Coronary Artery Disease: Improved Reproducibility of Calcium Scoring with an Electron-Beam CT Volumetric Method

**PURPOSE:** To assess the variability and reproducibility of a volumetric calcium score calculated with electron-beam computed tomographic (CT) scans of coronary arteries.

**MATERIALS AND METHODS:** Two sets of electron-beam CT scans were obtained in patients with coronary calcification (group A) or known risk factors for coronary arterial disease (group B). The second set of scans was obtained after a brief interval (group A, n = 52) or after 1 year with no risk modification (group B, n = 27). Traditional (plaque area and attenuation) and volumetric calcium scores were calculated for each patient and lesion.

**RESULTS:** The median percentage change for individual lesions in group A was 13% for the volumetric and 19% for the traditional score. The overall reduction in error with the volumetric score was 40% ($P < .001$). The median percentage change for group A patient totals was 9% for the volumetric and 15% for the traditional score ($P < .001$). In group B patients, the median volumetric score increased by 44% after 1 year.

**CONCLUSION:** The volumetric score showed better reproducibility than the traditional score, and its variability was considerably less than the score increase in untreated patients after 1 year. The reproducibility of the volumetric method makes it useful for assessing the progression of coronary arterial disease on serial electron-beam CT studies.

Electron-beam computed tomography (CT) is an extremely sensitive tool for the identification of coronary arterial calcification, which is known to be a marker of coronary arterial disease (1–7). The study of the progression and regression of established coronary atherosclerosis may be one of the most interesting clinical applications of this technology, but thus far this application has been hampered by the limited reproducibility of the calcium score currently in use (7).

To calculate the traditional calcium score (TCS) described by Agatston et al (2), the computer software multiplies the area of a calcified plaque by an assigned coefficient selected on the basis of the highest attenuation measured in the area. Minimal variations in estimated plaque attenuation or area on serial studies obtained in the same patient can result in substantially different score calculations.

In this study, we analyzed the applicability of a volumetric calcium scoring method to electron-beam CT. The score is calculated on the basis of isotropic interpolation, which has been in use in the field of medical imaging for several years (8–11). The value obtained with this method represents a volume and not an abstract number derived from the multiplication of the attenuation and area of a calcified plaque and may have an important application in the study of the progression of atherosclerotic coronary arterial disease.

To analyze the reproducibility of this method, 52 patients underwent two scanning procedures within a few minutes of each other. Twenty-seven additional patients under-
went two scanning procedures at a 1-year interval without having received any therapy for coronary arterial disease or having made changes to their diet or smoking habits. Our goal was twofold: to assess whether this volumetric method results in improved interscan reproducibility compared with that of the TCS and to verify that the measurement error of the volumetric method is substantially smaller than the increase in plaque size measured after a 1-year follow-up. If our hypothesis should prove to be correct, this volumetric scoring method could be used reliably in follow-up studies of the progression of coronary arterial disease.

MATERIALS AND METHODS

Patients

All patients had measurable coronary arterial calcifications on the initial electron-beam CT scan. Two separate groups of patients were studied: Patients in group A (n = 52) underwent two studies within a few minutes of each other after brief ambulation between the studies. The group A patients were consecutive patients referred by primary care physicians for screening purposes. Patients in group B (n = 27), who had known risk factors for coronary arterial disease, underwent two scanning procedures separated by 1 year; during that interval, the patients undertook no risk modification.

To ensure the continuity and homogeneity of the interpretations of findings, a single expert investigator (T.Q.C.) reviewed all scans. The study was conducted according to standard ethical criteria for clinical research and was approved by our internal review board. Written informed consent was obtained from each patient after the nature of the study had been fully explained.

CT Procedures

All patients underwent electron-beam CT with an Imatron C-100 scanner (Imatron, South San Francisco, Calif). Imaging was performed with a 100-msec acquisition time and a 3-mm section thickness. A total of 40 sections were obtained during two breath-holding periods. Scanning was electrocardiographically triggered at 80% of the R-R interval. All areas of calcification within the borders of a coronary artery and that had a minimal attenuation of 130 HU were analyzed. Images were obtained with a 30-cm² field of view (pixel size, 0.586 mm). To avoid scoring miscalculations, scans with artifacts produced by motion, breathing, cardiac arrhythmias, or erroneous electrocardiographic gating were excluded from the study. The TCS and the calcium volumetric score (CVS) were calculated for each individual calcified plaque and for each patient. Analyses of calcified plaques were performed with the aid of software (NEoramd; Scimage, Los Altos, Calif) installed on a workstation.

