Published in final edited form as:

Int J Cardiol. 2012 May 3; 156(3): 295–302. doi:10.1016/j.ijcard.2010.11.011.

Flat-Panel Versus 64-Channel Computed Tomography for *In Vivo* Quantitative Characterization of Aortic Atherosclerotic Plaques

Ibrahim Aboshady, MD, Dianna D. Cody, PhD, Evan M. Johnson, PhD, Amir Gahremanpour, MD, Deborah Vela, MD, Kamal G. Khalil, MD, Herbert L. DuPont, MD, James T. Willerson, MD, L. Maximilian Buja, MD, and Gregory W. Gladish, MD
Texas Heart Institute at St. Luke's Episcopal Hospital, Houston, Tex. (I.A., A.G., D.V., H.L.D., J.T.W., L.M.B.); The University of Texas Health Science Center, Houston, Tex. (I.A., D.V., K.G.K., H.L.D., J.T.W., L.M.B.); The University of Texas MD Anderson Cancer Center, Houston, Tex. (D.D.C., E.M.J., G.W.G.); Baylor College of Medicine, Houston, Tex. (K.G.K., H.L.D.)

Abstract

Background—Flat-panel computed tomography (FpCT) provides better spatial resolution than 64-channel CT (64-CT) and may improve *in vivo* quantitative assessment of atherosclerotic plaques.

Methods and Results—Lesions in 184 aortic histology sections from 6 Watanabe heritable hyperlipidemic rabbits were quantitatively compared with 64-CT (image thickness, 0.625 mm) and FpCT (image thickness, 0.150 mm) images. Images were re-oriented perpendicular to the vessel centerline. For detecting plaque, FpCT and 64-CT were not significantly different (sensitivity, 76 % vs 66%; $P=NS$). Although FpCT was significantly more sensitive (42 % vs 0%; $P<0.001$) for detecting eccentric lesions, the area under the curve (AUC) for FpCT (0.6) was not significantly different from that for 64-CT (0.45; $P=NS$). In detecting plaques with $\leq 10\%$ lipid (low attenuation foci), FpCT was significantly more sensitive than 64-CT (24% vs 0.7%; $P<0.01$) and had a significantly greater AUC (0.6 vs 0.5; $P<0.006$). Additionally, FpCT was more sensitive (65% vs 0%; $P<0.01$) in detecting plaques with $\leq 5\%$ calcium (high attenuation foci) but not in detecting branch points. Both FpCT and histology allowed us to detect low-attenuation foci as small as 0.3 mm in diameter, whereas 64-CT allowed us to detect only low-attenuation foci ≥ 1.5 mm in diameter.

Conclusions—Flat-panel CT seemed to have more potential for quantitative screening low-risk small atherosclerotic lesions, whereas 64-CT was apparently more useful when imaging established, well-characterized lesions particularly when measuring the vascular wall thickness in a rabbit model of atherosclerosis.

© 2010 Elsevier Ireland Ltd. All rights reserved.

Corresponding Author: Ibrahim Aboshady, MD, Texas Heart Institute, 6700 Bertner Ave, Houston, TX 77030; Houston, TX, 77030. Telephone 832-355-5080; fax 832-355-6812; IAboshady@heart.thi.tmc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Portions of the data described in this manuscript were presented at the 2008 Scientific Sessions of the American Heart Association, New Orleans, Louisiana, November 8, 2008.

Disclosures

- Dianna D. Cody, PhD: Medical Technology Management Institute, Milwaukee, WI, Modest, Speakers Bureau.
- The other authors have nothing to disclose.

Keywords

aorta; atherosclerosis; cardiovascular imaging; computed tomography; vulnerable plaque

Acute coronary syndrome often results when plaque ruptures or erodes.¹ Quantitative evaluation of plaque morphology is important because lipid-rich plaques are prone to rupture and precipitate acute myocardial infarction.^{2–4} The lack of sensitive and specific noninvasive diagnostic tools has hindered effective early detection and assessment of thrombosis-prone patients and lesions.

The imaging techniques available today for early assessment of atherosclerotic lesions have significant shortcomings, resulting in a “detection gap”: a difference between the number of cases detectable by current imaging modalities and the overall prevalence of the disease.⁵ However, recently developed noninvasive imaging methods, such as multidetector computed tomography (MDCT) (eg, 64-channel CT [64-CT]), have been used to characterize coronary plaques, coronary thrombi, carotid plaques, and aortic atherosclerotic lesions.^{6–7} Additionally, MDCT enables clinicians to image vessel-wall plaques for calcium deposits, angiographic stenosis, and lipid content.^{8–9}

Typical MDCT scanners use small x-ray detectors and a cone-pyramid-shaped x-ray beam. Flat-panel detectors (FPD), which were primarily developed for conventional radiographic applications, are being studied for their potential value in MDCT.^{11–13} Systems that use FPD can achieve higher spatial resolution than conventional CT applications,^{14–15} especially when imaging high-contrast structures, so these systems could enhance 3D angiography.¹⁶ Initial reports on flat-panel CT (FpCT) prototype systems show that they can image small vascular structures (eg, structures within *ex vivo* coronary arteries).¹⁷ Few FpCT prototypes exist, so information on technical specifications is scarce.¹⁸

In this study, we compared the ability of FpCT and 64-CT scanning to characterize and quantify aortic atherosclerotic lesions *in vivo* in a rabbit model of atherosclerosis. We hypothesized that FpCT would identify, characterize, and morphologically quantify small atherosclerotic lesions and their constituents more effectively than 64-CT.

