Eur J Nucl Med Mol Imaging (2013) 40:325–330
DOI 10.1007/s00259-012-2287-5

ORIGINAL ARTICLE

Temporal evolution of administered activity in cardiac gated SPECT and patients' effective dose: analysis of an historical series

C. Marcassa · O. Zoccarato · P. Calza · R. Campini

Received: 24 July 2012 / Accepted: 19 October 2012 / Published online: 21 November 2012

Abstract

Purpose Myocardial perfusion imaging contributes >20 % of the average medical radiation exposure to the population in the USA. Imaging protocols able to achieve a radiation exposure ≤9 mSv in 50 % of the studies by 2014 have been recommended. The aim of this study was to analyse the temporal evolution of administered activities in patients scheduled for dual-day ^{99m}Tc tracer gated single photon emission computed tomography (SPECT) and to compare different dose administration protocols in terms of patients' effective dose.

Methods Patients evaluated from 1 July 2002 to 31 January 2012 were allocated according to the protocol adopted: group 1: fixed activity according to diagnostic reference level: 740 MBq up to 80 kg (adapted for weight <60 kg); 900 MBq 80–100 kg, 1,110 MBq >100 kg, standard filtered back-projection (FBP) reconstruction; group 2: weight-adjusted activity: 8 MBq/kg up to 1,110 MBq, standard FBP reconstruction; and group 3: 4 MBq/kg, UltraSPECT wide beam reconstruction (WBR) reconstruction. A dual-head Anger camera (GE Helix) was used.

Results A total of 9,060 patients were allocated to different groups: 4,751 in group 1, 2,844 in group 2 and 1,465 in group 3. The stress+rest administered activity was 1,617±180 in group 1, 1,136±260 in group 2 and 682±164 MBq in group 3 (all $p<0.001$). Patients' effective dose was 13.7±3 in group 1, 9.5±2.8 in group 2 and 5.7±1.6 mSv in group 3 (all $p<0.001$). The 50th percentile was 12.6 in group 1, 9.1 in group 2 and 5.3 mSv in group 3. The effective dose received by the dedicated cardiologists was 2.1, 1.5 and 1.0 μSv/exam in group 1, group 2 and group 3 periods, respectively (all $p<0.001$).

Conclusion A significant reduction over time in the administered activity for gated SPECT was achieved; accordingly, a significant reduction in patients' exposure was obtained. A simple weight-adjusted strategy with 8 MBq/kg immediately fulfils the recommendations to limit exposure. In selected group 3 patients, a stress-only strategy allows for studies with <3 mSv exposure. Thus, at least the adoption of a new reconstruction algorithm is strongly encouraged, and suggested tracer activities for cardiac gated SPECT are to be revised.

Keywords Myocardial perfusion imaging dosimetry · Gated SPECT · Radiation exposure

Preliminary results were presented at the Annual EANM Congress, Milan, Italy, October 2012.

O. Zoccarato · P. Calza · R. Campini
Nuclear Medicine Dept, S. Maugeri Fnd, IRCCS,
Scientific Institute of Veruno,
Veruno, Italy

C. Marcassa (✉)
Cardiology Dept., S. Maugeri Fnd, IRCCS,
Scientific Institute of Veruno,
V. Per Revislate 13,
28010 Veruno, Italy
e-mail: claudio.marcassa@fsm.it

Introduction

Ischaemic heart disease is the leading cause of morbidity and mortality in developed countries. Diagnosis and treatment of ischaemic heart disease often require the use of techniques and procedures that employ some amount of radiation. Consequently, a significant increase in exposure of the population to ionizing radiation due to medical imaging has been observed since the 1980s. [1–3]

Recent retrospective studies on a cohort of about one million US people report that computed tomography and nuclear imaging together represent only 20 % of the total number of procedures but they contribute more than 75 % of the total effective dose to the population [4]. Other authors reported that cardiac imaging is responsible for 20 % of the collective effective dose [5].

