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EXPERT CONSENSUS DOCUMENT

ACCF/ACR/AHA/NASCI/SAIP/SCAI/SCCT 2010 Expert Consensus Document on Coronary Computed Tomographic Angiography

A Report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents

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Preamble

This document was developed by the American College of Cardiology Foundation (ACCF) Task Force on Clinical Expert Consensus Documents (ECDs) and cosponsored by the American College of Radiology (ACR), American Heart Association (AHA), American Society of Nuclear Cardiology (ASNC), North American Society for Cardiovascular Imaging (NASCI), Society of Atherosclerosis Imaging and Prevention (SAIP), Society for Cardiovascular Angiography and Interventions (SCAI), and Society of Cardiovascular Computed Tomography (SCCT) to provide

a perspective on the current state of computed tomographic angiography (CTA). ECDs are intended to inform practitioners and other interested parties of the opinion of the ACCF and document cosponsors concerning evolving areas of clinical practice and/or technologies that are widely available or new to the practice community. Topics are chosen for coverage because the evidence base, the experience with technology, and/or the clinical practice are not considered sufficiently well developed to be evaluated by the formal ACCF/AHA practice guidelines process. Often the topic is the subject of ongoing investigation. Thus, the reader should view the ECD as the best attempt of the ACCF and document cosponsors to inform and guide clinical practice in areas where rigorous evidence may not be available or the evidence to date is not widely accepted. When feasible, ECDs include indications or contraindications. Some topics covered by ECDs will be addressed subsequently by the ACCF/AHA Practice Guidelines Committee.

The task force makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest to inform the writing effort. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur. The relationships and industry information for writing committee members and peer reviewers are published in Appendix 1 and Appendix 2 of the document, respectively.

Robert A. Harrington, MD, FACC, FAHA
Chair, ACCF Task Force on
Clinical Expert Consensus Documents

1. Introduction

1.1. Writing Committee Organization

The writing committee consisted of acknowledged experts in the field of CTA, as well as a liaison from the ACCF Task Force on Clinical ECDs, the oversight group for this document. In addition to 2 ACCF members, the writing committee included 2 representatives from the ACR and AHA and 1 representative from ASNC, NASCI, SAIP, SCAI, and SCCT. Representation by an outside organization does not necessarily imply endorsement.

1.2. Document Development Process

1.2.1. Relationships With Industry and Other Entities

At its first meeting, each member of the writing committee reported all relationships with industry and other entities relevant to this document topic. This information was updated, if applicable, at the beginning of all subsequent meetings and full committee conference calls. As noted in the Preamble, relevant relationships with industry and other entities of writing committee members are published in Appendix 1.

1.2.2. Consensus Development

During the first meeting, the writing committee discussed the topics to be covered in the document and assigned lead authors for each section. Authors conducted literature searches and drafted their sections of the document outline. Over a series of meetings and conference calls, the writing committee reviewed each section, discussed document content, and ultimately arrived at consensus on a document that was sent for external peer review. Following peer review, the writing committee chair engaged authors to address reviewer comments and finalize the document for document approval by participating organizations. Of note, teleconferences were scheduled between the writing committee chair and members who were not present at the meetings to ensure consensus on the document.

1.2.3. External Peer Review

This document was reviewed by 15 official representatives from the ACCF (2 representatives), ACR (2 representatives), AHA (2 representatives), ASNC (1 representative), NASCI (2 representatives), SAIP (2 representatives), SCAI (2 representatives), and SCCT (2 representatives), as well as 10 content reviewers, resulting in 518 peer review comments. See list of peer reviewers, affiliations for the review process, and corresponding relationships with industry and other entities in Appendix 2. Peer review comments were entered into a table and reviewed in detail by the writing committee chair. The chair engaged writing committee members to respond to the comments, and the document was revised to incorporate reviewer comments where deemed appropriate by the writing committee.

In addition, a member of the ACCF Task Force on Clinical ECDs served as lead reviewer for this document. This person conducted an independent review of the document at the time of peer review. Once the writing committee documented its response to reviewer comments and updated the manuscript, the lead reviewer assessed whether all peer review issues were handled adequately or whether there were gaps that required additional review. The lead reviewer reported to the task force chair that all comments were handled appropriately and recommended that the document go forward to the task force for final review and sign-off.

1.2.4. Final Writing Committee and Task Force Sign-Off on the Document

The writing committee formally signed off on the final document, as well as the relationships with industry that would be published with the document. The ACCF Task Force on Clinical ECDs also reviewed and formally approved the document to be sent for organizational approval.

1.2.5. Document Approval

The final version of the document, along with the peer review comments and responses to comments were circulated to the ACCF Board of Trustees for review and approval. The document was approved in November 2009. The document was then sent to the governing boards of the ACR, AHA, ASNC, NASCI, SAIP, SCAI, and SCCT for endorsement consideration, along with the peer review comments/responses for their respective official peer reviewers. ACCF, ACR, AHA, NASCI, SAIP, SCAI, and SCCT formally endorsed this document. This document will be considered current until the ACCF Task Force on Clinical ECDs revises or withdraws it from publication.

1.3. Purpose of This Expert Consensus Document

This document presents an expert consensus overview of the current and emerging clinical uses of coronary CTA in patients with suspected or known coronary artery disease (CAD). Since the evidence base for this technology is not felt to be sufficiently mature to support a clinical practice guideline at present, this ECD offers an alternative vehicle in which the state of the art of coronary CTA can be described without the requirement to provide explicit recommendations accompanied by formal ratings of the quality of available evidence.

The intention of this document is to summarize the strengths and weaknesses of current clinical uses of coronary CTA as reflected in the published peer-reviewed literature and as interpreted by the writing committee. The document is not intended primarily as either a comprehensive literature review or as an instruction guide for those interested in performing or interpreting coronary computed tomography (CT) angiograms. The document also does not offer specific statements rating the appropriateness of various potential clinical uses of coronary CTA, as this has been dealt with in the ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 Appropriateness Criteria for Cardiac Computed Tomography and Cardiac Magnetic Resonance Imaging (1). Finally, this document does not address the evaluation of coronary calcium using CT, except as it pertains to CTA studies in patients with suspected or known CAD, since this topic has also been covered in the ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain (1a).

2. Executive Summary

Advances in CT imaging technology, including the introduction of multidetector row systems with electrocardiographic gating, have made imaging of the heart and the coronary arteries feasible. The potential to obtain information noninvasively comparable to that provided by invasive coronary angiography has been the major driving force behind the rapid growth and dissemination of cardiac CT imaging. In the future, the ability of CTA to provide information not currently available from invasive angiography may provide the basis for a major shift in how patients with atherosclerotic cardiovascular disease are classified and managed. Currently, cardiac CTA can provide information about coronary anatomy and left ventricular (LV) function that can be used in the evaluation of patients with suspected or known CAD.

The technology for performing coronary CT angiograms is evolving at a rate that often outpaces research evaluating its incremental benefits. Multidetector CT technology prior to 64-channel or "slice" systems should now be considered inadequate for cardiac imaging (except for studies limited to assessing coronary calcium). The incremental value of recently introduced CT hardware with 128-, 256-, and 320-channel systems over 64-channel systems has not yet been determined. As with any diagnostic technology, coronary CTA has technical limitations with which users should be familiar, and proper patient selection and preparation are important to maximize the diagnostic accuracy of the test. Most cardiac CTA examinations result in a large 4-dimensional (4D) dataset of the heart obtained over the entire cardiac cycle. Physicians who interpret these examinations must be able to analyze the image data interactively on a dedicated workstation and combine knowledge of the patient with expertise in coronary anatomy, coronary pathophysiology, and CT image analysis techniques and limitations. In addition, integration of coronary CTA data into clinical practice requires that the results be evaluated in terms of what was known diagnostically and prognostically before the test was performed and, thus, what incremental information the test provides. The ability of a test such as coronary CTA to provide incremental diagnostic information that alters management (as contrasted with increasing diagnostic certainty alone) is heavily dependent both on the pretest probability and on the alternative diagnostic strategies considered.

The published literature on the diagnostic accuracy of 64-channel coronary CTA compared with invasive coronary angiography as of June 2009 consists of 3 multicenter cohort studies along with over 45 single-center studies, many of the latter involving fewer than 100 patients. This literature reflects careful selection of study subjects and test interpretation by expert readers, typically with exclusion of patients who would be expected to have lower quality studies, such as those with irregular heart rates (e.g., atrial fibrillation), obesity, or inability to comply with instructions for breath holding. In addition, because the cohorts for these studies were assembled from patients referred for invasive coronary angiography, they do not necessarily reflect, in terms of obstructive CAD prevalence or clinical presentation, the population to which coronary CTA is most likely to be applied in clinical practice. Accepting these caveats, some consistent conclusions emerge from this literature that may be useful in clinical decision making. In these studies,

overall sensitivity and specificity on a per-patient basis are both high, and the number of indeterminate studies due to inability to image important coronary segments in the select cohorts represented is less than 5%. In most circumstances, a negative coronary CT angiogram rules out significant obstructive coronary disease with a very high degree of confidence, based on the post-test probabilities obtained in cohorts with a wide range of pretest probabilities. However, post-test probabilities following a positive coronary CT angiogram are more variable, due in part to the tendency to overestimate disease severity, particularly in smaller and more distal coronary segments or in segments with artifacts caused by calcification in the arterial walls. At present, data on the prognostic value of coronary CTA using 64-channel or greater systems remain quite limited. Furthermore, no large-scale studies have yet made a direct comparison of long-term outcomes following conventional diagnostic imaging strategies versus strategies involving coronary CTA.

As with invasive coronary angiography, the results of coronary CTA are often not concordant with stress single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI). The differences in the parameters measured by MPI ("function" or "physiology") and CTA ("anatomy") must be considered when making patient management decisions with these studies. Of note, a normal MPI does not exclude the presence of coronary atherosclerosis although it does signify a very low risk of future major adverse events over the short to intermediate term. Conversely, coronary CTA allows detection of some coronary atherosclerotic plaques that are not hemodynamically significant. The optimal management of such disease has not been established. Neither test can presently identify with any reasonable clinical probability nonobstructive coronary plaques that might rupture in the future and cause acute myocardial infarction (MI). Invasive coronary angiography has a similar limitation.

Studies comparing coronary CTA with fractional flow reserve (FFR) measured as part of invasive coronary angiographic studies complement the MPI comparisons described in the preceding text by showing that coronary CTA anatomic data do not provide very accurate insights into the probability that specific lesions will produce clinically significant ischemia. Similar observations have been made about the relationship of FFR data and the anatomic information provided by invasive coronary angiography.

In the context of the emergency department evaluation of patients with acute chest discomfort, currently available data suggest that coronary CTA may be useful in the evaluation of patients presenting with an acute coronary syndrome (ACS) who do not have either acute electrocardiogram (ECG) changes or positive cardiac markers. However, existing data are limited, and large multicenter trials comparing CTA with conventional evaluation strategies are needed to help define the role of this technology in this category of patients.

Coronary CTA imaging of patients with prior coronary bypass surgery yields very accurate information about the state of the bypass grafts but less accurate information about the native arteries distal to the bypasses and the ungrafted arteries. Because chest pain after bypass surgery might be associated with disease progression in either a graft or a native coronary artery, the difficulty of accurately assessing the native vessels is an important limitation for the clinical use of coronary CTA in the post-bypass patient.

Coronary stents pose some significant technical challenges for coronary CTA, since the metal in the stents may create several types of artifacts in the images. Special algorithms are now routinely used that may reduce some of these artifacts during image reconstruction. The literature suggests that in patients who have large diameter stents, good image quality, and whose clinical presentation suggests low-to-intermediate probability for restenosis, 64-channel coronary CTA can be used to rule out severe in-stent restenosis. There are no studies that directly compare a coronary CTA strategy with an invasive coronary angiography strategy in patients with coronary stents, and such data will be required to understand the efficiencies and tradeoffs of these 2 strategies in this population.

The literature on the assessment of LV function using cardiac CTA in patients with suspected or known CAD is much smaller than that for diagnostic coronary imaging. One likely reason is that echocardiography already provides a readily available, noninvasive means of assessing ventricular function and wall motion and does so without exposing patients to ionizing radiation or iodinated contrast agents.

Available comparisons with cardiovascular magnetic resonance (CMR) suggest that CTA estimation of LV ejection fraction is accurate over a wide range of values. Accuracy may, however, be reduced at higher heart rates due to difficulties in capturing end-systolic and end-diastolic phases accurately. Use of some newer strategies to reduce the radiation dose of coronary CTA studies, such as sequential scanning, will eliminate the ability to assess LV function with the same study.

The writing committee considered several emerging applications where empirical data were deemed insufficient to support development of a consensus. Imaging of noncalcified coronary plaques may in the future become a useful application for coronary CTA, but it has no role in current practice since there are insufficient data to assess its clinical utility. CTA assessment of total atherosclerotic burden and potential plaque vulnerability similarly will require substantial additional technical development and clinical investigation to define their potential value in patient management.

The writing committee identified 3 areas without consensus: the interpretation of incidental noncardiac findings on the CT examination, the use of coronary CTA in asymptomatic subjects, and the "triple rule-out" examination of patients with acute chest pain in the emergency department.

Use of coronary CTA raises 2 important safety issues: 1) the amount of radiation absorbed by the body tissues; and 2) the exposure to iodinated contrast agents that have the potential to produce allergic reactions and acute renal injury. Median effective radiation dose (which is a calculated rather than empirically measured quantity) for coronary CTA with current technology was 12 mSv in a cross-sectional international study of 50 sites (both academic and community) assessed in 2007. Individual sites in this study varied from a median of 5 to 30 mSv. In a 15-hospital imaging registry in Michigan in 2007, prospective use of a set of best practice radiation dose reduction recommendations resulted in a reduction in the average scan effective radiation dose from 21 mSv to 10 mSv with no reduction in image quality.

Several preliminary economic studies using claims data and/or modeling have examined the use of coronary CTA in the diagnostic evaluation of suspected coronary disease and in the evaluation of acute chest pain in the emergency department. Within the limits imposed by the data available, these studies suggest that a diagnostic strategy using coronary CTA may potentially reduce both the time spent in the diagnostic process and the overall costs of clinical evaluation in selected populations, particularly in lower-risk subjects who otherwise would have been subjected to more expensive and possibly less accurate testing strategies. However, longer-term empirical studies will be required to establish the full economic impact of this technology in contemporary practice.

3. Perspective and Scope of This Document

This document focuses on the perspective of clinicians caring for patients with suspected or known CAD in evaluating the potential current uses for cardiac CTA. Therefore, the use of cardiac CTA for other primary clinical questions, such as the diagnosis of pulmonary embolism, pulmonary parenchymal disease, pericardial disease, cardiac masses, arrhythmogenic right ventricular dysplasia, thoracic aortic disease, and congenital heart disease will not be directly addressed. Such disorders, of course, are relevant to the subject matter of this report when they are identified by the cardiac CT angiogram as a possible cause of the patient's symptoms. This report does consider cardiac CT angiographic estimation of LV ejection fraction and evaluation of regional wall-motion abnormalities because these findings may help refine the assessment of the severity and clinical relevance of CAD. Detection of coronary calcium by CT has been addressed in the ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by CT in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain (1a), and therefore will not be considered here except where assessment of coronary calcification is relevant to the performance and interpretation of coronary CTA. Information provided by coronary CTA that is relevant to the patient with suspected or known CAD is considered to the extent made possible by the available published evidence. The writing committee felt that abstracts and oral presentations were not sufficiently reliable sources to be used in the construction of this document.

4. Coronary CT Angiography: Brief Overview of the Technology

Noninvasive coronary imaging requires a system capable of acquiring motion-free, high spatial resolution images within less than 20 seconds, while patients are holding their breath. Current generation 64-channel multidetector row computed tomography (MDCT) fulfills these requirements reasonably well (2). This section will briefly review selected technical and interpretive issues specifically relevant to the performance of MDCT coronary imaging. Readers of the literature should not be confused by the fact that several equivalent terms are used to refer to this technology, including multidetector CT, multidetector row CT, multislice CT, and multichannel CT.

Appropriate patient selection and preparation are major preimaging determinants of image quality. Key aspects of the imaging process include heart rate and rhythm control, the proper timing of the scan relative to the introduction of the intravenous contrast bolus into the circulation, and minimization of patient motion. Interactive image reconstruction techniques are critical to proper diagnostic interpretation but cannot remedy deficiencies in collection of raw radiographic data. The determinants of patient radiation dose and the trade-offs between radiation dose and image quality are discussed in Section 11, Safety Considerations.

