HEART REVIEW

Non-invasive coronary angiography using multislice computed tomography

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Non-invasive methods for detection of coronary atherosclerosis have been limited to indirect markers, such as myocardial perfusion or wall motion during exercise or pharmacological stress. However, advances in multislice computed tomography (MSCT) not allow sufficient spatial resolution for direct non-invasive imaging of the coronary arteries. This review focuses on imaging techniques and clinical applications of MSCT in human studies. Published studies of the diagnostic accuracy of MSCT in native coronary arteries and bypass grafts indicate excellent sensitivity and specificity for detection of 50% diameter stenosis. MSCT is particularly good for evaluating the origin and course of anomalous coronary arteries. MSCT offers the ability to visualise both the lumen and wall of artery, as well as to quantify coronary classification. Further technical developments promise to render MSCT the ideal non-invasive tool for direct visualisation of the coronary arteries.

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Invasive coronary angiography has long been the reference standard for the detection of coronary atherosclerosis. It is generally safe, with a serious complication rate of <1/1000.[1] At present, over 4 million cardiac catheterisations are performed yearly in the United States. Of these, up to 27% have either angiographically normal coronary arteries or minimal atherosclerosis.[2] Given the expense of cardiac catheterisation and the desire to use this valuable resource for therapeutic rather than diagnostic purposes, there is a strong impetus to develop non-invasive means of accurately detecting coronary atherosclerosis. This review focuses on multislice computed tomography (MSCT) for coronary artery imaging.

CALCIUM SCORING

Electron beam computed tomography (EBCT) has long been available for detection of coronary calcium deposits as a surrogate marker for coronary atherosclerosis. EBCT uses a rotating electron beam and a stationary tungsten target, which allows very fast scan times, and prospective ECG gating. This is important because the heart, unlike other organs, is in constant motion. EBCT does not require iodinated contrast and therefore cannot distinguish between soft plaque, the arterial wall and the blood within the lumen of the artery. The only identifiable part of the coronary artery is calcium within an atherosclerotic plaque. This is identified by high *x* ray attenuation values (Hounsfield units >130 HU). Although high calcium scores are sensitive for the presence of significant coronary artery disease (CAD), an American College of Cardiology/American Heart Association consensus panel did "not recommend EBCT for diagnosing obstructive CAD because of its low specificity." Furthermore, calcium scoring cannot identify "soft" plaque, which may be more prone to plaque rupture and acute coronary syndromes.

Accordingly, calcium scoring by EBCT is probably best used as a risk factor for CAD rather than as a diagnostic test. With the advent of 16 and now 64 slice scanners, the temporal resolution of MSCT is now on par with EBCT, and MSCT can substitute for EBCT in the evaluation of coronary calcium.[3] In head-to-head comparisons, MSCT tends to have better spatial resolution and contrast-to-noise ratios, which leads to improved detection of pathology in smaller and more distal portions of the coronary tree.[4–6]

MULTISLICE COMPUTED TOMOGRAPHY

MSCT scanners employ an *x* ray beam and multiple detectors. The patient is placed on a table, which moves through the rotating *x* ray beam, producing a spiral scan. Early MSCT instruments used four detectors; current clinical MSCT scanners use 16 or 64 detectors. These acquire volumetric data with a nearly isotropic voxel of roughly 0.4×0.4×0.5 mm, exceeding current MRI scanners in spatial resolution. Postprocessing of acquired raw data is typically performed after the scan by the interpreting physician. Several techniques can be used for reconstruction of the data, including curved reformat, three-dimensional rendering, as well as standard oblique, saggital and coronal views. Axial (ie, raw) data can also be evaluated if there is any question as to whether artefact has crept into the reconstruction algorithms (fig 1). As many of these views are reconstructions of a raw dataset, there are opportunities for artefacts to appear in the final images.

TECHNIQUE/PROTOCOL FOR SCANNING

The predominant issues with MSCT imaging of the coronary arteries are all motion related. Images must be acquired at a portion of the cardiac cycle where it is most motionless, typically during diastole. In EBCT, the scanner can be turned off and on with such rapidity that it is possible to

Abbreviations: CAD, coronary artery disease; EBCT, electron beam computed tomography; LAD, left anterior descending; MSCT, multislice computed tomography; RCA, right coronary artery

