Comparison of high efficiency CZT SPECT MPI to coronary angiography

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Background. **The recently introduced cadmium zinc telluride (CZT) SPECT cameras have the potential to reduce radiation exposure to patients and shorten imaging time. So far, there has been only one small study comparing the results of high efficiency CZT SPECT myocardial perfusion imaging (MPI) to invasive coronary angiography.**

Methods. **All patients who had either a Tc-99m sestamibi or Tl-201 SPECT MPI study using a CZT camera (GE Discovery NM 530c) over a 1-year period followed by a coronary angiogram within 2 months were included. Only patients with a history of CABG surgery were excluded. Standard stress protocols were employed. Rest images were acquired for 5 min and stress supine and prone images for 3 min each. Both MPI studies and coronary angiograms were interpreted by blinded readers. A standard 17-segment model was employed for MPI interpretation, and coronary angiograms were interpreted for the presence of obstructive epicardial coronary artery disease (CAD) defined as ≥70% luminal narrowing. Correlation was based on the ability to diagnose obstructive epicardial CAD.**

Results. **Of the 3,111 patients who underwent SPECT imaging using the CZT camera during this time period, 230 patients qualified for the correlation study (mean age 64.2 ± 11.0 years old, 69% male, and 49% had a history of intracoronary stenting). Tc-99m was used in 76% vs Tl-201 in 24% of the studies. Exercise stress was performed in 60% of patients and vasodilator pharmacologic stress in 40%. Sensitivity was 95%, normalcy rate was 97%, and accuracy was 69% for detecting obstructive CAD.**

Conclusions. **In this so far largest correlation study between coronary angiography and high efficiency CZT SPECT imaging, a high sensitivity and accuracy for detecting obstructive epicardial CAD was found for this new SPECT camera technology. (J Nucl Cardiol 2011;18:595–604.)**

Key Words: Myocardial perfusion imaging: SPECT • coronary artery disease • diagnostic and prognostic application • Technetium-99m • Thallium-201

INTRODUCTION

Although extensively utilized in the management of patients with known or suspected coronary artery disease (CAD), myocardial perfusion imaging (MPI) technology is over 50-years old and suffers from known limitations, most notably long image acquisition times and radiation exposure. The recently introduced camera systems with optimized acquisition geometry, collimator design, and reconstruction software have the potential to improve image quality with significantly shorter image acquisition times and reduced isotope doses.[1] The Discovery NM 530c (GE Healthcare, Haifa, Israel) is one of the new high efficiency cardiac cameras and is based on a multi-pinhole design and an array of cadmium zinc telluride (CZT) pixilated detectors. The use of CZT detectors improves the energy and spatial resolution while the use of simultaneously acquired views gives complete and consistent angular data.[2]

Previous studies have validated CZT SPECT myocardial perfusion with conventional SPECT. An initial study on the D-SPECT camera (Spectrum Dynamics, Caesarea, Israel) found high image quality with an

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equivalent level of diagnostic confidence with traditional tracer doses when compared with conventional SPECT.[3] A second study again compared high-speed SPECT to conventional SPECT using standard isotope doses in a multicenter setting.[4] Initial studies using the Discovery NM 530c camera with conventional isotope doses found comparable diagnostic performance compared to conventional SPECT with significantly shorter acquisition times.[5-7] Preserved image quality and diagnostic performance with reduced tracer doses has also been shown.[8]

So far there has only been one published study with 56 patients correlating CZT SPECT myocardial perfusion imaging (MPI) to invasive coronary angiography.[9] The objective of this study was to evaluate the correlation of high efficiency CZT SPECT MPI to invasive coronary angiography in a larger, clinically relevant population.

METHODS

Study Design

In a study protocol approved by our institutional IRB, we prospectively evaluated all the patients who presented to the Mount Sinai Non-Invasive Cardiology Laboratory over a 1-year period (June 2009 to May 2010) for a clinically indicated Tc-99m sestamibi or Tl-201 SPECT MPI stress test using a CZT camera (GE Discovery NM 530c). Patients who underwent an invasive coronary angiogram within 2 months of the MPI were identified. Only patients with a history of coronary artery bypass grafting (CABG) surgery were excluded.

Imaging and Stress Protocol

Standard imaging protocols as endorsed by the American Society of Nuclear Cardiology (ASNC) were used for all the patients.[10] A rest–stress or stress-first imaging sequence was employed using Tc-99m sestamibi. If stress-first images demonstrated normal perfusion and normal left ventricular function, then rest imaging was not performed. The lower isotope dose imaging time was 5 min and the higher isotope dose imaging time was 3 min. A stress-redistribution imaging sequence was employed using Tl-201. Redistribution images were not done if stress perfusion and left ventricular function were normal. Tl-201 imaging time was 5 min for both stress and redistribution images. Tl-201 use was mostly based on Tc-99m shortages, but was used specifically in selected patients for viability detection. Image acquisition began 30-60 min after tracer injection for Tc-99m and 10 min after injection for Tl-201. All supine stress images were gated. Post-stress left ventricular ejection fraction (EF) was determined using commercial software (QGS, Cedars-Sinai, Los Angeles, CA). Supine and prone stress images were acquired in all the patients when technically possible. Prone imaging time was the same as the supine imaging time but gating was not performed.