Methods

Animal Model

Animal studies were approved and performed according to the guidelines of the Animal Welfare Committee at the University of Texas Health Science Center, Houston, Texas. The study sample comprised 184 histology sections from 6 homozygous Watanabe heritable hyperlipidemic (WHHL) rabbits (age, 2–3 years).^{19–20} These sections were compared with correlated images from FpCT and 64-CT. The rabbits received a regular, nonfat diet and were *in vivo* scanned in the Small Animal Imaging Facility at The University of Texas MD Anderson Cancer Center. The rabbits were placed under general anesthesia and then intubated. Manual breath-hold operations were performed with equipment already in hand. A radiographic contrast medium, Omnipaque 350 (2 mL/kg, total dose <250 mL), was administered via the marginal ear vein for CT imaging.

Clinical 64-Channel Computed Tomography (64-CT)

The LightSpeed Volume Computed Tomography scanner (GE Healthcare, Milwaukee, Wis) is a clinical scanner with 64 data channels and a maximum x-ray beam width of 40 mm.

Gated acquisition was not possible because of the rabbits' high heart rate (~300 beats/minute).

The following scan variables were used: 80 kVp, 675 mA, 0.4 seconds/rotation, pitch 0.516, 64×0.625 -mm detector configuration, small body scan field-of-view (SFOV), 18-cm display field-of-view (DFOV). A second scan protocol was also used: 120 kVp, 200 mA, 0.4 seconds/rotation, pitch 0.516, 64×0.625 -mm detector configuration, small body SFOV, and 18-cm DFOV. Both protocols were first executed without intravenous contrast enhancement. The images were not processed for dual-energy information. This part of the study was done to confirm that use of one kV setting over the other was justified. Post-contrast scanning was performed 30, 60, and 90 seconds after contrast was injected into the ear vein: 120 kVp, 200 mA, 0.4 seconds/rotation, pitch 0.516, 64×0.625 -mm detector configuration, small body SFOV, 18-cm DFOV. All images were 0.625 mm thick and were generated with the standard algorithm.

Flat-panel Computed Tomography (FpCT)

A prototype with a dual-panel rotating gantry and a commercial Performix CT x-ray source Figure 1 was designed, constructed, and tested at the General Electric (GE) Global Research Center (Niskayuna, NY) in conjunction with The University of Texas MD Anderson Cancer Center. The commercially available amorphous silicon fluoroscopic flat-panel x-ray detectors offer 200 μ native resolution. Rotation speed options for this scanner are 2, 4, or 8 seconds/rotation. At present, helical and gated image acquisitions are not feasible.

All images were collected 30 seconds after iohexol injection by using 500 views per rotation, and each rotation covered 4.3 cm in the z-axis (table) direction. The standard reconstruction algorithm was used to generate all images. Pre-contrast: 120 kV, 40 mA, 4 sec and 80 kV, 150 mA, 4 sec (2 sets of images). Post-contrast: 80 kV, 150 mA, 4 sec.

Image Generation and Analysis

With an automated tool (Vessel Analysis, AW Workstation, GE Healthcare), multiplanar reformatted images were created perpendicular to the center line of the aorta along its entire imaged length. Voxel sizes were $0.20 \times 0.20 \times 0.625$ mm for 64-CT and $0.20 \times 0.20 \times 0.20$ mm for FpCT. Because Hounsfield unit (HU) values produced by the FpCT scanner are not very reliable (and differ substantially from those produced by clinical CT scanners), HU parameters were not used for image segmentation. This was done visually, using a consistent window width (800) and window level (100) selection.

Image registration was accomplished by using images that had been reoriented (perpendicular to the vessel centerline) and then by using a specific distance from the aortic valve as a landmark. Small images (16-mm field of view) were created at 1-mm intervals along the aorta's center line. Four sets of images were created: one set of minimum-thickness images and one set each of 2-mm thick volumetric images created by using average-, maximum-, and minimum-intensity projection methods. Measurements were performed only on the 2-mm-thick, average-intensity projection slices. We used the other projections and thin images to confirm the identification of small high-attenuation (calcium) and low-attenuation (lipid) foci. Histologic sections were cut in the same configurations as the radiologic images (see below).

For each image, we measured minimum and maximum wall thickness and the number and size of low- and high-attenuation foci. Wall-thickening, when present, was considered eccentric if <80% of the vessel's circumference was involved, concentric if $\geq 80\%$ was involved, and both concentric and eccentric if the wall was thick throughout but significantly thicker along 1 aspect. An eccentric plaque's extent was quantified as the

percentage of lesion circumference involved. We determined the diameter of the largest calcific and lipid collections and their distance from the lumen, and we recorded the percentage of the plaque that consisted of lipid and calcific components. Additionally, if a subintimal low-attenuation layer was present, the percentage of the vessel circumference involved was recorded. Standard graphics tools were used for all measurements.