Despite current risk estimates for cardiac imaging procedures which are just projections from the available epidemiological evidence, due to the absence of direct evidence from cardiac imaging, recently, the growing use of imaging procedures has raised concerns about the risks of exposure to low-dose ionizing radiation in the general population, in particular of malignancy [6, 7].

Thus, scientific societies focused their attention on producing recommendations aimed at reducing radiation exposure in cardiac imaging. Concerning myocardial perfusion imaging (MPI), imaging protocols that will achieve a radiation exposure of no more than 9 mSv in 50 % of the studies by 2014 have been recommended [8]. Several strategies can be adopted to contain patients' exposure [9, 10]. New iterative reconstruction algorithms have been recently proposed for cardiac gated single photon emission computed tomography (SPECT) with ^{99m}Tc tracers, allowing for studies with reduced count statistics. This allows for half-dose, or even lower, cardiac gated SPECT, with image quality and quantitative data comparable to standard-dose studies [11–14].

The aim of the present study was twofold: to analyse the temporal evolution in the administered activities in patients scheduled for a dual-day ^{99m}Tc-sestamibi gated SPECT study and to compare different activity administration protocols in terms of patients' and staff's exposure.

Materials and methods

Data related to gated SPECT studies consecutively performed in our institution from 1 July 2002 to 31 January 2012 were retrospectively retrieved from our institutional database. Patients scheduled for a dual-day stress-rest ^{99m}Tc-sestamibi gated SPECT were allocated according to the study protocol adopted into group 1: patients injected with a fixed activity of tracer according to the diagnostic reference level suggested by the Italian Association of Nuclear Medicine (740 MBq up to 80 kg, proportionally adapted for weight <60 kg, 900 MBq 80–100 kg and 1,110 MBq more than 100 kg); group 2: patients injected with a weight-adjusted activity: 8 MBq/kg up to a maximum of 1,110 MBq; and group 3: patients injected with 4 MBq/kg and studies reconstructed with a new iterative reconstruction algorithm (wide beam reconstruction, WBR, by UltraSPECT).

A conventional dual-head Anger camera (Millennium VG, GE), equipped with a low-energy high-resolution collimator, was used in all studies, with the following acquisition parameters: 180° acquisition, 60 projections, 64× 64 matrix, pixel size 6.3 mm and 8 frames/cycle gated acquisition. Group 1 and group 2 studies were reconstructed with a conventional filtered back-projection (FBP) algorithm (Butterworth 0.5–10). Group 3 studies were reconstructed with an ordered subset expectation maximization (OSEM)-modified iterative reconstruction algorithm (WBR), as previously described [13]. No attenuation or scatter correction was performed.

Patients' exposure and detrimental effects

According to Italian and European regulations, the injected activities are recorded. Patients' effective dose was estimated according to published data as follows: 0.0079 mSv/MBq for a stress study and 0.009 mSv/MBq for a rest study [15, 16]. The probability of detrimental effect was estimated, according to published data, on the basis of the approximated overall fatal risk coefficient ($0.05 \times Sv^{-1}$) as recommended by the International Commission on Radiological Protection (ICRP) [17]

Staff exposure

The evaluation of the effective dose of the physician dedicated to performing the stress test and injecting the tracer was monitored with film badges for whole-body dose equivalent; monthly badge reports were reviewed retrospectively over the entire study period.

Statistical analysis

Data are reported as mean±SD. When appropriate, 95 % confidence intervals (CI) are reported. Analysis of variance (ANOVA) was used to compare differences between groups and trends over time. Categories were compared with the chi-square test. A p value <0.05 (two-tailed) was considered significant.

