The Cardiac Society of Australia and New Zealand

Noninvasive Coronary Artery Imaging: Current Clinical Applications

These guidelines were revised by Dr Gary Liew, Profs Michael Feneley and Stephen Worthley on behalf of the Imaging Subcommittee of the CSANZ.

The guidelines were reviewed by the Continuing Education and Recertification Committee and ratified at the CSANZ Board meeting held on Friday, 26th November 2010.

Summary Points

1. Multidetector computed tomography (MDCT) is currently the preferred noninvasive modality that can reliably image coronary arteries.
2. Cardiac magnetic resonance imaging (MRI) has limited indications, including assessing suspected coronary anomalies and assessing complex congenital heart disease in expert centres.
3. The strength of MDCT is to rule out significant coronary artery disease (CAD) in a low-intermediate risk population with symptoms. This has been demonstrated in multi-centre trials.
4. Other appropriate indications for coronary CTA include:
    a. Investigation of equivocal or uninterpretable stress tests;
    b. Evaluation of suspected coronary anomalies / complex congenital heart disease;
    c. Evaluation of new onset heart failure / cardiomyopathy of unknown aetiology;
    d. Mapping of coronary vasculature including internal mammary arteries before repeat CABG;
    e. Evaluation of left bundle branch block;
    f. Excluding significant CAD before non-coronary cardiac surgery.
5. It is not appropriate to perform coronary CTA on patients who have known significant CAD or a high pre-test probability of CAD.
6. Use of MDCT to evaluate acute chest pain in the emergency department has been studied in a number of single-centre trials. While the results are encouraging, we await multi-centre randomized trials and cost-effectiveness studies before recommending routine use locally.
7. The evaluation of patients with stents and CABGs has limitations, but may be appropriate in select scenarios.
8. Stenosis severity should be reported in defined ranges rather than assigning a specific percentage, and comment should be made on the type of plaque involved.
9. Radiation exposure should be kept to a minimum in line with the ALARA principle. Radiation dose-saving measures should be routinely employed where appropriate.
10. Expertise in the performance and interpretation of coronary CTA scans is very important.

INTRODUCTION

Coronary artery disease (CAD) remains a leading cause of death in western societies. In Australia, it affects nearly 640,000 people and accounts for 18% of all deaths.[1] The identification and appropriate investigation of patients with coronary artery disease are central components for subsequent treatment and improvements in the health of those patients. Despite the various biomarkers and functional tests available for risk stratification, for some patients we look for the reassurance of anatomical information on the coronary vasculature. This is usually done via coronary angiography, which remains the gold standard for luminal assessment but carries some risks due to its invasive nature. Furthermore, the proportion of patients who have normal coronary angiograms has remained relatively stable at 15%, with a higher proportion of normal studies in women.[2, 3]

The ability to provide this anatomical information noninvasively would be an attractive and probably safer alternative to coronary angiography. Two technologies which have undergone evaluation for this purpose are multidetector computed tomography (MDCT) and magnetic resonance imaging (MRI). This document will review both modalities but the main focus will be on MDCT because the technology has improved tremendously in recent years to a stage where widespread availability and implementation are possible. A comprehensive review of other functional imaging modalities and risk stratification tools / biomarkers is beyond the scope of this document. The topic of coronary artery calcium scoring is dealt with in a different document from CSANZ.

MULTIDETECTOR COMPUTED TOMOGRAPHY (MDCT)

Technology

The challenges in imaging the coronary vessels were to overcome cardiac motion and be of sufficient quality to reliably detect a lesion. Initial CT technology involved fixed detectors in the form of 'electron beam CT' which provided very good temporal resolution (50 – 100 ms) but poor spatial resolution and long scan times (>20 s). They were used primarily for detection and quantification of coronary calcium,[4] and it was not until the 1990s that the first coronary CT angiogram was described.[5]

The development of MDCT with increasing numbers of finer detectors and faster gantry rotation times has resulted in improved spatial and temporal resolution to provide satisfactory images of the coronaries during diastole when there is least motion (Table 1).

Table 1. Timeline and improvements in MDCT.

