Diagnostic Performance of a Novel Cadmium-Zinc-Telluride Gamma Camera System Assessed Using Fractional Flow Reserve

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Background: Although the novel cadmium-zinc-telluride (CZT) camera system provides excellent image quality, its diagnostic value using thallium-201 as assessed on coronary angiography (CAG) and fractional flow reserve (FFR) has not been validated.

Methods and Results: To evaluate the diagnostic accuracy of the CZT ultrafast camera system (Discovery NM 530c), 95 patients underwent stress thallium-201 single-photon emission computed tomography (SPECT) and then CAG within 3 months. Image acquisition was performed in the supine and prone positions after stress for 5 and 3 min, respectively, and in the supine position at rest for 10 min. Significant stenosis was defined as ≥90% diameter narrowing on visual estimation, or a lesion with <90% and ≥50% stenosis and FFR ≤0.75. To detect individual coronary stenosis, the respective sensitivity, specificity, and accuracy were 90%, 64%, and 78% for left anterior descending coronary artery stenosis, the respective sensitivity, specificity, and accuracy were 90%, 64%, and 78% for left anterior descending coronary artery stenosis, the respective sensitivity, specificity, and accuracy were 90%, 64%, and 78% for left anterior descending coronary artery stenosis, and 83%, 47%, and 60% for right coronary artery (RCA) stenosis. The combination of prone and supine imaging had a higher specificity for RCA disease than supine imaging alone (65% vs. 47%), with an improvement in accuracy from 60% to 72%.

Conclusions: Using thallium-201 with short acquisition time, combined with prone imaging, CZT SPECT had a high diagnostic yield in detecting significant coronary stenosis as assessed using FFR. (Circ J 2014; 78: 2727–2734)

Key Words: Cadmium-zinc-telluride camera; Coronary artery disease; Fractional flow reserve; Single-photon emission computed tomography

Thus, we retrospectively evaluated the diagnostic value of this CZT gamma camera system using thallium-201 in patients with suspected CAD, on CAG and FFR.

Methods

Subjects
We retrospectively studied 95 consecutive patients with suspected or known CAD who had undergone both thallium-201 SPECT and CAG between March 2012 and August 2013. Clinical grounds for suspected or known CAD were based on clinical symptoms, coronary risk profile, electrocardiographic (ECG) findings or past medical history. Patients requiring routine angiographic follow-up after successful percutaneous coronary intervention (PCI) were also included. Patients with acute
myocardial infarction or unstable angina within 1 month before the study and those with advanced atrioventricular block, severe left ventricular (LV) hypertrophy, such as from aortic stenosis or hypertrophic cardiomyopathy, were excluded. There were 80 men and 15 women, aged 66±12 years (range, 47–88 years). Hypertension was observed in 76 patients, diabetes mellitus in 37, and dyslipidemia in 55. Written informed consent for invasive CAG was obtained from all the participants. The study was approved by the Ethics Committee of Tokyo Medical University (No. 2650).

Stress MPI
The study protocol of stress MPI is shown in Figure 1. Exercise MPI with thallium-201 was performed in 29 patients using the 1-day protocol. Symptom-limited multi-step exercise using a bicycle ergometer was also done. Thallium-201 (74 MBq) was given at 85% of age-adjusted predicted maximum heart rate (target heart rate), or when chest pain, or ST-segment depression ≥0.1 mV, or leg fatigue developed. Exercise was then continued for 1 min at the previous level. Immediately after this last exercise session, ECG-gated SPECT was acquired. Four hours later, thallium-201 ECG-gated SPECT at rest was also obtained.

Adenosine triphosphate (ATP) stress MPI with thallium-201 was carried out in 66 patients using the 1-day protocol. Anti-ischemic agents were withdrawn 24 h before SPECT. Patients were also requested not to drink any beverage containing caffeine for at least 12 h before the test. ATP disodium (0.16 mg·kg⁻¹·min⁻¹) was given i.v. for 5 min, and then 3 min after this thallium-201 (74 MBq) was given i.v. Image acquisition was started immediately after stress application. Thallium-201 ECG-gated SPECT images at rest were acquired 4 h later.