4.1. Patient Selection and Preparation

Image quality of coronary CTA is improved by achieving a slow, regular heart rate, excluding very obese patients, selecting patients able to cooperate with instructions to be motionless and to hold their breath during imaging, and by assessing the presence and distribution of coronary calcification. All of these are evident from an initial patient evaluation except coronary calcification, which is typically assessed during the precontrast scans taken at the start of imaging. At present, there is no firm consensus on the extent of coronary calcification that precludes a technically adequate coronary CT angiogram. Innovations in the scanning process currently under investigation may reduce the importance of this issue in the future.

Patient preparation steps include achieving intravenous access, typically in an antecubital vein suitable for contrast administration at a flow rate of 4 to 6 mL/s, and administering preprocedure beta blockade when needed to achieve the desired heart rate and rhythm. Administration of sublingual nitroglycerin can be used to enhance coronary vasodilatation at the time of imaging. Rehearsal of the

breath hold with the patient improves compliance, serves to decrease patient anxiety, and may lessen motion artifact as a result. The rehearsal of breathing instructions can also be used as an opportunity to identify any unusual effects that might occur to heart rate and regularity from breath holding in individual patients.

4.2. Coronary CT Image Acquisition

CT is an excellent method of creating high-resolution, volumetric images of body structures that can be held relatively stationary. In such situations, current generation CT systems can resolve very small, submillimeter, abnormalities. Movement of the target organ creates the need for high-temporal resolution to reduce motion-related blurring artifacts. Two kinds of motion, respiratory and cardiac, must be controlled during CT imaging of the coronary arteries. Careful patient selection and preimaging coaching can control respiratory motion via a voluntary breath hold. Breath-hold times on 64-channel systems for a cardiac CTA range from 10 to 15 seconds (may be shorter on systems with 128 channels or higher) and are well within the capability of most patients, even those with respiratory compromise. Strategies to "control" cardiac motion rely on a combination of pharmacology and technology. The coronary arteries move in a complex pattern through space during each cardiac cycle. Each coronary artery moves at a different velocity and in a different pattern from the others, and even the individual segments of each coronary do not move uniformly (3). Because coronary artery velocity and acceleration during the cardiac cycle increase with higher heart rates, preimaging heart rate control with beta blockers is commonly used to slow coronary motion and is an important part of patient preparation (4). In 1 multicenter international study of 1965 patients undergoing coronary CTA, 12% of subjects were on daily beta blockers prior to study and an additional 46% received beta blockers in preparation for their scan (5). As the heart rate decreases, the phase of relative cardiac quiescence in mid- to late-diastole (at approximately 60% to 75% of the R to R interval) widens. With a sufficiently slow heart rate, typically between 50 to 65 beats per minute, ECG gating can be used to select (retrospectively) the portion of the cardiac cycle for image reconstruction where the motion of each coronary segment is at a minimum. Due to different patterns of motion during the cardiac cycle, the optimal images for defining details of the right coronary artery may occur in a different phase of the cardiac cycle from the optimal images of the left coronary artery.

4.2.1. Temporal Resolution of a CT Scan

The temporal resolution of a CT scan, or the ability to resolve separate points in time, is determined in CT acquisition by the time required to acquire the data for reconstruction of a single transverse section or "slice." Thus, the speed of gantry rotation (the gantry contains both the X-ray source and the detector array and is rotated around the patient during imaging) is one of the primary determinants of the temporal resolution of the MDCT scan. The minimum gantry rotation time on current generation scanners (the time required to complete a 360° rotation) is between 280 and 400 ms, depending on the manufacturer and model. Tremendous centrifugal forces are created by the need to spin the imaging components inside the gantry around the patient and significant further increases in rotation times are limited by the ability of current mechanical components to withstand such forces. Thus, alternative methods have been employed to further improve temporal resolution. The routine use of half-scan reconstruction results in an effective temporal resolution of approximately one half the time required for the CT gantry to complete a single 360° rotation or approximately 140 to 200 ms (6). Other methods include the use of partial scan reconstructions from multiple adjacent cardiac cycles to improve effective temporal resolution. In 2007, a "dual-source" CT scanner was introduced that contained 2 X-ray sources and 2 sets of detectors offset 90° from each other in the CT gantry (7). This configuration is able to achieve an additional improvement in temporal resolution (to approximately 83 ms) by combining the data from the 2 detectors using just 90° of gantry rotation as opposed to the required 180° of gantry rotation needed with a single-source system (8). However, half-scan and partial-scan reconstructions may decrease spatial resolution due to misregistration artifacts. For reference, conventional invasive angiography using 30 frames per second has a temporal resolution of approximately 33 ms (9).

4.2.2. Spatial Resolution of a CT Scan

Spatial resolution of a CT scan is defined in terms of the in-plane or x-y axis resolution and the through-plane or z-axis resolution. The *x-y spatial resolution* of a CT scan is the smallest distance between 2 high-contrast objects that still allows recognizing the objects as separate. Modifiable parameters that can affect in-plane resolution include the reconstruction algorithm that translates the projection data into planar images, the reconstructed field of view and the image matrix size (typically 512 × 512 pixels). The principal limit on the *z-axis*, or *"slice" resolution* (along the patient's long axis), lies in the detector array geometry. Within the detector array are rows of array elements, which are typically 0.4 to 0.6 mm in size along the z-axis. Thus, a "64-detector row CT" generally has 64 rows of detectors in its detector array. The width of the X-ray beam is collimated (i.e., physically limited) in relation to the width of the detector array, which can vary among different CT systems from 20 to 160 mm along the z-axis.

During data acquisition, the CT system records the "raw" scan data and converts it to X-ray attenuation Hounsfield units (HUs). This file of raw projection data is used to reconstruct axial images, most commonly using a filtered back-projection algorithm (a standard algorithm for reconstructing CT images). Each image is reconstructed into a

512 × 512 matrix for display. If the reconstructed image has, for example, a field of view of 260 mm, the pixels in the resulting image would have a nominal size of 0.5 mm × 0.5 mm (i.e., 260 mm/512=0.5 mm). With detector elements measuring 0.6 mm along the z-axis (see the preceding text), this example would result in each volume data element, or voxel, measuring 0.5 mm × 0.5 mm × 0.6 mm in the x, y, and z dimensions, respectively. These 3-dimensional (3D) "voxels" have the desirable property of being "near-isotropic": each voxel of the dataset has nearly the same size in all 3 dimensions. What this means practically for physicians is that the data can be displayed on a workstation in any plane or orientation without sacrificing spatial resolution. This capability is critical for cardiac and coronary imaging and allows visualization of the heart in the axial planes acquired as well as the short axis, vertical long axis (2-chamber), and horizontal long axis (4-chamber), all from the same acquisition. For coronary imaging, the near isotropic datasets provide views of each coronary artery segment along both its long axis and short axis (i.e., cross section).

For a coronary luminal diameter of about 3 mm, a cross section reconstructed from a CT scan with cubic voxel dimensions of 0.5 mm per edge will display the diameter of the lumen using about 6 voxels. Because disease cannot be resolved at the subvoxel level, the voxel size relative to the object being imaged defines the limits of quantitative resolution. Thus, grading of coronary lesions with coronary CTA can be done at the ordinal level, but full quantification remains problematic (10). For reference, invasive coronary angiography has a spatial resolution of about 0.16 mm (9). Thus, a 3-mm coronary artery lumen would be displayed using about 18 pixels, providing the opportunity for much more accurate quantification of disease affecting the coronary artery lumen.

The number of longitudinal detector rows/data channels that can independently measure X-ray attenuation simultaneously determines the volumetric coverage of the CT scanner, or the amount of the cardiac volume (which in adults is about 12 cm in the axial dimension) that is imaged with each CT gantry rotation. Using current generation 64-channel scanners, routine submillimeter imaging can be performed with scan durations of 10 to 20 seconds and longitudinal coverage of 20 to 40 mm of cardiac anatomy per gantry rotation. However, a 64-channel CT system that involves 32 detector rows and 2 focal spot positions (32 × 2=64 data channels) does not have the same volumetric coverage as a system with 64 detector rows. To cover the entire heart in the most common mode of scanning, multiple 360° gantry rotations gated to the cardiac cycle are used as a motorized table moves the patient through the CT scanner. Thus, the X-ray beam traces a continuous helical (spiral) path around the section of the patient's body being imaged.

Some institutions are now also using 128-channel scanners, and both 256- and 320-channel scanners have been introduced (11). The latter configurations offer the potential to image the entire heart during a single heartbeat (12,13). While this sounds like a theoretically attractive next step in CT technology, substantial technical challenges are imposed by the creation of CT scanners that require the use of a cone X-ray beam as wide as 16 cm in the z-axis direction. Although volumetric coverage is increased with these new scanners, increasing the number of detector rows does not by itself improve spatial or temporal resolution above that provided by 64-channel scanners. The benefits and limitations of these newly introduced CT scanners will not be known until formal analyses of image quality, diagnostic accuracy, radiation dose, and clinical performance are evaluated in appropriate large multicenter studies.

Coronary CTA examinations are typically performed using nonionic intravenous contrast medium with high iodine concentration (greater than or equal to 300 to 350 mg I/mL) to assure adequate opacification of the coronary artery lumen and sufficient contrast with the arterial wall. This contrast injection is followed by injection of normal saline to "push" contrast through the venous capacitance of the upper extremity and the right heart structures (14). The contrast injection should result in a high-level plateau of arterial opacification (greater than 300 to 350 HUs) during CT image acquisition. Several different methods, including the use of a test bolus and automated bolus tracking, are available to ensure that the period of maximum concentration of intravenously administered contrast material in the coronary arteries is properly synchronized with the period of scan acquisition. If the contrast bolus arrives either too early or too late, coronary image quality will be diminished, and diagnostic information may be lost. Adult coronary CTA requires the use of a high injection rate, typically 4 to 6 mL/s, with the duration of injection and the volume of intravenous contrast agent prescribed based on the structures to be imaged and the specifics of the CT systems used to acquire the exam.

4.3. Image Reconstruction and Interpretation

Image reconstruction is the process of converting raw CT attenuation data into axial (i.e., transverse) sections. Although much of the process involves the use of proprietary mathematical algorithms developed by each manufacturer, some elements are under the control of the technician working with the study. Decisions that must be made during this initial processing of the data include use of options for noise reduction and correction for any evident blurring or motion artifact. In order to find the part of the cardiac cycle that best captures motion-free images of the right and left coronary arteries, multiple phases of the cardiac cycle may need to be reconstructed and examined. Decisions about this are operator specific, with some choosing to create up to 20 reconstructions at 5% increments of the R to R interval (from 5% to 95%). Thus, a coronary CT angiogram may result in 350 to over 5000 transverse sections available for physician examination, with most

coronary CT angiograms falling into a range of 1500 to 3000 images.

The final phase of the CT angiogram study is the creation of 2-dimensional (2D) reformatted images and 3D volume-rendered images from the transverse reconstructions. The approach to interpretation of a CT coronary angiogram varies by operator, but some general principles can be described. For most experts, the source transverse sections supplemented with oblique reformations are the primary tools for interactive interpretation of coronary CTA examinations (15). In addition, interpretation of the transverse sections provides a general understanding of the anatomic relationships of the heart and coronary arteries with surrounding structures such as the great vessels, nonvascular mediastinal structures, lungs, and pleura. Comparisons of abnormalities detected on reformatted or 3D-rendered images with the source transverse sections may help to minimize errors in interpretation related to postprocessing artifacts.

Multiplanar reconstruction images can be oriented along any plane within the imaged volume, making it possible to view the long and short axis of the coronary artery segments and the cardiac chambers. Curved planar reformation images can be created manually or by using vessel centerline tracking algorithms to display the course of a coronary artery. Curved planar reformation images display the coronary artery as if it were stretched along a hypothetical straight line. Distortion is a concern with these reconstructions, particularly if vessel tortuosity creates difficulties for the computer's vessel-tracking calculations. Branch points can similarly be problem areas. The maximum intensity projection is a visualization technique that combines data from a user defined "slab" (i.e., multiple adjacent "slices") to produce a single summary image that displays the maximum intensity along each projection through the slab from the perspective of the display (or viewer). This allows the course of a contrast-filled coronary artery to be viewed as if one could see through the slab instead of only being able to see the portion of the artery on the surface of the slab. To look at the full length of a coronary artery, a "sliding slab" technique may be used that allows the operator to move the slab along the entire course of the artery interactively (16).

Volume rendering provides a 3D reconstruction that can be useful for displaying large amounts of data in a single view. The technique requires removing structures through editing or by setting levels of opacity (windows) for display. Volume rendering can be valuable for understanding the distribution of coronary arterial supply to the underlying myocardium and the position and course of coronary bypass grafts but is not considered reliable for detecting and grading coronary stenoses. Neither volume-rendering images nor maximum-intensity projection images are sufficient by themselves for assessing the distribution and severity of coronary atherosclerosis.

As workstation capabilities improve, more complex reconstructions become possible, potentially reducing the amount of physician time required for each study. At present, reconstruction is highly operator dependent. The extent to which variations among operators may influence the quality of diagnostic information provided has not been empirically tested. In addition, there are no universally accepted conventions or standards for the display of cardiac or coronary images, in contrast with echocardiography and nuclear cardiology. The SCCT has recently published a consensus document covering the interpretation and reporting of coronary CTA studies (17). The complexity of the physician–computer interaction poses substantial challenges to those desiring to assess the performance of this technology, since it may be difficult to assess whether specific aspects of this interaction vary across centers and practices, and if so, whether the differences improve or impair diagnostic performance.

5. Diagnostic Imaging of Coronary Arteries: Important Concepts

There are 2 basic diagnostic approaches to symptomatic patients with chest pain, loosely referred to as "anatomic" and "functional." Anatomic tests, such as coronary CTA and invasive coronary angiography, provide direct radiographic visualization of the structural features of the coronary artery lumen. Invasive coronary angiography creates a 2D coronary "lumenogram." By moving the fluoroscopy unit, or by using a biplane system, multiple projections of the lumen of each coronary artery can be obtained. To estimate coronary artery stenosis severity from this technique, one must compare any evident narrowing of the luminal outline with presumably normal adjacent segments to allow estimation of a "percent diameter stenosis." This visual grading process, which is still the standard clinical method of interpretation used in catheterization laboratories around the world, has a high degree of intra- and interobserver variability (18–20). Computer-assisted interpretation, which could serve to reduce at least some of this variability, has not yet been accepted into routine clinical practice.

Invasive coronary angiography is considered the "reference standard" for diagnostic coronary testing, despite the foregoing limitations, for several reasons. First, until the advent of 16-channel CT coronary angiography, it was the only method of directly visualizing the lumens of coronary arteries that was suitable for routine clinical use. Second, the assessment of luminal stenosis severity on coronary angiography, typically summarized in a very simple 1-, 2-, or 3-vessel obstructive disease ranking, has been repeatedly demonstrated to be one of the most important prognostic factors in patients with coronary disease (21,22). Finally, the results of invasive coronary angiography have formed the basis for revascularization treatment selection decisions for almost 40 years. Thus, invasive coronary angiography is the reference standard in coronary assessment primarily because

of the extensive evidence documenting its value in patient management and secondarily because of its higher spatial and temporal resolution compared with alternative coronary imaging options.

The extensive evidence base relating invasive angiography results to prognosis and patient management cannot necessarily be extrapolated to the findings of coronary CTA. However, it is worth noting that invasive coronary angiography itself has undergone major changes in imaging methodology, evolving from an analog film image intensifier system to digital image generation using flat-panel detectors. No empirical studies have yet examined whether this change in technology, which has had a significant impact on the fundamental imaging characteristics as well as radiation exposure, has altered the relationships between test results and patient outcomes.

Coronary CTA provides information about the coronary lumen that approximates the information available from invasive coronary angiography. In addition, it provides information about the presence of nonobstructive plaque in the vessel walls. Invasive coronary angiography is subject to uncertainties about whether the reference segment itself is diseased with plaque and whether the luminal narrowing is concentric or eccentric (19). Coronary CTA is able to image the plaque that is external to the lumen and display its relationship with the lumen. As with invasive coronary angiography, visual grading of coronary segment narrowing by ranges of stenosis is the current standard of practice and has been shown to provide useful clinical information relative to invasive coronary angiography (10,23). Quantitative coronary CTA has been used in some research applications but is not currently a routine part of clinical interpretation (24–26). In a recent multicenter study, visual and quantitative assessments of stenosis severity by coronary CTA were quite similar (23).