The Discovery NM 530c is equipped with a multiple pinhole collimator and 19 stationary CZT detectors simultaneously imaging 19 cardiac views. System design enables imaging of a three-dimensional volume imaged simultaneously by all detectors. Patients were imaged in the supine position with arms placed over the head. Automated heart positioning in the quality field-of-view was assisted by using real-time persistence imaging. Although the detector could be rotated by the gantry if required for positioning, once acquisition was started there was no detector or collimator motion. Penalized maximum likelihood iterative reconstruction adapted to the Discovery NM 530c three-dimensional geometry was used to create transaxial slices of the left ventricle. No correction for scatter or attenuation was performed.[5]

Standard exercise and pharmacologic protocols as endorsed by ASNC were used for all the patients.[11,12]

Isotope dose was weight based and dependant on the protocol performed. For a standard 1-day rest–stress Tc-99m protocol, the rest dose was 5-10 mCi based on the three weight groups (<200, 200-250, and >250 lbs) and the stress dose was 15-30 mCi based on the same weight ranges. The stress-first Tc-99m protocol employed a low stress dose of 12.5 mCi if the weight was <200 lbs and 25-30 mCi if the weight was >200 lbs. If needed rest doses for a 1-day stress–rest Tc-99m protocol were 15-30 mCi based on the three weight groups (<200, 200-250, and >250 lbs) while the rest dose for a 2-day stress–rest Tc-99m protocol was 10-25 mCi based on the same weight ranges. For a standard 1-day stress-redistribution Tl-201 protocol, 2.5-3.5 mCi of Tl-201 was used based on the three weight groups (<150, 150-200, and >200 lbs).

End Points

Patient demographics, stress test variables, and tracer doses were prospectively collected at the time of stress testing in the Nuclear Cardiology Database. Pre-test risk of coronary disease was based on the ACC/AHA scoring system which utilizes age, gender, and presenting symptom.[13]

MPI studies were read by consensus opinion by two of three board certified nuclear cardiologists (WLD, LBC, and MJH) who were blinded to clinical information, stress test results, and the results of the coronary angiogram. Quantitative perfusion scoring of the rest and stress (supine and prone) images was performed using a 17-segment model and a 5-point scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe, and 4 = absent).[14] A combined stress score was also calculated from the aggregate supine and prone reads. The percent total perfusion deficit was calculated by dividing either the summed rest or stress score by 68 and multiplying by 100.[4] The presence of obstructive CAD and the associated vessel or vessels were determined by consensus opinion of the two readers. The final interpretation involved a visual combination of both supine and prone results. Gated SPECT images, left ventricular volumes, and EF were considered in the final assessment of the presence of obstructive coronary disease.

Coronary angiograms were read by a board certified interventional cardiologist (JMS) who was blinded to the results of the MPI study. Presence of obstructive epicardial CAD was defined as $\geq$70% luminal narrowing. The presence of coronary stents, myocardial bridges, collateral vessels, and coronary anomalies was also noted.

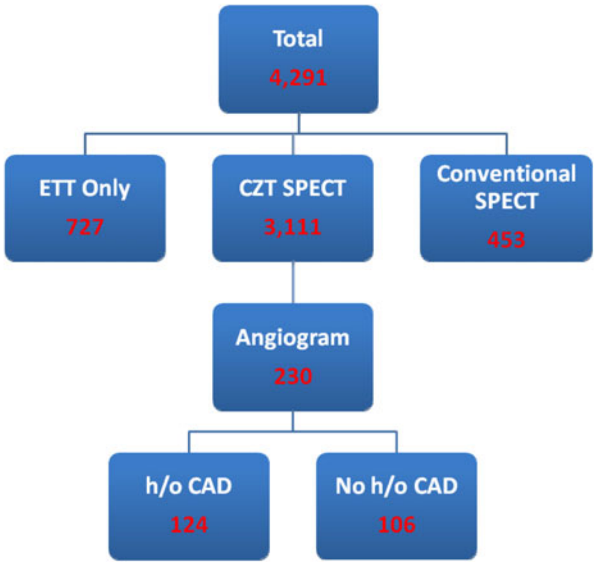

Figure 1. Flow diagram of patient testing over the 12-month period.

Normalcy rate was determined in a group of patients with a pre-test likelihood of disease of <5% based on the ACC/AHA scoring system including those who did not undergo coronary angiography.

Statistics

Continuous variables are presented as mean ± SD. Comparisons among continuous variables were done using two-tailed Student's *t*-tests. Chi-squared tests or Fisher's exact tests for smaller sample sizes were used for comparing categorical variables. A *P*-value of <.05 was considered significant. Statistical analysis was performed using GraphPad Instat 3.1, Prism 5.0, and SPSS 19.

