

# CARDIAC COMPUTED TOMOGRAPHY: IS IT READY FOR PRIMETIME?

John J. Mahmarian

*From Methodist OeBailey Heart Center, Houston, Texas*

## INTRODUCTION

The last decade has witnessed dramatic improvements in computed tomography (CT) technology with the development of both electron beam (EB) and multi-detector (MD) CT systems. EBCT provided the first attempt at high-resolution "freeze frame" images of the heart and coronary arteries, with 50 msec image acquisition times obviating distortion and blurring of the continuously moving myocardium. Developments in MDCT have included increasing gantry speeds to improve temporal resolution and the addition of multiple detector arrays that allow submillimeter spatial resolution and reduced image acquisition times.

Although EBCT has higher temporal resolution than MDCT and lower radiation exposure through prospective triggering of the X-ray beam at a specific time in the cardiac cycle, MDCT provides higher spatial resolution and is generally more accessible to the medical community. Both techniques can be used to assess cardiac structure, determine the presence and extent of coronary artery calcification and provide high-resolution, noninvasive coronary angiography.

The following article describes the current proposed uses of cardiac CT and its potential integration with other imaging modalities such as stress tomographic myocardial perfusion imaging (SPECT).

## CORONARY ARTERY CALCIUM SCORING - SCREENING FOR CORONARY ARTERY DISEASE

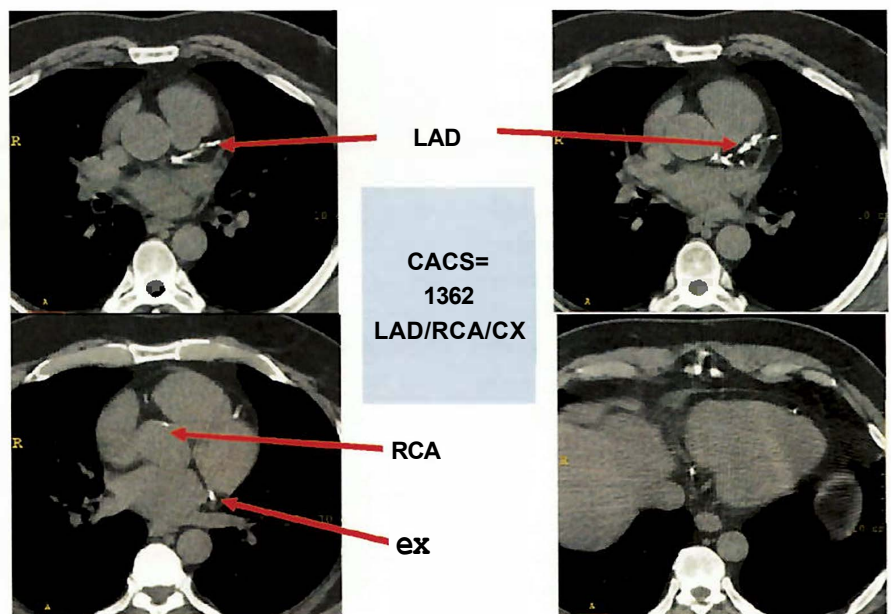
Despite improvements in the treatment of patients with advanced coronary artery disease (CAD), early detection and prevention remains the best long-term solution. While traditional risk factor analysis defines populations at risk for CAD, the commonly used Framingham risk score is imprecise at identifying CAD in asymptomatic individual patients. CT scanning can detect coronary artery calcification, which is highly specific for the presence of coronary atherosclerosis and increases relative to the extent of CAD (Figure 1).<sup>1</sup>

The coronary artery calcium score (CACS) is based on the extent and density of coronary calcification and can be used to guide therapeutic decision making, determine the need for additional diagnostic testing and predict subsequent patient outcome. Subjects with a CACS of 0 represent approximately 40% of all screened patients,<sup>2</sup> have a very low likelihood (<0.5%)

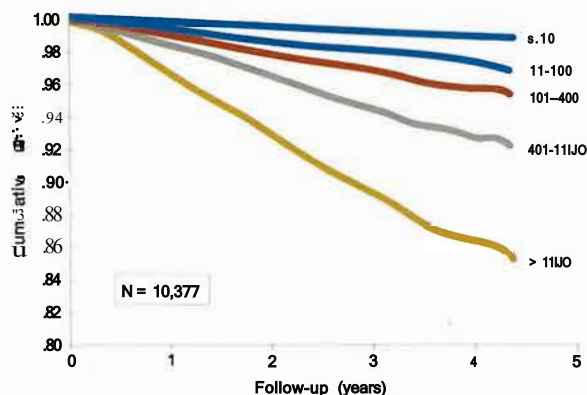
of significant (>50%) coronary artery stenosis<sup>3</sup> and have an excellent long-term prognosis (Figure 2).<sup>4</sup>

Multiple studies in more than 20,000 patients have shown an increase in cardiac event rates with higher CACS.<sup>4,10</sup> and