Calculation of the TCS

The TCS was calculated according to the method described by Agatston et al (2). This score was derived by placing an area of interest over each calcified coronary artery focus that had a minimal attenuation of 130 HU. The computer software measured the plaque area and the maximal attenuation within each region of interest. A score was then calculated by multiplying the measured area by an attenuation coefficient based on the peak CT number (coefficient 1 for peak attenuation = 131-200 HU; coefficient 2 for peak attenuation = 201-300 HU; coefficient 3 for peak attenuation = 301-400 HU; coefficient 4 for peak attenuation ≥ 401 HU). The sum of the individual scores measured within the borders of each coronary artery was used to compute the final TCS.

Calculation of the CVS

The method of isotropic interpolation is described in depth in several specialized publications (8-11). Here, we give a simplified description of the method as it is applied to the extraction of a CVS from electron-beam CT scans. The voxel size on electron-beam CT scans obtained with a 3-mm section thickness and a typical field of view of 30 cm² (pixel size = 0.586 mm) corresponds to 0.586 × 0.586 × 3 = 1.03 mm³.

With the technique of isotropic interpolation, the input data set is sampled at several intermediate cross sections between the original sections (10). For the purpose of calculating the CVS, the size of the intermediate cross sections is chosen to correspond to the size of the pixel in use. In the example given above the voxel size is now 0.586 × 0.586 × 0.586 = 0.201 mm³. The smaller size of the interpolated voxel allows a more precise volume reconstruction of the structure under analysis compared with that possible with the original voxels. By using a linear intensity distribution calculated on the basis of the plaque attenuation measured at the level of the reference section and the distance of the voxel from the reference section, each interpolated voxel is assigned a numeric value. All voxels with a value greater than 130 are used in the final three-dimensional reconstruction of the calcified plaque. The reconstruction is performed automatically by the software according to a fast, three-dimensional region-growing algorithm, and the plaque is viewed as a series of interconnected voxels with a value greater than 130. The final score is presented as a whole number to facilitate comparison with the TCS, although it actually is a volume estimated as a fraction of a cubic centimeter. For the purpose of presenting it as a whole number, the measured CVS is multiplied by 1,000.

Statistical Analysis

As the baseline of the relative accuracy of the CVS and the TCS, we used the absolute difference between scan measurements relative to their mean: |x₁ - x₂| / [(x₁ + x₂) / 2] × 100, where x₁ is the measurement from the first scan and x₂ is the measurement from the second scan; we

<p>| Table 1 Average TCS and CVS Levels per Lesion by Artery in Group A |
|-----------------------|-----------------|-----------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>Variable and Coronary Artery</th>
<th>No. of Lesions</th>
<th>Minimum</th>
<th>Maximum</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
<th>Mean*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCS¹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>112</td>
<td>0.7</td>
<td>546</td>
<td>8</td>
<td>27</td>
<td>65 (10)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>35</td>
<td>0.5</td>
<td>844</td>
<td>5</td>
<td>20</td>
<td>61 (34)</td>
<td></td>
</tr>
<tr>
<td>Left circumflex</td>
<td>28</td>
<td>0.7</td>
<td>84</td>
<td>3</td>
<td>11</td>
<td>29 (19)</td>
<td></td>
</tr>
<tr>
<td>CVS²</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>112</td>
<td>0.6</td>
<td>401</td>
<td>7</td>
<td>20</td>
<td>53 (49)</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>35</td>
<td>0.9</td>
<td>628</td>
<td>5</td>
<td>18</td>
<td>60 (78)</td>
<td></td>
</tr>
<tr>
<td>Left circumflex</td>
<td>28</td>
<td>0.8</td>
<td>65</td>
<td>3</td>
<td>11</td>
<td>26 (16)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Number in parentheses is the standard error of the mean.
² Variable is the mean TCS calculated from the first and second scans.
³ Variable is the mean CVS calculated from the first and second scans.
TABLE 2

Variability in the Replication of CVS and TCS: Lesion-by-Lesion Analysis in Group A

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Lesions</th>
<th>Minimum</th>
<th>Maximum</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
<th>Mean*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage change in CVS</td>
<td>175</td>
<td>0</td>
<td>200</td>
<td>4</td>
<td>13</td>
<td>28</td>
<td>22 (2)</td>
</tr>
<tr>
<td>Percentage change in TCS</td>
<td>175</td>
<td>0</td>
<td>200</td>
<td>9</td>
<td>19</td>
<td>46</td>
<td>35 (3)</td>
</tr>
<tr>
<td>Percentage change in TCS minus percentage change in CVS</td>
<td>175</td>
<td>-55</td>
<td>133</td>
<td>-2</td>
<td>7</td>
<td>21</td>
<td>13 (2)</td>
</tr>
</tbody>
</table>

Note.—Equations for calculating percentage change in CVS and TCS are given in the text.

