Cardiac Computed Tomography: Current Practice and Future Applications

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Cardiac computed tomography (CT) has continued to make great strides in cardiovascular imaging. New advances and refinements in technology have enabled CT to render astonishingly detailed images. Cardiac CT depends on a high temporal resolution to minimize coronary artery movement–related motion artifacts. There is ongoing debate as to the position of CT in the algorithm of diagnostic imaging in the realm of the cardiovascular sciences. There is a definite role for cardiac CT in patients with chest pain who have low or intermediate probability of coronary artery disease; a negative result on cardiac CT angiography could potentially exclude significant coronary artery disease and thus obviate further expensive workup. Further advancements in technique and validation of results will help establish CT on firmer ground. Such developments should proceed in tandem with reimbursement practices that encourage use of this tool in the right clinical context.

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Key words: Cardiac computed tomography • Vulnerable plaque • CT angiography • Cardiovascular imaging

The gold standard for visualization of the coronary arteries in clinical practice has been invasive coronary angiography, and the use of this technique as a diagnostic tool has increased manifold in the past 3 decades.[1] There has been increasing interest in the development of less invasive and more cost-effective techniques for the evaluation of the coronary arteries. Although invasive angiography is the gold standard for the assessment of obstructive coronary lesions, this modality has been associated with discrepancies in terms of clinicopathologic results. These include operator-dependent variables, such as visual estimation of the severity of lesions.[2]

Of the many imaging modalities being investigated, cardiac computed tomography (CT) seems to be the most promising. CT has evolved into a powerful clinical tool since its pioneering introduction in 1972 by Sir Godfrey N. Hounsfield, DSc. Any imaging modality for the heart must combine a high temporal resolution, to avoid rapid cardiac motion artifact, with a high spatial resolution, to visualize the intricate and complex anatomy of the heart. Cardiac CT thus depends on a high temporal resolution—albeit one that is less than magnetic resonance imaging (MRI) and conventional angiography—to minimize coronary artery movement–related motion artifacts.[3] Theoretically, a temporal resolution of 19 ms would be required to completely suppress motion artifacts arising from cardiac and pulmonary movement, but this technology does not yet exist.[4] The administration of an iodinated contrast agent increases CT attenuation and permits visualization of the coronary artery lumen.[5] In this context, it is worth noting that there is a linear relationship between voxel signal intensity (image brightness) and the x-ray linear attenuation coefficient, which is scaled relative to air and water and converted to an integer. This measurement is expressed as Hounsfield units (HU).[6]

The Evolution of Cardiac CT

The technology behind cardiac CT has continued to evolve since the introduction of the first electron beam computed tomography scanner in the 1980s (also called *cine CT* or an *ultrafast CT scanner*). Four-slice CT was introduced in 2000, 16-slice CT was introduced in 2002, and 64-slice CT was introduced in 2004. Most recently, we have also seen the introduction of the 256-slice and 320-slice scanners.

The less than satisfactory diagnostic yield of 16-slice CT was established by Kaiser and colleagues,[7] who found that the overall diagnostic sensitivity of this test for significant coronary artery disease (CAD) was 86%, but that the specificity was only 49%. Improvements in temporal resolution and scan times have resulted in the introduction of a new generation of scanners. There is a definite role for cardiac CT in patients with chest pain who have low or intermediate probability of CAD; a negative result on cardiac computed tomography angiography (CTA) could potentially exclude significant CAD and thus obviate further expensive workup.[8] In a study comparing 64-slice cardiac CT with quantitative coronary angiography, cardiac CT was found to have significant diagnostic accuracy with sensitivity of up to 95% and specificity of up to 90% per patient for stenoses.[9] Table 1 summarizes the results of 2 meta-analyses that evaluated the sensitivity and specificity of multislice computed tomography (MSCT).[10,11] Both these studies used conventional coronary angiography as the reference standard.