RESULTS

Demographics

A total of 4,291 patients presented to the Mount Sinai Non-Invasive Cardiology Laboratory over this

Table 1. Patient demographics

	Entire cohort N = 4291	Angiogram cohort N = 230	*P*-value
Age (years)	62.1 ± 13.6	64.2 ± 11.0	.02
Gender			<.0001
Male	2183 (50.9%)	158 (68.7%)	
Female	2108 (49.1%)	72 (31.3%)	
BMI (kg/m^2)	28.7 ± 6.9	27.9 ± 5.0	.08
Cardiac risk factors			
Diabetes	1213 (28.3%)	91 (39.6%)	.0003
Hyperlipidemia	2628 (61.2%)	186 (80.9%)	<.0001
Hypertension	2927 (68.2%)	185 (80.4%)	.0001
Smoking[#]	2141 (49.9%)	121 (52.6%)	.46
Family h/o CAD	547 (12.7%)	43 (18.7%)	.01
Known CAD			
Documented CAD	1285 (29.9%)	122 (53.0%)	<.0001
PCI	950 (22.1%)	113 (49.1%)	<.0001
CABG	322 (7.5%)	N/A	
Presenting symptoms			
Chest pain	2842 (66.2%)	170 (73.9%)	.02
Shortness of breath	2756 (64.2%)	159 (69.1%)	.15
ACC/AHA risk			
High	286 (6.7%)	47 (20.4%)	<.0001
Intermediate	3016 (70.3%)	151 (65.7%)	.15
Low	832 (19.4%)	31 (13.5%)	.03
Very low	157 (3.7%)	1 (0.4%)	.02

[#] Any smoking, past or present.
CAD, Coronary artery disease; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass grafting.

1-year period with 3,111 undergoing stress MPI on the CZT camera (Figure 1). A total of 230 patients without a history of CABG surgery subsequently underwent invasive coronary angiography within a 2-month period, 124 of which had documented CAD and 106 had no known history of CAD.

The characteristics of the patients from the entire year and who underwent angiography are found in Table 1. In the angiogram cohort, the mean age was 64.2 ± 11.0 years old with a majority (69%) being male and an average BMI of 27.9 ± 5.0 kg/m^2. The majority (86%) of patients was intermediate or high ACC/AHA pre-test risk and there was a higher proportion of patients with cardiac risk factors and CAD in the angiogram cohort as expected. Table 2 describes the MPI characteristics of the cohort with approximately three-fourths using Tc-99m and one-fourth employing Tl-201. More patients underwent exercise stress (60%) than pharmacologic stress (40%). In the overall cohort, 69.8% had normal perfusion which shrank to 15.7% in the angiogram group, and the average EF was 62% compared to 56% in the angiogram group.

Angiogram Results

Out of all of the patients who underwent stress MPI with a CZT camera during the year time period and did not have a history of CABG, 7.4% subsequently underwent invasive coronary angiography within 2 months of their MPI based on clinical decisions. Patients had their angiograms on average 13.1 days (standard deviation 16.2 days) after their stress MPI. Coronary angiography was normal in 12% of patients, non-obstructive CAD was diagnosed in 33%, and obstructive CAD in 55% of the patients (Table 3). Most patients with coronary disease had single vessel disease,

Table 2. Stress MPI characteristics

	Entire cohort N = 4291	Angiogram cohort N = 230	*P*-value
Isotope			
Tc-99m	2585 (60.2%)	175 (76.1%)	<.0001
Tl-201	979 (22.8%)	55 (23.9%)	.76
ETT only	727 (16.9%)	N/A	
Stress protocol			
Stress-only	1945 (54.6%)	43 (18.7%)	<.0001
Rest-stress	1217 (34.1%)	120 (52.2%)	<.0001
Stress-rest	402 (11.3%)	67 (29.1%)	<.0001
Isotope dose (mCi)			
Tl-201	3.2 ± 0.5	3.1 ± 0.4	.003
Tc-99m stress-only	20.1 ± 9.3	19.0 ± 8.7	.08
Tc-99m full study	38.1 ± 9.4	39.9 ± 9.1	.005
Stressor			
Exercise	2513 (58.6%)	138 (60.0%)	.72
Bruce	1563 (60.5%)	92 (62.6%)	.30
Modified Bruce	455 (17.6%)	24 (16.3%)	.94
Manual	567 (21.9%)	31 (21.1%)	.99
Pharmacologic	1778 (41.4%)	92 (40.0%)	.72
Adenosine	349 (19.6%)	20 (21.7%)	.86
Dipyridamole	1050 (59.1%)	48 (52.2%)	.25
Dobutamine	17 (1.0%)	1 (1.1%)	.93
Regadenoson	362 (20.4%)	23 (25.0%)	.48
MPI results			
Perfusion results			
Normal	2486 (69.8%)	36 (15.7%)	<.0001
Abnormal	1074 (30.1%)	194 (84.3%)	<.0001
EF (%)	62% ± 14%	56% ± 14%	<.0001

Tc-99m, Technitium-99; *Tl-201*, Thallium-201; *ETT*, exercise treadmill test; *mCi*, millicurie.