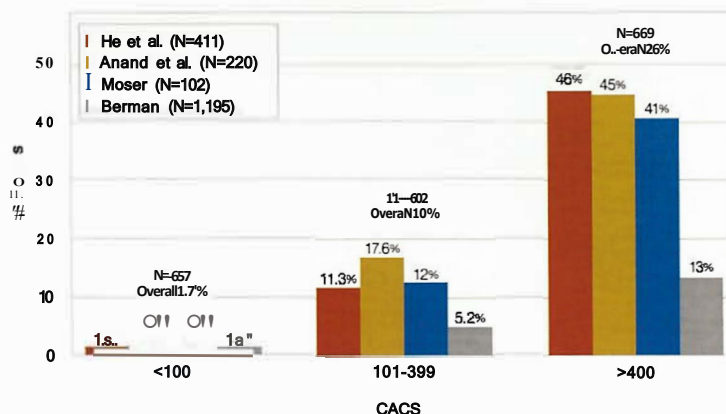
independent of biomarkers (C-reactive protein)<sup>11</sup> or risk predicted by clinical variables (i.e. Framingham Score).<sup>4-6,9</sup> Consistent with these prognostic studies, the likelihood of stress-induced ischemia increases with a higher CACS as



**Figure 1.** Representative multidetector CT scan showing extensive coronary artery calcification (arrows) in all three major coronary arteries. The coronary artery calcium score (CACS) was severe at 1362. Cx = circumflex; LAD = left anterior descending; RCA = right coronary artery



**Figure 2.** Survival curves based on CACS as determined by electron beam computed tomography in 10,377 subjects. A >1% mortality/year occurs when the CACS exceeds 400. Abbreviations as in Figure 1.



**Figure 3.** Relationship between coronary artery calcium score (CACS) results and an abnormal stress tomographic myocardial perfusion (SPECT) study. Patients with a CACS <100 have a low likelihood of SPECT positivity with a dramatic increase when the CACS is >400.

assessed by myocardial perfusion SPECT imaging. Published studies from investigators at Methodist DeBakey Heart Center and others<sup>12-14</sup> indicate that less than 2% of patients with a CACS <100 will have ischemia by stress SPECT, whereas this increases to more than 40% in the 10% of patients who have a CACS >400 (Figure 3).

Patients with coronary calcification should be treated the same as those with documented obstructive CAD, with aggressive risk factor modification and treatment of hyperlipidemia. Recent guidelines recommend that patients with a CACS <100 not undergo additional functional testing with stress SPECT unless they develop symptoms suggestive of ischemic heart disease, whereas patients with a CACS >400 should routinely be referred for functional testing due to the high but variable likelihood of significant CAD and silent myocardial ischemia.<sup>15,16</sup>

Patients with a moderate CACS of 100-400 may warrant further diagnostic testing depending on their risk factor profile and symptom status. It is generally recommended that asymptomatic men over age 45 and women over age 55 undergo CT screening for coronary artery calcification.<sup>16</sup> Recent studies also suggest that routine CT calcium

scoring may be warranted in patients who have a normal initial SPECT study since approximately 12% of them will have severe calcification and 18% will have a CACS >100/17

### CT CORONARY ANGIOGRAPHY

Contrast-enhanced CT coronary angiography became the next predictable technologic advancement beyond CAC scoring alone.<sup>18-36</sup> Both 16- and 64-slice multidetector CT scanners can be used to noninvasively visualize the coronary arteries.<sup>24,36</sup> Although there is little difference in diagnostic accuracy between these systems, the 64-slice scanners reduce the breath hold requirement by allowing faster acquisition of all CT image slices. However,

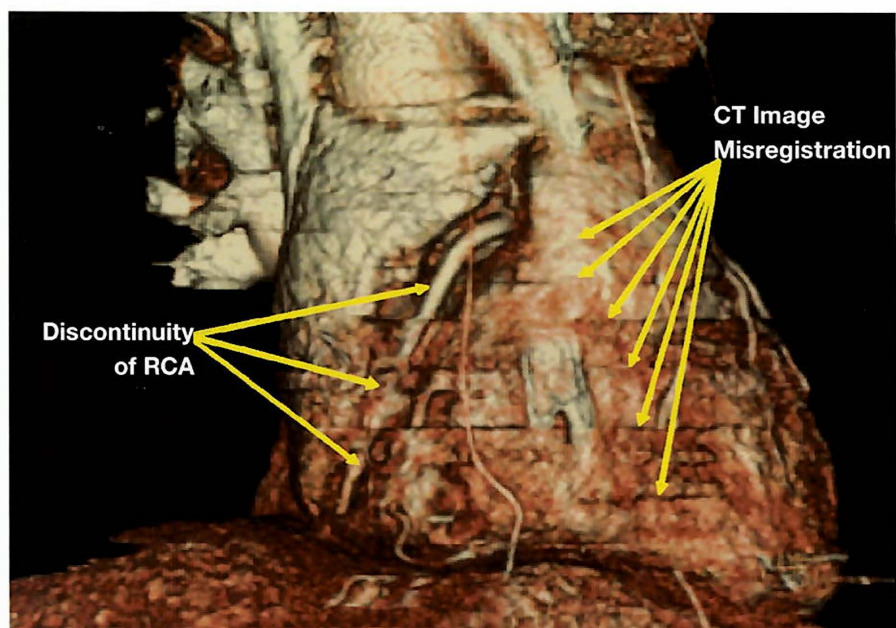
the temporal resolution (i.e. imaging time per slice) is similar for both 16 and 64 MDCT systems since this is dependent on gantry rotation speed and not the number of detectors.

