

# Triple-Rule-Out CT Angiography for Evaluation of Acute Chest Pain and Possible Acute Coronary Syndrome<sup>1</sup>

Ethan J. Halpern, MD

Triple-rule-out (TRO) computed tomographic (CT) angiography can provide a cost-effective evaluation of the coronary arteries, aorta, pulmonary arteries, and adjacent intrathoracic structures for the patient with acute chest pain. TRO CT is most appropriate for the patient who is judged to be at low to intermediate risk for acute coronary syndrome (ACS) and whose symptoms may also be attributed to acute pathologic conditions of the aorta or pulmonary arteries. Although a regular cardiac rhythm remains an important factor in coronary CT image quality, newer CT scanners with 64 or more detector rows afford rapid electrocardiographically (ECG) gated imaging to provide high-quality TRO CT studies in patients with a heart rate of up to 80 beats per minute. Injection of iodinated contrast material ( $\leq 100$  mL) is tailored to provide simultaneous high levels of arterial enhancement in the coronary arteries and aorta ( $>300$  HU) and in the pulmonary arteries ( $>200$  HU). To limit radiation exposure, the TRO CT examination does not include the entire chest but is constrained to incorporate the aortic arch down through the heart. Scanning parameters, including prospective ECG tube current modulation and prospective ECG gating with the “step-and-shoot” technique, are tailored to reduce radiation exposure (optimally, 5–9 mSv). When performed with appropriate attention to timing and technique, TRO CT provides coronary image quality equal to that of dedicated coronary CT angiography and pulmonary arterial images that are free of motion artifact related to cardiac pulsation. In an appropriately selected emergency department patient population, TRO CT can safely eliminate the need for further diagnostic testing in over 75% of patients.

© RSNA, 2009

<sup>1</sup> From the Department of Radiology, Thomas Jefferson University, 132 S 10th St, Philadelphia, PA 19107-5244. Received December 31, 2008; revision requested February 5, 2009; revision received February 10; accepted February 18; final version accepted February 25. **Address correspondence to** the author (e-mail: [ethan.halpern@jefferson.edu](mailto:ethan.halpern@jefferson.edu)).

© RSNA, 2009

**E**valuation of chest pain in the emergency department (ED) is a public health issue of great consequence. According to the most recent available health statistics report from the Centers for Disease Control and Prevention, evaluation of acute chest pain and related symptoms was the second most common reason for a visit to the ED by a female adult and the most common reason by a male adult in the United States in 2006 (1). Chest pain accounted for 6 392 000 ED visits and 1 976 000 hospital admissions. Overall, suspected heart disease and chest pain were the most common reasons for direct admission from the ED and accounted for 2 492 000 hospital admissions in 2006.

The differential diagnosis of chest pain is a complex problem for the ED physician. The diagnosis of acute coronary syndrome (ACS) includes unstable angina, non-ST-elevation myocardial

infarction, and ST-elevation myocardial infarction. Of patients presenting to the ED with symptoms of ACS, only 25% ultimately have a confirmed diagnosis of ACS at the time of discharge (2). The failure rate for diagnosis of ACS among patients presenting to the ED is in the range of 2%–5% (3,4) but may be as high as 29% at low-volume centers (5).

Patients in whom the diagnosis of ACS is missed tend to be younger and to have an atypical presentation and a nondiagnostic electrocardiogram (ECG) (6). The missed diagnosis of ACS is a common reason for litigation against ED physicians and accounts for up to 25% of the total malpractice liability of ED physicians (7). On the other hand, uncertainty in the diagnosis of ACS results in the practice of defensive medicine and begets an increased number of diagnostic tests and hospital admissions (8). The cost of negative inpatient cardiac evaluations is estimated at \$6 billion in the United States each year (9).

rapid triage to cardiac catheterization and intervention. On the other hand, when a patient's presentation clearly suggests a noncardiac diagnosis, coronary evaluation is not required and is not cost effective. The remaining patients suspected of having ACS must be cleared of this diagnosis prior to discharge. Given the potentially life-threatening consequences of missing a diagnosis of ACS, a high negative predictive value is critical for discharging patients with possible ACS.

The negative predictive value of coronary CT angiography for ACS will depend on the prevalence of coronary disease in the study population. A recent multicenter trial (15) demonstrated a 99% negative predictive value of coronary CT angiography for coronary disease at both the patient and the vessel levels in a population with a disease prevalence of less than 25%, establishing coronary CT angiography as an effective noninvasive examination to rule out obstructive coronary artery stenosis. Although another recent multicenter trial (16) demonstrated a negative predictive value of only 83% for coronary CT angiography, that study evaluated a population with a high (56%) prevalence of obstructive coronary disease. On the basis of the results of these studies of dedicated coronary CT angiography, it is likely that TRO CT will be most effective in a population with a low prevalence (<50%) of obstructive coronary disease.

For those with a low risk of ACS who are evaluated with conventional nuclear stress testing, only one-third of patients with a positive or indeterminate stress test result are found to have clinically significant coronary disease at the time of catheterization (17). For the evaluation of

### Essentials

- The primary goal of triple-rule-out (TRO) CT in the emergency department is to facilitate the safe rapid discharge of patients judged to be at low to intermediate risk of acute coronary syndrome.
- The detection of noncoronary lesions that explain the presenting complaint is a major advantage of the TRO CT examination over nuclear stress testing.
- TRO studies are most appropriate and cost-effective when there is a suspicion for acute coronary syndrome along with other diagnoses such as pulmonary embolism, acute aortic syndrome, or nonvascular disease in the thorax.
- An optimized TRO protocol provides excellent image quality for aortic and coronary and pulmonary arterial evaluation while minimizing contrast agent dose and radiation exposure.
- Attention to the details of patient preparation, contrast agent administration, and timing of the scan is the key to high-quality TRO studies.

### Clinical Role of Triple-Rule-Out CT

Numerous studies have demonstrated good to excellent diagnostic accuracy of dedicated coronary computed tomographic (CT) angiography for evaluation of coronary disease (10), with excellent negative predictive values (11,12). However, few reports have described the application of CT as part of the triple-rule-out (TRO) examination with a dedicated TRO injection and scan protocol (13).

TRO CT is a tailored ECG-gated examination designed to evaluate the aorta, coronary circulation, pulmonary arteries, and the middle to lower portion of the chest with a single scan. Application of the TRO examination for evaluation for suspected ACS in the ED is possible because of advances in CT technology that provide greater z-axis coverage with improved temporal resolution and decreased radiation dose. A recent survey of radiology practices found that 33% used CT in the ED for the work-up of chest pain and that 18% were using a TRO protocol (14).

All patients with ACS require hospital admission, and many will benefit from

#### Published online

10.1148/radiol.2522082335

**Radiology** 2009; 252:332–345

#### Abbreviations:

ACS = acute coronary syndrome  
ECG = electrocardiogram  
ED = emergency department  
MIP = maximum intensity projection  
TRO = triple rule out

Author stated no financial relationship to disclose.

patients presenting to the ED who are judged to be at low risk for ACS, coronary CT angiography is at least as accurate as nuclear imaging (18) and allows the safe and rapid discharge of low- to intermediate-risk ACS patients (19–21). Results of a recent study (22) suggest that in low- to moderate-risk patients, a CT triage model is less costly and more effective than strategies based on either stress echocardiography or stress ECG testing. The authors of another recent study (23) concluded that “compared to the other strategies, immediate CTA [CT angiography] is safe, identified as many patients with coronary disease, had the lowest cost, had the shortest length of stay, and allowed discharge for the majority of patients.” TRO CT precludes the need for additional diagnostic testing in over 75% of patients with low to intermediate risk of ACS and provides the additional advantage of helping find noncoronary diagnoses that explain the presenting complaint in 11% of ED patients (24). TRO CT eliminates the need for separate dedicated studies for coronary disease, aortic dissection, pulmonary embolism, and other acute chest conditions. In a properly selected population, coronary CT can provide a cost-effective evaluation (25) with reduced diagnostic time, lower costs, and fewer repeat evaluations for recurrent chest pain, as compared with standard diagnostic evaluation (26).

Among patients who present to the ED with a low to moderate risk of ACS and who are evaluated with TRO CT, a minority (<10%) are subsequently evaluated with conventional cardiac catheterization. Among those ED patients who are studied with both TRO CT and cardiac catheterization, few normal cardiac catheterization results would be expected (24). Since it would not be ethical to subject most patients with a low to moderate risk of ACS to cardiac catheterization, there are no studies that confirm the negative predictive value of TRO CT relative to conventional arteriography in the ED population. Nonetheless, if the quality of coronary imaging obtained with TRO CT is equivalent to that of dedicated coronary CT angiography, one would expect the same high diagnostic accuracy and negative

predictive value that have been documented with dedicated coronary CT angiography.

