Noninvasive Coronary Angiography by Contrast-Enhanced Electron Beam Computed Tomography

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Summary: Electron beam computed tomography (EBCT) is a cross-sectional imaging method with high temporal and spatial resolution. So far, it has mainly been applied for the detection of coronary artery calcifications which permit the very sensitive detection of coronary atherosclerosis even in the very early stages. However, after intravenous injection of a contrast agent, EBCT also permits the direct visualization of the coronary artery lumen. For these investigations, a volume data set is acquired that consists of 40 axial cross-sections of the heart (3 mm slice thickness). To evaluate the coronary arteries as to the presence of stenoses and occlusions, various forms of post-processing, including shaded surface display, maximum intensity projection, and multiplanar reconstruction, are applied. The sensitivities and specificities for the detection of coronary artery stenoses and occlusions are about 90%. Best results are obtained for coronary artery bypass grafts, the left main coronary artery, and the left anterior descending coronary artery, while reduced image quality impairs the results for the right coronary artery and the left circumflex coronary artery.

Key words: computed tomography, coronary angiography, coronary disease, electron beam computed tomography

Introduction

Annually, about 1.1 million coronary angiograms are performed in the United States. The replacement of some of these invasive diagnostic procedures by noninvasive methods would be desirable. However, many attempts to image the coronary arteries noninvasively have failed. The main problems are the small diameter of the coronary vessels and their rapid motion during the cardiac cycle, which is additionally superimposed by movements due to respiration. Promising results have been reported for magnetic resonance (MR) coronary angiography of the coronary arteries, starting in about 1993. In a clinical context, the application of MR coronary angiography currently seems restricted to the visualization of atypical origins and courses of the coronary vessels, while reliable evaluation of the coronary arteries as to the presence of occlusions and stenoses does not yet seem clinically feasible.

Because of its unique combination of high spatial and temporal resolution and the fact that image acquisition can be triggered to the electrocardiogram (ECG), electron beam computed tomography (EBCT, “cine CT,” “ultrafast CT”) is ideally suited for the imaging of the coronary arteries. So far, the method has mainly been applied to visualize and quantify calcifications of the coronary arteries. This so-called “calcium screening” has been shown to permit early and reliable diagnosis of coronary artery disease. The presence of coronary calcifications in EBCT also has high prognostic significance.

Since 1995, several groups have used EBCT in combination with intravenous injection of a contrast agent to visualize the inner lumen of the coronary arteries, thereby permitting direct imaging of coronary artery stenoses and occlusions. This review attempts to summarize the imaging protocols, schemes for data evaluation, and clinical results as well as the problems and future perspectives of this method.

Imaging Protocol

To visualize the coronary arteries by EBCT, a volume data set of the heart is acquired within one breathhold. To achieve vasodilation, nitrates should be given prior to the investigation (e.g., 0.8 mg of nitroglycerin s.l.). Image acquisition is done in a high-resolution mode with an acquisition time of 100 ms per image and an image matrix of 512 × 512. A field of view of 15 to 18 cm permits coverage of the complete cardiac volume with highest possible spatial resolution, but exact positioning of the volume data set as well as careful timing of contrast injection are crucial to achieve optimal image quality. A...
three-step imaging protocol has proven useful and is described herein.

**Determination of Heart Position**

The patients are investigated head first in supine position. To locate the heart position, the scanner’s multislice mode is used to acquire eight axial cross-sections of the chest (7 mm slice thickness, 4 mm gap after every other section) without contrast enhancement. On these cross-sections, the position of the ascending aorta is determined.\(^{15, 16}\) As an alternative, if a coronary calcification examination is performed in the patient, the obtained data set can be used to position further acquisitions.\(^{17, 18}\)

**Measurement of Contrast Agent Transit Time**

Exact timing of contrast injection is important to achieve optimal image quality. Several methods can be used to estimate the circulation time, including the injection of magnesium sulfate or indocyanine green. However, the most reliable measurements can be achieved by test injection of a contrast agent:\(^{15, 17}\) A bolus of 10 ml of contrast agent is injected intravenously (4 ml/s). After a delay of 10 s, 10 axial cross-sections of the chest at the level of the ascending aorta are acquired in single-slice mode (acquisition time 100 ms) and are triggered to the ECG at 80% of the R-R interval, with one image following every other heart beat. In this way, a time-density curve within the ascending aorta covering 20 heart beats can be obtained, and the exact contrast agent transit time from injection to maximum enhancement in the aortic root can be measured (Fig. 1). In addition, this serves to double-check the positioning of the following volume data set.

