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Scatter and cross-talk correction for one-day acquisition of ^{123}I-BMIPP and ^{99m}Tc-tetrofosmin myocardial SPECT

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Objective: ^{123}I-15-(*p*-iodophenyl)-3-(*R*,*S*)-methylpentadecanoic acid (BMIPP) and ^{99m}Tc-tetrofosmin (TET) are widely used for evaluation of myocardial fatty acid metabolism and perfusion, respectively. ECG-gated TET SPECT is also used for evaluation of myocardial wall motion. These tests are often performed on the same day to minimize both the time required and inconvenience to patients and medical staff. However, as ^{123}I and ^{99m}Tc have similar emission energies (159 keV and 140 keV, respectively), it is necessary to consider not only scattered photons, but also primary photons of each radionuclide detected in the wrong window (cross-talk). In this study, we developed and evaluated the effectiveness of a new scatter and cross-talk correction imaging protocol. ***Methods:*** Fourteen patients with ischemic heart disease or heart failure (8 men and 6 women with a mean age of 69.4 yr, ranging from 45 to 94 yr) were enrolled in this study. In the routine one-day acquisition protocol, BMIPP SPECT was performed in the morning, with TET SPECT performed 4 h later. An additional SPECT was performed just before injection of TET with the energy window for ^{99m}Tc. These data correspond to the scatter and cross-talk factor of the next TET SPECT. The correction was performed by subtraction of the scatter and cross-talk factor from TET SPECT. Data are presented as means ± S.E. Statistical analyses were performed using Wilcoxon's matched-pairs signed-ranks test, and $p < 0.05$ was considered significant. ***Results:*** The percentage of scatter and cross-talk relative to the corrected total count was 26.0 ± 5.3%. EDV and ESV after correction were significantly greater than those before correction ($p = 0.019$ and 0.016, respectively). After correction, EF was smaller than that before correction, but the difference was not significant. Perfusion scores (17 segments per heart) were significantly lower after as compared with those before correction ($p < 0.001$). ***Conclusions:*** Scatter and cross-talk correction revealed significant differences in EDV, ESV, and perfusion scores. These observations indicate that scatter and cross-talk correction is required for one-day acquisition of ^{123}I-BMIPP and ^{99m}Tc-tetrofosmin SPECT.

Key words: fatty acid metabolism, myocardial perfusion, one-day acquisition, scatter, cross-talk

INTRODUCTION

MYOCARDIAL ISCHEMIA and function can be evaluated clinically by electrocardiographically (ECG) gated cardiac imaging using ^{99m}Tc-labeled perfusion agents.[1–3] Radiolabeled fatty acids are also used to evaluate myocardial ischemia because free fatty acids are major energy sources under normal aerobic conditions.[4,5] Due to its prolonged myocardial retention, ^{123}I-15-(*p*-iodophenyl)-3-(*R,S*)-methylpentadecanoic acid (BMIPP) is suitable for single photon emission tomography (SPECT).[6,7] The distributions of perfusion agents and markers of fatty acid

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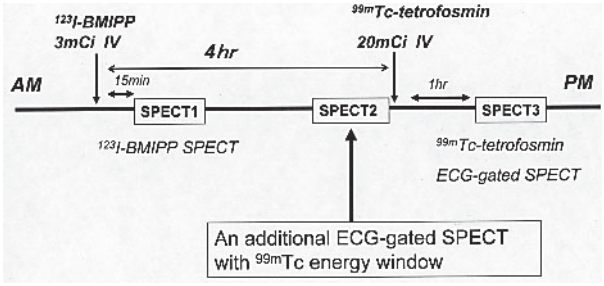

Fig. 1 The routine one-day acquisition protocol consisted of SPECT1 and SPECT3. ^{123}I-BMIPP SPECT (SPECT1) was performed in the morning and ^{99m}Tc-tetrofosmin SPECT (SPECT3) was started about 4 hours later. An additional SPECT acquisition (SPECT2) was performed just before the injection of ^{99m}Tc-tetrofosmin to assess the scatter and cross-talk factor due to ^{123}I-BMIPP.