Injection and scan techniques for TRO CT studies vary considerably from one institution to another, resulting in inconsistent image quality. Some radiologists are reluctant to perform TRO studies because of an impression that the TRO examination is too technically challenging or that the quality of the coronary artery study is compromised in the TRO examination. The goals of this article are to discuss various approaches to patient preparation, bolus timing, contrast agent administration, and ECG gating and to describe a straightforward optimized technique for performance of TRO CT studies. An optimized TRO protocol should minimize contrast agent dose and radiation exposure to the patient while providing coronary arterial image quality equivalent to that of a dedicated coronary CT angiogram, pulmonary arterial image quality equivalent to that of a dedicated CT pulmonary arteriogram, and high-quality imaging of the thoracic aorta without pulsation artifact.

### Patient Selection

Appropriate patient selection is crucial to the cost-effective application of TRO CT (Fig 1). Patients who are at high risk for ACS, with elevated cardiac biomarkers or acute ECG changes, should be admitted to the hospital and are likely to benefit from direct triage to cardiac catheterization for diagnostic purposes and timely intervention. In the remaining patients suspected of having ACS, the goal of TRO CT is to exclude the diagnosis of coronary disease or to define an alternative diagnosis that might explain the presenting symptoms.

Patients who are likely to have a high burden of calcified coronary plaque, because they have known coronary disease (including patients with previous myocardial infarction, chronic angina, or a stent, as well as patients who have undergone bypass) are less likely to benefit from the coronary imaging performed with TRO

CT, although the TRO study may still be useful with respect to the aorta, pulmonary arteries, and other intrathoracic conditions. The degree of coronary disease is often overestimated in these patients owing to blooming of calcified plaque, such that it is impossible to exclude clinically significant coronary disease. Older patients with multiple cardiac risk factors are more likely to have extensive coronary calcification (27). An indeterminate coronary CT evaluation is much more likely in patients with an elevated calcium score (score > 400–1000) (28). In such patients, a calcium scoring study may be useful prior to TRO CT to define whether the patient is a candidate for TRO CT.

An acceptable clinical history for TRO CT includes a symptom complex that raises the suspicion of ACS, including symptoms such as chest pain, shortness of breath, syncope or near syncope or neck, shoulder, back, or arm pain not appearing to be musculoskeletal in nature. Patients should be negative for initial cardiac biomarkers (myoglobin and troponin-I) and should not have new ECG changes suggestive of myocardial ischemia. Ideally, these patients should have signs, symptoms, and laboratory data that might be interpreted as consistent with ACS or other causes of

**Figure 1**

- Clinical presentation: low to moderate risk of ACS
- Clinical presentation: non-ACS diagnosis considered
- Negative biomarkers (myoglobin and troponin-I)
- Normal ECG or nonspecific changes
- No history to suggest extensive coronary calcium
- Not recommended for patients with bypass or stents
- Patient able to tolerate CT and hold breath
- Cardiac rhythm acceptable for ECG-gated scan
- Adequate renal function

**Figure 1:** Patient selection criteria for TRO CT.

chest pain, including pulmonary embolism and acute aortic syndrome.

In selected patients who test positive for low levels of biomarkers, TRO CT may be appropriate when the clinical impression favors pulmonary embolism or acute aortic syndrome or when there is a need to exclude ACS but there is no immediate intention of sending the patient for invasive cardiac catheterization. When clinical suspicion is truly limited to ACS, a dedicated coronary CT angiogram is preferred, as it will involve less contrast material and expose the patient to a lower radiation dose. Age, sex, and clinical presentation are well-validated parameters that can be used to define a population with possible ACS that would be appropriate for TRO CT (29). While traditional cardiac risk factors such as a family history of coronary disease, hypercholesterolemia, hypertension, and others clinical parameters may be important long-term prognostic markers, such risk factors are of limited clinical value in diagnosing ACS in the ED setting and in triaging these patients (30).

The presence of a cardiac arrhythmia presents a challenge for ECG-gated coronary imaging but is no longer an absolute contraindication. Sinus bradycardia is the preferred heart rhythm for TRO CT. In the absence of a clinical contraindication, a  $\beta$ -blocker should be administered prior to TRO CT. Both heart rate and ectopy are reduced after treatment with an intravenous  $\beta$ -blocker (31,32).

New CT technology provides improved temporal resolution, with the capability of scanning the entire heart in one to two heartbeats (as compared with four to five beats for most 64-section scanners). This new technology has reduced both the required phase window for diagnostic imaging of the coronary arteries and the effects of variability in heart rhythm on coronary image quality (33).

The decision as to whether a patient should be excluded from undergoing TRO CT owing to a cardiac arrhythmia must be based on an assessment of the magnitude of the arrhythmia and the specific

capabilities of the scanner that will be used for the study. A regular heart rate of up to 80 beats per minute is no longer a contraindication for many new scanners, including dual-source scanners and single-source scanners with a gantry rotation time faster than 300 msec. An irregular tachyarrhythmia poses a more difficult problem, but the degree of contraindication depends on the frequency of ectopic beats.

Allergies to contrast material and renal insufficiency are relative contraindications to administration of iodinated contrast material for TRO studies. The presence of asthma, acute heart failure, severe cardiomyopathy, or hypotension may limit the use of  $\beta$ -blockers to control heart rate and thus may reduce the quality of the TRO CT images. A history of recent cocaine use or a drug screen positive for cocaine is also a relative contraindication to the use of  $\beta$ -blockers for the scan (34), although this contraindication remains controversial (35). Recent use of a phosphodiesterase inhibitor is a relative contraindication to the administration of nitroglycerin for coronary vasodilatation during CT, but this does not represent a contraindication to TRO CT.

#### CT Hardware and Radiation Issues

TRO CT requires a longer scanning length than does dedicated coronary CT angiography. A mean scanning length of 20 cm is required to image the chest from above the aortic arch through the caudal aspect of the heart. To perform this scan during a single breath hold, the scanner should be capable of imaging the required volume with an ECG-gated technique in no more than 15 seconds. This requirement limits TRO CT studies to scanners with at least 64 detector rows.

TRO studies are associated with a higher radiation dose when compared with dedicated coronary CT angiography examinations because of the longer scanning length. Our typical scan parameters include a tube voltage of 120 kVp and a mean effective tube current of 600 mAs per section (where effective

milliamperere-seconds equals tube milliamperes times gantry rotation time divided by pitch). Heavier patients weighing over 200 lbs (>91 kg) are scanned with higher tube current of 800–1000 mAs, on the basis of a subjective estimate of patient body habitus by the attending radiologist. In our experience, mean effective TRO radiation dose for patients evaluated in helical scan mode without tube current modulation averages 18 mSv and is decreased to 8.75 mSv among patients evaluated with tube current modulation (36). Mean effective tube current and/or tube voltage can be decreased in smaller patients to reduce radiation dose.

Until recently, all coronary CT angiography studies have been performed with a helical acquisition (with or without tube current modulation). In patients with a very stable heart rate, newer scanners can acquire a TRO CT study with prospective ECG gating by using the “step-and-shoot” axial mode to further reduce radiation dose to 5–6 mSv. Prospective ECG gating should be reserved only for patients with a very stable heart rate, since any change in cardiac rhythm will either prolong the scan time (as the scanner waits for the next “normal” heartbeat) or result in degraded image quality from cardiac motion.

Images obtained with prospective ECG gating are more sensitive to minor variations in heart rate and cannot provide information about cardiac function and regional wall motion. Nonetheless, in appropriately selected patients evaluated with proper attention to technique, prospective ECG gating of coronary CT angiography can be used to reduce radiation dose while maintaining image quality (37,38).

CT imaging, and coronary CT in particular, has been criticized as an important source of radiation exposure to the population (39,40). Recent advances in CT technology, however, allow a dramatic decrease in radiation dose with coronary CT. The effective radiation dose for a TRO CT scan with a state-of-the-art scanner compares favorably with the dose of a nuclear stress test, the dose from which has been re-

ported to range from 10 to 17 mSv (41). When one considers that the conventional work-up in a patient with chest pain presenting to the ED is likely to include a negative nuclear stress test result, as well as another diagnostic radiologic examination such as a chest CT or a ventilation-perfusion study, application of a TRO CT study to an appropriate patient population may actually reduce the per-patient radiation exposure for diagnostic studies during the ED evaluation.