Results

Study population

The study cohort consisted of 9,060 patients consecutively scheduled for a dual-day stress-rest sestamibi gated SPECT study from 01 July 2002 to 31 January 2012. The study cohort was allocated according to the protocol adopted: group 1: from 1 July 2002 to 1 May 2007 (period 1), 4,751 patients; group 2: from 2 May 2007 to 30 April 2010 (period 2), 2,844 patients; and group 3: from 01 May 2010 to 31 January 2012 (period 3), 1,465 patients. The

Table 1 Clinical characteristics of the three study cohorts

	Group 1	Group 2	Group 3
n	4,751	2,844	1,465
Age, years	71±11**	73±11	74±10
Age >65 years, %	74*	77	81
Gender, % (M/F)	62/38	63/37	63/37
Weight (kg)	75±14	75±15	76±15
BMI (kg/m^2)	27.3±4.4	27.4±4.7	27.6±4.8
Stressor, % (exercise/dipyridamole)	47/53	48/52	48/52
Previous MI, %	10*	6	5
Previous CABG, %	16	18	16
Previous PTCA, %	23	25	27

BMI body mass index, *MI* myocardial infarction, *CABG* coronary artery bypass grafting, *PTCA* percutaneous coronary angioplasty

*$p<0.01$ vs groups 2 and 3

**$p<0.001$ vs groups 2 and 3

patients in groups 2 and 3 were slightly older than group 1, according to the aging of the general population, and less frequently were evaluated after a recent acute myocardial infarction (Table 1).

Effective dose of radiation

The average activity injected at stress and rest in the three groups is reported in Table 2. The average cumulative effective dose significantly reduced from 13.7±2.7 mSv in group 1 to 9.5±2.4 mSv in group 2 ($p<0.001$) and a further reduction was documented in group 3 (5.7±1.2 mSv, $p<0.001$ vs groups 2 and 3) (Figs. 1 and 2). The percentile curves of the cumulative estimated patients' effective dose in the three groups are reported in Fig. 3 and the trend in the 50th percentile at stress, rest and cumulative is reported in Table 3. A significant reduction over time in the cumulative (stress+rest) 50th percentile was documented and the suggested target of 9 mSv in at least 50 % of the study for a complete stress-rest evaluation was already obtained in group 2 patients, studied from 02 May 2007 to 30 April 2010 (Fig. 3).

The probability of detrimental effects was estimated in group 1 as 0.685×10^{-3} (95 % CI 0–1.3), in group 2 as

Table 2 ^{99m}Tc-Sestamibi average activities injected at stress and rest studies in the three study groups

	Group 1	Group 2	Group 3	*p*
Stress, MBq	808±97	571±130	342±82	All <0.001
Rest, MBq	807±95	565±121	340±83	All<0.001

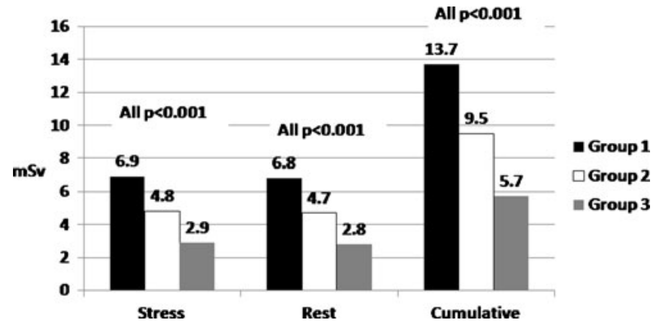

Fig. 1 Estimated effective dose at stress, rest and cumulative in group 1 (*black bars*), group 2 (*white bars*) and group 3 (*grey bars*)

0.485×10^{-3} (95 % CI 0–1.3) and in group 3 as 0.285×10^{-3} (95 % CI 0–1.1), corresponding to 1:1,460 patients, 1:2,105 patients and 1:3,509 patients, in group 1, group 2 and group 3, respectively. Thus, a 1.4-fold and 2.4-fold reduction in groups 2 and 3, respectively, as compared to group 1 was documented.

When the exposure of the physician dedicated to performing the stress test and injecting the tracer was analysed, a significant reduction over time was observed in the exposure (normalized by the number of studies performed) from 2.1 μSv/study in group 1 to 1.5 μSv/study in group 2 and to 1.0 μSv/study in group 3 (all $p<0.001$), which is more than 50 % reduction (Fig. 4).

