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Comparison of spiral and electron beam tomography in the evaluation of coronary calcification in asymptomatic persons

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Abstract

Recently, investigators have begun evaluating the ability of spiral computed tomography (sequence scan mode-SEQ) to measure coronary calcium. Electron Beam Tomography (EBT) and SEQ studies were performed in 10 women and 23 men, with a mean age of 54±9 years. The EBT study was performed within 4 weeks (mean 11 ±4 days) of the SEQ with no clinical interval event (MI, revascularization). The mean EBT calcium score (Agatston method) was 52.1 ±58.6, with a range of 0 to 175. The SEQ mean score was 60.1±71.1 (range 0 to 253). There were 7 persons with scores of 0 on both scans, and 9 persons with scores of zero on either EBT or spiral CT, but not both. Three persons had negative EBT studies where SEQ detected calcium, and 6 persons had EBT detected calcium and negative SEQ studies. The six patients with negative SEQ and positive EBT studies had a mean score of 47±25.7 (range 9 to 99). The remaining sixteen persons had coronary calcium detected on both studies. As compared to EBT, spiral CT had a sensitivity of 74% and a specificity of 70%, for an overall diagnostic accuracy of 73%. The positive and negative predictive values were 85 and 54%, respectively for SEQ in this study. The absolute difference in scores between the two tests was 29.1 +/-28.5 (mean±S.D.). The inter-test variability, defined as the mean values of the differences between the calcium scores in the two scans on the same subjects divided by the mean of the two scores (Absolute Difference between tests/mean), was 84.5% in this study. In asymptomatic persons, spiral CT (using SEQ) provides a limited sensitivity (74%) and specificity (70%) for coronary calcium when compared to EBT. Caution should be used when evaluating the results of spiral CT coronary calcium especially in patients with relatively low calcium scores (<200). © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Electron beam tomography; Spiral computed tomography; Coronary calcium

1. Background

It has been established that the presence of coronary calcium is always indicative of coronary atherosclerosis [1]. Several non-invasive imaging techniques have been used to detect coronary calcium (CC) [2], including; chest radiography [3], fluoroscopy [4], conventional [5] and spiral computed tomography [6,7], (CT). However, the decreased temporal and spatial resolution, slow acquisition times and inability to prospectively gate images to the electrocardiogram limit the accuracy of these modalities. Electron beam tomography (EBT), by acquiring images of the proximal coronary arteries, detects CC, which has been shown to be highly correlated with the presence of coronary artery disease [2,8]. The detection of CC, as measured with EBT, has been recently shown to have considerable potential for noninvasively identifying patients at increased risk of developing coronary artery disease

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[9-13]. Recent studies have documented the ability of this methodology to track progression or regression of atherosclerosis using cholesterol-reducing medications [14,15].

Recent advances in spiral CT imaging have renewed clinicians' interests in utilizing this modality to evaluate CC. For this reason, we have conducted a comparative study to evaluate the relative abilities of spiral CT and EBT to measure CC in an asymptomatic population.

2. Methods

2.1. Patient population

Thirty three subjects who underwent spiral CT evaluation of CC underwent EBT coronary artery scanning within 4 weeks. Persons were asymptomatic, with no known cardiovascular disease (no angina, revascularization, previous myocardial infarction or stroke). Patients were referred for calcium scans to evaluate for cardiovascular risk. Patients had, on average, 1.6 known cardiac risk factors at the time of scanning.

2.2. Spiral CT scan protocol

Scanning was performed using a Siemens Somatom Plus 4A (Siemens AG, Forchheim, Germany). Persons were scanned in the non-spiral 240° partial sequence scan mode (SEQ), slice thickness was 3 mm, tube current was 90 mA, and tube voltage was 120 kV without ECG-triggering. Images were acquired at end-inspiration with each breathhold. The slice-by-slice sequence mode of the subsecond (750 ms per 360°) conventional CT scanner allows for a 240° partial scan with 500 ms effective acquisition time. Interscan delay (1.5 s between slices) required the acquisition of two cluster scan series consisting of 20 slices each. The persons were instructed to hold their breath twice for 30 s each with a respiration delay of 30 s between each cluster series. The scans started just below the carina, and the entire coronary tree was imaged. Scoring was done using the Agatston method [16] with a threshold of 130 Hounsfield units. The lesion score was calculated by multiplying the lesion area by a density factor derived from the maximal Hounsfield unit within this area, as originally described by Agatston for EBT scanning [16]. A total calcium score was determined by summing individual lesion scores from each of four anatomic sites (left main, left anterior descending, circumflex, and right coronary arteries) in all 40 slices. The spiral CT scans were scored by a radiologist with extensive experience in cardiac anatomy and coronary calcium. The spiral CT scans were scored blinded to the results of the EBT scans.