### TRO CT Technique and Image Quality

High-quality coronary imaging is essential to distinguish patients with coronary disease from those in whom ACS may be excluded. Careful attention to patient preparation (Fig 2), scan technique (Fig 3), and injection technique (Table) will result in optimal, homogeneous aortic, coronary, and pulmonary arterial opacification and in coronary image quality that is equal to that obtained with dedicated coronary CT angiography (42). ECG gating of TRO

studies eliminates motion artifact related to cardiac pulsation and, therefore, provides superior definition of the pulmonary arterial tree as compared with dedicated pulmonary CT angiography without ECG gating. The discussion that follows is directed primarily toward performance of the TRO study with a 64 detector-row scanner.

### Patient Preparation and Monitoring

To minimize ectopy in the cardiac rhythm during coronary CT angiography, patients should refrain from stimulants such as caffeine on the day of the examination. However, unlike typical outpatients scheduled for coronary CT angiography, TRO CT patients typically present directly from the ED and cannot be instructed to modify their dietary intake prior to the scan. Nonetheless, the use of intravenous  $\beta$ -blockers allows rapid control of heart rate and reduction of ectopy in ED patients sent for TRO CT.

Adequate intravenous access is necessary to deliver a rapid contrast

agent bolus for coronary CT angiography. An 18–20-gauge intravenous catheter is placed into a large vein in the antecubital fossa. The intravenous catheter should be tested with a rapid saline flush to ascertain that there is no extravasation and that the patient does not experience pain during injection. A painful intravenous injection can result in a sudden change of heart rate during contrast agent administration, with degradation of image quality.

To reduce inadvertent compression of the subclavian vein during contrast agent injection, the arm with the intravenous catheter should not be extended above the patient's head. With the patient lying in a supine position, I prefer to extend the arm with the intravenous line directly in front of the patient. To maintain the patient's comfort and to keep the arm out of the gantry, the extended hand is rested on the gantry during the scan.

ECG leads are positioned above and below the level of the scan to prevent streak artifact. The ECG trace should be

### Figures 2, 3

- Withhold caffeine and other cardiac stimulants prior to the study
  - Good intravenous access (preferably 18 gauge)
  - Proper positioning of the arm with the IV catheter directly in front of the patient and resting on the gantry, to prevent subclavian vein compression
  - Saline injection at rapid rate to test intravenous catheter
  - ECG lead placement for clear R-waves
  - $\beta$ -Blockers (2.5–30 mg IV) to achieve sinus bradycardia
  - Sublingual nitroglycerin 2–3 minutes before CT angiography
  - Practice a small breath hold for 15 seconds
- 2.
- Heart is positioned at the center of the gantry to maximize resolution
  - Acquisition begins 1–2 cm above the aortic arch
  - Caudal extent is programmed to extend through the base of the heart, but real-time monitoring is used to terminate the scan as soon as the base of the heart is imaged
  - CT angiography begins 5 seconds after contrast material enters left atrium
  - Cranial-to-caudal direction of acquisition is preferred
  - Standard scan parameters: mean effective mAs of 600 at 120 kVp
- 3.

**Figure 2:** Technique for patient preparation for TRO CT. IV = intravenous.

**Figure 3:** Technique for performing TRO CT.

### Contrast Material Injection Protocols for Coronary CT Angiography and TRO CT

Examination Type	First Phase	Second Phase	Injection Rate
Dedicated coronary CT angiography	70 mL of iodine 350	40 mL of saline	5.5 mL/sec
TRO CT	70 mL of iodine 350	50 mL of diluted contrast agent (25 mL iodine 350 plus 25 mL saline)	5.0 mL/sec
Extended (18–20 sec) TRO CT (see Fig 4)	80 mL of iodine 350	70 mL of diluted contrast agent (35 mL iodine 350 plus 35 mL saline)	5.0 mL/sec

Note.—Iodine 350 = 350 mg of iodine per milliliter.

Figure 4



**Figure 4:** TRO CT angiogram of neck and chest in 24-year-old woman with history of Marfan syndrome who presented with acute onset of chest pain radiating into the neck. Clinical suspicion was high for aortic dissection with possible extension into coronary arteries or great arteries in the neck. Scan was obtained with prospective ECG gating and 120 mL of iodinated contrast material. First phase of injection was increased to 80 mL of contrast agent while second phase was increased to 40 mL of contrast agent plus 40 mL of saline to compensate for increased scanning time needed to include carotid arteries. **(a)** Coronal slab maximum intensity projection (MIP) image demonstrates enhancement of aorta, pulmonary arteries, and great vessels extending from the aortic arch with no dissection. **(b)** Oblique slab MIP image demonstrates normal aortic arch and descending thoracic aorta. **(c)** Oblique coronal slab MIP image demonstrates normal left ventricular outflow tract extending into proximal part of aortic arch. However, there is air in tissues of the neck surrounding great vessels (arrows). **(d)** Coronal slab MIP image through the trachea demonstrates extensive emphysematous changes in mediastinum. On further questioning, patient complained of an episode of intense coughing the previous night, just before symptoms began. Mediastinal air was thought to represent the cause of symptoms and was likely related to a ruptured pulmonary bleb (never seen). Patient recovered without further interventional therapy.

evaluated immediately before the scan, with the patient's arms raised into the position that will be used for the scan. It is important to be certain that the ECG leads will not be pulled off of the patient when the table moves for the scan. A clearly defined R-wave is necessary to ensure adequate ECG gating. If necessary, leads should be repositioned to obtain a clearly defined R-wave.

Baseline heart rate and blood pressure are obtained before and during administration of  $\beta$ -blockers and after the procedure. A stable blood pressure should be documented before the patient is returned to the ED.

The ideal heart rate for ECG-gated studies is a slow regular rhythm, usually a sinus bradycardia at 50–60 beats per minute (43). Although precise control of heart rate may be less critical with dual-tube CT scanners or with newer scanners that have a faster gantry rotation and improved temporal resolution, image quality is optimized and radiation dose is minimized with a regular cardiac rhythm.

Oral  $\beta$ -blockers may be given in the ED at least 1 hour before the scan for control of heart rate. However, heart rate often increases with the level of anxiety when the patient is placed on the CT table. I prefer to administer metoprolol tartrate intravenously when the patient is on the CT table. Intravenous metoprolol has an onset of action within 1–3 minutes (as compared with 1–2 hours for an orally administered dose) and allows better titration of heart rate prior to contrast agent injection.  $\beta$ -Blockers may alter vascular tone, cardiac rhythm, and myocardial contractility and can promote bronchospasm. Metoprolol should be used with caution, and may be contraindicated in patients with heart block, uncompensated heart failure and asthma.

In the interest of improving patient throughput, administration of metoprolol is performed during acquisition of the scout topogram and setup of the bolus-tracking images before coronary CT angiography. Patients who arrive with a heart rate in the range of 60–65 beats per minute are given an initial intravenous dose of 2.5 mg of metoprolol. Patients who arrive with a heart rate