Functional tests assess the ability of coronary arteries (including their collateral vessels) to provide a sufficient blood supply to the myocardium both at rest and during exercise or pharmacological stress. The detection of myocardial ischemia using this approach relies on measuring parameters such as LV blood flow/perfusion patterns or LV function and wall-motion patterns that reflect the impact of reduced blood supply and its consequences. Functional testing data therefore reflect both the severity and consequences of obstructive CAD and are prognostically incremental to anatomic imaging in several important clinical settings (27,28). The apparent dissociation between anatomic imaging results and functional test results can be attributed to several issues (Table 1). Thus, despite the detailed anatomic information it provides, CTA may not eliminate the need for assessing the functional significance of lesions of intermediate or indeterminate severity.

Table 1. Reasons for Dissociation Between Anatomic Imaging Test Results and Functional Test Results

- Diameter stenosis is a crude indicator of resistance to blood flow. Coronary blood flow is proportional to the fourth power of the radius of the cross-sectional vessel area.
- Other anatomic features can affect pressure gradient across a stenosis, including morphology and length of stenosis, entrance, and exit angles.
- Tone of myocardial microvasculature is also important in modulating antegrade and collateral components of coronary blood flow.
- The gold standard used to define ischemia will affect the apparent performance of diagnostic tests for ischemia (29).
- The ischemia-producing potential of intermediate severity lesions (e.g., 50% to 70% diameter stenosis) is particularly difficult to assess (30–33).

6. Assessment of Left Ventricular Function: Important Concepts

LV function, as reflected by the ejection fraction, is the single most important prognostic parameter in patients with established CAD. In addition, LV size and regional wall-motion data can influence decisions about appropriate therapies. Several methods provide quantitative evaluation of LV function, including transthoracic echocardiography (TTE), gated SPECT, radionuclide angiography, invasive left ventriculography, and cardiovascular magnetic resonance. LV assessment by CTA is based on use of retrospective gating with reconstruction of up to 20 phases of the cardiac cycle including end-systole and end-diastole. Many of the desired LV functional calculations can be automated using the workstation software, although some operator interaction with manual correction is often required. Clinical use of these CT-derived data requires proper understanding of features unique to coronary CTA compared to other more familiar methods of assessing LV structure and function measures. Values for LV volume, LV ejection fraction, and LV mass for cardiac CTA have recently been reported from a series of 103 apparently healthy adults free of hypertension and obesity (mean age 51 years) (34).

The temporal resolution of current-generation 64-channel multidetector scanners, reviewed briefly in Section 4, Coronary CT Angiography: Brief Overview of the Technology, is less than that of echocardiography and invasive LV angiography. Cardiovascular magnetic resonance can generate images with higher average temporal resolution secondary to acquiring data over multiple cardiac cycles. Limited temporal resolution of CTA is primarily relevant at higher heart rates and with the use of single-source MDCT scanners because fewer discrete time points of the cardiac cycle can be properly reconstructed, and may produce inaccuracies in LV parameter measures due to improper identification of end-diastole and end-systole. At heart rates between 55 to 65 beats per minute, however, current 64-channel CTA provides sufficient cine frame rates to provide LV function information with accuracy comparable to other noninvasive and invasive modalities.

7. General Issues in Clinical Test Evaluation

7.1. Key Clinical Questions

Clinicians caring for a patient with suspected or known CAD typically consider 3 types of questions. First, is coronary disease present in this patient, and if present, what is its current extent? This is a *diagnostic question* and effectively addresses the likelihood of certain findings if a reference standard test was performed. As discussed in the preceding text, invasive coronary angiography is the current reference standard diagnostic test for defining the presence and severity of obstructive CAD based on luminal stenosis. However, this status is based more on demonstrated value in defining prognosis and choosing treatment than on documented ability to provide accurate and reproducible assessment of the extent and severity of coronary atherosclerosis. Other technologies that can image the diseased vessel wall, such as intravascular ultrasound (IVUS), CMR, and optical coherence tomography, may actually be a more appropriate reference standard for some aspects of CTA's diagnostic performance given the ability of CTA to image the vessel wall in addition to the lumen.

Second, is this patient likely to suffer a major fatal or nonfatal cardiovascular event in the foreseeable future? This is a *prognostic question* and addresses the ability of CTA to help stratify risk.

Third, will CTA help clinicians alter management in ways that lead to reduced risk of major adverse clinical events? This is a *therapeutic question* and addresses the ability of the information derived from the test to help clinicians alter patient outcome.

7.1.1. Assessing Diagnostic Accuracy

Research studies evaluating novel diagnostic tests should consider using study designs that minimize biases and maximize generalizability. These designs often include the following features: 1) selection of the study patients consecutively or at random from the target population at multiple centers; 2) performance of both the new test of interest and the reference standard test (e.g., coronary CTA and invasive coronary angiography) in all patients in random order; 3) interpretation of both tests by multiple readers who are completely blinded to any clinical information including the results of other tests and who reflect the spectrum of readers likely to interpret the test in clinical practice; 4) assessment of intra- and interobserver variability for both studies. These methodological ideals have rarely been achieved in practice for any noninvasive imaging test, due to logistics, funding, and other barriers. As a consequence, a number of important biases may distort measured diagnostic performance. For example, most studies of the diagnostic accuracy of CTA have focused on patients who were already referred for invasive coronary angiography (24,35). While this study design is appropriate if CTA will be used as a direct replacement for invasive angiography, it is not ideal if the study population is substantially different from the one in which the test is most likely to be used clinically. Although recognition of such potential biases is an important part of the due diligence involved in vetting any new test for clinical practice, it is also important to recognize that virtually all the tests already accepted as a part of routine clinical practice, including stress nuclear and stress echo tests, had similar bias problems in their initial assessment and reported diagnostic performance (36). A few of the more important bias problems that occur regularly in the diagnostic testing literature are summarized in Table 2.

Table 2. Common Problems in Assessing Diagnostic Performance of Diagnostic Tests

Study Population Biases
• Population chosen to evaluate performance of diagnostic test is not the one in which the test will be used in practice.
Verification Biases
• Not all patients evaluated with new test also get reference standard test.
• Use of reference standard test influenced by results of new test being evaluated.
Interpretation Biases
• Clinical interpretation used for research without a separate research-level interpretation.
• Spectrum of readers/interpreters does not reflect the eventual community of practitioners who will use the test.
Analysis Biases
• Exclusion of indeterminate or uninterpretable tests in evaluation of diagnostic accuracy parameters.

What clinicians most want to know from the use of tests for diagnostic purposes are the post-test probabilities: "given the observed test result, what is the new (revised) probability my patient does/does not have disease?" These probabilities are often referred to as "predictive values," but this latter term has been a source of confusion to many in that it implies that these probabilities are fixed performance characteristics of diagnostic tests. Post-test probability, on the other hand, clearly indicates an estimate that is a revision of an earlier estimate (the pretest probability). To calculate these probabilities, one can employ Bayes' formula for simple cases or logistic regression models for more complex cases. Most of the predictive value/post-test probabilities reported in the coronary CTA literature are calculated from the study sample using 2×2 tables of sensitivity/specificity versus obstructive CAD present/absent. Because these estimates are valid for the study population from which they were derived, they may not be relevant to other patient populations. The critical factor to remember is that post-test probabilities may vary importantly according to pretest probability, and a given reported "predictive-value" figure does not apply across all possible pretest probabilities.

7.1.2. Likelihood Ratios and Receiver-Operator Characteristic Curves

Likelihood ratios and receiver-operator characteristic (ROC) curves provide 2 useful and complementary ways of

summarizing diagnostic test accuracy. Neither is dependent on disease prevalence per se, although both are affected by changes in the distribution of the severity of disease in the population being tested. A likelihood ratio is the likelihood of a given test result in a patient with disease relative to the same test result in a patient without disease (37). For a positive test, the likelihood ratio is calculated as (sensitivity/[1 − specificity]), and higher values indicate that the test in question is more accurate at identifying patients with disease, particularly if the value is 10 or greater. For a negative test, the likelihood ratio is calculated as ([1 − sensitivity]/specificity), and values less than 0.1 indicate a test particularly accurate at ruling out disease.

ROC curves display in graphical form the relationship between the true positive rate of a test (its sensitivity) and its false positive rate (1 − specificity) because the definition of a "positive" test is varied. Calculation of the area under the ROC curve provides a useful numeric summary measure that ranges from 1.0 (a perfect test) to 0.5 (a completely noninformative test). Statistical comparison of the ROC areas for 2 or more tests assessed in the same study population may be used to identify the more accurate test providing that the curves are of similar shape.

7.1.3. Assessing Prognostic Value

Because not all diagnosed disease is clinically important, some have argued that a better sense of the value of a test comes from its ability to stratify risk or prognosis. Adequate prognostic studies require large samples and often long periods of follow-up. Hence, relatively young technologies such as coronary CTA often lack such data in the initial years of their clinical life. Problems arise in this literature when researchers attempt to circumvent some basic structural requirements of prognostic studies in order to generate data more quickly. A few of the more relevant caveats for prognostic studies of diagnostic tests are summarized in Table 3.

Table 3. Common Problems in Assessing Prognostic Value of Diagnostic Tests

Choice of End Point
• End point chosen is either not clinically relevant or not objectively verifiable.
• All-cause mortality end point is chosen but other clinically relevant outcomes are not also measured.
• Classification of cause of death is often problematic, even with an independent events committee.
• "Harder" nonfatal end points, such as nonfatal MI, require proper use of verification testing (e.g., ECG, serum markers) or they may be missed.
• "Softer" nonfatal end points, such as revascularization and hospitalization, often represent arbitrary decisions by clinicians rather than surrogates for disease progression.
Completeness of Follow-Up
• Patients who are lost to follow-up often have worse prognoses, and their omission from a prognostic study can introduce serious biases.
Intervening Treatments or Events
• If a new test being studied affects subsequent use of prognosis-modifying therapies (e.g., medications, revascularizations), the relationship between test results and patient outcome may be obscured.
Statistical Power and Number of End Points
• Number of useable follow-up events, not number of patients, determines the statistical power of a prognostic analysis. (Useful rule of thumb is 5 to 10 outcome events are needed for each prognostic variable/covariate considered in the analysis.)

ECG indicates electrocardiogram; and MI, myocardial infarction.

7.1.4. Assessing Therapeutic Value

Determination of the therapeutic value of a diagnostic test is problematic because a test's effects are inherently indirect. Unlike a drug or device that is intended to have a direct impact on a symptom or disease, diagnostic tests can only improve outcome by providing new information that prompts changes of behavior among clinicians, patients, or both. No prospective randomized trials have yet examined whether the current commonly used strategies of stress testing improve patient outcomes. Nonetheless, therapeutic value has been demonstrated in clinical trials for some diagnostic tests. Trials of invasive versus conservative management in ACS essentially tested diagnostic strategies (early versus deferred invasive coronary angiography) that were closely linked to decisions about revascularization, which in turn had the potential to affect outcome (38,39). Randomized trials have shown that screening mammography (40) and abdominal aortic ultrasonography (41) save lives. Stratified analyses of treatment trials have shown that troponin can be used to identify patients who will benefit from invasive management of ACS (42). However, the proposition that diagnostic tests must be directly shown to affect patient outcomes before being considered fully validated for clinical practice is controversial because few tests ever reach this level of validation, and adequate funding for such trials is extremely difficult to obtain.

Typically, the value of additional prognostic data (including anatomic imaging findings) has been tested by calculating improvement in predictive information content, as reflected by statistical model likelihood chi-square values or p values and/or showing adjusted hazard ratios. Other approaches include calculation of c-indexes (43,44) and proportion of subjects with reclassified risk (45). Measures such as these that reflect only statistical improvements in information, however, do not necessarily translate into changes in clinical decision making. Without demonstrating this latter effect, there is limited possibility of altering patient outcomes and thus the true incremental value of the test in clinical practice may be overestimated (44).

8. Current Coronary CT Angiography Applications

8.1. Diagnostic Accuracy of Coronary CT Angiography in Stable Patients With Suspected CAD

A number of carefully done systematic reviews have examined the diagnostic performance of coronary CTA since the advent of 64-channel CT in 2004. Each represents a

somewhat different point in the evolution of the evidence base supporting this technology (46–52). In general, these studies have concluded that diagnostic accuracy has improved as the technology evolved from 4- to 16- to 64-channel machines, along with a decrease in the number of non-assessable coronary segments. As noted earlier, while the proof of concept for coronary CTA as a clinical tool was clearly shown by studies of 16-channel CT, present state-of-the-art performance is not considered achievable with less than 64-channel scanners due to improvements in temporal and spatial resolution.

Over 45 single-center studies have been published as of June 2009 examining the diagnostic performance of 64-channel CT in the identification of obstructive coronary disease in comparison with invasive coronary angiography in various populations (50). This literature largely reflects the performance of expert readers studying highly selected convenience samples of patients. This literature serves primarily to extend the proof of concept that coronary CTA can, under various selected circumstances, correctly identify both patients with and patients without significant coronary stenosis, as defined by invasive angiography. The strength of these data lies in the relative consistency of reported performance despite the variety of institutions studying different target patients and using somewhat different methods to perform and interpret the studies. Weaknesses include the small sample sizes, with most of the studies reporting on fewer than 100 patients, and the obvious biases inherent in studying a convenience sample already preselected for cardiac catheterization. A related issue is the inclusion in many studies of patients in whom the diagnosis of CAD was known or very probable, such as patients with a history of MI or patients with prior revascularization. Although many of these reports are deficient in relevant clinical details about the patients studied, a few not only provide important clinical descriptors but also use these data to formally estimate pretest probability of CAD with previously validated predictive models (53,54). The majority of studies used CT machines from the same vendor, and many employed the same workstation for post-processing as well. The number of interpreters for each study, whether they worked independently or in consensus, the use of prospective blinding to clinical and other test data, and the details of the coronary CTA review and interpretation process (including which types of reformations were used to identify and grade coronary lesions) varied substantially in this literature. Interpretation of the reference invasive coronary angiogram also varied with some investigators using quantitative coronary angiography and others using visual stenosis assessment only. Some reports defined significant disease as greater than or equal to 50% diameter stenosis, some as greater than or equal to 70%, and a few examined both. In addition, some studies excluded small-diameter segments (e.g., less than 1.5 to 2.0 mm), while others evaluated all segments regardless of size.

Studies have generally been consistent in finding less than or equal to 5% of patients had nonevaluable scans (in whole or in part). Nevertheless, significant potential for publication bias exists. Studies demonstrating poorer performance are much less likely to be submitted to journals or favorably received by the peer review process. In the most recent review covering studies published through November 2007, average per-patient sensitivity for identifying obstructive CAD was 98%, with average per-patient specificity of 88% (50). Likelihood ratios for a positive test averaged 8.0, while likelihood ratios for a negative test averaged less than 0.1. Individual study specificities were reported over a much broader range than sensitivities, and samples with higher pretest probabilities tended to report a lower specificity. The mean prevalence of obstructive CAD in these studies was 61%. Post-test probabilities for a negative test (probability that the patient did not have disease given a negative test result, or "negative predictive values") averaged 96% and post-test probabilities for a positive test averaged 93% but with a range from 64% to 100%.

Recently, 3 multicenter studies have been completed comparing 64-channel coronary CTA with conventional angiography. These studies are notable both for the fact that they are the first multicenter studies of contemporary coronary CTA diagnostic performance and that they used careful research methodology in the collection and interpretation of the CT and comparison catheterization data. However, as with the single institution papers, they are limited by focusing on a population already selected for coronary angiography. They also largely reflect the performance of expert coronary CTA readers rather than community-based readers. The CORE 64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) study was conducted at 9 international centers and enrolled 316 symptomatic patients age 40 years or more with suspected or known coronary disease. Patients with calcium scores less than 600 were referred for invasive coronary angiography, 291 (92%) of which completed coronary CTA prior to invasive coronary angiography (23). All centers used the same vendor's 64-channel CT system. Standardized scanning protocols were used, including nitroglycerin administration and use of radiation reduction algorithms (55). Independent blinded core laboratories analyzed the data, both visually and using quantitative methods. Lesions greater than or equal to 50% by quantitative coronary angiography in any vessel greater than 1.5 mm in diameter were considered obstructive. The median age of the study population was 59 years, and 74% were men. Fifty-eight percent had angina at the time of study, 20% had a prior MI, and 10% had a previous percutaneous coronary intervention. The prevalence of obstructive CAD by quantitative coronary angiography was 56%. Over 99% of 3782 coronary segments were suitable for quantitative evaluation by CT. On a per-patient–based analysis, the sensitivity of quantitative coronary CTA for detection of a greater than or equal to 50% diameter stenosis was 0.85,

with a specificity of 0.90. The likelihood ratio for a positive test was 8.5, while that for a negative test was 0.17. The post-test probability of significant CAD after a positive test was 0.91, while the post-test probability that disease was truly absent after a negative test was 0.83. Two patients had significant reactions to the contrast medium given for the studies. CTA was similar to invasive coronary angiography in its ability to identify, based on the presence of greater than 50% obstructive stenosis, those patients who were subsequently referred for revascularization. In addition, the formulation of CT data into a modified Duke prognostic CAD index correlated moderately well with the same index constructed from invasive coronary angiographic data ($r=0.81$).

The ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) study prospectively enrolled 245 patients with typical or atypical chest pain who were referred for invasive coronary angiography at 16 (predominantly nonacademic) U.S. sites and agreed to have a coronary CTA prior to their catheterization (56). All CT studies were performed with the same 64-channel CT system. The CT studies were interpreted by a consensus of at least 2 of 3 independent readers (2 academic, 1 nonacademic) blinded to all clinical and diagnostic test data. No coronary segments were excluded due to inability to evaluate the extent of stenosis. A single reader who was blinded to all clinical and CT data interpreted the invasive coronary angiograms. Patients with known coronary disease were excluded. Of the 245 patients enrolled, 15 were excluded for failure to complete both study tests. The remaining 230 patients had a mean age of 57 years, and 59% were men. Symptom status at the time of testing was not reported. By quantitative coronary angiography, disease prevalence was 25% for any stenosis greater than or equal to 50% and 14% for any stenosis greater than or equal to 70%. On a per-patient basis (including 3 patients with discordant readings among the 3 readers), sensitivity of coronary CTA was 94% to 95%, depending on the cutpoint chosen to represent a positive invasive coronary angiogram, and specificity was 82%. The likelihood ratio for a positive test was 5.5 to 5.6 with the likelihood ratio for a negative test 0.06 to 0.07. Post-test probability for a negative test (negative predictive value) was 99% for both disease definitions, but post-test probability after a positive test was 48% (with disease prevalence of 14%) to 64% (with disease prevalence of 25%).

Three university hospitals in the Netherlands prospectively enrolled 433 symptomatic patients age 50 to 70 years who were referred for invasive coronary angiography (October 2004 to June 2006) (57). Of these, 62 patients declined a research coronary CTA, and 11 patients were excluded for various technical reasons, leaving a study population of 360 subjects. No patients or coronary segments were excluded due to impaired image quality from either motion or coronary calcium. Patients with previous revascularization were excluded. All CT studies were performed within 2 weeks before or after invasive angiography. Each center used a CT machine from a different vendor. Three cardiologists unaware of the CT results graded each invasive angiogram. Significant coronary disease was recorded when the luminal diameter stenosis was greater than or equal to 50%. Teams of 2 observers unaware of the invasive angiogram results graded the CT studies. Scans from each center were interpreted by a team from 1 of the other 2 centers. The mean age of the study population was 60 years, and 68% were men. Forty-two percent had typical angina, 21% had unstable angina, and 14% had a non–ST-segment elevation MI. The prevalence of significant coronary obstructive disease was 68%; sensitivity for CTA was 99% with a specificity of 64%. Two patients with single-vessel disease were missed. CT classified 41 patients with angiographically insignificant disease as having significant coronary disease: 1-vessel disease in 20 patients, 2-vessel disease in 11 patients, 3-vessel disease in 7 patients, and significant left main disease in 3 patients. The likelihood ratio for a positive test was 2.7 and for a negative test was 0.02.

In October 2009, the National Heart, Lung, and Blood Institute funded the PROMISE (PROspective Multicenter Imaging Study for Evaluation of Chest Pain) trial, a randomized trial of initial anatomic strategy using a 64-slice or higher coronary CTA versus an initial functional stress testing strategy in 10 000 low- to intermediate-risk patients (58). The primary outcome is a composite clinical event including death and MI, and follow-up will average 2.5 years.

8.1.1. Coronary Anatomic Subgroup Data

Although patient-level accuracy data are most directly relevant to patient management decisions, anatomic subgroup data can provide supplementary insights into areas of coronary CTA strengths and weaknesses. In that regard, it is particularly relevant to note that accuracy of coronary CTA for the highest-risk CAD subgroups seems very good. In 13 studies, coronary CTA had a pooled sensitivity of 100% and specificity of 99% for detection of significant left main coronary disease (50). In the left anterior descending (LAD) artery, sensitivity was 93% and specificity was 95%. In the left circumflex artery, sensitivity was 88% with a specificity of 95%. In the right coronary artery, sensitivity was 90% with a specificity of 96%.

At the coronary segment level, of over 27 000 segments reported, 7.8% were unevaluable (50). In 9 studies, sensitivity in proximal segments was 93% with a specificity of 95%. Results were similar in midsegments, but in distal segments, sensitivity was 80% with a specificity of 97%. The negative likelihood ratio for distal segments was 0.2, indicating that a finding of no distal disease by coronary CTA is not as conclusive as the same finding in a more proximal segment where the negative likelihood ratio was 0.07.

8.1.2. Comparison of Coronary CT Angiography With Stress Perfusion Imaging

The contrast between "anatomic" and "functional" diagnostic testing has been reviewed earlier. Two different types of studies have been performed to compare the diagnostic performance of coronary CTA with stress MPI in identifying obstructive CAD. The majority use the myocardial perfusion study as the reference standard in lieu of invasive angiography (59–61). Several additional studies have reported on patients who received coronary CTA, stress myocardial perfusion testing, and invasive coronary angiography, which permits more comparisons to be performed but are limited by virtue of being small, very select study groups (33,62). This literature reinforces findings from the diagnostic angiography literature showing that negative coronary CTA results using contemporary equipment and analysis/interpretation methods provides a reliable exclusion of clinically significant coronary disease. However, the occurrence of discordant patients with 1 test "positive" and the other "negative" highlights the impact of different reference standards in assessing the performance of coronary CTA. A few examples serve to illustrate these issues.

Lin et al. (60) studied 163 symptomatic patients without known CAD who underwent both coronary CTA and exercise stress testing with SPECT imaging. The median time between exams was 111 days, indicating that this was a convenience sample that was subject to undefined selection biases. Thirty-nine patients (24%) had obstructive plaques identified on 64-channel CT, while 105 (64%) had nonobstructive plaque identified. Fifteen of 39 patients with obstructive coronary disease had normal exercise perfusion scans. Several scores reflecting various aspects of the extent and severity of CAD were predictive of the presence of severe myocardial perfusion defects. However, there was no association between the distribution of coronary plaque by CT and the presence of exercise perfusion defects on nuclear imaging.

Ninety-two low-risk chest pain patients (with negative ECG and serum marker results) seen in the William Beaumont Hospital Emergency Department underwent rest/stress MPI and 64-detector coronary CTA as part of a prospective study (63). Seven patients (8%) were excluded because of uninterpretable coronary CTA scans leaving 85 patients in the analysis (mean age 49 years, 53% men). Chest pain was the presenting symptom in 94%. Both MPI and coronary CTA were negative in 66 patients (78%), and both were positive in 6 patients (7%). When judged against the composite outcome of either definite ACS or significant CAD by invasive angiography in the subsequent 30 days, the sensitivity of stress nuclear imaging was 71% and coronary CTA was 86%, while the specificity was 90% and 92%, respectively.

A total of 114 patients (mean age 60 years, 85% intermediate pretest probability by Diamond and Forrester algorithm) presenting to the outpatient clinic of Leiden University with chest pain but without known CAD who had been referred for MPI underwent coronary CTA as well within 1 month (33). The first 28 patients were studied with 16-channel MDCT, while the remainder were studied with 64-channel scanners. Sixty-eight percent of patients had normal myocardial perfusion scans. Thirty-six percent of patients undergoing coronary CTA had no CAD, while 29% had nonobstructive plaques. When the coronary CTA was normal (n=41), 90% also had a normal MPI. In the 40 patients with obstructive CAD on coronary CTA, abnormal MPI was observed in 50%, one third of which showed fixed defects; and two thirds, reversible defects.

Ninety-six patients referred to the University of Zurich for invasive angiography for known or suspected CAD were asked to also undergo both MPI and 64-channel coronary CTA, in that order (62). Seven patients did not undergo coronary CTA because of atrial fibrillation, and 11 patients declined invasive angiography. The remaining 78 patients (mean age 65 years, 55% men) formed the study population. Twenty-four percent had known CAD and prior revascularization. Coronary CTA was uninterpretable in 5 patients, and the responsible segments were assumed to be diseased in an "intention-to-diagnose" analysis. By invasive angiography, 46 patients (63%) had significant CAD (diameter reduction of greater than or equal to 50% by quantitative analysis). MPI showed a defect in 29 of the 46 patients, of which 19 were reversible. In a patient-based analysis, coronary CTA had a sensitivity of 94% and specificity of 64% for identification of patients with any perfusion defect. The positive and negative likelihood ratios were 2.6 and 0.10, respectively. Performance did not materially improve when only reversible MPI defects were considered. Logistic regression analysis revealed a relationship between the percentage stenosis at quantitative coronary angiography and MPI results defined either as any perfusion defect or as a reversible defect only. Similar results were observed for coronary CTA-defined stenosis and MPI results. Based on ROC curve analysis, invasive angiography and coronary CTA results had a similar ability to identify patients who would have a defect on MPI. These data were interpreted as showing that coronary CTA was as accurate as invasive angiography in identifying patients with functionally significant CAD.

Taken together, these studies suggest that MPI and coronary CTA measure different parameters relevant to ischemic heart disease. Of note, a normal MPI does not exclude the presence of coronary atherosclerosis, but it does signify a very low risk of short- to mid-term adverse cardiac events. Conversely, coronary CTA allows detection of atherosclerotic plaques that are not hemodynamically significant. The optimal management of such nonobstructive disease is not established.

8.1.3. Comparison of Coronary CT Angiography With Fractional Flow Reserve

Three groups have examined coronary CTA data using intracoronary FFR data as the reference standard for hemodynamically significant obstructive disease (64–66). These data complement the MPI comparisons described above by showing that coronary CTA anatomic data do not provide very accurate insights into the probability that specific lesions will produce clinically significant ischemia. The following studies illustrate these points.

A retrospective study from Erasmus University identified 79 patients (mean age 60 years) over a 3-year period (2004 to 2007) who had coronary CTA (either 64-channel or dual source) and also had invasive coronary angiography with FFR measurement of a single discrete lesion (59). Patients with prior revascularization were excluded. A coronary stenosis was considered significant if it was 50% or more by visual assessment or by quantitative measurement. An FFR value less than 0.75 was considered functionally significant. Agreement between coronary CTA and invasive angiography was found in 49% of the 89 lesions of interest. Fifteen of the 16 lesions significant by FFR were also significant by coronary CTA. Overestimation by coronary CTA occurred in 44 lesions. Sensitivity and specificity of coronary CTA for FFR-defined hemodynamically significant lesions were 94% and 40%, respectively.

In a prospective study of 81 patients from Belgium, diagnostic accuracy of coronary CTA judged against functional significance assessed by FFR was fair with a sensitivity of 79%, specificity of 64%, positive likelihood ratio of 2.2, and negative likelihood ratio of 0.3 (65). Decision making based on coronary CTA results would have led to revascularization in patients without ischemia in 22% and inappropriate deferral in 7%.

8.2. Prognostic Evaluation of Coronary CT Angiography in Stable Patients With Suspected Coronary Disease

The hallmarks of a clinically informative prognostic study have been summarized earlier in this document. Due to the relatively short time interval that has elapsed since the clinical introduction of 64-channel CT scanners, no studies have yet been reported with this technology that have adequate statistical power to test the independent prognostic value of coronary CTA (i.e., using multivariable analysis methods). However, Min and colleagues (67) have reported on the relationship between all-cause mortality and coronary CTA results in 1127 patients using a 16-channel CT. Patients presented with stable symptoms thought to represent possible obstructive CAD and had coronary CTA as their primary diagnostic imaging test. By pretest assessment, 30% were low probability for significant CAD, 50% were intermediate probability, and 20% were high probability. Mean follow-up was 16 months. Cumulative survival in the low-probability patients was 99%, while that in the intermediate-probability patients was 97% and in the high-probability patients was 92%. In multivariable analysis, the presence of plaque in greater numbers of coronary arteries along with the severity of stenosis observed and the presence of plaque in the left main coronary artery were predictors of mortality. A summary measure of the extent and severity of CAD (a modified Duke Coronary Disease Index) was also independently prognostic. Patients with no detectable plaque by coronary CTA (n=333 or 30% of the cohort) had a 0.3% mortality rate, indicating that a completely negative study was associated with a very low risk of death over the subsequent 15 months.

A study from Harbor-UCLA described the follow-up of 2538 patients who underwent coronary CTA by electron-beam tomography (68). The subjects had a mean age of 59 years, and 70% were men. Symptom status was not reported. Follow-up averaged 78 months. The extent of significant disease, described as the number of diseased vessels, was a significant prognostic factor beyond conventional risk factor and demographic data. Coronary calcium added modest prognostic information to the extent of CAD. While this study has the longest follow-up to date of the prognostic studies using coronary CTA, several caveats should be considered. First, using electron-beam tomography provided voxels that were significantly longer in the z-axis (3 mm) than in the x- and y-axes (0.34 mm each). How this affected the accuracy of diagnostic classification is unclear. Second, lack of a complete clinical descriptor set makes assessment of incremental clinical value subject to some residual uncertainty.

A study from 3 centers in Europe enrolled 541 patients (2003 to 2007) with chest pain, a positive stress test, or a high risk for CAD (69). Patients had both a coronary CTA (94% with a 64-channel CT system) and a gated-SPECT MPI study within 3 months of each other and no interval event between them. Mean age was 59 years, and 59% were men. Four percent of patients were excluded due to an uninterpretable CT study, 7% were lost to follow-up, and 8% underwent an elective revascularization within 60 days of imaging and were excluded. The remaining 439 patients were followed for a median of 1.8 years and experienced 23 events (5.2%): 8 deaths (2 cardiac), 8 nonfatal MIs, and 7 hospitalizations for unstable angina. In multivariable analysis, significant obstructive coronary disease with 50% or greater stenosis added independent prognostic information to baseline risk factors and MPI results, but any atherosclerosis on CT did not. Importantly, both the CT and MPI results added significant prognostic information to each other. In addition, the presence of noncalcified plaque on CT added independent prognostic information to both CT stenosis and MPI results. The small number of follow-up events in this study and the restricted set of baseline clinical variables included in the analyses limit the conclusions that can be drawn.

Another way to view the outcomes resulting from a particular clinical strategy employing coronary CTA is to

consider both events and management choices made after the test. However, a proper control group is needed to define what would have happened with standard management (without coronary CTA). In a study from Ontario of 7017 consecutive patients undergoing invasive coronary angiography from January 2005 to February 2007, the effect of introducing a cardiac CT program in February 2006 was to decrease the frequency of normal invasive studies from 32% before the program to 27% after the program (70). In 3 academic centers in Alberta without cardiac CT programs, the normal invasive coronary angiography rate during the same period in 11 508 patients remained stable at 30%.

8.3. Use of Coronary CT Angiography in the Assessment of Patients With Acute Chest Pain

The diagnostic accuracy of coronary CTA in patients with suspected stable obstructive coronary disease (reviewed in the preceding text) has typically been studied in patients already referred for coronary angiography. In contrast, in the studies of coronary CTA use in the assessment of acute chest pain patients in the emergency department, coronary CTA results have often been compared with expert clinical assessment of the final diagnosis, using combined clinical and marker data. A strength of this literature is the avoidance of the need to study patients preselected for invasive angiography. It is notable that 2 studies randomized the use of coronary CTA and that several used careful methodology to define their study population and assess clinical outcomes (71–73). However, as with the diagnostic accuracy literature for coronary CTA, studies in this area are primarily single-center reports that describe the findings of experienced observers in small numbers of patients.