Detectors	Year introduced	Temporal resolution	Detector width	Coverage (z-axis)
4	1999	400 ms	1.0 – 1.5 mm	0.6 cm
16	2001	190 – 250 ms	0.5 – 0.75 mm	1.2 cm
64	2004	165 -200 ms	0.5 – 0.625 mm	2.9 - 4 cm
64 x 2 DSCT	2005	83 ms	0.6 mm	2.9 cm
256	2007	135 ms	0.625 mm	8 cm
320	2007	175 ms	0.5 mm	16 cm
128 x 2 DSCT	2008	75 ms	0.6 mm	4 cm*

DSCT denotes dual source CT. *Coverage of whole heart possible with high-pitch protocol

The majority of coronary CT angiograms performed today are done on 64-detector systems, which require a stable regular heart rate of <65 beats per minute, breath hold of <10 seconds and about 5 heart beats to image the entire heart. Due to these limitations, there may be potential artefacts introduced by motion, breathing, ectopic beats or arrhythmias. From the common platform of 64-detectors, the various manufacturers have adopted different pathways which improve on the variables of resolution, speed, coverage or a combination of these.

Resolution

The spatial resolution of a CT system is largely limited by the detector width. An axial CT image is made up of three dimensional voxels which have an in-plane resolution (x and y – axis) and usually worse through-plane (z-axis) resolution. The shape of this voxel is therefore a rectangular block rather than a perfect cube. This can be a limitation when performing certain image manipulations or reformats as there will be some interpolation of data. This issue is becoming less evident in modern 64-detector systems. Some manufacturers have produced an isotropic or cubic voxel from the outset (e.g. Toshiba – 0.5 x 0.5 x 0.5 mm) while others have adopted a multi-sampling approach. Using a flying focal spot in the z-axis, it is possible to improve on the spatial resolution; e.g. a detector width of 0.6mm may result in an isotropic resolution of 0.33mm from oversampling (Somatom Definition AS, Siemens Medical, Germany).

Recently, one manufacturer has introduced a high-definition scanner with an in-plane spatial resolution of 0.23mm with 64-detectors (Discovery CT750 HD, GE Healthcare, USA). This is approaching the spatial resolution of invasive coronary angiography, which is 0.20 – 0.25mm. Utilizing a novel statistical iterative reconstruction algorithm (ASIR), Min and colleagues were able to demonstrate better visualization of coronary stents and greater intraluminal stent area compared with conventional CT systems.[6]

Speed

Apart from trying to decrease gantry rotation times, a breakthrough in improving true temporal resolution occurred with the introduction of dual source CT (DSCT). This technology involved two sets of tubes and detectors placed 90 degrees apart in the gantry to obtain images with only a quarter rotation. This has resulted in good image quality at higher heart rates[7, 8] and even in atrial fibrillation.[9]

Towards the end of 2008, the second generation DSCT scanner was introduced with two sets of 128-detectors capable of even faster gantry rotation and ultra-high pitch (Definition Flash, Siemens Medical, Germany). The two set of detectors are imaging mostly different areas of the heart as the gantry rotates. This has enabled both speed and coverage of the whole heart in 250ms and within one heart beat.[10, 11]

Dual energy CT (DECT) usually involves the two tubes of a DSCT system emitting two different energies (e.g. 80kV and 140kV), resulting in different attenuation values from the absorption of energies by the objects in question.[12] Each voxel or point in tissue will have two CT values (Hounsfield Units) and the analysis is conducted based on "three-material decomposition" of the resulting images. It has the ability to discriminate between iodine and calcium in phantom models and vasculature of cadavers.[13] In future, this technology may allow more accurate assessment of coronary plaque and stenosis by better discrimination between bright contrast, calcium and other plaque components.

Coverage

In late 2007, manufacturers released 256 (Philips) and 320-detector systems that are capable of volumetric whole organ scans. Although the temporal resolution may be similar to 64-detector systems, the 320-detector (Aquilion ONE, Toshiba, Japan) is capable of imaging the whole heart in one heart beat thereby providing images free from step-artefacts.

Radiation

As coronary CT angiography is increasingly performed in different healthcare settings around the world, the issue of radiation exposure has become a major concern in recent times. An early study comparing 16 and 64 detector systems reported mean effective doses of 10mSv and 15mSv respectively, when no dose-saving measures were employed.[14] Radiation exposure is generally higher for women (10 – 21mSv) compared to men (7 – 15mSv), largely due to breast tissue.[15]

A simple strategy to limit radiation is to scan only the organ of interest rather than from the carina to below diaphragm. An increase in scan length of 1cm can lead to a 5% increase in the radiation.[16] In helical or retrospectively triggered scanning, x-rays are emitted throughout the cardiac cycle. Every manufacturer provides ECG-gated dose modulation, which decreases the tube current by up to 80% during systole, and only provides full current during the brief diastolic period of interest. This method has been shown to reduce radiation by 25-40%.[14, 16-18]

