COMPUTED TOMOGRAPHIC IMAGING WITHIN NUCLEAR CARDIOLOGY

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This Information Statement addresses the Complementary Roles of Nuclear Cardiology and Cardiac CT in the Current Healthcare Environment.

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CURRENT HEALTH CARE ENVIRONMENT FOR NEW CV TECHNOLOGY

Since the introduction of clinical nuclear cardiology nearly three decades ago, SPECT has become the most widely applied imaging technique for the evaluation of patients with known or suspected coronary artery disease (CAD). The striking increase in the utilization of SPECT in recent years has been driven by the documentation of its superior diagnostic and prognostic accuracy resulting in more cost-efficient and clinically effective patient care. Application of this robust evidence base has resulted in enhanced continuity of care between the primary care physician and nuclear cardiologist. With the recent addition of gated imaging, the evaluation of regional wall motion and quantification of ejection fraction has further improved the diagnostic and prognostic accuracy of the test. As a result, gated SPECT is now commonplace and at the heart of clinical cardiovascular management.

For the nuclear cardiologist, the development of cardiac computed tomography (CT), especially with hybrid systems including SPECT-CT and PET-CT modalities, have a similar potential for adding value to our current nuclear cardiology armamentarium. Of particular interest to most nuclear cardiologists is the potential for a hybrid system to provide attenuation correction for SPECT thereby further improving diagnostic accuracy.

Although notably used for screening for pre-clinical disease, the application of coronary calcium scoring (CCS) may provide anatomical correlates for SPECT physiological flow data that may enhance predictive accuracy for the extent and severity of CAD and more precisely guide medical management decisions in diagnostic patient cohorts. Furthermore, the combination of SPECT-CT or PET-CT may soon provide an evaluation of coronary anatomy in the same setting as perfusion imaging and offer even more clinical efficacy than the high levels we currently enjoy.

Careful evaluation and perhaps incorporation of these new modalities has become critical since some medical specialties have begun initiatives to exclude cardiologists from interpreting and obtaining reimbursement for newer cardiovascular imaging modalities, such as CT and magnetic resonance imaging. While some suggest that cardiac imaging by cardiovascular specialists leads to inappropriate self-referral and higher health care costs, evidence exists that the performance of cardiac imaging at the point-of-care leads to timely incorporation of more clinically relevant interpretations into quality patient care.[1-3] The exceptional growth rates in the field of nuclear cardiology have been promoted by the large body of evidence demonstrating that SPECT imaging results in added value and enhanced patient care.[2-3] This evidence has also been a guiding force in supporting current reimbursement levels. The American Society of Nuclear Cardiology (ASNC) has been the leading force responsible for the development and promoting of clinical guidelines, laboratory and physician standards and certification for practicing nuclear cardiologists as well as nuclear medicine specialists and radiologists.[4] Based on the experience within nuclear cardiology, restricting imaging access or interpretation based upon specialty alone and not guided by a knowledge base would likely have a detrimental effect on patient care. Since nuclear cardiologists are leaders in the cardiac SPECT and PET fields, it is appropriate that they participate in the development of SPECT-CT and PET-CT, taking a leading role in guiding clinical research and focusing clinical applications and utilization of new methodologies into areas of medical need.

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The current information statement seeks to evaluate the potential value of adding CT to SPECT/PET imaging and to focus research into areas of distinct promise for combined imaging of SPECT/PET-CT. Thus, the aims of this document are to: 1) review the current state of cardiovascular CT applications, 2) encourage the development of a solid evidence-base for hybrid imaging, and 3) facilitate the development of physician and laboratory certification standards and training guidelines that will result in high quality patient care–the ultimate *benchmark* for effectively guiding health care policy.

FUTURE PROMISE OF SPECT-CT AND PET-CT

Hybrid or dual-modality imaging offers clinical applications for each cardiac imaging technique, as well as those based on the unique value of a combined, co-registered SPECT-CT or PET-CT image. Dual-modality imaging presents an opportunity for using a single piece of equipment for distinctly different purposes, such as the determination of perfusion, function, and metabolism (PET-SPECT) or coronary calcification and angiography. Hybrid devices are rapidly evolving to incorporate state-of-the-art, high-speed multislice CT technology, along with the latest PET and SPECT detector systems. Therefore, a laboratory may use these hybrid devices for multiple purposes, thereby reducing space requirements compared to installation of two separate systems, as well as reducing overall financial cost involved in the purchase of both CT and PET-SPECT cameras.

SPECT imaging may utilize CT data to precisely quantify radiopharmaceutical activity and more accurately define geometric relationships. Synergy in combining CT with PET or SPECT may also be found in a variety of applications. CT-based attenuation correction is an obvious application of hybrid technology and is already in rather widespread clinical use. Substantial improvements in diagnostic accuracy have been realized, largely through improved specificity.[5] It is likely that CT-based attenuation correction with perfusion imaging will improve the detection of severe and extensive CAD. In addition, a template from CT data may be constructed to minimize errors and to be used as a model for reconstruction of accurate quantitative tracer uptake and retention.[6] Both image quality and quantitative accuracy may therefore be improved with CT. The ability for co-registration of anatomic landmarks with physiologic data makes SPECT-CT or PET-CT an ideal tool for molecular imaging. Such techniques are critical for the development of radionuclide imaging of many new potential targets, including angiogenic substrates, inflammation, neurohumoral activity, atherosclerotic plaques, hypoxia, apoptosis, and necrosis. Although the exact clinical value of these methods is not yet defined, the expansion of nuclear cardiology into molecular processes will require instrumentation advances, including rigorous anatomic localization. Finally, combined CT with PET or SPECT offers the promise that one device will address diverse manifestations of cardiovascular disease pathophysiology, including perfusion, function, and anatomy. This may prove to be a "turnkey" method for a noninvasive assessment of patients with known or suspected CAD.

CURRENT EVIDENCE ON CT IMAGING

CT Assessment of Coronary Calcification

Electron beam tomography (EBT) or multidetector spiral computed tomography (MDCT) measurement of coronary calcium and the assessment of myocardial perfusion and function using myocardial perfusion SPECT are established risk markers in the noninvasive assessment of patients with suspected CAD. Coronary calcium scoring (CCS) and myocardial perfusion / function are very different in the information that they provide about the patient. In brief, the CCS provides unique anatomical information regarding coronary atherosclerostic burden while myocardial perfusion scintigraphy assesses the physiologic significance of coronary stenoses and provides information regarding resting hypoperfusion or stress-induced ischemia. As a result, the techniques appear highly complementary. For the clinician, risk detection may provide an assessment of long- (with CT) and short-term (with SPECT) prognosis by including measurements from both CT coronary calcium and gated myocardial perfusion SPECT imaging. The value of near- and long-term risk prediction is that it may then be used to guide ensuing medical and surgical management decisions. Although SPECT is of established value and may provide adequate testing, in some cases, the addition of CCS data may prove helpful for patients without a prior CAD diagnosis.