Investigators from the William Beaumont Hospital randomized low-risk acute chest pain patients to coronary CTA (n=99) versus usual standard of care (n=98) protocols (72). Low risk was based on the Goldman-Lee algorithm. Coronary CTA patients with minimal disease were discharged; those with stenosis greater than 70% underwent catheterization, whereas cases with intermediate lesions or nondiagnostic scans underwent stress testing. Outcomes included safety (freedom from major adverse events over 6 months), diagnostic efficacy (clinically correct and definitive diagnosis), and time and cost of care. In the CTA-alone arm, 67 patients had normal coronary arteries and were sent home, while 8 with severe disease were referred for invasive evaluation. The remaining 24 patients required stress testing, owing to intermediate severity lesions or nondiagnostic scans. Of these, 21 of 24 (88%) had negative stress nuclear studies and were discharged. Overall, 88 of 99 (89%) patients in the coronary CTA arm were discharged home from the emergency department. In the usual care arm, 93 of 98 patients (95%) had negative nuclear stress tests and were discharged home. Of the remaining 5, 3 had invasive coronary angiography and 2 were discharged to outpatient follow-up. During the index visit, CTA evaluation reduced diagnostic time compared with standard care (3.4 h versus 15.0 h, $p<0.001$) and lowered costs ($1586 versus $1872; $p<0.001$).

Investigators at Seoul National University randomized 268 acute chest pain patients (mean age 58 years) to 64-channel coronary CTA or conventional care (71). Final diagnosis of ACS was made in 29% of the study cohort by 2 cardiologists independently using data from the clinical record 1 month after discharge. Coronary CTA use had no effect on the rate of diagnosis of ACS but was associated with fewer admissions deemed unnecessary in the intermediate probability group and with a decreased hospital length of stay, which seemed to occur primarily among high-risk patients. One patient in the conventional strategy had a nonfatal MI by Day 30, while no events occurred out to 30 days in the coronary CTA strategy.

At Massachusetts General Hospital, the ROMICAT (Rule Out Myocardial Infarction Using Computer Assisted Tomography) study prospectively enrolled 368 acute chest pain patients (39% women, mean age 53 years) with an inconclusive initial emergency department evaluation (including an initial ECG without ischemia and a normal initial troponin) in a protocol to receive a 64-channel coronary CTA scan (74). Screening for the study took place during weekdays over 2 years (2005 to 2007). Patients with known CAD were excluded. All physicians involved in the management of these patients were blinded to the coronary CTA results. Coronary CTA studies were evaluated independently for the presence of any coronary atherosclerotic plaque, as well as for significant coronary artery stenosis (greater than 50% stenosis) by 2 experienced observers who were blinded to all the clinical data. Among the 368 study patients, 31 (8.4%) were judged to have had ACS. Over a 6-month follow-up, none of the patients without ACS had a clinical outcome event. The time required to perform the CT scan averaged 16 minutes from the time of arrival in the imaging room, scans took an average of 14 seconds to perform, and average interpretation time was 9 minutes. By coronary CTA, 50% of patients were completely free of CAD, 31% had nonobstructive plaque, and 19% had significant obstructive CAD. Comparing the presence of any coronary plaque with the consensus diagnosis of ACS, coronary CTA had a sensitivity of 100% and a specificity of 54%, with a positive likelihood ratio of 2.2 and a negative likelihood ratio of 0.02. The presence of obstructive CAD had a sensitivity of 77% and a specificity of 87% for the consensus diagnosis of ACS, with a positive likelihood ratio of 5.9 and a negative likelihood ratio of 0.3. Of the 34 patients with significant obstructive CAD by CT, 14 were not diagnosed as having ACS, and none of these patients had a follow-up event out to 6 months.

A prospective study from the University of Pennsylvania enrolled 586 patients with suspected ACS who had a low Thrombolysis In Myocardial Infarction (TIMI) risk score and received a coronary CTA study (75). Four hundred seventy-six (84%) were discharged home after their CT

study, and none of these patients had a death or nonfatal MI out to 30 days.

Overall, these results reinforce the data from the stable angina studies showing that a negative coronary CTA study improves diagnostic certainty for ruling out significant coronary disease in a low-risk acute coronary population.

8.4. Use of Coronary CT Angiography in Preoperative Evaluation of Patients Before Noncoronary Cardiac Surgery

One potential role for CTA may be for preoperative evaluation of cardiac patients who are referred for noncoronary cardiac surgery. Several small studies have reported high diagnostic accuracy in these patients (76–80). The largest study to date consisted of 70 patients, of whom 31 had aortic stenosis (44%), 24 had mitral insufficiency (34%), 9 had aortic insufficiency (13%), and the remainder had other valvular or congenital lesions. On a per-patient basis, sensitivity and specificity were 100% (18 of 18 patients with significant CAD) and 92% (48 of 52 patients without significant CAD), respectively (78). The corresponding negative likelihood ratio is 0.01, which means a negative test would be associated with a very low post-test probability of disease for patients with low- and intermediate-pretest probabilities. Assuming that all patients previously would have been referred for invasive angiography, coronary CTA allowed the 48 patients (69%) in the study cohort with negative CT findings to avoid this procedure. However, a positive coronary CTA requires confirmation with invasive coronary angiography to establish the need for and extent of bypass surgery.

8.5. Use of Coronary CT Angiography in the Follow-Up of Cardiac Transplant Patients

Another potential application for coronary CTA is the evaluation of the cardiac transplant patient. Most transplant centers perform "routine" annual coronary angiography beginning 1 year after surgery, and the majority of these annual angiograms are negative. Absence of angiographic CAD is an important predictor of survival without adverse events in heart transplant patients (81). However, because of the diffuse and concentric nature of transplant vasculopathy (82), patients with clinical events often do not have angiographically "significant" disease, and IVUS is the method of choice for the detection of angiographically silent plaques in such patients (83). In contrast to invasive coronary angiography, coronary CTA permits visualization of atherosclerotic changes of the vessel wall including those associated with transplant vasculopathy. Sixty-four–channel coronary CTA has been tested in 2 small single-center studies (20 patients each), as a possible replacement for "routine" annual coronary catheterization with or without IVUS (84,85). Although getting the transplanted heart to the target heart rate can be difficult, the study from the Massachusetts General Hospital obtained diagnostic quality images in 83% of coronary segments. Sensitivity for identifying coronary stenosis or coronary plaque judged by invasive coronary angiography plus IVUS was 70% with a specificity of 92% (84).

8.6. Use of Coronary CT Angiography in Patients With Prior Coronary Bypass Surgery

In general, imaging of vein grafts with coronary CTA is less challenging than imaging the native coronary arteries primarily because of their larger size (typically 3 to 4 mm diameter) and reduced mobility compared with the epicardial coronary vessels and because they usually are not calcified. Assessment of internal mammary grafts is somewhat more difficult due to artifacts caused by metal clips and their smaller size (1 to 2 mm diameter) (86). Accuracy of coronary CTA for assessing graft stenosis has been shown to be somewhat lower than for assessing graft occlusion. Assessing the adequacy of the distal anastomotic site is more difficult than either patency or stenosis of the graft itself, due to the frequent presence of calcification and/or clips at the site and greater motion of this portion of the graft.

If coronary CTA is to supplant the need for invasive coronary angiography in prior coronary artery bypass graft surgery (CABG) patients, then it must be able to provide accurate information in 4 areas: 1) patency of grafts; 2) presence of stenoses in grafts; 3) the status of the proximal and distal anastomoses; and 4) the presence of significant lesions in the native coronary arteries both downstream from the grafts and in ungrafted segments.

In the most recent meta-analysis on the diagnostic accuracy of 64-channel coronary CTA, 6 studies were found (through November 2007) involving a total of approximately 350 CABG patients (50). Coronary CTA was able to detect complete occlusion of grafts with a sensitivity of 97% and a specificity of 100% (calculated on a per-graft rather than a per-patient basis). Considering both significant stenosis and occlusion, sensitivity was 98% and specificity was 97%. The positive likelihood ratio was substantially above 10 with a negative likelihood ratio of 0.02, indicating that coronary CTA can rule in or rule out graft disease with a high degree of certainty in patients with an intermediate pretest probability of disease (in the 50% range).

Assessing the native coronary arteries distal to the anastomosis is significantly more challenging than assessing grafts since they tend to be small and sometimes heavily calcified. In a study of 50 post-CABG patients from the University of Erlangen, 9% of all coronary segments in the native coronary arteries (either ungrafted arteries or grafted arteries distal to the graft) were unevaluable, due primarily to severe calcification or motion artifacts (87). In the evaluable segments, coronary CTA had a sensitivity of 86% with a specificity of 76% for significant stenoses. When the unevaluable segments were classified as diseased, the diagnostic accuracy for the detection of significant stenoses was 78%. Although these values reflect an improvement over previous scanner generations, they are still lower than

reported for studies performed with 64-channel CT in patients without previous bypass surgery. Because chest pain after bypass surgery might be associated with new stenosis of a graft or a native coronary artery, the difficulty of accurately assessing the native vessels is an important limitation for the clinical use of coronary CTA in patients after CABG.

From a technical standpoint, there are also differences in coronary CTA for the post-CABG patient compared to the patient without grafts. Patients with grafts are routinely studied from the level of the aortic arch to the diaphragm, compared to the level of the carina in patients who have not had prior CABG. In order to fully examine the patient with internal mammary grafts, some investigators have suggested a need to cover to the level of the clavicle so that subclavian stenosis can be ruled out. This increased coverage results in a need for a greater amount of contrast, longer breath hold, and greater amount of radiation. With 64-channel scanners, the longer breath hold is usually clinically insignificant, but the contrast and radiation increases remain (86).

8.7. Use of Coronary CT Angiography in Patients With Prior Coronary Stenting

The evaluation of stents by MDCT is significantly more difficult than the evaluation of coronary artery segments without stents, even using current generation 64-channel MDCT scanners. At least 3 different types of artifacts may complicate the imaging of coronary stents with coronary CTA.

- *Motion artifacts* are the most common reason in most series for unassessable stented coronary segments. These can be seen even with controlled heart rates and reconstruction techniques designed to optimize temporal resolution. Motion artifacts tend to exacerbate the other types of artifacts noted here.
- *Beam hardening artifacts* occur because the metal of the stent struts absorbs much more of the lower-energy portion of the X-ray beam than the surrounding soft tissues. As a result, the X-rays that are not absorbed and reach the detector array have a higher proportion of high-energy X-ray photons than expected in the standard reconstruction algorithms used for cardiac CT. The result is a "blooming artifact" that causes the stent struts to appear thicker in reconstructed images than they actually are. In some cases, the blooming may extend into the arterial lumen, interfering with the ability to assess the presence and extent of disease. Special reconstruction algorithms (called convolution algorithms or kernels) are now routinely used for coronary CTA studies in patients with coronary stents in order to (partially) correct for this beam hardening.
- *Partial volume averaging* is an artifact that may affect the voxels immediately adjacent to stent struts. When individual voxels contain information both from low-attenuation tissue (coronary artery, noncalcified plaque) and higher-attenuation coronary stent struts or coronary calcium, the image reconstruction algorithms assign average HUs to the voxels in question (averaging the higher- and lower-attenuation data into 1 summary attenuation value for that voxel). One result of this effect can be a loss of the sharp edge delineating the stent and the lumen. Since partial volume averaging is related to spatial resolution, it tends to be a greater problem in stents in smaller-diameter artery segments.

Some insights into the effects of these artifacts on stent imaging with coronary CTA can be obtained from in vitro studies, which have the advantage of eliminating some of the complexities of patient imaging, such as motion. An in vitro study of 68 different stents using 64-channel MDCT imaging found that use of special reconstruction algorithms improved visualization of the stent lumen and reduced blooming artifact at the cost of a modest increase in noise in the images (88). Stent luminal diameter measurements with electronic calipers averaged 57% of the true lumen diameter, with the best results (from an imaging perspective) at about 70% of true diameter. Different stent compositions and structures appeared to be associated with variations in the extent of residual artifact, suggesting that stents cannot all be regarded as equivalent in evaluating diagnostic coronary CTA performance. Similar results from the same group were obtained studying 29 different stent types using dual-source CT (89). A second in vitro study examined the effect of different amounts of in-stent stenosis and vessel diameter on 64-channel MDCT results (90). All 4 stents studied were associated with some blooming artifact leading to underestimation of the true stent diameter. Of vessels 3-mm or greater, no nonstenotic or low-grade stenotic vessel was misdiagnosed as an intermediate- or high-grade stenosis.

In the most recent meta-analysis of 64-channel coronary CTA covering studies published through September 2008, 14 studies of patients with prior coronary stenting were identified (91). In this relatively small, highly selected population, the prevalence of in-stent restenosis (greater than 50% diameter) was 20%, and pooled data showed a sensitivity of 90% and a specificity of 91% when only assessable segments were considered. In 5 studies where the nonassessable segments could also be included, sensitivity was 79% with specificity 81%.

The criteria for assessing the quality of stent images and the willingness to interpret images with some artifact evidence likely vary among investigative groups. In 1 careful study from the Massachusetts General Hospital, coronary CTA images of 54 stents in 44 patients were graded for image quality by 2 independent observers (92). A 64-channel MDCT scanner was used, and image reconstruction employed an algorithm known to reduce beam-hardening artifacts. Thirty of 54 stents (56%) were judged assessable by virtue of being free from major lumen distorting artifacts. Stent size was an important determinant of the

results. Stents 3.5 mm or larger (100%) were judged assessable; 80% of 3 mm and 33% of stents smaller than 3 mm were judged assessable. The major limits to assessability were partial volume averaging and beam hardening effects.

Thus, in a patient *known to have larger stents* and whose clinical presentation suggests low-to-intermediate probability for restenosis, 64-channel coronary CTA may be a reasonable alternative to invasive angiography to rule out significant in-stent restenosis, presuming high image quality can be obtained. Further research will be needed to validate the diagnostic accuracy data from the most recent 64-channel coronary CTA studies and to examine additional potential determinants of diagnostic accuracy, such as gender and diabetes, which can influence stent size and probability of restenosis. Some of the concepts suggested by in vitro studies related to variations in diagnostic performance among different individual stents will require validation in much larger studies than have been performed to date. In addition, outcome studies are needed that evaluate strategies of coronary CTA use and their influence on downstream testing and therapy.

8.8. Other Patient Subgroup Data

Other specific populations of interest that have been reported on include women, patients with left bundle-branch block, patients with LV dysfunction of possible ischemic etiology, and patients with atrial fibrillation. In each case, preliminary data are available in the form of 1 or several studies, each from a single center, using patients referred for invasive angiography.

Three studies have examined the diagnostic performance of 64-channel coronary CTA in women versus men (93–95). The Leiden study of 52 women and 51 men found no difference in accuracy, while the Rotterdam study in 123 women and 279 men found similar overall sensitivities but lower specificities in women (94,95). However, in the per-segment analysis, sensitivities in women were lower in the distal segments and side branches compared with those seen in men (94). A third study from Humboldt University in Berlin of 50 women and 95 men reported a lower overall sensitivity for women (70% versus 95% for men) and a higher rate of nondiagnostic examinations (14% versus 4% for men), due at least in part to the smaller size of coronary arteries in women (93).

Noninvasive stress tests have reduced accuracy in patients with left bundle-branch block, and invasive angiography is often required to clarify an uncertain diagnosis. An initial study of the diagnostic accuracy of 64-detector scanning has been reported in 66 patients with complete left bundle-branch block (mean age 69 years) admitted for invasive coronary angiography (96). Significant coronary disease, defined as greater than 50% diameter stenosis, was found in 44%. No coronary CTA study was excluded from analysis. CT correctly identified 35 of 37 (95%) patients without significant stenosis and 28 of 29 (97%) patients with significant stenosis on invasive coronary angiography. On a per-vessel basis, specificity was high but sensitivity was low for the circumflex (59%) and the right coronary artery (52%).

The performance of 64-channel coronary CTA in patients with dilated cardiomyopathy of uncertain etiology has been studied in 93 patients (mean age 65 years) who were referred for invasive catheterization (97). Significant coronary disease was defined as greater than 50% stenosis in 2 orthogonal views using quantitative coronary angiography. The prevalence of coronary disease was 46%, and 33% of the cohort were felt to have ischemic heart failure. Patients with single-vessel disease were considered nonischemic unless the lesion was in the left main or proximal anterior-descending artery. No patient was excluded from analysis. Coronary CTA correctly identified 92% of patients without CAD and 98% of patients with CAD. All patients with left main or 3-vessel disease were correctly identified. Coronary CTA also correctly identified 97% of patients without and 90% of patients with ischemic heart failure.

