Contrast Use in Cardiac CTA Applications

Cardiac CT in the emergency room

Coronary calcium scoring, coronary CT angiography, and triple rule-out studies are powerful and efficient new tools in the triage of patients with chest pain.

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Chest pain is one of the most common reasons for presentation to the emergency room (ER). Perhaps one third of patients with chest pain will eventually be diagnosed with acute coronary syndromes. Many chest-pain patients have equivocal clinical findings, however, including normal cardiac enzyme levels and a nondiagnostic electrocardiogram (ECG). The potentially fatal consequences of inadvertently discharging a patient with acute myocardial infarction (MI) leads to approximately 2.8 million unnecessary inpatient hospital admissions each year in the United States, at an annual cost of ≥$6 billion.

Multislice computed tomography (CT) has the potential to more effectively triage patients who present to the ER with chest pain. Through the use of coronary calcium scoring, coronary CT angiography (CTA), and triple rule-out studies, CT can quickly determine whether a patient has significant coronary artery stenosis, aortic dissection, or pulmonary embolism. The potential for more accurate and efficient triage must be balanced against the limitations of performing CT in the ER setting, however. These include increased radiation exposure, the need for heart rate control, and difficulties in contrast administration.

Coronary calcium scoring

The negative predictive value of coronary calcium scoring for significant coronary artery disease (CAD) is very high. Four studies with a total enrollment of approximately 7500 patients have shown that 95% to 99% of symptomatic patients with a coronary calcium score of 0 have normal coronary arteries. A study from the Mayo Clinic evaluated whether CT could be used as a triage tool for patients who present to the ER with chest pain. The study involved 100 patients with no known history of coronary disease, normal or nondiagnostic ECG findings, and normal cardiac enzyme concentrations.

In addition to electron-beam CT (EBCT), patients were evaluated by treadmill exercise testing, coronary angiography, radionuclide stress testing, and/or echocardiography. In this population, with a low pretest likelihood of disease, 54% of patients had a coronary calcium score of 0. All were found to be free of significant coronary disease by other testing methods, giving CT a negative predictive value of 100%. Sensitivity was 100% and specificity was 63%.

The authors concluded that in patients with normal initial cardiac enzyme concentrations and normal or indeterminate ECG findings, EBCT could safely be used to guide discharge decisions without further testing. This finding has been reproduced in 3 other studies. The largest study, which has extended enrollment to 1000 patients, found that CT had a negative predictive value of 99% for significant coronary disease or MI.

A study by Georgiou et al examined the prognostic implications of an elevated coronary calcium score in patients with chest pain and a nondiagnostic ECG. The study enrolled 225 patients, each of whom was examined by EBCT in the ER. After an average of 4 years of follow-up, investigators observed a strong relationship between the baseline coronary calcium score and the rate of cardiac events, including MI and death. A score of 0 was associated with an excellent prognosis (annual event rate 0.6%), whereas a coronary calcium score >400 was associated with a much worse prognosis (annual event rate of 13.9%).

Coronary CTA

There are limited data on the use of coronary CTA in the ER setting. Gallagher et al prospectively evaluated 85 patients with low-risk chest pain, using both rest-stress sestamibi nuclear imaging and 64-slice multidetector CT. Patients with a reversible perfusion defect on myocardial perfusion imaging or abnormal findings on CT (stenosis >50% or calcium score >400) were referred for invasive angiography. All patients were followed-up within 30 days to document any evidence of major adverse cardiac events. The authors concluded that the accuracy of multidetector CT was at least as good as that of stress myocardial perfusion imaging.
imaging for the detection and exclusion of an acute coronary syndrome.

A study by Raff et al., from the same institution, took this finding a step further, prospectively randomizing low-risk patients with chest pain to 64-slice CTA in the ER or standard care, including serial cardiac enzymes, ECG, and rest-stress nuclear imaging. A total of 67% of patients had a negative multislice CT scan, defined as absent or minimal calcification and luminal stenosis <30%, and were rapidly discharged home with a diagnosis of noncardiac chest pain. Eight percent of patients had a >70% stenosis on coronary CTA and were referred for invasive angiography. The remaining patients, who had either an intermediate-grade stenosis or an unreadable CT, were referred for nuclear stress testing.