Table 3. Results of invasive coronary angiography

Angiogram characteristic	Patients undergoing angiography	
	All patients N = 230	No known CAD N = 106
Stenosis		
Normal	27 (11.8%)	23 (21.7%)
Stenosis < 70%	76 (33.0%)	37 (34.9%)
Stenosis ≥ 70%	127 (55.2%)	46 (43.4%)
Any coronary artery stenosis		
Left Main	6 (2.6%)	3 (2.8%)
LAD	191 (83.0%)	73 (68.9%)
LCx	162 (70.4%)	62 (58.5%)
RCA	173 (75.2%)	65 (61.3%)
None	27 (11.8%)	23 (21.7%)
Number of vessels ≥ 70%		
0 Vessel disease	103 (44.8%)	60 (56.6%)
1 Vessel disease	75 (32.6%)	24 (22.6%)
2 Vessel disease	34 (14.8%)	12 (11.3%)
3 Vessel disease	18 (7.8%)	10 (9.4%)

LAD, Left anterior descending artery; *LCx*, left circumflex artery; *RCA*, right coronary artery.

and in those patients with no previously known CAD, most patients had non-obstructive CAD or a normal coronary angiogram.

Normalcy Rate

A total of 65 patients had very low (<5%) pre-test risk of CAD and their characteristics can be seen in Table 4. Once patients with abnormal left ventricular function were excluded, 62 remained. Two out of the sixty-two had a summed stress score of >3, resulting in a normalcy rate of 96.8%. These two patients were both women aged 50 and 59-years-old without symptoms of chest pain or shortness of breath. Both were inpatients undergoing the test with pharmacologic stress for preoperative screening for non-cardiac surgery. Both had type II diabetes, hypertension, and hyperlipidemia and they both had a total stress perfusion deficit of 14%.

Comparison to Angiography

In the entire cohort of patients who underwent an invasive angiogram over this 1-year period, the sensitivity of CZT SPECT for detecting obstructive CAD was 94.5% and the specificity was 36.9% (Table 5). When patients with previous diagnosis of CAD, those with abnormal left ventricular function (left ventricular EF <50%), and those with conduction abnormalities (left bundle branch block and paced ventricular rhythm) were excluded, sensitivity remained high at 91.7% and specificity increased to 55.6%.

We next performed an ROC curve analysis using the total perfusion deficit calculated from the quantitative assessment of perfusion in patients with no known coronary disease, normal left ventricular function, and no conduction abnormalities (left bundle branch block and paced ventricular rhythms) (Figure 2). The area under the curve for all the patients was 0.699 (0.631-0.767, 95% CI) which improved to 0.720 (0.647-0.792, 95% CI) when combined supine and prone imaging was used. The area under the curve further improved to 0.769 (0.664-0.874, 95% CI) and 0.816 (0.716-0.916, 95% CI) when only patients with no known CAD, normal left ventricular function, and no conduction abnormalities (no left bundle branch block or paced ventricular rhythm) were analyzed with and without prone imaging. A per vessel analysis in all-comers did not reveal any marked differences in the test characteristics based on individual coronary arteries (Figure 3).

Test characteristics for the CZT camera were also evaluated based on various patients and test characteristics such as isotope (Tc-99m vs Tl-201), stressor (exercise vs pharmacologic), BMI (obese vs non-obese), presence of known CAD, and left ventricular function (normal or abnormal) (Table 6). Tl-201 demonstrated higher sensitivity but lower specificity than Tc-99m. The

Table 4. Characteristics of patients with a very low (<5%) risk of CAD used to calculate the normalcy rate

	Very low pre-test risk of CAD N = 62
Age (years)	44.2 ± 11.6
Gender	
Male	8 (12.9%)
Female	54 (87.1%)
BMI (kg/m^2)	27.3 ± 7.2
Cardiac risk factors	
Diabetes	16 (25.8%)
Hyperlipidemia	22 (35.5%)
Hypertension	31 (50.0%)
Smoking#	28 (45.2%)
Family h/o CAD	7 (11.3%)
Presenting symptoms	
Chest pain	9 (14.5%)
Shortness of breath	11 (17.7%)
Isotope	
Tc-99m	46 (74.2%)
Tl-201	16 (25.8%)
Stress protocol	
Stress-only	56 (90.3%)
Rest-stress	6 (9.7%)
Stress-rest	0 (0%)
Isotope dose (mCi)	
Tl-201	3.0 ± 0.7
Tc-99m stress-only	18.4 ± 8.6
Tc-99m full study	26.9 ± 10.5
Stressor	
Exercise	31 (50.0%)
Pharmacologic	31 (50.0%)

Any smoking, past or present.

use of stressor did not result in pronounced differences in sensitivity or specificity while sensitivity was lower in obese patients. Known CAD and abnormal left ventricular function both resulted in lower specificity.