Discussion

In the present study, a significant reduction over time in patients' dosimetry was observed. A simple weight-adjusted activity of injected tracer was able to reduce the estimated exposure by 30 % (from 13.7 mSv in group 1 to 9.5 mSv in group 2, $p<0.001$). The additional use of a new

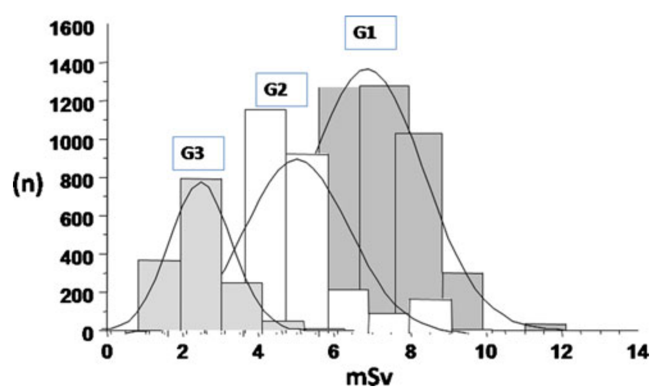

Fig. 2 Gaussian-fitted frequency distribution of stress studies' effective dose in the three groups. A significant leftward shift was observed from group 1 (*grey bars*) to group 2 (*white bars*) and group 3 (*light grey bars*)

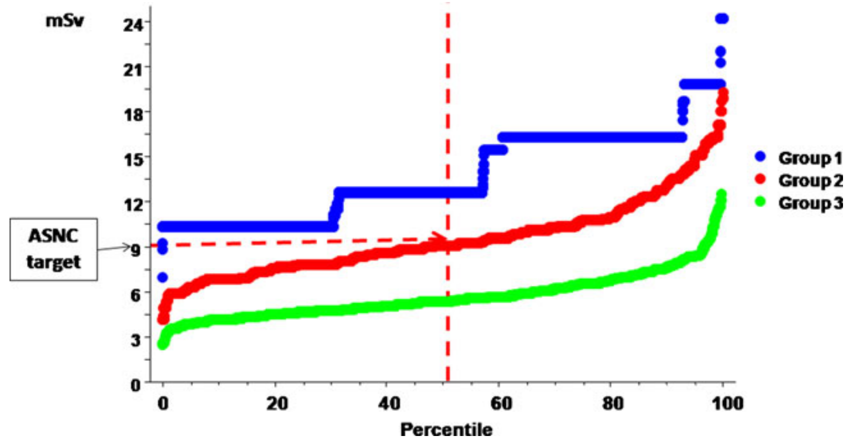

Fig. 3 Percentile curves of the effective cumulative dose in group 1 (*blue*), group 2 (*red*) and group 3 (*green*). *Dotted lines* indicate the target suggested by the American Society of Nuclear Cardiology of 50 % of studies with a cumulative effective dose less than 9 mSv [8]

reconstruction algorithm (WBR) was able to further reduce patients' effective dose by an additional 40 % (from 9.5 mSv in group 2 to 5.7 mSv in group 3, $p<0.001$); the total reduction in patients' exposure from group 1 to group 3 was almost 60 %. At the same time, a significant reduction, greater than 50 %, in the staff exposure was also documented. Finally, in select group 3 patients, a stress-only strategy would be able to reduce patients' exposure to as low as <3 mSv.

As a matter of fact, the combination of weight-adjusted tracer activity and the use of WBR, a new OSEM-derived iterative reconstruction algorithm, significantly reduced both patients' and staff's exposure and was able to reach the suggested target of a patient's exposure of 9 mSv or less in more than 50 % of our population. Several softwares are now available from different vendors to reconstruct gated SPECT studies acquired with fast protocol (half-time or less), with image quality comparable to that of standard time acquisition. Several studies demonstrated that these softwares are able to provide good quality images also in studies obtained with reduced tracer activity. In particular, with WBR we demonstrated that performance and image quality was comparable to that of conventional FBP, allowing for either half-time or half-dose studies [11–14]

New SPECT camera technologies, with high sensitivity solid-state detectors and utilizing advanced reconstruction algorithms, also allow lower doses of injected activity for diagnostic studies as compared to conventional Anger cameras [18–21]. These systems, however, are more expensive and almost exclusively dedicated to cardiac studies.