Histopathology

All aortic specimens were formalin-fixed, paraffin-embedded, and serially sectioned at 2- to 2.5-mm intervals from the left subclavian artery to the iliac bifurcation (mean arterial length examined, 46 ± 16 mm; range, 16–74 mm). Sections (5- μ m thick) were stained with hematoxylin, eosin, and Movat pentachrome to characterize and identify plaque components: lipid deposits, calcific deposits, and fibromuscular tissue. Specimens were not decalcified. Although complex plaques can develop in WHHL rabbits, excessive calcification, comparable to that attainable in human coronaries with advanced atherosclerosis, was not expected from these samples. Thus, standard tissue processing and fixation methods were used.

Images of each arterial ring were captured with an Olympus BX61 microscope equipped with a color digital camera (Olympus DP70, 12.5 mega-pixel resolutions). Morphometric analysis of parameters similar to those used in the radiologic image analysis (described above) was performed with Olympus MicroSuite software (Olympus America, Melville, NY). The acquired measurements were recorded and tabulated for comparison and correlation with the radiologic data.

For each 5- μ m section of the paraffin-embedded specimens, the same radiologic variables (above) were measured. Measurements of the vascular wall were made in 2 different low-power (4 $\times$) fields and then averaged. We defined lipid pools as morphologically distinct spaces comprising clear, needle-shaped cholesterol clefts and/or clear, bubbly, granular, mostly anucleate necrotic debris of foam cells. Lipid pool areas averaged 5.3 ± 3.2 mm² (range, 1.00–16.36 mm²). Thus, segments were considered positive for lipid if their measured area was ≥ 1.00 mm². A thin fibrous cap was defined as a cap ≤ 65 μ m thick. Inflammation was defined as the presence of ≥ 25 mononuclear round cells per field in H&E-stained sections under $\times 40$ magnification.²⁹

Statistical Analysis

Descriptive statistics were computed for the FpCT, 64-CT, and histopathologic data sets. Contingency tables were generated to compare the different methods. In previous studies, we observed that the imaging techniques and histopathologic examination produced consistent results.^{21–23} Agreement was measured with the Lin concordance coefficient (and Bradley-Blackwood F ratio), Bland-Altman analysis, and the Pitman test for difference between variance for continuous variables and Kappa statistics for categorical variables. Sensitivity, specificity, and receiver operating characteristic (ROC) curves were computed for 64-CT and FpCT and compared to those of histology as the gold standard.²⁴ The McNemar test was used to examine differences between sensitivities and specificities.²⁵ Stata version 11.0 (StataCorp College Station TX) was used for data analysis.

Statement of Responsibility

The authors had full access to the data and take responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

The analysis involved correlating both continuous and categorical data among the 3 modalities. Both imaging modalities easily discriminated calcific from non-calcific deposits. Histologic examination revealed calcific deposits and lipid pools that correlated with the imaging results (Figure 2). Neither imaging modality provided sufficient detail to allow measurement of the thickness of the fibrous caps over the larger lipid pools.

Only FpCT images provided the spatial resolution necessary to distinguish lipid from fibrous wall-thickening and to identify normal-thickness wall. The histopathologic data for plaque eccentricity and circumference, number of lipid pools and minimal distance from the vascular lumen correlated better with the FpCT data than with the 64-CT data. Both FpCT and histologic examination could detect lipid pools (low-attenuation foci) as small as 0.3 mm in diameter; 64-CT allowed us to detect only lipid pools ≥ 1.5 mm in diameter. In both FpCT and histology images, but not 64-CT images, we identified lesions containing $<5\%$ lipid and calcific deposits <1 mm in diameter.

According to the Lin concordance coefficient, the Bland-Altman plot, and the Pitman test, neither 64-CT nor FpCT measurements of wall thickness (minimum and maximum) correlated well with histologic measurements. However, in measuring minimal wall thickness, 64-CT was better correlated with histology than was FpCT, and the Bradley-Blackwood F ratio showed that the Lin coefficient and the Pitman test results were not interchangeable (Table 1, 2). In detecting plaques of any shape, FpCT and 64-CT were not significantly different in terms of sensitivity (76 % vs 66%; $P=NS$), specificity (28% vs 50%; $P=NS$), and overall area under the ROC curve (AUC) (Table 3).

For imaging plaques with eccentric shapes, FpCT was more sensitive than 64-CT (42% vs 0%; $P<0.001$); however, the AUC for FpCT was not significantly greater than for 64-CT (0.6 vs 0.45; $P=NS$). When compared to histology, both techniques were similarly accurate in quantifying lipid and calcium in the plaques. However, FpCT was more sensitive than 64-CT in detecting plaques with $\leq 10\%$ lipid content (24.2% vs 0.67%; $P<0.001$), and FpCT had a greater AUC (0.6 vs 0.5; $P<0.006$) (Table 3; Figures 3 and 4). Also, FpCT was more sensitive than 64-CT in detecting plaques with $\leq 5\%$ calcium content (6.25% vs 0%; $P<0.01$), but the AUCs of the two imaging techniques were not significantly different (Table 4). For detecting branch points, 64-CT and FpCT were not significantly different (Table 5). Thus, overall, FpCT was significantly more sensitive than 64-CT in detecting eccentrically shaped plaques and plaques consisting of $\leq 5\%$ calcium. For imaging eccentrically shaped plaques, FpCT is not only significantly more sensitive than 64-CT but also appears to be better test that strikes a more favorable balance between sensitivity and specificity.