The extent of coronary artery calcification is commonly quantified on CT using one of two scores: the Agatston score (CCS) or the calcium volume score (CVS). The CCS is derived based on the x-ray attenuation coefficient, or a CT number, measured in Hounsfield units, and the area of calcium deposits (total study time is about 10 minutes). The CVS is commonly applied for serial evaluation of calcium changes. The mean interscan reproducibility is in the range of 8-12%; varying greatest with smaller scores.

There are several important relationships between myocardial perfusion SPECT results and outcomes that have been established. Most notably, in large populations undergoing gated SPECT, there is a directly proportional relationship between cardiac mortality and the extent and severity of the scan abnormality.[7] The normal MPS scan has been clearly established as providing strong evidence of a very low short-term risk (2 years),[8] while in the uncomplicated patient, a mildly abnormal scan has been reported to have a <1% per year mortality risk,[7] except in several patient subgroups for whom angiography should be considered (e.g., patients with a low ejection fraction,[9] transient ischemic dilation of the left ventricle,[10] or high clinical risk, such as diabetes mellitus).[11] Thus, the evidence is substantial that current nuclear cardiology techniques are effective in guiding patient management decisions.

Assessment of the presence of subclinical coronary atherosclerosis also provides an opportunity to identify patients that are at risk for developing clinical CAD over the long term, and as such may define patients not otherwise recognized by standard clinical assessments who may benefit from aggressive risk factor modification. In current clinical practice, coronary calcium scanning is increasingly being applied for this purpose. A compendium of evidence is supportive of a strong directly proportional relationship between the tomographic assessment of coronary calcium and the overall amount of coronary plaque (calcified and noncalcified) as determined at postmortem examination.[12] Studies have shown that the presence of coronary artery calcification by EBT indicates the presence of histologically determined coronary atherosclerosis and that the CCS is directly related to the total atherosclerotic plaque burden present in the epicardial coronary arteries.[12-13]

These findings are consistent with studies correlating coronary calcium and coronary angiographic findings demonstrating that significant CAD (>50% stenosis) by angiography is almost universally associated with the presence of coronary artery calcium.[14-30] In the largest patient series, only 0.5% of patients (n=940) with a normal CT had significant CAD, predicting equally well in both genders.[27] These results further indicate that the extent of coronary calcium is a more precise barometer of obstructive CAD than the mere presence of calcium.[27-29] Assessment of coronary calcium allows for the detection of atherosclerotic lesions often long before they become hemodynamically significant. In contrast, stress nuclear cardiology techniques (as with all stress imaging methods) require a physiologically significant stenosis before an abnormality becomes evident.

The CCS has also been widely shown to have important prognostic information. In contrast to myocardial perfusion scintigraphy, which provides useful information across the spectrum of patients with known as well as suspected CAD, the application of CCS appears to be limited to the patient population without known CAD. It is unlikely that assessment of coronary calcium in patients with known CAD will provide useful discrimination of patients requiring further assessment for the purpose of determining whether there is a need for considering coronary revascularization. Furthermore, even in patients without known CAD, the assessment of cardiac events using the CCS does not contain information attributable to SPECT (i.e., the extent and severity of perfusion deficits and the presence or degree of ventricular dysfunction) regarding the likelihood of benefit from revascularization.

The bulk of evidence shows that the CCS provides incremental information over conventional risk factors in assessing risk of all-cause death and hard cardiac events.[31-37] For example, in the largest series reported to date, Shaw et al.[33] reported on a cohort of >10,000 asymptomatic patients, in which, the 5-year risk-adjusted (all-cause) death rates ranged from 1.0% to 5.0% for CCS ≤10 to >1,000, providing incremental information over that provided by conventional risk factor analysis alone. The vast majority of the evidence documents that the relative risk of mortality or "hard" cardiac events, such as death or myocardial infarction, increase proportionally with the extent of coronary calcification.

Furthermore, evidence from the South Bay Heart Watch study[37] reveals that the CCS added to the Framingham Risk Score in prediction of nonfatal myocardial infarction or cardiac death in asymptomatic individuals but that the predictive value of CT measurements is dependent upon the pretest risk in the population. Specifically, in a population of 1,029 asymptomatic subjects with at least one coronary risk factor (but no diabetes), the CCS was predictive of risk among subjects with an intermediate risk Framingham risk score (≥ 10% risk (or ~1% / year) risk of hard cardiac events). Their data suggested that the CCS did not provide useful added risk assessment for subjects with a low risk Framingham risk score. Data from this study and summarized in the most recent 34th Bethesda conference on atherosclerotic imaging supports screening strategies including CT imaging in patients with an intermediate Framingham risk score (10-year risk of coronary heart disease death or myocardial infarction in the range of 6%-20%).[38]

Of supplemental importance to SPECT imaging, recent data notes that when the CCS is clustered with additional risk parameters that higher risk patient subsets can be identified. In a recent publication, Park et al.[35] found that a high sensitivity C-reactive protein (Hs-CRP, an inflammatory marker) acted synergistically with CCS measures augmenting the relative risk ratios for CAD death or myocardial infarction. These results indicate that, in asymptomatic populations, combining risk markers may provide an effective means for identifying asymptomatic cohorts who may have event rates approaching that seen in our current SPECT populations.

To date, higher risk asymptomatic cohorts with CCS and elevated Hs-CRP,[35] diabetes,[31] and perhaps the metabolic syndrome are at substantially greater risk of events, despite being asymptomatic, and perhaps could benefit from additional risk stratification with SPECT. A challenge for this new paradigm in imaging asymptomatics is how and when imaging for prevention can interface and link with current ischemia testing. Evidence is unfolding that SPECT imaging is the modality providing a key to integrative management of those with high risk subclinical disease.

Serial Coronary Calcium Scoring and Preventive Therapy

Current evidence is supportive that patients with CCS ≥100 merit aggressive anti-atherosclerosis therapy (being treated according to secondary prevention guidelines). In this vein, a literature base has been developing as to the role of CT in serial monitoring of atherosclerotic disease progression in asymptomatic individuals. At the core of serial monitoring is the application of coronary calcium as a surrogate measure of risk. For serial monitoring, changes in the calcium volume score between the first and second CT scan are used to define disease progression/stabilization following intercurrent initiation of risk-reducing therapies. From several series,[40-46] serial CCS measurements were applied to assess atherosclerotic progression following intercurrent statin therapy. In general, these results indicate that statin treated patients have yearly mean coronary calcium progression (defined as percent change (% Δ) in calcium volume score) of approximately 10% as compared with a ≥40% Δ in untreated individuals ($p<0.0001$). Interestingly, from the Callister series,[40] for those patients who achieved an LDL (reduction) <120 mg/dl, atherosclerotic regression, as noted by a reduced calcium volume score of −7%±23% ($p=0.01$) was observed. In the first prospective, randomized controlled trial of sequential CT scanning performed 1 year apart (n=66 patients whose baseline LDL>130 mg/dl),[44] a crossover treatment design was utilized where patients were off and on treatment with 0.3 mg/day of cerivastatin. The results of this trial revealed that treatment with cerivastatin resulted in a marked reduction in LDL cholesterol (~35%) and attenuated progression in the calcium volume score (median progression = 9% / year on treatment versus 25% progression during the untreated portion of the study, $p<0.0001$). Although differential treatment benefits have been reported,[42-43] a synopsis of evidence supports that statin therapy slows the propagation of vascular calcification and this effect was dramatically noted in patients who maintained an LDL cholesterol <100 mg/dl where the rate of calcium progression was effectively halted.