Data were acquired in list mode using the high-speed CZT camera with pinhole collimation (Discovery NM 530c; GE Healthcare, Haifa, Israel). New gamma camera system is equipped with a multiple-pinhole collimator and 19 stationary CZT detectors that simultaneously focus on the heart to maximize the efficiency of SPECT images. The CZT pixels are 2.46×2.46 mm in size and each detector contains 32×32-pixel 5-mm-thick elements. The stationary array simultaneously acquires all the views necessary for tomographic reconstruction, saving the time required by conventional cameras for acquisitions while rotating around the subjects. Image acquisition was performed in the supine and prone positions after stress for 5 min and 3 min, respectively, and in the supine position at rest for 10 min. For prone position imaging, patients lay prone on the table and the detectors rotated underneath the table. Interpretation of the inferior wall was considered with prone position imaging, which can decrease the frequency of attenuation artifacts in the inferior wall. Prone position imaging was used for no other purpose. SPECT images were reconstructed on a workstation (Xeleris; GE Healthcare) using a new dedicated iterative algorithm with integrated collimator geometric modeling, using maximum penalized likelihood iterative reconstruction to obtain perfusion images in standard axes. For both stress and rest image reconstruction, 70 iterations were done. A Butterworth filter (order 15; cut-off frequency, 0.28 cycles/cm) was applied to the reconstructed slices. When obtaining ECG-gated images, the R-R interval was divided by the R wave trigger into 8 equal portions. End-diastolic and end-systolic MPI was obtained with this method. Eighty-six of 95 patients (91%) were in sinus rhythm during image acquisition. No scatter or attenuation corrections were made.

Image Analysis
In accordance with a previous method, each SPECT image was divided into 17 segments. The radiopharmaceutical accumulation in the myocardium was visually evaluated by 2 cardiologists (blinded to clinical data) using a 5-grade scale: 0, normal; 1, slight reduction of uptake; 2, moderate reduction of uptake; 3, severe reduction of uptake; or 4, absence of radioactive uptake. The sum of the scores for all the segments during exercise and at rest was termed the summed stress score (SSS) and the summed rest score (SRS), respectively. SSS minus SRS was defined as the summed difference score (SDS). MPI was considered as positive for myocardial ischemia in individual coronary territory when SDS in each territory was ≥1. Disagreements in image interpretation were resolved by consensus after extensive discussion. Each reconstructed short-axis

Figure 1. Study protocol of stress myocardial perfusion imaging. ATP, adenosine triphosphate disodium.
Circulation Journal Vol.78, November 2014

Significant coronary stenosis were analyzed on a per-vessel basis. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant variables. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant variables. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant variables. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant variables.

Student’s t-test was used to compare the means of the continuous variables. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant coronary stenosis were analyzed on a per-vessel basis.

CAG and FFR
All patients underwent CAG within 3 months of SPECT. Multi-direction CAG was performed according to Judkin’s method. The degree of coronary artery stenosis was visually rated according to the criteria of the American Heart Association, and intracoronary pressure was measured in cases of intermediate lesion on CAG, defined as lesion with <90% and ≥50% diameter narrowing on visual estimation.

A 0.014-in. guidewire with a mounted pressure sensor (PressureWireTM; Radi Medical Systems, Uppsala, Sweden) was placed across the lesion. To induce a maximal hyperemic vasodilation, 8 mg and 12 mg of papaverine hydrochloride, a vasodilator of resistance vessels, were injected into the right and left coronary arteries, respectively. Under conditions of maximum hyperemia, simultaneous recording of aortic pressure and distal coronary pressure was performed. FFR was calculated as the ratio of hyperemic mean distal coronary pressure to mean aortic pressure.8,22,23 Significant coronary stenosis was defined as ≥90% diameter narrowing on visual estimation or as a lesion <90% and ≥50% stenosis with FFR ≤0.75.23

Statistical Analysis
The results are given as mean ± SD, or number and frequency. Student’s t-test was used to compare the means of the continuous variables. Sensitivity, specificity, and accuracy of the CZT-gamma camera system using thallium-201 in detecting significant coronary stenosis were analyzed on a per-vessel basis.