Investigators analyzed such parameters as diagnostic accuracy, time to diagnosis, and length of stay. All favored cardiac CT. For example, 75% of patients had immediate triage based on the findings of multislice CT, resulting in a 77% reduction in average diagnostic time (from 15.0 to 3.4 hours) and a 16% reduction in average ER costs. In addition, there were no significant differences in the incidence of major adverse cardiac events in the 2 groups. No patient discharged home on the basis of a negative CT scan was found to have CAD during 6-month follow-up.

These findings suggest the potential for coronary CTA and coronary calcium scoring to play an important role in the ER triage of patients with chest pain. They come from a single study and a single institution, however, and must be confirmed by further research. A multicenter study is under development.

A key step in ensuring both the safety and the cost-effectiveness of CT as a triage tool is the selection of a reasonable threshold for referral for further testing. Raff et al. set the threshold low, at a 30% stenosis. At Harbor–University of Los Angeles (UCLA) Medical Center, we use 50% stenosis as the threshold for identifying a positive examination.

Triple rule-out

In a triple rule-out examination, multislice CT is used to evaluate 3 leading causes of chest pain: coronary disease, aortic dissection, and pulmonary embolism. CT has proven to be highly accurate in the evaluation of each of these conditions.
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Studies are needed to determine whether it is possible to achieve, in a single examination, images that are diagnostic for all 3 conditions, and whether CT will be equally accurate when the 3 studies are combined into 1.

A small study from Italy used a triple rule-out protocol to evaluate 23 patients with equivocal chest pain. All underwent contrast-enhanced ECG-gated 64-slice CT of the thorax. Of the 23 patients, 11 had no pathological findings, 2 had extensive pulmonary embolism, and 2 had <50% coronary artery stenosis. An additional 8 patients had significant CAD (>50% stenosis). In this last group, invasive angiography confirmed the CT findings in all cases. Patients without CT findings were discharged the same day. The average length of hospitalization and the total hospital charges were significantly lower in study patients as compared with matched controls. The authors concluded that ECG-gated 64-slice CTA of the entire thorax is technically feasible and enables rapid determination of cardiac and noncardiac causes of chest pain.

The first diagnosis addressed by the triple rule-out examination is obstructive CAD (Figure 1). Although there are limited studies on the use of coronary CTA in the ER setting, this application has the potential for widespread use. Within seconds, multislice CTA can rule out significant CAD or triage patients to cardiac catheterization.

**FIGURE 2.** A triple rule-out examination shows aortic dissection arising in the descending aorta. The coronary and pulmonary arteries were normal in this patient. (A through C) These angiographic views of the coronary arteries reveal no stenosis. (D) A sagittal view shows an aortic dissection originating in the descending thoracic aorta and continuing into the iliac bifurcation. (E) An axial slice depicts an aortic dissection. (F) An endoscopic view of the aortic dissection.
Summary data from a new American Heart Association Scientific Statement demonstrates a 98% negative predictive power for cardiac CT to exclude significant angiographic stenosis.\textsuperscript{14} Not all vessels are visualized by coronary CTA, however, and careful attention must be paid to the details of contrast administration and image acquisition in order to achieve sufficient image quality.

Nearly a decade ago, Rubin\textsuperscript{14} showed that CT had a sensitivity and specificity of 100% for aortic dissection. One of the most important advantages of CT is its ability to not only detect aortic dissection but also to visualize the dissection from the origin of the great vessels through the entire length of the aorta (Figure 2). Multislice CTA has completely replaced transesophageal echocardiography for this application in our institution.

The triple rule-out examination has a potentially important role in the diagnosis of pulmonary embolism (Figure 3); however, data on this application are limited. There are few, if any, published studies on the use of 64-slice CT for the evaluation of suspected pulmonary embolism. Clinical experience with earlier-generation scanners suggests it is possible to visualize third-, fourth-, and perhaps even fifth-generation branches of the pulmonary arteries.\textsuperscript{15}

It is reasonable to question the need for a triple rule-out examination. One might wonder how often an ER physician is likely to suspect pulmonary embolism, aortic dissection, and CAD in the same patient. Figure 4 shows a rare case in which a triple rule-out study actually detected all 3 conditions in a single patient. The patient had aortic dissection, pulmonary embolism, dense calcific plaque in 1 coronary artery, and at least 1 occluded coronary bypass graft.

