Prospective evaluation of ultrafast cardiac computed tomography for determination of coronary bypass graft patency

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ABSTRACT Twenty-five consecutive patients with 68 independent (single distal anastomosis) saphenous vein aorto coronary and 12 internal mammary bypass grafts (27 to left anterior descending, 10 to diagonal, 23 to left circumflex, 20 to right coronary artery) entered a reader-blinded, prospective, standardized study to establish the accuracy of ultrafast (cine) cardiac computed tomography (CT) for determining graft patency compared with invasive angiography. All patients underwent imaging after injection of 35 to 45 ml of meglumine diatrizoate (Renografin-76; 7 to 9 ml/sec for 5 sec) into an arm vein. Electrocardiographically triggered images were acquired over eight to 16 tomographic levels at 1 cm intervals from aortic arch to mid left ventricle. Criteria for graft patency were contrast opacification on at least two noncontiguous levels and contrast density-time curves morphologically similar to that of the aorta. Ultrafast CT correctly determined that 46 of 48 bypass grafts were patent and 31 of 32 were occluded (sensitivity, specificity, and accuracy 96%, 97%, and 96%); there were no interpretation errors in 23 (92%) of the 25 patients. Accuracy was independent of vessel bypassed and not different for saphenous veins (96%) compared with internal mammary bypasses (100%). This study establishes a 20 min outpatient intravenous injection technique that is highly accurate for determining patency of coronary artery bypass grafts.


CORONARY ARTERY bypass graft surgery has become a well-established therapy for many patients with ischemic heart disease. Premature occlusion of the bypass grafts, involving about 20% of them by 1 year and then 2% to 5% each year thereafter,1–4 is the major limiting factor in the success of this approach, affecting symptom recurrence, ventricular function, and survival.4–7 Identification of patients with incomplete revascularization is fundamental to their management, especially when symptoms or acute ischemic events mandate differentiation of graft closure from progression of native coronary disease. Hospitalization for invasive angiographic evaluation of grafts remains the current management standard, since noninvasive methods have been either inaccurate or impractical. Because our preliminary experience indicated that ultrafast (cine) computed tomography (CT) had the potential for evaluating grafts in a minimally invasive way,8 this prospective, blinded study was designed to establish the accuracy of this method for determining patency or occlusion of coronary artery bypass grafts.

Methods

Patients. Based on preliminary indications of clinical utility8 and previous experiences with standard computed tomographic assessment of grafts,9–13 222 patients underwent ultrafast CT evaluation of their bypass grafts between May 1985 and September 1986. Twenty-five patients (age 64 ± 8 years; 75% men) with 70 independent (single distal anastomoses) saphenous vein bypass grafts and 15 internal mammary bypass grafts also underwent clinically indicated invasive angiographic evaluation of their grafts without change in symptoms, clinical status, or electrocardiogram between the tests. Angiography was performed within 1 month in 20 patients and between 2 and 5 months after ultrafast CT in the other five patients. The patients had from one to five grafts (average 3.4) and had had bypass surgery 2 weeks to 11 years previously. The invasive angiographic evaluation of three grafts was technically unacceptable because of lack of demonstration of a stump and failure to perform a biplane aortic root injection. Ultrafast CT determi-
nation of the status of two grafts was precluded because of numerous metallic surgical clips along the course of an internal mammary graft in one case and because the lowest acquisition was just below the proximal anastomosis of an aorto-right coronary saphenous vein graft in a second patient. Therefore, 80 grafts were evaluated in this study.

**Coronary angiography.** Selective graft angiography was performed by four experienced angiographers using the Judkins or Sones approaches. Grafts were cannulated and injected with 4 to 8 ml of meglumine diatrizoate (Renografin-76) and visualized in at least two projections.

Occluded grafts were identified by a stump or by non-visualiza-
tion on biplane aortography after aortic root injection of at least 30 ml of contrast solution. Angiograms were interpreted independently by separate observers who were unaware of the results of ultrafast CT.

**Ultrafast computed x-ray tomography**

*Instrumentation.* In this study we used the Imatron C-100 multislice rapid-acquisition ultrafast CT scanner. Images are acquired in 50 msec and have a spatial resolution of 2 line-pairs/cm (full-width half maximum approximately 2.5 mm). A high-energy electron beam is electromagnetically swept around a 210° stationary semicircular tungsten target ring, which generates x-ray images on a corresponding but inverted 216 degree detector ring above the patient. Eight milliseconds are required for the electron beam to reset for additional images on the same target ring or on any one of the other three adjacent rings. The scanner was preset in its "flow" mode, in which all four target rings are scanned once in rapid succession after the R wave triggers.