Atrial fibrillation poses a particular challenge to coronary CTA imaging for 2 main reasons: because heart rates are typically higher than 60 beats per minute, and because R to R intervals are irregular. Higher heart rates require use of a CT with very high temporal resolution in order to capture the coronary images without motion-related blurring, while irregular R to R intervals makes the use of data from more than 1 cardiac cycle in the image reconstruction process subject to misregistration errors. One small study has reported on an initial experience of coronary CTA in 15 patients (mean age 58 years) with atrial fibrillation and suspected coronary disease referred for invasive angiography (98). Imaging was done with a 64-channel dual-source CT, which provides a nominal temporal resolution of about one fourth of a gantry rotation or about 83 milliseconds. The mean heart rate during imaging of the study cohort was 84 plus or minus 9 beats per minute. Of 225 segments, 6% to 7% were judged to be of too-poor quality to be interpreted, primarily due to residual cardiac motion. Imaging of the heart in a single cardiac cycle, recently demonstrated to be feasible with 256-detector scanners, could theoretically eliminate the need for stable heart rhythms during scanning (99).

8.9. Assessment of Global and Regional Left Ventricular Function

The literature on the assessment of LV function using cardiac CTA in patients with suspected or known CAD is much smaller than that reviewed earlier in this document for diagnostic coronary imaging. One likely reason is that echocardiography already provides a readily available, noninvasive means of assessing ventricular function and wall motion and does so without exposing patients to ionizing radiation or iodinated contrast agents.

To create the images needed for assessment of ventricular function with retrospectively gated CTA studies, axial datasets are typically reconstructed at 5% to 10% increments

through the R to R interval. This provides a 4D volumetric dataset for analysis that can be viewed as a cine loop in the standard views, including 2- and 4-chamber views and short-axis views. Ejection fraction can be estimated visually or quantitatively using tracings of the ventricular chamber in diastole and systole.

The only meta-analysis to date covered publications through March 2006 and found only 4- and 16-channel CTA comparisons with CMR. These studies involved a total of 252 patients (100). Assessment of the left ventricle by CTA was performed using short-axis cine images that spanned the length of the entire LV, as is customary with CMR. The difference between LV ejection fraction measured with CMR and with CTA averaged 1.7% (CTA mean 52.9% versus CMR 54.6%). For the subset of studies using 16-channel machines, the difference was less than 1%.

More recent comparisons of 64-channel coronary CTA and CMR have confirmed the results of these earlier studies showing the close correlation of ejection fraction measured by these 2 techniques. In a retrospective study of 63 patients from Kyoto University who had the 2 studies within 2 weeks of each other, the mean ejection fraction difference was 0.22±4.2% (r=0.97) (101).

A study from Massachusetts General Hospital compared 64-channel CTA with 2D echo and with SPECT estimates of LV ejection fraction (102). Thirty-six patients had cardiac CTA and echo or SPECT imaging within 3 months. The overall correlation between CT and the other 2 imaging modes was very good (57±15% versus 58±13%, r=0.86) with the strongest correlation between CT and SPECT (r=0.90). A separate study from the same institution examined correlations between 64-channel CT and 2D echo in 25 patients with ejection fractions less than 45% who had both tests within 4 weeks (103). Ejection fraction by CT was 38±12% versus 36±8% for echo (r=0.67). Regional wall motion was assessed using a 17-segment model with a 4-point scale and showed modest agreement (kappa=0.61).

9. Emerging Applications

Topics included in this section are those for which the data are not yet deemed sufficient to support development of consensus opinions.

9.1. Noncalcified Coronary Plaque Imaging and Its Potential Clinical Uses

Several imaging technologies have been used to study atheroma progression or regression during life in patients. IVUS has been used in coronary arteries (104–110), external ultrasound has been used to measure carotid intimal medial thickness (111), and magnetic resonance has measured aortic and carotid atheroma (112). In each instance, serial imaging has been capable of measuring statistically significant change over time in atheroma burden as well as differential responses between active treatment and control populations. Given the ability of coronary CTA to image the coronary arterial wall, it may be possible to use this test to monitor atheroma burden over time. At present, such applications are considered of uncertain clinical utility and have been limited to research uses.

9.2. Assessing Atherosclerotic Burden

In order to detect changes in atherosclerotic burden over time, it is necessary to be able to accurately define the presence and extent of disease in each segment of the coronary tree. A meta-analysis of coronary CTA detection of coronary plaque in comparison with IVUS covering publications through April 2008 found 14 studies involving 340 patients (113). Sensitivity of coronary CTA on the lesion level averaged about 90%, while per-segment sensitivity was lower at 81% to 86%. At the vessel level, coronary CTA was more sensitive for calcified plaque than noncalcified plaque. This literature has a number of important limitations, including the small sample and the fact that IVUS is performed only in selected arteries usually to clarify the significance of an intermediate lesion. A full comparison of IVUS and coronary CTA data in all segments is unlikely to be feasible.

Comparison of coronary CTA and histology in postmortem coronary artery specimens has shown that the atherosclerotic plaques themselves undergo variable enhancement after contrast injection (114). While calcified and noncalcified plaques can be differentiated by CT, persuasive evidence supporting reliable subclassification of noncalcified plaques as lipid-rich versus fibrous-based on CT attenuation numbers is not currently available (25,115–121). If differences in plaque density could be reliably measured, such measures could be used to monitor treatment-induced or natural progression and regression of coronary atheroma (122,123).

Quantifying plaque burden with coronary CTA has also proven difficult. The primary limitations include accurate definition of the adventitial border, spatial resolution (currently approximately 0.4 mm), and artifacts created by calcified atheroma. At present, coronary CTA is best suited for analysis of plaque burden in the larger proximal coronary segments.

A few examples can serve to illustrate the current state of research in this area. In a study from the University of Erlangen of 41 patients who underwent 64-channel coronary CTA and were found to have only noncalcified plaques, 2 independent observers calculated the volume of plaque in proximal coronary segments (124). Interobserver variability of these measurements varied significantly by artery, with the lowest variability in the LAD (17±10%) and the greatest in the circumflex (32±13%). In the LAD, the average volume of atheroma was 150 mm^3. There was a significant inverse correlation between plaque volume and variability. In addition, studies with higher image quality exhibited less variability in measurement of plaque.

In a follow-up investigation from this same group, 50 patients with single noncalcified atherosclerotic lesions of the left main or proximal LAD artery who had a previous 64-channel coronary CTA had a follow-up research coronary CTA done at least 12 months after the first one using the same methods (125). Only patients with ideal baseline images were selected for study. Two independent readers analyzed CT datasets in random order. Readers were blinded to each other's readings as well as to clinical information and to information about whether the study was baseline or follow-up. Plaque areas were manually traced in serial 1-mm sections and the total volume of plaque was calculated by multiplying area by reconstruction increment (which yielded the height or depth of the lesion). The difference in volume between the second and the first scan was divided by the interval in years between the 2 scans to yield the annualized rate of change. Mean time to the second scan was 16.8 months. Mean interobserver variability was 16±12%, confirming the investigators' earlier work that LAD and left main artery images gave reasonably reproducible estimates for plaque volume. The mean noncalcified plaque volume in the 50-patient sample increased from 92±81 mm^3 on baseline scans to 115±110 mm^3 at follow-up, representing a mean annualized progression rate of 22%. Eighty-four percent of patients showed progression, while 16% showed regression. Neither the baseline plaque volume nor the baseline low-density lipoprotein (LDL) or high-density lipoprotein levels nor the use of statins appeared to have any influence on the rate of progression. The generalizability of these findings from this very select group of patients is unclear, but the fact that the 50-patient sample was chosen from a parent cohort of 1134 consecutive coronary CTA patients indicates that much more work will be needed to prove these methods are ready for general clinical use.

Several pilot studies have used coronary CTA to study treatment effects on atheroma. Investigators from Chiba University studied 21 patients with 16-detector CT before and after 1 year of treatment with atorvastatin 10 mg daily (126). One noncalcified plaque was followed for each patient. No significant change in atheroma area was seen after treatment, during which mean LDL cholesterol fell from 122 mg/dL to 96 mg/dL. There was, however, a significant (but weak) direct correlation between the final LDL cholesterol level and the degree of plaque area change ($r=0.39$, $p<0.05$). Additionally, the average density (assessed by HU) in the studied plaque increased significantly over the treatment period, suggesting the possibility of a favorable alteration in plaque composition.

9.3. Identification of Vulnerable Plaques

In addition to atherosclerotic burden, some initial investigations have been performed to evaluate the ability of coronary CTA to identify "vulnerable" plaques based on their apparent composition. In 1 small study from Beijing of 26 patients who underwent 64-channel MDCT and IVUS, plaque analysis software using HU ranges was not able to distinguish between lipid-rich and fibrous plaques (127). In a study from Hiroshima University, 21 patients had 64-channel coronary CTA and IVUS studies focusing on 38 noncalcified lesions (128). The mean CT density of hypoechoic lesions was significantly lower than that of hyperechoic lesions. There was also good agreement between the 2 tests in the amount of calcium evident in the plaques.

An investigation of 50 patients (25 stable, 25 with ACS) from Leiden University compared 64-channel MDCT plaque composition (noncalcified versus mixed versus completely calcified) with virtual histology IVUS (129). On coronary CTA, 32% of plaques in ACS patients were noncalcified and 59% were mixed. In stable CAD patients, 61% of plaques were completely calcified. In virtual histology IVUS, several features suggesting vulnerable plaque composition were more prevalent in the ACS patients. On both coronary CTA and IVUS, composition of culprit and nonculprit plaques appeared identical.

9.4. Left Ventricular Enhancement Patterns

Several studies have used MDCT to evaluate the LV myocardium in patients with prior MI. A retrospective study of 202 patients (63±13 years) attempted to detect previous MI in patients referred for 64-channel coronary CTA (130). Significant differences were noted between attenuation values of infarcted versus normal myocardium (56±23 HU versus 124±19 HU, $p<0.01$). Thinning of myocardial walls was noted only in chronic MIs ($p<0.01$).

MDCT has also been evaluated for the prediction of improvement in LV parameters after MI. In one such study, 26 patients (53±9 years) underwent MDCT and TTE within 1 week of acute MI, with a follow-up TTE at 3 months (131). MDCT evaluation examined early perfusion defects (ED) as well as delayed enhancement (DE). In myocardial segments considered abnormal by TTE, both ED and DE were associated with nonrecovery. Conversely, myocardial segments with lower prevalence of ED and DE were associated with recovery as assessed by TTE.

10. Areas Without Consensus

The 3 topics included in this section (incidental extracardiac findings, use in asymptomatic high-risk individuals, and the "triple rule-out" in the emergency department) have been the subject of some empirical research, but the data overall are not yet sufficiently clear to support the development of a consensus.

10.1. Incidental Extracardiac Findings

The literature describing the prevalence of extracardiac abnormalities in cardiac CT studies, the extent of their clinical significance, and the impact on patient health remains insufficient to answer the important clinical and policy questions raised by this aspect of the test's use. In the few published studies, there is considerable variation in how

incidental findings are categorized, and the specific definition applied to a "clinically significant finding," ranging from one that requires follow-up or clinical correlation to one that needs immediate evaluation or treatment. Data are even scarcer concerning the clinical implications of these incidental findings, with only 5 studies reporting on therapeutic consequences after short-term follow-up (132–136). No data are available documenting the impact these incidental findings have on long-term patient outcome, the costs associated with additional evaluations and treatments, or potential increased anxiety caused for the patient and physician.

Extracardiac findings detected with cardiac CT have an overall prevalence ranging from 20% to 53% of cases using electron-beam CT (134,137) and 15% to 67% of cases using MDCT (132,133,136,138–141). Considering the broad use of the term "clinically significant finding" in the studies to date, a more informative classification of incidental findings would be as follows: 1) benign finding: no clinical importance, requiring no additional work-up or follow-up; and 2) clinically significant finding: potentially or definitely important lesion requiring additional investigation. This second category can be subdivided into indeterminate findings requiring clinical correlation or follow-up, and major findings requiring immediate evaluation or management. Using this classification, approximately 4% to 25% of findings are reported to be potentially significant, requiring clinical correlation or follow-up, and 5% to 11% are reported to be major, requiring immediate evaluation or intervention.

Opinions vary greatly as to the importance of routinely reporting noncardiac findings in a coronary CTA study, in large part because of the deficiencies in empirical outcome and cost data (142). Some have argued that reporting of noncardiac findings would lead to additional costs and anxiety to the patient without proven benefit (143). Those holding such opinions may use filters to reduce the "maximum" field of view allowable, which limits the amount of mediastinum, lung, breast, and other thoracic structures that are reconstructed, although it does not completely exclude such structures. Others advocate reconstructing the examination with a full field of view to identify all incidental findings and report on their clinical significance (133,140,144). They point out that CT differs from the other cardiac imaging modalities by providing high-resolution diagnostic information about other organs besides the heart, with no extra radiation to the patient. Moreover, for symptomatic patients, typically with chest pain or shortness of breath, and an intermediate or high pretest probability of a noncardiac cause of the symptoms, extracardiac findings may not be "incidental."

In a series of 254 patients from Seoul who underwent coronary CTA, a noncontrast low-dose whole thoracic scan was used to screen for unrecognized extracardiac lesions (145). The coronary CT study was then reconstructed with a small field of view. In 20% of patients, an extracardiac abnormality was found on the initial thoracic scan that required additional work-up, treatment, or follow-up, while such findings were noted in 2% of patients from the contrast coronary CT study.

In the prospective ROMICAT study involving 395 acute chest pain patients presenting to the Massachusetts General Hospital Emergency Department, 45% of the patients had 1 or more incidental findings with 19% having 2 or more such findings (135). Noncalcified pulmonary nodules were most common (24%), followed by liver cysts (7%) and calcified pulmonary nodules (4%). Adjudication by an outcomes committee determined that 1.3% of patients (n=5) had their management changed by the incidental finding (pneumonia, pneumothorax, gallstones). An additional 4% were felt to have findings with the potential to alter future management (including hiatal hernia and thoracic aortic aneurysm). Further diagnostic imaging studies were recommended for 21% of patients (n=81), including those with noncalcified pulmonary nodules, contrast-enhancing liver lesions, and mediastinal lymph nodes. At 6 months, 3 patients had received biopsies as a result of the initial incidental CT finding, and in 2 patients, cancer was diagnosed and successfully removed.

Of specific concern with cardiac MDCT is the problem of incidental noncalcified pulmonary nodules. While substantial data are emerging from lung cancer screening studies of high-risk populations, the populations referred for cardiac CT are different, and caution should be used in extrapolating results of lung cancer screening trials to cardiac CT scanning. The reported prevalence of indeterminate pulmonary nodules discovered at cardiac CT that prompted radiological follow-up is reported to range between 1% and 20%. In the study of cardiac CT scans by Onuma et al. (136), for the 61 noncalcified lung nodules identified, 33 patients went on to have further investigations, and 2 of the nodules were found to be malignant after 6-month follow-up. In the ROMICAT study discussed in the preceding text, 245 of 395 patients had incidental findings of noncalcified pulmonary nodules, and 1 biopsy was done within 6 months, revealing adenocarcinoma (135). Follow-up data are not available for the other studies. Overall, the prevalence of indeterminate nodules found at cardiac CT is much lower than the reported prevalence of noncalcified lung nodules in high-risk lung cancer screening populations. Guidelines for management of small pulmonary nodules detected on CT have been published (146).

The 2008 revision of the cardiology fellowship training guidelines recommends that level 2 and 3 training include the review of 150 cardiac CT cases for incidental findings and a review of a dedicated teaching file of 25 cardiac CT cases featuring the presence of significant noncardiac pathology (147). Although this experience serves as an introduction to the topic, it cannot provide expertise in recognizing the full spectrum of pathology that can be found in the thorax outside the heart and in the regions of the upper abdomen that may be seen in some studies. In the worst case, the interpretation of noncardiac structures by physi-

cians without training in cross-sectional imaging of the thorax could lead to missed diagnoses that have immediate consequences on patient health; alternatively, it may result in increased and unnecessary follow-up and referral for insignificant findings that have been misinterpreted.

10.2. Use of Coronary CT Angiography in Asymptomatic High-Risk Individuals

For many individuals, the process of atherosclerotic plaque formation in coronary arteries begins early in life (148). Autopsy studies of young adults dying from traffic accidents, homicides, and suicides have found that 60% between the ages of 30 and 39 years have LAD plaques of AHA grade 2 or higher (fatty streaks and more advanced lesions) (149). Furthermore, those younger individuals with multiple risk factors have a higher subsequent rate of atherosclerotic involvement (150). Developing an accurate method of identifying younger asymptomatic patients with early atherosclerosis who might benefit from intensified risk factor modification to prevent or retard the onset of clinical disease represents an intuitively sensible response to such observations. Currently, the Framingham risk score (FRS) is often used for this purpose (151).