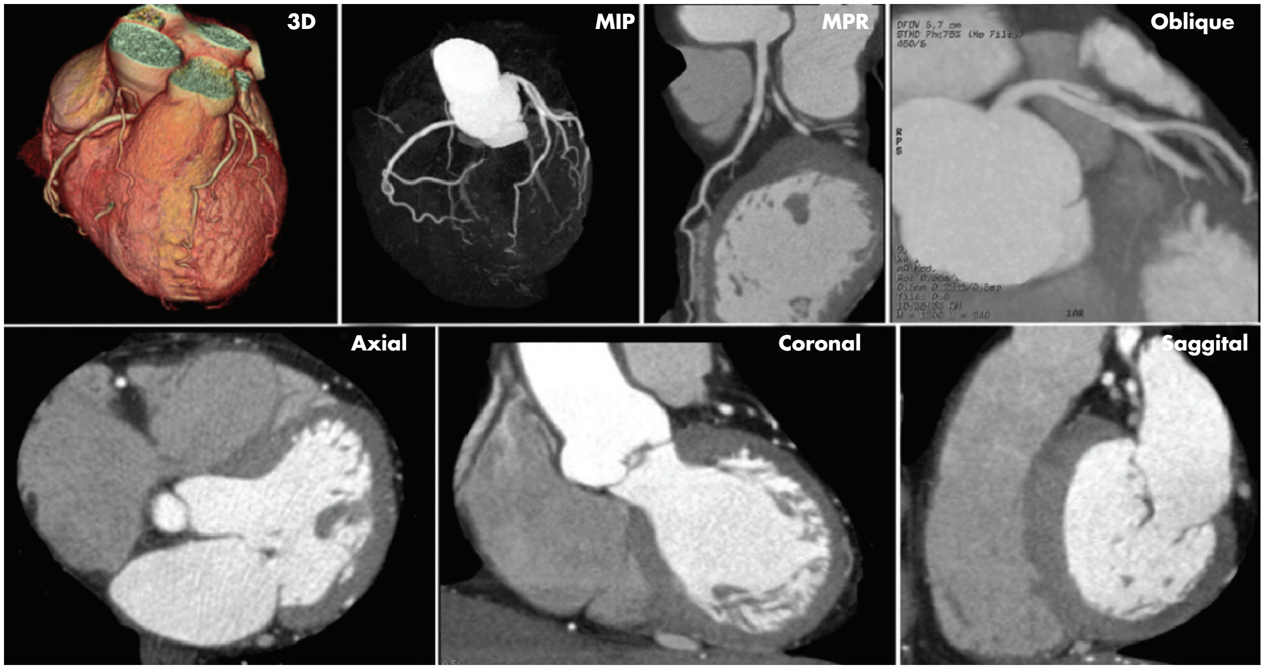

Figure 1 64-slice cardiac images of a normal heart and coronary arteries. These include three-dimensional (3D), maximum intensity pixel (MIP), as well as curved reformat and oblique views of the left main and left anterior descending arteries. Axial, coronal and saggital views give information concerning chamber size, wall thickness and (to a lesser degree) valvular structure. MPR, multi-planar reformat.

prospectively gate the scan and acquire images only during a specified part of the heart cycle. Multislice coronary CT usually uses retrospective gating, in which the entire cardiac cycle is acquired and then only end-diastolic images are reconstructed. The advantage with prospective imaging is that it involves less radiation exposure to the patient. The advantage to retrospective gating is that since images have been acquired during the entire cardiac cycle it is possible to evaluate cardiac function (ie, ejection fraction). Current MSCT scanners have the option of modulating the amount of radiation given during a particular part of the cardiac cycle, allowing reduction of the total radiation dose while still acquiring information throughout the whole cycle.

Controlling the heart rate and rhythm are of paramount importance to the acquisition of a CT coronary angiogram. With newer 64-detector instruments, excellent images can be obtained with heart rates <80 beats/min. However, optimal images are obtained with a heart rate <60. This may require intravenous β-blockade at the time of scanning. Even more important than heart rate is heart rhythm. Irregular rhythms confound the ability of the scanner to gate to the cardiac cycle, especially with retrospective gating. Thus, patients with atrial fibrillation or frequent atrial or ventricular ectopy are prone to motion artefacts.

Breath holding is mandatory for coronary CT scanning. With coronary CT imaging, overlapping slices are required as only a portion of the cardiac cycle is used. This mandates breathholds of approximately 25 s for 16-detector scanners. With 64-slice technology, this breathhold is reduced to approximately 5 s. The shorter scan time reduces the likelihood of poor scan quality due to respiratory motion artefact, as well as potential patient movement and heart rate variability (fig 2).

CT coronary angiography involves at least two separate scans, with separate breathholds of varying lengths. The first scan is a "scout" image, which is taken without contrast. It is a relatively low-resolution (and low-radiation) scan obtained at a slice thickness of several millimetres. Using this initial scan, the location of the left main coronary can be determined. At this point, timing of the contrast bolus can be achieved in one of