X-ray exposure changes in a linear fashion with tube current (mA) but with the square of the tube voltage (kV). Therefore, a reduction from 120kV to 100kV in small to moderate body masses (e.g. <85 kg) could result in a radiation exposure drop of 46 – 64%.[14, 16] Recently, non-helical scanning, where the exposure is prospectively triggered to occur only in diastole ("step-and-shoot") has resulted in reductions in radiation of about 80% without compromising diagnostic quality.[16, 19] Patients need to have low heart rates (<60 bpm) and a stable rhythm without ectopics or much heart rate variability. While the radiation exposure will vary depending on whether temporal "padding" is employed, effective doses for prospective scanning are around 2-3mSv for modern 64-detector systems[20, 21] and <1mSv is achievable with second generation DSCT.[22]

The PROTECTION I study was an international multi-vendor observational study into radiation exposure involving nearly 2,000 patients from 21 university and 29 community hospitals.[16] The vast majority (96%) were studied using 64-detector scanners but there was a wide range of effective doses across different manufacturers (median 9 – 19mSv) as well as across different sites using machines from the same manufacturer. ECG-gated dose modulation was applied in 38% of patients but only 5% had tube voltage reduction (100kV) and 6% employed prospective scanning. In a recent sub-analysis, prospective scanning incurred much less radiation compared to retrospective scanning (3.6 v 11.2 mSv) without impairing diagnostic image quality.[23]

In a recent multi-centre trial of nearly 5,000 patients, implementation of dose reduction techniques resulted in a 53% decrease in radiation exposure from a median of 21mSv to 10mSv without deterioration in diagnostic quality.[24] The intervention involved education of a physician and radiographer at each participating site and implementation of adequate patient preparation, use of beta-blockers and nitrates, limiting scan length, ECG-gated dose modulation and using 100kV tube voltage when appropriate. The most significant change was use of 100kV, and the greatest improvements were made by smaller community hospitals.

We recommend adopting the following strategies for reducing radiation where appropriate:

1. **Limiting the scan volume to the organ of interest**
2. **Prospectively triggered scanning.**
3. **ECG-gated dose modulation**
4. **Reducing tube voltage to 100kV in smaller patients (<85kg; BMI <30)**

Diagnostic Accuracy

Comparisons between 16 and 64 detector systems have reported superior performance of 64-MDCT.[25-27] Many studies involving 16-MDCT excluded vessels <1.5 mm from analysis. There is a tendency to overestimate lesion severity, especially in calcific plaques due to blooming artefact.[28] Despite the improvements of 64-MDCT, the image quality of segments >2.0mm remains better than those <2.0mm,[29] and proximal better than distal.[30, 31]

Since the introduction of 64-detector systems, numerous single-centre studies comparing the accuracy of coronary CTA with traditional coronary angiography for significant stenoses have been published. Most had less than 100 patients and used a binary cut-off of 50% stenosis in their analyses. Meta-analyses of these studies have been performed (Table 2).

Table 2. Meta-analyses of native coronary arteries studied with 64-MDCT.

Author	Year	Analysis	reporting	Sensitivity	Specificity	PPV	NPV
Abdulla[32]	2007	Patients	1251	98%	91%	93%	97%
		Segments	18920	86%	96%	83%	97%
Mowatt[15]	2008	Patients	1286	99%	89%	93%	100%
		Segments	14199	90%	97%	76%	99%
Stein[30]	2008	Patients	2045	98%	88%	93%	96%
		Segments	27099	90%	96%	73%	99%

PPV denotes positive predictive value; NPV, negative predictive value.

From these pooled results, it is clear that coronary CTA has excellent negative predictive value but somewhat variable positive predictive value. Therein lies its strength as a tool to rule out significant CAD. The lower sensitivity and higher specificity of the analyses by segment are expected because patients are defined as having CAD if any segments are positive for significant disease. The percentage of non-evaluable segments range from 4 to 8%. The left main coronary artery has the best sensitivity (91-100%) and specificity (100%) while the mid-right coronary has the worst (81% and 95%, respectively).[30, 31]

The prevalence of CAD in these meta-analyses was high, around 60%, which impacts the predictive values. Meijboom et al. studied the accuracy of 64-MDCT in symptomatic patients with low (13%), medium (53%) and high (87%) estimated pre-test probability of CAD, and found 100% NPV in the low-to-intermediate group but 89% in the high group.[33]

In recent times, results from multi-centre and sometimes multi-vendor validation trials of 64-MDCT have been published (Table 3). The CORE64 trial was a highly anticipated single vendor, international multi-centre trial of 291 patients comparing 64-MDCT to conventional angiography.[34] The authors reported almost 100% of segments were evaluable but excluded patients with high calcium scores (>600) and vessels <1.5mm. The poor NPV of 83% was attributed to the high prevalence of CAD (56%) in the study population. Although the study

found that MDCT could accurately identify the presence of significant CAD and those requiring subsequent revascularization, the authors concluded that coronary CTA with the 64-MDCT technology examined could not replace conventional coronary angiography.