*Acquisition protocol.* The protocol has been described previously. In brief, patients undergo imaging after a 4 hr fast. If there is a history of allergy to contrast medium, antihistamine and steroid premedication is begun the evening before study. Patients are positioned supine and perpendicular to the scanner gantry. All imaging is performed with held expiration, either at end-inspiration or end-expiration. In those without internal mammary bypasses, a localization scan is used to identify the level of the most cephalad surgical clip, or, in the absence of metallic clips, the most caudal portion of the aortic arch. For patients with internal mammary bypasses, the top scan occurs 1 cm above the cephalad border of the aortic arch. Renografin-76 is then injected (7 to 9 ml/sec for 5 sec) into an antecubital vein via a 16- or 18-gauge 1½ inch or 2 inch catheter. Scanning normally begins 7 to 10 sec after injection. In patients with cardiac failure, pulmonary disease, or atrial fibrillation, arm-to-tongue circulation time is determined with an intravenous injection of 1 ml of 50% magnesium sulfate diluted in 9 ml of saline. In such cases, imaging begins at 70% of the measured circulation time. When programmed for flow mode acquisitions, images are acquired at every, every other, or every third R wave, dependent on whether heart rate is less than 78, between 79 and 100, or over 100 beats/min, respectively. All patients in this study had I0 such images at each of eight scanning planes. Total image acquisition time is therefore 10 to 30 beats. Reconstruction of one level requires 3 min (18 sec/image). If the lowest scanning plane is not at least 4 cm below the level of the lowest proximal anastomosis, a second eight-level sequence is acquired with a second injection of contrast.

*Image interpretation.* The ultrafast CT images were interpreted by two observers who knew from the operative reports which grafts had been placed at the time of surgery, but who were blinded to the results of angiography. Images were examined in both closed-loop movie format and in a static display that permitted quantitative analysis of density changes in the graft over time. Criteria for graft patency were opacification of the graft on at least two noncontiguous levels (figure 1) and contrast density-time curves morphologically similar to that of the aorta (figure 3). The former criterion is used to decrease false positive interpretations due to occluded grafts with patent stumps; the latter is used to distinguish pulmonary veins from patent grafts, which in cross-section occasionally have similar appearance and location.

**Data and statistical analysis.** Sensitivity was defined as the number of grafts patent on ultrafast-CT and angiography divided by the number of grafts patent on angiography; specificity was defined as the number of grafts occluded on CT and angiography divided by the number of grafts occluded on angiography. Accuracy was the number of ultrafast CT determinations in agreement with angiography divided by the total number of studied grafts. Results were analyzed for all grafts, for those to each of the major coronary arteries, and for saphenous vein compared with internal mammary bypasses. Differences were tested for significance with Fisher’s exact test.

**Results**

Because each study was limited by scanner geometry to a maximum of 8 cm, 21 of the 25 patients required a second injection of contrast material to visualize the extent of all grafts. The total amount of contrast medium administered varied from 35 to 105 ml.

Angiography determined that 48 bypass grafts were patent, 20 to the left anterior descending, three to the diagonal, 13 to the left circumflex or circumflex marginal, and 12 to the right coronary or right posterior descending coronary arteries. Thirty-two grafts were occluded, identified by stump cannulation (31 grafts) or nonvisualization on an aortic root injection (one graft). Seven of the occluded grafts were to the left anterior descending, seven to the diagonal, eight to the right coronary, and 10 to the left circumflex arteries. Of the patent grafts, 37 were saphenous veins; 31 of the 32 occluded grafts were saphenous veins.

Figure 1A shows a typical eight-level ultrafast CT study in which circumflex, diagonal, and right coronary artery saphenous vein grafts are patent. Each graft is seen as it exits the aortic root and then in cross-section in sequential caudal planes as it travels to the distal anastomosis. The stump of a left anterior descending graft is visualized in frame 3 and is shown in a close-up in figure 1B. Figure 2 demonstrates both an occluded and a patent saphenous vein graft. The occluded graft is visible but does not opacify with contrast. Its time-density curve is flat in comparison with that of the aorta (figure 3).

Ultrafast CT correctly identified 46 of 48 (sensitivity 96%) of the patent and 31 of 32 (specificity 97%) of the occluded grafts. Diagnostic accuracy was 96%, and correct interpretation of all grafts occurred in 23 of the 25 patients (92%). In the two patients whose results of ultrafast CT differed from angiographic findings, the discrepancy involved one of three grafts in one and two of four grafts in the other.
The sensitivity, specificity, and accuracy of ultrafast CT for individual coronary vessels is shown in table 1. There was no significant difference in sensitivity, specificity, or accuracy for graft patency of bypass grafts traveling to any of the major coronary arteries.