Spearman’s correlation coefficient was used to estimate the correlation between FFR and SDS of investigated coronary territory. P<0.05 was regarded as a statistically significant difference. The computations were performed using SPSS (version 11.0; SPSS, Chicago, IL, USA).

Results
Patient Characteristics
Subject clinical characteristics, including medication at the time of the study, are summarized in Table 1. The mean patient age was 66 years, and 84% were men. The mean body mass index was 25 kg/m². Previous myocardial infarction occurred in 20 patients (21%), of whom 15 were treated with PCI during the acute phase. Remote PCI was performed in 32 patients (34%). Among classical coronary risk factors, the prevalence of hypertension was the highest, and that of diabetes mellitus was 39%.

All of the 95 patients underwent both stress MPI using the CZT-gamma camera system and CAG successfully. Among the 95 patients, left main or 3-vessel CAD was observed in 22 patients (23%), 2-vessel CAD in 21 (22%), 1-vessel CAD in 22 (23%), and insignificant lesions in the remaining 30 (32%). Among 285 major coronary arteries evaluated, 76 were regarded to have intermediate lesions and were measured with pressure-derived myocardial FFR. Of these 76 intermediate lesions, the average FFR was 0.76 ± 0.09, with 29 lesions having FFR ≤0.75 and 45 lesions with FFR ≤0.80. Applying an FFR criterion of ≤0.75 for a functionally significant stenosis, the number of significant stenoses was 55 in the left anterior descending (LAD) coronary artery, 40 in the left circumflex (LCx) coronary artery, and 35 in the right coronary artery (RCA). The remaining 209 arteries were judged to have either a severe stenosis with ≥90% diameter narrowing (n=90), or a mild stenosis with ≥50% diameter narrowing (n=35).
Diagnostic Performance of CZT Gamma Camera SPECT

Diagnostic performance of the CZT gamma camera system on a per-vessel basis is shown in Figure 2. To detect individual coronary stenosis, for an FFR cut-off of 0.75, the respective sensitivity, specificity, and accuracy were 90%, 64%, and 78% for LAD stenosis, 78%, 84%, and 81% for LCx stenosis, and 83%, 47%, and 60% for RCA stenosis (Figure 2A). The combination of prone and supine imaging resulted in a higher specificity for RCA disease than supine imaging alone (65% vs. 47%), with an improvement in accuracy from 60% to 72% (Figure 2B). When the FFR cut-off was set at ≤0.80 for functional severity of coronary stenosis,10,11 the CZT SPECT combined with supine and prone imaging showed 85% sensitivity, 69% specificity, and 79% accuracy for LAD stenosis, 76% sensitivity, 85% specificity, and 81% accuracy for LCx stenosis, and 82% sensitivity, 68% specificity, and 74% accuracy for RCA stenosis (Figure 2C). An example of MPI taken in both the supine and prone positions is shown in Figure 3: a patient with no significant coronary artery stenosis had an apparent inferior wall defect in the supine position that was not detected in the prone position after stress.

Table 4. LV Parameters vs. Presence of Abnormal MPI

<table>
<thead>
<tr>
<th></th>
<th>Normal MPI (n=7)</th>
<th>Abnormal MPI (n=77)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>At rest</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>LV end-diastolic volume (ml)</td>
<td>89±50</td>
<td>87±34</td>
<td>0.885</td>
</tr>
<tr>
<td>LV end-systolic volume (ml)</td>
<td>39±33</td>
<td>43±29</td>
<td>0.924</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>60±10</td>
<td>55±14</td>
<td>0.675</td>
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<tr>
<td>After stress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV end-diastolic volume (ml)</td>
<td>93±55</td>
<td>91±33</td>
<td>0.919</td>
</tr>
<tr>
<td>LV end-systolic volume (ml)</td>
<td>43±38</td>
<td>44±29</td>
<td>0.721</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>57±10</td>
<td>55±14</td>
<td>0.384</td>
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</tbody>
</table>

Data given as mean±SD. LV, left ventricular; MPI, myocardial perfusion imaging.