2.3. Electron beam coronary scan protocol

The EBT studies were performed with an Imatron C-150XL Ultrafast° CT scanner (Imatron, South San Francisco, CA) in the high resolution volume mode, using a 100 ms exposure time, 630 mA electron gun current, and 130 kV electron gun current. Electrocardiographic triggering was employed, so that each image was obtained at the same point in diastole, corresponding to 60% of the RR interval. Proximal coronary artery visualization was obtained without contrast medium injection, and at least 30 consecutive images were obtained at 3 mm intervals beginning one centimeter below the carina and progressing caudally to include the coronary arteries. The entire coronary tree was visualized on every study. The EBT scans utilized a threshold of 130 Hounsfield units (Hu) for identification of a calcific lesion and scoring was done using the Agatston method as described above. The EBT scans were scored by a cardiologist with extensive experience with coronary calcium, blinded to the results of the spiral CT scans. Total radiation exposure by EBT is approximately 0.7 Rad per person [17], and 1.2 Rad with spiral CT [18].

2.4. Statistical analysis

All values are reported as mean±standard deviation. Data were analyzed using chi square and Fisher's exact test for comparing categorical variables. The Wilcoxon rank sum test was used for comparing continuous variables. Analysis of variance (ANOVA) was performed to demonstrate the influence of cardiac motion artifacts of SEQ in comparison to EBT. All tests of significance were two-tailed, and significance was defined at the 0.05 level

or below. All statistical analysis were performed using the SAS software system [19].

3. Results

3.1. Patient population

Both EBT coronary scanning and spiral CT (using SEQ) were performed in 10 women and 23 men, with a mean age of 52 ± 9 years. The EBT study was performed within 4 weeks (mean 11±4 days) of the conventional CT with no significant clinical event in the interval (MI, stroke or revascularization). No patients reported any history of cardiac or pulmonary disorders at the time of the EBT study. The mean heart rate at the time of the EBT study was 81 ± 12 beats per min.

3.2. Calcium scores

The mean EBT calcium score was 52.1 ±58.6, with a range of 0 to 175 (median score 28). The SEQ mean score was 60.1 ±71.1 with a range of 0 to 253 (median 47). There were 7 persons with scores of 0 on both scans, and 9 persons with scores of zero on either EBT or SEQ, but not both (7/16 or 44% with negative tests by both modalities). Three persons had negative EBT studies and calcium detected on spiral CT. Two of the three had pericardial calcification or beam hardening artifact near the distribution of the circumflex artery (see Fig. 1), misclassified as coronary calcium by spiral CT. Six persons had positive EBT studies and negative spiral CT studies. These patients had a mean score of 47±25.7 (range 9 to 99). Four of the six persons had most or all of the detected calcium in the distribution of the right coronary artery. The remaining sixteen persons had CC detected by both studies. Spiral CT tended to generate higher mean and median calcium scores, but the difference was not statistically significant (P – 0.10). Thus, if EBT is considered the gold standard, spiral CT had a sensitivity of 74% and a specificity of 70%, for an overall diagnostic accuracy of 73%. The positive and negative predictive values were 85% and 54%, respectively for spiral CT in this study. There were no significant differences in men as compared to women in this study (P>0.05).

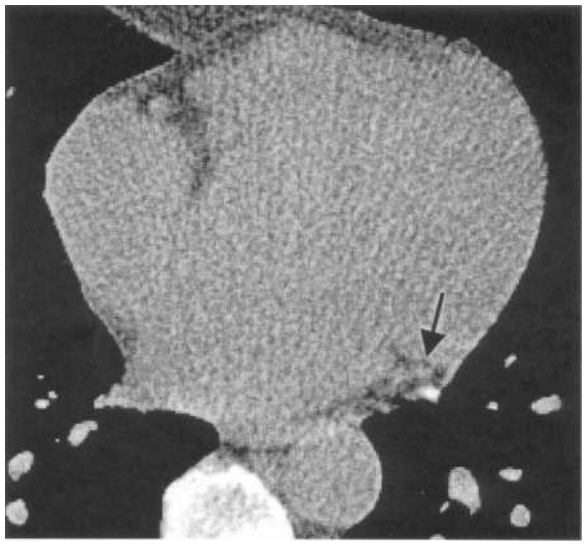

Fig. I. An electron beam tomography scan of a patient with pericardial calcification (arrow) in the region of the circumflex coronary artery. With short acquisition times, the circumflex artery (black arrow) could be clearly distinguished from this calcified focus (white arrow).