The 184 lesions were classified according to American Heart Association (AHA) criteria (Table 6).²⁶ Of the 48 lesions classified as type II by histology, 42 were also classified as type II by FpCT and 35 by 64-CT. FpCT was significantly more sensitive than 64-CT in detecting all types (Table 6).

Discussion

We found that in hyperlipidemic rabbits, FpCT imaging allows better identification, quantification, and characterization of most measured aortic atherosclerotic plaque components than 64-CT scanning, with the exception of wall thickness. First, FpCT and 64-CT were equally useful in distinguishing calcific from non-calcific deposits,²⁷ but only in FpCT images were we able to distinguish lipid from fibrous wall-thickening. Second, noninvasive imaging with FpCT enabled us to measure the different components of atherosclerotic plaques. Very small high-attenuation foci and lesions that included a small

percentage of lipids could be identified in both FpCT images and histologic sections, but not in 64-CT images. The histopathologic data for plaque eccentricity and circumference, the number of low-attenuation foci, and the minimal distance of each component from the vascular lumen correlated better with the FpCT data than with the 64-CT data.

With the introduction of MDCT, computed tomography has reached a level that allows the identification of vessel-wall plaque components with accuracy similar to that of invasive techniques such as angiography or transesophageal echocardiography. As noted by Smith and colleagues,²⁸ contrast-enhanced, cardiac-gated MDCT is effective in identifying many different causes of acute aortic syndrome, including acute aortic dissection, penetrating atherosclerotic ulcer, intramural hematoma, and unstable thoracic aneurysm.

Another study by Choi and colleagues²⁹ partly supports our data in revealing some limitations on the clinical utility of MDCT. The investigators found that, despite the sophistication of their CT technique, there was overlap in the mean CT densities of plaques with small and large necrotic cores. Inoue et al³⁰ used MDCT to compare the CT density of plaque between patients with acute coronary syndrome (ACS) and those with stable angina. Number of plaques did not differ between the 2 groups, but minimum CT density was significantly lower in patients with ACS (25 ± 15 HU) than in patients with stable angina (71 ± 16 HU; range, 46–101 HU; $P < 0.001$). Similarly, minimum plaque density was significantly lower in culprit coronary segments (26 ± 16 HU) than in non-culprit segments (48 ± 17 HU) in 15 ACS patients with multiple plaques. The investigators' approach was to use plaque CT density as a potential indicator of vulnerability. In contrast, in the current study, we analyzed detailed morphometric measurements to assess plaque behavior. Also, we did not use HU units, because the prototype CT scanner does not provide reliable values of HU. Instead, we used relative differences among grey levels and visual assessment of images.

Several other investigators have assessed the various capabilities and limitations of MDCT. Achenbach et al³¹ studied the applicability and image quality of contrast-enhanced coronary artery visualization by MSCT with retrospective electrocardiographic gating. Moselewski et al³² compared measurements of cross-sectional coronary atherosclerotic plaque and vessel areas by 16-slice MDCT versus intravascular ultrasound. Some authors^{33–35} have shown that MDCT identifies plaque calcification, distribution, and positive remodeling more accurately than ultrasound. These studies showed the advantages of MDCT over ultrasound and indicated the need for more accurate quantification of plaque components by imaging for predicting plaque rupture and assessing plaque vulnerability.

When classified according to the AHA classification system, most of the lesions we examined were, histologically, at stage II–V. It was evident that, in classifying the lesions, FpCT data was more accurate than MDCT and closer to histology. Nikolaou and co-workers³⁶ also found that the morphologic classifications of lesions made by the two imaging modalities were comparable and were close to the classifications made by histologic examination.

In a previous study that used the same FpCT scanner, FpCT with standard reconstruction algorithms produced images with a spatial resolution of 19 lp/cm, whereas 64-CT images had a spatial resolution of only 7 lp/cm (at 10% modulation transfer function for both techniques).¹⁸ In the present study, FpCT's enhanced spatial resolution allowed us to detect lipid pools (low-attenuation foci) that were 5 times smaller than those detected by 64-CT (0.3 vs 1.5 mm), and FpCT enabled the radiologist to identify lesions containing <5% lipid and calcific deposits of <1 mm diameter.

The FpCT system was designed to dramatically increase spatial resolution. Recently, FpCT has been used to detect microcalcification in the breast,³⁷ evaluate stent mechanics,³⁸ define fine structures in temporal bone,³⁹ and diagnose other non-atherosclerosis-related conditions.^{40–43} Recently, Korosoglou et al⁴⁴ described a different new technique in which a special magnetic resonance imaging sequence (inversion recovery with on-resonant water-suppression) is used to locate areas of supramagnetic nanoparticle uptake. As Fishbein⁴⁵ has pointed out, this technology may eventually provide insights into plaque biology that will enable us to identify plaque features that predict and, perhaps, cause plaque rupture.

