Annals of Nuclear Cardiology Vol. 9 No. 1 68–72

ORIGINAL ARTICLE

Optimization of ^{201}Tl Dosage in a Simultaneous Acquisition Rest ^{99m}Tc/Stress ^{201}Tl Dual-Isotope Myocardial Perfusion Single-Photon Emission Computed Tomography with Semiconductor Gamma Camera

Shonosuke Sugai, MD[1)], Naoya Matsumoto, MD[1)], Ayano Makita, MD[1)], Keiichiro Kuronuma, MD[1)], Yasuyuki Suzuki, MD[1)], Yoshitaka Hori, RT[2)], Shunichi Yoda, MD[3)], Yasuo Okumura, MD[3)], and Yasuo Amano, MD[2)]

Received: September 4, 2023/Revised manuscript received: October 10, 2023/Accepted: October 12, 2023

Abstract

***Background*: The use of ^{201}Tl in myocardial perfusion single-photon emission computed tomography (SPECT) is predominantly not recommended because of the higher radiation exposure of ^{201}Tl compared to ^{99m}Tc agent. However, the advent of new gamma cameras with semiconductor detectors has made it possible to reduce the ^{201}Tl dose and lower radiation exposure. In our hospital, the dose of ^{201}Tl is adjusted according to the patient's body mass index (BMI), with 50 MBq for BMI<25 and 74 MBq for BMI≥25. The dose of ^{201}Tl during simultaneous acquisition dual-isotope myocardial perfusion SPECT (MPS; stress ^{201}Tl and rest ^{99m}Tc agent) exceeds 9 mSv/examination when 74 MBq of ^{201}Tl is administered. In order to further reduce the radiation dose, optimization of the ^{201}Tl dose was investigated.**

***Methods*: Two hundred and eighty consecutive patients who underwent stress MPS using simultaneous acquisition dual-isotope protocol (SDI protocol) for the estimation of ischemic heart disease were included. Patients with prior myocardial infarction were excluded. Correlations between BMI and acquisition time were determined in patients receiving 50 MBq (n=154) or 74 MBq (n=126) of ^{201}Tl. In addition, linear regression analysis was used to determine the slope and intercept to derive a linear functional equation, and the theoretically optimal ^{201}Tl dose was evaluated.**

***Results*: The correlation coefficient between BMI and acquisition time in the ^{201}Tl 50 MBq group was 0.532 (P< 0.00001) and in the ^{201}Tl 74 MBq group was 0.478 (P<0.00001), both showing a positive correlation. Linear regression analysis yielded two equations: y=0.52x-0.32 (^{201}Tl 50 MBq group) and y=0.41x-0.69 (^{201}Tl 74 MBq group). Linear function equation results indicated that patients with BMI between 25 and 30 could be examined within approximately 15 minutes with 50 MBq of ^{201}Tl.**

***Conclusion*: Considering examination efficiency, a single acquisition time of less than 15 minutes is ideal. Theoretically, patients with BMI less than 30 could be examined within approximately 15 minutes with 50 MBq of ^{201}Tl.**

Keywords: 201Thallium (^{201}Tl) dosage, Acquisition time, Cadmium-zinc-telluride, Myocardial perfusion, Single-photon emission computed tomography

Ann Nucl Cardiol 2023; 9 (1): 68–72

The ratio of ^{201}Tl to ^{99m}Tc for stress myocardial perfusion single-photon emission computed tomography (SPECT) in Japan was approximately 1:1 in 2016, which is a higher ratio than in United States and Europe (1). However, ^{201}Tl has a higher radiation exposure than ^{99m}Tc, and the IAEA Nuclear Cardiology Protocols Study (INCAPS) study suggested that patients under 70 years of age should not be examined with ^{201}Tl (2). The American Society of Nuclear Cardiology has

