B). Recalculating the counts in the left ventricle for the rest examination to correspond to an injected activity of 3.1 MBq/kg showed no statistical difference between patients >110 kg and patients <110 kg (*p* = 0.59, Figure 1C).

The total numbers of reconstructed counts for the stress examination on the conventional gamma camera were 4.29E5 ± 1.48E5, 5.94 ± 1.40E5, and 8.26 ± 2.96 E5 for patients <110, 110–120, and >120 kg, respectively (Figure 2A). Recalculating the total number of counts corresponding to an administered activity of 2.5 MBq/kg for the two patient groups >110 kg resulted in a number of counts of 4.42E5 ± 1.43E5 for the conventional gamma camera, which did not differ from the number of counts in patients <110 kg (*p* = 0.24) (Figure 2B). The recalculation of counts in the left ventricle for the rest examination to correspond to an



◀ **Figure 1.** The total number of reconstructed counts in the left ventricle on the CZT camera for the **A** current activity administration schedule at stress (<110 kg: 2.5 MBq/kg, 110-120 kg: 430 MBq, >120 kg: 570 MBq), **B** if 2.5 MBq/kg would have been administered at stress, and **C** if 3.1 MBq/kg would have been administered at rest.

injected activity of 3.1 MBq/kg showed no statistical difference between patients >110 kg and patients <110 kg ($p = 0.14$; Figure 2C).

The acquisition of the stress examination was undertaken at a mean of 56 minutes after the injection for exercise and 67 minutes after the injection for pharmacological stress. For the conventional camera, the counts in the myocardium were $5.29E5 \pm 2.63E5$ and $4.50E5 \pm 2.65E5$ for exercise and pharmacological stress, respectively (p value = 0.16). For the CZT camera, the counts in the myocardium were $1.90E5 \pm 5.96E4$ and $1.69E5 \pm 5.64E4$ for exercise and pharmacological stress, respectively (p value = 0.07).