A triple rule-out examination can visualize additional pathology, including aortic aneurysm; coarctation of the aorta; pericardial thickening, calcification, and effusion; interstitial lung disease; pneumothorax; and pneumonia.

Limitations

The triple rule-out examination has several limitations and challenges (Table 1), one of the largest being contrast administration. It is difficult to deliver contrast so as to achieve optimal opacification of not just the right heart, left heart, and coronary arteries but also the pulmonary arteries. The timing of contrast injection and the duration of contrast enhancement require special attention. Typically, this means either administering a larger contrast dose than would be used for coronary CTA—\(\geq 100 \text{ mL}\)—or using a multiphasic protocol with a long secondary injection of mixed contrast at a low flow-rate.

Another limitation of the triple rule-out study is the need to achieve good heart rate control in order to perform a high-quality study that yields definitive information on both coronary calcification and arterial obstruction. The goal heart rate of \(\leq 60 \text{ bpm}\) is particularly difficult to achieve in the ER setting. The patient’s heart rate is likely to be high as a result of anxiety, stress, and pain. The use of beta-blockers may be appropriate in patients with coronary disease or aortic dissection, but may not be indicated in patients with pulmonary embolism. Whether the study should be performed at all in the absence of good heart rate control is an open question.

Just as with coronary CTA, patients may be ineligible for a triple rule-out examination because of arrhythmias, renal dysfunction, or allergies to contrast material. Obesity and calcification also interfere with the quality of the study.

The radiation dose associated with a triple rule-out study can reach 25 to 40 mSv. A key reason for the high radiation dose is the need for retrospective ECG gating. The motion of the lungs is even greater than that of the heart. In fact, to prospectively capture motion-free images of the lungs and pulmonary arteries would require a temporal resolution of 18 msec, as compared with 35 msec for the heart. Therefore, in order to visualize small-branch vessels and small pulmonary emboli, it is useful to gate image acquisition in both the heart and lungs. Many triple rule-out protocols specify gating from the apex of the heart through the diaphragm. A slow pitch, thin slices, and redundant overlap each increase the radiation dose.

Are the diagnostic findings worth the radiation dose? From the perspective of an ER physician, the answer is yes. A leading cause of malpractice suits against ER physicians is misdiagnosis of chest pain. An imaging examination that can rule out coronary disease, aortic dissection, and pulmonary embolism with \(>90\%\) accuracy will be widely used; however, it is a decision that is likely to be driven less by science than by practicality.

One way to reduce the radiation dose is to use a thin-slice mode through the heart and a thick-slice mode for the remainder...
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of the study. This is a more challenging protocol for radiologic technicians to implement, however. At Harbor–UCLA Medical Center, we use a third approach that involves performing 2 separate scans. First, we perform coronary CTA, which delivers a radiation dose of 10 to 12 mSv with dose modulation. We then perform lung CT, using thicker slices without overlap, for an additional radiation dose of 4 to 5 mSv. This approach is much easier for the radiologic technicians to implement and results in a lower total radiation dose, shorter breath-hold times, and a similar contrast dose, as compared with a single thin-slice scan.

An additional advantage of this approach is that cardiac CT and lung CT studies can be read by different physicians with appropriate subspecialty expertise. Health insurers will generally pay for both scans and interpretations, as they are each done for different indications.

A shortage of experienced CT technologists makes it difficult to offer the triple rule-out examination 24 hours a day. Even if a skilled technologist is available, performing a triple rule-out study in the middle of the night but deferring reading of the study until the next morning exposes the physician and the hospital to liability. Therefore, the most sensible approach may be to limit triple rule-out studies to normal business hours, when both the technologist and the interpreting physician are available.

Under the auspices of the American College of Cardiology, a multidisciplinary committee recently released appropriateness criteria for cardiac CT.16 It indicates that a triple rule-out examination is potentially appropriate for the exclusion of obstructive coronary disease, aortic dissection, and pulmonary embolism in patients with an intermediate pretest probability for at least 1 of these conditions, assuming the ECG shows no ST-segment elevation and initial enzymes are negative.

Perfusion imaging

CT myocardial perfusion imaging is the subject of active research. Early studies have produced promising results. Mahnken et al17 evaluated whether contrast-enhanced multislice CT was comparable to contrast-enhanced magnetic resonance imaging (MRI) for depiction of acute MI. The study involved 28 post-MI patients who underwent 16-slice CTA and, within 5 days, gadolinium-enhanced MRI. All studies were completed within 2 weeks of an acute MI.