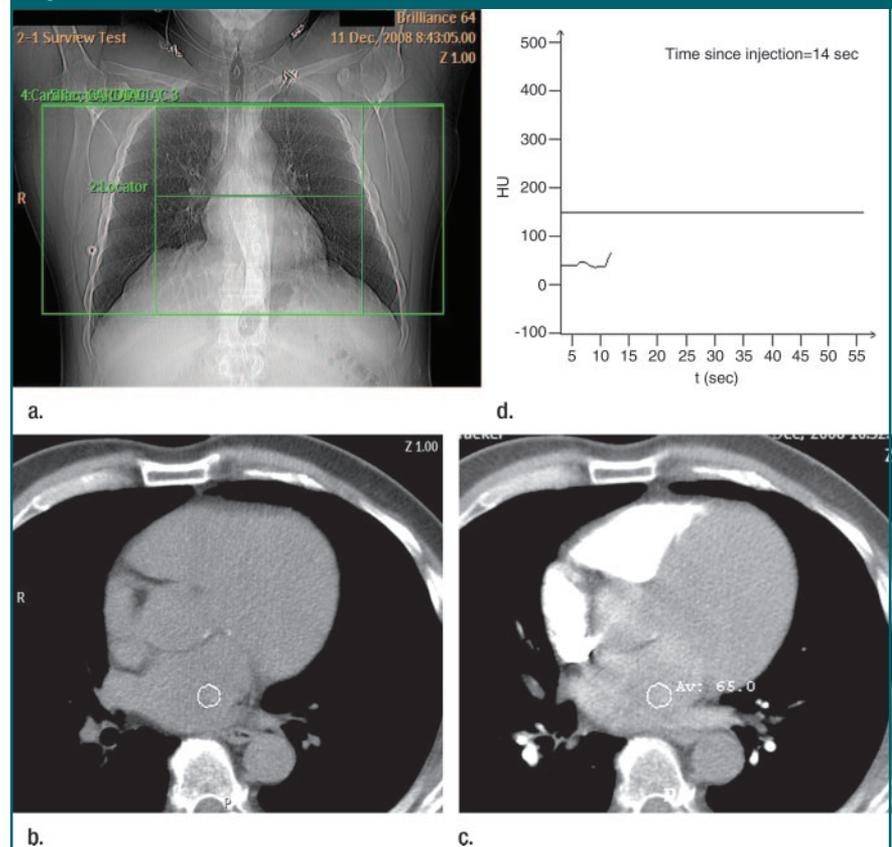
faster than 65 beats per minute are given an initial intravenous dose of 5 mg. After allowing several minutes to observe the effect of the first dose, additional doses of 5 mg are administered every 3–5 minutes until the target heart rate is achieved. A minority of patients with acute chest pain and/or shortness of breath will present with a tachycardia that does not respond to  $\beta$  blockade. It is unusual to administer more than 20 mg of metoprolol since patients who do not respond with a lower heart rate after the first 10–20 mg are unlikely to respond to a higher dose. For patients who continue to respond slowly to administration of an intravenous  $\beta$ -blocker, the maximum intravenous dose that I will administer is 30 mg. The patient's heart rate and blood pressure are monitored after every dose, and no further  $\beta$ -blocker is given if systolic pressure declines below 100 mm Hg.

To achieve maximum coronary vasodilatation for the study, sublingual nitroglycerin is administered 2–3 minutes before the start of TRO CT (44). A recent study suggests that pretreatment with sublingual nitroglycerin may improve the diagnostic accuracy of coronary CT (45). As with metoprolol, nitroglycerin is not administered if the systolic blood pressure declines below 100 mm Hg.

Although nitroglycerin and  $\beta$ -blockers can combine to cause hypotension, this is not generally a problem on the CT table with the patient in the supine position. Nitroglycerin does result in a reflex tachycardia, but this is not generally a problem when patients have received a  $\beta$ -blocker prior to the study. Relative contraindications to nitroglycerin include clinical scenarios such as hypovolemia and idiopathic hypertrophic subaortic stenosis or recent use of a phosphodiesterase inhibitor, where nitroglycerin may induce profound hypotension.

After administration of nitroglycerin, I generally practice the breath hold with the patient. The patient is instructed to take a slow small breath and to hold it for 15 seconds. A large inspiratory effort draws more unopacified blood from the inferior vena cava and may reduce the level of intravascular opacification during scanning (46). If

**Figure 5**



**Figure 5:** Scan setup and bolus-tracking images. **(a)** Coronal scout topogram. Scan levels are planned within the green rectangle. Starting level for scan is at the inferior margin of the clavicular heads, just above the aortic arch. Inferior margin of the scan is set below the base of the heart. To limit radiation to the patient, CT angiographic acquisition is monitored in real time and manually stopped as soon as the base of the heart is imaged. Note that setup specifies two reconstruction fields of view. Smaller (25-cm) field of view is used for evaluation of aorta and coronary anatomy. Larger field of view is used to evaluate pulmonary arteries, lungs, and chest wall. **(b)** Precontrast bolus-tracking image. Table height and patient position are adjusted so that heart is centered in the scanning area. CT resolution is maximized at center of the gantry. A region of interest (circle) is defined in the left atrium. **(c)** Low-dose bolus-tracking images are obtained every 2 seconds, beginning 5 seconds after start of the contrast agent injection. This image demonstrates early opacification of left atrium. CT angiography was manually started at this time. **(d)** Graph shows that scanning is programmed to begin 5 seconds after initial opacification of left atrium reaches 100 HU above baseline (horizontal line at 150 HU in this plot). To maximize use of the contrast dose, however, scanning is manually started by the technologist as soon as contrast material enters left atrium. Manual start time is approximately 2 seconds earlier than the density would have triggered an automatic start to the scan. The programmed start line serves as a backup in the event the technologist fails to start the scan earlier.

the patient takes a large practice breath, I ask the patient to repeat the practice exercise and take a smaller breath. Although the breath hold may seem like a trivial detail, it is important to practice the breath hold so that the patient is prepared for the length of the breath hold that will be required for the scan.

### Setting Up the Scan

The TRO CT examination must include the entire thoracic aorta, as well as the heart. On the basis of inspection of the scout topogram, TRO scans are programmed to start 1 cm above the aortic arch, usually at the inferior margins of the clavicular heads (Fig 5). Because radiation dose to the pa-

tient is directly proportional to the length of the scan, the lung apices above the level of the aortic arch are not included. Although 5% of patients with pulmonary embolism have an isolated upper lobe embolus (47), an isolated subsegmental pulmonary embolus above the level of the aortic arch is extremely uncommon and is very unlikely to be detected with CT angiography. In the early days of spiral CT, before the introduction of multisection CT scanners, dedicated pulmonary CT angiography was generally limited to a distance of 10–12 cm from the aortic arch down through the inferior pulmonary veins (48). Excluding the apices from TRO CT reduces the scan length by approximately 4–5 cm, which we estimate is associated with a 15%–20% reduction in effective radiation dose.

Many centers traditionally acquire CT pulmonary arteriography studies in the caudal-to-cranial direction to reduce the effect of respiratory motion in the lower lobes (49,50). Others have suggested advantages to scanning in the cranial-to-caudal direction for CT pulmonary arteriography (51). As discussed below, the cranial-to-caudal scanning direction is favored for TRO studies because of additional considerations related to timing of the contrast agent injection and patient heart rate. Although scanning is programmed to continue through the base of the heart, the TRO CT angiography acquisition is monitored in real time and is manually stopped as soon as the base of the heart is imaged. Manual stopping of the scan at the heart base can reduce scanning length by 1.5–2.0 cm. The radiation dose estimates of 8.75–18 mSv cited earlier were obtained before we routinely began terminating the scan in real time once the base of the heart was imaged. We estimate that the use of real-time monitoring to reduce acquisition length can reduce the radiation dose by another 7%–10%.

#### Contrast Agent Injection and Timing of Image Acquisition

The goal of contrast agent administration for dedicated coronary CT angiography is to maintain a high level of enhancement in the coronary arteries (52). Coronary opacification demon-

strates a strong correlation with the rate of injection, as well as with the concentration of iodine in the contrast material (53,54). For TRO CT studies, a reasonable enhancement goal is an attenuation level higher than 300 HU in the coronary arteries and higher than 200 HU in the pulmonary arteries.

Standard injection techniques used for dedicated coronary CT angiography result in suboptimal opacification of the pulmonary arterial circulation (55). Opacification of the pulmonary arteries requires an extended contrast agent injection to maintain contrast on the right side of the heart during the scan. However, it is important not to have full strength contrast material in the superior vena cava at the time of the scan, because this can cause a streak artifact that may limit image quality.

Studies of aortic CT angiography have demonstrated an advantage to the biphasic injection of contrast material (56). A high-injection-rate uniphasic injection of contrast material results in a peak of contrast enhancement during a short interval, with attenuation minima at the beginning and/or end of the acquisition. A biphasic injection protocol can be tailored to provide a more homogeneous enhancement profile over time. To optimize both coronary and pulmonary arterial enhancement for TRO CT, I prefer a biphasic contrast agent injection protocol to provide an intense homogeneous level of contrast enhancement in the left-sided circulation (aorta and coronary arteries) with a slightly lower homogeneous level of enhancement in the right-sided circulation. A rapid flow rate is maintained throughout the injection to minimize the effect of venous return from the inferior vena cava.

Although preheating of contrast material is not required to obtain a rapid flow rate, preheating up to a temperature of 37°C prior to injection reduces the viscosity of the contrast material and facilitates a rapid flow rate at lower injection pressures (57).