* Number in parentheses is the standard error of the mean.

Refer to this as the percentage change (12, 13). For both the CVS and the TCS, the distributions of the percentage change values across lesions and across patients were very positively skewed. Consequently, the range and quartiles (50th [median], 25th, and 75th percentiles) of each distribution provide useful descriptive statistics of the relative accuracy of each measure. To study the relative accuracy of the two methods, we analyzed the differences between the percentage change in the TCS and that in the CVS by lesion and by patient total for group A patients. Finally, we compared the replication error in the measurement of the CVS in group A patients with the change in the CVS in group B patients during the 1-year follow-up. We used analyses of variance to analyze the average difference in the accuracy between the TCS and the CVS per lesion and per patient. The Wilcoxon rank-sum statistic was used to make inferences about median differences in accuracy. To accommodate the positive skew in the distribution of percentage change values, the Mood test was used to analyze the overall median relative accuracy of the CVS. Finally, nonparametric tolerance limits were constructed to interpret the relevance of various levels of the relative change in a patient’s CVS.

RESULTS

Table 1 provides a descriptive summary of the distribution of TCS and CVS levels across lesions by type of artery in group A patients, where the level per lesion is the average of the measurements from each of the two scans. Of the 175 lesions, 112 (64%) were in the left anterior descending coronary artery, 35 (20%) were in the right coronary artery, and 28 (16%) were in the left circumflex coronary artery. The distributions of the TCS and CVS levels across lesions were positively skewed so that the mean levels were uniformly higher than the median levels in each artery, and the largest values of both the TCS and the CVS were in the left anterior descending and right coronary arteries.

Group A Lesions: CVS and TCS Reproducibility

Table 2 illustrates the greater overall precision of the CVS relative to that of the TCS by showing the comparison of the distributions of the percentage change in the two types of measurement between scans obtained in group A patients. This table shows that the mean percentage change in the CVS (22%) was substantially lower than that of the TCS (35%) and indicates that there was a 37% overall reduction in error. This comparison of means is misleading given that the distribution of values was positively skewed. However, the findings were confirmed by use of the median percentage change in the CVS across lesions, which was 32% lower than that of the TCS. The median percentage change in both measures was relatively constant across types of artery (for the left anterior descending, right coronary, and left circumflex arteries, respectively, the percentage change in CVS was 14%, 11%, and 14% and that in TCS was 21%, 18%, and 18%). These median values were not significantly different across artery type (P = .65 for CVS and P = .76 for TCS; Mood test for equality).

These summary statistics underscore the greater precision of the CVS compared with that of the TCS. To document the statistical significance of the greater precision of CVS measurements, we analyzed the distribution of differences in percentage change values between the TCS and the CVS by lesions. The percentage change in the TCS between scans was larger than that in the CVS for 123 (70%) of the 175 lesions. The median difference by lesion in percentage change values between the TCS and the CVS (ie, median percentage change in TCS – median percentage change in CVS] × 100) was 7% (95% confidence interval: 4%, 11%) and did not change significantly in an artery-by-artery analysis (P = .66). Thus, the CVS measurements were significantly more precise than those of the TCS (P < .001, Wilcoxon rank-sum test), and this result was consistent across arteries.

Figure 1 shows the regression line for relative change in the CVS versus the corresponding relative change in the TCS for the 175 lesions. (Note that in this case we used the relative change in each measurement, (x2 – x1)/[(x1 + x2)/2], rather than the absolute percentage change). This analysis indicates that the average variability of the CVS was only 53% as large as that of the TCS.

Figure 2 is a plot of the percentage change in CVS values versus ln[1 + (CVS1 + CVS2)/2]. This plot shows that the relative accuracy of the CVS improves as the mean CVS per lesion increases. For 120 lesions with an average CVS of greater than 7.5, the median percentage change in the CVS was 8%, whereas the median percentage change for the entire sample was 13% (median improvement, 38%).