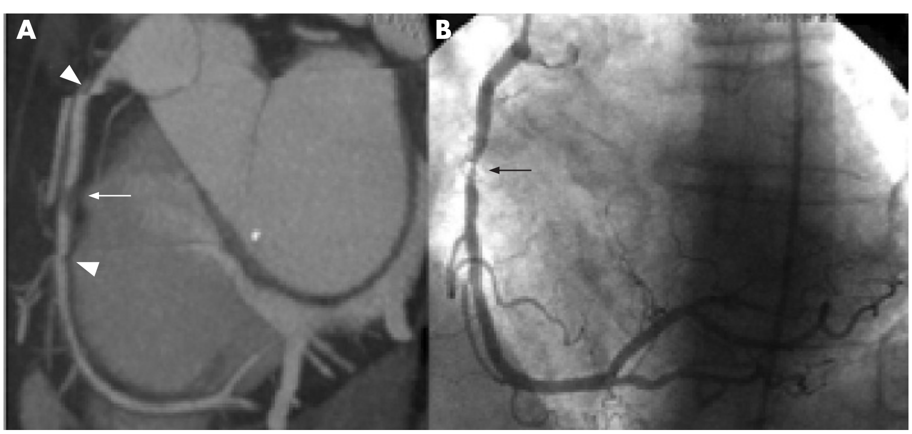

Figure 2 64-slice coronary CT (A) and conventional coronary angiogram (B) demonstrating a "high-grade" lesion (arrow) in the mid-right coronary artery. Note that there are two areas of registration artefacts (arrowheads) which could be mistaken for stenosis.

Table 1 Accuracy of multislice computed tomography in detecting stenosis of >50% diameter

Author	Number of pts/seg	Type of patient	Analysis by segment Sens	Spec	PPV	NPV	Analysis by patient Sens	Spec	PPV	NPV
16-slice MSCT										
Achenbach[8]	22/83	No symptoms	82	86	91	76	NR	NR	NR	NR
Herzog*[9]	38	Chest pain	NR	NR	NR	NR	72	100	100	80
Schuijf[10]	45/450	Chest pain	85	89	71	95	NR	NR	NR	NR
Mollet[11]	128/1384	Stable angina	92	95	79	98	100	86	97	100
Hoffman[12]	33/530	Known CAD	63	96	64	96	86	82	90	75
Achenbach[13]	50/128	Suspected CAD	100	83	NR	NR	94	96	69	99
Kuettner[14]	60/780	Suspected CAD	72	97	72	97	NR	NR	NR	NR
Ropers[15]	77/62E	Suspected CAD	92	93	NR	NR	85	78	82	81
Hoffman[16]	103/1384	Suspected CAD	95	98	87	99	97	87	90	95
Kopp[17]	102/1200	Suspected CAD	93	97	81	99	NR	NR	NR	NR
Nieman[18]	58/231	Suspected CAD	95	86	90	97	NR	NR	NR	NR
Schuijf[19]	31/277	HTN	93	96	88	98	95	80	91	89
Burgstahler[20]	10/21	Prior CABG	86	100	75	86	NR	NR	NR	NR
Schlosser[21]	48/131	Prior CABG	96	95	81	99	NR	NR	NR	NR
Martuscelli[22]	93/285	Prior CABG	97	100	NR	NR	NR	NR	NR	NR
Burgstahler[23]	13/43	Prior CABG	83	93	89	100	NR	NR	NR	NR
64-slice MSCT										
Leber[24]	55/798	Stable angina	73	97	NR	NR	88	85	NR	NR
Leschka[25]	67/1005	Suspected CAD	94	97	87	99	100	100	100	100
Raff[26]	70/1065	Suspected CAD	86	95	66	98	95	90	93	93
Pugliese[27]	35/494	Stable angina	99	96	78	99	100	90	96	100

CABG, coronary artery bypass graft; CAD, coronary artery disease; E: evaluable segments (excluding artefacts); HTN, hypertension; NR, not reported.
*used a definition of stenosis of 75% diameter.

two ways. A test bolus of ~10 ml of iodinated contrast can be given, while a region of interest (ROI) is placed in the aorta at the level of the left main coronary. Continuous low-level scanning is performed, and a contrast timing peak is then obtained, which determines the transit time from the intravenous line (typically a large-bore, antecubital intravenous) to the arrival at the level of the coronaries. Using this timing bolus, the final scan is performed with the true contrast bolus. Alternatively, continuous low-level scanning can be performed at the level of the left main coronary. Contrast is injected into the venous system, and the full scan is "triggered" once a peak level is obtained. In our experience, a single sublingual nitroglycerine tablet (0.4 mg) given a few minutes before the contrast injection improves image quality, and so this is given before the final coronary scan.

Some institutions perform calcium scoring as part of their routine protocol before contrast injection. Although this does incur a slightly greater radiation dose to the patient, it can be used instead of the scout images, and can give additional prognostic information. Calcium scores cannot be obtained from a contrast study, so if one is required as part of the patient's workup, it needs to be performed as a separate scan.[7]

ACCURACY OF MSCT IN DETECTING CORONARY STENOSIS

Table 1 shows the sensitivity and specificity and predictive values of MSCT coronary angiography in published studies. In most of these studies, a significant coronary lesion is defined as stenosis of ⩾50% diameter detected by quantitative coronary angiography (QCA).