Table 5. Scintigraphic Findings vs. Presence of Prior MI

<table>
<thead>
<tr>
<th></th>
<th>Prior MI (+) (n=20)</th>
<th>Prior MI (−) (n=74)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summed score</td>
<td></td>
<td></td>
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<tr>
<td>Summed stress score</td>
<td>14.8±9.9</td>
<td>11.2±7.6</td>
<td>0.151</td>
</tr>
<tr>
<td>Summed rest score</td>
<td>6.5±5.9</td>
<td>3.8±4.4</td>
<td>0.027</td>
</tr>
<tr>
<td>Summed difference score</td>
<td>8.3±6.3</td>
<td>7.4±5.0</td>
<td>0.537</td>
</tr>
<tr>
<td>At rest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV end-diastolic volume (ml)</td>
<td>93±21</td>
<td>86±38</td>
<td>0.261</td>
</tr>
<tr>
<td>LV end-systolic volume (ml)</td>
<td>48±21</td>
<td>41±31</td>
<td>0.335</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>50±13</td>
<td>57±14</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Data given as mean±SD. LV, left ventricular; MI, myocardial infarction.

<50% diameter narrowing (n=119) on visual estimation. Among these, 18 territories (LAD; 4; RCA; 9; LCx, 5) were supplied by collateral circulation. Among these 18 coronary territories with collateral circulation, total occlusion was found in 14, and ≥99% coronary stenosis was found in 4 patients. Coronary angiographic findings are listed in Table 2.

MPI

Abnormal MPI results were observed in 86 of the 95 patients (91%). The average SSS, SRS, and SDS in all patients were 12.0±8.2 (range, 0–36), 4.4±4.8 (range, 0–22), and 7.6±5.3 (range, −2 to 21), respectively. Among the 86 patients, an abnormal perfusion area in the LAD coronary arterial territory was observed in 61 (71%), in the LCx territory in 40 (47%), and in the RCA territory in 50 (58%; Table 3).

LV volumetric and functional analyses with ECG-gated SPECT were successfully completed in 84 patients (88%). On volumetric and functional analysis, LV end-diastolic volume, LV end-systolic volume, and LV ejection fraction were similar in the normal (n=7) and abnormal (n=77) MPI groups, both at rest and after stress (Table 4).

In patients with previous myocardial infarction (n=20), the average SRS (6.5±5.9 vs. 3.8±4.4; P=0.027) was greater and LV ejection fraction at rest (50±13% vs. 57±14%; P=0.039) was less than in those without (n=74), whereas the average SSS (14.8±9.9 vs. 11.2±7.6), SDS (8.3±6.3 vs. 7.4±5.0), LV end-diastolic volume at rest (93±21 ml vs. 86±38 ml), and LV end-systolic volume at rest (48±21 ml vs. 41±31 ml) were similar (Table 5).

The correlation between FFR and SDS of 76 investigated coronary territories was analyzed. A significant negative correlation was observed between FFR and SDS on thallium scintigraphy (r=−0.401; P=0.003).

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Discussion

Major Findings

The present study has shown that the CZT gamma camera system using thallium-201 has good diagnostic value, with sensitivity of 78–90%, specificity of 64–84%, and accuracy of 72–81% in detecting an individual coronary artery stenosis. The highest sensitivity of 90% was found in detecting LAD stenosis, while the highest specificity of 84% was observed in detecting LCx stenosis. Although the diagnosis of coronary stenosis in the RCA was based on the data acquired in the
Patients with angiographically normal coronary arteries are likely to have abnormal stress MPI. Indeed, only 9% of the present patients had normal stress MPI, but underwent CAG because of routine angiographic follow-up after successful PCI. In a recent comparison study of positron emission tomography with technetium-99m sestamibi SPECT, Bateman et al noted sensitivity of 38–71%, specificity of 84–88%, and accuracy of 72–80% in detecting individual coronary stenosis with the standard Anger camera system.

The specificity obtained in that study is similar to the present result, although the sensitivity was lower than that obtained in the present study. Thus, using thallium-201 with a short acquisition time, CZT SPECT has a good diagnostic yield in detecting significant coronary stenosis, at least similar to that of established MPI with the standard Anger camera system.

The diagnosis of multi-vessel CAD is considered to be important because standard SPECT evaluation is known to often underestimate this high-risk subset due to balanced ischemia. To overcome this diagnostic challenge, numerous studies reported the usefulness of scintigraphic markers, such as transient ischemic dilatation and LV dyssynchrony.