Additional outcome evidence is available to support the notion that patients with accelerated progression have a worsened event-free survival. In 2 series of 817 and 495 asymptomatic individuals undergoing serial CT scanning and ~4 years of outcome evaluation, the rate of *progression* was more than double for patients who had an acute myocardial infarction during follow-up (~45% for patients with events versus ~21% for event-free survivors, $p<0.0001$).[45-46] This evidence is noteworthy because independent of changes in LDL cholesterol, serial measurements of coronary calcium identified at-risk asymptomatic individuals. Thus, when applying serial CT imaging: 1. High risk individuals are those with a CCS ≥400; 2. Those patients with high risk scores have progressive disease at higher rates than individuals with lower baseline CCS. Thus, patients with higher baseline CCS should be considered for risk reduction therapy; and 3. Patients whose second scan (performed at least 1 year apart) exhibits a change in the CCS >30%-40% are at high risk for acute myocardial infarction in the 3-5 years following testing. In simplistic terms, important components of serial CT scanning are: the degree of risk resides in the baseline and follow-up scan as well as the magnitude of change between two scans. The intensity of management (i.e., risk reduction strategies) should therefore be tailored and aggressively focused on those high risk patients as determined by these three components noted during serial CT imaging.

Integrating CT and SPECT to Guide Medical Management Decisions

For SPECT imaging, the assessment of the amount of ischemia is central to risk stratification. Recent evidence in a diagnostic cohort of 10,627 patients revealed that patients undergoing medical therapy as their initial treatment had superior survival to those patients referred to revascularization in the setting of no or mild ischemia.[39] By contrast, patients undergoing revascularization had an increased survival benefit over patients undergoing medical therapy when moderate to severe ischemia (>10% of the total myocardium) was detected by myocardial perfusion SPECT. These findings suggest a new paradigm: rather than identify patient risk, the goal of myocardial perfusion imaging in a combined testing strategy is the identification of patients who may benefit from revascularization or anti-ischemic or risk-reduction intervention. Assessment of the amount of ischemia is central to this prediction of benefit—an assessment provided by myocardial perfusion imaging but not by the assessment of atherosclerotic burden provided by CT measurement of coronary calcium. How the combination

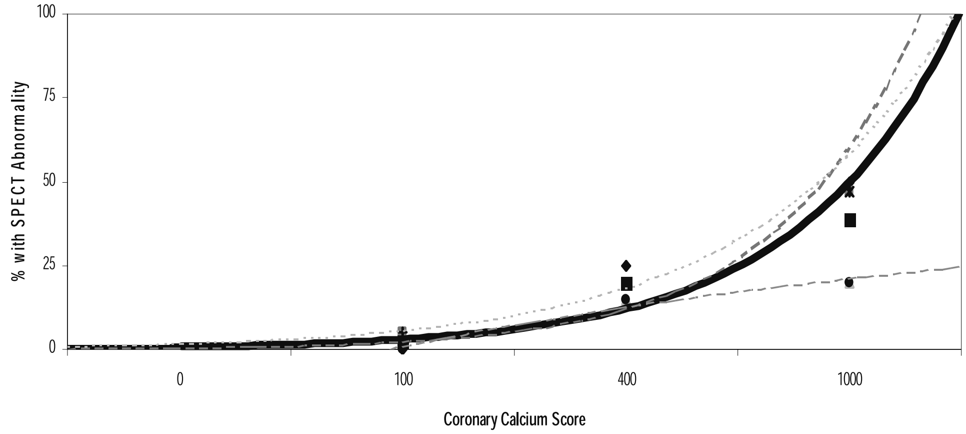

Figure 1. A Compilation of Evidence on the Relationship Between Coronary Calcium Measures and the Rate of SPECT Abnormalities. The predictive line is derived using an exponential regression function projecting through a range of coronary calcium scores from 0 to >1,000. This model includes average, median, and range estimates for the likelihood of a SPECT abnormality by the Coronary Calcium Score. Based upon this model, 1 in 50 patients with a calcium score <100 will have an abnormal SPECT and ~1 in 3 to 1 in 4 patients with calcium scores ≥400 will have an abnormal SPECT scan.

of coronary calcium scanning and SPECT might improve risk assessment is the subject of ongoing research.

Recent trials have compared the CCS to physiologic parameters of myocardial perfusion using stress SPECT.[47-50] By examining the relationship between the CCS and the frequency of an abnormal SPECT study, these reports have been consistent in providing evidence that there is a linear relationship between CCS and SPECT abnormalities (Figure 1). The exceedingly low cardiac event rate in subjects with a CCS <100 is consistent with angiographic studies indicating a comparably low likelihood of significant CAD and an extremely low incidence of stress-induced myocardial ischemia (~2%) in such individuals. Thus, studies to date have consistently provided evidence that those patients with CCS <100 generally do not benefit from stress SPECT.

Development of a strategy using a threshold of CCS >400 as a "trigger" for performing a stress SPECT study has recently been evaluated. (Figure 2).[47-49] This proposed testing strategy to selectively recommend stress SPECT for patients with a high CCS is based on the finding that these patients have an intermediate likelihood of having silent myocardial ischemia with its attendant high short-term risk for cardiac events. In the first report by He et al.,[47] large ischemic perfusion defects by SPECT were confined to subjects who had a CCS of ≥400. In the larger study by Berman et al.[49] nearly three-fourths of patients with ischemia, including those with large ischemic perfusion defects, had a CCS ≥400. These results further indicate that the likelihood of myocardial ischemia by SPECT is closely related to the absolute CCS and, based upon published reports, it is expected that ~1 in 3 to 1 in 4 individuals with a CCS ≥400 will have silent ischemia on SPECT imaging. In the study of Berman et al.,[49] the frequency of ischemic SPECT was also seen to increase when the CCS was >90th percentile for age and gender, resulting in the addition of the category of CCS >100 and >90th percentile to the category of asymptomatic patients deserving of consideration for myocardial perfusion SPECT (Figure 2).

