Non-invasive coronary artery imaging – new and evolving techniques

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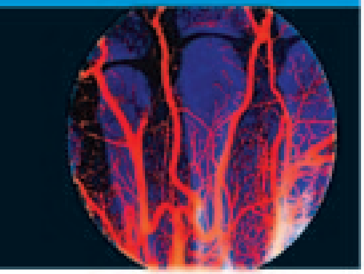

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Dr Anand is currently working on the early detection of coronary heart disease in patients with diabetes. His other research interests include non-invasive cardiovascular imaging, such as coronary angiography by electron beam computed tomography, myocardial perfusion imaging and echocardiography.

Abstract

The inherent limitations of invasive coronary angiography have led to the development of several non-invasive coronary artery imaging techniques. These techniques include electron beam computed tomography (EBCT), magnetic resonance imaging (MRI) and, most recently, multislice computed tomography (MSCT). This article discusses the relative merits and ultimate clinical potential of each of these techniques. Non-invasive techniques are useful for the detection of flow-limiting coronary artery stenoses and provide quantification of coronary atherosclerotic plaque burden and characterisation of plaque composition. Therefore, they have the potential to identify vulnerable plaques. Currently, computed tomography (CT) techniques (EBCT and MSCT) appear to permit the most robust coronary artery imaging compared with MRI. Future studies are needed to define specific areas for potential clinical application of non-invasive coronary artery imaging techniques.

Introduction

Invasive coronary angiography has been the gold standard during the past 50 years for establishing the presence, location and severity of epicardial coronary artery stenoses.[1] While providing exceptional spatial resolution and a general 'road map' of the coronary arterial tree for catheter-based or surgical interventions, this technique is invasive, costly[2,3] and associated with a small but definite risk of morbidity (1.5%) and mortality (0.15%).[4–6] Invasive coronary angiography also requires a brief hospitalisation or a period of observation for several hours after the procedure in a specialised monitoring unit. Hence, a convenient, non-invasive and safe method for coronary angiography is likely to provide significant clinical and economic benefits for most patients with suspected luminal coronary stenosis.[7]

Recent advances in computed tomography (CT) and magnetic resonance imaging (MRI) have resulted in a surge of interest in non-invasive coronary artery imaging. This article reviews the techniques currently available for non-invasive coronary artery imaging, i.e. electron beam computed tomography (EBCT), multislice computed tomography (MSCT) and MRI, and will discuss their capabilities, advantages and disadvantages.

Electron beam computed tomography

EBCT (GE Imatron, San Francisco, California) is a cross-sectional imaging technique similar to conventional CT. However, unlike conventional CT, which uses a rotating X-ray tube, EBCT uses a static row of detectors and a moving beam of electrons to produce the X-ray photons, thus permitting a rapid image acquisition time of 50 to 100 milliseconds per slice (temporal resolution). This process also results in a low radiation dose of 1 to 2 millisieverts (mSv).[8] Furthermore, when combined with prospective electrocardiographic (ECG) triggering and

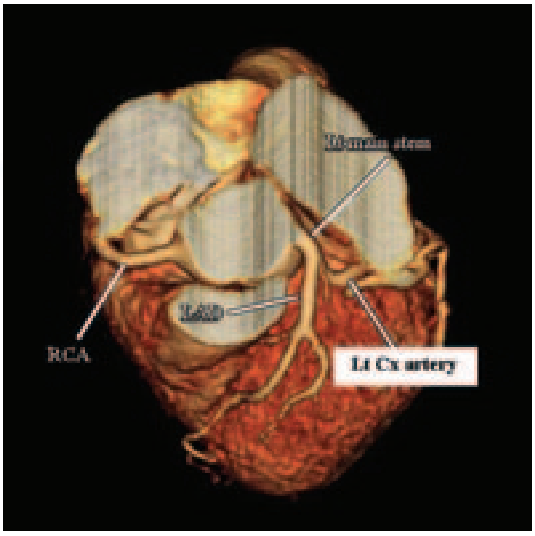


Figure 1. EBCTA of a 58-year-old woman, which shows the left main stem, proximal, mid- and distal segments of the left anterior descending (LAD), left circumflex (Lt Cx) and right coronary arteries (RCA). The patient presented with atypical chest pain and her risk factors included hypertension and a positive family history of premature CAD. Her exercise electrocardiogram was positive with horizontal ST segment depression in the anteroseptal leads at peak exercise. Coronary calcium imaging by EBCT revealed a coronary calcium score of zero. EBCTA did not reveal any obstructive coronary artery disease.