DOI: 10.17996/anc.23-00010

1) Department of Cardiology, Nihon University Hospital, Tokyo, Japan
2) Department of Radiology, Nihon University Hospital, Tokyo, Japan
3) Division of Cardiology, Department of Medicine, Nihon University School of Medicine, Tokyo, Japan

proposed that more than 50% of all examinations should be performed with an radiation dose of 9 mSv or less (3). However, ^{201}Tl is known to have better extraction fraction of blood flow and higher sensitivity in detecting ischemic myocardium compared to ^{99m}Tc (4). In addition, it has been reported that ^{201}Tl improves the diagnostic performance of multi-vessel lesions by measuring washout rate (5). Recently, the advent of semiconductor gamma cameras (D-SPECT) has made it possible to reduce the dose of radioisotope tracer (especially, ^{201}Tl) and reduce radiation exposure (6, 7). We use the simultaneous acquisition rest ^{99m}Tc/stress ^{201}Tl dual-isotope myocardial perfusion SPECT (MPS; SDI protocol) reported by Makita and Sugai et al. in our hospital and adjust the ^{201}Tl dose according to the patient's body mass index (BMI), with 74 MBq for BMI ≥ 25 and 50 MBq for BMI < 25 (8, 9). In the SDI protocol, the effective dose of isotopes is less than 9 mSv per examination when 50 MBq of ^{201}Tl is administered, but the radiation exposure dose exceeds 9 mSv when 74 MBq of ^{201}Tl is administered. In this study, optimization of ^{201}Tl dosage was investigated to further reduce the radiation exposure dose.

Methods

Patient population

The study included 280 consecutive patients who had undergone stress MPS using the SDI protocol between December 29th, 2021 and February 15th, 2023 to evaluate ischemic heart disease, and were classified into two groups: ^{201}Tl 50 MBq group (n=154) with BMI < 25 and ^{201}Tl 74 MBq group (n=126) with BMI ≥ 25. Patients with a history of prior myocardial infarction were excluded.

Stress MPS protocol

The SDI protocol reported by Makita et al is as follows (8), initially, 125 MBq of ^{99m}Tc-Tetrofosmin (Nihon Medi-Physics, Tokyo, Japan) or ^{99m}Tc-methoxy isobutyl isonitrile (MIBI; PDRadio pharma, Tokyo, Japan) was injected to visualize resting myocardial perfusion. Then, patients underwent a 6-minute vasodilator stress using an adenosine infusion (120 μg/kg/min; PDRadio pharma Tokyo, Japan). At 3 min after the start of the adenosine infusion, 50-74 MBq of ^{201}Tl was injected to visualize stress myocardial perfusion; patients with BMI >25 received 74 MBq of ^{201}Tl and those with BMI <25 received 50 MBq of ^{201}Tl. After the end of loading, 100 ml of carbonated water is ingested before the first acquisition to eliminate the effect of extracardiac tracer accumulation (10). Subsequently, the first simultaneous rest ^{99m}Tc/stress ^{201}Tl acquisition performed using D-SPECT in an upright position. After a meal break for about 60 minutes, a second simultaneous rest ^{99m}Tc/redistribution ^{201}Tl acquisition of the SDI protocol was performed in an upright position. When imaging with D-SPECT, the patient seats in an upright position and the semiconductor detector is placed a close to the chest wall as possible to obtain sufficient photon counts. the semiconductor detector is placed parallel to the backrest, but the angle is adjusted if it could not be parallel due to obesity or breasts. The first and second acquisition were performed with electrocardiogram (ECG)-gated imaging. Both stress and rest ECG-gated images are taken with ^{201}Tl and ^{99m}Tc agents, respectively, but since ECG-gated parameters are more appropriate for measurement with ^{99m}Tc images, stress ^{99m}Tc (1st acquisition) and rest ^{99m}Tc (2nd acquisition) are used for quantitative gated SPECT (QGS) evaluation.

The acquisition time was determined by the number of gamma-ray counts of left ventricle, with a target left ventricular count of 1.0 M count. The manufacturer's recommended left ventricular photon count is 0.5 M counts or higher, but the target count value was set at 1M counts or higher to account for errors.

Statistical analysis

Statistical analysis was performed using EZ-R to determine the correlation between BMI and first acquisition time (min) for the ^{201}Tl 50 MBq or 74 MBq groups (11). Linear regression analysis was used to determine the slope and intercept to derive a linear functional equation to determine the theoretical optimal dose of ^{201}Tl.