It is noteworthy that only ~10% of patients undergoing CT imaging have CCS ≥400, indicating that only a small fraction of patients referred for CCS would require further testing by SPECT, and that proceeding to coronary angiography with a high score and a normal SPECT is exceedingly rare. These observations are important in allaying the fears of third party payors that measuring the CCS is going to result in a marked increase in unnecessary testing. The current evidence is supportive that the combination of CCS and SPECT is more effective than SPECT alone in determining the need for aggressive medical therapy in diagnostic populations.

However, additional research is still required on the fully integrative role of CT and SPECT. For example, there is a wide range of CCS in patients with normal myocardial perfusion SPECT, thus exposing an important limitation relevant to all forms of stress testing in that they do not effectively screen for subclinical atherosclerosis. For instance, only 22% of patients with a normal SPECT study had no evidence of CCS; 56% had a CCS ≥ 100 and 31% had a CCS ≥ 400.[49] Thus, critical

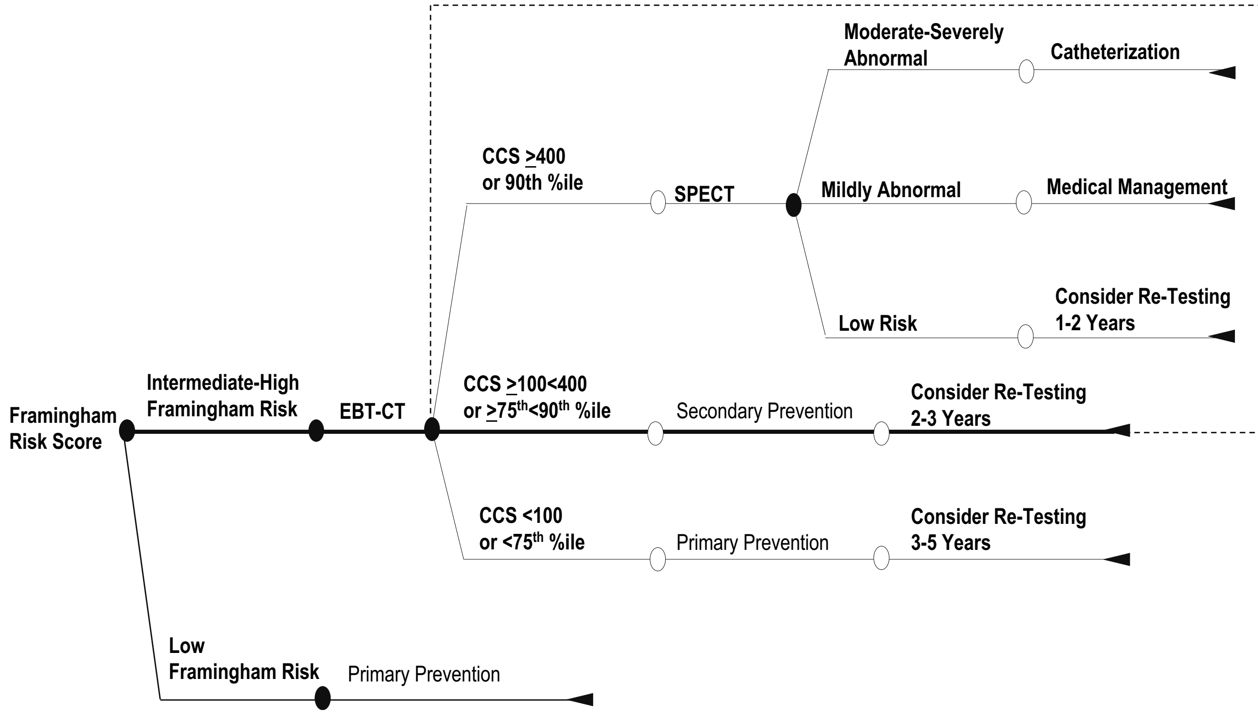

Figure 2. Preliminary Patient Management Strategy for Using Computed Tomographic (CT) Coronary Calcium Scores (CCS) and Ischemia Testing with SPECT Imaging In Asymptomatic, Intermediate-High Risk Individuals. The dotted box indicates patients who will be treated to secondary prevention goals.

evidence is still required to estimate the short-term prognosis of patients with high CCS and normal stress perfusion SPECT. Accordingly, a preliminary observation noted that patients with prognostically important CCS who have normal MPS have a very low risk of hard cardiac events.[51] On the basis of the preliminary data and the knowledge of the excellent short-term prognosis of patients with normal myocardial perfusion SPECT, even in the presence of established CAD, it is reasonable to hypothesize that such patients might be at low *short-term* risk but high *long-term* risk for cardiac events. Therefore, CCS may unmask a larger subgroup of patients who should receive more aggressive anti-atherosclerotic intervention than would have been indicated based on the results of MPS testing alone. Future study that incorporates the follow-up data from patients undergoing both studies will determine which patients with normal stress imaging tests are best suited for undergoing subsequent CCS.

Noninvasive CT Angiography for Stable (Non-High-Risk) Chest Pain Populations

Currently, invasive contrast coronary angiography remains the standard for defining the extent and severity of coronary anatomy. Its *advantages* include a very high spatial resolution, the capacity to define the entire endoluminal surface including the presence of plaque rupture, and the ability to proceed directly to coronary intervention in the same procedure. However, there are disadvantages that include an inability to define the true extent of atherosclerosis and the presence of eccentric arterial remodeling,[52] procedural risks (i.e., complications including those related to the arterial puncture, receiving iodinated contrast, radiation, and catheter vascular or arterial trauma, including rare myocardial infarction and more common branch vessel compromise associated with percutaneous coronary intervention) as well as procedural charges, which often exceed $5,000.[53-54] Moreover, a substantial number of procedures are not followed by intervention, because the coronary arteries are normal or show minimal irregularities without obstructive CAD.