Next, we explored the differences in patient characteristics and MPI results between true positive and false positive patients in those with no known CAD, normal left ventricular function, and no conduction abnormalities (no left bundle branch block or paced ventricular rhythm). The summed stress scores of true positives and false positives as well as the scores of true negatives and false negatives were found not to be statistically different (Figure 4). Demographic characteristics of patients with true positives and false positives were compared in Table 7, and except for a greater proportion of hypertension in the true positive group than in the false positive group, the two groups were similar.

Table 5. Comparison of CZT SPECT MPI to coronary angiography in the detection of obstructive (≥70%) epicardial CAD in all-comers and in the usual select population of no known coronary disease, normal left ventricular function, and no conduction abnormalities (left bundle branch block and paced ventricular rhythms)

All patients N = 230	
Sensitivity (%)	94.5
Specificity (%)	36.9
(+) Predictive value (%)	64.9
(−) Predictive value (%)	84.4
Accuracy (%)	68.7
No known CAD, NL EF, NL conduction N = 82	
Sensitivity (%)	91.7
Specificity (%)	55.6
(+) Predictive value (%)	62.3
(−) Predictive value (%)	89.3
Accuracy (%)	71.6

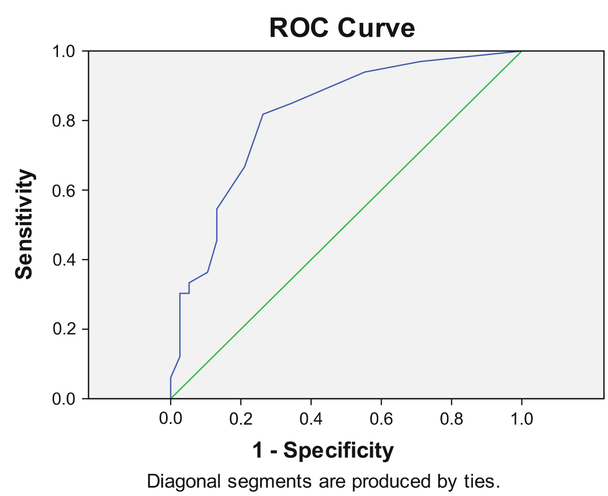

Figure 2. ROC curve derived from combined supine and prone summed stress score from patients with no known coronary disease, normal left ventricular function, and no conduction abnormalities (left bundle branch block and paced ventricular rhythms).

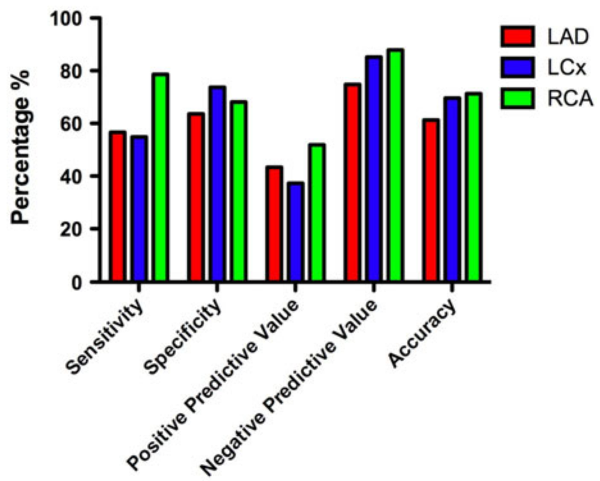

Figure 3. Per vessel analysis of CZT SPECT MPI's ability to diagnose obstructive (≥70% stenosis) epicardial CAD.

DISCUSSION

In this so far largest correlation study, to our knowledge, between invasive coronary angiography and high efficiency CZT SPECT imaging, a high sensitivity and accuracy for detecting obstructive epicardial CAD was found for this new SPECT camera technology. Previous studies have shown that CZT image quality was superior to conventional SPECT,[15] diagnostic accuracy was non-inferior to conventional SPECT while imaging time was decreased,[4-6] and isotope dose can be reduced below conventional amounts.[8] In this study, the sensitivity for the detection of a ≥70% epicardial stenosis was >90% in consecutive patients in routine clinical practice which included patients with suspected CAD, known CAD, post-PCI patients, obese patients, those with normal and abnormal left ventricular function, and conduction abnormalities. The results were similar for both tracers (Tc-99m and Tl-201) and all stressors (exercise and vasodilators). The normalcy rate in low-risk patients (pre-test likelihood of disease of <5%) was excellent at 97%.