Investigators compared the area of MI as determined by the 2 imaging techniques. There was good agreement between contrast enhancement patterns on late-enhancement MRI and late-enhancement CTA. The results were not as concordant on early-phase imaging. The authors concluded that late-enhancement CT appears to be as reliable as delayed contrast-enhanced MRI in assessing infarct size and myocardial viability in acute MI.

These and other investigators continue to evaluate the potential of CT myocardial perfusion imaging in human and animal studies. If this technique comes to fruition, it will represent another breakthrough in CT and another reason for performing cardiac CT in the ER.

Table 1. Practical limitations of triple rule-out CT angiography

- Beta-blockers are required for coronary CTA, but may not be safe in patients with pulmonary embolism
- High radiation dose: approximately 25 to 40 mSv from a single scan; 14 to 18 mSv from separate coronary CT and chest CT scans
- Not available 24 hours a day (lack of experienced technologists, readers, and physician supervision)
- Increased contrast volume (>100 mL)
- Obesity and calcifications limit interpretation
- Patient exclusion criteria:
  - Rapid heart rate
  - Arrhythmias
  - Renal dysfunction
  - Contrast allergies

FIGURE 4. CT angiography reveals (A) an aortic dissection of the transverse aorta and (B) a pulmonary embolism of the right pulmonary artery, dissection involving the ascending and descending aorta, and dense calcific plaque in the circumflex artery. (C) A volume-rendered image depicts a patent left internal mammary artery and a diseased saphenous vein graft.
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Conclusion
Multislice CT has the potential to more effectively triage patients who present to the ER with chest pain. Coronary calcium scoring is highly accurate for ruling out significant coronary disease. It may overlook noncalcific plaque but represents a good first step and should be incorporated early into the work-up of patients with chest pain. There are limited data on the use of coronary CTA in the ER, but in other settings, this diagnostic tool has proven to have a high negative predictive value, assuming sufficient image quality. The triple rule-out examination has the potential to rule out coronary disease, aortic dissection, and pulmonary embolism in a single study with >90% accuracy. It will likely have widespread appeal in the ER. Finally, research into CT myocardial perfusion imaging is in its early stages. It offers the potential for another critical breakthrough in cardiac CT.

References

Discussion
Elliott K. Fishman, MD:
Thanks very much, Matt, for a terrific talk. I just want to make one clarification. When I mentioned we do the scan in the morning, that’s the nuclear studies, not the CT scans. We don’t wait for the CTs in the morning, and we’re starting the ER program, as well. I agree with you that the biggest challenge is the technical side. The reading is the second challenge. So we’re doing a sort of a compromise, in that we’ll do the cardiac CT until 11:00 PM, and then from 11:00 PM to 7:00 AM we’re not going to do it. Another big challenge is getting the best technologist in at that hour.

I have a question. When you’re doing the triple rule-out and you’re doing the two acquisitions, do you inject the second time, or do you go with that first bolus?

Matthew Budoff, MD:
It depends on the order. If we’re looking for pulmonary embolism, and that’s a serious consideration, then we usually do the heart first. Then we’ll do a second bolus for the venous enhancement and right side enhancement, so we would need a second bolus to get good contrast opacification in the pulmonary arteries.

We have been doing thicker slices and full studies to try to get a full PE study. Gating is better, but we can always look back at the cardiac gated studies, at least for the proximal pulmonary arteries, and our radiologists are looking at those studies to get the most important, clinically significant pulmonary emboli.

Fishman: Even for routine pulmonal studies, we don’t gate. The whole literature is without gating basically. When you say “thick,” do you mean 3 or 5 mm?

Budoff: We vary between the two thicknesses, but we mostly prefer 3 mm instead of 5. But a lot of literature was done with 5-mm slices.

Achenbach: I really like the concept of 2 separate scans, but they would, of course, be best if the cardiac scan was read first, and then the decision was made to go on to do a full chest scan. This way, if you have a patient who has a coronary lesion and has to go to the angiogram, then you can save the radiation and additional contrast that you would spend if you did the chest scan, and rather use it in the cath lab. So the optimal thing would be to read the cardiac scan before you then go on to the complete chest.