Table 3. Prospective multi-centre validation trials of 64-MDCT

Author	Year	Analysis reporting		Sensitivity	Specificity	PPV	NPV
Miller[34]	2008	Patients	291	85%	90%	91%	83%
Meijboom[35]	2008	Patients	360	99%	64%	86%	97%
		Segments	5297	88%	90%	47%	99%
Budoff [36]	2008	Stenosis >50%		95%	83%	64%	99%
		Stenosis >70%		94%	83%	48%	99%

PPV denotes positive predictive value; NPV, negative predictive value.

At the end of 2008, Meijboom et al. reported the results of a multi-centre, multi-vendor trial of 64-MDCT.35 Their specificity and PPV were much lower than other studies, which may in part be due to inclusion of all segments regardless of image quality. This is closer to the real world situation in which a non-evaluable segment or stenosis >50% will probably result in an invasive angiogram. Another factor could be the high pre-test probability of disease in their population.

The ACCURACY trial by Budoff et al. was somewhat different in that they studied 230 symptomatic low (25%) CAD prevalence patients scheduled to have coronary angiograms and provided analysis by stenosis >70% in addition to the usual >50% cut-off.[36] They included patients with heart rates >65bpm, high calcium scores and obesity. They showed that NPV remained high and specificity is comparable to other noninvasive stress imaging tests at both cut-offs.

The high negative predictive value of coronary CTA has received further support with a study showing freedom from significant cardiac events for 18 months if the coronary CTA was normal.[37] This study of 1,256 patients who were followed for up to 2 years looked at composite endpoints of death, AMI or hospitalization due to unstable angina in a population with very low event rates. They also found that coronary CTA provided additional prognostic value to the Framingham Risk Scores (FRS), with non-obstructive CAD having a lower event rate and obstructive CAD having a higher event rate than predicted by the FRS alone. Another study of 436 symptomatic patients reported that those patients with minimal or no CAD on coronary CTA were free from events at 3 years of follow-up: a NPV of 100%.[38] The prevalence of CAD was 14% and they estimated significant cost savings (USD 15,300/patient) compared to conventional angiograms in their local healthcare system.

Cost-effectiveness

In Australia, there has been one study on behalf of the Medical Services Advisory Committee (MSAC) into the cost-effectiveness of coronary CTA for symptomatic patients who were otherwise referred for invasive coronary angiography.[39] They used a cost-utility analysis and the outcome was given as incremental cost per quality of adjusted life year gained (QALY). Using a total procedure cost of $3,035 for an invasive coronary angiogram and $1,020 for a

coronary CTA, MSAC concluded that coronary CTA is a cost-effective strategy offering a higher health-related quality of life for symptomatic patients with up to 65% pre-test risk of CAD.

Quantitative assessment of stenosis

Most of the literature so far has used the binary cut-off of 50% stenosis in validating MDCT against coronary angiogram. In clinical practice and with invasive coronary angiography, further quantification of lesion severity is desirable to decide whether revascularisation is indicated. A few studies have compared stenosis severity on coronary CTA with quantitative coronary angiography (QCA) and intravascular ultrasound (IVUS).[34, 36, 40-43] Although the correlations were good, there were large standard deviations (up to ±25%) in quantifying stenoses with current 64-MDCT systems.

Based on these studies, the Society of Cardiovascular Computed Tomography (SCCT) has published guidelines on the interpretation and reporting of coronary CTA, recommending that stenoses be graded in broad ranges rather than assigning a specific number (Table 4).[44]

Table 4. Recommended stenosis grading

Normal	Absence of plaque and no stenosis
Minimal	<25% stenosis
Mild	25% – 49% stenosis
Moderate	50% - 69%
Severe	70% - 99%
Occluded	100%

Although MDCT has the potential to characterize plaque composition, there is much overlap in CT values (HU) in the various types of non-calcified plaques (e.g. lipidic or fibrous).[43, 45] The SCCT has recommended that plaques be described as "calcific," "non-calcific" or "mixed."[44]

Recommendations

- **Coronary CTA should be performed on systems with ≥64-detectors;**
- **Coronary CTA is best-validated in low-intermediate risk groups with symptoms;**
- **MDCT has a high negative predictive value and can rule out significant CAD in the appropriate population;**
- **Limitations of MDCT do not allow stenosis quantification in the same manner as invasive coronary angiography. Coronary CTA reports should use stenosis grading as recommended in Table 4, along with comments on the type of plaque;**
- **Lesions which are >50% on MDCT should be verified by another modality.**