Table 1 Patients' characteristics

Patient No.	Age/Sex	Diagnosis	Defect (TET)	Defect (BMIPP)	Mismatch
1	52/M	UA	–	–	–
2	79/F	S/O MI	–	–	–
3	83/M	DCM	–	–	–
4	55/F	MI	Sep	Sep	–
5	67/M	MI	Inf	Inf	+
6	86/F	MI	Ant	Ant	–
7	94/F	CHF	–	–	–
8	63/M	VA	–	–	–
9	70/F	MI	Inf	Inf	+
10	76/M	UA	–	–	–
11	45/M	DCM	–	–	–
12	53/M	CHF	–	–	–
13	76/M	S/O MI	–	–	–
14	73/F	DCM	–	–	–

US: unstable angina, MI: myocardial infarction, DCM: dilated cardiomyopathy, CHF: chronic heart failure, VA: vasospastic angina, Sep: septum, Inf: inferior wall, Ant: anterior wall, Mismatch (+): BMIPP defect area > tetrofosmin defect area.

metabolism frequently do not agree in ischemic myocardial disease and cardiomyopathy.[6–11] Therefore, both types of cardiac imaging are important for evaluation of cardiac conditions. In some hospitals, both ^{99m}Tc-labeled perfusion agents and ^{123}I-BMIPP are used on the same day to minimize both the time required for the procedure and the degree of inconvenience to patients and medical staff. However, as the emission energies of ^{123}I (159 keV) and ^{99m}Tc (140 keV) are similar, it is necessary to consider not only scattered photons but also primary photons of each radionuclide detected in the wrong window (cross-talk). In the present study, we developed a new correction method for one-day acquisition of both ^{123}I-BMIPP and ^{99m}Tc-tetrofosmin SPECT. In addition, the usefulness of this method was assessed by comparing end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (EF), and perfusion scores before and after correction using the Cedars-Sinai quantitative gated SPECT program.[12–14]

MATERIALS AND METHODS

Patients

Fourteen consecutive patients with ischemic heart disease or heart failure (8 men and 6 women with a mean age of 69.4 yr, ranging from 45 to 94 yr) who presented at Hiraka General Hospital, Yokote, Japan, between August and October 2002 were enrolled in this study (Table 1).

Acquisition protocol and correction method

The one-day acquisition protocol used in this study is shown in Figure 1. The routine protocol consisted of SPECT1 and SPECT3. First, myocardial SPECT was obtained (SPECT1) after injection of ^{123}I-BMIPP (111 MBq: 3 mCi). About four hours later, ECG-gated SPECT was acquired 60 min after injection of ^{99m}Tc-tetrofosmin (370 MBq: 10 mCi) (SPECT3). In this study, an additional SPECT (SPECT2) was acquired just before injection of ^{99m}Tc-tetrofosmin according to the same protocol used for SPECT3. These data correspond to the scatter and cross-talk factor of SPECT3, and correction for scatter and cross-talk was performed by subtraction of SPECT2 from SPECT3.

SPECT

SPECT was performed with a 2-detector gamma camera (Millennium MG; General Electric Medical Systems, Milwaukee, WI) equipped with low-energy, general-purpose collimators, with the detectors set to form an angle of 90°. The energy window for ^{99m}Tc was symmetrical 140 keV with 20% width. Thirty-two equidistant projections were acquired over 180° in a 64 × 64 matrix from the 45° right anterior oblique projection to the 45° left posterior oblique projection. Acquisition of ECG-gated images was performed with 40 s per 6° angular step. At each projection, 8 frames were acquired per cardiac cycle. Transaxial slices with a thickness of 4.7 mm pixels were reconstructed using a Butterworth filter (order, 5.0; critical frequency, 0.35 cycles per pixel) and the filtered backprojection method (ramp filter) on a processing computer (eNTEGRA; General Electric Medical Systems). No attenuation correction was applied.

