Published in final edited form as:

J Nucl Cardiol. 2013 October ; 20(5): . doi:10.1007/s12350-013-9735-x.

High-Efficiency SPECT MPI: Comparison of Automated Quantification, Visual Interpretation, and Coronary Angiography

W. Lane Duvall, MD*, Piotr J. Slomka, PhD†, Jim R. Gerlach, CNMT†, Joseph M. Sweeny, MD*, Usman Baber, MD*, Lori B. Croft, MD*, Krista A. Guma, CNMT*, Titus George, CNMT*, and Milena J. Henzlova, MD*

*Mount Sinai Medical Center, Mount Sinai Division of Cardiology (Mount Sinai Heart)

†Cedars-Sinai Medical Center, Artificial Intelligence in Medicine Program

Abstract

Background—Recently introduced high-efficiency (HE) SPECT cameras with solid-state CZT detectors have been shown to decrease imaging time and reduce radiation exposure to patients. An automated, computer derived quantification of HE MPI has been shown to correlate well with coronary angiography on one HE SPECT camera system (D-SPECT), but has not been compared to visual interpretation on any of the HE SPECT platforms.

Methods—Patients undergoing a clinically indicated Tc-99m sestamibi HE SPECT (GE Discovery 530c with supine and prone imaging) study over a one year period followed by a coronary angiogram within 2 months were included. Only patients with a history of CABG surgery were excluded. Both MPI studies and coronary angiograms were reinterpreted by blinded readers. One hundred and twenty two very low (risk of CAD < 5%) or low (risk of CAD < 10%) likelihood subjects with normal myocardial perfusion were used to create normal reference limits. Computer derived quantification of the total perfusion deficit (TPD) at stress and rest was obtained with QPS software. The visual and automated MPI quantification were compared to coronary angiography (70% luminal stenosis) by receiver operating curve (ROC) analysis.

Results—Of the 3,111 patients who underwent HE SPECT over a one year period, 160 patients qualified for the correlation study (66% male, 52% with a history of CAD). The ROC area under the curve (AUC) was similar for both the automated and visual interpretations using both supine only and combined supine and prone images (0.69-0.74). Using thresholds determined from sensitivity and specificity curves, the automated reads showed higher specificity (59-67% versus 27-60%) and lower sensitivity (71-72% versus 79-93%) than the visual reads. By including prone images sensitivity decreased slightly but specificity increased for both. By excluding patients with known CAD and cardiomyopathies, AUC and specificity increased for both techniques (0.72-0.82). The use of a difference score to evaluate ischemic burden resulted in lower sensitivities but higher specificities for both automated and visual quantification. There was good agreement between the visual interpretation and automated quantification in the entire cohort of 160 unselected consecutive patients ($r = 0.70-0.81$, $p < 0.0001$).

Conclusions—Automated and visual quantification of high-efficiency SPECT MPI with the GE Discovery camera provide similar overall diagnostic accuracy when compared to coronary angiography. There was good correlation between the two methods of assessment. Combined supine and prone stress imaging provided the best diagnostic accuracy.

Address for Correspondence: W. Lane Duvall, MD Mount Sinai Medical Center, Box 1030 One Gustave L Levy Place New York, NY 10029 Telephone: (212) 241-7054 Fax: (212) 426-6376 william.duvall@mountsinai.org.

Addendum: The patients analyzed in the current study were also included in an earlier study which correlated CZT SPECT MPI to coronary angiography irrespective of tracer (Tc-99m or Tl-201).(21)

Keywords

CZT SPECT MPI; High-Efficiency SPECT MPI; Automated Quantification; Coronary Angiography

Introduction

Recently introduced high efficiency Cadmium Zinc Telluride (CZT) camera systems with novel collimation methods have helped overcome historical limitations of myocardial perfusion imaging (MPI) by significantly shortening image acquisition times and reducing administered activity.(1) In parallel, methods for automated, quantification of MPI studies have been developed to modernize and improve the reliability and reproducibility of MPI.(2) These techniques have been studied in recent years demonstrating reproducibility,(3) favorable comparison to visual interpretation,(2, 4) good correlation with coronary angiography,(5-8) and the ability to predict cardiac events.(9)

The two commercially available CZT SPECT cameras, D-SPECT (Spectrum Dynamics, Caesarea, Israel) and Discovery NM 530c (GE Healthcare, Haifa, Israel),(10) have been validated by comparison to conventional SPECT using standard radiopharmaceutical activity (11-17) as well as lower administered activity.(18-20) There have now been four published studies correlating conventional administered activity CZT SPECT MPI to invasive coronary angiography,(5, 16, 21, 22) and two studies addressing the accuracy of low administered activity CZT SPECT MPI.(23, 24) One of these compared automated computer analysis to coronary angiography with good results and is the only implementation of automated quantification applied to CZT SPECT (D-SPECT camera) to date.(5) However, to date no study has examined the automated quantification of data from the GE Discovery camera, which has a unique collimation and reconstruction system based on multipinhole design.