The reported specificity of stress SPECT MPI in this study and in previous ones using conventional SPECT is relatively low from 53 to 100%.[16,17] A ''referral bias'' in which SPECT MPI has become a gatekeeper for the cardiac catheterization laboratory explains this relative lack of specificity.[16] In routine clinical practice, as examined in this study, patients with normal myocardial perfusion are usually not referred for angiography and, therefore, the occasional patient who has normal coronary arteries on angiography is almost always referred because of abnormal perfusion imaging. When only a subsample of patients initially tested subsequently receives the definitive assessment, a number of selection biases come into play including ''work-up bias'' and ''verification bias.''[18] Because sensitivity and specificity vary widely as a consequence of selection bias, the accuracy of a test will vary based on the population in which it was determined.[19] Because of this referral bias, the true specificity of clinical SPECT MPI is impossible to assess, and normalcy rate has been used instead as a surrogate. The reported normalcy rate ranges from 85% for Tl-201 to 95-100% for Tc-99m SPECT MPI,[16] and this study found a normalcy rate of 97% in this clinical cohort. Lower specificity in this study may also be due to a lower prevalence of obstructive disease in the cohort (55%) and lack of robust attenuation correction.

In comparison to conventional SPECT, sensitivity was similar and specificity was inferior than that of CZT SPECT. During the calendar year of 2008, all patients at our institution were imaged on a conventional SPECT camera (Vertex Plus with Vantage Pro, Philips/ADAC Laboratories) as we did not yet have a CZT camera, so we examined all patients who underwent SPECT MPI over this 1-year period. Out of the 3,443 patients who had a SPECT MPI, 260 patients without a history of CABG underwent an invasive coronary angiogram within 2 months of the MPI (the same inclusion criteria as the CZT cohort). Sensitivity was 90.3%, specificity was 23.2%, while the positive predictive value was 67.1%, negative predictive value 57.9%, and overall accuracy was 65.8%. We also performed the analysis in the subgroup (N = 107) with no known CAD, normal left ventricular function, and no conduction abnormalities with little change in the sensitivity (86.5%) and the specificity (23.6%). These data would suggest that the selection bias in routine clinical practice results in lower specificities than the populations studied in clinical trials of MPI.[20]

There has been one other published study on the correlation of high efficiency CZT SPECT MPI and coronary angiography.[9] The camera system studied was the D-SPECT which uses CZT solid-state detector columns with wide-angle tungsten collimators. This study included 56 patients, of those 34 (61%) had obstructive CAD (≥70% stenosis), and 22 (39%) had non-obstructive (<70% stenosis) CAD. All of the included patients underwent invasive coronary angiography within 6 months of their CZT SPECT MPI. Using an automated quantification method and analyzing upright, supine, and combined images, sensitivity ranged from 88% to 94% and specificity ranged from 59% to 86%. Patients with known CAD, cardiomyopathy, valvular heart disease, or change in symptoms between their MPI and angiogram were excluded.

Whether invasive coronary angiography alone is the true ''gold standard'' for the diagnosis of physiologically significant CAD remains debatable. In this study,

Table 6. Test characteristics of CZT SPECT MPI compared to coronary angiography for the detection of obstructive (≥70%) CAD in select patient subgroups

	All patients N = 230	Tc-99m N = 175	TL-201 N = 55
Sensitivity (%)	94.5	92.6	100
Specificity (%)	36.9	39.5	27.3
(+) Predictive value (%)	64.9	64.0	67.3
(−) Predictive value (%)	84.4	82.1	100
Accuracy (%)	68.7	68.0	70.9
	All patients N = 230	**Exercise N = 138**	**Pharmacologic N = 92**
Sensitivity (%)	94.5	96.0	92.3
Specificity (%)	36.9	34.9	40.0
(+) Predictive value (%)	64.9	63.7	66.7
(−) Predictive value (%)	84.4	88.0	80.0
Accuracy (%)	68.7	68.1	69.6
	All patients N = 230	**BMI < 30 N = 148**	**BMI ≥ 30 N = 82**
Sensitivity (%)	94.5	96.6	89.5
Specificity (%)	36.9	35.6	38.6
(+) Predictive value (%)	64.9	69.4	55.7
(−) Predictive value (%)	84.4	87.5	81.0
Accuracy (%)	68.7	72.3	62.2
	All patients N = 230	**No known CAD N = 106**	**Known CAD N = 124**
Sensitivity (%)	94.5	93.5	95.1
Specificity (%)	36.9	48.3	20.9
(+) Predictive value (%)	64.9	58.1	69.4
(−) Predictive value (%)	84.4	90.6	69.2
Accuracy (%)	68.7	67.9	69.4
	All patients N = 230	**EF < 50% N = 62**	**EF ≥ 50% N = 168**
Sensitivity (%)	94.5	100	92.1
Specificity (%)	36.9	16.7	43.0
(+) Predictive value (%)	64.9	65.5	64.6
(−) Predictive value (%)	84.4	100	82.9
Accuracy (%)	68.7	67.7	69.0

specificity was markedly decreased in patients with previous PCI due to higher numbers of ''false positive'' perfusion results. The obvious cause of false positive perfusion results would be previous infarction which occurred either prior to or in the setting of PCI which opened the culprit vessel, resulting in a patent vessel on subsequent angiography. This group of patients also has advanced CAD, decreased coronary flow reserve, endothelial dysfunction, and likely small vessel disease. Thus, perfusion defects on MPI may also reflect non-uniform hyperemic coronary flow better than the results of a conventional contrast ''luminogram.'' It is quite possible that invasive coronary angiography underestimates physiologically significant disease, rather than