A dual-source CT system that incorporates 2 x-ray tubes and 2 corresponding detectors offset by 90 degrees offers considerable advantages (SOMATOM® Definition, Siemens, Forchheim, Germany).[12] Dual-source computed tomography (DSCT) scanners with 0.32-second gantry rotation time are able to afford a temporal resolution as low as 83 ms independent of heart rate for CTA and functional evaluation.[13] DSCT without β-blocker premedication has been studied against coronary angiography for diagnostic accuracy. The results showed that DSCT retained high diagnostic accuracy, even in patients with high heart rates.[14] A recent study has found that artifacts in DSCT scans are mainly

Table 1
Sensitivity and Specificity of Cardiac CT

Meta-Analysis	Technique	Sensitivity (95% CI)	Specificity (95% CI)
Vanhoenacker PK et al[10]	64-slice	93% (88-97)	96% (96-97)
54 studies*	16-slice	83% (76-90)	96% (95-97)
	4-slice	84% (81-88)	93% (91-95)
Sun Z and Jiang W[11]	Segment-based	83% (79-89)	93% (91-96)
47 studies	Vessel-based	90% (87-94)	87% (80-93)
	Patient-based	91% (88-95)	86% (81-92)

*Data refer to detection of more than 50% stenosis per segment.
CT, computed tomography; CI, confidence interval.

due to calcified plaque and misregistration. It was found that once the artifacts were recognized, they did not pose an impediment to scan readability.[15]

The value of cardiac CT in an emergency department (ED) setting is being investigated, and it promises to be a valuable tool for ED physicians. Chest pain is one of the most common causes of presentation to the ED and a leading cause of malpractice suits against ED physicians.[16] In a triple rule-out examination that can be performed in the ED, CT is used to evaluate with great accuracy 3 leading and potentially fatal causes of chest pain—coronary disease, pulmonary embolism, and aortic dissection—in a single study with greater than 90% accuracy.[17] Sixty-four–slice cardiac CT performed in the ED had a high positive predictive value for predicting acute coronary syndrome, and a negative study indicated low likelihood of major cardiovascular events.[18] Furthermore, it has been established that a certain subset of patients with acute coronary syndrome–type symptoms can be diagnosed as having noncoronary causes of chest pain and discharged home without adverse clinical outcomes.[19,20] There is immense potential for multidetector computed tomography (MDCT) to improve the management of select patients with chest pain in an ED setting. However, more information from randomized clinical trials is urgently needed before CT can become part of the diagnostic algorithm or potentially replace existing tests like myocardial perfusion scintigraphy (MPS).[21]

Noncalcified or Vulnerable Plaque

The term *vulnerable plaque* was initially coined by William C. Little, MD. He based this terminology on serial angiographic studies of patients with myocardial infarction, which showed that a culprit lesion need not have produced severe luminal occlusion before an acute coronary occlusion. Rather, a nonobstructive lesion could become "vulnerable" and thereby become obstructive given the appropriate triggers.[22]

Although coronary angiography can grossly identify features like plaque disruption, luminal thrombosis, and calcification, it fails to delineate qualitative features of the plaque.[23] Detection of asymptomatic CAD has been in the limelight more recently since the publication of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force report.[24] Here, the authors argue that detection of subclinical atherosclerosis by imaging motivates lifestyle changes in patients and decreases disease burden in the population, which eventually translates into health care dollars saved. It must be mentioned in this context that the SHAPE Task Force and its recommendations have generated much controversy in the scientific community. Although in a strict pathophysiological sense, the vulnerable plaque is the main orchestrator of disease in CAD, it is abetted in the process by vulnerable (thrombosis-prone) blood and also by vulnerable (arrhythmia-prone) myocardium. This finding gave rise to the concept of the "vulnerable patient," as proposed by Naghavi and colleagues.[25] Traditional population-based screening tools, including the Framingham risk score, identify the extremes in terms of risk—the high and the low—but are thought to vastly underestimate the intermediate-risk group, which is thought to provide the major substrate of CAD in a given population.[24] Noncalcified atherosclerotic lesions are thought to be positively correlated with the vulnerable plaque and, thus, with the vulnerable patient. These lesions are associated with lower CT density, positive remodeling, and adherent spotty calcium, features that may indicate plaque vulnerability.[26]

Detection of the Vulnerable Plaque

In most patients, an acute myocardial infarction is often the first clinical event that heralds the onset of CAD; most patients are entirely asymptomatic prior to the event. The acute event is commonly caused by rupture or, less often, by erosion of coronary atherosclerotic plaques, many of which are not associated with significant luminal stenosis before the event.[27] Thus, identifying vulnerable plaques in these asymptomatic individuals assumes great importance because of the potential for early intervention that could delay the progression of events that would otherwise culminate in an acute coronary event. The histologic parameters known to be associated with the vulnerable plaque include plaque size, positive remodeling, a large necrotic core, a thin fibrous cap, macrophage infiltration, and plaque vascularization.[27]