The objective of this study was to evaluate the applicability of the automated perfusion analysis based on normal limits to this new type of device and examine the agreement of automated assessment of CZT SPECT MPI with standard visual interpretation and invasive coronary angiography in an unselected clinical population. Furthermore, we sought to evaluate the value of combined supine-prone automated and visual analysis for this new device.(4, 6)

Methods

Study Design

In a study protocol approved by our institutional IRB, we retrospectively evaluated all 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 SPECT MPI stress test using a CZT camera (GE Discovery NM 530c).(1, 13) Patients who then underwent an invasive coronary angiogram within 2 months after the MPI were identified. Patients with a history of coronary artery bypass grafting (CABG) surgery were excluded. A subset of patients without known coronary artery disease (CAD), without a history of percutaneous coronary intervention (PCI), and without decreased left ventricular function (EF < 50%) was also analyzed.

Imaging and Stress Protocol

Standard imaging protocols as endorsed by the American Society of Nuclear Cardiology (ASNC) were used for all patients.(25) 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, rest imaging was not performed. The lower radiopharmaceutical dose imaging time was 5 minutes and the higher radiopharmaceutical dose imaging time was 3 minutes. Image acquisition began 30-60 minutes after tracer injection. All supine stress images were gated. Post stress left ventricular ejection fraction (EF) was determined using commercial software (QGS, Cedars-Sinai, Los Angeles, CA). Both supine stress images were acquired in all patients and prone stress images acquired when physically possible for the patient to do so. Prone imaging time was the same as the supine imaging time (3 or 5 minutes) but gating was not performed. Rest images were acquired in the supine position.

Standard exercise and pharmacologic protocols as endorsed by ASNC were used for all patients.(26, 27)

Radiopharmaceutical activity was weight based and dependent on the protocol performed. For a standard one day rest-stress Tc-99m protocol, the rest administered activity was 185-370 MBq (5-10 mCi) based on three weight groups (<200 lbs, 200-250 lbs, >250 lbs) and the stress administered activity was 555-1110 MBq (15-30 mCi) based on the same weight ranges. The stress-first Tc-99m protocol employed a low stress administered activity of 462.5 MBq (12.5 mCi) if the weight was <200 lbs and 925-1110 MBq (25-30 mCi) if the weight was >200 lbs. If needed the rest administered activity for a one day stress-rest Tc-99m protocol was 925-1110 MBq (25-30 mCi) if the weight was <200 lbs and became a two day stress rest Tc-99m protocol if the weight was >200 lbs with a rest administered activity of 925-1110 MBq (25-30 mCi).

End Points

Patient demographics, stress test variables and administered activity was prospectively collected at the time of stress testing in the Nuclear Cardiology Database. Pretest risk of coronary disease was based on the ACC/AHA scoring system which utilizes age, gender, and presenting symptom.(28) Chest pain and shortness of breath were both considered anginal equivalents for the purposes of the scoring system.

Visual Analysis—MPI studies were read by consensus opinion by two board certified nuclear cardiologists (WLD, LBC, or 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 five-point scale (0 = normal, 1 = mild, 2 = moderate, 3 = severe, 4 = absent).(29) A combined stress score was also calculated from the aggregate supine and prone reads. In this process, perfusion defects present in the stress prone images which were not present in the stress supine images (and vice versa) were routinely considered to be artifactual. The visual percent of abnormal myocardium was calculated by dividing the summed rest or stress score by 68 and multiplying by 100.(12) Gated SPECT images, left ventricular volumes, and ejection fraction were available during the visual assessment of myocardial perfusion.

Creation of Normal Limits—For generation of normal limits of perfusion by CZT SPECT using the GE Discovery camera, a group of males and females with very low (< 5%) or low (< 10%) pretest risk of coronary disease and a normal resting ECG who exercised to 85% of their predicted maximal heart rate with a negative ECG response were selected for the normal reference database. Pretest risk of coronary disease was based on the ACC/AHA scoring system.(28) None of the patients used for the creation of normal limits were included in the angiogram cohort. Additionally, as per previous practice in generating normal limits, the patients had normal stress and rest images by visual assessment of supine

and prone images (visual summed score < 3) and normal left ventricular function by gated images.(2)