The absolute difference in scores between the two tests was 29.1±28.5 (mean±S.D.). A Bland-Altman plot is demonstrated in Fig. 2 [20]. The inter-test variability between EBT and spiral CT, defined as the mean values of the differences between the calcium scores in the two scans on the same subjects divided by the mean of the two scores (*Difference between tests*/mean), was 84.5% in this study. The linear regression equation to compare EBT to SEQ values was EBT=0.66(SEQ)+ 16.07, with a correlation factor of 0.68 (see Fig. 3).

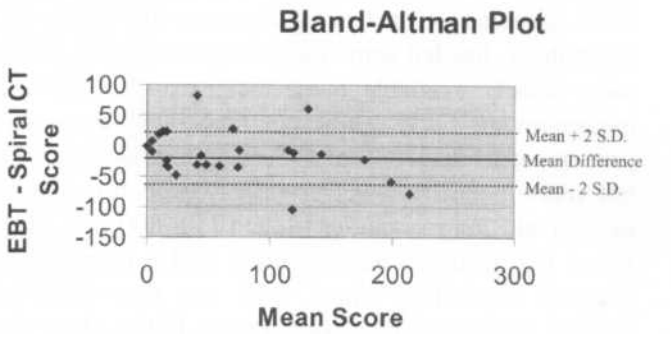

Fig. 2. A Bland-Altman plot comparing the differences between electron beam tomography and spiral CT against the mean. The dashed lines define 2 standard deviations above and below the mean difference for these modalities. CT=Computed Tomography; EBT=Electron Beam Tomography; S.D.=Standard Deviation.

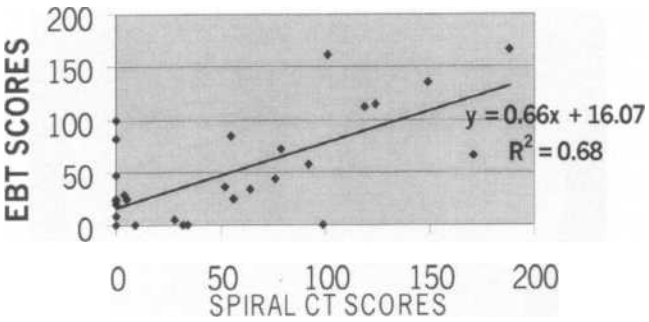

Fig. 3. A linear regression comparing electron beam tomography scores against the spiral CT scores in the same patients. CT=Computed Tomography; EBT=Electron Beam Tomography.

4. Discussion

Recent advances in the detection and quantification of CC using EBT have led to a renewed interest in screening for CC as an early marker of coronary heart disease. Electron beam tomography, with its ability to acquire images in 100 ms and gate to the electrocardiogram (to minimize coronary motion), provides clinicians with a safe and non-invasive means to detect and measure coronary calcium [2]. The sensitivity of EBT for obstructive coronary artery disease is above 95%, and was 99% for multivessel disease in a large multicenter study [8]. In comparison, a study of helical CT to angiography demonstrated a 88% sensitivity for obstructive coronary disease [21]. A study recently reported the use of serial EBT studies as a potential tool to track progression of disease with statin drug therapy [14,15], and this modality is now used to track the efficacy of therapy in some patients. However, the limited availability of EBT, coupled with recent advances in spiral CT technology, has led some investigators to study other, more widely available mechanical scanners for CC measurement. Early studies demonstrated some improvement in detection of CC over fluoroscopy [22], but reproducibility was very poor, probably due to excessively long scanning times (750-800 ms) [23]. Spiral CT scanners have recently had a decrease in scanner acquisition times, and are now able to acquire an image in 250-500 ms [24]. Also, the recent ability to prospectively gate images to the electrocardiogram has further increased interest in spiral CT as a method to evaluate CC [25]. A study by Carr et al. [24] involved no prospective gating, and acquired approximately 400 images of the heart, discarding those which did not occur at the proper time in diastole. With limited-life X-ray tubes in the conventional CT system (not present in the EBT system), maintenance and long-term costs are markedly increased utilizing conventional CT in this manner.

