

Tomographic Plaque Imaging with CT: Technical Considerations and Capabilities

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X-ray computed tomography (CT) is widely available in the world and has the ability to provide high-definition, thin-section imaging of any body part. In particular, CT over the past decade has been shown in numerous publications to allow for quantitation of coronary calcification, a proven surrogate for coronary artery atheromatous plaque. Electron beam tomography (EBT) and multidetector CT (MDCT) have been studied for these purposes. However, there are methodological differences between types of CT scanners and precision of calcium scoring is a function of their individual technical capabilities and limitations. These technical aspects are detailed here. Although MDCT has shown considerable improvements in recent years, EBT remains the clinical reference standard for noninvasive definition of atherosclerotic plaque.
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X-ray computed tomography (CT) can provide exquisite, rapid, high-resolution imaging of the body and in particular the heart (and vascular system in general). Tomographic imaging by CT has had significant advances in temporal and spatial resolution to facilitate noninvasive cardiac imaging. In particular, both electron beam tomography (EBT) and multidetector CT (MDCT) have shown applicability, under certain defined circumstances, for coronary artery imaging and atherosclerotic plaque identification.

Coronary lumen imaging of the major epicardial coronary arteries using CT during intravenous contrast administration is now not only feasible but is in routine use in some clinical settings. Coronary artery imaging by CT without contrast administration has focused on identification of mural coronary calcification.

Full discussions of the clinical integration of CT coronary lumen (CT coronary angiography) and quantification of coronary calcium (as a surrogate

to estimation of coronary plaque burden) by EBT/MDCT are to be found elsewhere in this issue. The current section details technical and practical issues regarding coronary atherosclerotic plaque imaging by CT, which then help define its capabilities and limitations for clinical usage. The focus will be on coronary calcium imaging.

Coronary Calcium and Atherosclerotic Plaque

Recent studies have confirmed that arterial calcium development is intimately associated with vascular injury and atherosclerotic plaque evolution and is largely controlled by common cellular and subcellular mechanisms.¹⁻⁴ Calcium can be seen in all degrees of atherosclerotic involvement and is an active process. Thus, the long held notion of so-called "degenerative" calcification of the coronary arteries with aging is not correct.

The incidence of coronary artery calcium by CT as a function of age has been shown to mimic that of the incidence of cardiovascular atherosclerotic disease in men and women. The data⁵ show the following: (1) the incidence of coronary artery calcium increases from only a few percent in the second decade of life to nearly 100% by the eighth decade in men and women; (2) the general incidence of coronary artery calcium in women is similar to that in men who are a decade younger; (3) this separation in prevalence with age is eliminated by approximately age 65 to 70, when the incidence of coronary calcium in women is similar to that of men of the same age. Although there is

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an increasing incidence of coronary calcification in patients, as one grows older, this simply parallels the increased incidence of coronary atherosclerosis with advancing age. Coronary artery calcium score, as a measure of the extent of coronary disease, also increases with age, but the magnitude of the estimated atherosclerotic plaque burden is quite different in men versus women.⁶

Atherosclerosis is the only disease known to be associated with coronary calcification.⁷⁻⁹ Recent studies have shown that calcium can be seen in all degrees of atherosclerotic involvement and is an active process.¹⁰⁻¹³ Coronary calcification is common in patients with known coronary artery disease^{14,15} and is strongly related to age, increasing dramatically after age 50.¹⁶⁻¹⁹ Since Faber²⁰ in 1912 noted that Mönckeberg's calcific medial sclerosis does not occur in the coronary arteries, atherosclerosis is the only vascular disease known to be associated with coronary calcification.

However, coronary plaque and its associated coronary calcification may have only a poor correlation with the extent of histopathologic stenosis,^{21,22} which in turn is largely accounted for as a result of individual variations in coronary artery remodeling. In situ coronary calcium, on the other hand, is associated with plaque size.²³

A fundamental requirement for the use of coronary calcium quantification by CT to define coronary artery plaque is to establish how these 2 measures relate to each other. Simon et al²³ and Rumberger et al^{24,25} at the Mayo Clinic initially examined random autopsy hearts and compared measures of coronary calcium using EBT as compared with direct histologic plaque areas and percent luminal stenosis. These studies determined that the total area of coronary artery calcification quantified by EBT is linearly correlated ($r = 0.90$) with the total area of histologic coronary artery plaque. Here, although the total atherosclerotic plaque burden was tracked by the total calcium burden, not all plaques were found to be calcified, and the total calcium area was around 20% of the total atherosclerotic plaque area. These data suggest that there may be a size of coronary plaque that is most commonly associated with coronary calcium but, in the smaller plaques, the calcium is either not present or is undetectable. An article by Baumgart et al²⁶ compared direct intracoronary ultrasound measures during angiography with EBT scanning and confirmed a direct association

of coronary calcium score with localization and extent of atherosclerotic plaques in vivo.