Quantitative Analysis—Stress supine and prone images were quantified separately using their respective supine and prone normal limits.(2) Rest images were quantified using the rest normal limits. Automatically generated myocardial contours were evaluated by an experienced technologist blinded to all results, and when necessary, contours were adjusted to correspond to the myocardium. The quantitative perfusion endpoint used was the total perfusion deficit (TPD), which reflects a combination of both defect severity and the extent of the defect in one parameter.(2)

It has been previously shown that a higher accuracy can be achieved by combining supine and prone images than with supine images alone for the detection of CAD using conventional SPECT by computing combined TPD (C-TPD).(6) C-TPD is calculated by limiting the TPD computation from the prone polar map to pixels which have been quantified as abnormal on supine images (mean absolute deviation >3.0). The same threshold is subsequently used for prone images but only in locations determined abnormal on supine images. In addition, as previously established in males, defects in the anterior wall on supine images were considered regardless of the prone image findings, and defects in the inferior wall on prone images were considered regardless of the supine findings.(6) The C-TPD parameter is then established for this combined analysis - analogous to the TPD derivation on standard supine images.

All quantitative analysis was performed in batch mode of de-identified data by a technologist blinded to any clinical or angiographic results.

The ischemic burden was determined by calculating the summed difference scores and TPD. For the automated quantification, a supine difference TPD was derived from the supine TPD – the rest TPD while the combined attenuation difference TPD was calculated by subtracting the rest TPD from the combined supine and prone TPD. For the visual quantification, a supine difference score and a combined difference score were calculated in a similar fashion.

Coronary Angiography Analysis—Coronary angiograms were read visually by a board certified interventional cardiologist (JMS) blinded to the results of the MPI study. The presence of obstructive epicardial coronary artery disease was defined as 70% luminal narrowing in the three epicardial vessels (left anterior descending (LAD), left circumflex (LCx), and right coronary (RCA)) and/or 50% stenosis of the left main. The presence of myocardial bridges, collateral vessels, and coronary anomalies was also noted.

Statistics

Continuous variables are presented as mean $\pm$ SD. Comparisons among continuous variables were done using two tailed Student's t-tests. Chi-squared tests were used to compare categorical variables. A p value of <0.05 was considered significant. Receiver operator curves (ROC) curves were generated comparing stress TPD from automated quantification or visual summed stress scores to obstructive coronary disease on angiography. Cutoff values for TPD for the automated quantification, summed stress scores for the visual reads, and difference TPD and scores were determined from the intersection of the sensitivity and specificity curves graphed by quantification value in the entire cohort of patients to maximize both sensitivity and specificity. Sensitivity, specificity, positive and negative predictive values, and accuracy for the prediction of obstructive coronary artery disease were obtained from these curves. Areas under the curve were compared using the Delong Delong Clarke-Person method (Analyse-it 2.2). Sensitivities and specificities were

compared using McNemar's test (Stata 12.1). Agreement between percent abnormal myocardium and TPD was analyzed using linear regression and Pearson's r correlation coefficient (GraphPad Prism 4). Other statistical analysis was performed using GraphPad Instat 3.1 and SPSS 19.

Results

Demographics

A total of 4,291 patients presented to the Mount Sinai Non-Invasive Stress Laboratory for a stress test over this one year period with 3,111 undergoing stress MPI on the CZT camera (Figure 1). A total of 160 patients without a history of CABG surgery subsequently underwent invasive coronary angiography within a 2 month period of their Tc-99m MPI study, and 59 of them had no known history of CAD and normal left ventricular function.

The characteristics of all the patients from the time period and those who underwent angiography are found in Table 1 and 2. In the angiogram cohort, the mean age was 63.6 ± 10.3 years old with a majority (66.3%) being male. The average BMI was 28.3 kg/m^2 and the majority (84%) of patients were intermediate or high ACC/AHA pretest risk and the angiogram cohort was older with a greater proportion of cardiac risk factors. In the overall cohort 69.8% had normal perfusion which decreased to 18.8% in the angiogram group. The angiogram group had fewer stress-only studies and more rest-stress or stress-rest studies as would be expected with the high rate of abnormal perfusion results.

Angiogram Results

One hundred and sixty patients underwent invasive coronary angiography within two months of their Tc-99m CZT SPECT MPI without a history of CABG surgery. Patients had their angiograms on average 13.8 ± 15.5 days after their stress MPI. Coronary angiography was normal in 12% of patients, nonobstructive CAD was diagnosed in 34%, and obstructive CAD in 54% of the patients (Table 3). Single vessel disease was the most common finding in patients with obstructive coronary disease. All three patients with left main stenosis 50% also had obstruction of 70% in at least one of the other three vessels (LAD, LCx, or RCA). Angiogram characteristics of the subgroup of 59 patients who had no known coronary artery disease and normal left ventricular function are also shown in Table 3.