Some investigators recommend using MDCT to identify obstructive coronary artery disease, evaluate its severity, and predict subsequent revascularization in symptomatic patients.^{46–48} Miller et al⁴⁹ state that MDCT cannot yet replace conventional coronary angiography. Hence, there is a need for more advanced technologies such as FpCT.

Sarwar and colleagues⁵⁰ recently used MDCT and FpCT to assess blooming artifacts in *ex vivo* coronary arteries, comparing the effectiveness of these imaging techniques with histopathologic examination in measuring areas of calcified plaque in 3 explanted human hearts. The investigators found that measurements made from the MDCT images overestimated the plaque area by 400% (4.61/1.15 mm), and that the predicted difference between the MDCT and histopathologic measurements was substantial (3.46 mm²; $P=0.018$). The FpCT images also overestimated plaque area, but to a much smaller extent (214%; 2.18/1.02 mm), and the predicted difference between FpCT and histopathologic measurements was smaller (1.16 mm²; $P=0.08$). The authors concluded that using FpCT to visualize calcified coronary plaques reduces the amount of blooming artifact. In addition, the authors noted that smaller calcified plaques could not be detected in the MDCT images. This finding is in concordance with ours.

In conclusion, in animal vessels similar in size to human coronary arteries, FpCT, with its high spatial resolution, appeared to better identify and quantify plaque components than 64-CT. Thus, FpCT is a promising tool for screening and characterizing plaque composition, especially in small lesions with fewer morphologic risk factors for rupture. FpCT could be more helpful than MDCT for early assessment of plaque vulnerability and predicting its future behavior. Additionally, FpCT may be useful in longitudinal studies of plaque development or for monitoring responses to experimental therapies in an animal model.

Acknowledgments

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology.⁵¹

Funding Sources

This work was supported in part by grants from the US Army Telemedicine and Advanced Technology Research Center (TATRC), the Texas Heart Institute, the National Institutes of Health (NIH 5 P30 CA016672 35), and the Roderick Duncan MacDonald Research Fund Committee at St. Luke's Episcopal Hospital.

References

1. Virmani R, Burke AP, Kolodgie FD, et al. Vulnerable plaque: the pathology of unstable coronary lesions. *J Interv Cardiol.* 2002; 15:439–446. [PubMed: 12476646]
2. Beilvert A, Cormode DP, Chabot F, et al. Tyrosine polyethylene glycol (PEG)-micelle magnetic resonance contrast agent for the detection of lipid rich areas in atherosclerotic plaque. *Magn Reson Med.* 2009; 62:1195–1201. [PubMed: 19780153]

3. Aikawa M, Rabkin E, Okada Y, et al. Lipid lowering by diet reduces matrix metalloproteinase activity and increases collagen content of rabbit atheroma: a potential mechanism of lesion stabilization. *Circulation*. 1998; 97:2433–2444. [PubMed: 9641696]
4. Shah PK. Inflammation and plaque vulnerability. *Cardiovasc Drugs Ther*. 2009; 23:31–40. [PubMed: 18949542]
5. Schuijf JD, Shaw LJ, Wijns W, et al. Cardiac imaging in coronary artery disease: differing modalities. *Heart*. 2005; 91:1110–1117. [PubMed: 16020614]
6. Itani Y, Watanabe S, Masuda Y. Aortic calcification detected in a mass chest screening program using a mobile helical computed tomography unit: relationship to risk factors and coronary artery disease. *Circ J*. 2004; 68:538–541. [PubMed: 15170088]
7. Langheinrich AC, Michniewicz A, Sedding DG, et al. Quantitative X-ray imaging of intraplaque hemorrhage in aortas of apoE^(-/-)/LDL^(-/-) double knockout mice. *Invest Radiol*. 2007; 42:263–273. [PubMed: 17414521]
8. Flohr T, Stierstorfer K, Bruder H, et al. New technical developments in multislice CT—Part 1: approaching isotropic resolution with sub-millimeter 16-slice scanning. *Rofo*. 2002; 174:839–845. [PubMed: 12101473]
9. Mitsutake R, Miura S, Zhang B, et al. HDL-associated factors provide additional prognostic information for coronary artery disease as determined by multi-detector row computed tomography. *Int J Cardiol*. 2010; 143:72–78. [PubMed: 19237208]
10. Bruder H, Kachelriess M, Schaller S, et al. Single-slice rebinning reconstruction in spiral cone-beam computed tomography. *IEEE Trans Med Imaging*. 2000; 19:873–887. [PubMed: 11127602]
11. Kalender WA. [The use of flat-panel detectors for CT imaging]. *Radiologe*. 2003; 43:379–387. [PubMed: 12764587]
12. Kotter E, Langer M. Digital radiography with large-area flat-panel detectors. *Eur Radiol*. 2002; 12:2562–2570. [PubMed: 12271399]
13. Ludwig K, Henschel A, Bernhardt TM, et al. Performance of a flat-panel detector in the detection of artificial erosive changes: comparison with conventional screen-film and storage-phosphor radiography. *Eur Radiol*. 2003; 13:1316–1323. [PubMed: 12764648]
14. Volk M, Hamer OW, Feuerbach S, et al. Dose reduction in skeletal and chest radiography using a large-area flat-panel detector based on amorphous silicon and thallium-doped cesium iodide: technical background, basic image quality parameters, and review of the literature. *Eur Radiol*. 2004; 14:827–834. [PubMed: 14968260]
15. Groh BA, Siewerdsen JH, Drake DG, et al. A performance comparison of flat-panel imager-based MV and kV cone-beam CT. *Med Phys*. 2002; 29:967–975. [PubMed: 12094992]
16. Jaffray DA, Siewerdsen JH. Cone-beam computed tomography with a flat-panel imager: initial performance characterization. *Med Phys*. 2000; 27:1311–1323. [PubMed: 10902561]
17. Knollmann F, Pfoh A. Image in cardiovascular medicine: coronary artery imaging with flat-panel computed tomography. *Circulation*. 2003; 107:1209. [PubMed: 12615803]
18. Ross W, Cody DD, Hazle JD. Design and performance characteristics of a digital flat-panel computed tomography system. *Med Phys*. 2006; 33:1888–1901. [PubMed: 16872096]
19. Clubb FJ, Cerny JL, Deferrari DA, et al. Development of atherosclerotic plaque with endothelial disruption in Watanabe heritable hyperlipidemic rabbit aortas. *Cardiovasc Pathol*. 2001; 10:1–11. [PubMed: 11343989]
20. Buja LM, Kita T, Goldstein JL, et al. Cellular pathology of progressive atherosclerosis in the WHHL rabbit: an animal model of familial hypercholesterolemia. *Arteriosclerosis*. 1983; 3:87–101. [PubMed: 6824499]
21. Gertz SD, Bodmann BG, Vela D, et al. Three-dimensional isotropic wavelets for post-acquisitional extraction of latent images of atherosclerotic plaque components from micro-computed tomography of human coronary arteries. *Acad Radiol*. 2007; 14:1509–1519. [PubMed: 18035280]
22. Gertz SD, Cherukuri P, Bodmann BG, et al. Usefulness of multidetector computed tomography for noninvasive evaluation of coronary arteries in asymptomatic patients. *Am J Cardiol*. 2006; 97:287–293. [PubMed: 16442381]