As shown in Table 1, the percentage of analyzable arteries increases significantly from 4- to 16-slice detector systems but with similar diagnostic accuracy across all systems when the artery can be properly assessed. CT coronary angiography is very effective at excluding the presence of significant CAD, with a negative predictive value approaching 100%. However, the severity of arterial stenosis is overestimated approximately 30% of the time due to technical issues of spatial and temporal resolution and inadequate visualization of the lumen due to excessive coronary

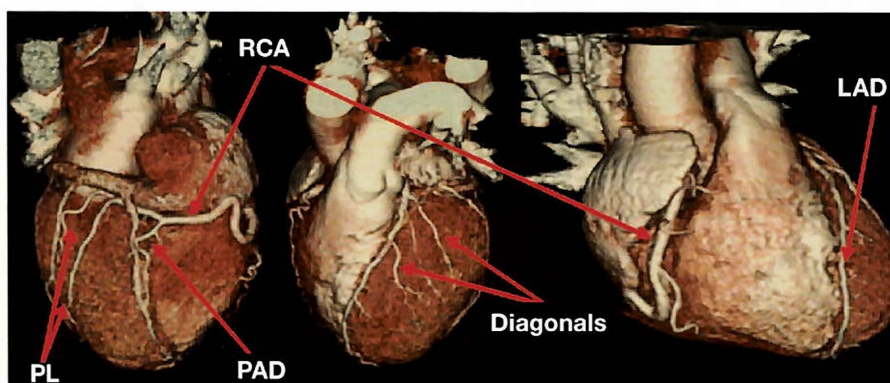
|                     | 4 Detector<br>(N=390) | 16 Detector**<br>(N=670) | 64 Detector<br>(N=129) |
|---------------------|-----------------------|--------------------------|------------------------|
| Analyzable Arteries | 70%                   | 90%                      | 89%                    |
| Sensitivity         | 80%                   | 85%                      | 82%                    |
| Specificity         | 96%                   | 95%                      | 96%                    |
| PPA                 | 76%                   | 76%                      | 64%                    |
| NPA                 | 97%                   | 97%                      | 98%                    |

\* Restricted generally to proximal and mid segments  
 \*\* Restricted generally to arteries >2mm

**Table 1.** Multidetector CT for identifying coronary artery stenosis.



**Figure 4.** Volume rendered view from a patient who moved during study acquisition. The misregistration of CT slice data prevented adequate coronary artery assessment. RCA = right coronary artery.



**Figure 5.** Volume rendered views of a CT angiography study acquired under optimal technical conditions. LAD = left anterior descending; PDA = posterior descending artery; PL = posterolateral branch; RCA = right coronary artery.

calcification or poor contrast opacification.<sup>34</sup> Thus, for patients in whom CT angiography detects significant stenosis, either invasive coronary angiography or a noninvasive functional assessment of ischemia is still recommended.

Proper patient preparation and screening for contraindications is essential for safely ensuring the highest quality studies (Table 2). Patients who have dysrhythmias are not optimal candidates for CT angiography since irregular rhythms will distort the images and render them uninterpretable. Due to the

limited temporal resolution of all current MDCT systems (~180 msec), heart rate needs to be reduced with beta-blockers (preferably below 65 beats/minute) to ensure imaging at end-diastole when there is minimal cardiac motion. This requirement may change in the future if dual source detector CT systems are shown to increase temporal resolution to <100 msec.<sup>37</sup> Adequate IV access is necessary since contrast is injected at 4-5 ml/sec. Of prime importance is a cooperative patient who can comply with directions and remain motionless

### Screen for contraindications

- Atrial fibrillation, bigeminy, trigeminy
- Severe asthma - inability to use beta-blockers
- Creatinine >1.5 mg/dl
- Pacemakers/defibrillators
- Contrast allergy
- Morbid obesity (BMI >40)
- Poor IV access (antecubital vein with 18-gauge IV)
- Inability to follow breath hold commands
- Inability to hold breath 10-20 seconds (depending on CT scanner)