CURRENT CLINICAL INDICATIONS

We have discussed the role of MDCT as a tool to rule out significant disease in patients with suspected CAD and stable symptoms. There are other specific clinical scenarios which may warrant its use. In 2006, a multi-society group including the American Colleges of Cardiology and Radiology, American Heart Association and other expert groups published guidelines on appropriateness criteria for both MDCT and MRI for cardiac applications.[46] Below is a summary of the MDCT indications at that time:

Table 5. Appropriate indications

1.	Evaluation of chest pain - intermediate pre-test probability of CAD • Unable to exercise or ECG uninterpretable
2.	Evaluation of chest pain – uninterpretable or equivocal stress test / imaging.
3.	Evaluation of acute chest pain (ED) • Intermediate pre-test probability • No ECG changes and normal cardiac enzymes
4.	Evaluation of suspected coronary anomalies
5.	Evaluation of CAD in new onset heart failure
6.	Assessment of complex congenital heart disease • Coronary & great vessel anomalies • Cardiac chamber & valves
7.	Evaluation of pulmonary vein anatomy prior to radiofrequency ablation for AF
8.	Coronary vein mapping prior to placement of biventricular pacemaker
9.	Repeat CABG – internal mammary and coronary artery mapping
10.	Technically difficult or limited images from echocardiogram or MRI • Evaluation of cardiac mass (tumour or thrombus) • Evaluation of pericardial conditions (mass, pericarditis, post cardiac surgery)

There are similar tables in the 2006 guidelines[46] for inappropriate and uncertain indications. Indications deemed inappropriate generally involved:

- asymptomatic patients;
- high pre-test probability of CAD (including positive stress test / imaging);
- positive cardiac enzymes or ST elevation on ECG.

Since the 2006 guidelines[46] were published, there have been several publications addressing additional indications for coronary CTA, and the multi-society group responsible for the 2006 guidelines released an updated expert consensus document on coronary CTA in May, 2010.[47] The additional indications for coronary CTA now supported are:

- Pre-operative assessment to rule out significant CAD prior to non-coronary cardiac surgery.[48] The prevalence of CAD in the 70 patients evaluated was 26%. The authors reported sensitivity was 100%, specificity 92%, PPV 82% and NPV 100%. The excellent NPV would have permitted the 69% of patients in the study with a negative

CTA to avoid invasive angiography. A history of angina was unreliable in predicting significant CAD. The subset of patients with aortic stenosis had higher coronary calcification, which led to an overestimation of stenosis (PPV 75%) but the excellent NPV of 100% was preserved.

- Detection of CAD in patients with left bundle branch block.[49] Stress testing / imaging may be difficult in this population. Invasive coronary angiography showed significant CAD in 44% of this group, with MDCT having a PPV of 91% and NPV 97%.
- Ruling out significant CAD in patients with dilated cardiomyopathy.[50] This study utilizing 16-MDCT in 61 patients with dilated cardiomyopathy of unknown aetiology was able rule out significant CAD with sensitivity 99%, specificity 96%, PPV 82% and NPV 99.8%. This indication is similar to the investigation of new onset heart failure, as outlined in Table 5.
- Alternative to invasive coronary angiography to detect CAD in the follow-up of patients following cardiac transplantation. Two small single-centre studies have examined this issue.[51, 52] The sensitivity for detecting either coronary stenosis or plaque when compared with the combination of invasive angiography plus IVUS was 70% with specificity 92%.[51]

Recommendations

- **Patients with indications as outlined in Table 5 are appropriate for evaluation with MDCT.**
- **Coronary CTA should not be performed in patients who have a high pre-test probability of CAD or are known to have significant CAD or acute coronary syndrome.**
- **Coronary CTA is appropriate in the investigation of patients with cardiomyopathy of unknown aetiology and patients with left bundle branch block.**
- **Coronary CTA is appropriate to rule out CAD in patients scheduled for non-coronary cardiac surgery. The CTA finding of a stenosis >50% or highly calcified plaque that precludes accurate assessment of stenosis severity will necessitate invasive angiography.**
- **Coronary CTA may be an appropriate alternative to invasive angiography in the routine follow up of patients after cardiac transplantation, although confirmation in larger studies is desirable.**

In addition, the following potential applications of coronary CTA were addressed in the 2010 Expert Consensus document, but the recommendations to be made on these issues are less clear at present or there is insufficient data to provide a consensus opinion:

Evaluation of Acute Chest Pain in the Emergency Department

The problem of acute chest pain in the emergency department (ED) can be taxing, not only on the staff but on the time and resources of the hospital system. More than 60% of chest pain presentations to ED in the USA are found not to have acute coronary syndrome, but physicians are reluctant to discharge patients because there is a reported 2% rate of missed AMI.[53, 54] Based on the ability of coronary CTA to rule out significant CAD in patients with stable symptoms, there have been a number of studies evaluating its use in acute chest pain. All were conducted in patients with initial negative cardiac enzymes and no ischaemic ECG changes.