CT Methods

This section will discuss methods related to coronary artery calcium identification. Specific methods of contrast-enhanced coronary lumen imaging using EBT and MDCT are discussed elsewhere.

EBT Methods

EBT is a mature Food and Drug Administration–approved body-imaging device developed over 20 years ago and is the only CT device specifically designed from inception for cardiac imaging. Although the technique can quantify ventricular anatomy and global and regional function²⁷ as well as myocardial perfusion,²⁸ it is currently best known for defining and measuring coronary artery calcified plaque and for performing noninvasive coronary angiography. To date, and specifically over the past decade, there have been nearly 1,000 articles published regarding the validation of EBT for coronary artery plaque and lumen imaging.

EBT (also referred to as “Ultrafast-CT,” GE/Imatron Inc., South San Francisco, CA) uses unique technology-enabling ultrafast scan acquisition times currently of 33 milliseconds, 50 milliseconds, 100 milliseconds, and multiples of 100 milliseconds (up to 1.5 seconds) per slice. There have been 3 iterations for EBT since it was introduced clinically in the early 1980s. The overall imaging methods have remained unchanged, but there have been improvements in data storage, data manipulation and management, data display, and spatial resolution. The original C-100 scanner was replaced in 1993 by the C-150, which was replaced by the C-300 in 2000. The current EBT scanner, the “e-speed” (GE/Imatron) was introduced in 2003. The “e-speed” is a multislice scanner and currently can perform a heart or body scan in one half the total examination time required by the C-150 and C-300 scanners. The “e-speed,” in addition to the standard 50 milliseconds and 100 milliseconds scan modes common to all EBT scanners, is capable of imaging speeds as low as 33 milliseconds, but as of this writing, no validation studies on the applicability of calcium scoring in

this mode are available. Thus, the current discussion of EBT will focus on the established methods of the C-150 and C-300 imaging systems.

EBT uses a stationary multisource/split-detector combination coupled to a rotating electron beam and produces serial, contiguous, thin-section tomographic scans in synchrony with the heart cycle. EBT is distinguished by its use of a scanning electron beam rather than a traditional x-ray tube and mechanical rotating device used in current "spiral" single and multiple detector scanners. The electron beam (cathode) is steered by an electromagnetic deflection system that sweeps the beam across the distant anode, a series of 4 fixed tungsten "target" rings. A stationary, currently dual level, detector lies in apposition to the tungsten target rings. Thus, as opposed to physically moving the x-ray tube in a circle about the patient, as is done by the mechanical CT (spiral) scanners, only the electron beam is moved in EBT.

Standardized methods for imaging, identification, and quantification of coronary artery calcium using EBT have been established.⁹ The scanner is operated in the high-resolution, single-slice mode with continuous, nonoverlapping slices of 3-mm thickness and an acquisition time of 100 milliseconds per tomogram. Patients are positioned supine, and, after localization of the main pulmonary artery, a sufficient number of tomographic slices are obtained to cover the complete heart through the left ventricular apex (usually 36 to 40 slices). Electrocardiographic triggering is done at end diastole at a time determined from the continuous ECG tracing recorded during scanning. Current clinical protocols for EBT perform triggering during the cardiac cycle as varied depending on the patient's resting heart rate. This is intended to minimize coronary motion artifacts because the ballistics of cardiac motion is highly dependent on resting heart rate.

The presence of coronary calcium is sequentially evaluated in all levels. Coronary calcium is defined as a hyperattenuating lesion above a threshold of 130 Hounsfield Units (HU) with an area of 3 or more adjacent pixels (at least 1 mm²). CT HU densities range from -1,000 (air), through 0 (water), and up to +1,000 (dense cortical bone). The "calcium score" developed by Agatston²⁹ and predicated on a 3-mm slice thickness is a product of the area of calcification per coronary segment and a factor rated 1 through 4 dic-

tated by the maximum calcium CT density within that segment. A calcium score is reported for a given coronary artery and segment and for the entire coronary system; however, most research studies have reported data related to the summed or total "score" for the entire epicardial coronary system.