![Fig. 1 Time-density curve obtained in the aortic root after bolus injection of a contrast agent. The first acquisition is started 10 s after the injection, subsequent acquisitions are obtained after every other heartbeat. Peak density in the aorta (110 Hounsfield Units) is observed 15 s after the injection.](image)

**Volume Data Set**

Because of the tortuous course of the coronary arteries, it is not possible to visualize the coronary vessels within one image. Therefore, a volume data set of the heart has to be acquired which permits evaluation of the coronary arteries by off-line post processing. Usually, 40 axial cross-sections of the heart are acquired within one breath hold, with one image following every heart beat at 80% of the R-R interval. A slice thickness of 3 mm with a table feed of only 2 mm generates overlapping cross-sections. If larger volumes have to be covered, for example, in patients with bypass grafts, contiguous cross-sections without overlap are acquired. Amounts of 120 to 160 ml of a contrast agent (30–35% iodine) are injected at a rate of 4 ml/s. From the initiation of contrast injection to the acquisition to the first image, a delay is maintained according to the individually determined contrast agent transit time (usually 15–25 s). Some authors have reported using 1.5 mm slice thickness without overlap.\(^{19}\) This reduces the covered volume to a 6 cm slab.

**Data Evaluation**

In the cross-sectional images of the heart obtained during and after contrast injection, the mean CT density with the coronary arteries is about 165–200 Hounsfield Units (HU), while the mean density of the myocardium (85–100 HU) and connective tissue (\(\approx 100\) HU) are significantly lower.\(^{15–17}\) This permits selective visualization of the coronary artery lumen filled with contrast agent.

In the contrast-enhanced EBCT scans, the coronary arteries can be clearly identified in the cross-sectional images obtained at different levels (Fig. 2). However, because of the tortuous course of the coronary vessels, the interpretation of the data sets as to the presence of stenoses and occlusions of coronary arteries can be very difficult. For this reason, various forms of image reconstruction are applied, usually after transferring the image data to dedicated workstations. The acquired continuous volume data sets allow for several modes of postprocessing.

**Shaded Surface Display**

The shaded surface display (SSD) is a true three-dimensional rendering technique. All pixels below a certain threshold are discarded and the remaining pixels are shaded according to a lighting model and depth from the observer (Fig. 3). In EBCT of the coronary arteries, the reconstruction threshold is usually chosen at 80 to 100 HU for optimal discrimination between the contrast-enhanced vessel lumen and the surrounding connective tissue, even though systematic investigations as to the optimal reconstruction threshold (which may vary from patient to patient) have so far not been conducted. Since overlapping structures such as the chest wall prevent visualization of the heart and parts of the coronary vessels because they can be covered by the pulmonary trunk and atrial
Fig. 2 (A, B) Axial electron beam computed tomography image at two different levels. Cross-sections of the coronary artery lumen can be clearly seen after the injection of a contrast agent.

Fig. 3 (A) Three-dimensional shaded surface display (SSD) reconstruction of the complete heart. The chest wall has been removed by segmentation. The pulmonary trunk and atrial appendages cover parts of the coronary arteries. (B) After manual segmentation to remove the pulmonary trunk and atrial appendages, all parts of the coronary vessels can be seen. (C) Further segmentation yields an isolated reconstruction of the coronary artery tree. (D) Maximum intensity projection. The same raw data as for the SSD reconstruction in (C) was used. In this two-dimensional projection technique, coronary calcifications can be visualized in the course of the coronary arteries. Reproduced from Ref. No. 16 with permission.
appendages, manual segmentation has to be performed before the coronary arteries can be visualized in the SSD reconstructions (Fig. 3). The reconstructions are rendered from different angles to show all parts of the coronary artery system. By further segmentation, everything but the coronary arteries can be removed to obtain reconstructions of the isolated coronary artery tree (Fig. 3).

Among the drawbacks of the SSD technique is the fact that all information concerning the density of structures above the reconstruction threshold is lost in the reconstruction process and the fact that manual editing is a potential cause of errors and can be very time consuming, especially if a display of the isolated coronary arteries is attempted.

Newer, so-called “volume rendering techniques” (VRT) generate images similar to the SSD, but they are not limited to the display of the rendered surface. Using varying opacities, the degree of which depends on each pixel’s CT attenuation, the reconstructions convey information about different CT densities within the reconstructed volume. The value of this form of reconstruction remains to be assessed.