One study of comparative data relating spiral CT and EBT have shown that even when spiral CT operates using accelerated scan times, calcific deposits are blurred due to cardiac motion, and small calcifications may not be seen [26].Two newer studies were recently reported, each involving symptomatic, older men undergoing both EBT and spiral CT. Since the two methods were compared over a large range of values (scores from 0 to 4000), a high correlation was seen [24,25]. However, both studies poorly correlated with EBT at lower scores, and the inter-test variability for both studies was significant. In one comparative study between EBT and spiral CT, Becker [27] demonstrated an overall 42% inter-test variation in older, symptomatic men. However, for those patients with non-obstructive coronary disease, the differences in scoring between modalities were much more significant. The mean score and standard deviation was 73.4±57 for EBT and 27.6± 35 for spiral CT, yielding a 91% inter-test variability.

Since multiple studies have documented that even low scores have prognostic significance [9,28], we undertook this study to evaluate the correlation between EBT and spiral CT in a typical screening population (younger, otherwise healthy patients who are at risk for coronary disease due one or more cardiac risk factors) [9,29]. Our study, showing weak correlation between EBT and SEQ at lower scores correlates well with previous work done with these modalities. The mean scores for EBT and SEQ, as well as the inter-test variability in our study was lower than reported by Becker for patients with non-obstructive coronary disease [27]. The finding of extensive calcification, and a good correlation over a large range of values in these studies, does not adequately address the significance of accurately measuring CC. All three previously reported studies of both modalities had variations of over 100 points on average [24,25,27], far too great to track atherosclerosis serially, accurately risk assess patients, and

most importantly, correctly differentiate persons with atherosclerosis from those without. The inter-test variability of our study (84.5%) is similar to other inter-test comparisons between EBT and spiral CT, but much higher than that reported for inter-scan variability between two EBT scans (8-29%) [30,31]. More importantly, management is now increasingly based upon the score category (0, 1-10, 11-100, 101-400, >400) or the percentile rank compared to other asymptomatic individuals [13,32]. The difference in scores leads to different category classification in a significant number of individuals (Fig. 4); an incorrect categorization which could significantly change how the patient will be managed.

The accuracy and reproducibility of any type of cardiac scanning is inversely proportional to the amount of subject motion. There are three reasons for this dependence: acquisition time, gating and respiratory motion. The first involves the time needed for acquisition of a single slice image. Conventional scanners, including spiral scanners, have image acquisition times (250-500 ms) that do not adequately `freeze' cardiac motion. The acquisition times of SEQ encompass 67% of the entire cardiac cycle (mean heart rate of 80 beats per min). Ritchie et al. [33] found that physiologic motion from both cardiac contractions and respiratory movement require imaging times of 19 ms to completely avoid motion artifacts. Boyd and Lipton [34] estimated that scan times of 30-50 ms would be necessary to minimize cardiac motion sufficiently to produce clinically useful images. Greater acquisition times increase artifacts manifested as black or white streaks, bands, dark spots, loss or resolution, or distortion of anatomy [35,36]. These observations illustrate the problems created with spiral CT's lqnger image acquisition times. The second reason cardiac scanning is dependent on lack of subject motion is related to electrocardiographic gating. Prospective gating has allowed for scanning during diastole, which has been shown to decrease cardiac motion by eliminating the effect of ventricular contraction. However, the heart still moves anteriorly during diastole due to ventricular recoil and atrial contraction. This substantial diastolic motion produces artifacts, particularly in the right coronary artery and left circumflex artery distributions [37,38]. This is one reason why slower scanning with spiral CT does not correlate well with EBT.

The partial volume effect is another source of error. This phenomenon occurs as the result of longer exposure times, potentially making less accurate but visually more pleasing images [33]. Thus, the image might look less noisy with longer exposure times, but