23. Wilner WT, Mazraeshahi RM, Aboshady I, et al. Quantification of roughness of calcific deposits in computed tomography scans of human coronary arteries. *Invest Radiol.* 2007; 42:771–776. [PubMed: 18030200]
24. Cohen J. A coefficient of agreement for nominal scales. *Psychol Meas.* 1960; 20:37–46.
25. Durkalski VL, Palesch YY, Lipsitz SR, Rust PF. Analysis of clustered matched-pair data. *Stat Med.* 2003; 22:2417–2428. [PubMed: 12872299]
26. Stary HC. Natural history and histological classification of atherosclerotic lesions: an update. *Arterioscler Thromb Vasc Biol.* 2000; 20(5):1177–1178. [PubMed: 10807728]
27. Aboshady I, Cody DD, Vela D, et al. Performance evaluation of flat-panel and 64 detector row CT for characterization of vulnerable plaque. *Am J Cardiol.* 2007; 100:15L.
28. Smith AD, Schoenhagen P. CT imaging for acute aortic syndrome. *Cleve Clin J Med.* 2008; 75:7–9. 12, 15–17 passim. [PubMed: 18236724]
29. Choi BJ, Kang DK, Tahk SJ, et al. Comparison of 64-slice multidetector computed tomography with spectral analysis of intravascular ultrasound backscatter signals for characterizations of noncalcified coronary arterial plaques. *Am J Cardiol.* 2008; 102:988–993. [PubMed: 18929698]
30. Inoue F, Sato Y, Matsumoto N, et al. Evaluation of plaque texture by means of multislice computed tomography in patients with acute coronary syndrome and stable angina. *Circ J.* 2004; 68:840–844. [PubMed: 15329505]
31. Achenbach S, Moselewski F, Ropers D, et al. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: a segment-based comparison with intravascular ultrasound. *Circulation.* 2004; 109:14–17. [PubMed: 14691045]
32. Moselewski F, Ropers D, Pohle K, et al. Comparison of measurement of cross-sectional coronary atherosclerotic plaque and vessel areas by 16-slice multidetector computed tomography versus intravascular ultrasound. *Am J Cardiol.* 2004; 94:1294–1297. [PubMed: 15541250]
33. Schoenhagen P, Tuzcu EM, Stillman AE, et al. Non-invasive assessment of plaque morphology and remodeling in mildly stenotic coronary segments: comparison of 16-slice computed tomography and intravascular ultrasound. *Coron Artery Dis.* 2003; 14:459–462. [PubMed: 12966267]
34. Uehara M, Funabashi N, Mikami Y, et al. Quantitative effect of Atorvastatin on size and content of non-calcified plaques of coronary arteries one year after Atorvastatin treatment by multislice computed tomography. *Int J Cardiol.* 2008; 130:269–275. [PubMed: 17707102]
35. Henein M, Nicoll R. Atherosclerosis and extensive arterial calcification: the same condition? *Int J Cardiol.* 2010; 141:1–2. [PubMed: 19969382]
36. Nikolaou K, Becker CR, Muders M, et al. Multidetector-row computed tomography and magnetic resonance imaging of atherosclerotic lesions in human ex vivo coronary arteries. *Atherosclerosis.* 2004; 174:243–252. [PubMed: 15136054]
37. Gong X, Vedula AA, Glick SJ. Microcalcification detection using cone-beam CT mammography with a flat-panel imager. *Phys Med Biol.* 2004; 49:2183–2195. [PubMed: 15248571]
38. Ebrahimi N, Claus B, Lee CY, et al. Stent conformity in curved vascular models with simulated aneurysm necks using flat-panel CT: an in vitro study. *AJNR Am J Neuroradiol.* 2007; 28:823–829. [PubMed: 17494650]
39. Gupta R, Bartling SH, Basu SK, et al. Experimental flat-panel high-spatial-resolution volume CT of the temporal bone. *AJNR Am J Neuroradiol.* 2004; 25:1417–1424. [PubMed: 15466345]
40. Garmer M, Hennigs SP, Jager HJ, et al. Digital radiography versus conventional radiography in chest imaging: diagnostic performance of a large-area silicon flat-panel detector in a clinical CT-controlled study. *AJR Am J Roentgenol.* 2000; 174:75–80. [PubMed: 10628458]
41. Hirota S, Nakao N, Yamamoto S, et al. Cone-beam CT with flat-panel-detector digital angiography system: early experience in abdominal interventional procedures. *Cardiovasc Intervent Radiol.* 2006; 29:1034–1038. [PubMed: 16988877]
42. Kakeda S, Korogi Y, Ohnari N, et al. Usefulness of cone-beam volume CT with flat panel detectors in conjunction with catheter angiography for transcatheter arterial embolization. *J Vasc Interv Radiol.* 2007; 18:1508–1516. [PubMed: 18057285]