Maximum Intensity Projection

Maximum intensity projection (MIP) renderings are two-dimensional projection images in which all pixels are assigned a gray-scale value that corresponds to their actual CT attenuation (Fig. 3). In these reconstructions, spatial information is lost due to overlap and projection, but the information, for example, concerning calcifications within the coronary arteries, is retained. Manual segmentation is necessary to remove everything but the coronary arteries and can be time consuming. Maximum intensity projection reconstructions have to be rendered from various angles to compensate for overlap, and in their appearance they resemble fluoroscopic angiograms.

Multiplanar Reconstruction

The continuous volume data set permits the generation of secondary images in arbitrary planes by postprocessing, called “multiplanar reconstructions” (MPR). These reconstructions require no thresholding, and all information concerning different CT attenuations is preserved. Because of the anisotropic nature of the volume data set, the spatial resolution of the generated multiplanar reconstructions depends on their orientation: the closer their orientation to the axial plane, the higher the spatial resolution of the reconstructed images. To visualize long segments of the curved coronary arteries within one image, multiplanar reconstructions are generated in oblique and double-oblique planes. Several views in different planes have to be rendered to cover the complete course of each coronary vessel.

To depict the complete course of the coronary arteries in one single image, “curved” multiplanar reconstructions can be used. For these reconstructions, the coronary artery is depicted in a curved plane that follows the course of the coronary vessel through the volume data set (Fig. 4). Curved multiplanar reconstructions have to be rendered separately for each coronary artery and, due to the anisotropic spatial resolution within the volume data set, the spatial resolution of the obtained images depends on the reference plane used and on the course of the artery (Fig. 4). While oblique, double-oblique, and curved multiplanar reconstructions can be rendered very quickly with dedicated software, the technique is limited due to the fact that separate reconstructions are necessary for every coronary artery and that side branches are not visualized.

Results of Patient Studies

The studies of EBCT coronary angiography that have been published so far comprise approximately 160 patients and healthy subjects. In unselected patient groups, the studies are technically adequate for evaluation in about 80 to 90% of cases.

In 11 healthy volunteers, Chernoff et al. determined the length of the continuously visualized coronary artery lumen. They found mean values of 65 mm for the left anterior descending coronary artery, 45 mm for the left circumflex, and 58 mm for the right coronary artery. These values compare favorably with similar investigations by MR imaging. The determination of the mean coronary artery diameters measured by EBCT in these 11 subjects yielded no significant difference compared with normal values reported in the literature.

Measurement of coronary artery diameters in EBCT SSD reconstructions of 10 patients with coronary artery disease yielded a correlation of $r = 0.83$ to the diameter measured at identical sites by quantitative coronary angiography. Due to better image quality, a closer correlation was found for the left main and left anterior descending coronary artery ($r = 0.87$). Partial volume effects lead to underrepresentation of very small coronary arteries and stenotic segments in the EBCT reconstructions, while a tendency toward overestimation of the diameter of large coronary vessels and bypass grafts was observed.

Concerning the detection of coronary artery stenoses and occlusions, overall sensitivities ranging from 74 to 90% and specificities from 91 to 95% were found in comparisons of EBCT with conventional x-ray coronary angiography.

Figure 5 shows an example of a high-grade coronary artery stenosis in the left anterior descending coronary artery in comparison with conventional angiography, as well as the result following coronary angioplasty. While the results for the left main and left anterior descending coronary artery are uniformly good, with sensitivities usually well above 90%, the results are worse for the right coronary artery and especially for the left circumflex coronary artery, as far as both technically adequate visualization of the vessels and detection of significant coronary artery stenoses are concerned.

Electron beam computed tomography also seems well suited for the demonstration of the short- and long-term suc-
cess of coronary revascularization: in 40 patients, it could be shown that restenoses following coronary angioplasty can be detected with a sensitivity of 94% by EBCT, and both occlusions and high-grade stenoses of coronary artery bypass grafts were detected with 100% sensitivity in a group of 25 patients (Fig. 6). While the value of EBCT coronary angiography as a screening method for coronary artery stenoses is still limited because of reduced image quality, especially of the left circumflex coronary artery, its application in the evaluation of patients after coronary revascularization seems clinically feasible.