Automated Quantification and Visual Reads

For generation of normal limits of perfusion, stress normal limits employed a group of 30 males and 48 females and rest normal limits used 24 males and 20 females. All subjects had very low (< 5%) or low (< 10%) pretest risk of coronary disease and a normal resting ECG and exercised to 85% of their predicted maximal heart rate with a negative ECG response and normal myocardial perfusion and left ventricular function by gated images. The demographics of these normals can be found in Table 4 and the quantification pattern of supine and prone images can be seen in Figure 2.

The supine only visual reads were compared to automated interpretation in all 160 patients who underwent coronary angiography. The ROC area under the curve (AUC) was similar for both assessment methods at 0.693 for the visual reads and 0.692 for the automated computer reads ($p = 0.96$). The supine images were also compared in the subgroup of 59 patients without known CAD and normal left ventricular function again with similar ROC AUC of 0.740 for the visual reads and 0.717 for the computer analysis ($p = 0.75$).

The combined supine and prone visual reads were compared to automated interpretation in the overall cohort which was reduced to 133 subjects as 27 subjects did not have prone

images to include in the analysis. There was no difference between the visual and automated quantification with an ROC AUC of 0.725 for the visual reads and 0.743 for the automated computer reads ($p = 0.63$). The combined supine and prone images were also compared in the subgroup of 48 patients without known CAD and normal left ventricular function (11 subjects without prone imaging) with an ROC AUC of 0.820 for the visual reads and 0.781 for the computer analysis ($p = 0.56$).

The ROC AUC improved with the addition of prone images to supine images for both visual and automated assessment methods in the angiogram cohort and in those selected patients without known CAD and normal left ventricular function. This was a non-significant trend in improvement moving from supine to supine-prone combined images in the full angiogram ($p = 0.13$) and selected ($p = 0.20$) visual cohorts and in the selected automated patients ($p = 0.32$). However, it reached statistical significance ($p = 0.014$) in the full angiogram cohort with automated quantification.

Thresholds for stress perfusion defects and ischemic burden were determined from analysis of the sensitivity and specificity curves and chosen to maximize both sensitivity and specificity (Table 5). A threshold of a TPD of 4% for the supine computer quantification and 3% for the combined supine and prone automated quantification were used. While a cutoff of a supine stress score > 8 and combined stress score > 4 were derived from the curves, the traditional summed stress score of > 3 was used to define abnormal for visual interpretation. With these thresholds applied to the supine and combined scores, the automated reads showed higher specificity (59-67% versus 27-60%, $p < 0.001$) and lower sensitivity (71-72% versus 79-93%, $p < 0.001$) than the visual reads. By including prone images sensitivity decreased slightly but specificity increased for both techniques ($p = \text{NS}$ comparing automated to visual reads). Automated quantification of supine images resulted in a sensitivity of 72% and specificity of 59% which changed to 71% and 67% with the addition of prone images. Visual interpretation found a sensitivity of 93% and specificity of 27% which changed to 79% and 60% with the addition of prone images. The exclusion of patients with known CAD and abnormal left ventricular function resulted in similar sensitivities but higher specificities for both assessment techniques ($p = \text{NS}$ comparing automated to visual reads).

An ischemic burden threshold of a TPD difference of 3.5% was used for the automated supine difference and 1.5% was used for the automated combined supine and prone difference. A threshold of 4 for the visual supine difference score and 1 for the combined difference score was used for visual quantification. For the automated quantification and visual interpretation of the entire angiogram cohort, the use of a difference score resulted in lower sensitivities but higher specificities (Table 6). The selected cohort with no known CAD and normal left ventricular function had relatively few patients due to lack of rest imaging in all patients making the results difficult to interpret.

There was significant agreement between the visual interpretation and automated quantification in the entire cohort of 160 unselected patients ($p < 0.0001$) (Figure 3). Supine images had an r value of 0.76 which increased to 0.81 when combined supine and prone images were used. Bland-Altman analysis of the entire angiogram cohort using supine-only images found the bias to be -7.1 ± 6.7 and for the combined images the bias was -3.9 ± 5.6 . The selected patients without known CAD and with normal left ventricular function also showed significant correlation ($p < 0.0001$) with r values of 0.70 and 0.78 for supine and combined supine and prone images. Bland-Altman analysis of the selected patients using supine-only images found the bias to be -5.6 ± 6.4 and for the combined images the bias was -2.9 ± 5.4 .