The major techniques that permit the identification of the vulnerable plaque are ultrasound, MRI, nuclear imaging, and MDCT.[28] A good majority of the ultrasound studies have been performed with carotid plaques, owing to the larger caliber and easy accessibility of these plaques.[29] Carotid artery intima-media thickness has also been studied extensively because it is thought to be a marker of adverse cardiovascular and cerebrovascular outcomes.[30] MRI-utilizing contrast, such as fibrin, nitric oxide, and ultrasmall particles of iron oxide, has been used for imaging the vulnerable plaque. Although intravascular ultrasound

(IVUS) is attractive because it affords direct visualization of the plaque, it tends to be invasive. Nuclear imaging, with its ability to identify metabolic processes, holds great promise and has been studied with respect to the identification of vulnerable plaques.[31] The uptake of ^{18}F-radiolabeled fluorodeoxyglucose into macrophages, which allows visualization of atherosclerotic plaques, has been studied with promising results.[32,33] A bewildering array of targets is available for radionuclide imaging, a detailed discussion of which is beyond the scope of this article. Other targets being explored include chemokines (MCP-1, VCAM-1), integrins involved in angiogenesis $\alpha_3\beta_3$, lipoproteins like LDL, platelet glycoprotein VI, apoptosis markers, and matrix metalloproteinases.[31]

Although total plaque and calcified plaque areas can be quantitated, many of the histopathological features mentioned earlier may not be amenable to evaluation by CT due to limitations of spatial resolution and soft tissue contrast.[34,35] However, in this context, it must be noted that therapy for CAD has systemic components, and thus a global assessment of plaque burden or coronary artery calcification (CAC) score provides invaluable information.[35]

New Applications for CT

MSCT, when combined with myocardial perfusion scan imaging, can be used to identify intermediate-risk (symptomatic or asymptomatic) patients. MSCT is a sensitive test, and myocardial perfusion scan imaging is a specific test. Combining the tests allows for integration of functional and anatomic assessment of CAD, thereby obviating the need for invasive angiography in certain patient subsets.[36] Another application is the use of calcium scores obtained by CT to detect high-risk patients within a low-risk population identified by MPS.[37] In a study that combined the use of calcium scores and stress single-photon emission computed tomography (SPECT), asymptomatic patients with an abnormal CAC score and baseline normal or low-risk results on stress SPECT who were referred for a second stress study experienced no increase in adverse cardiac events.[38]

CT has also made forays into the assessment of myocardial viability. The ability of MDCT to accurately identify and characterize morphologic features of acute and healed myocardial infarction has been demonstrated in animal models.[39] Adenosine stress-contrast enhanced MSCT has been shown to be a potential alternative to MPS because it can show myocardial ischemia by adenosine and also demonstrate coronary stenosis.[40]

CT has been shown to compare favorably with IVUS in measurements of atherosclerotic plaque and the lumen area.[41] The improved spatial resolution offered by MDCT enables visualization of aortic valve anatomy and pathology.[42,43]

Limitations and Disadvantages

The major limitations of CTA that have imperiled its widespread acceptance are motion artifacts, restrictions based on body mass index (which must be > 30 kg/m^2), and radiation exposure. The presence of artifacts relates to movement of cardiothoracic structures, such as the lungs and coronary blood vessels, and also to high heart rates (> 70 beats/min) and arrhythmias. The presence of intracoronary calcium also makes certain segments of scans unreadable. It has been noted that although there is an inverse relationship between image quality and heart rate and heart rate variability, diagnostic accuracy of cardiac CT was not significantly affected by these factors. However, significant calcium burden (calcium score > 1000) was found to be the major factor that decreased diagnostic accuracy with regard to CTA, and it should be an indication to review the reason for the CTA study and the clinical utility of the data that will be obtained, taking into consideration the experience of the interpreting physicians prior to proceeding with the study (Table 2).[20,44-46]

Another major disadvantage associated with cardiac CT is radiation exposure. In a study by Einstein and colleagues,[47] lifetime cancer attributable risk for standard 64-slice CT scans ranged from 1 in 143 for a 20-year-old woman to 1 in 3261 for an 80-year-old man. The radiation dose associated with a 64-slice CT is 3 to 7 times higher than that associated with a routine body CT scan.[48] The mean effective radiation dose from coronary angiography is 5.6 mSv, which is about half the radiation exposure associated with CTA.[49] Using prospective electrocardiogram-triggering or step-and-shoot mode, radiation is applied only at a preset time in the cardiac cycle, resulting in high diagnostic image quality with an effective radiation dose as low as 2.6 mSv.[50]