Results

Patient characteristics

Patient background characteristics is shown in Table 1, with 154 patients in the ^{201}Tl 50 MBq group and 126 patients in the ^{201}Tl 74 MBq group. ^{201}Tl 50 MBq group was significantly older and BMI and total effective dose (^{201}Tl + ^{99m}Tc agent) were significantly lower compared to ^{201}Tl 74 MBq group (age: 73 [64, 80] vs 68 [58.25, 89], p<0.001, BMI: 22.59 [20.26, 23.795] vs 28.16 [26.76, 30.80], p<0.001, total effective dose: 8.25 [8.15, 8.36] vs 11.97 [11.86, 12.08], P< 0.001).

Relationship between BMI and acquisition time

The regression coefficient between BMI and acquisition time for each dose of ^{201}Tl is shown in Figure 1. The regression coefficient for the ^{201}Tl 50 MBq dose group was 0.532 (P< 0.00001) and for the ^{201}Tl 74 MBq dose group was 0.478 (P< 0.00001), both showing positive correlation. Linear regression analysis revealed two equations: y=0.52x-0.32 (^{201}Tl 50 MBq group) and y=0.41x-0.69 (^{201}Tl 74 MBq group) (Figure 2). Patients with a BMI between 25 and 30 who had previously received 74 MBq of ^{201}Tl could theoretically be tested within approximately 15 minutes with a 50 MBq dose.

Table 1　Patient Characteristics

	50 MBq dose group	74 MBq dose group	
n	154	126	P value
Age	73 [64, 80]	68 [58.25, 89]	<0.001
Male sex (%)	106 (68.8)	103 (81.7)	ns
BMI (kg/m^2)	22.59 [20.26, 23.79]	28.16 [26.76, 30.80]	<0.001
Acquisition time/1M count (min)	11.15 [9.66, 12.54]	11.06 [9.29, 12.59]	ns
Total effective dose (mSv)	8.25 [8.15, 8.36]	11.97 [11.86, 12.08]	<0.001

BMI, body mass index

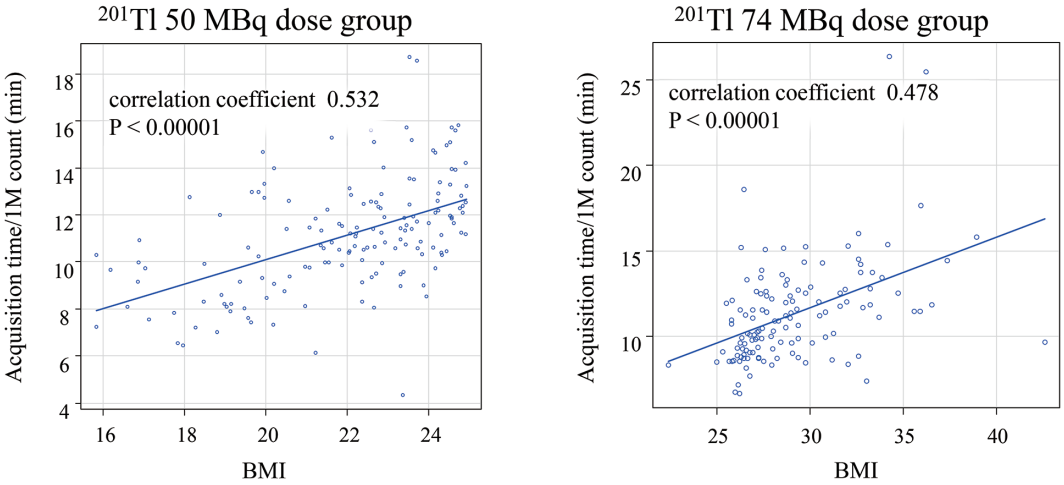

Figure 1　Scatter plot and correlation between BMI and imaging time.