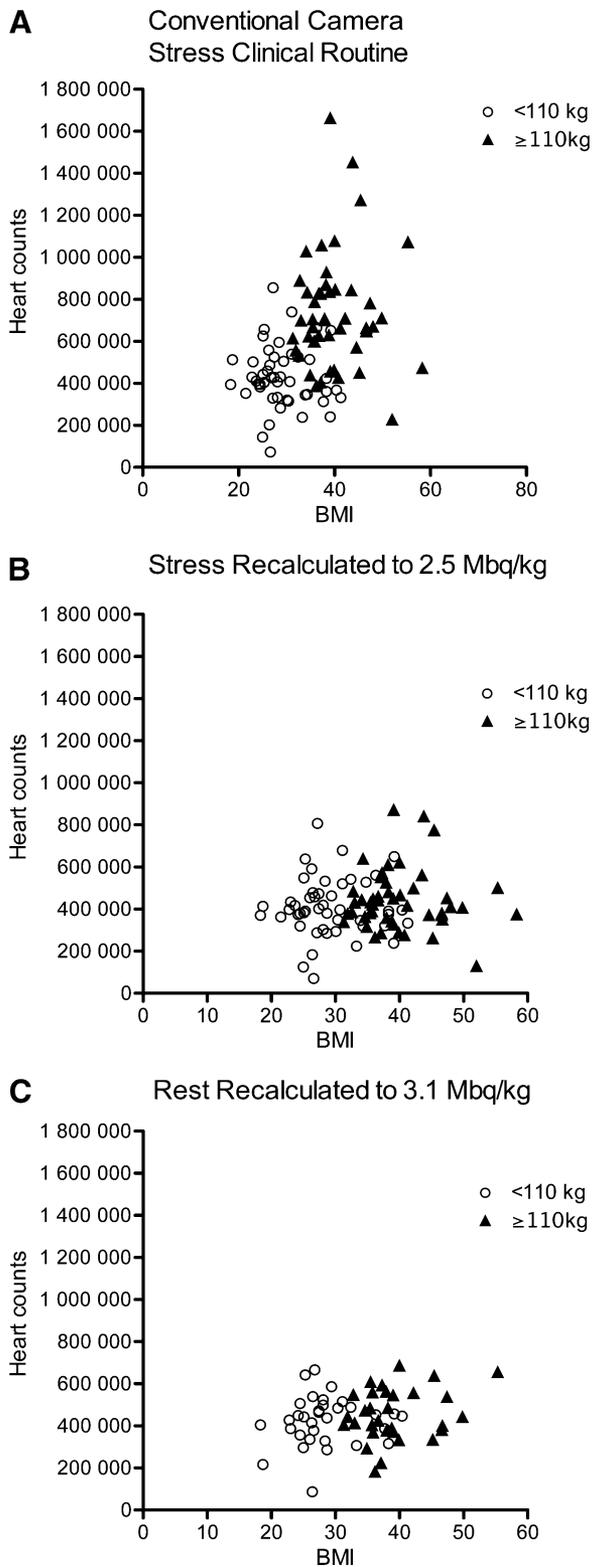
IMAGE QUALITY AND ISCHEMIA SCORE

Sixteen of the patients with a body weight over 110 kg (112-193 kg, BMI 31-58) were reimaged in the conventional gamma camera, or alternatively, and the listmode files from the CZT camera were resampled to create images that correspond to an injected activity of 2.5 MBq/kg. The scores of the image quality for the two reviewers are shown in Table 3. The mean value of the evaluated image quality for the two administration schedules was equal ($p = 1.0$). Examples of the image quality for the current administration protocol and a liner protocol of 2.5 MBq/kg can be seen in Figure 3.

There was no significant difference in SSS (summed stress score) ($p = 0.27$) for quantification of ischemia when comparing images reconstructed to reflect 4 MBq/kg (median 2.0, range 0-36) with images reconstructed to reflect 2.5 MBq/kg (median 3.5, range 0-35; bias \pm SD = 1.1 ± 3.5). The interobserver variability of SSS was 0.7 ± 1.8 .

Radiation Exposure

Figure 4 shows the mean absorbed dose to whole body as a function of body weight when administered according to the ASNC guidelines, the EANM guidelines, our current activity administration schedule, and for an administration of 2.5 MBq/kg.



◀**Figure 2.** The total number of counts in the left ventricle for the conventional gamma camera for the **A** current activity administration schedule at stress (<110 kg: 2.5 MBq/kg, 110–120 kg: 430 MBq, >120 kg: 570 MBq), **B** if 2.5 MBq/kg would have been administered at stress, and **C** if 3.1 MBq/kg would have been administered at rest.

The effective dose for the stress examination using a linear administration schedule of 2.5 MBq/kg body weight for a 120 kg patient would decrease from 4.0 mSv (570 MBq) to 2.1 mSv (300 MBq) in stress.

DISCUSSION

This study shows that it is possible to use a linear administration schedule of 2.5 MBq/kg body weight for MPS on patients with a body weight ranging from 51 kg to 193 kg (BMI 18–58) using a CZT gamma camera or a conventional gamma camera with a resolution recovery reconstruction algorithm. This will significantly reduce the effective dose to the patient compared to the EANM/ASNC guidelines.

The findings in the present study show that the traditional proportionally higher administered activity or prolonged acquisition time for obese patients is not necessary for MPS. The higher proportion of attenuation and scattered photons in fat tissue had no detectable influence on image quality and ischemia quantification. Therefore, an administration schedule based on a linear increase of activity, 2.5 MBq/kg, can be used also for obese patients without loss of counts due to attenuation. Using an administration schedule of 2.5 MBq/kg reduces the radiation dose with 30% in stress compared to the clinically used protocol for a 120 kg patient. Reducing the administered activity is not only beneficial for the patient but also advantageous for the staff taking care of the patient.

Millions of MPS studies are performed each year worldwide. Thus, reducing the administered activity will result in a decreased collective dose, both for patients and staff, and consequently a decreased risk associated with ionizing radiation exposure. Reducing the administered activity may also be important to prolong the use of MPS in the predicted worldwide deficiency of ^{99m}Tc.