An early prospective blinded study by Hoffmann et al. included coronary CTA on 103 patients at admission to rule out ACS. The absence of significant stenosis accurately

predicted the absence of ACS (NPV 100%).[55] On the other hand, the PPV was only 47%, indicating a large number of false positives. In a subsequent study (ROMICAT),[56] the authors screened 1,869 patients but only enrolled 368 (20%). About 50% of these patients had a negative coronary CTA, with a NPV of 100% for ACS but poor PPV. For patients with a low-to-intermediate pre-test probability of ACS, MDCT may be a useful triage tool in ED.

Similarly, another study of 58 patients found that of the 60% of patients with a negative coronary CTA, none had AMI or death after discharge after 15 months follow-up.[57] The authors reported an excellent NPV of 97% and poor PPV of 52%.

Goldstein and colleagues conducted a single-centre randomized trial of MDCT for ED chest pain versus the usual management, which was a nuclear stress test.[58] MDCT patients with non-significant lesions were discharged, those with a severe (>70%) stenosis underwent invasive coronary angiography, and those with a moderate stenosis underwent stress testing. MDCT immediately triaged 75% of patients to discharge or invasive coronary angiography, with the remainder undergoing stress testing. Patients were followed-up for 6 months, and both the MDCT and the usual nuclear stress pathways were found to be 100% safe. Compared to the usual standard of care, the MDCT strategy saved time (3.4 v 15 hours), costs ($1,586 v $1,872) and resulted in fewer repeat evaluations for recurrent chest pains (2% v 7%).

In a prospective study of 85 patients with chest pain in the ED, all underwent MDCT and nuclear stress imaging to determine accuracy in excluding significant CAD and events at 30 days.[59] Both MDCT and nuclear imaging had high NPVs (99% and 97%, respectively) but poor PPVs (50% and 38%, respectively). The accuracy of MDCT was similar to nuclear stress imaging in this low-risk cohort.

In Australia, there has been a recent publication utilizing DSCT in the evaluation of acute chest pain in 89 patients.[60] It was a prospective observational study with follow-up to 1 year. The result of the coronary CTA was not given to the treating team, and all patients underwent subsequent stress testing and standard care. Coronary CTA identified all patients with a severe stenosis requiring invasive coronary angiography. It identified 3 of 4 patients with a subsequent positive troponin. None of the patients died or had AMI in the follow-up period.

The 'Triple Rule-Out' CT Scan

MDCT already has proven clinical accuracy for the diagnoses of aortic dissection and pulmonary embolism, while coronary CTA studies for acute chest pain have been promising. The idea of a 'triple rule-out' scan protocol to exclude all three potentially fatal conditions has been proposed.[61-63] There are technical limitations to the protocol, involving rapid scanning of the entire chest, streak artefact from the right heart, optimal timing of the contrast bolus and extra radiation (up to 50%).[64] The optimal scanning protocol for each target of the scan is compromised by targeting all three issues simultaneously. A feasibility study of 50 patients with atypical chest pain using a novel protocol with 64-MDCT yielded good-quality images but 8 patients were excluded from coronary analysis due to artefacts.[65] A recent study of 31 patients using the new second generation DSCT to perform the triple rule-out protocol resulted in only 4.1mSv of radiation compared with 20mSv using conventional MDCT, although only 85% of coronary segments were diagnostic versus 93% with conventional MDCT.[66]

Recommendations:

- **Use of coronary CTA in the evaluation of acute chest pain is feasible and shows promise, but more data from multi-centre randomized trials on outcomes are needed before routine use is recommended.**
- **It should be performed in low-to-intermediate risk patients without ECG changes or positive cardiac enzymes. Algorithms for integrating MDCT into chest pain evaluation pathways may need to be tailored for local facilitation of workflow.**
- **Preliminary data on time saved and cost-effectiveness in the USA are encouraging but this needs to be studied locally.**
- **Currently, we cannot recommend adopting a 'triple rule-out' strategy for use of MDCT in the evaluation of acute chest pain.**