Problems and Outlook

In the published studies, the image quality in about 10 to 15% of the investigations was too poor for evaluation, ranging from 6% for the proximal left anterior descending coronary artery to 26% for the proximal left circumflex coronary artery. Several factors can contribute to degraded image quality. Movement artifacts affect mainly the right and left circumflex coronary artery in their mid segments (Fig. 7). Faster scan times are necessary to eliminate these artifacts, because the current scan speed of 100 ms in the high-resolution mode is insufficient for complete prevention of motion artifacts from cardiac pulsations. In addition, mainly the left circumflex, but also the right coronary artery, have close anatomic relationships to venous structures such as the coronary sinus and atrial appendages, which can be a potential source of error in manual segmentation of the data sets. All vessel segments can be affected by trigger or respiration artifacts. These artifacts can be detected in surface display reconstructions, since they affect all of the surface of the heart, but they might be difficult to detect and cause false-positive de-
Fig. 5  A 65-year-old patient with a high-grade stenosis of the left anterior descending coronary artery in angiography (A) and electron beam computed tomography (EBCT) (B, C). After angioplasty, normalization of the lumen diameter is documented by EBCT (D). Reproduced from Ref. No. 16 with permission.

Fig. 6  High-grade stenosis in a bypass graft to the left anterior descending coronary artery in electron beam computed tomography (A) and coronary angiography (B). Reproduced from Ref. No. 26 with permission.
tection of stenoses in other forms of image reconstruction (Fig. 7). Finally, calcifications of the coronary vessels have a similar or higher CT density than the contrast-enhanced vessel lumen and can therefore cause false-negative results in SSD reconstructions. They have also been cited as a cause for false-positive results in multiplanar reconstructions. Heavily calcified vessel segments therefore have to be excluded from the evaluation.

Compared with magnetic resonance coronary angiography, EBCT has several advantages. The spatial resolution is superior to that of MR imaging and the overall acquisition time is considerably shorter. Conventional MR coronary angiography sequences require repeated breathholds with severe problems originating from misregistrations due to the patient’s inability to reproduce the level of in- or expiration exactly. Only navigator-echo based respiratory gated sequences, which are not yet widely available, can eliminate the need for repeated breathholds. Patients with metallic implants are excluded from MR imaging, and claustrophobia can be a problem. However, MR angiography can be performed without injection of a contrast agent and does not involve exposure to ionizing radiation.

To improve the results of EBCT coronary angiography, modifications of the scanner would be desirable. Shorter scan times would reduce motion artifacts. Improved in-plane spatial resolution would help reduce partial volume effects and might permit compensation for calcifications within the coronary arteries by introducing an additional upper threshold for reconstruction. As long as only one scan can be acquired in every cardiac cycle, the number of scans that make up the volume data set cannot be significantly increased, since the breathhold cannot be extended over more than 30 to 40 s. This also prevents further reduction of the slice thickness; therefore, simultaneous acquisition of several cross-sections would be desirable.

Even without changes in the scanner characteristics, there is room for improvement. Modifications of the investigation protocol could contribute to higher image quality. By introducing suitable table slew and tilt, the imaging plane could be oriented more parallel to the left circumflex and right coronary artery, and thereby making use of the higher in-plane spatial resolution, visualization of these vessels could be improved. Optimal timing of image acquisition within the cardiac cycle could reduce motion artifacts. The currently most widely used value of 80% of the R-R interval might not be optimal for imaging of the vessel segments within the coronary groove, since atrial contraction during end-diastole causes rapid movement of the base of the heart. Further theoretical, phantom, and patient investigations have to be conducted to optimize EBCT coronary angiography results.

Acquisition of a static volume data set might not even be the best and only way to investigate stenoses of the coronary arteries. Very promising results have been reported for time-density measurements in the coronary arteries after bolus injection of a contrast agent using the scanner’s multislice mode to investigate the patency of coronary artery stents. These results warrant further investigation.

Conclusion

Because of its unique temporal resolution, electron beam computed tomography is especially suited for cardiac imaging. Even though mainly applied to detect coronary calcifications, recent studies have demonstrated that cardiac EBCT in combination with intravenous injection of a contrast agent permits imaging of the coronary vessel lumen and detection of coronary artery stenoses and occlusions. Very reliable results are obtained for the left main and left anterior descending coronary artery as well as for venous bypass grafts, while motion artifacts and anatomic difficulties currently reduce the diagnostic value for the right and especially for the left circumflex coronary artery. Even though improvements in scanner design and in the investigation protocol are warranted,
clinical applications of the method, for example in the follow-up after coronary revascularization, seem possible.

References