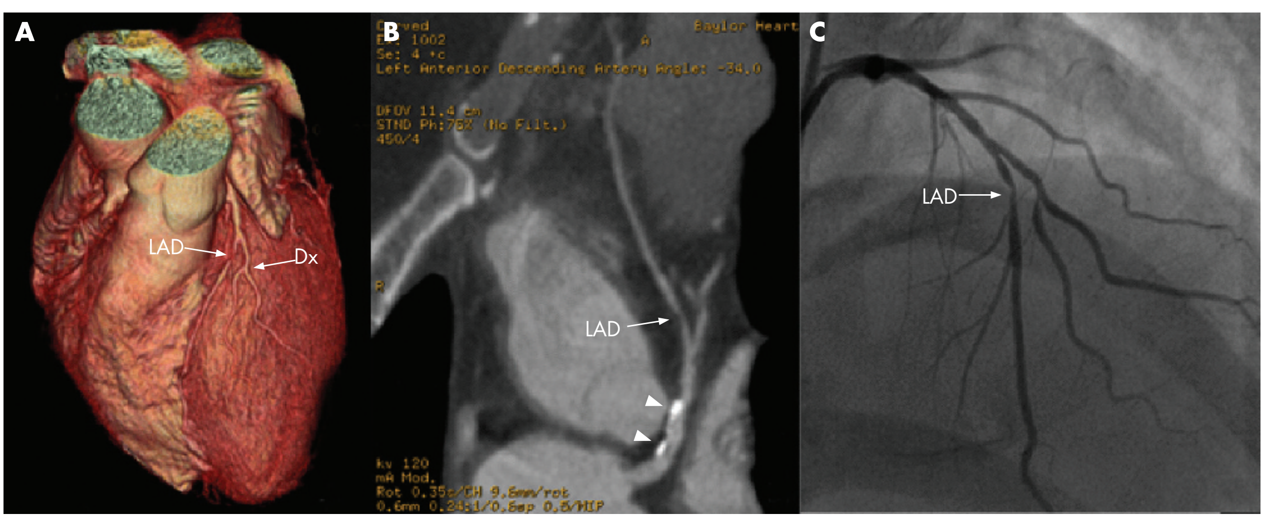

Figure 3 64-slice coronary CT of a patient with typical angina. Three-dimensional reconstruction (A) as well as curved reformatted images (B) demonstrate a high-grade lesion which is entirely of soft plaque (arrow) in the left anterior descending (LAD). Calcified plaque is seen more proximally in the vessel (arrowheads). Invasive angiography (C) confirmed these findings. Dx, diagnosis.

Sensitivity and positive predictive value are good in most studies.[8–27] Moreover, there is a very high specificity and negative predictive value. This is very important, because it suggests that CT coronary angiography can rule out severe coronary atherosclerosis in the face of symptoms or equivocal functional tests. It must be recognised that these good results are obtained when technically inadequate scans or patients with rapid heart rates or arrhythmias are excluded. Nevertheless, it seems that in patients with good quality studies, the test is very accurate for detecting of significant coronary artery disease compared with invasive coronary angiography (fig 3). There are currently no long-term data regarding outcomes for patients who have negative tests.

CLINICAL APPLICATIONS FOR MSCT

There are currently no published guidelines for the clinical application of CT coronary angiography. Patients who have chest pain, but who are of low-to-moderate risk or have equivocal stress tests are ideal candidates for CT coronary angiography as are patients who are asymptomatic but who are a very high risk for early or severe cardiovascular disease. For particularly anxious patients with atypical chest pain, the combination of a low-risk stress test and a negative CT coronary angiogram is a powerful tool for reassurance (figs 4 and 5). Often more important, the ability to demonstrate mild coronary atherosclerosis can lead to lifestyle and diet changes, as well as encouraging compliance with medical therapy.

We do not currently use this test as a stand-alone preoperative modality. However, it is possible that, in future, the preoperative evaluation for non-cardiac surgery could rely heavily on a negative CT coronary angiogram. In addition, patients at low risk for CAD who are scheduled for valve surgery or repair of congenital heart disease could potentially undergo MSCT instead of invasive catheterisation. Finally, it may be useful in situations where traditional stress imaging methods are notoriously difficult, such as left bundle branch block.