Coronary stent imaging

Evaluation of in-stent restenosis (ISR) has always been challenging due to metal artefacts, partial volume effects and beam hardening, with a high percentage of unevaluable stents in the past.[67, 68] Improvements with 64-MDCT and DSCT have decreased the proportion of unevaluable stents to 12%.[69] Stent diameter of <3.0 mm has been identified as a major predictor of an unevaluable stent.[70] The mean sensitivities (91%) and specificities (94%) were high and the NPV (98%) was excellent, but the PPV (63%) was poor.[69] A sub-study of the multi-centre CORE 64 trial was recently published, which found evaluability also decreased with thicker stent struts.[71] About 80% of stents in that study were <3.0mm diameter and only 64% were evaluable, with poor PPV (57%) and NPV (80%). An early study evaluating ISR in left main stents (post-dilated diameter 4.0mm) found the overall accuracy for simple left main stents was 98% but for complex bifurcation stents, it was 83%.[72] Recent technological advancements in spatial resolution with so-called 'high definition' MDCT show promise, with better intra-luminal stent quantification.[6]

Recommendations:

- **Routine use of MDCT to evaluate in-stent restenosis cannot be recommended currently, but this situation is likely to change with evolving technology.**
- **Assessment of stents is currently feasible in the setting of stent diameters >3.0mm and in simple left main stents.**

Coronary Artery Bypass Grafts

The assessment of CABGs has always been much easier than native coronary arteries due to their relatively larger size and immobility. Even with 4-detector[73] and 16-detector systems,[74, 75] the image quality was good, but the evaluation of distal anastamose and native vessels has been challenging. With 64-MDCT, 100% of grafts were evaluable with excellent NPV (100%) and PPV (92%).[76] However, the native coronaries are often extremely diseased and calcified, particularly in the smaller distal vessels beyond the graft anastomoses, resulting in a high NPV (96%) but low PPV (44%).

Consequently, the multi-society guidelines published in 2006 rated the use of MDCT in CABGs and native coronary arteries as 'uncertain,' with a borderline score for appropriateness.[46] The new 2010 guidelines[47] are similarly equivocal, noting the excellent accuracy for graft assessment but the limitations of assessing the anastomoses and native vessels.

Recommendations:

- **Use of MDCT in patients with CABGs can only be recommended to assess graft patency. Assessment of the native coronaries can be challenging currently but may improve with improvements in technology.**
- **It may also be used when invasive angiography fails to demonstrate a graft or adequately assess its patency.**
- **It is appropriate to use MDCT for surgical planning of repeat CABG to map internal mammary arteries, grafts and native coronary arteries.**

Chronic Total Occlusions

Percutaneous coronary intervention (PCI) for chronic total occlusions (CTO) can be a most difficult challenge involving excessive time, contrast and radiation. Success rates are poor[77, 78] due to failure to cross the lesion with guide-wires.[79] The operator sometimes does not know the length of the occlusion, the course of the occluded vessel or the extent of calcification. It was not appreciated until recent years that MDCT could visualize segments of vessel beyond occlusion sites due to collateral filling with contrast.[80] Mollet et al. found occlusion length, a blunt stump and calcification to be predictors of PCI procedural failure.[80] Similarly, an Australian study found heavy transluminal calcification on MDCT to be an independent predictor of procedural failure.[81]

More recently, a larger study of 142 CTOs found severe calcification, length of calcification and calcification at the entry point of the occlusion to be factors in procedural failure.[82] The authors found that the mean effective radiation dose for PCI was 39mSv and for coronary CTA was 22 mSv, and questioned if the extra radiation was warranted. However, with current dose-reduction strategies, radiation doses for prospective coronary CTA could be as low as 2-3 mSv.

There are no trials to date comparing the efficacy of a pre-PCI coronary CTA to routine care in CTO intervention. One assumes the information derived from a pre-PCI coronary CTA may change interventional strategies in terms of employing different guide-wires and approaches, or may result in a decision not to attempt the procedure.