The lack of widespread acceptance of this technique and also its unsettled position in clinical evaluation algorithms make CT unattractive in terms of reimbursement. From a practice standpoint, cardiac CT is a diagnostic and prognostic test. This role should be considered in the context of data from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showing that percutaneous coronary intervention plus stenting and optimal medical therapy is no better at preventing

Table 2
Consensus Update on Appropriate Use of CTA for Cardiac CT

Role of CAC in asymptomatic patients
- CAC is useful in detecting subclinical atherosclerosis in all ethnic groups
- It is most useful in risk stratification of subjects with an intermediate Framingham risk score (10% to 20% 10-year risk)

CTA in asymptomatic patients
- At this time, CTA cannot be recommended for screening purposes
- Plaque characterization, although possible, cannot be generalized to all populations due to scan variability

CTA in symptomatic patients with suspected CAD
- CTA is useful in patients with equivocal or discordant results on stress perfusion or wall motion studies
- CTA cannot be recommended at this time to assess the effectiveness of medical therapy for CAD
- CTA may be more sensitive than nuclear stress testing for 3-vessel or left main disease

CTA in symptomatic patients with known CAD
- These patients benefit more from heart catheterization

CTA in assessment of acute chest pain in the emergency department
- Exclusionary criteria limit the number of evaluations possible
- Patients with positive cardiac enzymes and/or EKG changes should not undergo CTA
- Although the "triple rule-out" approach has its merits, it may be best to perform a higher quality study for the specific indication based on risk stratification

CTA in patients with known CAD poststenting
- In general, catheterization is better than CTA, especially if classic angina is present

CTA in post-CABG patients
- Functional assessment by MPI or echocardiography is better, not least because of artifacts from surgical clips

CTA and calcium score
- A separate CAC estimate is not required, and the amount of calcium can be inferred from the CTA itself

CTA, computed tomography angiography; CT, computed tomography; CAC, coronary artery calcification; CAD, coronary artery disease; EKG, electrocardiogram; CABG, coronary artery bypass grafting; MPI, myocardial performance index.
Adapted with permission from Poon M et al.[54]

future events than optimal medical therapy alone in patients with stable CAD.[51]

Conclusion

Although MSCT appears to hold much promise, many clinicians are skeptical about its actual role in the diagnosis of CAD. Flohr and colleagues[13] have noted that a temporal resolution better than 100 ms, submillimeter spatial resolution, and examination times no longer than 10 seconds are prerequisites for incorporation of CCT into clinical algorithms. Such a degree of temporal resolution could potentially eliminate the need to control the patient's heart rate by β-blockade.

There is a dearth of clinical algorithms in place with CT to help clinicians develop cogent diagnostic and treatment plans. This is in stark contrast to the current clinical thinking and decision-making tree developed with coronary angiography and various other imaging modalities (eg, nuclear imaging). This potentially might change as CT use becomes more refined and guidelines fall into place regarding clinical decision-making based on CT. Furthermore, new clinical trials, such as the Study of Perfusion and Anatomy's Role in CAD (SPARC), are aiming to determine the impact of stress-perfusion, CTA, and combined perfusion-anatomy imaging on post-test resource utilization as assessed by referral rate to catheterization within 90 days of the index study. Thus, CTA and stress-perfusion imaging may evolve into complementary studies in the evaluation of CAD.[52]

At this time, it is hard to ignore some of the deficiencies and distinct disadvantages with CT that make coronary angiography a much more appealing—albeit more invasive and expensive—procedure. Tables 3 and 4 summarize the current indications thought to be appropriate for cardiac CT and also provide a recent consensus update on the matter.[53,54]

Technological innovation continues to advance the limits of medical imaging. Older techniques are being perfected, with the addition of sophisticated newer advancements, as in the evolution of MDCT. Researchers have inspired new ways of looking at disease states in cardiovascular disease based on quantitative and qualitative data gathered from sources such as molecular imaging and ligand-incorporated microbubbles in contrast echocardiography. Some of the novel approaches in development have yet to find applications in practice, given considerations regarding cost and validation against accepted standards of imaging—in many cases, contrast angiography, IVUS, or necropsy.