The biphasic injection is timed so that the first phase of the injection opacifies the left heart while the second phase opacifies the right heart during

TRO CT. More specifically, for a 64-detector scanner, the biphasic injection consists of 70 mL of undiluted contrast material (350 mg of iodine per milliliter) followed by 25 mL of contrast material diluted with 25 mL of saline, all injected at 5.0 mL/sec (Table). To make efficient use of the contrast agent bolus, imaging is triggered on the basis of opacification of the left atrium, which begins 2–3 seconds before opacification of the descending aorta. Scanning begins 5 seconds after the contrast agent enters the left atrium (Fig 5), so that the aorta and coronary arteries are in the plateau phase of peak enhancement during the CT angiographic acquisition. The injection volume and rate are optimized for a scanning time of approximately 14–15 seconds. In the event of a significantly longer scan time—such as that which may occur if there is an arrhythmia when using prospective ECG gating or when the CT angiogram is extended in length—the injection would need to be prolonged to ensure adequate pulmonary opacification (Table). When the TRO study is properly timed, the first phase of the injection opacifies the coronary arteries during image acquisition (Figs 6, 7), while the second phase of the injection provides simultaneous homogeneous enhancement of the pulmonary arteries (Figs 8, 9). The thoracic aorta is also homogeneously enhanced and optimally evaluated (Figs 10, 11). A review of our TRO studies demonstrates that this technique provides a mean enhancement level of 300–350 HU in the aorta, pulmonary arteries, and coronary arteries (42).

Several variations of this biphasic injection protocol have been proposed. In one variation, a biphasic injection is used with undiluted contrast material (320 mg of iodine per milliliter), but the flow rate starts at 5 mL/sec and is then reduced to 3 mL/sec to avoid overloading the right heart and superior vena cava with dense contrast material (58,59). The reduced flow rate in the second phase of the injection provides a longer injection time and reduces streak artifact from the superior vena cava. A 50-mL saline flush is applied as a third phase to flush the con-

trast agent that remains in the arm veins into the right heart.

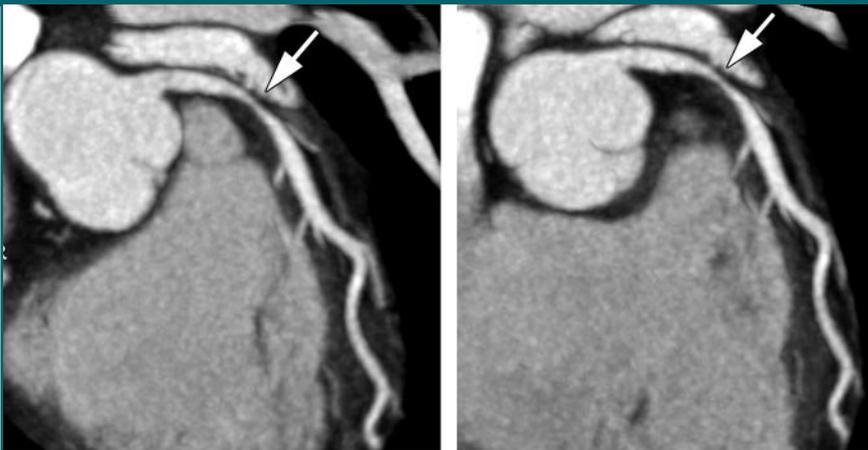
An alternative triphasic technique involves a first phase with 50 mL of undiluted contrast material (350 mg of iodine per milliliter) followed by 50 mL of 60% contrast agent-to-40% saline and

then by 30 mL of saline, each injected at 4.5 mL/sec (60). Contrast material is diluted in the second phase of the injection to reduce streak artifact from the superior vena cava. The use of diluted contrast material with a faster flow rate has a theoretic advantage over the use

of full-strength contrast material at a slower rate. The faster injection rate results in greater filling of the venous system from the injection, greater filling of the right atrium from the superior vena cava, and less variation related to unopacified venous flow from the inferior vena cava.

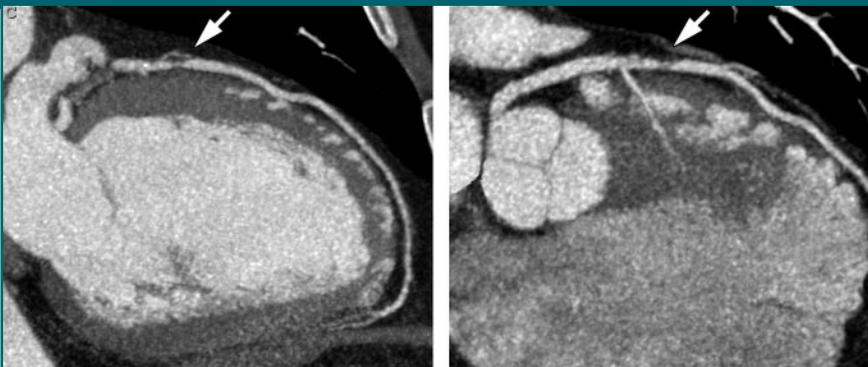
Although I do use a saline flush for dedicated coronary CT angiography, I do not use a saline flush for TRO CT studies. In my experience the saline flush can result in complete washout of contrast material from the right heart

**Figure 6**



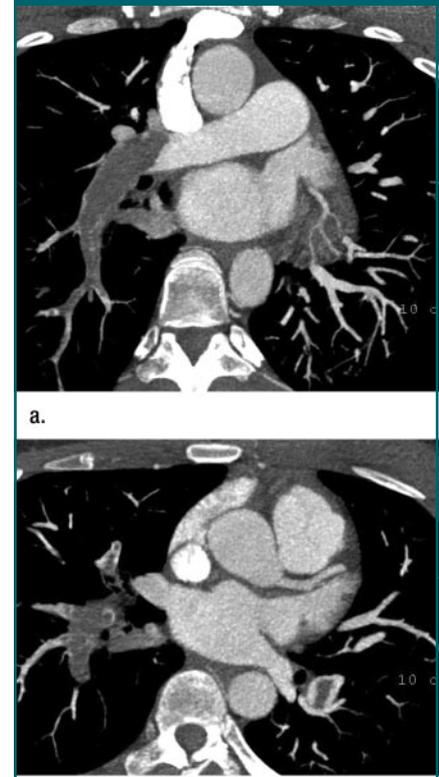
**a.** **b.**  
**Figure 6:** TRO CT angiogram in 37-year-old woman with no relevant cardiac history who presented with sudden onset of chest pain while at work. TRO demonstrated a smooth 75% stenosis of the left anterior descending artery (arrow). Patient was treated with angioplasty. Slab MIP images of (a) left anterior descending artery in long axis of the aortic root and (b) left anterior descending artery in orthogonal obliquity in the short axis of the aortic root.

**Figure 7**



**a.** **b.**  
**Figure 7:** TRO CT angiogram in 51-year-old athletic man with no relevant cardiac history who presented with atypical chest pain while resting at home. TRO CT images demonstrate irregular narrowing of left anterior descending artery (LAD; arrow). Patient was treated with angioplasty. (Bright spots projecting just below LAD correspond to contrast material in interstices of right ventricle between trabeculations adjacent to interventricular septum. These are imaged along with septum owing to the thickness of the slab MIP projection.) (a) Slab MIP image of LAD along the long axis of the left ventricle. (b) Slab MIP image of LAD in an orthogonal obliquity along short axis of the aortic root.

**Figure 8**



**a.** **b.**  
**Figure 8:** TRO CT angiogram in 31-year-old woman with chest pain that was atypical for angina but without severe shortness of breath. TRO CT demonstrates bilateral pulmonary embolism with normal aorta and coronary arteries. (a) Oblique coronal slab MIP image demonstrates large thrombus in right pulmonary and interlobar pulmonary arteries with extension into right lower lobe segmental branches. (b) Axial slab MIP image demonstrates bilateral pulmonary embolism with a smaller thrombus also present in left pulmonary artery.