MDCT does offer several *advantages* over the invasive approach. That is, as a noninvasive procedure requiring only intravenous access, the risk of arterial vascular trauma is eliminated. It can also effectively define coronary anomalies affecting the origin of the coronary vessels and can potentially define the presence and location of significant coronary lesions. Furthermore, MDCT can be completed in a relatively short time compared to other noninvasive evaluation of CAD such

Technique (n of studies)	Total N of Segments	Positive Segments with CAD	Negative Segments with CAD
4-Slice - CTA (10)	4,047	449 / 561	172 / 3,486
8-Slice CTA (2)	503	72 / 90	10 / 413
16-Slice CTA (2)	501	133 / 142	34 / 359
Summary CTA (14)	**5,051**	**654 / 793**	**216 / 4,258**

p<0.0001 for each comparison

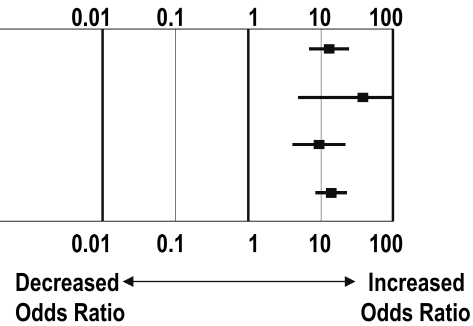

Figure 3. Forest Plot of the summary odds ratio of 4- (n=10 reports), 8- (n=2 reports), and 16- (n=2 reports) slice computed tomographic angiography (CTA) for the diagnosis of coronary artery disease (CAD) stenosis ≥50%. The summary odds ratio depicts the rate of CAD stenosis ≥50% in positive versus negative CTA segments as based upon 14 published reports. This evidence reveals that in the setting of a visualized obstructed arterial segment on CTA, there is an approximately 11-fold higher likelihood of a significant stenosis ≥50% on coronary angiography.

as stress SPECT. Nevertheless, several *disadvantages* of the technique remain. Iodinated contrast load requirements remain similar to those of invasive coronary angiography. The radiation exposure may exceed that of invasive angiography.[53-56] However, the most important limitation to date is technical in that the technique remains suboptimal in its ability to precisely and consistently detect the presence and location of anatomic coronary lesions. The obstacles for routine use of CT angiography are multifactorial and include: 1) substantial movement of the coronary arteries during the cardiac cycle and the limitations of temporal resolution of MDCT technology that involves rapid rotation of heavy collimated detectors; 2) spatial resolution limitations; 3) artifacts caused by overlying calcium or stents that can obscure the presence of luminal narrowing; 4) the need for a slow and regular heart rate during the bolus first-pass acquisition. All of these limitations can reduce the portion of the coronary arterial tree that can be accurately scrutinized and renders this technique, currently, as a research tool.

As a result of these limitations, the reported sensitivity and specificity for anatomic CAD have thus far been less than ideal. Kuettner and colleagues recently reported their findings in a series of 66 patients undergoing MDCT imaging[57] noting an overall sensitivity and specificity of 68% and 99% for evaluable segments. However, 43% of segments were not evaluable, yielding an overall sensitivity of 43%. In a recent series of 77 patients undergoing 16-slice MDCT, Ropers et al.[58] found a sensitivity of 85% by patients and 73% by lesion site. Thus, the overall specificity was 78%.[58] In an earlier study of 59 patients using a 16-slice MDCT, Nieman et al. found a sensitivity and specificity of 95% and 86% respectively by coronary artery lesions.[59] Clearly these studies are limited by their small numbers and do not necessarily reflect the current state of a rapidly evolving technology. Thus more data will be needed before the true role of MDCT will be established by clinical practice. As technology improves, however, one can expect the accuracy of the imaging technique to correspondingly improve. CT coronary angiography is technically much more challenging than coronary calcium scanning. For the latter, results with MDCT are generally accepted to be equivalent to those of EBCT if scanners with 4 or more slices and detector rotation times of <=500 are used. For CT coronary angiography, greater numbers of slices and faster rotation times are even more critical. It is widely held that scanners with at least 16 detectors are needed, along with the rotation time of <=500 msec. CT technology is rapidly improving, and even recent articles use scanncers that are not state-of-the art. For example, current generation MDCT scanners are available offering rotation times close to 300 msec, 0.4 mm cubic isotropic resolution, and expanded coverage reducing the scan time to less than 10 seconds. In addition to higher resolution, these advances will allow imaging at higher heart rates, use of less iodinated contrast, less heart rate change during acquisiton, and should result in a higher proportion of evaluable studies.

Currently, the main clinical value appears to be the high negative predictive value, allowing the exclusion of obstructive CAD (Figure 3).[60] The positive predictive value is however hampered by various issues. First, it should be noted that MDCT cannot yet provide reliable quantification of stenotic lesions, and quantification is not possible in regions with dense coronary calcium. Second, many patients have already been diagnosed with

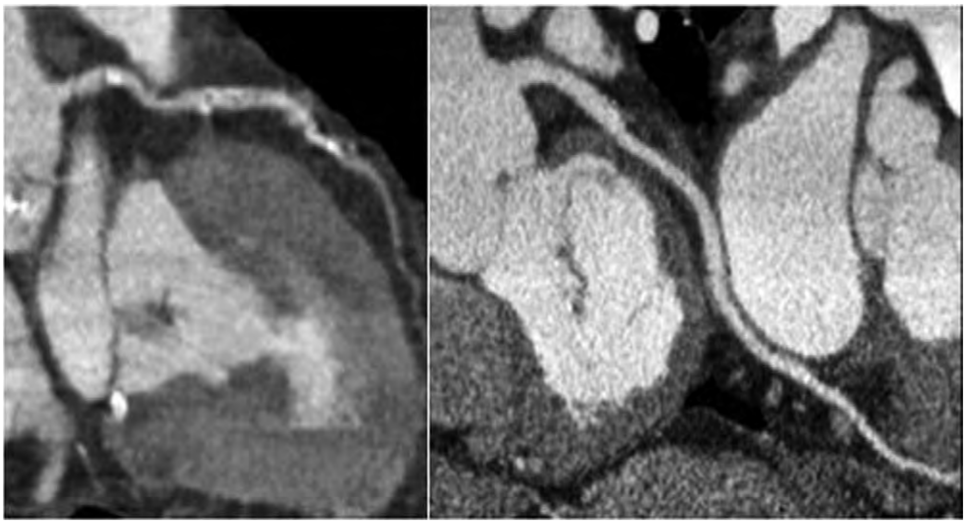

Figure 4. In this case example of CTA, the left anterior descending is diffusely diseased on the left panel and the obtuse marginal branch is normal (right panel).

CAD (with a history of myocardial infarction, bypass surgery or percutanous intervention) and need testing for new symptoms or for risk assessment purposes. In these patients, anatomy is often complex with many abnormalities. In these patients, MDCT may show many lesions, but the hemodynamic consequences of these abnormalities, needed for adequate therapeutic decision making, may not be clear. In patients with stents, MDCT can detect stent patency but cannot accurately assess in-stent restenosis.[61] Third, in patients with many lesions, identification of the culprit lesion is not possible. In particular, patients with diabetes have extensive and diffuse lesions. The potential consequences are that: 1. the number of patients referred for cardiac catheterization will increase instead of decrease and 2. luminology may determine patient management and the so-called oculostenotic reflex will result in many interventions. To avoid these potential consequences, integration of the anatomic information provided by MDCT with hemodynamic information provided by SPECT or PET is needed.