Quantification of coronary artery calcium using EBT scanning has been proven as a valid surrogate for atherosclerotic plaque burden and as a measure of the severity of coronary disease in direct pathologic comparison studies²⁵ regardless of age or gender²⁴ and in clinical studies using coronary angiography³⁰ and intravascular ultrasound²⁶ as reference standards.

MDCT Methods

The current generation of MDCT systems are capable of acquiring 4, 8, or 16 (and potentially soon 32) levels of the heart simultaneously with ECG gating in either a prospective or retrospective mode. The MDCT differ from single-slice helical or spiral CT systems principally by the design of the detector arrays and data acquisition systems that allow the detector arrays to be configured electronically to acquire multiple levels of various slice thickness simultaneously. Thus, in the current 16-channel MDCT systems 16 slices can be acquired at nominally 1.25-mm slice widths for cardiac imaging. As of 2003, 4-channel MDCT systems are the most widely deployed with an estimated installed base in the United States of over 2,000 and only a few 16-channel systems are installed.

In MDCT systems, like the preceding generation of single-slice helical scanners, the x-ray photons are generated within a specialized x-ray tube mounted on a rotating gantry. The patient is centered within the bore of the gantry such that the array of detectors is positioned to record incident photons after traversing the patient. Within the x-ray tube, a tungsten filament allows the tube current to be increased (mA), which proportionately increases the number of x-ray photons for producing an image. This is a design difference with current generation EBT systems, which use a fixed mA. The attenuation data (after passing from the source, through the body, and incident on the detector array) are recorded and transformed through a filtered back projection into the CT

image. This final step is common to both EBT and MDCT. Helical and MDCT systems have 2 principal modes of scanning that are dependent on whether the patient on the CT couch is stationary (axial mode) or moved at a fixed speed relative to the gantry rotation (helical mode). The axial mode uses prospective ECG triggered at predetermined offset from the ECG detected R wave analogous to EBT (but at a physically slower speed per image than EBT) and is the current mode for measuring coronary calcium at most centers using MDCT. This mode is preferred mainly because of issues of keeping the radiation dose similar to that of EBT (see later discussion on radiation dosimetry).

Current MDCT systems allow 4, 8, or 16 slices to be obtained within a single heartbeat. The temporal resolution of a helical or MDCT system is determined by the gantry speed, which determines the number of views per second possible. To reconstruct each slice 180° plus the angle of the fan beam is required, typically a total of 220° of rotation. For a 16-channel system with 0.4-second rotation, the temporal resolution is 0.244 seconds or 244 milliseconds for a 50-cm display field of view (FOV). By reducing the display FOV to the 20 cm to encompass the heart, the number of views can be reduced too, theoretically further improving temporal resolution for a 16-channel scanner to approximately 200 milliseconds. The majority of MDCT systems in 2003 have gantry speeds of 0.5 to 0.75 seconds and temporal resolution of 320 to 500 milliseconds per image when used for measuring coronary calcium, as compared with 100 milliseconds or less for EBT.

The rapid evolution of MDCT, although potentially of great value for coronary artery calcium (CAC) quantitation, makes current application of guidelines for MDCT uses more confusing. All comparisons between MDCT and EBT data show good group correlation values, but with each improvement in MDCT speed and slice profile the correlation with EBT is found to be better despite the strong claims of comparability declared by vendors of preceding generations. Another issue relates to the image slice thickness used for imaging, which varies between manufacturers. The issue of slice thickness and the effects on calcium scoring are discussed in a later section.

Variability and Calibration

When comparing measurement devices, calibration to an external standard is crucial for comparability between both EBT and MDCT over time. Significant variability in the measurement of the 130 HU threshold has been documented within and between EBT scanners even when serviced and maintained at the same site.³¹ Use of an external calibration phantom was shown to reduce scanner variation with EBT by 25%. Because there may be measurement errors both within the same and between different EBT systems (largely because of differences of FOV settings, thus affecting spatial resolution), comparison of MDCT systems to EBT by definition will include the measurement error of the EBT system plus the measurement error with MDCT. Furthermore, differences in scanner calibration, equipment age, hardware and software versions, power, and reconstruction kernel will result in differences in CT scanners (EBT or MDCT) for measuring CT numbers at the threshold for measurable calcified plaque. The articles by Goldin and Yoon³² and Carr et al³³ both document how agreement at various cut points can be influenced based on whether a threshold of 90 HU or 130 HU was defined as threshold for measurable calcified plaque and document the need for calibration of the calcium score.