**No caffeine for at least 12 hours prior to study**

**NPO for two hours**

**Beta-blockers to reduce heart rate, preferably <65 BPM**

### Patient education

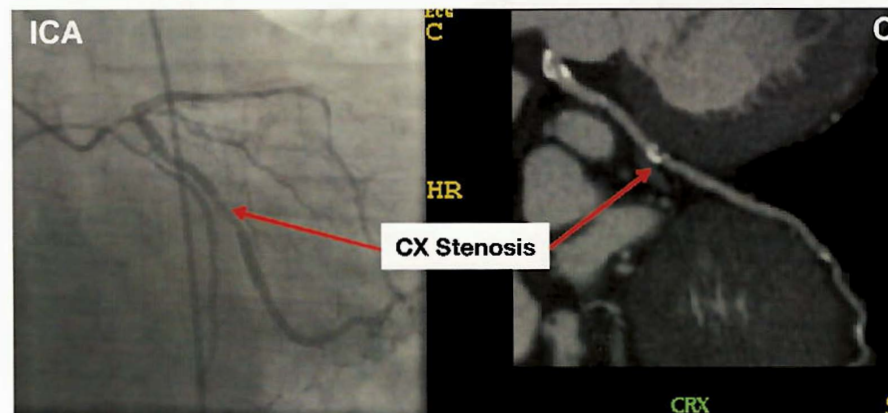
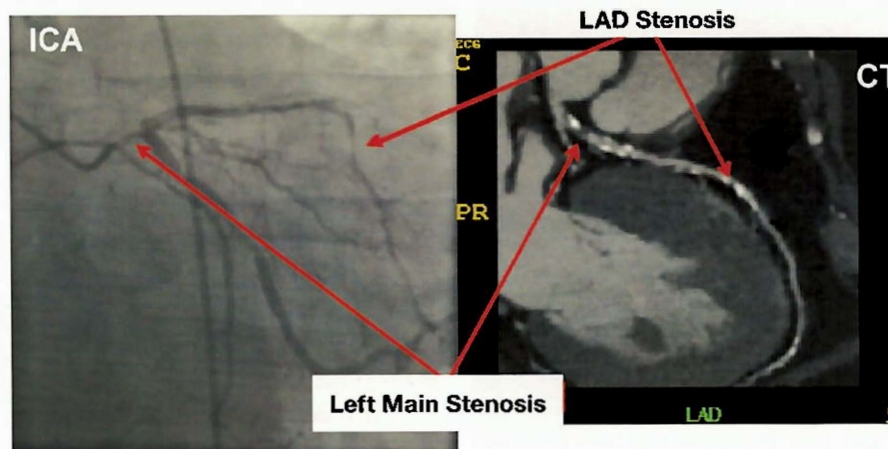
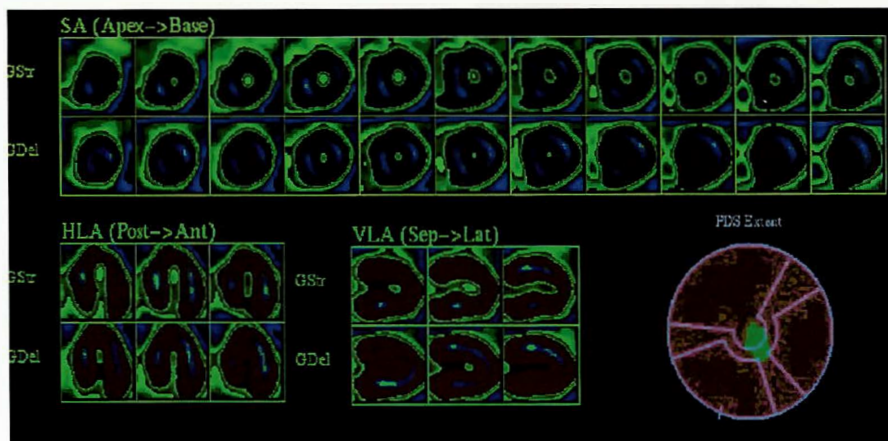
- Breath hold
- Motion
- Contrast bolus effects

**Table 2.** Proper patient preparation and screening prior to CT angiography.

throughout the 10-20 second breath hold that is required for image acquisition. Any chest motion resulting from coughing, swallowing or breaching will result in misregistration of the CT image and a suboptimal study (Figure 4). Additional contraindications include severe asthma with the inability to receive beta-blockers, renal insufficiency from the 80-120 ml of contrast administered or a known allergy to iodinated contrast materials. Diabetics taking metformin must discontinue using it the morning of the study and for several days thereafter. Excellent images can be obtained when patients are properly selected and prepared for CT angiography (Figure 5).