Figure 9



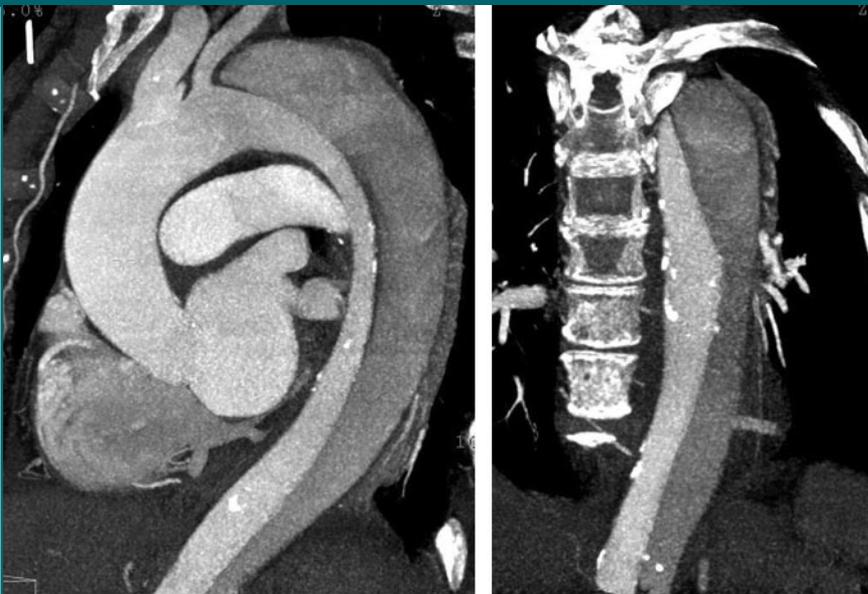
**a.** **b.**  
**Figure 9:** (a) Sagittal and (b) coronal slab MIP images from TRO CT angiogram in 40-year-old man with chest pain and tachycardia show left upper lobe pulmonary embolus extending into an apical segmental branch of left pulmonary artery (arrow). Coronary arteries and aorta were normal.

and result in a nondiagnostic pulmonary arteriogram when the acquisition time is prolonged or when the start of image acquisition is delayed by a slow right-to-left contrast material transit time. I prefer to leave some of the diluted contrast material from the second phase of injection in the patient's arm rather than risk using a saline flush that may wash the contrast out of the pulmonary circulation. When scanning time must be increased for additional z-axis coverage, the injection may be prolonged with additional contrast material. (Fig 4 demonstrates a carotid plus TRO CT study requiring 20 seconds for acquisition.)

There are different approaches among centers to the directionality used for acquiring TRO studies. If the patient is unable to hold his or her breath for the full acquisition, it is best to use caudal-to-cranial scanning, so that the heart is imaged before the patient begins to breathe. The cranial-to-caudal scanning direction used in my protocol introduces an additional 5 seconds between the breath hold and the cardiac portion of the scan. In my experience, the heart rate is more variable when the patient first takes a breath and tends to plateau at a rate slightly below the baseline level at 5–15 seconds after the patient takes a breath. For the majority of patients who have no trouble holding their breath, scanning in a cranial-to-caudal direction affords better coronary image quality by imaging the heart during this respiratory-induced plateau of the heart rate. Furthermore, since contrast material must pass through the pulmonary arterial tree before it enters the coronary arteries, optimal enhancement in the pulmonary circulation is achieved before optimal coronary arterial enhancement. A scan performed in the cranial-to-caudal direction can be started a few seconds earlier than a scan performed in the caudal-to-cranial direction and can take advantage of the earlier enhancement in the pulmonary circulation to reduce the overall contrast material load.

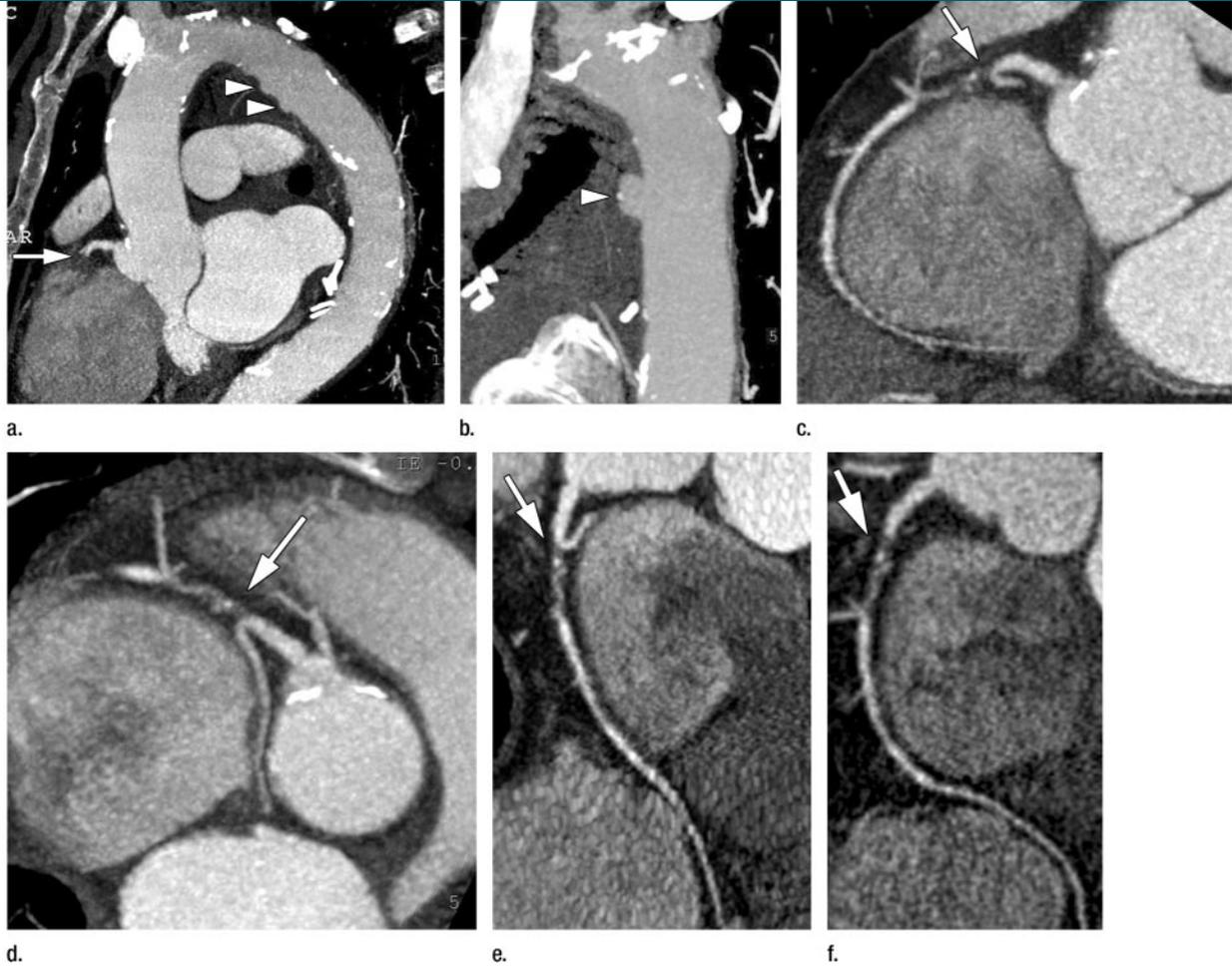
Timing of contrast agent injection

Figure 10



**a.** **b.**  
**Figure 10:** TRO CT angiogram in 79-year-old woman with recent onset of vague chest discomfort. TRO CT demonstrates type B aortic dissection extending from distal aortic arch to descending aorta. (a) Oblique slab MIP image shows entire aortic arch with dissection flap extending into the abdomen. (b) Coronal slab MIP image again demonstrates the dissection with asymmetric enhancement of true and false lumina.

Figure 11



**Figure 11:** TRO CT angiogram in a 74-year-old man with history of coronary disease and pulmonary embolism who presented with progressive chest pain over 6 months that became acutely worse on the day of presentation. Diagnosis of pulmonary embolism, a primary clinical consideration, was excluded at CT. **(a)** Oblique slab MIP image demonstrates ectatic aortic arch with atherosclerotic calcification and suggestion of two areas of aortic ulceration (arrowheads). Arrow = proximal right coronary artery. **(b)** A different obliquity on the slab MIP shows one of the ulcers, which measured 10 mm in width and extended 8 mm beyond the expected contour of the aorta (arrowhead). Comparison with earlier studies (not shown) demonstrated no notable change in appearance of the aortic ulcers. **(c)** Left anterior oblique slab MIP shows high-grade stenosis or possible proximal occlusion (arrow) in proximal right coronary artery. **(d)** Axial slab MIP confirms high-grade stenosis or possible occlusion (arrow) in proximal right coronary artery. **(e, f)** Curved MIP images of right coronary artery confirm the lesion (arrow) in proximal right coronary artery. Presence of ischemia in inferior wall and inferoseptum was confirmed with stress testing.

and image acquisition is a critical component of the study. When scanning is timed to begin 5 seconds after contrast material first appears in the left atrium, image acquisition corresponds to the “peak plateau” of contrast enhancement in the coronary circulation. The entire TRO study can be performed with 100 mL of contrast material with current 64-section scanners. Even faster scanning times with shorter injections may be achieved with newer CT systems that use 256 or 320 detector rows.