Examining obese patients with the GE Discovery 530 CZT camera has been reported to be challenging^{21,27} due to the limited quality field of view (QFOV) associated with this camera. For patients with a large body habitus, it may be difficult to obtain an

Table 3. The result of the image quality for the current administration schedule with fixed activity (110-120 kg: 430 MBq, >120 kg: 570 MBq) and for images corresponding to an administered activity of 2.5 MBq/kg in 16 patients (112-193 kg, BMI 31-58). The first eight patients were examined on a convention gamma camera, BMI 34-58, and the last eight on a CZT camera, BMI 31-38

| Patient | Reviewer 1 | | Reviewer 2 | |
|---------|-----------------------|------------|-----------------------|------------|
| | Current adm. schedule | 2.5 MBq/kg | Current adm. schedule | 2.5 MBq/kg |
| 1 | 3 | 3 | 3 | 2 |
| 2 | 3 | 4 | 2 | 3 |
| 3 | 3 | 4 | 3 | 3 |
| 4 | 4 | 3 | 3 | 2 |
| 5 | 3 | 4 | 2 | 3 |
| 6 | 2 | 2 | 2 | 1 |
| 7 | 4 | 3 | 3 | 3 |
| 8 | 3 | 3 | 2 | 2 |
| 9 | 3 | 3 | 3 | 3 |
| 10 | 3 | 3 | 2 | 3 |
| 11 | 4 | 4 | 4 | 4 |
| 12 | 4 | 3 | 4 | 3 |
| 13 | 3 | 3 | 3 | 3 |
| 14 | 4 | 3 | 3 | 3 |
| 15 | 3 | 4 | 3 | 4 |
| 16 | 4 | 4 | 4 | 4 |
| Mean: | 3.3 | 3.3 | 2.9 | 2.9 |

acceptable position of the myocardium within the QFOV, where an off center position may introduce artifacts in the images.²⁸ Therefore, it is important to show that a linear administration schedule of 2.5 MBq/kg in obese patients can be used also for conventional MPS as has been shown in the present study. This is also valid for patients with large breasts that have to be examined with conventional MPS cameras for the same reason as above.²⁹ It is difficult to triage if it will be possible to correctly position the patient by body weight or BMI but an experienced technologist can by visual inspection of the patient determine if a correct position will be possible as long as the heart is normally positioned in the body.

Using a linear schedule for administered activity in the stress examination will according to this protocol give an administered activity in the rest examination that is also linear to the body weight. For a 2-day protocol, the result from the stress examination found in this study could potentially also be used for the rest examination with a linear weight-based schedule.

LIMITATIONS

The findings in the present study should be interpreted in the light of limitations. Only a few patients ($n = 4$) with a weight >120 kg were examined on the CZT camera (17 patients with a body weight between 110 and 120 were included). This was due to the fact that most of these patients could not be examined in this camera because the heart could not be positioned within the fixed QFOV related to the body habitus of these patients.

NEW KNOWLEDGE GAINED

Linear low-dose administration of ^{99m}Tc-tetrofosmin for MPS is feasible over a wide range of body weights including obese patients for examination not only with new generation of gamma cameras, CZT, but also using a conventional gamma camera applying the new generation of reconstruction algorithms taking into account depth-dependent OSEM-Resolution Recovery.