Finally, we used analyses of variance to test for patient and artery effects. In one analysis, the effect of "artery" was nested within the "patients" factor. This is appropriate if one assumes that artery effects are potentially different for each patient. For the other analysis, we used type of artery as a covariate with two degrees of freedom. This latter design assumes that the artery effect would be relatively constant across patients. Both analyses indicated that there were no significant differences among arteries or patients with respect to the relative precision of the CVS and TCS (for all effects, P > .6).

Group A Patients: Reproducibility of Total CVS and TCS

Among the 52 patients in group A, the median value of the average CVS and TCS across patients was 58 and 64, respectively. Thirty-nine (75%) of these patients had a mean CVS of less than 210 and a mean TCS of less than 336. The mean percentage change was 18% for CVS and 29% for TCS (22% and 35%, respectively, across lesions), which represents a 38% overall reduction in error. The median percentage change was 9% for the total CVS (25th percentile, 4%; 75th percentile, 20%) and 15% for the total TCS (25th percentile, 9%; 75th percentile, 37%). This measurement error was smaller than that in the analysis of individual lesions, where the median percentage change was 13%.
and 19% for CVS and TCS, respectively. The greater accuracy of the total patient scores was expected, because in relative terms sums are usually more stable than individual measurements.

The relative error in CVS measurements was smaller than that in TCS measurements in 38 (73%) of the 52 patient totals. The mean difference in percentage change between the TCS and the CVS patient totals was 12% ± 3 (standard error of the mean), and the median difference was 8% (95% confidence interval: 4%, 14%). This difference between the TCS and the CVS for patient totals was significant (P < 0.001, Wilcoxon rank-sum test).

As was the case with the analysis of individual plaques, there was a tendency for the precision of the repeated measurements of the total CVS to improve above a threshold level, which in this case was established at 30 (Fig 3, Table 3). Accordingly, we conducted a separate analysis of the reproducibility of the CVS in 35 patients with an average CVS greater than 30. We found that the median percentage change in the CVS was 6% (25th percentile, 2%; 75th percentile, 12%), whereas the corresponding median in the entire sample was 9%, as was reported earlier in this article.

Subtraction of the Attenuation Cofactor from the TCS

One of the main reasons for the poor reproducibility of the TCS may be the inclusion in its calculation of an arbitrary attenuation cofactor. To verify this hypothesis, we used the results in 17 group A patients to compare the interscan variability of the CVS, the TCS, and a modified TCS in which the attenuation cofactor was eliminated. These patients were selected because they showed a substantial change in peak plaque attenuation between the first and second CT examinations, with a marked increase in the calculated total TCSs obtained 5 minutes apart. The median percentage change in the CVS, the TCS, and the modified TCS was 13%, 40%, and 25%, respectively. This indicates that a 15% absolute improvement in the percentage change in the TCS (with an improvement in the relative discrepancy between the TCS and the CVS from 68% to 48%) can be obtained simply by eliminating the attenuation cofactor. Of note, the median percentage change for both the CVS and the TCS was higher in this group of patients than in the entire cohort, which probably indicates a selection of particularly difficult cases and the statistical effect of the small number of patients in the subgroup. However, the expected frequency of the occurrence of peak attenuation changes in practice cannot be predicted.

Group B Patients: Relative Change in the CVS

For group B patients, the relative change in CVS was calculated with respect to the initial baseline CVS measurement by using \( \frac{[CVS_2 - CVS_1]}{CVS_1} \times 100 \). All patients in this group had an initial CVS of greater than 30. The variability of the CVS observed in the replication study with patients in group A was small relative to the average change in CVS mea-

Figure 1. Graph shows the results of the regression of relative changes in the CVS versus relative changes in the TCS per lesion. On average, the variability of the CVS was only 5.3% as large as that of the TCS.

Figure 2. Plot shows the percentage change in the CVS versus \( \ln[1 + \left| \frac{CVS_1 + CVS_2}{2} \right| (\ln[1 + Mean(CVS)]) \] per lesion. A value of 2.1 on the x axis corresponds to a CVS of 7.5.

Figure 3. Plot shows the percentage change in CVS versus \( \ln[1 + \left| \frac{CVS_1 + CVS_2}{2} \right| (\ln[1 + Mean(CVS)]) \] per patient. A value of 3.4 on the x axis corresponds to a CVS of 30.
There was a change in the CVS that is indicative of true progression of atherosclerotic disease (rather than simple replication error). To determine the level of change in the CVS that is indicative of true progression of atherosclerotic disease (rather than simple replication error), we analyzed the tolerance limits of the replication error in the CVS in group A patients with a baseline CVS greater than 30. We concluded that this method demonstrated superior reproducibility compared with that of the TCS, at both the level of the individual lesion and the level of the total patient score. Reproducibility of the CVS improved even further in patients with a CVS greater than 30. Of note, the variability of the CVS was substantially smaller than the measured increase in the CVS found in untreated patients at the end of 1 year. There are several considerations that help explain our findings.