CT itself is breaking new barriers with the ongoing competition between major medical equipment manufacturers. Recent arrivals on the scene include Aquilion® ONE (Toshiba American Medical Systems, Inc., Tustin, CA), which performs up to 320 slices and Brilliance iCT (Philips, Amsterdam, The Netherlands), which performs 256 slices. It has been noted that 320-slice CTA obviates over-scanning and over-ranging, and thus has the potential to decrease radiation exposure.[55]

Table 3
Mean Effective Radiation Dose for Various Studies

Examination	Mean Effective Dose (mSv)
Coronary angiography	5.6
PTCA	6.9
Coronary angiography and PTCA	9.3
PTCA and stent implantation	9
Coronary angiography with PTCA and stent implantation	13
Nuclear imaging (SPECT)	15-20

PTCA, percutaneous transluminal coronary angioplasty; SPECT, single-photon emission computed tomography.
Data from Betsou S et al[59] and Cury RC et al.[20]

Table 4
Criteria for Cardiac CT

Indication
Detection of symptomatic CAD Chest pain syndrome • Intermediate pretest probability of CAD • EKG is uninterpretable or patient is unable to exercise Evaluation of suspected coronary anomalies • Acute chest pain • Intermediate pretest probability of CAD • No EKG changes, and serial enzymes are negative
Detection of CAD with prior test results • Uninterpretable or equivocal stress test
Morphology • Assessment of complex congenital heart disease • Evaluation of coronary arteries in new onset heart failure patients
Evaluation of intracardiac and extracardiac structures • Evaluation of cardiac masses • Patients with technically limited images from echo, MRI, or TEE • Evaluation of pericardial conditions • Evaluation of pulmonary vein anatomy prior to invasive radiofrequency ablation for atrial fibrillation • Noninvasive coronary vein mapping prior to placement of a biventricular pacemaker • Noninvasive coronary arterial mapping, including internal mammary artery mapping, prior to repeat cardiac surgical revascularization
Evaluation of aortic and pulmonary disease • Evaluation of suspected aortic dissection or thoracic aortic aneurysm • Evaluation of suspected pulmonary embolism

CAD, coronary artery disease; EKG, electrocardiogram; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.
Adapted from *Journal of the American College of Cardiology,* Volume 48, Hendel RC et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging. Pages 1475-1497.[53]

As with any other new development in medicine, cost-benefit analyses and issues related to insurance and reimbursement must be resolved before the use of CCT can become more widespread and acceptable. Cost savings have been noted to result from the use of CCT, as opposed to catheterizations, in patients with mildly abnormal or equivocal myocardial perfusion scans.[56] On December 13, 2007, the Centers for Medicare and Medicaid Services released a Proposed National Coverage Decision Memorandum for cardiac CTA. It restricts coverage for use of cardiac CTA to symptomatic patients with chronic stable angina at intermediate risk of CAD or symptomatic patients with unstable angina at low risk of short-term death and intermediate risk of CAD. All other uses of cardiac CTA for the diagnosis of CAD would be noncovered.[57] However, on March 12, 2008, the Centers for Medicare and Medicaid Services released a final-decision memorandum for cardiac CTA indicating that a national coverage determination on CT is not appropriate at this time.[58]

In the annals of cardiovascular imaging, the concept of "gatekeeper" has gained currency. Despite initial promises, it appears that CT must be perfected and advanced further to be able to usurp nuclear cardiology as the gatekeeper to the cardiac catheterization laboratory. The American Heart Association, which takes a position regarding this matter in its 2007 statement notes, states that although CT is a promising tool, radiation doses, reproducibility, and validation studies must be considered when choosing this technique. The applications that are the most promising are the use of CTA to obtain calcium scores to perform risk assessment in asymptomatic individuals and to rule out coronary stenoses in certain subsets of patients. ■

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Main Points

- Although invasive angiography is the gold standard for the assessment of obstructive coronary lesions, this modality has been associated with discrepancies in terms of clinicopathologic results. Of the many imaging modalities now being investigated, cardiac computed tomography (CT) seems to be the most promising.
- Cardiac CT depends on a high temporal resolution to minimize coronary artery movement–related motion artifacts.
- There is a definite role for cardiac CT in patients with chest pain who have low or intermediate probability of coronary artery disease; a negative result on cardiac CT angiography could potentially exclude significant coronary artery disease and thus obviate further expensive workup.
- In the emergency department, CT can be used to evaluate with great accuracy 3 leading and potentially fatal causes of chest pain—coronary disease, pulmonary embolism, and aortic dissection—in a single study with greater than 90% accuracy.
- Identification of vulnerable plaque in asymptomatic individuals offers the potential of early intervention that could delay the progression of events that would otherwise culminate in an acute coronary event. The major techniques that permit the identification of the vulnerable plaque are ultrasound, magnetic resonance imaging, nuclear imaging, and multidetector computed tomography.
- The major limitations of CT angiography that have imperiled its widespread acceptance are motion artifacts, restrictions based on body mass index (which must be > 30 kg/m^2), and radiation exposure.

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