### SUMMARY

While still evolving, CT coronary angiography has already proven effective at diagnosing significant CAD (Figure 6), assessing coronary artery bypass graft (Figure 7) and stent patency (Figure 8) and identifying coronary artery anomalies (Figure 9).<sup>38,40</sup> CT angiography may also ultimately characterize and quantify the presence and extent of



**Figure 6.** Representative case illustrating the integration of CT coronary angiography and exercise SPECT results. This 52 year-old asymptomatic man was referred for SPECT due to nonspecific ST changes on the ECG. He exercised 6-1/2 minutes on the Bruce protocol, had no cardiac symptoms but developed 2.5 mm ST segment depression in the inferolateral leads. The SPECT images show only a small 4% ischemic defect in the apex (A). CT coronary angiography (CTA) was performed to define whether he had limited stenosis to the distal left anterior descending (LAD) or more advanced coronary artery disease. Although severe stenosis of the distal LAD was seen on CT, the patient also had severe stenosis of the left main extending into the proximal LAD (B) as well as moderate stenosis of the circumflex artery (Cx) (C). A good correlation was seen between invasive coronary angiography (ICA) and CTA. The patient underwent coronary artery bypass surgery for treatment of his left main stenosis.

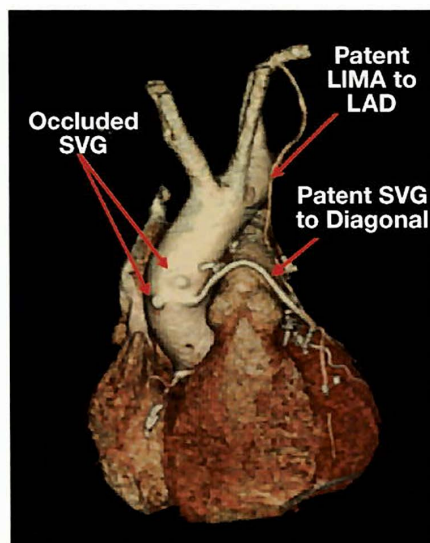
both calcified and noncalcified atherosclerotic plaque, which might better refine risk stratification.<sup>41-43</sup>

Another important area of research is the fusion of anatomic CT data with the functional information obtained during stress myocardial perfusion SPECT. Methodist DeBakey Heart Center currently has a SPECT-CT system that will allow coregistration of CT and nuclear perfusion data sets. This fusion of information should improve the diagnostic accuracy of CT and SPECT results (Figure 10) and more precisely tailor percutaneous coronary interventions by identifying which arteries in a specific patient supply ischemic myocardium.

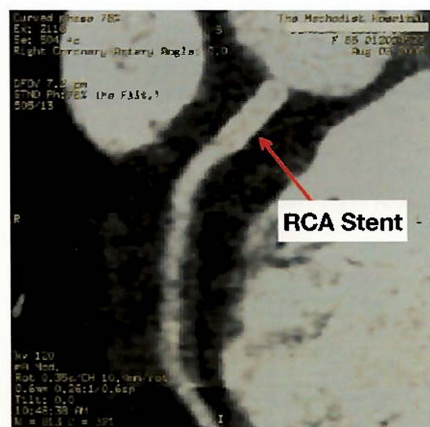
Finally, CT angiography will function as an essential roadmap for hot spot nuclear tracers currently being developed to target specific components of unstable atherosclerotic plaque. These future applications of fusion technology may better identify which patients with ischemia are at high risk for clinical events and thereby better guide therapeutic decision making.

## REFERENCES

1. 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.
2. He ZX, Hedrick TD, Pratt CM, Verani MS, Aquino V, Roberts R, Mahmarian J. Severity of coronary artery calcification by electron beam computed tomography predicts silent myocardial ischemia. *Circulation*. 2000 Jan 25;101:244-51.
3. Haberl R, Becker A, Leber A, Knez A, Becker C, Lang C, 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 Feb;37(2):451-1.
4. 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. *Radiology*. 2003 Sep;228(3):826-33.

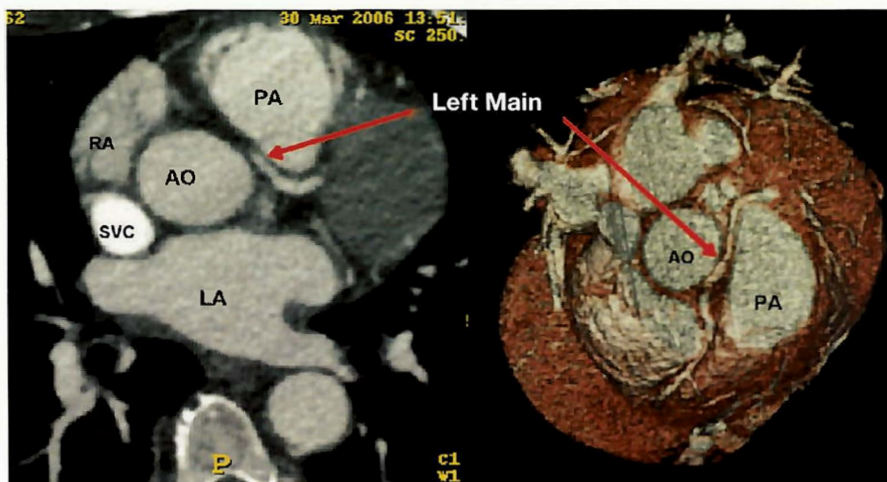


**Figure 7.** Representative volume rendered image of a patient with prior coronary artery bypass grafting. Saphenous vein graft (SVG) stumps are easily seen as well as a patent graft to the first diagonal and a patent left internal mammary artery (LIMA) graft to the distal left anterior descending (LAD) coronary artery.