Thus, the combination of SPECT and MDCT modalities appears to be a classic "win-win" situation: MDCT provides incremental information over SPECT and PET in detection of early atherosclerosis and can provide improvements through optimal attenuation; SPECT and PET provide incremental information over MDCT by assessing the hemodynamic significance of lesions. Moreover, MDCT does not only allow assessment of calcified plaques, but soft plaques can also be visualized, and with newer MDCT technology, assessment of plaque constitution will be feasible. It is anticipated that the integration of plaque constitution and information on inflammatory activity (as may become possible with new PET tracers) may further help to identify vulnerable plaques.

Two case illustrations of CT angiography are depicted in Figures 4 and 5.

HEALTH CARE POLICY ISSUES

With the introduction of any new diagnostic technology, there are numerous health care policy issues that must be considered and the introduction of cardiovascular CT systems is not an exception. The major issues facing the assimilation of this technology into mainstream cardiology practice include: 1) the development

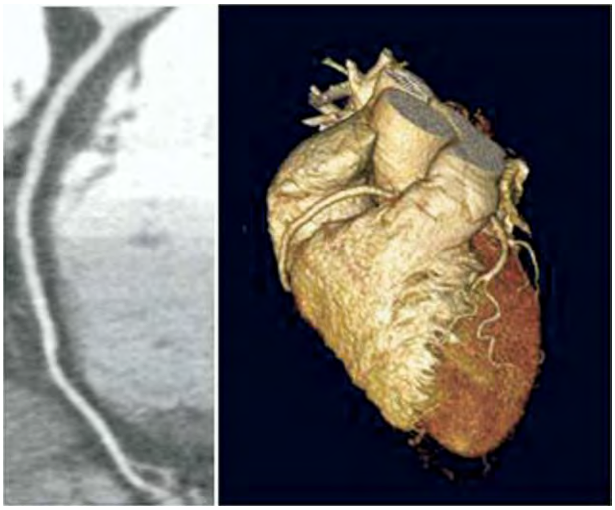

Figure 5. This case example of CTA illustrates a patent right coronary artery (left panel) including a 3-dimensional view

of a sufficient evidence base upon which to guide utilization of the technology and patient management, 2) physician and technologist training and certification, and 3) reimbursement.

Evidence from properly conducted clinical studies published in peer-reviewed journals should drive medical practice, similar to what has transpired with gated SPECT imaging. Studies should be conducted that establish the clinical effectiveness of cardiovascular CT technology including diagnostic accuracy, incremental clinical value, and its impact on the determination of prognosis. As discussed in this statement, there is a growing body of evidence regarding the incremental prognostic value of CT but additional evidence is required in order to refine testing and treatment algorithms for asymptomatic and symptomatic patient cohorts.

Nuclear cardiologists have extensive experience in utilizing risk stratification data in SPECT interpretation and patient management and thus extending this reasoning to CT applications would be an effortless transition as compared with other specialty groups. With the inclusion of CT anatomy, nuclear cardiologists experience focusing on cardiovascular physiology would be a natural extension of adding to a more powerful clinical scan interpretation improving image accuracy and clinical decision making.

The cost-effectiveness of these new hybrid technologies must also be evaluated. From the recent 34th Bethesda Conference on atherosclerotic imaging, there is a paucity of available cost-effectiveness literature upon which to guide health care policy decisions as well as reimbursement. It again should be noted that there is extensive data on the cost-effectiveness of SPECT and this data has been useful for guiding US and international health policy on imaging.[62,63] This latter statement is critical as coronary calcium scanning, for example, is largely restricted to self-pay patients. This inequity to access disportionately harms lower socioeconomic patient subsets. As a result, current reimbursement for CT and/or combined SPECT-CT or PET-CT for cardiovascular indications are currently not in place and inconsistently applied but will require precise definition to reflect the magnitude of clinical work necessary for optimally combined imaging. ASNC, with extensive experience in this arena, can provide guidance to both public and private payors.

In the related regulatory environment, there is the potential that inter-specialty “turf” conflicts could develop potentially limiting access of qualified practitioners to this new technology. Such strategies may only further exacerbate the existing “detection gap” for cardiovascular disease.[64] Strategies aimed at developing guidance documents for asymptomatic coronary screening with CT should be developed similar to that for breast, colon, and lung cancer. Standards for technical quality and focusing on the quality of scan interpretation and reporting of results will also need to be established. Certification and accreditation bodies, such as has occurred in nuclear cardiology with the Certification Board of Nuclear Cardiology (CBNC) and The Intersocietal Commission for the Accreditation of Nuclear Medicine Laboratories (ICANL) should be fostered to create standards for cardiac CT testing and oversight.

Technologists and physicians, both those currently in training and those in practice, will require appropriate training in these new technologies. Though the federal government has regulated the use of radioisotopes, increasingly individual states have acquired oversight of the use of radiation and administration of radioactive substances. Organizations like ASNC will have to work with states to implement appropriate guidelines regarding the training and certification of healthcare professionals providing these new services. To facilitate the availability of new technology in all regions of the country, eventually including rural areas where there is frequently limited access to individuals trained in the latest technologies, consideration should be made to allowing “cross-over” training for CT and nuclear medicine technologists. Similarly, “cross-over” training will have to be addressed for physicians, including cardiology fellows, radiology residents, and nuclear medicine residents as well as for cardiologists, nuclear medicine physicians, and radiologists currently in practice.

CONCLUSIONS

Though there are many challenges to be met in the health care policy arena related to the introduction of cardiovascular CT technologies, none are insurmountable and there is experience in related areas to guide us based upon the substantial experience within ASNC. Historically, nuclear cardiologists have played a leading role in the field of cardiac imaging by developing new imaging techniques as well as providing a wealth of knowledge of the accuracy of nuclear imaging as based upon risk stratification and, more recently, cost effectiveness data to guide health care policy decisions. The experience within ASNC in developing nuclear cardiology as well as in contributing to the growth and clinical knowledge in cardiac CT can foster and potentially lead the development and growth of cardiovascular CT.

From a review of the current evidence and future possibilities of cardiac CT, there appears to be substantial promise for the complementary role for CT imaging with PET or SPECT. Current developments in the field of CT imaging will allow for multiple new indications for noninvasive imaging that span a spectrum of cardiac applications resulting in further added value to the field of nuclear cardiology. Nuclear cardiology methods may allow greater clinical information to be derived from CT by the provision of functional information, potentially important when questionable abnormalities are observed by CT. Based on years of imaging expertise and the incorporation of science and quality into clinical practice, nuclear cardiologists and the American Society of Nuclear Cardiology are well suited to participate in the leadership, development, research, and practice of CT-based cardiac imaging.