### Image Interpretation

Interpretation of TRO CT studies includes evaluation of the coronary arteries, as well as of other vascular and nonvascular structures. Most of the noncoronary structures are evaluated with axial 3–5-mm-thick images. Thinner sections may be obtained when needed for further evaluation of abnormalities detected on the 3–5-mm sections. For patients without substantial coronary disease, I prefer to evaluate

the coronary arteries with a combination of thin-section (0.6–0.8-mm) axial images and slab (5-mm) MIP reconstructions (Figs 6, 7).

Slab MIP images are reconstructed in real time during the interpretation session so that no additional technologist effort is required. It is important to be certain that each segment of each coronary artery is evaluated in multiple projections by rotating the slab MIP images on a workstation. The aorta and pulmonary arteries are evaluated with

the same viewing tools as are used for the coronary circulation (Figs 8–10). For more complicated cases where vascular calcifications or complex plaque are present, vessel-tracking software is useful to create curved MIP views that facilitate visualization of the coronary arteries in multiple planes (Fig 11).

For those patients scanned with a conventional helical acquisition, multiphase reconstructions are obtained at 10% increments throughout the cardiac cycle. Cardiac wall motion is evaluated on a workstation in standard echocardiographic projections, including four-, three-, and two-chamber and short-axis views. Any abnormality of regional wall motion should be correlated with the corresponding vessel on the coronary CT angiogram to search for and/or confirm a stenosis. Identification of a wall motion abnormality can confirm that a coronary artery lesion is functionally significant.

In a patient who does not have a high pretest likelihood of obstructive coronary disease, normal findings on a coronary CT angiogram serve to eliminate any further need for a diagnostic coronary work-up (61). In the practice at my institution, the diagnosis of ACS is effectively ruled out by a TRO CT scan that demonstrates normal coronary arteries or no more than minimal coronary disease (<25% stenosis). When there is more than minimal disease, further cardiac work-up may be appropriate. Although both calcified and noncalcified plaques may be associated with ACS, mixed calcified-and-noncalcified plaques with a predominantly noncalcified component are better correlated with ACS (62). The authors of one recent study (63) suggest that positive vascular remodeling, low-attenuation plaque, and spotty calcification in coronary plaques are associated with ACS. Unfortunately, the anatomic information provided by coronary CT angiography in the presence of substantial coronary disease may not be definitive for the functional diagnosis of ACS. Clinical trials are needed to define whether there is an appropriate appearance of coronary plaque and/or degree of coronary stenosis that can definitively in-

clude or exclude acute coronary syndrome. In the future, perfusion CT will be combined with coronary CT angiography to provide a more accurate diagnostic tool for evaluation of ACS.

### Conclusion

The TRO CT examination can be a powerful tool for evaluation and triage of patients with a low to moderate risk of ACS in whom diagnostic catheterization is not indicated. However, unlike most CT studies that can be performed by a technologist using a simple protocol, TRO CT studies require more individualized attention. Careful consideration regarding patient selection, patient preparation, and injection and scanning techniques will result in high-quality TRO CT studies to evaluate the aorta, coronary circulation, pulmonary arteries, and adjacent intrathoracic conditions. When compared with conventional management of acute chest pain in the ED, appropriate application of TRO CT can reduce (a) time for patient triage, (b) number of required diagnostic tests, (c) ED costs, and (d) radiation exposure to the patient.

**Acknowledgments:** The author acknowledges the assistance of Anish Koka, MD, and Kevin Takakuwa, MD, who reviewed the manuscript and provided insightful suggestions.

### References

- Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Nat Health Stat Report* 2008;7:1–38.
- Pope JH, Selker HP. Acute coronary syndromes in the emergency department: diagnostic characteristics, tests, and challenges. *Cardiol Clin* 2005;23(4):423–451, v–vi.
- Pope JH, Aufderheide TP, Ruthazer R, et al. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000;342(16):1163–1170.
- Christenson J, Innes G, McKnight D, et al. Safety and efficiency of emergency department assessment of chest discomfort. *CMAJ* 2004;170(12):1803–1807.
- Schull MJ, Vermeulen MJ, Stukel TA. The risk of missed diagnosis of acute myocardial infarction associated with emergency department volume. *Ann Emerg Med* 2006;48(6):647–655.
- Rusnak RA, Stair TO, Hansen K, Fastow JS. Litigation against the emergency physician: common features in cases of missed myocardial infarction. *Ann Emerg Med* 1989;18(10):1029–1034.
- Karcz A, Korn R, Burke MC, et al. Malpractice claims against emergency physicians in Massachusetts: 1975–1993. *Am J Emerg Med* 1996;14(4):341–345.
- Katz DA, Williams GC, Brown RL, et al. Emergency physicians' fear of malpractice in evaluating patients with possible acute cardiac ischemia. *Ann Emerg Med* 2005;46(6):525–533.
- Storrow AB, Gibler WB. Chest pain centers: diagnosis of acute coronary syndromes. *Ann Emerg Med* 2000;35(5):449–461.
- Meijer AB, O YL, Geleijns J, Kroft LJ. Meta-analysis of 40- and 64-MDCT angiography for assessing coronary artery stenosis. *AJR Am J Roentgenol* 2008;191(6):1667–1675.
- Marano R, De Cobelli F, Floriani I, et al. Italian multicenter, prospective study to evaluate the negative predictive value of 16- and 64-slice MDCT imaging in patients scheduled for coronary angiography (NIMISCAD-Non Invasive Multicenter Italian Study for Coronary Artery Disease). *Eur Radiol* 2009;19(5):1114–1123.
- Hamon M, Morello R, Riddell JW, Hamon M. Coronary arteries: diagnostic performance of 16- versus 64-section spiral CT compared with invasive coronary angiography—meta-analysis. *Radiology* 2007;245(3):720–731.
- Gallagher MJ, Raff GL. Use of multislice CT for the evaluation of emergency room patients with chest pain: the so-called “triple rule-out”. *Catheter Cardiovasc Interv* 2008;71(1):92–99.
- Thomas J, Rideau AM, Paulson EK, Bisset GS 3rd. Emergency department imaging: current practice. *J Am Coll Radiol* 2008;5(7):811–816e2.
- Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol* 2008;52(21):1724–1732.
- Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008;359(22):2324–2336.
- Khare RK, Powell ES, Venkatesh AK,