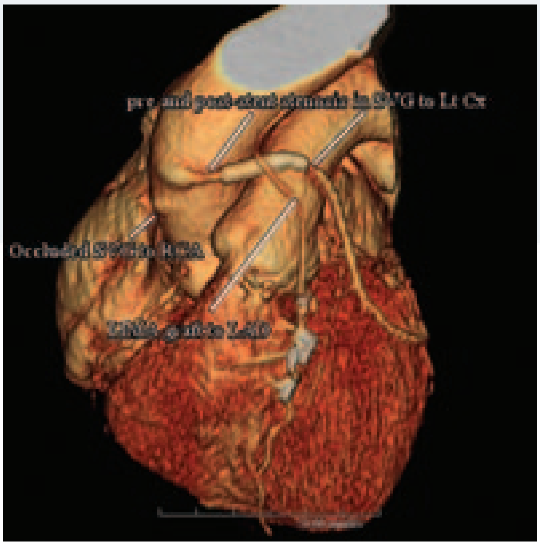


Figure 2a. EBCTA of a 64-year-old man, which shows a patent left internal mammary artery (LIMA) graft to the left anterior descending artery (LAD), a left circumflex (Lt Cx) vein graft with significant obstructive disease both proximal and distal to the stent, and an occluded RCA vein graft. In addition, he had severe native coronary disease. The patient presented with dyspnoea on exertion and his risk factors included previous history of CAD as well as an equivocal exercise electrocardiogram.

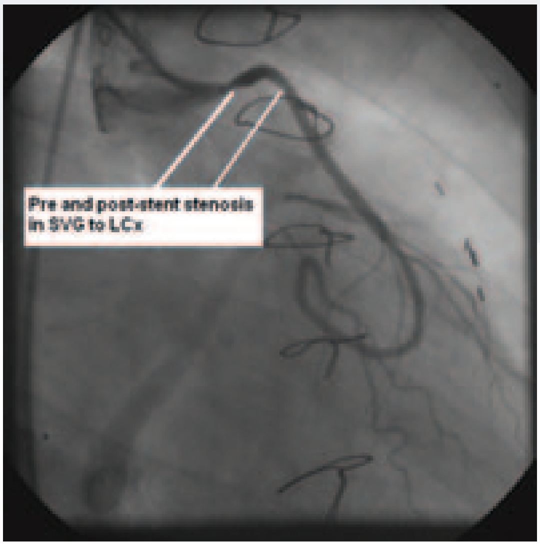


Figure 2b. Invasive coronary angiogram, which confirmed the findings of the EBCTA.

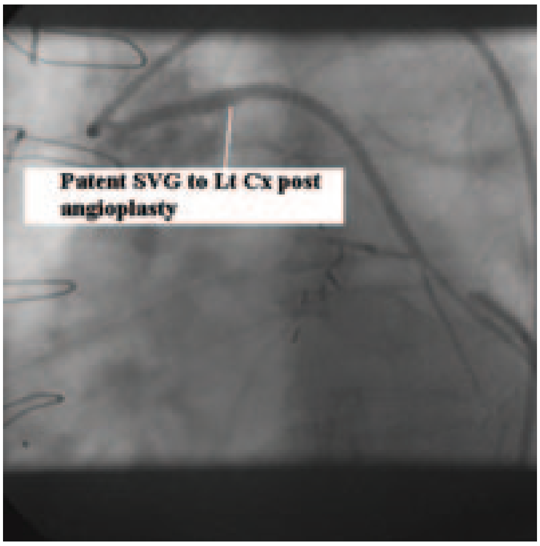
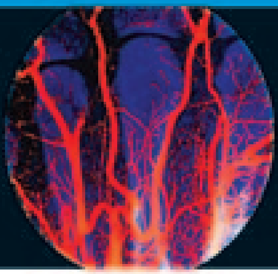