Imaging protocols, tracer selection and hardware are only parts of the principle of "as low as reasonably achievable" (ALARA), and in line with the importance of justification of all studies involving ionizing radiation, an appropriate patient selection according to appropriateness criteria and clinical guidelines is the initial and equally important component of a programme of radiation exposure reduction. Moreover, in selected patients, a stress-only approach has been documented to provide accurate diagnostic and prognostic evaluation, with a reduced radiation exposure [22]

Radiation-related side effects

Great emphasis has recently been placed on the issue of patients' radiation safety by physicians, patients and by the media. The risk of cancer in the range of a "low-dose" level of ionizing radiation (<100 mSv) is largely based on the "linear no-threshold" model extrapolated from follow-up of survivors of the atomic bomb explosions in Hiroshima and Nagasaki, Japan, in 1945 [6, 7, 9]. According to these assumptions, the lifetime risk of malignancy related to

Table 3 Trend in the 50th percentile for stress and rest studies and cumulative

	Group 1	Group 2	Group 3
Stress	6.3	4.6	2.7
Rest	6.3	4.4	2.6
Cumulative	12.6	9.1	5.3

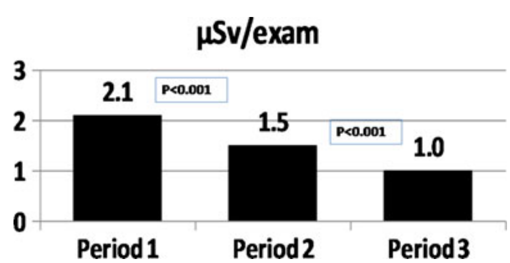

Fig. 4 Trend in average physician's exposure. A significant reduction (>50 %) was documented from period 1 to period 3

MPI is in the range of 1:2,000 patients for a 10 mSv effective dose. Results from the present study suggest that the combination of a weight-adjusted tracer activity with WBR is able to reduce the estimated risk up to 1:3,509, with a 2.4-fold reduction as compared to a fixed-dose protocol. In Italy the MPI rate is in the range of 1,700 stress-rest study/million inhabitants; with a low-dose approach, approximately more than 400 MPI-related malignancies over 10 years could be avoided. Furthermore, the majority of patients undergoing nuclear stress tests, in our population, are above 65 years of age. The lifetime risk of a radiation-related malignancy is much lower in older adults than children and fertile women. Thus, the risk of adverse events due to a serious heart disease or the risk of missing a serious cardiovascular diagnosis is much greater than the theoretical risk of radiation-related harm.

Limitations

The present report is based on a retrospective analysis. A prospective study would be required to verify the impact of low-dose protocols on patients' long-term incidence of radiation-induced side effects. However, this would require a very large sample size (in the range of hundreds of thousands of subjects) with a very long-term follow-up. Results of the present study are based on tracer activities optimized for our gated SPECT camera, study protocols and the iterative algorithm employed (WBR) and do not necessarily apply to other camera systems or softwares. Each centre should define the optimal tracer activity according to its own protocols, reconstruction software and camera system in order to match image quality and radiation protection. Finally, attenuation correction was not performed in our population, so the impact of CT scan on global patients' exposure was not assessed. Recent contributions, however, suggest that also for the use of CT in a hybrid imaging protocol, either for attenuation correction or non-invasive CT coronary angiography, low-dose protocols can be adopted [23–25]. With low-dose protocols, attenuation correction is expected to increase patients' exposure by approximately 13 % for two correction maps (stress and rest); however, CT coronary angiography implies at least a 36 % additional exposure also with the newer low-dose protocol (Fig. 5)

Conclusion

A simple change in the administered dose protocols can result in a significant reduction in patients' exposure and allows the recommendations from scientific societies to be fulfilled. Further reductions can be obtained with new iterative reconstruction algorithms, with a 240 % concomitant reduction in the probability of malignancy. This could be particularly important in patients undergoing multiple evaluation over time. In selected patients, a stress-only strategy allows for studies with <3 mSv exposure. Thus, according to our results, to reduce patients' and staff's exposure, at least a software implementation should be encouraged and, accordingly, activities to be used for cardiac gated SPECT are to be revised. Finally, an update of the diagnostic reference limits should be considered.