Spatial Resolution

Spatial resolution is important in all 3 dimensions when measuring coronary plaque. Even if limited to the proximal coronary arteries, the vessels course obliquely along the Z (longitudinal) plane as well as within the X-Y (transverse) imaging plane. The inplane resolution of both EBT and MDCT systems is equivalent at the same display fields of view. For a display FOV of 26 cm (preferred for EBT scanning) and 35 cm, the respective pixel areas are 0.26 mm² and 0.46 mm², respectively. The Z dimension is determined by the slice collimation that with current protocol for coronary calcium is 3 mm for EBT but varies between manufacturers from 2.5 mm to 3.0 mm for MDCT. Because even the proximal coronary arteries are often less than 5 mm in diameter, this can easily result in an effect termed "partial volume averaging." This can be explained as an object, in this case a small calcified plaque, having dramatically different CT numbers related to whether it is

centered within 1 slice or divided between 2 adjacent slices. Difficulties in measuring small plaques and distinguishing them from image noise is an established limitation of current methods and likely contributes to the observed variability with both EBT and MDCT when performing repeated scans in the same individual.^{34,35} Improved spatial resolution in the Z axis will reduce this source of measurement error and is possible with current MDCT systems^{36,37} and with the latest generation of EBT.

Imaging Speed/Temporal Resolution

Overall CT image quality is dependent on multiple factors throughout the imaging sequence. These include image noise, blurring, spatial resolution, and other factors related to both the imaging device and patient. In the case of measuring calcified plaques of various sizes, temporal resolution, spatial resolution, and image noise are important to varying degrees. Cardiac CT is dependent on having a high temporal resolution to minimize coronary motion. By coupling rapid image acquisition with ECG gating (MDCT) or triggering (EBT), images can be acquired in specific phases of the cardiac cycle. Studies have indicated that temporal resolutions of 19 milliseconds are needed to suppress all pulmonary and cardiac motion.³⁸ Cardiac magnetic resonance motion studies of the coronary arteries indicate that the rest period of the coronary artery varies significantly between individuals, with a range of 66 to 333 milliseconds for the left and 66 to 200 milliseconds for the right coronary artery³⁹ and that for mapping coronary flow, temporal resolution of 23 milliseconds may be required for segments of the right coronary artery.^{40,41} Current generation cardiac CT systems that create images for measuring calcified plaque at 100 milliseconds (EBT) and 220 to 500 milliseconds (MDCT) cannot totally eliminate coronary artery motion in all individuals (except possibly for the “e-speed” EBT scanner operating in the 33-millisecond mode). Motion artifacts are especially prominent in the mid-right coronary artery, in which the ballistic movement of the vessel may be as much as 2 to 3 times its diameter with the twisting and torsion of the heart during a single cardiac cycle. Blurring of plaques secondary to coronary motion increases in systems with slower acquisition speeds. The result-

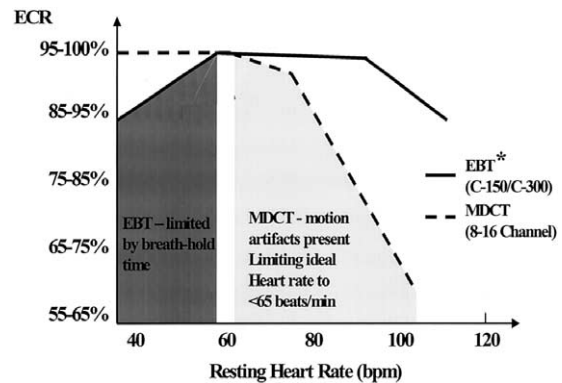


Fig 1. ECR (evaluable case rate) versus resting heart rate (beats/min) for EBT versus MDCT. *These limitations do not apply to the “e-speed” version of EBT (see text for details).

ing artifacts tend to increase apparent plaque area (“blooming”) and decrease plaque density and thus alter calcium score measurements. It should be noted that using more detectors (ie, 2 v 4 v 8 v 16 detector/channel systems) does not improve the temporal resolution of the images obtained. In a recent study of MDCT, a majority of noninvasive angiography cases could not be fully evaluated because of motion artifacts, especially when the heart rate was >65 beats per minute.⁴² Thus, increasing numbers of detectors with MDCT will not decrease motion artifacts. The images from MDCT are best when the resting heart rate is <65 beats/min; at faster heart rates, motion artifacts become more dominant. Generally, the higher x-ray flux (mA = tube current × scan time) available with MDCT devices leads to images with somewhat better signal-to-noise ratio and higher spatial resolution when compared with EBT. This occurs at a cost of increased radiation depending on the scanner and protocol used.