The main limitations of the TCS reside in the fact that the third spatial dimension of a calcified plaque is not taken into consideration and in the introduction of an arbitrary attenuation scaling factor. Hence, a minimal variation in the area or attenuation of a plaque may cause substantial variability in scoring between repeated CT studies.

The aging of an atherosclerotic plaque entails progressive accumulation of calcium and fibrous tissue (7,16,17). This process may translate into an increase in plaque attenuation over time, with a sub-

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**TABLE 3**

Comparison of CVS between Group A and Group B Patients with CVS Greater than 30

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
<th>Minimum</th>
<th>Maximum</th>
<th>25th Percentile</th>
<th>Median</th>
<th>75th Percentile</th>
<th>Mean*</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Mean CVS &gt; 30†</td>
<td>35</td>
<td>0</td>
<td>36</td>
<td>2</td>
<td>6.0</td>
<td>12</td>
</tr>
<tr>
<td>First CVS &gt; 30†</td>
<td>35</td>
<td>-30</td>
<td>23</td>
<td>-4</td>
<td>-0.7</td>
<td>9</td>
<td>0.8 (2.0)</td>
</tr>
<tr>
<td>B‡</td>
<td>27</td>
<td>6</td>
<td>116</td>
<td>21</td>
<td>44.0</td>
<td>82</td>
<td>52.0 (7.0)</td>
</tr>
</tbody>
</table>

* Number in parentheses is the standard error of the mean.
† The measure was [(CVS1 - CVS2) / [(CVS1 + CVS2)/2] × 100, where CVS1 and CVS2 are the CVSs from the first and second scans, respectively.
‡ The measure was [(CVS1 - CVS2) / CVS1] × 100, where CVS1 and CVS2 are the CVSs from the first and second scans, respectively.

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**DISCUSSION**

In this study, we assessed the value of a volumetric score—the CVS—to improve the reproducibility of serial electron-beam CT measurements. We carefully excluded from the analysis all cases with misregistration artifacts, because we were interested in the actual reproducibility of this method and its comparison with the traditional scoring method under ideal circumstances. The volumetric method demonstrated superior reproducibility compared with that of the TCS, at both the level of the individual lesion and the level of the total patient score. Reproducibility of the CVS improved even further in patients with a CVS greater than 30. Of note, the variability of the CVS was substantially smaller than the measured increase in the CVS found in untreated patients at the end of 1 year. There are several considerations that help explain our findings.

The main limitations of the TCS reside in the fact that the third spatial dimension of a calcified plaque is not taken into consideration and in the introduction of an arbitrary attenuation scaling factor. Hence, a minimal variation in the area or attenuation of a plaque may cause substantial variability in scoring between repeated CT studies.

The aging of an atherosclerotic plaque entails progressive accumulation of calcium and fibrous tissue (7,16,17). This process may translate into an increase in plaque attenuation over time, with a sub-
sequent increase in the TCS (18). Because of the use of scalar attenuation coefficients with a sudden shift of the weighting for small changes in attenuation (ie, a coefficient of 2 for an attenuation of 299 HU and a coefficient of 3 for an attenuation of 302 HU), an increase in the TCS may not necessarily indicate an increase in plaque size but rather a simple increase in plaque attenuation. The results of our limited analysis of the reproducibility of the TCS after elimination of the attenuation cofactor support this opinion, although the CVS still showed superior results.

The volumetric score we propose is not directly affected by either the area or the peak attenuation of a plaque, although the minimal attenuation of 130 HU necessary for an interpolated voxel to be included in the reconstructed plaque is determined on the basis of the attenuation in the reference section.