Table 2 compares the sensitivity, specificity, and accuracy of ultrafast CT for assessing patency of saphenous vein compared with internal mammary bypass grafts. Although the diagnostic accuracy for internal mammary grafts was 100%, accuracy for saphenous veins (96%) was not statistically different.

Analysis of errors. All three errors occurred in two patients. In one case, angiography showed an occluded diagonal and a patent left anterior descending graft, whereas the ultrafast CT interpretation was that the diagonal graft was patent and the left anterior descending graft was occluded. Retrospective unblinded review led to the same misinterpretation, probably caused by the distal anastomosis occurring within an interslice gap. Four other patients had this combination of two grafts (2 = both closed; 1 = both patent; 1 = left anterior descending patent, diagonal closed), all with correct ultrafast CT assessments. The only other error occurred with a left anterior descending graft that appeared on ultrafast CT to be filling with contrast; because opacification was faint and the graft appeared thin at all levels, it was interpreted to be patent but highly pathologic. Contrast angiography 2 weeks later revealed faint thrombus staining of an essentially occluded graft. This was classified as an interpretative error but may have represented progression of disease to occlusion in the interval between testing.

Excluded grafts. Three grafts not visualized by angiography were excluded because stumps were not demonstrated and aortic root injections were not performed. The clinical interpretation was that these grafts were closed. In all three, ultrafast CT showed patent grafts. In one of the three, repeat invasive angiography confirmed that the graft was patent. Both the grafts excluded because of a technically inadequate ultrafast CT study were patent on angiography. The internal mammary graft was not visualized on any of 12 levels, but because there was a metallic clip on each level with associated scatter artifact, patency or occlusion could not be determined. The proximal right coronary saphenous vein graft was visualized in the eighth and lowest imaged level; because it was seen in only one slice, patency could not be differentiated from a stump and no interpretation could be rendered.

Complications. There were four significant complications among the 222 consecutive patients examined in this study. Three were minor but caused discomfort. One patient with preexistent renal failure (creatinine 3.4 mg/dl) developed transient oliguria requiring hospitalization. Two patients, neither requiring treatment, developed venous inflammation that extended 2 to 6
FIGURE 1B. High-magnification image of frame 3 from figure 1, showing appearance of the stump of an occluded left anterior descending graft (curved arrow).

FIGURE 2. One of 80 images at peak aortic root opacification in a patient with a patent (open arrow) circumflex and an occluded (closed arrows) left anterior descending graft. The occluded graft is visualized because of faint calcification of enclosed thrombus.
cm proximally from the site of contrast injection. One patient had arm swelling associated with axillary vein thrombosis, which resolved with local and anti-inflammatory therapy.

Discussion

Overall accuracy and accuracy for individual vessels. This study establishes that cardiac ultrafast CT is a sensitive and specific outpatient test for determining patency of individual saphenous vein and internal mammary bypass grafts. Its accuracy is superior to that of other minimally invasive and noninvasive methods,16-25 including that recently reported for exercise biplane radionuclide ventriculography26 and magnetic resonance imaging.27,28 With the rapid and minimally invasive ultrafast CT method, complications were rare (1.8%), cost was low, and x-ray exposure was markedly reduced (3 rads skin dose to the sharply collimated 8 cm scanned region of thorax, less than 25% of the average x-ray exposure in our laboratories during invasive graft studies) compared with invasive graft angiography. Accuracy was achieved despite a relatively large number (3.4, range 1-5) of relatively aged (3 ± 4 years) grafts per patient.

Alternative modalities. Noninvasive evaluation of bypass graft patency has largely depended on indirect evidence. Their status has been inferred from the electrocardiographic response to exercise,16,19,26 the distribution of myocardial thallium-201 at peak exercise compared with rest,17,18,22,25 and the performance of regional myocardium during exercise radionuclide ventriculography.26 However, regional myocardial infarction, ischemia for reasons other than graft occlusion (including progression in the native circulation), and multiple grafts to overlapping myocardial territories are common pitfalls in inferring graft status from these tests.26