References

1. www.nasci.org/NASCI-Newsletters/NASCIBeat%20December%202003.htm, access date: August 16, 2004.
2. Levin DC, Parker L, Intenzo CM, Sunshine JH. Recent rapid increase in utilization of radionuclide myocardial perfusion imaging and related procedures. Radiol 2002;222:144-8.
3. Levin DC, Rao VM, Maitino AJ, Parker L, Sunshine JH. Comparative increases in utilization rates of ultrasound examinations among radiologists, cardiologists, and other physicians from 1993 to 2001. J Am Coll Radiol 2004;I:549-52.
4. www.asnc.org; access date: August 16, 2004.
5. Koepfli P, Hany TF, Wyss CA, Namdar M, Burger C, Konstantinidis AV, Berthold T, von Schulthess GK, Kaufmann PA. CT attenuation correction for myocardial perfusion quantification using a PET/CT hybrid scanner. J Nucl Med 2004;45:537-42.
6. Da Silva AJ, Tang HR, Wong KH, Wu MC, Dae MW, Hasegawa BH. Absolute quantification of regional myocardial uptake of 99m-Tc-sestamibi with SPECT. Experimental validation in a porcine model. J Nucl Med 2001; 42:772-9.
7. Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, Friedman J, Diamond GA. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation 1998; 97:535-43.
8. Shaw LJ, Hendel R, Lauer MS, Borges-Neto S, Alazraki N, Burnette J, Krawczynska E, Cerqueira M, Maddahi J, for the Myoview Multicenter Registry. Prognostic value of normal exercise and adenosine Tc-99m tetrofosmin SPECT imaging: results from the multicenter registry in 4,728 patients. J Nuc Med 2003;44:134-139.
9. Sharir T, Germano G, Kang X, Lewin HC, Miranda R, Cohen I, Agafitei RD, Friedman JD, Berman DS. Prediction of myocardial infarction versus cardiac death by gated myocardial perfusion SPECT: risk stratification by the amount of stress-induced ischemia and the poststress ejection fraction. J Nucl Med 2001;42: 831-7.
10. Abidov A, Bax JJ, Hayes SW, Cohen I, Gerlach J, Kang X, Friedman JD, Germano G, Hachamovitch R, Berman DS. Transient ischemic dilation ratio of the left ventricle is a significant predictor of future cardiac events in patients with otherwise normal myocardial perfusion SPECT. J Am Coll Cardiol 2003;42:1818-25.
11. Berman DS, Kang X, Hayes SW, Friedman JD, Cohen I, Abidov A, Shaw LJ, Amanullah AM, Germano G, Hachamovitch R. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men. Impact of diabetes mellitus on incremental prognostic value and effect on patient management. J Am Coll Cardiol 2003;41:1125-33.
12. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. Circulation 1995;92:2157-62.
13. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: A histologic study of 723 coronary artery segments using nondecalcifying methodology. J Am Coll Cardiol 1998;31:126-133.
14. Rumberger JA, Sheedy PF, Breen JF, et al. Coronary calcium, as determined by electron beam computed tomography, and coronary disease on arteriogram. Effect of patient's sex on diagnosis. Circulation 1995;91:1363-1367.
15. Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827-832.
16. Breen JF, Sheedy PF, Schwartz RS, et al. Coronary artery calcification detected with ultrafast CT as an indication of coronary artery disease. Radiol 1992;185:435-439.
17. Bielak LW, Kaufmann RB, Moll PP, et al. Small lesions in the heart identified at electron beam CT: Calcification or noise? Radiol 1994;192:631-636.
18. Kaufmann RB, Sheedy PF, Maher JE, et al. Quantity of coronary artery calcium detected by electron beam computed tomography in asymptomatic subjects and angiographically studied patients. Mayo Clin Proc 1995;70:223-232.
19. Braun J, Oldendorf M, Moshage W, et al. Electron beam computed tomography in the evaluation of cardiac calcification in chronic dialysis patients. Am J Kidney Dis 1996;27:394-401.
20. Budoff MJ, Georgiou D, Brody A, et al. Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease. A multicenter study. Circulation 1996;93:898-904.
21. Fallavollita JA, Brody AS, Bunnell IL, et al. Fast computed tomography detection of coronary calcification in the diagnosis of coronary artery disease. Comparison with angiography in patients <50 years old. Circulation 1994;89:285-290.
22. Baumgart D, Schmermund A, George G, et al. Comparison of electron beam computed tomography with intracoronary ultrasound and coronary angiography for detection of coronary atherosclerosis. J Am Coll Cardiol 1997;30:57-64.
23. Schmermund A, Baumgart D, Gorge D, et al. Coronary artery calcium in acute coronary syndromes: A comparative study of electron-beam computed tomography, coronary angiography, and intracoronary ultrasound in survivors of acute myocardial infarction and unstable angina. Circulation 1997;96:1461-1469.
24. Kennedy J, Shavelle R, Wang S, et al. Coronary calcium and standard risk factors in symptomatic patients referred for coronary angiography. Am Heart J 1998;135:696-702.
25. Bielak LF, Rumberger JA, Sheedy PF, et al. Probabilistic model for prediction of angiographically defined obstructive coronary artery disease using electron beam computed tomography calcium score strata. Circulation 2000;102:380-385.
26. Shavelle DM, Budoff MJ, LaMont DH, et al. Exercise testing and electron beam computed tomography in the evaluation of coronary artery disease. J Am Coll Cardiol 2000;36:32-38.
27. Haberl R, Becker A, Leber A, et al. Correlation of coronary calcification and angiographically documented stenoses in patients with suspected coronary artery disease: Results of 1,764 patients. J Am Coll Cardiol 2001;37:451-457.
28. Rumberger JA, Sheedy PF, Breen JF, et al. Electron beam computed tomographic coronary calcium score cutpoints and severity of associated angiographic lumen stenosis. J Am Coll Cardiol 1997;29:1542-1548.