Budoff: Absolutely. I agree with you. It’s just a practical matter of getting people to and from the scanner. Half of the time is spent getting the patient on the table and setting them up on the table, so the techs don’t want to have to take them off the table, and then start again.

Stephan Achenbach, MD:
No, I understand. The best thing would...
be to have a physician there and read the cardiac CT scan. Then, if the patient needs to go to the cath lab, go to the cath lab. Then, if the coronaries are clear, we’ll do the rest of the test.

FISHMAN: It makes a lot of sense. By doing them very close, you’re doing them one after another, you don’t have to give much additional contrast. If you waited for someone to review the study, you’d have to do another reasonable-size bolus.

ACHENBACH: Roughly 50 mL would probably be enough, wouldn’t it?

FISHMAN: Pulmonary emboli are hard to see with 50 mL.

BUDOFF: We used less on the second study because we do them in rapid succession. We do use smaller boluses.

FISHMAN: If you just go back and forth from one to the other, and you’re doing 80 mL on the cardiac, you probably can get by with 40 or 50 mL on the pulmonary side, if you waited only a few seconds.

BUDOFF: Right. We found the contrast dose is about the same if you do 2 versus 1, because if we did 1, we’re going to give a longer bolus, and then each study is optimized. We have to measure this better, but the radiation dose is approximately 50% of what you would have done if you did it all as 1 study. So, if you forget about the billing issues and the interpretation issues in the U.S. (where only 1 physician is supposed to get their hands on a study), it would have been much more practical for us to have 2 studies done.

SAMUEL WANN, MD, MACC: Is there any rationale for that even on a standard cardiac study? I do look at the proximal pulmonary arteries and usually make a stock statement about the major pulmonary arteries, given the limitations of the coronary study, that there are no major pulmonary emboli. It seems to me that a lot of times in the emergency room that’s enough. I tell the guys when they ask for a triple rule-out, if they want a pulmonary angiogram, they ought to order it. But we do read the pulmonary arteries. There is some contrast in them, but it’s suboptimal. I wonder what data there are, or what your opinions are. I’m concerned, of course, that the small subsegmental pulmonary emboli are not clinically irrelevant, but don’t make much difference to patient outcome anyway.

ACHENBACH: Not for the outcome perhaps, but of course, that would be an explanation for the patient’s chest pain, and could prevent further testing in some other direction, as you say is more than pulmonary embolism somewhere.

WANN: Chest pain is often vague and it may be difficult to establish a causal relationship even if there is known pathology.

BUDOFF: Not only that, but how do we treat that patient? Every therapy is either indicated or contraindicated based on 1 of the 3 diagnoses, and we think the aortic dissection is old because there is some calcification in the wall of the dissection plane lower down, and maybe the acuity is the pulmonary embolism, but you’re still not going to heparinize or anticoagulate a patient with a large type A and B dissection. So, on that patient, we are stuck to watch and wait, and almost do nothing for the patient, even though we made 3 diagnoses.

WANN: So you say that detecting small subsegmental pulmonary emboli could prove an explanation of chest pain? I guess I challenge you to prove that to me.

ACHENBACH: I’m not saying it’s sufficiently been explained, but if you find a reason, at least you have some reasoning that you might not do something crazy for other testing that you otherwise would be doing.

FISHMAN: I think the other issue about doing it your way with the 2 doses is that people try to do too many things at one time. They do each one of them equally poorly. They have a poor coronary study. Dissection is probably the easiest to see, right? But if you have a poor PE study, and you have a poor coronary study, then you end up with nothing.

There is something we need to be careful about. I’m sure your hospitals are probably similar in that there are certain patients who come in 2 or 3 times a year for chest pain. It’s impossible to tell a clinician that since the last 3 were negative, there’s no PE. You can’t go far with that. But, I think we have to figure out some rules to say: if you had a coronary CTA within the last X months or X years, and it’s negative, we’re not going to do it again. We need to know if there’s some magic number where you can say that.

ACHENBACH: It depends on negative. I mean, if you have no calcium and no plaque visible, I think then you can be pretty sure. But if you had a CTA before that showed something like a 40% to 60% narrowing, we consider it significant at that point, and then the patient comes back 3 months later, he might have more.

FISHMAN: I agree there. But the situation I mean is when it’s normal.

ACHENBACH: Entirely clear.