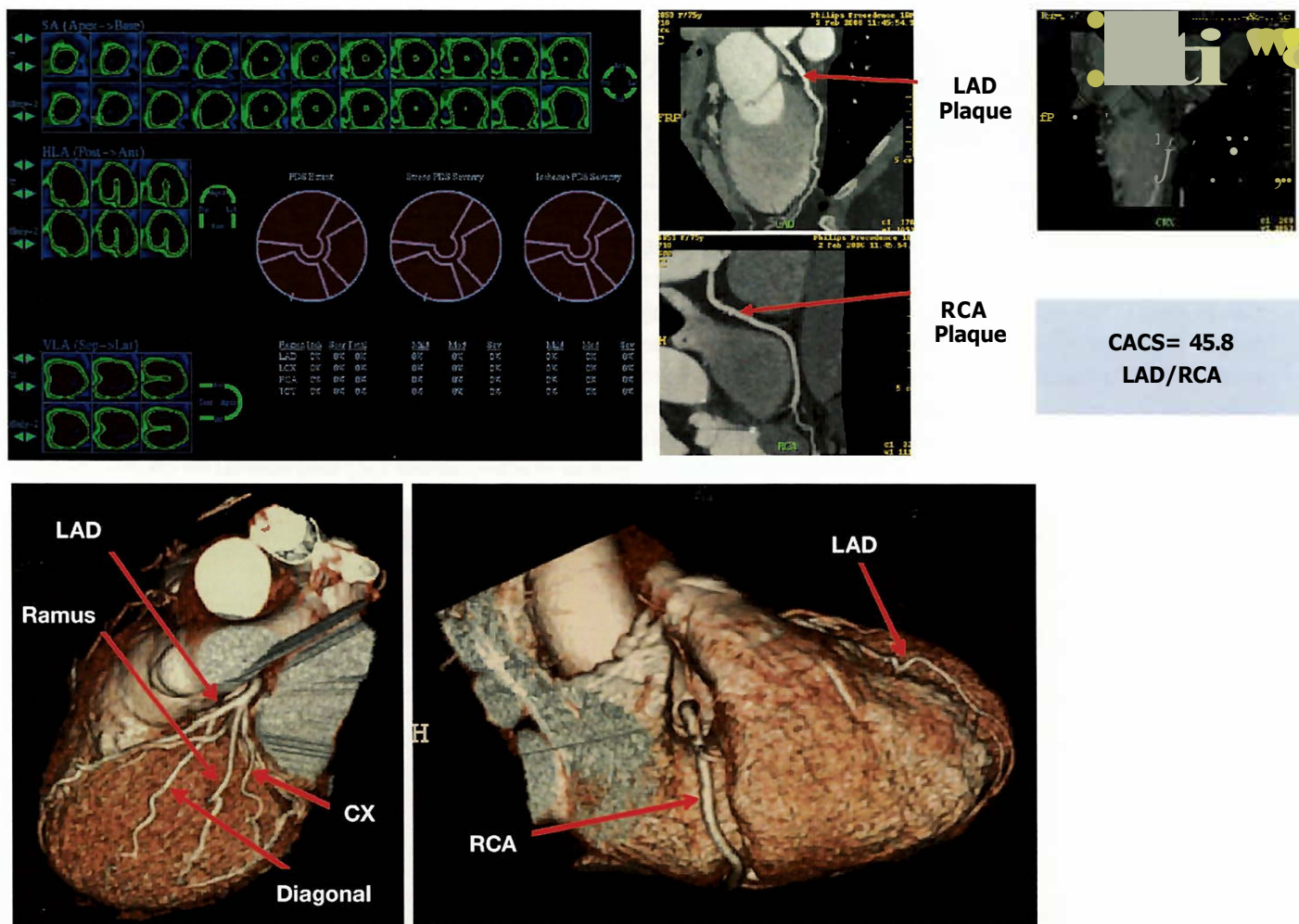
**Figure 8.** A patent stent in the proximal right coronary artery is well visualized.