Therefore, in the guidelines for coronary revascularization, the European Society of Cardiology recommended measurement of FFR in cases of intermediate lesion on CAG, defined as lesions with <90% and ≥50% diameter narrowing on visual estimation. In accordance with this guideline, we used FFR measurements for the same grade of coronary narrowing.

**Comparison With Previous Studies**

In earlier SPECT studies the diagnostic value of the standard Anger camera system in detecting individual coronary artery stenosis was 65–91% in sensitivity, 83–96% in specificity, and 87–92% in accuracy. Compared with these results, the current study may indicate a lower specificity for the CZT gamma camera system, but this lower specificity is explained by referral bias in current clinical practice because patients with normal stress MPI are rarely referred for CAG.

In contrast, patients with angiographically normal coronary arteries are likely to have abnormal stress MPI. Indeed, only 9% of the present patients had normal stress MPI, but underwent CAG because of routine angiographic follow-up after successful PCI. In a recent comparison study of positron emission tomography with technetium-99m sestamibi SPECT, Bateman et al noted sensitivity of 38–71%, specificity of 84–88%, and accuracy of 72–80% in detecting individual coronary stenosis with the standard Anger camera system. The specificity obtained in that study is similar to the present result, although the sensitivity was lower than that obtained in the present study. Thus, using thallium-201 with a short acquisition time, CZT SPECT has a good diagnostic yield in detecting significant coronary stenosis, at least similar to that of established MPI with the standard Anger camera system.

The diagnosis of multi-vessel CAD is considered to be important because standard SPECT evaluation is known to often underestimate this high-risk subset due to balanced ischemia. To overcome this diagnostic challenge, numerous studies reported the usefulness of scintigraphic markers, such as transient ischemic dilatation and LV dyssynchrony. The addition of transient ischemic dilatation and LV dyssynchrony to standard perfusion analysis with myocardial SPECT improves diagnostic accuracy. In the current study, however, we evaluated the diagnostic accuracy of the CZT gamma camera system in detecting individual coronary stenosis using the stan-
This reconstruction algorithm is adversely affected by extracardiac radiotracer activity. Askew et al found that a considerable number of cardiac segments was deemed uninterpretable when SPECT was acquired in the early phase due to the presence of non-cardiac activity, such as hepatic or bowel activity. To overcome this shortcoming, many investigators delayed the initiation of data acquisition until 60–90 min after technetium radiotracer injection, to reduce hepatic activity. Hepatic clearance of technetium, however, depends on the stress method, while insufficient clearance was often observed after pharmacologic stress. Contrary to the aforementioned approach, this reconstruction algorithm was used for reconstruction of the acquired datasets.

Figure 3. Post-exercise thallium-201 single-photon emission computed tomography and coronary angiography (CAG) of a 54-year-old man with suspected coronary artery disease. (A) Perfusion defect is noted in the inferior wall on post-stress supine imaging. Post-stress prone imaging is normal, showing that the apparent perfusion defect is secondary to soft-tissue attenuation. (B) Subsequent CAG showed no significant coronary artery stenosis. LCA, left coronary artery; RCA, right coronary artery.

CZT Gamma Camera System

One of the fundamental differences between the CZT camera and the Anger camera lies in the reconstruction method. While a standard Anger camera uses filtered backprojection reconstruction, the new CZT camera applies maximum penalized likelihood iterative reconstruction. Based on integrated collimator geometry modeling, 40 and 50 iterations of the algorithm were used for reconstruction of the acquired datasets.
we used thallium-201 with this new CZT camera system because this radiotracer has good heart-to-organ activity ratios for the liver and spleen, irrespective of the stress method. Indeed, two-thirds of the present patients required pharmacologic stress, partly due to their older age. With this approach, reduction of scan time (including prone acquisition) from 15 min to 8–10 min and reduction of radiotracer dose from 111 MBq to 74 MBq were possible, compared with the standard Anger camera system.