There are situations in which CT coronary angiography is useful after an invasive catheterisation has already been performed. MSCT is particularly well suited for defining the exact origin and course of anomalous coronary arteries identified by conventional coronary angiography[28] (fig 6). Like intravascular ultrasound, MSCT is able to demonstrate pathology in the wall of the artery, and not just define obstruction of the lumen. In this manner, coronary angiogram can often give a more total view of coronary pathology, including evaluation of

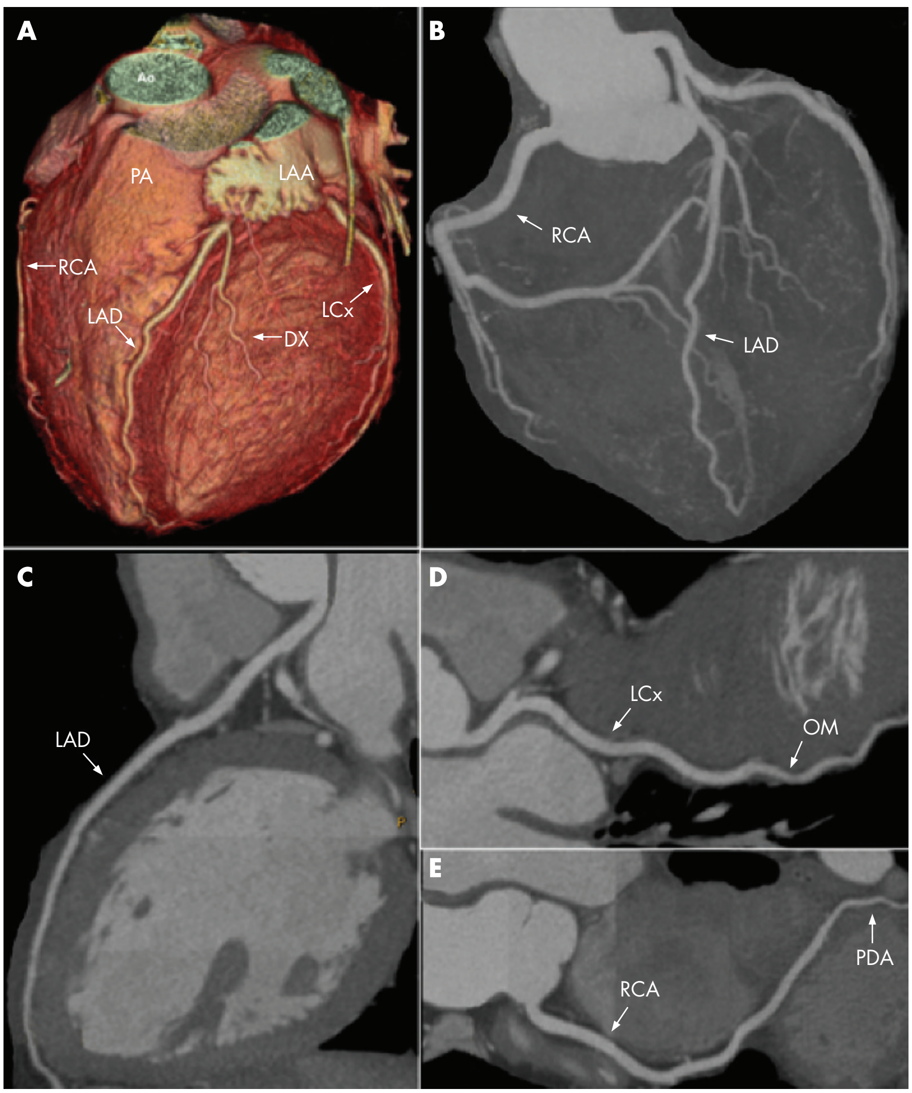

Figure 4 64-slice coronary CT images of a normal coronary tree. Multiple reconstructions are seen: three-dimensional (A), which gives a good overview of the course of the arterial tree in relation to the larger structures of the heart; maximum intensity pixel (MIP) view (B), which can highlight areas of calcified plaque; curved reformatted views (C–E), which are primarily used to determine the extent and severity of both soft and calcified plaque. Dx, diagnosis; LAA, left atrial appendage; LCx, left circumflex; Pa, pulmonary artery.