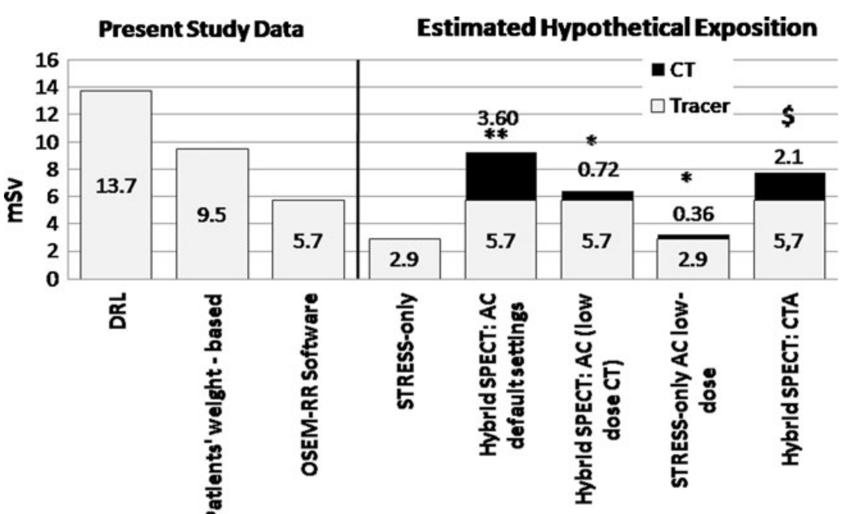

Fig. 5 Expected patients' exposure according to the tracer dose and imaging protocol adopted. *Gray bars* indicate the expected patients' exposure related to gated SPECT, *black bars* indicate the contribution of CT source in hybrid imaging. *AC* attenuation correction, *CT* computed tomography, *CTA* computed tomography angiography, *DRL* diagnostic reference limits. **Estimated exposure based on a dual slice CT system with default AC acquisition parameters (130 kV_p; 60 mAs; pitch 1.5) for an average 20-cm scan length. Stress plus rest AC maps. *Stress plus rest AC estimated exposure with low-dose systems, based on data from [23. $Estimated hypothetical exposure with a low-dose acquisition protocol using an ECG-driven tube current modulation, a body mass index-adapted tube voltage modulation and prospective ECG-triggered sequential scanning. Data from [25]

Conflicts of interest None.