Direct evaluation of grafts has also been possible noninvasively. Pulsed Doppler echocardiography, digital subtraction angiography, nuclear magnetic resonance imaging, and standard computed tomography have all been investigated. Specificity for detecting closed grafts (56%) is unacceptably low for Doppler echocardiography.21 Digital angiography provides excellent results when contrast is injected into the aortic root23 but lacks in overall accuracy when performed via peripheral venous injection.23,24 Preliminary reports of magnetic resonance imaging show the results to be inconclusive concerning closed grafts and to be time consuming.27,28

Standard computed tomography has been studied extensively for determining coronary bypass graft patency, with accuracies ranging from below 80% to greater than 95%.9-13 This approach has the disadvantage that a greater amount of contrast medium is frequently required for an entire study, the sources of potential error, especially in patients with three to five grafts, are greater and there is little prospect of differentiating patent but highly diseased grafts from normal grafts.13 Because of these shortcomings, computed
Tomography has not achieved acceptance despite recognition of its potentially high accuracy more than a half decade ago. Because invasive angiography has remained the standard for determining graft patency, premature graft closure, now known to be an occurrence of significant frequency,\textsuperscript{1,4} often goes undetected.

Generalizability of findings. Normal patent saphenous vein bypass grafts range in diameter from 3 to 6 mm, while internal mammary bypasses are generally 2 to 4 mm in diameter. The spatial resolution of the Imatron C-100 is 2 line-pairs/centimeter or about 2.5 mm full-width half maximum. Therefore a number of factors may be relevant in generalizing these results to large numbers of patients before further study. First, saphenous vein bypass grafts tend to develop diffuse narrowings and atherosclerosis as they age. Therefore the technique might be expected to be less accurate in evaluating the patency of aged grafts. In this study, 20 grafts had been placed more than 4 years earlier. There was no trend toward decreased accuracy in this group: the three errors occurred in two patients with bypass surgery 4 months and 6 years before ultrafast CT. Second, it would seem that internal mammary bypass grafts should be more difficult to assess by ultrafast CT because they are narrower and the common practice of applying metallic surgical clips along the length of these grafts to control bleeding can obscure the graft in cross-sectional planes. The perfect discrimination between patent and occluded internal mammary bypasses seen in this study may reflect the large number of tomographic levels (eight to 16) available for review and the fact that there was only one occluded internal mammary graft. Independent study with a larger number of occluded internal mammarys is recommended to confirm the accuracy of ultrafast CT for evaluating their patency. Third, this study was confined to non-complex grafts. The distal limb of combination saphenous vein bypass grafts will require separate study; presumably their length and possibly their greater mobility, associated with their lying on the myocardium, will be relevant factors in the ability of ultrafast CT to assess them.

Technical details. Optimal graft visualization requires that the series of images precede contrast bolus arrival at the graft and continue sequentially as the bolus reaches peak intensity and washes out. Our acquisition protocol was satisfactory in most cases. In a few patients with atrial fibrillation and varying heart rates during contrast injection, the bolus was not optimally imaged and repeat study was required.

Patient movement, including respiration, was not a problem in the 25 patients of this study, but in our experience this can lead to interpretation difficulty in some cases. Repeat study at the same outpatient visit has been required because of patient movement in about 2% of the total patient population. Patient movement sufficient to invalidate an examination using ultrafast CT is minimal compared with other techniques requiring longer acquisition times.

Limitations and future research. The high accuracy of ultrafast CT for determining bypass graft patency demonstrated in this study encourages active research in a number of areas. The role of nonionic contrast agents, which may be less noxious locally and have less renal toxicity, should be explored. Minor hardware and software modifications would allow table incrementation through the gantry during a graft study so as to preclude the necessity of more than one contrast injection to view the entire length of all grafts. The capability of this technique to differentiate diseased but patent from healthy patent grafts must be explored. Improved spatial resolution is anticipated and this may permit direct visual assessment of the status of patent grafts. More promising, however, is recent research suggesting that ultrafast CT can potentially measure graft flow.\textsuperscript{29} All of these improvements would make ultrafast CT a superior screening test for bypass graft status. Because details of proximal and distal anastomoses and the distal vasculature are not provided by ultrafast CT, definitive graft study may continue to require invasive angiography.

Conclusion. This study establishes ultrafast CT to be a highly accurate outpatient technique for determining the patency of both independent saphenous vein and internal mammary bypass grafts. Because it is minimally invasive and because previous noninvasive approaches have had significant limitations and inaccuracies, this is the first technique that holds promise for replacing invasive angiography for the routine evaluation of patients for coronary bypass graft patency. It may be especially useful for epidemiologic studies designed to establish the contribution of risk factors and interventions in the maintenance of graft patency.

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