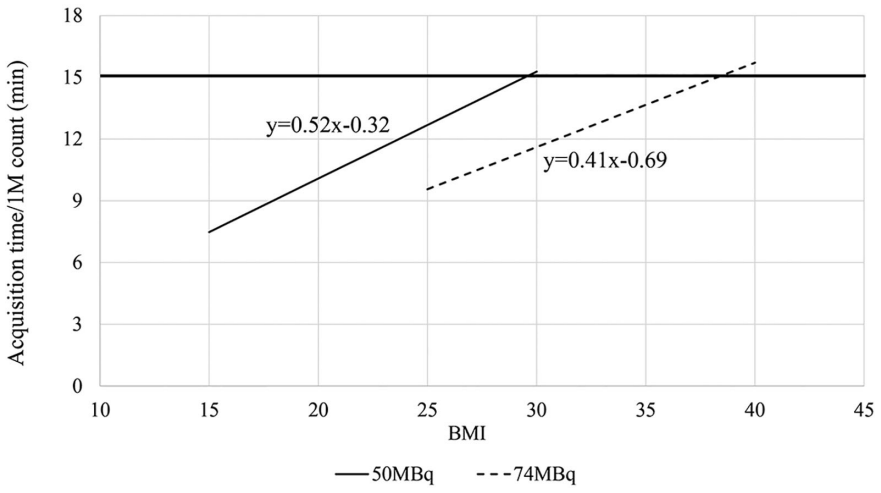

Figure 2　Linear regression line between BMI and imaging time.

Discussion

Although the advent of cadmium zinc telluride gamma cameras has made it possible to shorten acquisition time, the typical acquisition time with conventional anger-type cameras is 15 minutes (12). Considering examination efficiency and patients' throughput, the ideal acquisition time is less than 15 minutes. Theoretically, patients with BMI less than 30 could be examined within approximately 15 minutes with a ^{201}Tl 50 MBq dose, and the dose could be further reduced for emaciated patients with BMI less than 20.

Patients with BMI <30 accounted for 86.4% of the total, and if these patients could be tested with 50 MBq of ^{201}Tl, it would reduce the exposure of most patients undergoing examination to less than 9 mSv. There were 33 patients with BMI <20, 11.8% of the total. For these patients, a further

reduction of the dose of ^{201}Tl was considered possible.

The use of ^{201}Tl is avoided worldwide due to its high radiation dose. However, ^{201}Tl is superior to ^{99m}Tc tracers in its higher extraction fraction and in its ability to assess viability through redistribution phenomenon. Higher extraction fraction of ^{201}Tl may increase the chance of ischemic myocardium detection and reduces the risk of missing ischemic myocardium. In addition, severely reduced perfusion defect observed in ^{99m}Tc imaging is likely to determine non-viable tissue. However, ^{201}Tl can evaluate viable myocardium properly by its redistribution property. The high photon count sensitivity of dedicated cardiac semiconductor gamma cameras (D-SPECT and Discovery NM 530c) has achieved the optimized radiation exposure in ^{201}Tl imaging. The present study is a simultaneous dual-isotope MPS using D-SPECT and it is not considered possible to apply the protocol to conventional Anger cameras. Since this study was not conducted with other semiconductor gamma cameras, the adaptation is limited to D-SPECT. However, it is thought that imaging with reduced ^{201}Tl dose and exposure dose is possible with semiconductor gamma camera.

Study limitations

Possible causes of prolonged examination time include, (1) small size of the left ventricle (LV), (2) presence of pericardial effusion, (3) fluid retention due to heart failure, and (4) distance from the collimator to the heart. In this study, there were 11 patients whose acquisition time exceeded 15 minutes with ^{201}Tl 50 MBq. LV sizes were obtained using end-diastolic volume from QGS software. However, the end-diastolic volume of patients whose acquisition time exceeded 15 minutes was not significantly different from that of patients whose acquisition time was less than 15 minutes (66 mL [61, 75] vs. 70 mL [54, 84.75], $P=0.565$). And there were no patients with pericardial effusion or heart failure among those whose acquisition time exceeded 15 minutes. Patients with high BMI have a longer distance from the body surface to the heart and a similarly longer distance from the collimator. Imaging with D-SPECT is performed in an upright sitting position, with the gamma detector as close to the chest wall as possible to obtain adequate counts. However, patients with high BMI may have a thicker chest wall that deviates from the D-SPECT region of interest. In the current study, we did not examine chest circumference, waist circumference, or the distance from the camera, and we were unable to evaluate the relationship between these factors and imaging time. Men may have a thicker lateral chest due to the development of the broad back muscles, and women may have distance and shielding issues due to the breasts. These multiple factors may affect acquisition time.