Figure 1 schematically shows the limitations of EBT versus MDCT for calcium scoring (and noninvasive angiography) as a function of resting heart rate. Evaluable case rate is an estimation of the percent of studies that would be successful under a given clinical condition. The C-150 and C-300 EBT systems take 100-millisecond scans but can acquire only 1 slice per cardiac cycle. The limitation of EBT at slow heart rates is that the required breath hold to acquire the required number of slices (up to 40) may be too long for some patients. Conversely, although MDCT can acquire

multiple cardiac slices per rotation, the slower temporal resolution per slice limits its practical ability to individuals with heart rates <65 beats/min. The “e-speed” B, which acquires dual high-resolution images at 33 to 50 msec/slice, can image the entire heart in one half the time of the prior EBT systems and thus has an ECR that is very high regardless of resting heart rate (up to 110-120 beats/min).

Studies Comparing EBT and MDCT for Calcium Scoring

Becker et al studied 100 patients comparing MDCT with EBT and reported a high correlation between the 2 modalities.⁴³ In this study, however, the percent variability between individuals was 32% for CAC scores. There were relatively few patients with scores <100, and the high correlation may have been driven by those individuals with high scores. Moreover, the level of individual precision was limited and the scores <100 appeared to have the most deviation by MDCT as compared with EBT. Although a high correlation indicates that these 2 measures have a linear relationship to one another, the spread about the line can still be significant and can limit use in individuals.

Knez et al⁴⁴ studied the diagnostic accuracy of MDCT compared with EBT in 99 symptomatic male patients. For quantification of CAC, the volumetric calcium score was determined. The results indicated excellent correlation between the 2 modalities ($r = .99$). The mean variability between the MDCT and EBT derived scores was 17%. Importantly, the study population had 26 patients with score ranging from 0 to 100, and the mean variability between the test was 20%, which was not significantly different from very high scores.

These studies were performed in older male symptomatic adults with a mean age above 60 years and a high range of calcium score values.^{43,44} The findings of extensive calcification and a good correlation over a large range of values, however, does not fully address the need to measure CAC scores accurately and reproducibly in a given individual. In addition, these high correlations may not apply as well to a younger asymptomatic population with generally much lower scores. The studies by Budoff,⁴⁵ Carr et al,³³ and Goldin and

Yoon³², each comparing EBT and helical CT, indicated a range of poor to fair and fair to excellent agreement at a series of clinical cut-points as proposed by Rumberger⁴⁶ using the Agatston score. However, the study by Carr et al³³ indicated that agreement could be improved by calibration of the Agatston score to an external standard.

It should be emphasized that the clinical value for CAC determination is to facilitate individual risk assessment, and thus scoring for a given patient should be as accurate as possible. However, for epidemiologic studies and investigations of coronary calcium in broad population groups, measures by MDCT and EBT may provide similar insight into the atherosclerotic process.

Signal Versus Noise

Early detection of calcified plaque is dependent on distinguishing the plaque from image noise. MDCT systems have reduced image noise compared with EBT systems. Image noise with EBT has been shown to have an association with body mass index,⁴⁷ which may result in falsely identifying noise as calcified plaque or overestimation of true plaque burden. On the other hand, the image blurring by MDCT may result in false-negative studies or underestimation of true plaque burden.

Prospective gated imaging has resulted in partial scan times of 220 to 500 milliseconds for MDCT; however, motion artifacts can be a significant drawback for measurements within a given individual. On the other hand, retrospective ECG gating is an alternative method for data acquisition; this enables one to reconstruct the images at a desired slice position. In a beating heart phantom study, ECG-gated volume coverage with MDCT (2.5-mm collimation) and overlapping image reconstruction (1-mm increment) was found to significantly improve the reliability of coronary arterial calcium quantification, especially for small plaques ($P < .05$).⁴⁸ Mean interexamination variability was reduced from 35 (6%, Agatston score, standard electron-beam CT) to 4 (2%; $P < .05$) (volumetric score).

As a result of clear reductions in errors by doing volume versus area (Agatston) scoring, noted in the original study by Callister et al⁴⁹ on volume scoring, all reported EBT scoring from clinical and research centers since 1998 has included both

measures, as is also now being advocated with the newer MDCT systems.