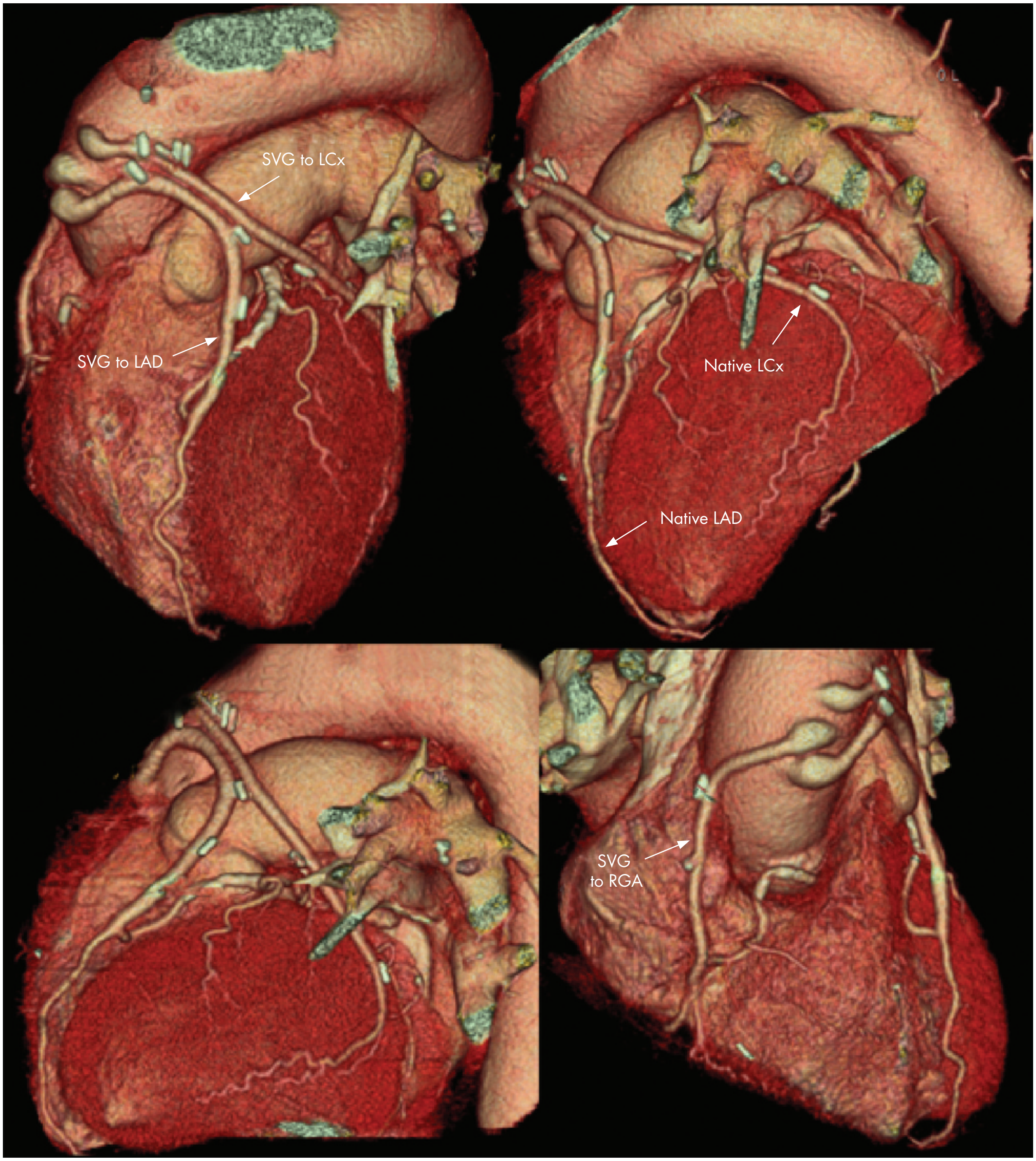

Figure 5 64-slice cardiac CT with multiple 3D reconstructions. Patent grafts to the left anterior descending (LAD), left circumflex (LCx) and right coronary artery (RCA) are seen. Three-dimensional reconstruction is the primary tool used to evaluate the overall patency of coronary bypass grafts with CT coronary angiography. In our institution, we have found that approximately 80% of patients who are sent for MSCT imaging of their coronaries for investigation of chest pain do not have subsequent catheterisation. The majority of these patients have had stress tests which were equivocal or technically positive. For example, a 45-year-old woman with risk factors for coronary disease and sharp, stabbing chest pain may have a stress echocardiogram as her next test of choice. If patients are unable to reach the target heart rate but have 1.5 mm of ST depression at peak exercise, even with normal wall motion, they are likely to have an invasive cardiac catheterisation. In our experience, these types of intermediate probability patients are ideal for MSCT coronary angiography to triage them to further invasive testing or medical management. SVG, saphenous vein graft.

the lumen, the amount of soft, fatty plaque, and calcified plaque burden in the coronary vasculature.[29–31] MSCT is also very well suited to evaluating the patency of coronary bypass grafts (fig 7), and in some cases may obviate the need for stress testing in some patients who have undergone bypass surgery.[21 32–36]

FUTURE DIRECTIONS

Scanners that are fast enough to acquire gated scans of the heart in 5 s are fast enough to acquire gated scans of the entire thorax in ~15 s. This opens the door for the so-called "triple rule out". In essence, a physician could diagnose coronary