In Figure 1, there were two cases in the 50 MBq group in which the imaging time exceeded 18 minutes, and two cases in the 74 MBq group in which the imaging time exceeded 25 minutes. None of the possible causes for the decrease in counts already listed in Limitation were applicable. There were no frequent body motions, and the posture during imaging was uniform. However, the distance and shielding from the gamma camera by the thickness of the chest wall, the broad back muscles, and the breast have not been examined. It is possible that these influences may be involved, and studies in the future that take them into account are considered necessary.

Conclusions

In patients with $25\leq BMI<30$, even if the dose of ^{201}Tl is reduced to 50 MBq, the acquisition time can theoretically be performed within about 15 minutes, and about 86.4% of all patients can be tested with a radiation exposure dose of 9 mSv or less.

Acknowledgments

None.

Sources of funding

None.

Conflicts of interest

None.

Reprint requests and correspondence:
Naoya Matsumoto, MD
Department of Cardiology, Nihon University Hospital, 1-6 Kanda Surugadai, Chiyoda-ku, Tokyo, Japan
E-mail: matsumoto.naoya@nihon-u.ac.jp

References

1. Otsuka R, Kubo N, Miyazaki Y, Kawahara M, Takaesu J, Fukuchi K. Current status of stress myocardial perfusion imaging pharmaceuticals and radiation exposure in Japan: Results from a nationwide survey. J Nucl Cardiol 2017; 24: 1850–5.
2. Einstein AJ, Pascual TNB, Mercuri M, et al. Current worldwide nuclear cardiology practices and radiation exposure: Results from the 65 country IAEA Nuclear Cardiology Protocols Cross-Sectional Study (INCAPS). Eur Heart J 2015; 36: 1689–96.
3. Cerqueira MD. Diagnosis and prognosis of coronary artery disease: PET is superior to SPECT: Con. J Nucl Cardiol 2010; 17: 678–82.
4. Klein R, Beanlands RSB, deKemp RA. Quantification of myocardial blood flow and flow reserve: Technical aspects. J Nucl Cardiol 2010; 17: 555–70.
5. Sugai S, Matsumoto N, Makita A, et al. Clinical utility of a slow ^{201}Tl washout rate in the detection of multi-vessel

coronary artery disease using a simultaneous acquisition rest ^{99m}Tc/stress ^{201}Tl protocol and a semiconducting gamma camera. Circ J 2022; 86: 1409–15.
6. Baumgarten R, Cerci RJ, de Nadai Costa A, et al. Radiation exposure after myocardial perfusion imaging with Cadmium-Zinc-Telluride camera versus conventional camera. J Nucl Cardiol 2021; 28: 992–9.
7. Mouden M, Timmer JR, Ottervanger JP, 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.
8. Makita A, Matsumoto N, Suzuki Y, et al. Clinical feasibility of simultaneous acquisition rest ^{99m}Tc/stress ^{201}Tl dual-isotope myocardial perfusion single-photon emission computed tomography with semiconductor camera. Circ J 2016; 80: 689–95.
9. Sugai S, Matsumoto N, Makita A, et al. A pitfall of simultaneous acquisition stress ^{201}Tl/rest ^{99m}Tc dual-isotope myocardial perfusion single-photon emission computed tomography with a semiconductor gamma camera. Ann Nucl Cardiol 2022; 8: 120–2.
10. Matsumoto N, Sato Y, Suzuki Y, et al. Usefulness of rapid low-dose/high-dose 1-day ^{99m}Tc-sestamibi ECG-gated myocardial perfusion single-photon emission computed tomography. Circ J 2006; 70: 1585–9.
11. Kanda Y. Investigation of the freely available easy-to-use software ‘EZR’ for medical statistics. Bone Marrow Transplant 2013; 48: 452–8.
12. Oddstig J, Hedeer F, Jögi J, Carlsson M, Hindorf C, Engblom H. Reduced administered activity, reduced acquisition time, and preserved image quality for the new CZT camera. J Nucl Cardiol 2013; 20: 38–44.