43. Lee SC, Kim HK, Chun IK, et al. A flat-panel detector based micro-CT system: performance evaluation for small-animal imaging. *Phys Med Biol*. 2003; 48:4173–4185. [PubMed: 14727760]
44. Korosoglou G, Weiss RG, Kedziorek DA, et al. Noninvasive detection of macrophage-rich atherosclerotic plaque in hyperlipidemic rabbits using "positive contrast" magnetic resonance imaging. *J Am Coll Cardiol*. 2008; 52:483–491. [PubMed: 18672170]
45. Fishbein MC. The vulnerable and unstable atherosclerotic plaque. *Cardiovasc Pathol*. 2010; 19:6–11. [PubMed: 18835793]
46. Min JK, Kang N, Shaw LJ, et al. Costs and clinical outcomes after coronary multidetector CT angiography in patients without known coronary artery disease: comparison to myocardial perfusion SPECT. *Radiology*. 2008; 249:62–70. [PubMed: 18796668]
47. Vanhoenacker PK, Heijenbroek-Kal MH, Van Heste R, et al. Diagnostic performance of multidetector CT angiography for assessment of coronary artery disease: meta-analysis. *Radiology*. 2007; 244:419–428. [PubMed: 17641365]
48. Duerinckx AJ. The nonculprit coronary lesion as seen by coronary CT angiography: what should we be looking for? *AJR Am J Roentgenol*. 2008; 191:439–440. [PubMed: 18647914]
49. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med*. 2008; 359:2324–2336. [PubMed: 19038879]
50. Sarwar A, Rieber J, Mooyaart EA, et al. Calcified plaque: measurement of area at thin-section flat-panel CT and 64-section multidetector CT and comparison with histopathologic findings. *Radiology*. 2008; 249:301–306. [PubMed: 18710960]
51. Coats AJ. Ethical authorship and publishing. *Int J Cardiol*. 2009; 131:149–150. [PubMed: 19046787]

Figure 1.

Flat-panel computed tomography (FpCT): a multipanel prototype CT system developed for the MD Anderson Cancer Center. The two 20×20 -cm flat panels are visible to the left of the gantry bore, and there is a seam region between flat-panel x-ray detectors. The physical gap between active areas in this configuration is approximately 2.5 cm.

Figure 2.

Micrographic, FpCT, and 64-CT images of the descending aorta and corresponding histologic sections. Voxel sizes were $0.20 \times 0.20 \times 0.625$ mm for 64-CT and $0.20 \times 0.20 \times 0.20$ mm for FpCT. Column 1, cross-sectional histologic sections stained with hematoxylin and eosin; Column 2, corresponding 64-CT images; Column 3, corresponding FpCT images; Column 4, longitudinal histologic sections stained with hematoxylin and eosin; Column 5, corresponding histologic sections stained with Movat pentachrome. A, Rabbit 5, 35 mm from aortic valve. The margins of the calcification are clearer on the FpCT images. Blooming artifact causes overestimation of calcification size on 64-CT. B, Rabbit 6, 37 mm from aortic valve. Both FpCT and 64-CT show non-calcified plaque between the calcification and lumen, but only FpCT shows the wall-thickening external to the calcification, as seen at histologic examination. C and D, FpCT and 64-CT images and corresponding histologic sections of the descending aorta (lower half). C, Rabbit 6, 32 mm from aortic valve. Low- and intermediate-attenuation components of plaque thickening are seen on FpCT but not 64-CT. These components correspond to an area of intraplaque hemorrhage seen at histologic examination. D, Rabbit 4, 48 mm from aortic valve. The 1.9-mm low-attenuation focus seen on FpCT (but not 64-CT) corresponds to focal wall-thickening and lipid pools seen at histologic examination.