Figure 2c. Invasive coronary angiogram, which demonstrates the patent Lt Cx vein graft after angioplasty with the insertion of a coated stent to the stenosed Lt Cx vein graft.

breath-holding during inspiration, EBCT allows imaging of a motion free heart during diastole (usually at 40% of the R–R interval).[9] EBCT also has a high in-plane spatial resolution (up to 13.5 line pairs per mm). In a clinical setting, the value of EBCT for the detection and quantification of coronary calcium, a marker for atherosclerosis, has been well established. The level of coronary calcium reflects the overall extent of histological[10] and clinical atherosclerosis.[11] Recent studies have revealed promising results with respect to the diagnostic[12,13] and prognostic potential of coronary calcium measurements in symptomatic and asymptomatic patients.[14–16]

The first studies that reported the use of EBCT angiography (EBCTA) for coronary artery visualisation were published in 1995.[17,18] Since these initial publications, several investigators have established the clinical value of EBCTA for the detection of stenoses in coronary arteries[19–22] (Figure 1), venous or arterial bypass grafts[23] (Figures 2a–c) and for the characterisation of coronary artery anomalies (Figure 3, overleaf).[24] EBCTA is typically carried out with 1.5 to 3 mm slices with a 1 mm slice overlap, which results in an approximate 40 second breath-hold time. Homogenous enhancement of the coronary arteries is obtained with intravenous administration of 120 to 160 ml non-ionic contrast media (iohexol or iodixanol) at 3 to 5 ml/second, through an 18-gauge cannula placed in the antecubital vein. The sensitivity and specificity of EBCTA for detecting obstructive coronary artery disease



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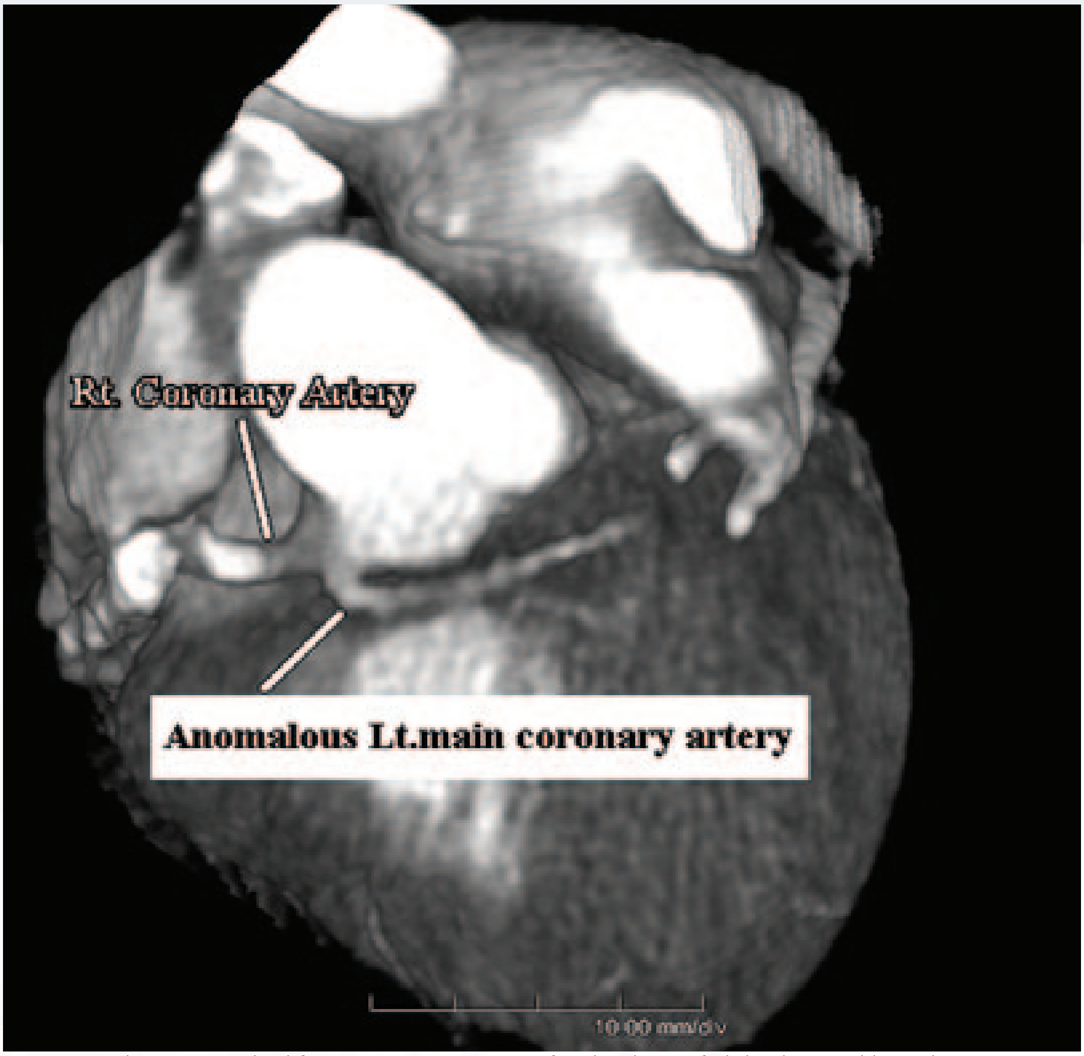