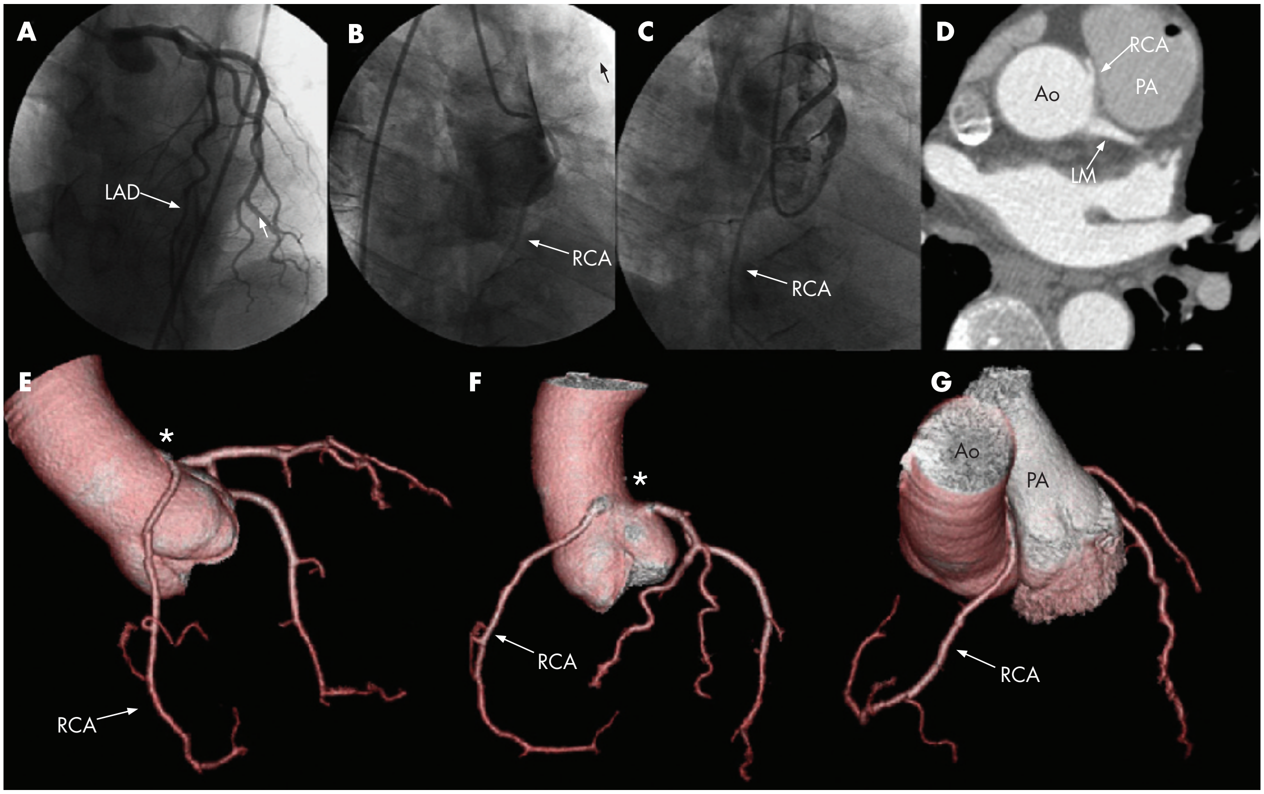

Figure 6 Anomalous right coronary artery (RCA). The invasive coronary angiogram was unsatisfactory (A–C) due to extreme anterior takeoff of the RCA and takeoff from the left coronary cusp. CT coronary angiogram clearly demonstrates the exact location of the takeoff of the RCA ostium. Axial slices (D) were extremely helpful in localising the separate ostium of the RCA and its distance from the left main coronary. Three-dimensional reconstruction (E, F) shows the RCA in relation to the left main (*). Reconstruction of the pulmonary artery (PA) trunk (G) allows additional localisation of the proximal course of the RCA, which is between the aorta (Ao) and PA.

disease, aortic dissection and pulmonary embolus with a single MSCT scan. In addition, it would be possible to diagnose pericardial effusion and pulmonary disease (ie, pneumonia, fibrosis) at the same time (a ''quintuple rule out''). The major problems with this type of scan are related to the timing of the scan relative to the contrast bolus, and the need for the interpreting physician to be familiar with cardiac, pulmonary, mediastinal and vascular pathology. Future developments in technology may include larger (eg, 256-detector) detector arrays or so-called ''flat panel'' scanners, all of which will have increased spatial resolution.[37] They would theoretically be able to image the entire heart in a single revolution, which would allow the entire coronary tree to be imaged in a single heartbeat.

CONTROVERSIES

There are several controversies which have been ignited by the advent of CT coronary angiography. The most prominent is the question of competence. Different medical subspecialties have stepped forward and promoted themselves as the logical owners of this type of imaging, including specialists in cardiology, radiology and nuclear medicine. Each type of physician brings different expertise to the interpretation of these images, and it is currently unclear whether any of these groups have a clear advantage in their interpretation.

Cardiologists have a large body of knowledge of plaque characteristics, and a wealth of information concerning the clinical care of these patients. In addition, they are the most knowledgeable when it comes to coronary anatomy, normal variations and anomalies. Radiologists have the most experience with the technology itself, are expert in the evaluation of axial anatomy and have an in-depth knowledge of radiation safety and CT physics. Nuclear medicine specialists who have particular training in cardiac imaging are also interested in this technology as a powerful adjunct to functional cardiac testing. There is a great deal of overlap with cardiologists and radiologists, many of whom read nuclear perfusion studies. A recent ACC/AHA task force published a set of guidelines for those practitioners who are interested in level 1, level 2 or level 3 training in the area of CT and MR cardiac imaging.[38]

CONCLUSION

Coronary angiography by MSCT is a promising technology that already appears to have superb sensitivity and specificity for detecting significant obstruction in the large epicardial coronary arteries. Because of its high spatial resolution and ability to image the arterial lumen and wall, further technological development will likely make this an important diagnostic tool for cardiovascular pathophysiology.