The FRS may not adequately assess risk for patients with unusually powerful comorbid conditions, such as peripheral arterial disease, long-standing or difficult to control diabetes, chronic kidney disease, smokers, and those with a family history of premature CAD. Additionally, young women, particularly those with early menopause, autoimmune disorders, or poorly controlled hypertension or hyperlipidemia, may be misclassified by traditional FRS assessment. A number of recent publications have suggested that it is possible to use calcium scoring, derived from noncontrasted CT scans of the heart, to improve risk stratification beyond the information provided by the FRS, particularly for patients who are in the Framingham intermediate risk group (i.e., FRS predicted 8-year risk of coronary heart disease death of 10% to 20%) (152).

Although current 64-channel coronary CTA can clearly detect calcified plaques as effectively as electron beam tomographic imaging, it adds the capability to image the noncalcified plaque, as discussed earlier in this document. What is lacking at present, however, is evidence specifically linking noncalcified plaques that are not obstructive with an independent clinically important increase in risk. In the large follow-up studies of coronary calcium in asymptomatic subjects, patients without significant calcium (which would include the patients with noncalcified plaques) had a very low event rate. In the St. Francis Heart study, this rate was around 0.1% per year (153).

Investigators from Seoul National University followed 1000 middle-age asymptomatic subjects (mean age 50 years) who were self-referred for 64-channel coronary CTA for a mean of 17 months (range 12 to 21 months, 97% complete) (154). Five percent of subjects had a stenosis greater than 50%, and 2% had a stenosis greater than 70%. Almost three quarters of these individuals had single-vessel obstructive disease with the lesions most often in the LAD artery. Four percent of subjects had only noncalcified plaques with 5 of 40 having a stenosis greater than 70%. In follow-up, the overall cohort had no cardiac deaths, 1 patient with unstable angina required hospitalization, and 14 patients were revascularized, the majority of which resulted from the coronary CTA findings. The prevalence of incidental noncardiac findings in this cohort and the additional tests and therapies that resulted from those findings were not reported.

To date there are no published trials evaluating the impact of specific therapy on clinical outcome in asymptomatic subjects identified as having only noncalcified atheroma by coronary CTA.

10.3. The "Triple Rule-Out" in the Emergency Department

The use of coronary CTA for the evaluation of patients with chest pain in the emergency department offers the potential to assess not only coronary artery stenoses as the cause of chest pain but also 2 other potentially life-threatening conditions: acute aortic syndromes and pulmonary embolism. Acute aortic syndromes include aortic dissection, intramural hematoma, and rupturing thoracic aortic aneurysm. This so-called "triple rule-out," however, poses specific logistic and conceptual challenges. The confidence and accuracy with which the pulmonary artery, aorta, and coronary arteries can be assessed by CT is related to the quality of contrast enhancement of each of these structures (155,156). The quality of contrast enhancement is, among other procedural issues, critically dependent on the timing of scanning relative to the beginning of contrast-medium injection (scan delay). Intravenously administered contrast material typically provides adequate opacification of the pulmonary arteries 8 to 12 seconds after the beginning of contrast injection, while opacification of the ascending aorta and coronary arteries occurs 8 to 10 seconds later.

An important challenge of the "triple rule-out" consists of achieving and maintaining adequate opacification of all 3 vascular beds of interest simultaneously while scanning proceeds between the apices of the lungs and the diaphragm over approximately 15 to 20 seconds with contemporary scanners (157). To avoid respiratory motion artifacts during scanning of the heart due to prolonged breath hold, scanning in the caudocranial direction may be preferable over the craniocaudal scanning typically used for coronary CTA (157,158). The needed field of view, section thickness, and scan length in the z-axis are different for the small-caliber and short coronary arteries than for the comparatively large-caliber and long pulmonary arteries and aorta. In fact, in the setting of an acute aortic syndrome, imaging of the abdominal aorta and iliac arteries together with the thoracic aorta is necessary for the recognition and characterization of critical malperfusion syndromes due to insufficient blood supply to the lower extremities and abdominal viscera and for the recognition of aortoiliac occlusive or aneurysmal

disease that might complicate the delivery of endografts indicated in the treatment of some aortic lesions (159). An appropriate scanning protocol for the "triple rule-out" will therefore represent a compromise between the optimal scan parameters for each component of the exam (158).

Subsequent image reconstruction from projection data benefits from ECG triggering or gating for the thoracic aorta and coronary arteries territories (159,160). The benefits and limitations of ECG gating have not been established for pulmonary artery CTA. However, the optimal field of view is smaller for the coronary arteries than for the pulmonary arteries and thoracic aorta. Also, the optimal time point during the cardiac cycle may vary substantially with heart rate for the coronary arteries, whereas the optimal timing relative to the cardiac cycle for reconstruction of the thoracic aorta is less narrow (160). More than 1 set of image reconstructions may be needed to optimally evaluate the thoracic aorta and the coronary arteries.

Only 2 studies to date have examined the use of CT to rule out more than 1 possible etiology of chest pain simultaneously in patients presenting to the emergency department (161,162). In the larger of the 2, from Thomas Jefferson University Hospital, all patients qualifying clinically for a "triple rule-out" in the emergency department one 8-hour day a week over a 1-year period were prospectively enrolled. Research assistants present in the emergency department during each enrollment day collected pretest clinical data. Scanning was done with a 64-channel CT from the lower margin of the clavicles to the estimated lower border of the heart (based on scout films) plus a 2-cm safety margin. Scan length was typically between 17 and 24 cm, and scans took between 12 and 15 seconds. The investigators used a 2-phase contrast injection: 70 mL of contrast followed by 25 mL of contrast mixed with an equal volume of saline, all injected at 5 mL/s. The objective was to visualize the coronary arteries with the undiluted contrast injection while simultaneously visualizing the pulmonary arteries with the dilute contrast from the second phase of the injection. A single experienced radiologist interpreted all the studies. Severe coronary stenosis was defined as greater than 70% luminal diameter narrowing. Two independent physicians defined final 30-day outcome using the clinical record plus follow-up contacts (98% complete). Of the 201 patients enrolled, 197 completed the protocol. Mean age was 49 years, 55% were women, and 46% were black. Baseline TIMI risk scores were 0 to 2 in 94% of patients. Diagnostic quality scans of the pulmonary arteries and aorta were obtained in 100% of patients. A clinically important extracoronary diagnosis that was felt to explain the patient's symptoms was found in 11%, including pulmonary embolism in 3 patients, aortic dissection in 1 patient, and pneumonia in 5 patients. Ten percent of patients had suboptimal image quality in at least 1 coronary artery. Most patients had minimal or no disease (88%), while 11% were found to have moderate-to-severe disease. For patients with no significant coronary disease, the post-test probability of ACS was less than 1%. One false-negative study was the result of observer error. No adverse outcomes were observed to 30 days. The mean effective radiation dose was estimated to be 18 mSv in patients without dose modulation and 8.7 mSv with prospective dose modulation.

Retrospective analysis of 64-channel coronary CTA datasets from 50 patients admitted to the emergency department with suspected ACS showed that a dedicated coronary CT protocol provides excellent visualization of the coronary arteries and proximal ascending aorta but did not show the pulmonary arterial system well enough to exclude pulmonary embolism (163).

The volume of contrast material required for a "triple-rule out" protocol exceeds the contrast volume that would be needed to examine any of the 3 vascular beds separately (157,158). In addition, a "triple rule-out" scanning protocol will have a higher radiation dose than typical chest CT or coronary CTA studies because of the section overlap needed to allow retrospective gating and the longer scan length. Radiation exposure is increased further when considering imaging of the legs to exclude deep venous thrombosis or imaging of the abdomen and pelvis when assessing an acute aortic syndrome. This is relevant because some of the patients with chest pain in the emergency department may be exposed to more ionizing radiation in the course of their work-up if radionuclide MPI or invasive coronary angiography is performed subsequently. In the Thomas Jefferson University Hospital study described in the preceding text, 21% of the "triple rule-out" protocol patients had subsequent stress MPI studies, and 7% had invasive angiography (162).

The occurrence of acute aortic syndromes or pulmonary embolism in the absence of suggestive symptoms and clinical context is uncommon (164), and emergency department physicians are usually not uncertain about all 3 cardiovascular conditions examined by the "triple rule-out" (165). Thus, routine use of a "triple rule-out" CT scan should not be used as a substitute for a careful clinical evaluation with targeted testing for the most likely causes of the patient's symptoms.

11. Safety Considerations

The 2 safety issues involved in use of coronary CTA are related to the dose of radiation delivered during imaging and the need to use iodinated contrast material. These risks will be briefly reviewed in this section.

11.1. Patient Radiation Dose

The typical doses of radiation reported to be associated with coronary CTA exceed those reported for invasive coronary angiography (Table 4).

Although substantial efforts have been directed toward reducing the radiation dose of CTA, most radiation safety experts subscribe to a model, discussed in the following text,

Table 4. Representative Values and Ranges of Effective Dose Estimates for Cardiac Studies

Examination	Representative Effective Dose Value (mSv)	Range of Reported Effective Dose Values (mSv)	Administered Activity (MBq)
Chest X-ray PA and lateral	0.1	0.05–0.24	N/A
Diagnostic invasive coronary angiogram	7	2–16	N/A
64-slice coronary CTA*			
Without tube current modulation	15	12–18	N/A
With tube current modulation	9	8–18	N/A
Prospectively triggered coronary CTA*	3	2–4	N/A
Percutaneous coronary intervention or radiofrequency ablation	15	7–57	N/A
Myocardial perfusion study			
Sestamibi (1-day) stress/rest	12	N/A	1480
Tetrofosmin (1-day) stress/rest	10	N/A	1480
Thallium stress/redistribution	29	N/A	130
Rubidium-82 rest/stress	10	N/A	2960
Myocardial viability study			
PET F-18 FDG	14	N/A	740
Thallium stress/reinjection	41	N/A	185

Adapted from Mettler et al. (166) and Strauss and Bailey (167). *64-slice multidetector-row computed tomography and prospectively triggered coronary CTA studies published since 2005 only.
CTA indicates computed tomographic angiography; FDG, fluorodeoxyglucose; MBq, megabecquerel; mSv, millisievert; N/A = not applicable; PA, posteroanterior; and PET, positron emission tomography.

which assumes that there is no safe dose of radiation and any exposure may increase the long-term risk of cancer. While such an assumption represents a "worst-case scenario," in order to minimize any future risk of cancer, it is reasonable to limit a patient's exposure to radiation by following some basic principles, including:

1. Ordering coronary CTA only in keeping with established appropriateness criteria for cardiac CT and CMR (1), and only if the clinical question at hand cannot be adequately addressed by other means (an update of appropriate use criteria for cardiac CT is expected in 2010 and an update of appropriate use criteria for CMR is planned).
2. Performing the CTA study with the minimum radiation dose required for adequate diagnostic quality.
3. Avoiding unnecessarily repeating coronary CTA.

Parameters of absorbed radiation dose, expressed in SI units of milliGray (mGy), reflect the energy absorbed by the body of a patient exposed to ionizing radiation (169). The radiation dose absorbed by patients cannot be measured easily. The effective radiation dose (E, expressed in units of millisieverts [mSv]) is the dose parameter most frequently quoted in the coronary CTA literature. E is a calculated, not measured, quantity meant to express the risk of a nonuniform partial-body exposure to radiation, for example of the chest, in patients undergoing coronary CTA, relative to the whole-body exposure to radiation experienced by Japanese survivors of atomic bomb explosions. Estimates of E are based on complex assumptions and simulations. They pertain to a generic mathematical model of a human body with a mass of 70 kg. The concept of E was developed for the purpose of radiation protection and cannot (and was never meant to) reflect individualized patient dose. As a rough, generic estimate of risk, E is mostly useful for comparing different imaging procedures or protocols and for optimizing protocols that involve exposure of multiple organ systems.

The numerical value of E for coronary CTA can differ depending on the method used to estimate E even though the radiation exposure is the same (170–172), and the values of E reported for coronary CTA in the medical literature during different eras may not be comparable to each other.

Because of the uncertainties related to the estimation of E, and because there is no measurable reference standard, E should be reported as ranges and not as single numerical values. Differences of estimates of E by a factor of less than 2 are unlikely to be clinically relevant. The range of E reported for coronary CTA in the medical literature as of 2008 is approximately 2 to 32 mSv (166), and the representative median value of E for coronary CTA with current technology is approximately 2 to 15 mSv, with the lowest values coming from centers using 64-channel dual-source CT in the "step and shoot" mode (173,174). The ranges and representative medians for E of other common imaging studies that use ionizing radiation are listed in Table 4.

The PROTECTION I (Prospective Multicenter Study On Radiation Dose Estimates of Cardiac CTA In Daily Practice) trial studied the estimated radiation dose associated with coronary CTA at 50 international study sites (21 university, 29 community) in 2007 (5). The median effective radiation dose was 12 mSv (interquartile range among centers 8 to 18 mSv, range 5 to 30 mSv). Small relative differences in estimated radiation dose were correlated with patient-related factors (patient weight, absence of sinus rhythm). Larger differences were correlated with use of specific strategies to reduce the study radiation dose and with differences in CT equipment (5).

In 2007, the Advanced Cardiovascular Imaging Consortium, a multicenter collaborative quality improvement program in Michigan, initiated a prospective best-practices radiation-dose reduction program at 15 sites (175). Relative to the control period, the program reduced estimated median radiation dose by 53%. Estimated effective dose was 21 mSv in the control period and 10 mSv in the intervention period. The proportion of scans considered of diagnostic quality was 89% in the control period and 92% in the intervention period, indicating no deterioration in image quality with the radiation-dose reduction protocols.

The risk of developing a malignancy as a stochastic effect of biologic damage resulting from radiation is extremely difficult to ascertain. Several authorities have advocated the "linear no-threshold" hypothesis, which proposes that the risk of malignancies increases linearly with radiation dose, without a threshold below which radiation cannot cause malignancies (176). Based on this hypothesis, the age- and sex-averaged lifetime risk of dying from a malignancy attributable to radiation exposure has been estimated to be approximately 5 to 7.9 in 100 individuals of the general population per 1 Sv of E (176,177). For a "normal" population, this would translate into an estimated average lifetime risk of approximately 0.05% to 0.08% of dying from a malignancy resulting from a typical coronary CT angiogram with an E of 10 mSv. This risk is superimposed on the 21% intrinsic population-averaged lifetime risk in the United States of dying of a malignancy.

In general, radiation exposure and dose are inversely related to image noise and, by implication, image quality. Efforts at decreasing radiation exposure and patient dose should aim to deliver an image quality that allows confident image interpretation. Assuming maintenance of a specific level of image noise, radiation dose decreases with:

1. Lower tube current (expressed in milliAmpere [mA] or the product of tube current and exposure time, expressed in milliAmpere seconds [mAs]).
2. Lower tube voltage (peak kiloVolt, kVp).
3. Greater slice thickness (mm).
4. Higher table advance per gantry rotation expressed as a fraction of the combined width of all slices acquired simultaneously (also referred to as "pitch," which is dimensionless). A higher value of pitch indicates faster table advance and, hence, less overlap of irradiation between successive gantry rotations (178).
5. Lower patient body mass (kg).

Technical options for reducing radiation exposure and patient dose by the practitioner of coronary CTA include:

1. Use of the lowest settings of tube current and tube voltage consistent with diagnostic image quality (179,180). In the PROTECTION I study, reduced tube voltage from greater than or equal to 120 to 100 kV was used in only 5% of subjects but was associated with an estimated 46% relative reduction in radiation dose and an improvement in image quality (5).
2. Use of ECG-controlled tube current modulation to reduce tube current during the portions of the cardiac cycle unlikely to be used for image reconstruction (typically systole) (180). Increasing the length of time during the cardiac cycle during which the tube current is reduced is more feasible in scanners with higher temporal resolution (181). If during image reconstruction the least degree of cardiac motion is found during the period of reduced tube current, the quality of images reconstructed at that phase of the cardiac cycle may not be optimal due to low signal-to-noise ratio. In the PROTECTION I study, ECG-controlled tube current modulation was used in 73% of patients who had spiral CT data acquisition and was associated with a 25% relative reduction in estimated radiation dose in multivariable analysis but no effect on image quality (5).
3. Prospective triggering or "step and shoot" mode with radiation output only during predetermined portions of the cardiac cycle (also called sequential scanning) (182). With the use of prospective triggering, the time point of optimal image quality with the least degree of cardiac motion may be missed altogether. In addition, this method of imaging does not allow for assessment of LV function since a full 4D dataset is not collected. In the PROTECTION I study, this method of scanning was used in only 6% of patients and was associated with a 78% relative reduction in estimated radiation dose relative to spiral scanning but no effect on image quality (5).
4. Heart-rate dependent increase of pitch (181), or eliminating slice overlap altogether (with area detectors or scanners that can cover the entire length of the heart in the z-direction with 1 gantry rotation).