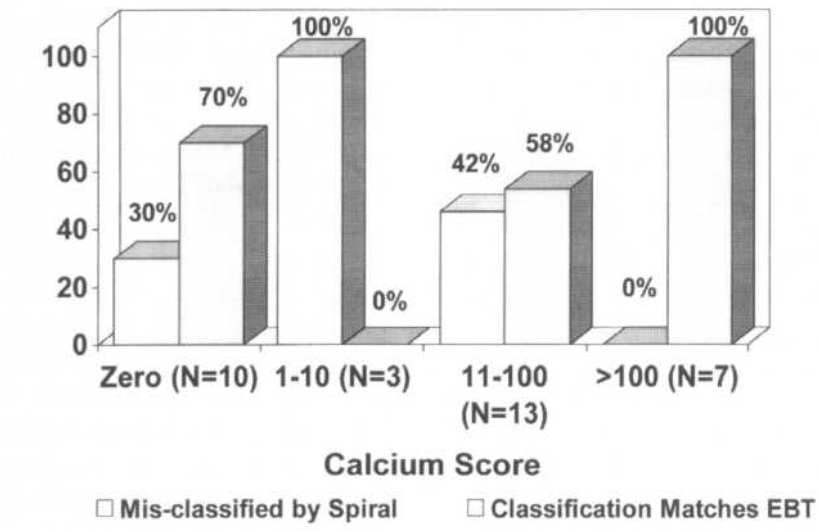

Fig. 4. A graph comparing the differences between coronary calcium scores by electron beam tomography and spiral CT. The categories chosen are most commonly used to classify patients for treatment.(32) The number of patients in each scoring category (determined by results of EBT) is listed with the scoring category. A majority of patients with scores <100 were classified differently by spiral and EBT results. CT=Computed Tomography; EBT=Electron Beam Tomography.

signal averaging will eliminate small foci of calcium. At an average heart rate of 80 beats per min, the right coronary artery will move half it's diameter during imaging at 250 ms scan acquisition [39]. This degree of motion may result in missed calcific deposits, one possible reason why some patients had positive scores by EBT and no calcium detected on corresponding SEQ images. The third reason for error is because of respiratory or cardiac motion, which causes the coronary arteries to move relative to the scanning table. Early studies with EBT reproducibility demonstrated high inter-scan variability, at least in part due to the need for two breath holds to cover the coronary anatomy [40-42].

The diagnosis of coronary calcium made in 3 patients with SEQ but not EBT might be due to misclassification of other calcium sources. Two patients reported to have circumflex calcification by spiral CT were found to have pericardial calcification or beam hardening artifacts in the region of the circumflex artery by EBT (Fig. 1). Pericardial calcification, beam hardening artifacts and mitral and aortic calcium contribute to the error seen with slower imaging, as motion artifacts cause these foci to be blurred in the region of the artery, making it impossible to distinguish the artery from the non-coronary calcific foci.

The results of this study, showing relatively low sensitivity (74%) and specificity (70%) for detection of coronary calcium with SEQ was disappointing. The widespread availability and lower cost of spiral CT is attractive as it could make coronary calcium screening a more widely available test. However, its only fair correlation with EBT and high false negative rate (26%) are concerning. The false negative scores by spiral CT are most likely the result of motion artifacts and partial voluming effect. A recent editorial highlighted concerns related to falsely reassuring patients with negative EBT scans [43]. These concerns will certainly be magnified with the use of spiral CT. If the objective of screening for CC is to find advanced disease, the use of fluoroscopy to detect extensive coronary calcium is a less expensive alternative, with a lower radiation dose than either CT approach [44]. However, the potential of EBT to accurately quantify and detect early coronary artery disease is appealing, especially because the atherosclerotic process can be retarded or reversed. EBT can also be used for longitudinal studies to test the efficacy of therapy to retard atherosclerosis.

5. Limitations

This was a limited study, incorporating only 33 persons undergoing scanning with both EBT and spiral CT. The ideal study might utilize intravascular ultrasound as a gold standard to compare EBT and spiral CT. For this study, as with other studies of EBT and spiral CT, EBT was considered the gold standard.

A large, potentially uncorrected error in CT screening is the use of 130 Hounsfield units as a threshold for scoring on spiral CT. This measure (used for EBT) was derived based upon the use of phantoms [45], histologic and pathologic studies [1,37], intravascular ultrasound [46]and angiographic correlation trials [2,8] to distinguish noise from calcification. There are no studies that evaluate the proper thresholds or areas to use with spiral CT scanners. Such research is needed prior to clinical use of spiral CT to detect coronary calcium. The different image acquisition protocol, exposure time, detector array and other factors may cause different thresholds for detecting calcium accurately and possibly different scoring algorithms may be required.

Until histopathologic, angiographic and prospective population studies are completed, clinicians should consider use of a spiral CT reporting method proposed by Moore for conventional CT [47], whereby moderate or extensive calcification is noted and reported as such. Current CC scoring data from conventional scans are disappointing, with an 88% sensitivity for angiographic disease [21] and poor inter-test variability when compared to EBT. Thus, while EBT is not the only means to evaluate for CC, it is the only method that has been sufficiently validated for clinical use. Future improvements in the CT scanners might lead to better reproducibility and accuracy, allowing use of these alternative modalities to measure CC. Until more validation studies are available, use of a more accurate, more reproducible methodology should be utilized when available to

accurately risk assess and track patients with subclinical coronary artery disease.

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