Figure 3. EBCTA showing an anomalous left main coronary artery originating from the right sinus of valsalva. The arrows delineate the preaortic or interarterial course of the left main coronary artery between the aorta and pulmonary trunk. These findings were confirmed by invasive coronary angiography (not shown).

ranges from 85% to 90%,[19–21,25,26] which is equivalent to that of stress testing using nuclear imaging or echocardiography.[27,28]

In published trials of EBCTA,[20, 21, 29] between 10% and 25% of coronary artery segments could not be adequately evaluated. In most cases, this is because of extensive coronary calcification: the overlap of density values between calcified plaques and the contrast-enhanced vessel lumen makes it difficult to accurately identify luminal stenosis in calcified segments and often leads to false-negative[19,30] and false-positive results.[18] For this reason, EBCTA is also unlikely to be useful in the evaluation of in-stent restenoses. Other factors contributing to inadequate image quality include motion artefacts caused by cardiac and respiratory motion (inadequate breath-hold), and ECG mistriggering (as a result of ventricular ectopics). Inadequate image quality is more common in the left circumflex and right coronary arteries because of their position in the atrioventricular groove, which is perpendicular to the imaging plane and in close proximity to the atria.[20]

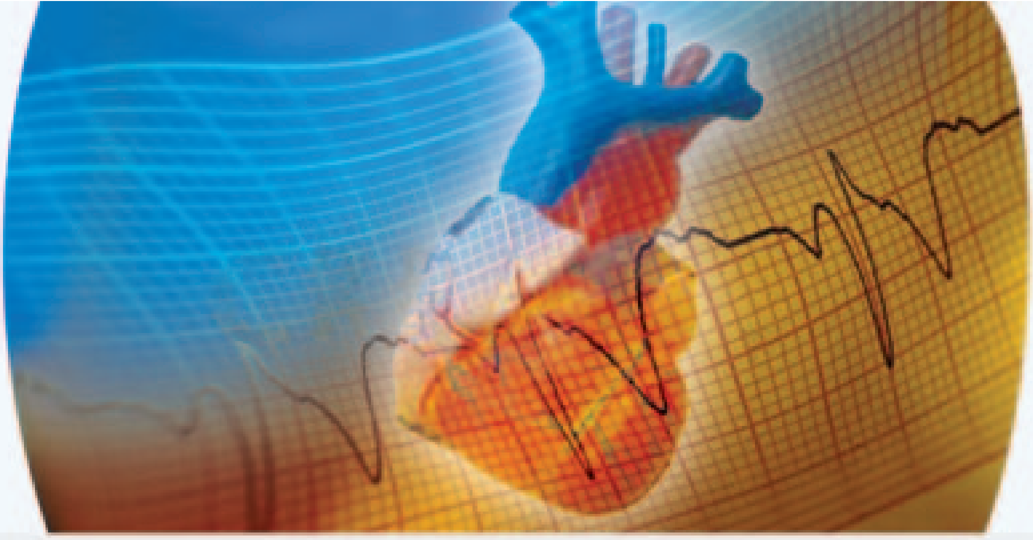

Table 1. Potential clinical applications of EBCTA.

Application	Clinical presentation
• Monitoring saphenous vein graft attrition non-invasively	• Asymptomatic patients who have undergone CABG >5 years ago
• Delineation of coronary venous anatomy	• Patients who require biventricular pacemaker implantation
• Alternative to stress testing and/ or invasive angiography	• A typical chest pain
	• Symptomatic patients with mild-to-moderate coronary calcification
	• Equivocal exercise electrocardiogram, exercise SPECT or stress echocardiogram
	• Newly diagnosed cardiomyopathy with low-to-intermediate risk for ischaemic coronary artery disease
	• Symptomatic patients with left bundle branch block
	• Atypical symptoms in patients who have had CABG
	• Patients requiring visualisation of anomalous coronary arteries

Abbreviations: CABG = coronary artery bypass grafting; SPECT = single photon emission computed tomography