11.2. Intravenous Contrast

Safe and effective use of contrast media is an important part of the clinical use of coronary CTA. Aside from allergic reactions, contrast medium-induced nephropathy is the major safety issue related to contrast administration. Contrast-induced nephropathy is a form of acute kidney injury whose pathogenesis is not well understood and is likely multifactorial. Possibilities that have been proposed include a direct toxic effect of contrast agent on the tubular epithelium, oxidative stress, ischemic injury, and tubular obstruction. Neurohormonal factors have also been implicated in the pathogenesis of contrast-induced nephropathy.

Contrast-induced nephropathy is often defined clinically by an arbitrary change in renal function. The 2 most common definitions are based on either an absolute change in serum creatinine of greater than 0.5 mg/dL or a greater than 25% increase in serum creatinine from baseline within 2 to 3 days following the exposure to the contrast agent (183). The increase in serum creatinine is often associated with adverse clinical outcomes including a higher mortality (184–187).

Risk factors associated with the development of contrast-induced nephropathy include: hypotension, congestive heart failure, chronic kidney disease, diabetes, age older than 75 years, anemia, and volume of contrast (188). An increasing incidence of contrast-induced nephropathy with estimated glomerular filtration rates below 60 mL/min/1.73 m^2 was established from retrospective analysis of clinical trials of patients undergoing coronary angiography. Such analysis underscores the importance of pre-existing renal impairment as a major risk factor for developing contrast-induced nephropathy (189).

The older, ionic, high-osmolar contrast agents are the media most likely associated with adverse events in both routine and high-risk patient populations. Among the newer low-osmolar or iso-osmolar contrast agents, there is no clear consensus on which is the better and safer contrast agent to use either intravenously or intra-arterially. Prospective randomized controlled trials comparing iso-osmolar with low-osmolar contrast agents have been inconclusive, and all contrast agents have the potential of causing contrast-induced nephropathy (190–195).

Current generation MDCT scanner technology specially designed for imaging human coronary arteries usually requires the use of a higher or even the highest concentration of iodine as well as faster injection rate to get the best possible coronary visualization (196,197). In general, intravenous administration of iodine-containing contrast media is associated with significantly lower incidence of contrast-induced nephropathy (0% to 21%) compared with the intra-arterial approach. The possible explanation for lower contrast-induced nephropathy rates with the intravenous approach include the use of lower doses of contrast, less sick patients with fewer chronic comorbidities, and fewer procedure-related complications that might precipitate an acute renal injury, such as dislodgment of atheromatous material be an intra-aortic catheter or significant hypotension (198–202).

The writing committee acknowledges the current controversies in this area, yet feels some measures to minimize the occurrence of contrast-induced nephropathy in patients referred for coronary CTA seem reasonable to apply across all protocols and patients. These should include screening patients by noting baseline serum creatinine levels and calculating glomerular filtration rates, noting any history of diabetes mellitus, CAD, peripheral vascular disease, and other underlying conditions that would make the patient high risk, avoiding preprocedural dehydration, limiting contrast agent dose as much as possible, and ensuring adequate hydration before and after contrast exposure. Since the physicians performing the coronary CTA are often not the physicians involved in the routine care of the patients to be studied, it is critical that both referring and performing physicians communicate about the need and plans for measures to minimize contrast-induced nephropathy. If both parties recognize the need to be vigilant on this score, errors of omission are less likely to occur than if each assumes the other is managing the preprocedure preparations.

12. Cost-Effectiveness Considerations

National expenditures on health care as a percentage of total gross domestic product continue to rise each year and now exceed 15% in the United States. One of the key concerns payers and policy makers have with any new test is that it will increase total medical expenditures, thereby exacerbating the already intense competition among healthcare and other priorities, such as education, transportation, and defense, for societal resources. Medical economic analyses can be very useful in helping to define the efficiency with which new medical technologies produce improvements in the public health. Careful economic analysis is required to define whether a new testing strategy may actually recoup some or all of its direct costs by eliminating the need for downstream tests that would otherwise be used. Of course, it is also possible that a new testing strategy may increase total testing costs in the long run by creating the need for follow-up tests that would not otherwise have been performed. In addition, even if the test does not "pay for itself" in that manner, cost-effectiveness analysis can define whether its use for defined clinical indications provides good value and make it a more attractive societal investment than other less efficient means of improving health.

In general, the literature on the economic effects of coronary CTA to date is very limited, comprising a few claims data analyses and several model-based analyses. The former are often limited by the inability to account for all the relevant clinical details that affect both pre- and post-test care patterns. The latter are often limited by the lack of empirical data relevant to the analysis, and by unrealistic assumptions about the patterns of care in the "real world."

The cost consequences of choosing MDCT versus SPECT MPI in patients without known CAD have recently been explored in a large insurance claims database (203). Comparing 1938 subjects who had an MDCT with 7752 subjects who had SPECT showed that initial MDCT was associated with 16% lower follow-up costs (approximately $450) exclusive of the costs of the test. Subjects who initially received an MDCT were more likely to get a SPECT in follow-up, while subjects who initially underwent SPECT were more likely to undergo subsequent invasive coronary angiography. At 9 months, rates of follow-up revascularization did not differ between the 2 groups. In this data sample, the overall 9-month rate of revascularization was about 2% with a CAD-related hospitalization rate of 4%, implying that the study population had a very low prevalence of significant CAD.

To date, several preliminary economic models of coronary CTA strategies have been published. Such efforts are obviously limited by the lack of empirical outcome data currently available and the resulting need to make major

unverifiable assumptions about outcomes resulting from a coronary CTA testing strategy relative to other management options. One model was created for the United Kingdom National Health Service in 2007 and considers alternative diagnostic workup strategies for a stable cohort with suspected CAD (48). The primary model was a short-term cost minimization model based largely on pooled diagnostic accuracy data for 8 different diagnostic testing strategies. Costs were assigned using U.K. prices: exercise ECG £66, exercise MPI £293, 64-channel MDCT £206, and invasive coronary angiography £320. Because MDCT had a better sensitivity and specificity compared with MPI and a lower cost, short-term modeling suggested that MDCT-based strategies would be more economically efficient than MPI-based strategies, although differences narrowed somewhat in patients with a higher pretest probability of disease. The least expensive strategy overall was exercise ECG followed by MDCT for patients who had a positive or indeterminate result. Need for invasive angiography in patients with a positive MDCT increased the testing costs by about 20% at a 10% pretest probability and by about 60% at a 50% pretest probability. The most expensive strategy at all pretest probabilities was exercise MPI as the initial test with invasive coronary angiography for a positive or indeterminate result. These results suggest that the high sensitivity of MDCT would allow MDCT-based strategies to provide an efficient (i.e., lower cost) evaluation of low pretest probability patients, since a negative test would allow invasive angiography to be avoided. However, the assumptions of this model need to be empirically validated since "real life" practice often deviates in a number of unanticipated ways from the "ideal" represented in decision models. In addition, U.S. prices would be expected to vary from those in the United Kingdom. Finally, the modeling does not consider the cost of incidental findings on MDCT that require additional work-up.

A cost-effectiveness model created by investigators from Harvard compared the costs and health outcomes of a coronary CTA-based evaluation strategy with a standard care strategy using biomarkers and stress testing in patients with acute chest pain (204). For this application, there are some empirical cost data from the Beaumont Hospital single-center randomized trial (72). The Harvard model considered hypothetical cohorts of 55-year-old men and women with acute chest pain being evaluated in the emergency department. The overall prevalence of ACS was assumed to be 10% with 2% having stable angina and 88% having nonanginal chest pain. In the usual care strategy, the investigators randomly allocated patients to 1 of 3 testing strategies: stress ECG, stress echo, or stress SPECT. The results in the usual care arm reflect the blending of equal amounts of those 3 strategies. In the men, the coronary CTA strategy increased costs per patient by $200 relative to usual care, while in women, the coronary CTA strategy saved $380. This model projected that the coronary CTA strategy would increase life expectancy by 10 days for men and 6 days for women. The incremental cost-effectiveness of the coronary CTA strategy in men was estimated at $6400 per quality-adjusted life year added, while for women the coronary CTA strategy was economically dominant (lower costs, better quality-adjusted survival). In sensitivity analysis, when the usual care strategy was changed to all patients receiving stress SPECT MPI, the coronary CTA strategy was found to be economically dominant for both genders.

In a second decision model–based analysis of the use of coronary CTA in patients presenting to the emergency department with low-risk chest pain, the strategy of MDCT from the emergency department had better outcomes and lower costs than observation unit care plus either stress ECG or stress echo (205).

The Beaumont Hospital randomized trial together with the 2 model-based analyses suggest that for low-risk acute chest pain patients (with pain that is clinically felt to be noncardiac), coronary CTA may provide an efficient evaluation strategy relative to conventional alternatives. Whether the strategy also modestly improves long-term outcomes, as the model-based analyses suggest, will require additional empirical data to determine. In addition, the extent to which these results apply to intermediate-risk acute chest pain patients is unclear at present.

13. Quality Considerations

The concept of quality in coronary CTA applies to patient selection, technical training, patient preparation, image acquisition, physician training, interpretation and reporting of results, and patient safety. The technical performance of coronary CTA with modern 64-channel machines is relatively uncomplicated and robust. However, the interpretative aspects of coronary CTA are inherently more challenging, as has been discussed in other sections of this document. It is important to note that the clinical studies on the diagnostic accuracy of coronary CTA reviewed earlier in this document typically followed detailed protocols for patient preparation and technician training. And while technicians from a broad array of backgrounds can be trained to perform these studies within a few weeks, acquisition technique does influence image quality and therefore can influence diagnostic accuracy. Each laboratory should have a routine that assures maximal patient safety and the best possible image quality. Physician training needed to perform and interpret these studies with a high level of quality requires the same sort of structured intensive training program needed for high-level competence in other forms of complex cardiovascular imaging. Thus, short stand-alone courses that attempt to fast track this process, by themselves, would be insufficient for this purpose. The 2005 ACCF/AHA Clinical Competence Statement on Cardiac Imaging With Computed Tomography and Magnetic Resonance (206), the 2006 ACR Practice Guideline for the Performance and Interpretation of Cardiac Computed To-

mography (207), the 2009 SCCT Guidelines for the Interpretation and Reporting of Coronary Computed Tomographic Angiography (208), the 2008 White Paper from the ACR and NASCI on structured reporting of coronary CTA (209), the 2008 ACCF/ACR/AHA/ASE/ASNC/HRS/NASCI/RSNA/SAIP/SCAI/SCCT/SCMR Health Policy Statement on Structured Reporting in Cardiovascular Imaging (210), and the ACR Clinical Statement on Noninvasive Cardiac Imaging (211) currently serve as reference points for the performance and interpretation of cardiac CT. Guidance documents such as these will need to be updated periodically as the technology of cardiac CT evolves and as the knowledge base supporting its clinical use matures. The 2005 ACCF/AHA Clinical Competence Statement on Cardiac Imaging With Computed Tomography and Magnetic Resonance largely preceded the widespread dissemination of 64-channel CT machines (206). Although it is impossible to know whether most readers today are level 2 or level 3 competent, having this statement as a reference point as the technology becomes more widely disseminated may assist in improving the overall interpretation quality for this test in practice. Board certification in cardiovascular CT by passing a written examination is offered by the Certification Board of Cardiovascular Computed Tomography (www.cbcct.org). Future studies are needed to address the impact of variability in test performance and interpretation on the ability of coronary CTA to alter clinical care and improve future outcomes. Other important needs include the development of appropriate quality measures and data standards that can allow monitoring of diagnostic performance and identify areas for quality improvement. Appropriate use criteria needs to be updated as the technology and supporting evidence base evolve. Finally, close monitoring of radiation exposure administered to patients is necessary to weigh the benefits of this noninvasive test and potential future unintended consequences and costs.

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APPENDIX 1. AUTHOR RELATIONSHIPS WITH INDUSTRY AND OTHER ENTITIES—ACCF/ACR/AHA/NASCI/SAIP/SCAI/SCCT 2010 EXPERT CONSENSUS DOCUMENT ON CORONARY COMPUTED TOMOGRAPHIC ANGIOGRAPHY

Committee Member	Consultant	Speaker	Ownership/ Partnership/ Principal	Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
Dr. Daniel B. Mark (Chair)	• AstraZeneca • Aventis • Medtronic, Inc. • Novartis	None	None	• Alexion Pharmaceuticals, Inc.* • Medicure* • Medtronic, Inc.* • National Institutes of Health/Agency for Healthcare Research and Quality* • National Institutes of Health/National Heart, Lung, and Blood Institute* • Pfizer* • Proctor & Gamble*	None	None
Dr. Daniel S. Berman	• Flava Pharma	None	None	• Astellas* • Bristol-Myers Squibb* • Siemens* • Tyco Mallinckrodt	None	None

Committee Member	Consultant	Speaker	Ownership/ Partnership/ Principal	Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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Dr. Mark A. Hlatky	None	None	None	None	None	None
Dr. John McB. Hodgson	None	• GE Medical	None	None	None	None
Dr. Michael S. Lauer	None	None	None	None	None	None
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Dr. Richard L. Morin	None	None	None	None	None	None
Dr. Debabrata Mukherjee	None	None	None	None	None	None
Dr. Michael Poon	None	None	None	None	None	None
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Dr. Jerome L. Hines	Official Reviewer—ACCF Board of Governors	None	• GE Healthcare	None	None	None	None
Dr. Mark A. Hlatky	Official Reviewer—ACCF Task Force on Clinical Expert Consensus Documents	None	None	None	None	None	None
Dr. Judd Hollander	Official Reviewer—AHA	None	None	None	• Siemens*	None	None
Dr. James K. Min	Official Reviewer—Society of Cardiovascular Computed Tomography	None	• GE Healthcare	None	None	None	None
Dr. John P. Mulrow	Official Reviewer—Society for Cardiovascular Angiography and Interventions	None	None	None	None	None	None
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Peer Reviewer	Representation	Consultant	Speaker	Ownership/ Partnership/ Principal	Research	Institutional, Organizational, or Other Financial Benefit	Expert Witness
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Dr. William A. Zoghbi	Official Reviewer—ACCF Board of Trustees	None	None	None	None	None	None
Dr. Suhny Abbara	Content Reviewer—Expert	• EZEM • Magellan Healthcare Inc. • Partners Imaging • Perceptive Informatics, Inc.	• Siemens	• Partners Imaging	• Bracco	None	None
Dr. K. Ananthasubramaniam	Content Reviewer—ACCF Imaging Council	None	None	None	None	None	None
Dr. Ralph Brindis	Content Reviewer—ACCF Appropriate Use Criteria Task Force	None	None	None	None	None	None
Dr. Pamela S. Douglas	Content Reviewer—ACCF Appropriate Use Criteria Task Force	• Northpoint Domain Scientific Advisory Board	None	• Northpoint Domain	• Abiomed • Amgen • Atritech • Edwards • Osiris • Viacor	• American College of Cardiology: board member; American Society of Echocardiography (nonvoting)	None
Dr. Victor A. Ferrari	Content Reviewer—ACCF Task Force on Clinical Expert Consensus Documents	None	None	None	None	None	None
Dr. Robert C. Hendel	Content Reviewer—ACCF Appropriate Use Criteria Task Force	• Astellas Pharma (noninvasive) • PHx Health (noninvasive)	None	None	• Astellas Pharma (noninvasive) • GE Healthcare (noninvasive)	None	• 2008: Represented defendant on diagnostic testing case regarding whether standard of care was followed in diagnostic evaluation for chest pain syndrome. Case closed, for defense.
Dr. Christopher Kramer	Content Reviewer—ACCF Imaging Council	None	• Merck/ Schering-Plough	None	• Astellas • GlaxoSmithKline • Merck • Siemens Healthcare	None	None
Dr. Wilfred Mamuya	Content Reviewer—Expert	None	None	None	None	None	None
Dr. Robert S. Rosenson	Content Reviewer—ACCF Task Force on Clinical Expert Consensus Documents	• Abbott • Anthera • AstraZeneca* • Daiichi Sankyo • LipoScience • Roche	None	• LipoScience*	None	• Grain Board	None
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