- Courtney DM. Diagnostic uncertainty and costs associated with current emergency department evaluation of low risk chest pain. *Crit Pathw Cardiol* 2008;7(3):191–196.
18. Gallagher MJ, Ross MA, Raff GL, Goldstein JA, O'Neill WW, O'Neil B. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low-risk chest pain patients. *Ann Emerg Med* 2007;49(2):125–136.
  19. Rubinshtein R, Halon DA, Gaspar T, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. *Circulation* 2007;115(13):1762–1768.
  20. Hollander JE, Chang AM, Shofer FS, McCusker CM, Baxt WG, Litt HI. Coronary computed tomographic angiography for rapid discharge of low-risk patients with potential acute coronary syndromes. *Ann Emerg Med* 2009;53(3):295–304.
  21. Chang SA, Choi SI, Choi EK, et al. Usefulness of 64-slice multidetector computed tomography as an initial diagnostic approach in patients with acute chest pain. *Am Heart J* 2008;156(2):375–383.
  22. Khare RK, Courtney DM, Powell ES, Venkatesh AK, Lee TA. Sixty-four-slice computed tomography of the coronary arteries: cost-effectiveness analysis of patients presenting to the emergency department with low-risk chest pain. *Acad Emerg Med* 2008;15(7):623–632.
  23. Chang AM, Shofer FS, Weiner MG, et al. Actual financial comparison of four strategies to evaluate patients with potential acute coronary syndromes. *Acad Emerg Med* 2008;15(7):649–655.
  24. Takakuwa KM, Halpern EJ. Evaluation of a “triple rule-out” coronary CT angiography protocol: use of 64-section CT in low-to-moderate risk emergency department patients suspected of having acute coronary syndrome. *Radiology* 2008;248(2):438–446.
  25. Ladapo JA, Hoffmann U, Bamberg F, et al. Cost-effectiveness of coronary MDCT in the triage of patients with acute chest pain. *AJR Am J Roentgenol* 2008;191(2):455–463.
  26. Goldstein JA, Gallagher MJ, O'Neill WW, Ross MA, O'Neil BJ, Raff GL. A randomized controlled trial of multi-slice coronary computed tomography for evaluation of acute chest pain. *J Am Coll Cardiol* 2007;49(8):863–871.
  27. Wexler L, Brundage B, Crouse J, et al. Coronary artery calcification: pathophysiology, epidemiology, imaging methods, and clinical implications—a statement for health professionals from the American Heart Association Writing Group. *Circulation* 1996;94(5):1175–1192.
  28. Hecht HS, Bhatti T. How much calcium is too much calcium for coronary computerized tomographic angiography? *J Cardiovasc Comput Tomogr* 2008;2(3):183–187.
  29. Fraker TD Jr, Fihn SD, 2002 Chronic Stable Angina Writing Committee, et al. 2007 chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to develop the focused update of the 2002 guidelines for the management of patients with chronic stable angina. *J Am Coll Cardiol* 2007;50(23):2264–2274.
  30. Han JH, Lindsell CJ, Storrow AB, et al. The role of cardiac risk factor burden in diagnosing acute coronary syndromes in the emergency department setting. *Ann Emerg Med* 2007;49(2):145–152.
  31. Fenster PE, Quan SF, Hanson CD, Coaker LA. Suppression of ventricular ectopy with intravenous metoprolol in patients with chronic obstructive pulmonary disease. *Crit Care Med* 1984;12(1):29–32.
  32. Quan SF, Fenster PE, Hanson CD, Coaker LA, Basista MP. Suppression of atrial ectopy with intravenous metoprolol in chronic obstructive pulmonary disease patients. *J Clin Pharmacol* 1983;23(8–9):341–347.
  33. Steigner ML, Otero HJ, Cai T, et al. Narrowing the phase window width in prospectively ECG-gated single heart beat 320-detector row coronary CT angiography. *Int J Cardiovasc Imaging* 2009;25(1):85–90.
  34. Lange RA, Hillis LD. Cardiovascular complications of cocaine use. *N Engl J Med* 2001;345(5):351–358. [Published correction appears in *N Engl J Med* 2001;345(19):1432.]
  35. Dattilo PB, Hailpern SM, Fearon K, Sohal D, Nordin C. Beta-blockers are associated with reduced risk of myocardial infarction after cocaine use. *Ann Emerg Med* 2008;51(2):117–125.
  36. Takakuwa KM, Halpern EJ, Gingold EL, Levin DC, Shofer FS. Radiation dose in a “triple rule-out” coronary CT angiography protocol of emergency department patients using 64-MDCT: the impact of ECG-based tube current modulation on age, sex, and body mass index. *AJR Am J Roentgenol* 2009;192(4):866–872.
  37. Hirai N, Horiguchi J, Fujioka C, et al. Prospective versus retrospective ECG-gated 64-detector coronary CT angiography: assessment of image quality, stenosis, and radiation dose. *Radiology* 2008;248(2):424–430.
  38. Shuman WP, Branch KR, May JM, et al. Prospective versus retrospective ECG gating for 64-detector CT of the coronary arteries: comparison of image quality and patient radiation dose. *Radiology* 2008;248(2):431–437.
  39. Brenner DJ, Hall EJ. Computed tomography: an increasing source of radiation exposure. *N Engl J Med* 2007;357(22):2277–2284.
  40. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. *JAMA* 2007;298(3):317–323.
  41. Thompson RC, Cullom SJ. Issues regarding radiation dosage of cardiac nuclear and radiography procedures. *J Nucl Cardiol* 2006;13(1):19–23.
  42. Halpern EJ, Levin DC, Zhang S, Takugawa. Comparison of image quality and arterial enhancement with a dedicated coronary CTA protocol versus a triple rule-out coronary CTA protocol. *Acad Radiol* (in press).
  43. Ferencik M, Nomura CH, Maurovich-Horvat P, et al. Quantitative parameters of image quality in 64-slice computed tomography angiography of the coronary arteries. *Eur J Radiol* 2006;57(3):373–379.
  44. Dewey M, Hoffmann H, Hamm B. Multislice CT coronary angiography: effect of sublingual nitroglycerine on the diameter of coronary arteries. *Rofo* 2006;178(6):600–604.
  45. Chun EJ, Lee W, Choi YH, et al. Effects of nitroglycerin on the diagnostic accuracy of electrocardiogram-gated coronary computed tomography angiography. *J Comput Assist Tomogr* 2008;32(1):86–92.
  46. Wittram C, Yoo AJ. Transient interruption of contrast on CT pulmonary angiography: proof of mechanism. *J Thorac Imaging* 2007;22(2):125–129.
  47. Oser RF, Zuckerman DA, Gutierrez FR, Brink JA. Anatomic distribution of pulmonary emboli at pulmonary angiography: implications for cross-sectional imaging. *Radiology* 1996;199(1):31–35.
  48. Remy-Jardin M, Remy J. Spiral CT angiography of the pulmonary circulation. *Radiology* 1999;212(3):615–636.
  49. Washington L, Goodman LR, Gonyo MB. CT for thromboembolic disease. *Radiol Clin North Am* 2002;40(4):751–771.
  50. Wittram C. How I do it: CT pulmonary angiography. *AJR Am J Roentgenol* 2007;188(5):1255–1261.

51. Hargaden GC, Kavanagh EC, Fitzpatrick P, Murray JG. Diagnosis of pulmonary emboli and image quality at CT pulmonary angiography: influence of imaging direction with multidetector CT. *Clin Radiol* 2006;61(7):600–603.
52. Cademartiri F, Mollet NR, Lemos PA, et al. Higher intracoronary attenuation improves diagnostic accuracy in MDCT coronary angiography. *AJR Am J Roentgenol* 2006;187(4):W430–W433.
53. Rist C, Nikolaou K, Kirchin MA, et al. Contrast bolus optimization for cardiac 16-slice computed tomography: comparison of contrast medium formulations containing 300 and 400 milligrams of iodine per milliliter. *Invest Radiol* 2006;41(5):460–467.
54. Rist C, Becker CR, Kirchin MA, et al. Optimization of cardiac MSCT contrast injection protocols: dependency of the main bolus contrast density on test bolus parameters and patients' body weight. *Acad Radiol* 2008;15(1):49–57.
55. Dodd JD, Kalva S, Pena A, et al. Emergency cardiac CT for suspected acute coronary syndrome: qualitative and quantitative assessment of coronary, pulmonary, and aortic image quality. *AJR Am J Roentgenol* 2008;191(3):870–877.
56. Fleischmann D, Rubin GD, Bankier AA, Hittmair K. Improved uniformity of aortic enhancement with customized contrast medium injection protocols at CT angiography. *Radiology* 2000;214(2):363–371.
57. Cademartiri F, Mollet NR, van der Lugt A, et al. Intravenous contrast material administration at helical 16-detector row CT coronary angiography: effect of iodine concentration on vascular attenuation. *Radiology* 2005;236(2):661–665.
58. Vrachliotis TG, Bis KG, Haidary A, et al. Atypical chest pain: coronary, aortic, and pulmonary vasculature enhancement at biphasic single-injection 64-section CT angiography. *Radiology* 2007;243(2):368–376.
59. Haidary A, Bis K, Vrachliotis T, Kosuri R, Balasubramaniam M. Enhancement performance of a 64-slice triple rule-out protocol vs 16-slice and 10-slice multidetector CT-angiography protocols for evaluation of aortic and pulmonary vasculature. *J Comput Assist Tomogr* 2007;31(6):917–923.
60. Litmanovich D, Zamboni GA, Hauser TH, Lin PJ, Clouse ME, Raptopoulos V. ECG-gated chest CT angiography with 64-MDCT and tri-phasic IV contrast administration regimen in patients with acute non-specific chest pain. *Eur Radiol* 2008;18(2):308–317.
61. Achenbach S. Computed tomography coronary angiography. *J Am Coll Cardiol* 2006;48(10):1919–1928.
62. Feuchtner G, Postel T, Weidinger F, et al. Is there a relation between non-calcifying coronary plaques and acute coronary syndromes? a retrospective study using multislice computed tomography. *Cardiology* 2008;110(4):241–248.
63. Motoyama S, Kondo T, Sarai M, et al. Multislice computed tomographic characteristics of coronary lesions in acute coronary syndromes. *J Am Coll Cardiol* 2007;50(4):319–326.