Figure 3.
Bland-Altman plot: Comparison of the potential of 64-CT and FpCT to detect plaque calcium $\leq 5\%$. The Y-axis represents the difference between each pair of scores of the two modalities, and the X-axis represents their average. The size of each circle reflects the number of paired observations represented by that circle.

Figure 4. Receiver operating characteristic (ROC) curves computed for 64-CT and FpCT compared to histologic findings (used as the "gold standard"). It showed FpCT is a better test for assessing both variables.

Table 1

Minimal Wall Thickness Measured by FpCT, 64-CT, and Histology

Comparison	Difference		Bland-Altman 95% limits of agreement		Pitman test of difference in variance		Lin concordance coefficient (95% CI)		Pearson correlation	
	Mean	SD	Mean	SD	r	P	ρ_c	P	r	P
Histology vs 64-CT	-0.199	0.154	-0.500	0.102	0.161	0.072	0.346	0.000	0.592	0.000
Histology vs FpCT	-0.257	0.260	-0.767	0.254	-0.179	0.027	0.024	0.54	0.048	0.541
64-CT vs FpCT	-0.025	0.235	-0.486	0.435	-0.218	0.006	0.478	0.000	0.490	0.000

Measurements are in mm.

Table 2

Maximal Wall Thickness Measured by FpCT, 64-CT, and Histology

Comparison	Difference		Bland-Altman 95% limits of agreement		Pitman test of difference in variance		Lin concordance coefficient (95% CI)		Pearson correlation	
	Mean	SD	Mean	SD	r	P	ρ_c	P	r	P
Histology vs 64-CT	-0.206	0.701	-1.608	1.197	-0.081	<0.001	0.346	<0.001	0.118	0.190
Histology vs FpCT	-0.367	0.574	-1.515	0.781	-0.524	<0.001	0.024	0.54	0.295	<0.001
64-CT vs FpCT	-0.142	0.722	-1.558	1.274	-0.354	<0.001	0.478	<0.001	0.147	0.062

Table 3Maximal Capabilities of 64-CT and FpCT in Detecting Plaque, Plaque Eccentricity, and Plaque Lipid Content $\leq 10\%$

	Plaque Detection			Eccentric Plaque			Plaque Lipid $\leq 10\%$		
	64-CT	FpCT	P	64-CT	FpCT	P	64-CT	FpCT	P
Sensitivity	66%	76.4%	NS	0%	42%	<0.001	0.7%	24%	<0.001
Specificity	50%	28%	NS	89%	70%	0.02	100%	90%	NS
AUC	.6	.5	NS	.5	.6	NS	.5	.6	.006
(+) Likelihood ratio	1.3	1		0	1.4		0	2.3	
(-) Likelihood ratio	0.7	0.9		1.1	.8		1	0.8	
PPV	92%	91%		0%	33%		100.0%	78%	
NPV	14%	11%		75 %	77%		39%	43%	

AUC indicates area under the receiver operating characteristic curve; NS, non-significant (ie, $P > .05$); PPV, positive predictive value; NPV, negative predictive value.

Table 4Potential of 64-CT and FpCT to Detect Plaque Calcium Content $\leq 5\%$

	64-CT	FpCT	P
Sensitivity	0%	6%	<0.001
Specificity	97%	96%	NS
AUC	0.5	0.5	NS
(+) Likelihood ratio	0	1.5	
(-) Likelihood ratio	1	0.9	
PPV	0%	18%	
NPV	87%	87%	

Table 5

Comparison of the Maximum Potential of 64-CT and FpCT to Detect Atherosclerotic Lesions at Vascular Branching Points

	64-CT	FpCT	P
Sensitivity	7%	9%	NS
Specificity	93%	87%	NS
AUC	.5	.5	NS
(+) Likelihood ratio	1.1	0.7	
(-) Likelihood ratio	0.9	1.0	
PPV	18%	14%	
NPV	83%	81%	

Table 6

Number of Lesions Identified by FpCT and 64-CT Imaging Compared to Histopathologic Sections as Gold Standard According to AHA Classification

Hist.	FpCT					64-CT					P
	II (n=48)	III (n=42)	IV (n=44)	V (n=50)	S	II (n=46)	III (n=58)	IV (n=47)	V (n=33)	S	
II (n=48)	42	4	2	0	88	35	9	3	1	73	0.008
III (n=38)	4	28	5	1	74	7	24	7	0	63	0.04
IV (n=47)	2	8	32	5	68	2	16	25	4	53	0.008
V (n=51)	0	2	5	44	88	2	9	12	28	55	0.001

Hist. indicates histopathologic examinations; S, sensitivity (%).