5. Raggi P, Callister TQ, Cooll B, He ZX, Lippolis NJ, Russo DJ, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron-beam computed tomography. *Circulation*. 2000 Feb 29;101(8):850-5.
6. Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. *J Am Coll Cardiol*. 2000 Oct;36(4):1253-60.
7. Wong ND, Hsu JC, Detrano RC, Diamond G, Eisenberg H, Gardin JM. Coronary artery calcium evaluation by electron beam computed tomography and its relation to new cardiovascular events. *Am J Cardiol*. 2000 Sep 1;86(5):495-8.
8. Kondos GT, Hoff JA, Sevruckov A, Davighus ML, Garside DB, Devries SS, et al. 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 May 27;107(20):2571-6.
9. Arad Y, Goodman A, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. *J Am Coll Cardiol*. 2005 Jul 5;46(1):158-65.
10. Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. *J Am Coll Cardiol*. 2005 Sep 6;46(5):807-14.
11. Park R, Detrano R, Xiang M, Fu P, Ibrahim Y, LaBree L, et al. Combined use of computed tomography coronary calcium scores and C-reactive protein levels in predicting cardiovascular events in nondiabetic individuals. *Circulation*. 2002 Oct 15;106(16):2073-7.
12. Moser KW, O'Keefe JH Jr, 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 Nov-Dec;10(6):590-8.
13. Anand DV, 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 Nucl Cardiol*. 2004 Jul-Aug;11(4):450-1.
14. Berman DS, Wong ND, Gransar H, Miranda-Peats R, Dahlbeck J, Hayes SW, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. *J Am Coll Cardiol*. 2004 Aug 18;44(4):923-30.
15. Brindis RG, Douglas PS, Hendel RC, Peterson ED, Wolk MJ, Allen JM, et al. ACCF/ASNC appropriateness criteria for single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI): a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group and the American Society of Nuclear Cardiology endorsed by the American Heart Association. *J Am Coll Cardiol*. 2005 Oct 18;46(8):1587-605.
16. Naghavi M, Falk E, Hecht HS, Jamieson MJ, Kaul S, Berman D, et al; for the SHAPE Task Force. From Vulnerable Plaque to Vulnerable Patient - Part III: Executive Summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report. *Am J Cardiol*. 2006 Jul 17;98(2A):2H-15H.
17. Thompson RC, McGhie AI, Moser A-W, O'Keefe JH Jr, Stevens TL, House J, et al. Clinical utility of coronary calcium scoring after nonischemic myocardial perfusion imaging. *J Nucl Cardiol*. 2005 Jul-Aug;12(4):392-400.
18. Knez A, Becker CR, Leber A, Ohnesorge B, Becker A, White C, et al. Usefulness of multislice spiral computed tomography angiography for determination of coronary artery stenoses. *Am J Cardiol*. 2001 Nov 15;88(10):1191-4.
19. Achenbach S, Giesler T, Ropers D, Ulzheimer S, Derlien H, Schulte C, et al. ii. Detection of coronary artery stenoses by contrast-enhanced, retrospectively electrocardiographically-gated, multislice spiral computed tomography. *Circulation*. 2001 May 29;103(21):2535-8.
20. Nieman K, Rensing BJ, van Geuns RJ, Munne A, Ligthart JM, Pattynama PM, et al. Usefulness of multislice computed tomography for detecting obstructive coronary artery disease. *Am J Cardiol*. 2002 Apr 15;89(8):913-8.
21. Vogl TJ, Abolmaali ND, Diebold T, Engelman K, Ay M, Dogan S, et al. Techniques for the detection of coronary atherosclerosis: multi-detector row CT coronary angiography. *Radiology*. 2002 Apr;223(1):212-20.
22. Giesler T, Baum U, Ropers D, Ulzheimer S, Wenke E, Mennicke M, et al. Noninvasive visualization of coronary arteries using



**Figure 9.** Coronary anomaly with the left main arising from the right sinus of Valsalva and tracking between the pulmonary artery (PA) and ascending aorta (AO). The patient had exertional chest pain and a stress echocardiogram demonstrating ischemia in the anterior wall. At the time of invasive coronary angiography, the left main ostium could not be found. CT angiography was diagnostic and the patient was referred for coronary artery bypass surgery. LA = left atrium; RA = right atrium; SVC = superior vena cava.