Until recently, adequate visualisation of distal coronary artery segments, side branches and collateral vessels with a luminal diameter <1.5 mm was not possible by EBCTA. However, recent improvements in EBCT scanner characteristics (better temporal resolution, reduced slice thickness, ability to perform multiphase angiography), imaging protocols and post-processing methods have significantly enhanced the robustness and reliability of this technique. In addition, these improvements have enhanced the visualisation of distal coronary artery segments and side branches (personal experience and personal communication: Dr Mathew Budoff, Harbor UCLA Medical Center, Los Angeles, California, 2003). Finally, EBCT can also provide an assessment of ventricular function and myocardial perfusion during the same examination session.

Clinical applications of EBCTA

EBCTA is a convenient and safe technique to identify obstructive coronary artery disease (CAD) non-invasively; therefore, it can be considered in many instances as a strong alternative to stress testing or an adjunct to conventional diagnostic coronary angiography in individuals with a low-to-intermediate likelihood of obstructive CAD.

In this respect, a number of clinical applications for EBCTA may be considered (Table 1).

Multislice computed tomography (MSCT)

Conventional spiral or helical CT has been limited by its slow X-ray rotational speed, which is 10 times slower than that of EBCT, and results in image blurring as a result of cardiac motion. However, these shortcomings have improved with the advent of MSCT (or multidetector computed tomography) in 1998. In MSCT, a single rotating X-ray tube provides a beam of photons that is received by several rows of detectors (usually four), effectively providing four axial slices for each tube rotation. Ongoing improvements in the rotational speed of MSCT scanners have further increased the number of tomographic slices imaged per rotation to 16, 32 or more, which results in: thinner sub-millimetre slices; higher spatial resolution; better contrast-to-noise ratio; and a shorter scan time

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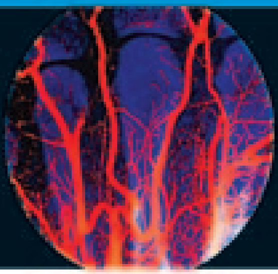

(approximately 20 seconds). In addition, given the robust imaging of other parts of the body and lower initial cost, the use of MSCT scanning is increasing rapidly, and its regional availability eclipses that of EBCT.