Table 7. True positives versus false positives in patients with no known coronary disease, normal left ventricular function, and no left bundle branch block or paced rhythm

	True positive N = 33	False positive N = 20	*P*-value
Age (years)	65.2 ± 9.7	62.0 ± 12.0	.29
Gender			
Male	22 (66.7%)	12 (60.0%)	.77
Female	11 (33.3%)	8 (40.0%)	
BMI (kg/m^2)	26.5 ± 4.3	29.3 ± 6.4	.06
Cardiac risk factors			
Diabetes	11 (33.3%)	5 (25.0%)	.76
Hyperlipidemia	26 (78.8%)	13 (65.0%)	.34
Hypertension	30 (90.9%)	10 (50.0%)	.002
Smoking	16 (48.5%)	9 (45.0%)	1.0
Family h/o CAD	10 (30.3%)	3 (15.0%)	.33
ACC/AHA risk			
High	7 (21.2%)	3 (15.0%)	.72
Intermediate	24 (72.7%)	15 (75.0%)	1.0
Low	1 (3.0%)	2 (10.0%)	.55
Very low	1 (3.0%)	0 (0%)	1.0
Isotope			.76
Tc-99m	23 (69.7%)	15 (75.0%)	
Tl-201	10 (30.3%)	5 (25.0%)	
Stressor			1.0
Exercise	22 (66.7%)	14 (70.0%)	
Pharmacologic	11 (33.3%)	6 (30.0%)	
Stress protocol			.73
Stress-only	6 (18.2%)	5 (25.0%)	
Rest-stress	12 (36.4%)	8 (40.0%)	1.0
Stress-rest	15 (45.5%)	7 (35.0%)	.57

Tc-99m, Technitium; *Tl-201*, Thallium.

MPI falsely diagnosing non-uniform coronary flow reserve. It is likely that the true ''gold standard'' involves a combination of both anatomy and physiology which hybrid MPI-CTA shows promise in being able to provide.[21]

LIMITATIONS

The study is limited by the single site clinical experience. The use of an entire year's worth of unselected clinical patients would, however, make the results more generally applicable. Coronary angiograms were performed for clinical indications on select patients and not uniformly on all patients. While performing angiograms on all patients undergoing MPI may have been possible in the past, the use of stress MPI as a clinical ''gatekeeper'' to the catheterization lab means that most patients referred for angiography have abnormal myocardial perfusion. This ''referral bias'' results in a selection bias for the determination of true sensitivity and specificity, but does reflect actual clinical practice. Another possible contributing factor to lower specificity is the absence of reliable attenuation correction. Correlation between MPI with a CZT camera with CT attenuation correction and coronary angiography is not yet available.

CONCLUSION

In this unselected group of patients over a 1-year-period of time, high efficiency CZT SPECT imaging demonstrated a high sensitivity and accuracy for detecting obstructive epicardial CAD with a greatly reduced imaging time. Because of the referral bias to invasive angiography, the true specificity of clinical SPECT MPI was not possible to accurately assess in this

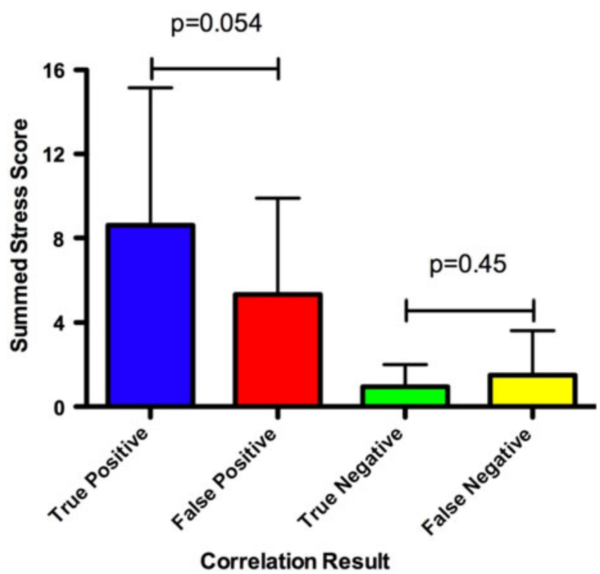

Figure 4. Comparison of summed stress scores in patients with no known coronary disease, normal left ventricular function, and no conduction abnormalities (left bundle branch block and paced ventricular rhythms) based on the correlation between CZT SPECT MPI and coronary angiography based on combined supine and prone scores.

cohort. The normalcy rate was very good (97%) and has been used as a surrogate for specificity.

References

1. Garcia EV, Faber TL, Esteves FP. Cardiac dedicated ultrafast SPECT cameras: New designs and clinical implications. J Nucl Med 2011;52:210-7.
2. Slomka PJ, Patton JA, Berman DS, Germano G. Advances in technical aspects of myocardial perfusion SPECT imaging. J Nucl Cardiol 2009;16:255-76.
3. Sharir T, Ben-Haim S, Merzon K, Prochorov V, Dickman D, Berman DS. High-speed myocardial perfusion imaging initial clinical comparison with conventional dual detector anger camera imaging. JACC Cardiovasc Imaging 2008;1:156-63.
4. Sharir T, Slomka PJ, Hayes SW, 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.
5. Esteves FP, Raggi P, Folks RD, Keidar Z, Askew JW, Rispler S, et al. Novel solid-state-detector dedicated cardiac camera for fast myocardial perfusion imaging: Multicenter comparison with standard dual detector cameras. J Nucl Cardiol 2009;16:927-34.
6. Buechel RR, Herzog BA, Husmann L, Burger IA, Pazhenkottil AP, Treyer V, et al. Ultrafast nuclear myocardial perfusion imaging on a new gamma camera with semiconductor detector technique: First clinical validation. Eur J Nucl Med Mol Imaging 2010;37:773-8.
7. Herzog BA, Buechel RR, Katz R, Brueckner M, Husmann L, Burger IA, et al. Nuclear myocardial perfusion imaging with a cadmium-zinc-telluride detector technique: Optimized protocol for scan time reduction. J Nucl Med 2010;51:46-51.
8. Duvall WL, Croft LB, Ginsberg ES, Einstein AJ, Guma KA, George T et al. Reduced isotope dose and imaging time with a high-efficiency CZT SPECT camera. J Nucl Cardiol 2011. doi:10.1007/s12350-011-9379-7.
9. Nakazato R, Tamarappoo BK, Kang X, Wolak A, Kite F, Hayes SW, et al. Quantitative upright-supine high-speed SPECT myocardial perfusion imaging for detection of coronary artery disease: Correlation with invasive coronary angiography. J Nucl Med 2010;51:1724-31.
10. Hansen CL, Goldstein RA, Berman DS, Churchwell KB, Cooke CD, Corbett JR, et al. Myocardial perfusion and function single photon emission computed tomography. J Nucl Cardiol 2006;13:e97-120.
11. Henzlova MJ, Cerqueira MD, Hansen CL, Taillefer R, Yao SS. ASNC announcement. J Nucl Cardiol. 2009;16:331.
12. Henzlova MJ, Cerqueira MD, Mahmarian JJ, Yao SS. Stress protocols and tracers. J Nucl Cardiol 2006;13:e80-90.
13. Hendel RC, Berman DS, DiCarli MF, Heidenreich PA, Henkin RE, Pellikka PA, et al. ACCF/ASNC/ACR/AHA/ASE/SCCT/SCMR/SNM 2009 appropriate use criteria for cardiac radionuclide imaging: A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the American Society of Nuclear Cardiology, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the Society of Cardiovascular Computed Tomography, the Society for Cardiovascular Magnetic Resonance, and the Society of Nuclear Medicine. Circulation 2009;119:e561-87.
14. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. J Nucl Cardiol 2002;9:240-5.
15. Duvall WL, Croft LB, Godiwala T, Ginsberg E, George T, Henzlova MJ. Reduced isotope dose with rapid SPECT MPI imaging: Initial experience with a CZT SPECT camera. J Nucl Cardiol 2010;17:1009-14.
16. Udelson JE, Dilsizian V, Bonow RO. Chapter 16—nuclear cardiology. In: Libby P, Bonow RO, Mann DL, Zipes DP, editors. Braunwald's heart disease: A textbook of cardiovascular medicine. Philadelphia, PA: WB Saunders; 2008.
17. Klocke FJ, Baird MG, Lorell BH, Bateman TM, Messer JV, Berman DS, et al. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging–executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging). Circulation 2003;108:1404-18.
18. Begg CB, Greenes RA. Assessment of diagnostic tests when disease verification is subject to selection bias. Biometrics 1983;39:207-15.
19. Diamond GA. Reverend Bayes' silent majority. An alternative factor affecting sensitivity and specificity of exercise electrocardiography. Am J Cardiol 1986;57:1175-80.
20. Diamond GA. Affirmative actions: Can the discriminant accuracy of a test be determined in the face of selection bias? Med Decis Making 1991;11:48-56.
21. Herzog BA, Husmann L, Buechel RR, Pazhenkottil AP, Burger IA, Valenta I et al. Rapid cardiac hybrid imaging with minimized radiation dose for accurate non-invasive assessment of ischemic coronary artery disease. Int J Cardiol 2010. doi:10.1016/j.ijcard.2010.08.023.