- contrast-enhanced multidetector CT: influence of heart rate on image quality and stenosis detection. *AJR Am J Roentgenol.* 2002 Oct;179(4):911-6.
23. Kuettner A, Kopp AF, Schroeder S, Rieger T, Brunn J, Meisner C, et al. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with angiographically proven coronary artery disease. *J Am Coll Cardiol.* 2004 Mar 3;43(5):831-9.
  24. Nieman K, Cademartiri F, Lemos PA, Raaijmakers R, Pattynama PM, de Feyter PJ. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. *Circulation.* 2002 Oct 15;106(16):2051-4.
  25. Ropers D, Baum U, Pohle K, Anders K, Ulzheimer S, Ohnesorge B, et al. Detection of coronary artery stenoses with thin-slice multi-detector row spiral computed tomography and multiplanar reconstruction. *Circulation.* 2003 Feb 11;107(5):664-6.
  26. Mollet NR, Cademartiri F, Krestin GP, McFadden EP, Arampatzis CA, Serruys PW, et al. Improved diagnostic accuracy with 16-row multislice computed tomography coronary angiography. *J Am Coll Cardiol.* 2005 Jan 4;45(1):128-32.
  27. Kuettner A, Beck T, Drosch T, Kettering K, Heuschmid M, Burgstahler C, et al. Diagnostic accuracy of noninvasive coronary imaging using 16-detector slice spiral computed tomography with 188 ms temporal resolution. *J Am Coll Cardiol.* 2005 Jan 4;45(1):123-7.
  28. Heuschmid M, Kuettner A, Schroeder S, Trabold T, Feyer A, Seemann MD, et al. ECG-gated 16-MDCT of the coronary arteries: assessment of image quality and accuracy in detecting stenoses. *AJR Am J Roentgenol.* 2005 May;184(5):1413-9.
  29. Kifer J, Cifuentes E, Legros G, Pasquet A, Grandin C, Van Beers BE, et al. Head-to-head comparison of three-dimensional navigator-gated magnetic resonance imaging and 16-slice computed tomography to detect coronary artery stenosis in patients. *J Am Coll Cardiol.* 2005 Jul 5;46(1):92-100.
  30. Kuettner A, Trabold T, Schroeder S, Feyer A, Beck T, Brueckner A, et al. Noninvasive detection of coronary lesions using 16-detector multislice spiral computed tomography technology: initial clinical results. *J Am Coll Cardiol.* 2004 Sep 15;44(6):1230-7.
  31. Hoffmann U, Milewski F, Cury RC, Ferencik M, Jang IK, Diaz LJ, et al. Predictive value of 16-slice multidetector spiral computed tomography to detect significant obstructive coronary artery disease in patients at high risk for coronary artery disease: patient-versus segment-based analysis. *Circulation.* 2004 Oct 26;110(17):2638-43.
  32. Mollet NR, Cademartiri F, Nieman K, Saia F, Lemos PA, McFadden EP, et al. Multislice spiral computed tomography coronary angiography in patients with stable angina pectoris. *J Am Coll Cardiol.* 2004 Jun 16;43(12):2265-70.
  33. Hoffmann MH, Shi H, Schmitz BL, Schmid FT, Lieberknecht M, Schulze R, et al. Noninvasive coronary angiography with multislice computed tomography. *JAMA.* 2005 May 25;293(20):2471-8.
  34. Garcia MJ, Lessick J, Hoffmann MH, CATSCAN Study Investigators. Accuracy of 16-row multidetector computed tomography for the assessment of coronary artery stenosis. *JAMA.* 2006 Jul 26;296(4):403-11.
  35. Raff CL, Gallagher MJ, O'Neill WW, Goldstein JA. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. *J Am Coll Cardiol.* 2005 Aug 2;46(3):552-7.
  36. Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, et al. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol.* 2005 Jul 5;46(1):147-54.
  37. Achenbach S, Ropers D, Kuettner A, Flohr T, Ohnesorge B, Bruder H, et al. Contrast-enhanced coronary artery visualization by dual-source computed tomography: initial experience. *Eur J Radiol.* 2006 Mar;57(3):331-5.
  38. Anders K, Baum U, Schmid M, Ropers D, Schmid A, Pohle K, et al. Coronary artery bypass graft (CABG) patency: Assessment with high-resolution submillimeter 16-slice multidetector-row computed tomography (MDCT) versus coronary angiography. *Eur J Radiol.* 2006 Mar;57(3):336-44.
  39. Schlusser T, Konorza T, Hunold P, Kuhl H, Schmermund A, Barkhausen J. Noninvasive visualization of coronary artery bypass grafts using 16-detector row computed tomography. *J Am Coll Cardiol.* 2004 Sep 15;44(6):1224-29.
  40. Gaspar T, Halon DA, Lewis BS, Adawi



**Figure 10.** Computed tomography for clarifying equivocal SPECT results. This 75-year old woman was referred for exercise SPECT due to a history of atypical chest pain. The patient exercised for seven minutes on the Bruce protocol but developed 2 mm ST-segment depression with chest pressure radiating to the jaw. The SPECT images (A) show normal perfusion. The post-stress ejection fraction by gated SPECT was 75%. CT angiography was performed to clarify whether significant coronary artery disease was present. The volume rendered images (B) show a high quality study. By CT, the patient had a mild CACS (45.8) with the coronary arteriograms showing no significant obstructive CAD (C). Abbreviations as in other figures.

- S. Schliamer JE, Rubinshtein R, et al. Diagnosis of coronary in-stent restenosis with multidetector row spiral computed tomography. *J Am Coll Cardiol.* 2005 Oct 18;46(8):1573-9.
41. Achenbach S, Moselewski F, Ropers D, Ferencik M, Hoffmann U, MacNeill B, et al. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: a segment-based comparison with intravascular ultrasound. *Circulation.* 2004 Jan 6;109(1):14-1
42. Leber AW, Knez A, Becker A, Becker C, von Ziegler F, Nikolaou K, et al. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intracoronary ultrasound. *J Am Coll Cardiol.* 2004 Apr 7;43(7):1241-1
43. Leber AW, Becker A, Knez A, von Ziegler F, Sirol M, Nikolaou K, et al. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. *J Am Coll Cardiol.* 2006 Feb 7;47(3):672-1