Initial studies using the new generation MSCT scanners have revealed promising results for the detection of obstructive CAD.[31–34] In a comparative study, Leber *et al*. found that MSCT coronary angiography had a marginally higher diagnostic accuracy than EBCTA, although the difference was not clinically significant.[31] The advantages of MSCT are offset by a higher radiation dose (6.7 to 13 mSv) compared with EBCTA (1.5 to 2 mSv) and invasive coronary angiography (2 to 2.5 mSv)[35] because of the use of retrospective ECG gating techniques. Furthermore, the temporal resolution of MSCT is limited by the X-ray tube rotational time (440 to 500 milliseconds). However, this can be improved to 210 milliseconds by interpolating only 180° of the acquired data. Figure 4 shows EBCTA

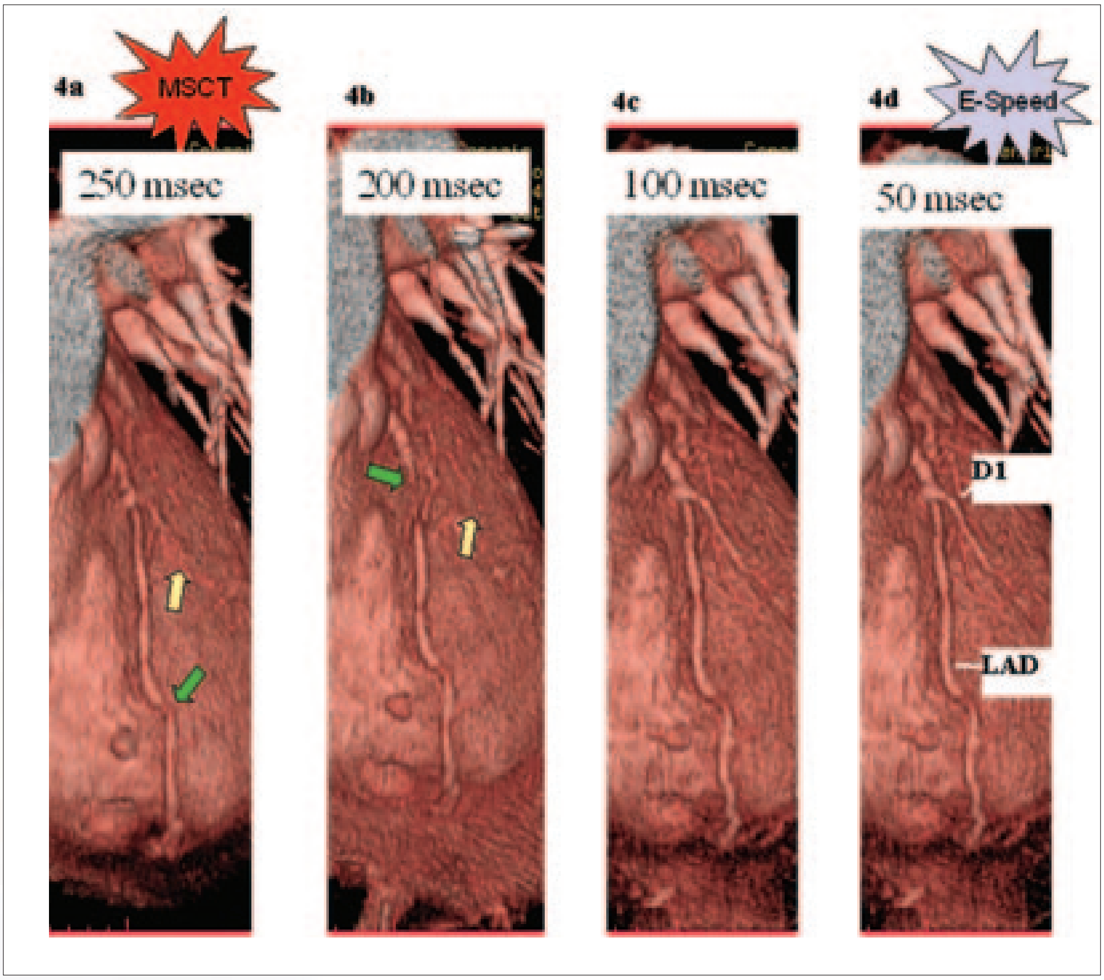

Figure 4. EBCTA acquired at (a) 250 milliseconds, (b) 200 milliseconds, (c) 100 milliseconds and (d) 50 milliseconds, with a spatial resolution of 13.5 line pairs per mm (e-speed, GE Imatron). It is apparent that diagnostic accuracy and image quality are significantly reduced at lower temporal resolutions: in images a and b, 'false stenoses' begin to appear in the proximal and distal left anterior descending artery (LAD) (green arrows), and smaller diagonal branches of the LAD (D1) are no longer clearly visualised (yellow arrows); in images c and d both the LAD and its diagonal branch are visualised.

images obtained at temporal resolutions of 50 and 100 milliseconds compared with simulated MSCT angiography images acquired at temporal resolutions of 200 and 250 milliseconds, using the same e-speed EBCT scanner (GE Imatron). As a result of slower slice acquisition times, the resting heart rate plays a major role in image quality of MSCT. Those patients with a heart rate >60 beats per minute require oral beta-blockers 1 hour before the procedure.[32,33] The high radiation dose associated with MSCT will continue to be a significant disadvantage compared with EBCTA, MRI and invasive coronary angiography.

Magnetic resonance imaging (MRI)

MRI is an attractive technique for non-invasive coronary artery imaging because of the lack of ionising radiation and the lack of requirement for iodinated contrast agents. In addition, its ability to assess left ventricular function, quantify myocardial blood flow, and evaluate myocardial perfusion and viability makes it an ideal candidate for the comprehensive evaluation of patients with suspected CAD.[36–38] However, MRI reaches its limits of spatial and temporal resolution when applied to visualising the coronary arteries.[39] The first clinical evaluation of MR coronary angiography was reported by Manning *et al*. in 1993 using two-dimensional breath-hold sequences.[40]