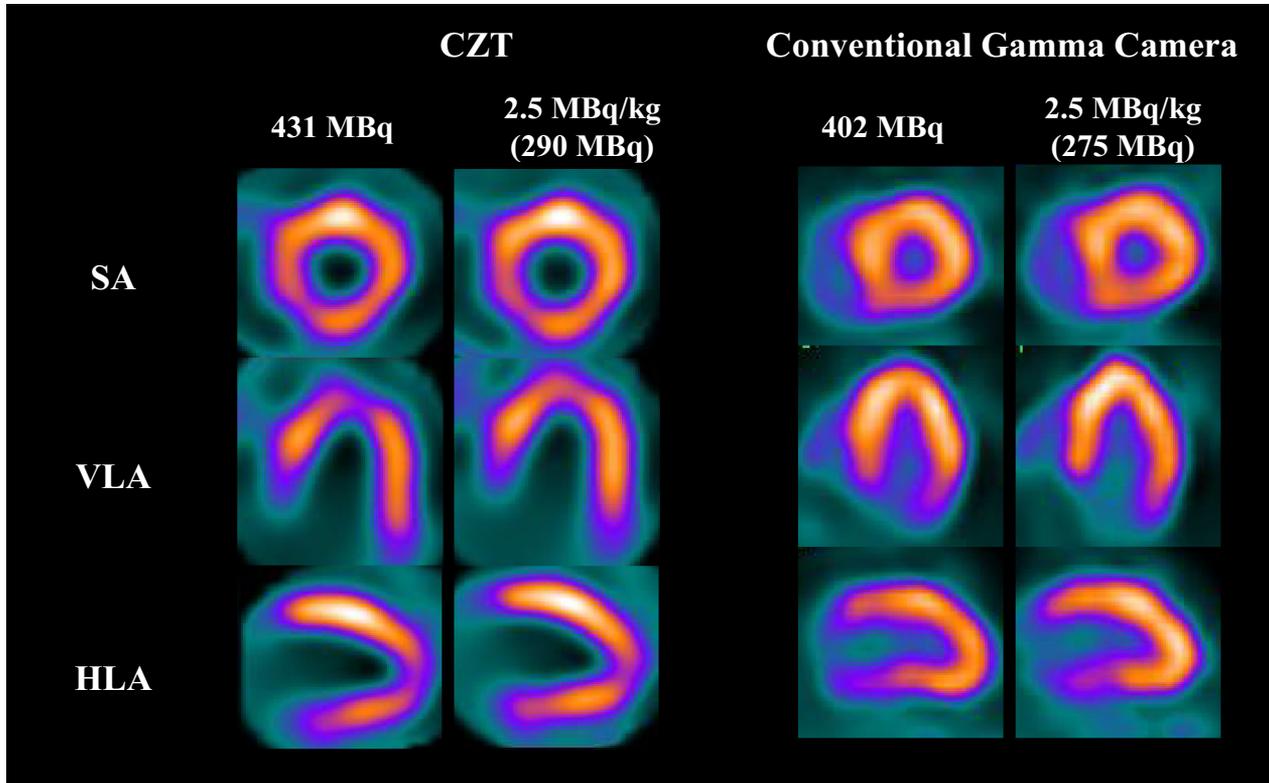


Figure 3. The image quality (stress examination) for two patients administered with 431 MBq (scanned on the CZT camera) and 433 MBq (scanned on the conventional gamma camera), according to the current protocol. The scanning was performed to current protocol (475 seconds for the CZT and 25 seconds/projection on the convention gamma camera) and with a reduced scan time to correspond to an administered activity of 2.5 MBq/kg.

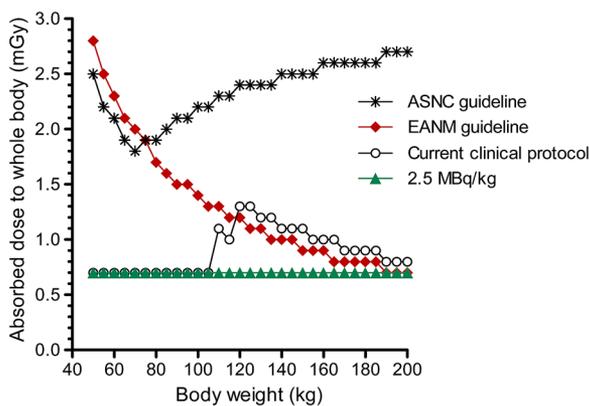


Figure 4. Mean absorbed dose from the stress examination to whole body as a function of body weight for administered activity at stress according to ASNC guidelines, EANM guidelines, our current clinical activity administration schedule, and 2.5 MBq/kg.

CONCLUSIONS

A linear administration schedule of 2.5 MBq/kg body weight can be applied for MPS of patients within a wide range of body weight (51-193 kg, BMI 18-58) using either a CZT gamma camera or a conventional gamma camera with a resolution recovery reconstruction algorithm. Thus, the radiation dose associated with MPS can be significantly reduced in obese patients.

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Disclosures

The authors, J Oddstig, C Hindorf, F Hedeer, J Jögi, H Arheden, M Hansson, and H Engblom, declare that they have no disclosures.

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