29. Guerci AD, Spadaro LA, Goodman KJ, et al. Comparison of electron beam computed tomography scanning and conventional risk factor assessment for the prediction of angiographic coronary artery disease. J Am Coll Cardiol 1998;32:673-679.
30. Schmermund A, Denktas AE, Rumberger JA, Christian TF, Sheedy PF, 2nd, Bailey KR, Schwartz RS. Independent and incremental value of coronary artery calcium for predicting the extent of angiographic coronary artery disease: comparison with cardiac risk factors and radionuclide perfusion imaging. J Am Coll Cardiol 1999;34:777-86.
31. Raggi P, Shaw LJ, Berman DS, Callister TQ. Prognostic value of coronary artery calcium screening in subjects with and without diabetes. J Am Coll Cardiol 2004;43:1663-9.
32. Detrano R, Hsiai T, Wang S, et al. Prognostic value of coronary calcification and angiographic stenoses in patients undergoing coronary angiography. J Am Coll Cardiol 1996;27:285-290.
33. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiol 2003;228:826-33.
34. O'Malley PG, Taylor AJ, Jackson JL, Doherty TM, Detrano RC. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol 2000;85:945-8.
35. Park R, Detrano R, Xiang M, Fu P, Ibrahim Y, LaBree L, Azen S. Combined use of computed tomography coronary calcium scores and C-reactive protein levels in predicting cardiovascular events in nondiabetic individuals. Circulation 2002;106:2073-7.
36. Kondos GT, Hoff JA, Sevrukov A, Daviglus ML, Garside DB, Devries SS, Chomka EV, Liu K. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. Circulation 2003;107:2571-6.
37. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. JAMA 2004;291:210-5.
38. Redberg RF, Vogel RA, Criqui MH, Herrington DM, Lima JA, Roman MJ. 34th Bethesda Conference: Task force #3–What is the spectrum of current and emerging techniques for the noninvasive measurement of atherosclerosis? J Am Coll Cardiol 2003;41:1886-98.
39. Callister TQ, Raggi P, Cooil B, et al. Effect of HMG-CoA reductase inhibitors on coronary artery disease as assessed by electron-beam computed tomography. N Engl J Med 1998;339:1972-1978.
40. Budoff MJ, Lane KL, Bakhsheshi H, et al. Rates of progression of coronary calcium by electron beam tomography. Am J Cardiol 2000;86:8-11.
41. Hecht HS, Harman SM. Comparison of effectiveness of statin monotherapy versus statin and niacin combination therapy in primary prevention and effects on calcified plaque burden. Am J Cardiol 2003;91:348-51.
42. Hecht HS, Harman SM. Comparison of the effects of atorvastatin versus simvastatin on subclinical atherosclerosis in primary prevention as determined by electronbeam tomography. Am J Cardiol 2003;91:42-5.
43. Achenbach S, Ropers D, Pohle K, et al. Influence of lipid-lowering therapy on the progression of coronary artery calcification: a prospective evaluation. Circulation 2002;106:1077-1082.
44. Raggi P, Callister TQ, Shaw LJ. Progression of Coronary Artery Calcium and Risk of First Myocardial Infarction in Patients Receiving Cholesterol-Lowering Therapy. Arterioscler Thromb Vasc Biol 2004;24:1272-1277.
45. Raggi P, Cooil B, Shaw LJ, Aboulhson J, Takasu J, Budoff M, Callister TQ. Progression of coronary calcium on serial electron beam tomographic scanning is greater in patients with future myocardial infarction. Am J Cardiol 2003;92:827-9.
46. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. Circulation 2002;105:823-9.
47. He ZX, Hedrick TD, Pratt CM, Verani MS, Aquino V, Roberts R, Mahmarian JJ. Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia. Circulation 2000;101:244-51.
48. Moser KW, O'Keefe JH, Bateman TM, McGhie IA. Coronary calcium screening in asymptomatic patients as a guide to risk factor modification and stress myocardial perfusion imaging. J Nucl Cardiol 2003;10:590-598.
49. Berman DS, Wong ND, Gransar H, Miranda-Peats R, Dahlbeck J, Hayes SW, Friedman JD, Kang X, Polk D, Hachamovitch R, Shaw L, Rozanski A. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol 2004;44:923-30.
50. Anand DJ, Lim E, Raval U, Lipkin D, Lahiri A. Prevalence of silent myocardial ischemia in asymptomatic individuals with subclinical atherosclerosis detected by electron beam tomography. J Nuc Cardiol 2004;11:450-457.
51. Berman DS, Wong ND, Gransar H, Miranda-Peats L, Arad Y, Hayes S, Friedman J, Polk D, Hachamovitch R, Rozanski A. Relationship between Stress Myocardial Perfusion SPECT and the Extent of Subclinical Atherosclerosis Assessed by CT Coronary Calcium (abstr). Circulation 2003;108:IV-634-5.
52. Nissen SE, Tsunoda T, Tuzcu EM, et al. Effect of recombinant ApoA-I Milano on coronary atherosclerosis in patients with acute coronary syndromes: a randomized controlled trial. JAMA 2003;290:2292-300.
53. Budoff MJ, Achenbach S, Duerinckx A. Clinical utility of computed tomography and magnetic resonance techniques for noninvasive coronary angiography. J Am Coll Cardiol 2003;42:1867-78.
54. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol 1999;33:1756-1824.
55. Knollmann FD, Hidajat N, and Felix R. CTA of the coronary arteries: comparison of radiation exposure with EBCT and multislice detector CT. Radiol 2000;217:364-365.
56. Morin RL, Gerber TC, McCollough CH. Radiation dose in computed tomography of the heart. Circulation 2003;107:917-922.
57. Kuettner A, Kopp AF, Schroeder S, Rieger T, Brunn J, Meisner C, Hueschmid M, Trabold T, Burgstahler C, Martensen J, Schoebel W, Selbman H-K, Claussen CD. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with angiographically proven coronary artery disease. J Am Coll Cardiol 2004;42:831-9.
58. Ropers D, Baum U, Pohle K, et al. Detection of coronary artery stenoses with thin-slice multi-detector row spiral computed tomography and multiplanar reconstruction. Circulation 2003;107:664-666.
59. Nieman K, Cademartiri F., Lemos PA, et al. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. Circulation 2002;106:2051-2054.
60. Schuijf JD, Bax JJ, Shaw LJ, de Roos A, van der Wall EE, Wijns W, Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multi-slice computed tomography for non-

invasive coronary angiography (abstract). J Am Coll Cardiol 2005 (in press).

61. Schuijf JD, Bax JJ, Jukema JW, Lamb HJ, Warda HM, Vliegen HW, de Roos A, van der Wall EE. Feasibility of assessment of coronary stent patency using 16-slice computed tomography. Am J Cardiol 2004;94:427-30.
62. Underwood SR, Anagnostopoulos C, Cerqueira M, Ell PJ, Flint EJ, Harbinson M, Kelion AD, Al-Mohammad A, Prvulovich EM, Shaw LJ, Tweddel AC; British Cardiac Society; British Nuclear Cardiology Society; British Nuclear Medicine Society; Royal College of Physicians of London; Royal College of Radiologists. Myocardial perfusion scintigraphy: the evidence. Eur J Nucl Med Mol Imaging 2004;31:261-91.
63. Shaw LJ, Hachamovitch R, Berman DS, Marwick TH, Lauer MS, Heller GV, Iskandrian AE, Kesler K, Travin MI, Lewin HC, Hendel RC, Borges-Neto S, Miller DD for the Economics of Noninvasive Diagnosis (END) Multicenter Study Group. The economic consequences of available diagnostic and prognostic strategies for the evaluation of stable angina patients: An observational assessment of the value of pre-catheterization ischemia. J Am Coll Cardiol 1999;33:661-669.
64. Pasternak RC, Abrams J, Greenland P, Smaha LA, Wilson PW, Houston-Miller N. 34th Bethesda Conference: Task force #1–Identification of coronary heart disease risk: is there a detection gap? J Am Coll Cardiol 2003;41:1863-74.