Current MRI protocols permit three-dimensional imaging of the coronary arteries using both free breathing, the 'navigator echo technique', and breath-hold techniques. MRI has so far shown only moderate diagnostic accuracy (sensitivity 50 to 83%, specificity 88 to 93%) compared with invasive coronary angiography for the detection of coronary stenosis.[39,41,42] The mean examination time of 70 minutes is also a problem for routine clinical practice compared with other non-invasive and invasive techniques.[43] Furthermore, a relatively low contrast-to-noise ratio and movement artefacts often prevent adequate visualisation of the coronary vessels. However, MRI techniques are continuing to evolve rapidly, and improved results may be expected soon. Of particular interest is the potential of MRI to characterise coronary atherosclerotic plaque composition and identify vulnerable plaques.[44]

Conclusion

MRI and CT imaging are emerging as the most promising complementary imaging modalities for: quantification of coronary atherosclerotic plaque burden, characterisation of plaque composition, and detection of flow-limiting coronary stenoses in patients with low-to-intermediate risk of ischaemic CAD. At present, CT techniques (EBCT and MSCT) provide better coronary artery visualisation, image resolution and enhanced diagnostic accuracy compared with MRI, although this may change with further technical advances in MRI. Recent studies have shown that the diagnostic accuracy of MSCT is almost equivalent to that of EBCT,[31] although EBCT (e-speed, GE Imatron) has a superior temporal resolution. While non-invasive techniques are unlikely to reach the same image quality as invasive coronary angiography in the future, they may play an important role in the clinical assessment of patients with atypical chest pain, equivocal stress tests, dilated cardiomyopathy and coronary bypass grafts. Future studies are required to evaluate the role of non-invasive coronary artery imaging techniques in appropriate clinical settings and selected patient populations.

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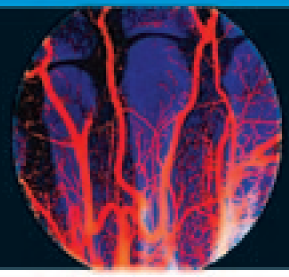

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