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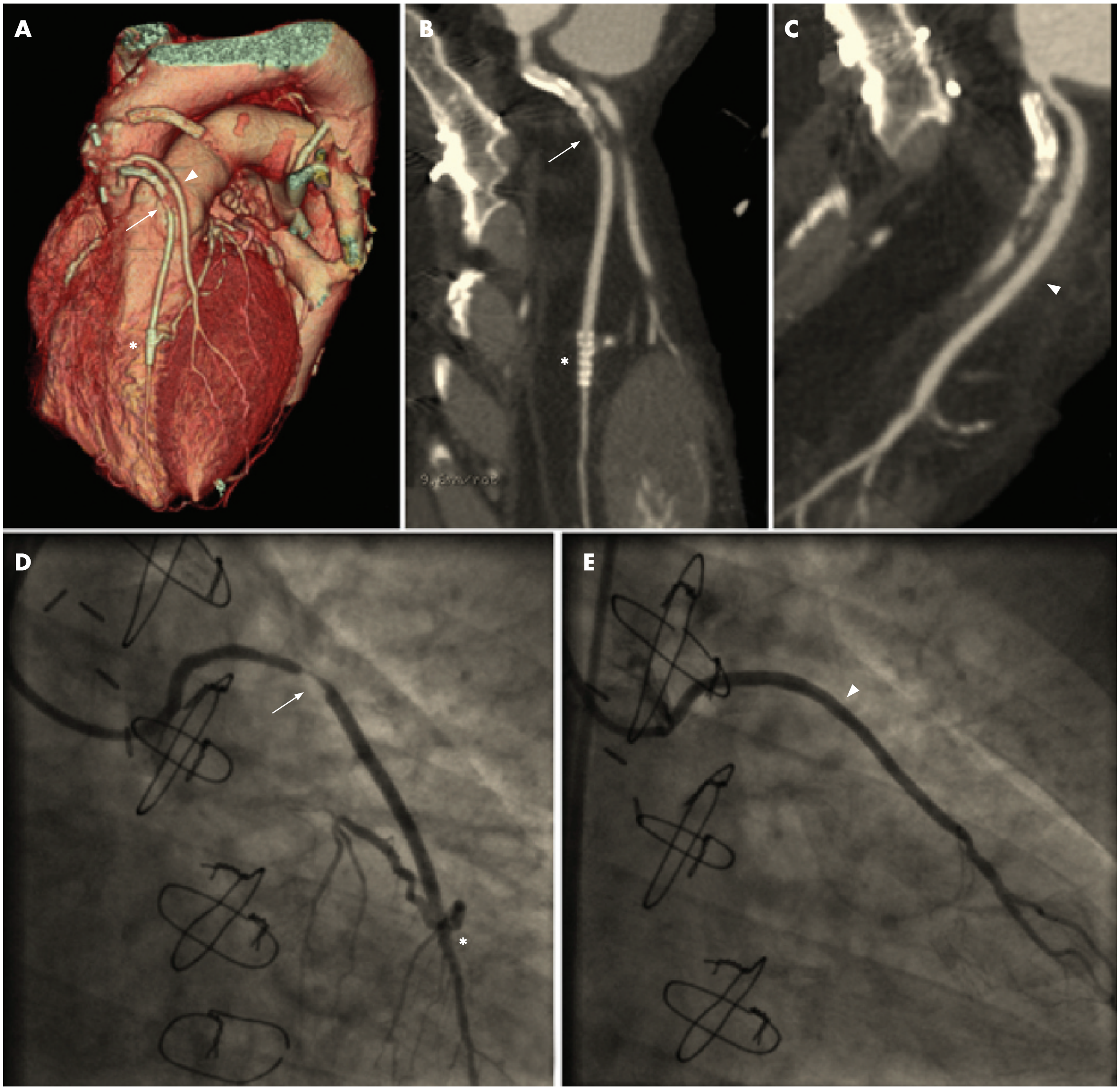

Figure 7 64-slice images of a patient who has undergone a coronary bypass. Three-dimensional reconstruction (A) clearly demonstrates bypass grafts to the lower anterior descending artery(LAD) (arrow) and diagonal branch (arrowhead). Curved reformatted images of the grafts show a ''high-grade'' lesion in the graft to the LAD (B) and a patent graft to the diagonal branch (C). A patent stent (*) is seen on the three-dimensional and the curved reformatted images. Invasive angiography (D,E) confirm these findings.

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