Recent studies have shown that MDCT with a retrospective ECG-gating algorithm showed a high correlation with coronary calcium scores determined using EBT in 60 patients⁵⁰ and a mean variability of 12% with Agatston and 7.5% with volumetric scoring,⁵¹ respectively. Whether the number of missed plaques may be reduced with retrospective ECG gating, small incremental reconstruction and thinner slices needs to be investigated. However, a limitation of retrospective gating is that the process is a very time-consuming manual analysis and often involves subjective selection of retrospectively gated CT sections. This process may also add significantly to the intertest variability of CAC scores for MDCT because it is highly operator dependent.

Radiation Exposure

One drawback of MDCT as compared with EBT is the higher radiation exposure to the patient.^{32,48,50-58} Radiation exposure from prospectively gated studies is much less than from retrospectively gated studies. The x-ray photon flux expressed by the product of x-ray tube current and exposure time (mA) is generally higher with MDCT. For example, 400 mA with 0.5-second exposure time yields 200 mA in MDCT versus 614 mA (fixed tube current) with 0.1-second exposure time yields 61.4 mA in EBT. The increase in radiation dose with MDCT compared with EBT has been estimated to range from 3 to 10 times higher, depending on the protocol used and whether prospective or retrospective gating is used.^{50,52,53} The most modern MDCT devices used in the retrospective imaging mode probably expose the patient to about 30 to 40 mGy (3-4 rad), equivalent to a conventional angiographic study, and up to 10-fold higher than the doses delivered during EBT of 3 to 4 mGy (0.3-0.4 rad).^{54,55}

The radiation dose estimation has a wide margin of error and depends significantly on the method of estimation. Furthermore, the distributions of radiation dose are different for MDCT and EBT. In EBT the maximum dose is delivered at the entrance surface to the patient's anatomy lying closest to the target ring (usually the posterior elements) because of the configuration of target rings, whereas in MDCT, the dose is uniform

around the patient and decreases toward the center. This results in a decreased dose distribution in EBT to organs lying anteriorly such as breasts. Thus, with MDCT, the effective dose in women is 25% higher than in men raising the mean dose from 30 mGy (3 rad) per study in men to 40 mGy (4 rad) per study in women.⁵⁴ In MDCT, using prospective gating, the radiation dose is lower than that of retrospective gated studies. However, results from a recent study showed that ECG-controlled tube current modulation allows significant dose reduction of 48% and 45% in men and women, respectively, while performing retrospectively ECG-gated MDCT of the heart.⁵⁸

Reproducibility of Calcium Scoring

A promise of these technologies is to accurately measure atherosclerosis burden and to track changes over time to assess efficacy of therapy.⁵⁹ This ability to assess progression is dependent on the reproducibility of the technologies. EBT interscan reproducibility has been shown to be approximately 10%, with interreader variability approximately 3% and intra-reader variability <1%.^{60,61} This has been significantly more problematic with MDCT. The interscan variability in several studies is 32% to 40%.^{62,63} A recent study showed that interreader variability with MDCT is problematic and suggested double reading all studies to better assess coronary calcium. In an article by Goldin and Yoon,³² mean interreader variability was 4.5% for electron beam CT versus 41.5% for spiral CT.³² However, large studies evaluating the reproducibility of MDCT are not yet available.

The previously mentioned studies support the idea that the age- and gender-based calcium score percentiles using EBT cannot always be applied to the results obtained with MDCT scanners in patients with CAC score <100; furthermore, these results may be altered by using slice thicknesses other than the 3 mm used for the foundation of the Agatston calcium scoring system. Moreover, it appears that the calcium scores from various MDCT scanner manufacturers differ (confounded by different slice thicknesses) and their ability to monitor disease progression or regression remains to be fully established. In addition, CAC scores obtained using gated retrospective reconstruction algorithms from spiral CT scanners may not be directly comparable to those

Table 1. Basic Description of CT Systems

	EBT	MDCT
Electron source (cathode)	Electron gun	Tungsten filament
Target (anode)	Tungsten rings in gantry	Tungsten anode in x-ray tube
Gantry	Fixed—electron beam rapidly sweeps across tungsten rings	Rotates—tube and opposing detectors rotate within gantry
Detectors	Matrix array	Matrix array
Image reconstruction (180° plus width of fan beam)	Partial scan/filtered back-projection sharp kernel	Partial Scan/Filtered back-projection Standard kernel
CT number scale	Hounsfield Unit (HU)	Hounsfield unit (HU)
mA	Fixed	User selectable
Exposure time for coronary calcium (temporal resolution)	100 msec (true prospective) at full FOV; 86 msec for “central time resolution”	230 msec (post processing) for 16-channel systems and longer for 8-, 4-, 2-, and channel systems (dependent on gantry rotation speed and detector design)
mAs	Fixed mA × exposure time	User selectable mA × exposure time
Heart rate limitations	<110 beats per minute	<65 beats per minute
z axis resolution	1.5 mm	≤1.0 mm