The results of previous analyses (19–22) of the reproducibility of the TCS have confirmed the large interscan variability of this measure. To evaluate the interscan reproducibility of this method, some investigators (19) limited their analysis of calcified coronary arterial plaques to the proximal 12 sections of a 20-section study. With this approach, the core question behind the need for a reproducible test is not addressed: Can the calcium score be used for follow-up studies? If this is the goal, one cannot afford to miss new, small, or peripheral lesions that may be important in future measurements. Other investigators (20) have used log-transform calculations to mathematically (but not practically) reduce the apparent, wide interscan variability of the TCS. Wang et al (12) concluded that the TCS is not accurate enough to use for serial studies in the same patient. In an attempt to improve the reproducibility of the TCS, Wang et al suggested the acquisition of thicker (6-mm) sections. Yet, although such a method could eliminate some of the motion artifacts, it would probably further impair the reproducibility and reliability for serial follow-up studies. In fact, it is conceivable that resorting to thicker sections may result in the neglect of small, new, and softer plaques that may grow to more sizable dimensions in the future.

Figure 5. Calcified plaque analysis in the same patient performed with electron-beam CT scans obtained 1 year apart (April 1996 and April 1997). The software automatically highlights in yellow all areas with an attenuation greater than 130 HU. The analysis is conducted with the transverse views (upper right and upper left); the sagittal views (lower right and lower left) allow the interpreting physician to examine the acquired three-dimensional data sets for the presence of motion artifacts. In this case, there were no motion artifacts. A detailed enumeration of each individual plaque detected in the coronary arteries is shown (upper middle and lower middle), with the CVS expressed in cubic centimeters (cc). The TCS is reported in the “Score” column, and the mean attenuation of each plaque is reported in the “Mean” column. For comparison with the TCS, the CVS is multiplied by 1,000. A summary of the two studies obtained at a 1-year interval (center) is shown for both the individual artery and the total score. There was progression of disease, with good agreement between the CVS and the TCS. Scr#1 = CVS from April 1996, Scr#2 = CVS from April 1997, CX = left circumflex coronary artery, LAD = left anterior descending coronary artery, RCA = right coronary artery, Scr#1 = TCS from April 1996, Scr#2 = TCS from April 1997.
Because both high sensitivity for the detection of calcified plaques and high calcium score reproducibility are necessary to follow the evolution of coronary atherosclerotic disease, a 6-mm section thickness may not be advisable. This opinion was indirectly supported by the recent observations of Broderick et al. (23). They demonstrated improved reproducibility of coronary arterial calcium scoring with the use of helical CT scans by using a volumetric method and lowering to 90 HU the threshold limit for the detection of a calcified plaque.

Several other factors that affect reproducibility should be taken into account. Of importance is the effect of partial volume averaging. The shape of a voxel obtained with electron-beam CT with a 30-cm² field of view is that of a parallelepiped with very uneven dimensions of 0.56 × 0.56 × 3 mm. This limits the reliable reproduction of the same plaque when it is imaged in different spatial planes. Further, a newly forming plaque often has an attenuation near to or lower than the minimal necessary attenuation of 130 HU, and bordering voxels may contain only the margins of a forming plaque. This is of great consequence in the calculation of the TCS, because the voxels that contain only part of a calcified plaque may be included in or discarded from the calculation of a final score simply on the basis of the detected average attenuation over the entire voxel. Finally (and always related to the effect of partial volume averaging), a very small plaque may cover one or two voxels at the first examination and three or four voxels at the second, just by virtue of a difference in the patient's position between examinations. A change of a few voxels with regard to such small values may result in a magnified error when mathematical calculations are applied to relative percentage changes. In fact, we demonstrated a greater inter-scan variability below a minimal threshold score both at the level of the individual lesion and at the level of the total patient score.

Other factors known to affect score reproducibility, such as motion and artifacts, were carefully avoided in our study. However, motion artifacts remain important drawbacks of the current technology (7). Our software allows on-screen visualization of the entire threedimensional data set and simultaneous analysis of a calcified plaque. This allows the interpreting physician to quickly assess the quality of the acquired data for the presence of motion artifacts before beginning the analysis (Figs 5, 6). More reliable electrocardiographic-triggering mechanisms and faster acquisition times will probably yield further improvements.

The CVS is based on a pathophysiological sound concept, and in our experience it showed excellent reproducibility. The application of the CVS will render electron-beam CT a highly reliable method for the study of the progression of established coronary atherosclerosis. Our analysis allowed us to determine which level of change in the CVS can be considered to be reliable evidence of the true progression of disease rather than mere replication error, thus providing important information for the practicing physician. Caution should be used when interpreting the small changes in calcified plaques observed on longitudinal studies as representative of clinically relevant disease progression. However, a measured change in the CVS in the range of 15% or greater at the end of follow-up has a high likelihood of representing true progression of disease.

References
14. Möhlenkamp S, Pump H, Schimpf S, et al. The progression of calcified plaques diff...