Discussion

This investigation found that automated and visual CZT SPECT MPI quantification provide similar overall diagnostic accuracy based on ROC AUC when compared to coronary angiography. This is the first time that the two methods of quantification have been compared to each other with coronary angiography as the gold standard. The agreement between the automated and visual assessments was high with correlation coefficients of 0.76-0.81. Sensitivity which ranged from 64-93% was higher with visual reads in the entire supine only group ($p < 0.001$) but similar between methods in all other groups. Specificity which ranged from 27-85% improved significantly with the addition of prone imaging and was higher with automated quantification in the entire supine only group ($p < 0.001$) but similar between methods in all other groups. The incorporation of ischemic burden using summed difference scores improved specificity further in both cohorts.

Previous work has shown that CZT image quality was superior to conventional SPECT,(18) diagnostic accuracy was non-inferior to conventional SPECT while imaging time was decreased,(12-14) and radiopharmaceutical activity can be reduced below conventional amounts.(19). There have also been a number of other published papers comparing CZT SPECT MPI to coronary angiography,(21-23, 30) but only one has used automated quantification software.(5) Sensitivity for the detection of obstructive epicardial disease was consistently high (87-95%) and specificity varied from 37-86% depending on subject exclusion criteria, referral bias for coronary angiography, and prevalence of CAD (43-83%) in the studied groups. The use of automated quantification with the D-SPECT camera in a select group of patients without known cardiac disease found excellent sensitivity (88-94%) and good specificity (59-86%) for detecting obstructive epicardial disease (70% stenosis), both of which improved with the combination of upright and supine images for resolving imaging artifacts.(5) In the current study when patients with known CAD and reduced left ventricular function were excluded, the specificity of the automated quantification was similar to that found in the D-SPECT camera while the sensitivity was lower.

This study is the first to demonstrate that blinded visual and automated quantification demonstrate similar overall accuracy based on ROC AUC analysis from comparison to coronary angiography. Previous work has already shown that the prognostic value of automated and visual analysis are similar.(9) Given these findings, it would be reasonable to advocate for the use of automated quantification as an independent validation of clinical reading to “double check” the accuracy of clinical interpretation. Given the strong correlation of the visual and automated quantification of the stress images seen in this study, the use of automated quantification may help facilitate greater use of stress-only protocols. Automated quantification could also be used as an independent standard in clinical trials.

In regards to the GE Discovery 530c CZT SPECT camera, the addition of prone imaging to supine only imaging greatly improved specificity and ROC AUC for both visual and automated analysis to the extent that it should be standard practice. The use of rest images and a difference TPD score also improved specificity as would be expected given rest images ability to identify attenuation artifact. The incorporation of gated data into automated quantification would also be expected to improve specificity further. The GE CZT SPECT camera does not provide a true raw rotating image to provide clues to the reader about attenuation artifacts such as overlying breast tissue or elevated hemi-diaphragms and may therefore be more dependant on attenuation correction with CT attenuation maps or attenuation reduction with prone imaging. This method of resolving artifacts, including attenuation artifacts, has already been shown to be beneficial by automated quantification in conventional and CZT SPECT imaging.(5, 6)

Limitations

The study is limited by the single site clinical experience and relatively small sample size. 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 laboratory means that most patients referred for angiography have abnormal myocardial perfusion. This “referral bias” which results in a selection bias for the determination of true sensitivity and specificity, typically results in decreased specificity. Previous work with this CZT SPECT camera has shown an excellent normalcy rate of 97%. (21) As small changes in the thresholds can greatly affect sensitivity and specificity, more patients may need to be analyzed to define appropriate quantification cutoffs with this new camera system. Different cutoffs may also be chosen if the automated quantification is being done to maximize sensitivity or specificity for a particular patient.

Conclusion

Automated and visual CZT SPECT MPI quantification provide similar overall diagnostic accuracy when compared to coronary angiography. Automated quantification has the potential to support clinical reads by “checking” their results. Furthermore, combined supine-prone stress imaging is needed for best diagnostic accuracy given its ability to greatly increase specificity.

Acknowledgments

This research was supported in part by grant R0HL089765-05 from the National Heart, Lung, and Blood Institute/ National Institutes of Health (NHLBI/NIH). Cedars-Sinai Medical Center receives royalties for the licensure of quantitative perfusion software, a portion of which is distributed to one of the authors (PS) of this manuscript.