obtained by EBT; this discrepancy may result in differences in risk stratification if one uses age- and gender-based percentile tables derived from EBT studies. Unfortunately, unlike the standards for EBT, no standards have been adopted to allow for comparable measurement of coronary artery using MDCT. The ideal acquisition protocol is a subject of controversy for MDCT; ungated imaging should not be done or the results interpreted only in a subjective and not objective manner. Recommendations for the standardization of coronary artery imaging by MDCT for prospective as well as retrospective ECG gating should be established in line with recommendations recently suggested by a group of German researchers and clinicians.⁶⁴

There are several areas regarding coronary artery calcium quantitation as it relates to use of EBT versus MDCT that require discussion. These involve temporal scan resolution and slice thickness during imaging. These issues also include intrinsic scan characteristics and revolve around other common parameters such as FOV and partial volume (or volume averaging) effects through the thickness of the tomogram.

Table 1 shows information regarding temporal and spatial resolution of the EBT and MDCT systems currently in clinical use. EBT has a “true” temporal resolution per image for coronary calcium quantitation of 100 milliseconds (86 milliseconds for “central time resolution”). Data from an entire 360 rotation of the scanning gantry are

not needed to produce CT tomograms. The requirement is only 180° (assuming symmetry), and this is referred to as a “central time resolution” or central temporal resolution. Commonly, MDCT scanner manufacturers refer to the temporal resolution of a 500-millisecond full rotation scanner as only 250 milliseconds for this reason. By using a variety of partial scan reconstruction methods that would require data from more than 1 full gantry rotation (and thus commensurate increases in radiation exposure), effective temporal resolutions as low as 125 milliseconds (for this example) would theoretically be possible. However, this type of temporal resolution applies only to a volume in the center of the image. For a complete scan to be created, data from 180° plus the width of the scanning or “fan” beam must be included. Fan beam widths for MDCT are variable, but in general are on the order of 40° to 50°. Thus, data from $180 + 40 = 220^\circ$ is nominally required to produce a complete tomographic section of the body. This physical constraint is what then can be used to calculate the “true” temporal resolution for any given MDCT scanner.

There are a variety of MDCT systems available that have been used or are advocated for use regarding coronary artery calcium measurements, and their true temporal resolutions range from 220 milliseconds (16-channel scanner) to 1,000 milliseconds (single-slice scanner). Motion artifacts during imaging in any given tomographic plane or through the volume of the tomogram

Table 2. Comparison of Coronary Calcium Scores (Agatston Method) in Population-Based Studies (Men Only): EBT (3.0-mm Slice Thickness) Versus MDCT (2.5-mm Slice Thickness) and Estimated Corrections for Slice Thickness

	Age	<40	40–44	45–49	50–54	55–59	60–64	65–70	>70
25th percentile	EBT	0	0	0	1	4	13	32	95
	MDCT	0	0	0	0	0	1	21	51
	MDCT*	0	0	0	0	0	1	17	43
50th percentile	EBT	0	1	3	15	48	113	180	360
	MDCT	0	0	0	7	35	59	136	211
	MDCT*	0	0	0	6	28	47	109	169
90th percentile	EBT	14	59	154	332	554	994	1299	1829
	MDCT	24	44	181	299	730	793	1452	1693
	MDCT*	19	35	145	239	584	634	1162	1354

*Estimated corrections for slice thickness.

(volume element or voxel) can alter the calcium measurements. At heart rates <65 beats per minute, the fastest of the MDCT systems result in limited motion artifacts, whereas systems with temporal resolution approaching 1,000 milliseconds (which would be the entire cardiac cycle at a heart rate of 60 beats per minute) will still confound the quantitation of coronary calcium.