**Importance of FFR for CAD Diagnosis**

In patients with coronary stenosis of moderate severity, evaluation of myocardial ischemia is challenging because the weak correlation between stenosis 40–70% of the diameter, as determined on CAG, and flow limitation during hyperemic stress is well recognized. A recent landmark study, the Fractional Flow Reserve versus Angiography for Multivessel Evaluation (FAME) trial, also noted better prognosis of CAD patients who were treated with PCI based on FFR compared with CAG-guided PCI. Despite this clear limitation of CAG for the diagnosis and treatment of intermediate coronary stenosis, previous diagnostic studies of myocardial SPECT for CAD used invasive CAG as the gold standard. Indeed, visual estimation of 50% coronary diameter narrowing using a caliper is subjective, whereas FFR=0.75 for an intermediate stenosis is objective and easily obtained by experienced personnel.

Applying these sophisticated FFR measurements, we examined a cut-off of not only ≤0.75 but also ≤0.80 for myocardial ischemia because the latter value was applied for the threshold for PCI in the FAME and FAME 2 trials. With this criterion for intermediate coronary stenosis, the CZT gamma camera system also had sensitivity of 76–85%, specificity of 69–85%, and accuracy of 74–81% in detecting individual coronary artery stenosis. Thus, the present study has demonstrated the good diagnostic value of the CZT gamma camera system using thallium-201, regardless of the FFR cut-offs for intermediate coronary stenosis of either ≤0.75 or ≤0.80.

**Study Limitations**

The present study had some limitations. Although FFR is the current gold standard for evaluating the physiological significance of epicardial coronary stenosis, there are some pitfalls related to FFR. In the case of LV hypertrophy, a lower ischemic threshold is observed as a result of the relatively inadequate capillary supply to the muscle mass. In LV hypertrophy, in addition, an increased perfusion gradient is noted between subepicardial and subendocardial layers, increasing the propensity for transmural steal. From the technical point of view, FFR will be artificially high in a submaximum hyperemic condition, and stenosis severity may be underestimated. Therefore, we excluded patients with severe left LV hypertrophy, such as from aortic stenosis or hypertrophic cardiomyopathy. In addition, FFR cut-offs have not been established in patients with acute myocardial infarction or on chronic hemodialysis. These limitations should be kept in mind when applying this sophisticated method.

In this study, LV volumes were relatively small even though ≥20% of patients had previous myocardial infarction. Given that 15 of 20 patients with previous myocardial infarction underwent early coronary reperfusion therapy with PCI, successful myocardial salvage may have prevented LV remodeling in most of the present patients. Therefore, good diagnostic yield of a CZT gamma camera system using thallium-201 may be limited to this particular group of patients. The diagnostic value of this system in patients with a large heart, such as those with LV remodeling, remains to be determined.

It was reported that for patients with morbid obesity, MPI on CZT cameras might often yield insufficient image quality. Because the body mass is too large for the size of the gantry, the patient’s heart cannot be positioned close enough to the detectors. As a result, for the patients with body mass index ≥40 kg/m² it is difficult to obtain diagnostic imaging quality on a CZT camera. In the present study, however, with Japanese subjects, the maximum body mass index was only 35 kg/m² and no such artifact was observed.

Another limitation is that the current study was done retrospectively in a single institution and included a small number of patients. Therefore, a prospective approach including multiple centers, with a large patient group, is necessary. In addition, although clinical evidence has shown that the cardiac event rates after normal SPECT are low, a recent study reported increased cardiac events in patients with functionally significant coronary stenosis as assessed on FFR. Based on these observations, it may be important to further evaluate the role of FFR in determining prognosis for patients with normal myocardial SPECT. Given that most patients with FFR <0.75 usually undergo PCI, a large prospective multi-center study is necessary to evaluate the prognosis for patients with FFR <0.75 and normal myocardial SPECT.

**Conclusions**

Using thallium-201 with a short acquisition time, combined with prone and supine imaging, CZT SPECT had a high diagnostic yield in detecting significant coronary stenosis as assessed on FFR. Although a modest reduction of scan time was established in the current study, to maximize the benefit of the CZT camera system, a further dose reduction of thallium-201 may be attainable.

**Acknowledgments**

We thank the Department of International Medical Communications at Tokyo Medical University for assistance with the manuscript.

**Disclosures**

Conflict of Interest: None declared.

**References**

8. Boden WE, O’Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk