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, Nishina H, Berman DS, Akincioglu C, Abidov A, Friedman JD, et al. Automated quantification of myocardial perfusion SPECT using simplified normal limits. *J Nucl Cardiol.* 2005; 12:66–77. [PubMed: 15682367]
3. Xu Y, Hayes S, Ali I, Ruddy TD, Wells RG, Berman DS, et al. Automatic and visual reproducibility of perfusion and function measures for myocardial perfusion SPECT. *J Nucl Cardiol.* 2010; 17:1050–7. [PubMed: 20963537]
4. Slomka PJ, Nishina H, Abidov A, Hayes SW, Friedman JD, Berman DS, et al. Combined quantitative supine-prone myocardial perfusion SPECT improves detection of coronary artery disease and normalcy rates in women. *J Nucl Cardiol.* 2007; 14:44–52. [PubMed: 17276305]
5. 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. [PubMed: 20956478]
6. Nishina H, Slomka PJ, Abidov A, Yoda S, Akincioglu C, Kang X, et al. Combined supine and prone quantitative myocardial perfusion SPECT: method development and clinical validation in patients with no known coronary artery disease. *J Nucl Med.* 2006; 47:51–8.
7. Slomka PJ, Fish MB, Lorenzo S, Nishina H, Gerlach J, Berman DS, et al. Simplified normal limits and automated quantitative assessment for attenuation-corrected myocardial perfusion SPECT. *J Nucl Cardiol.* 2006; 13:642–51.

8. Xu Y, Fish M, Gerlach J, Lemley M, Berman DS, Germano G, et al. Combined quantitative analysis of attenuation corrected and non-corrected myocardial perfusion SPECT: Method development and clinical validation. *J Nucl Cardiol.* 2010; 17:591–9.
9. Xu Y, Nakazato R, Hayes S, Hachamovitch R, Cheng VY, Gransar H, et al. Prognostic value of automated vs visual analysis for adenosine stress myocardial perfusion SPECT in patients without prior coronary artery disease: a case-control study. *J Nucl Cardiol.* 2011; 18:1003–9. quiz 10-4.
10. Slomka PJ, Patton JA, Berman DS, Germano G. Advances in technical aspects of myocardial perfusion SPECT imaging. *J Nucl Cardiol.* 2009; 16:255–76.
11. 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 angler camera imaging. *JACC Cardiovasc Imaging.* 2008; 1:156–63. [PubMed: 19356422]
12. 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. [PubMed: 20430269]
13. 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.
14. 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.
15. 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. [PubMed: 20008999]
16. Gimelli A, Bottai M, Giorgetti A, Genovesi D, Kusch A, Ripoli A, et al. Comparison between ultrafast and standard single-photon emission CT in patients with coronary artery disease: a pilot study. *Circ Cardiovasc Imaging.* 2011; 4:51–8. [PubMed: 21068188]
17. Songy B, Lussato D, Guernou M, Queneau M, Geronazzo R. Comparison of myocardial perfusion imaging using thallium-201 between a new cadmium-zinc-telluride cardiac camera and a conventional SPECT camera. *Clin Nucl Med.* 2011; 36:776–80. [PubMed: 21825848]
18. 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. [PubMed: 21069489]
19. 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 accepted.
20. Nkoulou R, Pazhenkottil AP, Kuest SM, Ghadri JR, Wolfrum M, Husmann L, et al. Semiconductor Detectors Allow Low-Dose-Low-Dose 1-Day SPECT Myocardial Perfusion Imaging. *J Nucl Med.* 2011; 52:1204–9. [PubMed: 21810589]
21. Duvall WL, Sweeny JM, Croft LB, Barghash MH, Kulkarni NK, Guma KA, et al. Comparison of high efficiency CZT SPECT MPI to coronary angiography. *J Nucl Cardiol.* 2011; 18:595–604. [PubMed: 21638154]
22. Fiechter M, Ghadri JR, Kuest SM, Pazhenkottil AP, Wolfrum M, Nkoulou RN, et al. Nuclear myocardial perfusion imaging with a novel cadmium-zinc-telluride detector SPECT/CT device: first validation versus invasive coronary angiography. *Eur J Nucl Med Mol Imaging.* 2011
23. Gimelli A, Bottai M, Genovesi D, Giorgetti A, Di Martino F, Marzullo P. High diagnostic accuracy of low-dose gated-SPECT with solid-state ultrafast detectors: preliminary clinical results. *Eur J Nucl Med Mol Imaging.* 2011
24. Duvall WL, Sweeny JM, Croft LB, Ginsberg E, Guma KA, Henzlova MJ. Reduced stress dose with rapid acquisition CZT SPECT MPI in a non-obese clinical population: Comparison to coronary angiography. *J Nucl Cardiol.* 2011
25. 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. [PubMed: 17174800]

26. Henzlova MJ, Cerqueira MD, Hansen CL, Taillefer R, Yao SS. ASNC Imaging Guidelines for Nuclear Cardiology Procedures: Stress protocols and tracers. *J Nucl Cardiol.* 2009; 16:331.
27. Henzlova MJ, Cerqueira MD, Mahmarian JJ, Yao SS. Stress protocols and tracers. *J Nucl Cardiol.* 2006; 13:e80–90. [PubMed: 17174798]
28. Hendel RC, Berman DS, Di Carli 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. [PubMed: 19451357]
29. 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. [PubMed: 11986572]
30. Duvall WL, Sweeny JM, Croft LB, Ginsberg E, Guma KA, Henzlova MJ. Reduced stress dose with rapid acquisition CZT SPECT MPI in a non-obese clinical population: Comparison to coronary angiography. *J Nucl Cardiol.* 2012; 19:19–27. [PubMed: 22147617]

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

Figure 2. 17-Segment normal average segmental uptake for supine and prone images in low likelihood subjects.

(B)

Figure 3.

Correlation between visual interpretation and automated quantification and Bland-Altman analysis with 95% limits of agreement for (A) supine images and (B) supine and prone images.

Table 1

Patient Demographics.

	Entire Cohort N = 4291	Angiogram Cohort N = 160	P value
Age (yrs)	62.1 ± 13.6	63.6 ± 10.3	0.17
Gender			0.0002
Male	2183 (50.9%)	106 (66.3%)	
Female	2108 (49.1%)	54 (33.8%)	
BMI (kg/m ²)	28.7 ± 6.9	28.3 ± 5.1	0.47
Cardiac Risk Factors			
Diabetes	1213 (28.3%)	63 (39.4%)	0.003
Hyperlipidemia	2628 (61.2%)	126 (78.8%)	<0.0001
Hypertension	2927 (68.2%)	130 (81.3%)	0.0007
Smoking *	2141 (49.9%)	87 (54.4%)	0.3
Family h/o CAD	547 (12.7%)	30 (18.8%)	0.04
Known CAD			
Documented CAD	1285 (29.9%)	83 (51.9%)	<0.0001
PCI	950 (22.1%)	80 (50.0%)	<0.0001
CABG	322 (7.5%)	N/A	-
Presenting Symptoms			
Chest Pain	2842 (66.2%)	120 (75.0%)	0.03
Shortness of Breath	2756 (64.2%)	106 (66.3%)	0.66
ACC/AHA Risk			
High	286 (6.7%)	31 (19.4%)	<0.0001
Intermediate	3016 (70.3%)	104 (65.0%)	0.18
Low	832 (19.4%)	24 (15.0%)	0.2
Very Low	157 (3.7%)	1 (0.6%)	0.07

* Any smoking, past or present

CAD = coronary artery disease

PCI = percutaneous coronary intervention

CABG = coronary artery bypass grafting

Table 2

Stress MPI Characteristics.

	Entire Cohort N = 4291	Angiogram Cohort N = 160	P value
Isotope			
Tc-99m	2585 (60.2%)	160 (100%)	<0.0001
Tl-201	979 (22.8%)	N/A	-
ETT Only	727 (16.9%)	N/A	-
Stress Protocol			
Stress-Only	1945 (54.6%)	35 (21.9%)	<0.0001
Rest-Stress	1217 (34.1%)	107 (66.9%)	<0.0001
Stress-Rest	402 (11.3%)	18 (11.3%)	0.51
Isotope Dose (mCi)			
Tl-201	3.2 ± 0.5	N/A	-
Tc-99m Stress-Only	20.1 ± 9.3	18.4 ± 8.5	0.02
Tc-99m Full Study	38.1 ± 9.4	39.8 ± 9.1	0.02
<i>Stressor</i>			
Exercise	2513 (58.6%)	96 (60.0%)	0.78
Bruce	1563 (60.5%)	66 (64.1%)	0.23
Modified Bruce	455 (17.6%)	16 (15.5%)	0.82
Manual	567 (21.9%)	21 (20.4%)	0.97
Pharmacologic	1778 (41.4%)	64 (40.0%)	0.78
Adenosine	349 (19.6%)	11 (17.2%)	0.75
Dipyridamole	1050 (59.1%)	37 (57.8%)	0.95
Dobutamine	17 (1.0%)	1 (1.6%)	0.63
Regadenoson	362 (20.4%)	15 (23.4%)	0.66
<i>MPI Results</i>			
Perfusion Results			<0.0001
Normal	2486 (69.8%)	30 (18.8%)	
Abnormal	1078 (30.2%)	130 (81.3%)	
Ejection Fraction (%)	62% ± 14%	57% ± 13%	<0.0001

Tc-99m = Technitium-99

Tl-201 = Thallium-201

ETT = Exercise Treadmill Test

mCi = millicurie

Full Study = Rest-Stress or Stress-Rest

Table 3

Results of Invasive Coronary Angiography.

Angiogram Characteristic	All Patients N = 160	No Known CAD or Cardiomyopathy N = 59
<i>Stenosis</i>		
Normal	19 (11.9%)	12 (20.3%)
Stenosis < 70%	54 (33.8%)	22 (37.3%)
Stenosis 70%	87 (54.4%)	25 (42.4%)
Left Main 50%	3 (1.9%)	2 (3.4%)
<i>Any Coronary Artery Stenosis</i>		
Left Main	40 (25.0%)	11 (18.6%)
LAD	52 (32.5%)	42 (71.2%)
LCx	34 (21.3%)	37 (62.7%)
RCA	50 (31.3%)	36 (61.0%)
None	19 (11.9%)	12 (20.3%)
<i>Number of Vessels 70%</i>		
0 Vessel Disease	19 (11.9%)	12 (20.3%)
1 Vessel Disease	50 (31.3%)	13 (22.0%)
2 Vessel Disease	25 (15.6%)	8 (13.6%)
3 Vessel Disease	12 (7.5%)	4 (6.85%)

LAD = Left Anterior Descending Artery

LCx = Left Circumflex Artery

RCA = Right Coronary Artery

Table 4

Demographic profile of the low-risk patients used to generate normal limits.

	<i>Rest</i>		<i>Stress</i>	
	Female Normals N = 20	Male Normals N = 24	Female Normals N = 48	Male Normals N = 30
Age (yrs)	61.4 ± 10.0	51.6 ± 5.5	45.5 ± 10.9	43.3 ± 4.7
Gender				
Male	0 (0%)	24 (100%)	0 (0%)	30 (100%)
Female	20 (100%)	0 (0%)	48 (100%)	0 (0%)
BMI (kg/m ²)	28.0 ± 5.3	28.6 ± 4.5	28.0 ± 8.1	28.4 ± 5.6
Cardiac Risk Factors				
Diabetes	6 (30.0%)	6 (25.0%)	12 (25.0%)	4 (13.3%)
Hyperlipidemia	16 (80.0%)	22 (91.7%)	17 (35.4%)	11 (36.7%)
Hypertension	17 (85.0%)	19 (79.2%)	25 (52.1%)	9 (30.0%)
Smoking *	11 (55.0%)	15 (62.5%)	16 (33.3%)	10 (33.3%)
Family h/o CAD	4 (20.0%)	9 (37.5%)	8 (16.7%)	4 (13.3%)
Presenting Symptoms				
Chest Pain	2 (10.0%)	0 (0%)	11 (22.9%)	0 (0%)
Shortness of Breath	3 (15.0%)	0 (0%)	12 (25.0%)	0 (0%)
ACC/AHA Risk				
High	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intermediate	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Low	15 (75.0%)	23 (95.8%)	0 (0%)	26 (86.7%)
Very Low	5 (25.0%)	1 (4.2%)	48 (100%)	4 (13.3%)

* Any smoking, past or present

Table 5

Results of clinical and automated readings using a cut off of a TPD of 4% for supine automatic quantification and 3% for combined automatic quantification, along with a stress score of >3 for visual assessment.

	Automated	Visual
<i>All Patients</i>		
<i>Supine (N=160)</i>		
AUC	0.692	0.693
Sensitivity	72%	93% *
Specificity	59%	27% *
<i>Combined Supine + Prone (N=133)</i>		
AUC	0.743	0.725
Sensitivity	71%	79%
Specificity	67%	60%
<i>No Known CAD or Cardiomyopathy</i>		
<i>Supine (N=59)</i>		
AUC	0.717	0.740
Sensitivity	72%	92.0%
Specificity	62%	38%
<i>Combined Supine + Prone (N=48)</i>		
AUC	0.781	0.820
Sensitivity	64%	77%
Specificity	85%	81%

*
p < 0.05

AUC = Area Under the Curve

Table 6

Results of clinical and automated readings using a cut off of ischemia corresponding to a TPD of 3.5% for supine only automated quantification and 1.5% for combined supine-prone automatic quantification. A threshold of 4 for the visual supine difference score and 1 for the combined difference score was used for visual quantification.

	Automated	Visual
<i>All Patients</i>		
<i>Supine Difference (N=122)</i>		
AUC	0.634	0.679
Sensitivity	63%	74%
Specificity	61%	59%
<i>Combined Supine + Prone Difference (N=102)</i>		
AUC	0.669	0.622
Sensitivity	63%	59%
Specificity	68%	62%
<i>No Known CAD or Cardiomyopathy</i>		
<i>Supine Difference (N=33)</i>		
AUC	0.637	0.639
Sensitivity	53%	63%
Specificity	64%	50%
<i>Combined Supine + Prone Difference (N=27)</i>		
AUC	0.645	0.582
Sensitivity	44%	56%
Specificity	82%	46%

*
p < 0.05

AUC = Area Under the Curve