Phantom studies

Phantom studies were performed with a dynamic myocardial phantom developed at Hokkaido University, Sapporo, Japan, as described in detail elsewhere.[15] Briefly, the phantoms consisted of hemi-ellipsoids, modeled as both endocardial and epicardial surfaces, and a thorax. The endocardial surface moves continuously towards and away from the epicardial surface to change the myocardial thickness, and thickening of the myocardium causes

a reduction in LV volume. LV volumes at end diastole and end systole were 143 m*l* and 107 m*l*, respectively, and the ejection fraction (EF) of this phantom was 25%.

Phantom studies consisted of Protocols 1, 2, and 3, in which the myocardial space was filled with 100 kBq·ml^{-1} of ^{99m}Tc solution, 100 kBq·ml^{-1} of ^{123}I solution, or a mixture of both 100 kBq·ml^{-1} of ^{99m}Tc solution and 100 kBq·ml^{-1} of ^{123}I solution, respectively. In this phantom study, the cardiac cycles were uniformly fixed at 60 cycles/min. All acquisitions were ECG-gated and obtained using a ^{99m}Tc window (symmetrical 140 keV with 20% width). SPECT images of Protocol 1 data were determined 'TRUE', while those of Protocol 3 were 'Uncorrected.' SPECT images of the subtraction of Protocol 2 from Protocol 3 were also reconstructed and determined 'Corrected.' EDV, ESV, and EF were calculated from these three SPECT images using the Cedars-Sinai quantitative gated SPECT program.[12–14]

Table 2 Results of phantom study

	EDV (m*l*)	ESV (m*l*)	EF (%)
True	93	79	15
Uncorrected	92	78	15
Corrected	93	78	16

Protocol 1: The myocardial space was filled with only ^{99m}Tc solution.
Protocol 2: The myocardial space was filled with only ^{123}I solution.
Protocol 3: The myocardial space was filled with a mixture of both ^{99m}Tc solution and ^{123}I solution.
True: Data from Protocol 1
Uncorrected: Data from Protocol 3
Corrected: The correction was performed by subtraction of Protocol 2 from Protocol 3.

Table 3 Results of clinical study

	Before correction	After correction	p
EDV (m*l*)	108.1 ± 16.7	111.0 ± 16.0	< 0.05
ESV (m*l*)	57.34 ± 14.0	58.8 ± 13.6	< 0.05
EF (%)	53.3 ± 4.7	52.5 ± 4.6	0.079
Perfusion Score	70.1 ± 14.7 (mean ± SD)	68.5 ± 15.5	< 0.05

Data processing

The 8-interval LV function was calculated from short-axis images using the quantitative gated SPET (QGS) algorithm developed by Germano et al.[12–14] Estimated LV function was based on LV volume, ejection fraction (EF), and perfusion score. Perfusion scores were expressed semiquantitatively with the maximum counts of segments, divided into 17 segments, given a value of 100.

Statistics

Data are presented as means ± S.E. Statistical analyses were performed using Wilcoxon's matched-pairs signed-ranks test, with $p < 0.05$ considered significant. All analyses were performed using SPSS version 10.0 (SPSS, Inc., Chicago, IL).

RESULTS

Phantom studies

Table 1 shows 'True,' 'Uncorrected,' and 'Corrected' EDV, ESV, and EF. The differences among them were small.

Clinical studies

The mean percentage of scatter and cross-talk relative to the corrected total count was 26.0 ± 5.3%. Table 2 shows the values of EDV, ESV, EF, and perfusion scores before and after correction. EDV and ESV were significantly larger after as compared with those before correction ($p = 0.019$ and 0.016, respectively). After correction, EF was smaller than that before correction, but the difference was not significant. Corrected perfusion scores (17 segments

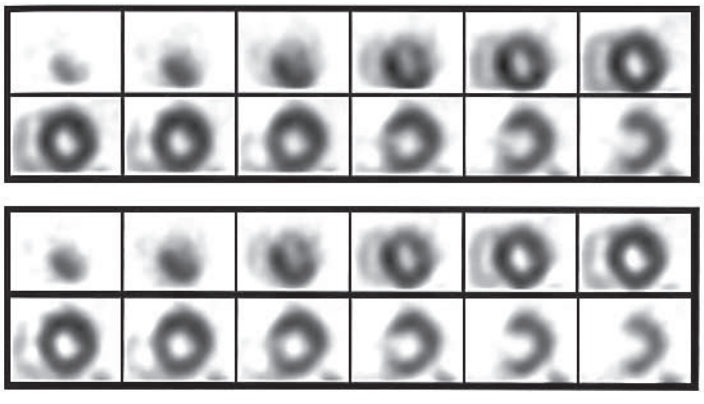

Fig. 2 An 86-year-old female with old myocardial infarction in the apical anterior wall (Pt. No. 6). Short-axis SPECT images of ^{99m}Tc-tetrofosmin before (*upper row*) and after (*below row*) the correction. The uptake in the septal–inferior wall before the correction is a little higher than that after the correction.

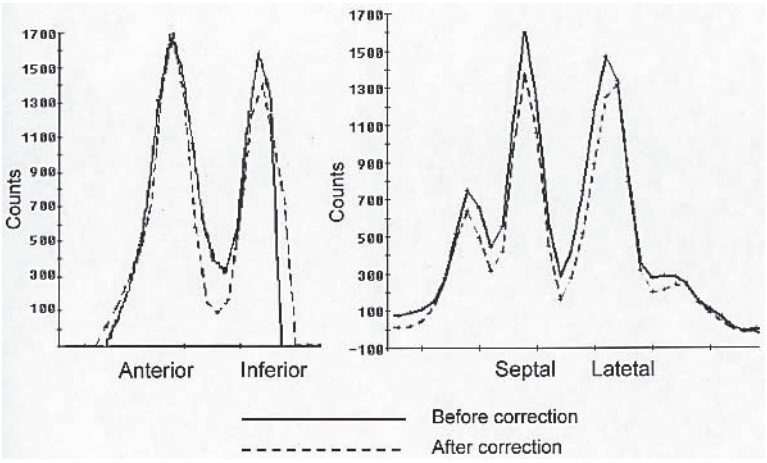

Fig. 3 Profile curve analysis of the myocardial wall before and after the correction. The left panel shows the anterior to inferior wall, and the right panel shows the septal to lateral wall on a short axis image at the midventricular level.

per heart) were significantly lower ($p < 0.001$) than those before correction.

Profile curve analysis

We performed profile curve analysis of an 86-year-old man with old myocardial infarction in the apical anterior wall. Figure 2 shows short-axis SPECT images before and after the correction. Figure 3 shows vertical and horizontal profile curves on the mid-ventricular short-axis slice. Profile curves before and after the correction did not match. Figure 4 shows circumferential profile curves at the mid-ventricular level. The difference in the profile before and after correction was more marked at the infero-septal wall.

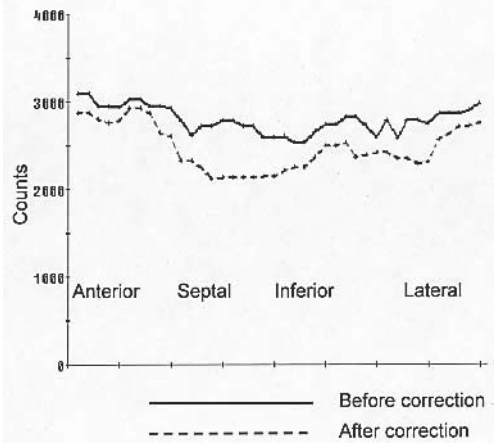

Fig. 4 Circumferential profile curve analysis of the myocardial wall before and after the correction. The difference before and after the correction increased from the septal to the inferior wall.