References

1. Lucas FL, DeLorenzo MA, Siewers AE, Wennberg DE. Temporal trends in the utilization of diagnostic testing and treatments for cardiovascular disease in the United States, 1993–2001. Circulation 2006;113:374–9.
2. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. Circulation 2007;116:1290–305.
3. Gerber TC, Carr JJ, Arai AE, Dixon RL, Ferrari VA, Gomes AS, et al. Ionizing radiation in cardiac imaging: a science advisory from the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention. Circulation 2009;119:1056–65.
4. Fazel R, Krumholz HM, Wang Y, Ross JS, Chen J, Ting HT, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. N Engl J Med 2009;361:849–57.
5. Einstein AJ. Effects of radiation exposure from cardiac imaging: how good are the data? J Am Coll Cardiol 2012;59:553–65.
6. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, National Research Council. Health risks from exposure to low levels of ionizing radiation: BEIR VII phase 2. Washington, DC: National Academies Press; 2006.
7. Laskey WK, Feinendegen LE, Neumann RD, Dilsizian V. Low-level ionizing radiation from noninvasive cardiac imaging: can we extrapolate estimated risks from epidemiologic data to the clinical setting? JACC Cardiovasc Imaging 2010;3:517–24.
8. 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.
9. Douglas PS, Carr JJ, Cerqueira MD, Cummings JE, Gerber TC, Mukherjee D, et al. Developing an action plan for patient radiation safety in adult cardiovascular medicine. Proceedings from the Duke University Clinical Research Institute/American College of Cardiology Foundation/American Heart Association Think Tank Held on February 28, 2011. J Nucl Cardiol 2012;19:534–50.
10. Slomka P, 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.
11. DePuey EG, Gadiraju R, Clark J, Thompson L, Anstett F, Shwartz SC. Ordered subset expectation maximization and wide beam reconstruction “half-time” gated myocardial perfusion SPECT functional imaging: a comparison to “full-time” filtered backprojection. J Nucl Cardiol 2008;15:547–63.
12. 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.
13. Marcassa C, Campini R, Zoccarato O, Calza P. Wide beam reconstruction for half-dose or half-time cardiac gated-SPECT acquisitions: optimization of resources and reduction in radiation exposure. Eur J Nucl Med Mol Imaging 2011;38:499–507.
14. Zafrir N, Solodky A, Ben-Shlomo A, Mats I, Nevzorov R, Battler A, et al. Feasibility of myocardial perfusion imaging with half the radiation dose using ordered-subset expectation maximization with resolution recovery software. J Nucl Cardiol 2012;19:704–12.
15. ICRP Publication 106. Radiation dose to patients from radiopharmaceuticals. Addendum 3 to ICRP Publication 53. Ann ICRP 2008;38:159–62.
16. Konijnenberg M. Physics and radiation exposure. In: Bucerius J, Ahmadzadehfar H, Biersack H, editors. 99mTc-Sestamibi. Berlin: Springer; 2012. doi:10.1007/978-3-642-04233-1_2.
17. The 2007 Recommendations of the International Commission on Radiological Protection. ICRP Publication 103. Ann ICRP 2007;37:1–332.
18. Duvall W, Croft L, Godiwala T, Ginsberg E, George T, Henzlova M. Reduced isotope dose with rapid SPECT MPI imaging: initial experience with a CZT SPECT camera. J Nucl Cardiol 2010;17:1009–14.
19. Sharir T, Slomka PJ, Hayes S, DiCarli MF, Ziffer JA, Martin WH, et al. Multicenter trial of high-speed versus conventional single-photon emission computed tomography imaging: quantitative results of myocardial perfusion and left ventricular function. J Am Coll Cardiol 2010;55:1965–74.
20. Gimelli A, Bottai M, Genovesi D, Giorgetti A, Di Martino F, Marzullo P. High diagnostic accuracy of low-dose gated-SPECT with solid-state ultrafast detectors: preliminary clinical results. Eur J Nucl Med Mol Imaging 2012;39:83–90.
21. Mouden M, Timmer JR, Ottervanger JP, Reiffers S, Oostdijk AHJ, Knollema S, et al. Impact of a new ultrafast CZT SPECT camera for myocardial perfusion imaging: fewer equivocal results and lower radiation dose. Eur J Nucl Med Mol Imaging 2012;39:1048–55.
22. Chang SM, Nabi F, Xu J, Raza U, Mahmarian JJ. Normal stress-only versus standard stress/rest myocardial perfusion imaging: similar patient mortality with reduced radiation exposure. J Am Coll Cardiol 2010;55:221–30.
23. Preuss R, Weise R, Lindner O, Fricke E, Fricke H, Burchert W. Optimisation of protocol for low dose CT-derived attenuation correction in myocardial perfusion SPECT imaging. Eur J Nucl Med Mol Imaging 2008;35:1133–41.
24. Pazhenkottil A, Herzog BA, Husmann L, Buechel RR, Burger IA, Valenta I, et al. Non-invasive assessment of coronary artery disease with CT coronary angiography and SPECT: a novel dose-saving fast-track algorithm. Eur J Nucl Med Mol Imaging 2010;37:522–7.
25. Gaemperli O, Saraste A, Knuuti J. Cardiac hybrid imaging. Eur Heart J Cardiovasc Imaging 2012;13(1):51–60.