The Issue of Slice Thickness

The Agatston calcium scoring was designed as an area measurement and is predicated on a 3.0-mm slice thickness. Although this is likely not the ideal tomographic slice thickness for coronary artery imaging, it was chosen historically because the original EBT scanning system in use at the time for research had 3.0 mm as the thinnest slice available. Current EBT systems are now able to perform scanning at 1.5 mm, and the latest MDCT systems can provide slice thicknesses that are ≤ 1 mm. However, current data are based on the traditional Agatston scoring algorithm, although other methods such as volume score and integrated area above background may prove to be more reliable in serial studies. Manufacturers of MDCT have thus sought to duplicate Agatston scoring to rival the data from EBT. This has resulted in changing in the initial threshold CT density (HU) for calcium from the traditional 130 HU²⁹ to 90 HU³³ to facilitate baseline similarities for calcium scores. Lowering the threshold can potentially reduce partial volume errors caused by motion artifact (which would result in missing some coronary calcium) and increases the overall sensitivity of the scanner for very small areas of

calcification. Some MDCT systems are capable of acquiring true 3.0-mm slices, whereas others acquire images at 2.5-mm slice thickness. The Agatston score is a nonlinear variable and information across the area of calcium within the tomogram is multiplied by 1, 2, 3, or 4 depending on the maximum HU within the area under interrogation. By sampling at 2.5-mm slice intervals rather than 3.0-mm slice intervals, the area is oversampled. If all parameters are the same, such as FOV and spatial resolution, a partial solution for estimating calcium scores done on a 2.5-mm scanner can be determined by adjusting the score by $2.5/3.0 = 0.8$ to compare the result using a 3.0-mm scanner.

Hoff et al⁶ using EBT and 3.0-mm slice thicknesses have published a very large population database. These same data have been applied by various individuals using various MDCT systems, implying that the data would be similar under similar conditions. However, this is not entirely true and depends on which scanner was used for imaging. The MDCT scanner used in the paper by Carr et al³³ used 3.0-mm slice thicknesses for the comparison. However, current scanners manufactured by vendors in Germany and Japan use a 2.5-mm slice thickness. Population data for studies done using an 8-channel MDCT, 2.5-slice thickness system⁶⁵ are shown in Table 2 and are compared with data using EBT as published by Hoff et al.⁶ The authors of the former paper indicated that the data from the MDCT scanner were similar to those found using EBT; however, they failed to note the issue of slice thickness in the calculations. The data show calcium scores for men only, across all ages examined, and for selected percentiles. The comparison calcium

scores, however, accounting for the differences in slice thicknesses, are shown in Table 2 below the published data. These data indicate that there can be considerable differences in absolute calcium scores depending on the scanner used and underlines the need for using data that are specific for the CT scanner used and depend on the amount of calcium present. These results underscore the need to use data that are specific to the machine used for scanning. In the future, a more universal scoring system may be possible that would be machine independent, but at present data derived from MDCT should be compared with caution with those derived from EBT.

Summary and Conclusions

EBT has undergone rigorous testing for reliability and validity and has proven to be useful in identifying individuals with, or at risk for, CHD. Although MDCT is a promising tool for coronary calcium scoring, more studies are needed comparing EBT and helical CT scans in the same patients, especially with calcium scores <100. MDCT studies evaluating progression, reproducibility, and plaque burden determined by independent methods like intravascular ultrasound or autopsy and outcomes studies are needed to fully evaluate its potential to measure and track atherosclerosis. MDCT currently provides patients a higher radiation dose and less clinical validation than EBT, although several groups have published promising data with this technique.

At present, EBT remains the reference standard for calcium scoring. It is also important to note that these results should only be applicable to the prospectively triggered sequential mode; however, its applicability to the newer 16-slice MDCT is also yet to be explored. The absence of CAC on EBT identifies a group of patients at very low risk of events with a very high sensitivity and negative predictive value ($\geq 99\%$) to identify patients with obstructive coronary artery disease,⁶⁶ showing a score of 0 (no coronary calcium) with EBT can virtually exclude those patients with obstructive CAD. Raggi⁶⁷ showed an annual event rate of only 0.36% for patients with scores of zero. Both the American College of Cardiology/American Heart Association writing group and the Prevention V Conference agreed that the negative predictive value of EBT is very high for short-term events.⁶⁸

Furthermore, Greenland et al⁶⁹ from the American Heart Association have suggested that EBT calcium scores can provide incremental data above conventional risk factors in patients at intermediate risk for a coronary event. It needs to be determined if a zero score derived from MDCT devices has the same prognostic and diagnostic significance in ruling out obstructive CHD as does a zero score from EBT. The same needs to be determined for a positive scan and the validity and reproducibility of the calcium scores by MDCT. Ideally, MDCT scanners should undergo validation studies to assess the comparisons to angiography, histology, and outcome data before widespread utilization.

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