FISHMAN: If a 35-year-old patient comes to the ER with acute chest pain, you rule out dissection. Then you go back to the records, and you see that he’s had 6 other of these rule-out PE and rule-out dissection. You need to be able to say, “Look, it was normal, not 30% or anything.”

BUDOFF: I think you can extrapolate from the cath data and say that you have at least a 5-year window during which it is very unlikely that they’re going to develop significant coronary artery disease over that period, and maybe even longer. We don’t have enough outcome data, but if you can add the calcium data in, if they had a calcium score of 0, we have a 5-year window for that, saying their event rates are low as well. So just adding the two together gives you more confidence that you have a 5-year window.

FISHMAN: I made that comment, particularly with Stephan here, because there is work to be done in cardiac CT. One of the issues with CT in general was this concern about detecting lung nodules. Everybody has a lung nodule, anywhere from 4-16, to 64-slice CT, there is no normal patient. Everyone has a 2-mm nodule. Now the societies have said that if it is <4 mm, forget about it. I think statements like that help guide practice. I can imagine that in the ER
setting you’ll have someone say, “Look, I don’t care if it was negative before. I’m telling you I want it anyway.” If you can have firm data that says whatever window you want to come up with, having guidelines would be very critical in that situation, particularly with the dose of cardiac CT being high.

ACHENBACH: Absolutely. The problem is that we need at least some data to develop guidelines. So we’ll have to wait a little before we can come up with guidelines.

WANN: I’m always concerned that the coronary CT is being held to a very, very high standard. We accept pulmonary CTA as the state-of-the-art gold standard test without much supporting data. Coronary CT is under great scrutiny. I don’t know of a whole lot of data supporting CTA of the renal arteries, yet it’s well accepted. It seems reasonable to me to accept it, but I point out a dichotomy between the level of proof being required for coronary CTA, and other applications.

ACHENBACH: If you look at the guidelines for the diagnosis of pulmonary embolism, they are very careful.

WANN: It’s what data they’re based on, though. It’s all expert opinion.

ACHENBACH: No. They’re based on studies that were performed. For example, if you have a clear rule-out of pulmonary embolism with spiral CT, then it is safe to withhold anticoagulation. These data are just starting to appear now. In the U.S., I don’t think there is a guideline that supports this, as far as I know. But I’ve done some research on this. There is a very recent guideline by the British Society of Radiology that says you can withhold anticoagulation. But if you look at the actual guidelines, they’re very, very slow to come out. According to my knowledge, there is no guideline in the U.S. that would support the use of spiral CT for pulmonary embolism rule-out.

CHIP GILKESON, MD: There may not be a guideline now, but there surely have been studies, though. Their outcome is that for a negative CT, for 6 months to a year, it’s good. It’s interesting, though, certainly from the ER perspective about the dreaded complication of a missed MI. Their standard of a miss is amazing. For example, in Charlie White’s data using 16-slice CT in his study of roughly 28 patients, there are 1 or 2 missed significant stenosis. I think there is a psychology, particularly from the ER, that they do not tolerate anything. With PE, 99% or small segmental emboli, okay. But there’s a psychology that any kind of miss, even 1%, in cardiac and coronary disease is not acceptable to the ER.

BUDOFF: That’s their lawsuit, that’s why. That’s their number one liability.

GILKESON: Right. That really is the drive I think.

ACHENBACH: If the cardiac CT report says there’s nothing, then at least they’re out of their liability problem.

BUDOFF: Yes, they shifted the liability to the interpreter.

FISHMAN: Right. I think that’s another issue. Since the guidelines of how people have managed with nuclear studies, it is very clear to change a guideline. It can be determined so that a negative CT means “good-bye, you’re out of the hospital in 2 hours.” That’s like, take a deep breath, swallow, and you’ve made a decision. Often in imaging, you come up with decisions that may let things change that rapidly. This will. You’re kicking the person out of the ER in a way that you wouldn’t have managed them before, and I think that’s where you need 100% accuracy. The concept of 99% is not going to work. I think we all would agree that the biggest growth in cardiac CT is going to be in the ER, and the biggest thing, really, is the challenge of staffing. At Hopkins, I think we have the world’s best technologists, and my techs would tell me that’s true. But even they admit that the people who work between 11:00 PM and 7:00 AM are a different group. Also, the fact that you don’t have your main physicians at that time and you don’t have your own nursing at that time makes it the most challenging of times.