DISCUSSION

To our knowledge, there have been no previous reports concerning scatter and cross-talk correction for one-day acquisition of ^{123}I-BMIPP and ^{99m}Tc-tetrofosmin myocardial SPECT. However, there have been a few reports concerning simultaneous acquisition of ^{123}I-BMIPP and ^{99m}Tc-MIBI SPECT.[16,17] These studies discussed optimal energy windows for ^{123}I and ^{99m}Tc acquisition to differentiate between the distributions of these two isotopes, but did not include correction for scatter or cross-talk. Although dual-isotope acquisition saves time, both of the images obtained may be impaired due to scatter and cross-talk. On the other hand, in our one-day method there is no possibility of impairment of ^{123}I-BMIPP images, and ^{99m}Tc-tetrofosmin images can be corrected.

Our clinical results showed significant differences between corrected and uncorrected EDV, ESV, and perfusion scores. However, no significant differences were observed in the phantom study, a discrepancy most likely due to the lack of liver uptake in the phantom. The percentage uptake of ^{123}I-BMIPP in the heart has been reported to be 5.4 ± 0.6% at 1.5 h, 5.1 ± 0.4% at 3 h, and 4.2 ± 0.6% at 6 h. In addition, that in the liver was reported to be 10.0 ± 1.1% at 1.5 h, 8.7 ± 1.2% at 3 h, and 7.8 ± 1.3% at 6 h,[18] and therefore liver uptake cannot be ignored. In this study, we used myocardial phantom without defects. It might be preferable if the phantom could demonstrate some defects or mismatches.

The profile curves were shown to be different before and after correction, and the difference was more marked at the septal or inferior wall. The circumferential curves also supported the tendency for the differences to be greater near the infero-septal wall. This was thought to be due to the scatter photons from the liver. The scatter photons generated by high ^{123}I-BMIPP uptake in the liver may cause overestimation of the uptake by the infero-septal wall in uncorrected images. This may be responsible for the differences in profile curves, resulting in

difference in QGS parameters regarding clinical data. This hypothesis is supported by the lack of differences in the phantom data.

Myocardial SPECT studies generally show a decreased inferior wall in the absence of true inferior wall hypoperfusion. This is a well-described empirical artifact in myocardial perfusion studies with a number of designations, including diaphragmatic artifact, inferior wall attenuation artifact, and liver artifact.[19] This phenomenon causes a decrease in not only the perfusion score in the inferior wall but also a reduction in the mean perfusion score. In the present study, the inferior wall uptake before correction was overestimated due to the scatter photons from the liver. Therefore, the mean perfusion score was significantly decreased after correction.

Our study has some limitations. First, we did not consider the effect of the difference in SPECT2 and SPECT3 acquisition time, which began about 3.5 h and 5 h after ^{123}I-BMIPP injection, respectively. The correction of not only time, but also biodistribution or washout in the heart and liver is not trivial. Second, SPECT2 and SPECT3 were obtained using a ^{99m}Tc energy window (symmetrical 140 keV with 20% width). However, a smaller energy width may decrease the scatter and cross-talk factor, and further studies are required to investigate this possibility. Third, our protocol needs a longer time than the routine protocol, and may produce some artifacts due to misregistration. These two SPECT studies will be done in two days in principle. Our protocol should be used when these studies must be done in a day.

CONCLUSIONS

The findings of the present study indicated that the scatter and cross-talk factor from ^{123}I-BMIPP uptake causes significant differences in the results of ^{99m}Tc-tetrofosmin studies on one-day acquisition. EDV and ESV were underestimated, while EF and perfusion scores were overestimated without correction. Thus, scintigraphies using ^{99m}Tc- and ^{123}I-labeled agents should ideally be performed on different days. If these tests must be performed on the same day, it is necessary to use correction for scatter and cross-talk.

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