Recommendations:

- **The use of MDCT to assess CTO may be useful in planning PCI of the lesion.**
- **Extensive calcification, especially at the entry site, and length of occlusion may predict procedural failure.**

Coronary CTA in Asymptomatic Individuals

The 2010 Consensus statement[47] - acknowledges the high prevalence of early stage atherosclerosis in young asymptomatic adults and the limitations of current clinical risk assessment tools, including the Framingham risk score. It cites recent evidence that coronary calcium scoring may improve risk stratification provided by the Framingham risk score.[83] It notes that while coronary CTA can additionally image non-calcified plaque, there is currently a lack of evidence linking non-calcified plaques that are non-obstructive with an independent increase in risk. Moreover, asymptomatic patients without coronary calcification have a very low event rate, around 0.1% per year.[84] There are also no published trials demonstrating improved outcomes after specific therapy in asymptomatic subjects with non-calcified coronary plaque on CTA. Nevertheless, the Consensus document does provide an extensive

review of the emerging CTA research on coronary plaque characterisation, the assessment of atherosclerotic burden, the natural history of plaque progression and its response to treatment, and the identification of vulnerable plaque. This research work does not yet provide a basis for recommending coronary CTA in asymptomatic subjects. As this research work progresses and with further technological improvements, it will become clearer whether coronary CTA will have a future role in asymptomatic subjects to aid individualisation of risk and/or response to treatment.

TRAINING & ACCREDITATION

Performance and reporting of cardiac CT requires competency in many areas. Practitioners should have a good understanding of technical aspects of CT, cardiac anatomy and pathology, as well as being able to identify extra-cardiac pathology which may occur in the field of view of a cardiac CT.

In 2009, the Australian New Zealand Conjoint Committee for the Recognition of Training in CT Coronary Angiography issued guidelines which exceed those of the ACC/AHA (www.anzctca.org). In summary, they recommended the following:

1. Level A – for independent supervision and reporting of cardiac CT.
    (i) Specialist in Cardiology, Radiology or Nuclear Medicine.
    (ii) Coursework – 40 hours, with at least 20 hours of interactive 'hands on' training under the supervision of a Level B (mentor level) specialist.
    (iii) Logbook of 150 cases verified by a Level B specialist. The 150 cases must include a minimum of 50 live cases (no more than 25 of the live cases can be achieved during a training course), 50 cases correlated with another imaging modality and/or appropriate clinical follow-up, 25 cases with non-coronary cardiac findings and 25 cases with non-cardiac findings. Live cases claimed outside a course must include the name of the claimant in the patient's report.

2. Level A – recertification.
    (i) Evaluation of 300 cases within a 3-year period recorded in a logbook.
    (ii) 30 cases correlated (as defined above).
    (iii) Maximum of 100 cases may be achieved via courses or library cases.

Logbooks will be subjected to random audits. For recertification purposes, live cases can be claimed by no more than two doctors, and only if each reporting doctor's name appears on the patient's report. The criteria for accreditation and recertification of a Level B (mentor level) specialist are more onerous, but essentially require a doubling of the Level A caseload requirements (www.anzctca.org).

Accreditation and training on the international front has largely been developed by organizations in USA. In 2005, the ACC/AHA along with other professional societies published guidelines on clinical competence in cardiac CT and cardiac MRI.[85] These guidelines have been informally adopted by the European Society of Cardiology.[69] One can apply to the SCCT for verification of one's cardiac CT experience. The SCCT has also issued guidelines on performance[86] and reporting of cardiac CT.[44] In 2008, board examinations were introduced by the Certification Board of Cardiovascular Computed Tomography for USA.

MAGNETIC RESONANCE IMAGING

MRI is a unique technology which allows noninvasive visualization of cardiovascular anatomy without ionizing radiation. However, there are some limitations, including long imaging time, the confined space in the scanner and the fact that MRI is contra-indicated in patients with certain metallic implants. MRI has the potential to provide information on cardiac anatomy, function (myocardial and valvular), perfusion and metabolism.

It has been almost 20 years since initial reports of MRI's ability to image the coronaries with breath-holds of up to 18s.[87] Often no exogenous contrast is needed for coronary MRA. Using bright-blood imaging sequences, image quality was good and compared favourably with invasive coronary angiography, with PPV 85% and NPV 95%.[88] However, the spatial resolution obtainable was approximately 1mm, and was not sufficient for routine clinical use. The development of MR 'navigator echo' allowed free breathing acquisition of coronary artery images over many minutes, reducing motion artefacts by analysing data when the diaphragm or heart were in a small range of positions.[89] With the advent of black-blood imaging and improvement in spatial resolution to 0.46 mm, visualization of the vessel wall in addition to the lumen was possible.[90] A direct comparison of bright-blood and black-blood techniques was made in a small trial.[91] There was no clear advantage to either technique but black-blood scans can be difficult to interpret because calcification and motion artefacts may lead to signal attenuation.[92]

The ability of MRI to evaluate CABGs has also been reported.[93, 94] Flow through bypass grafts was able to be measured, and when incorporated with MRI images, yielded high sensitivity (96%) and specificity (92%) in detecting obstructive stenoses >70%.[94] However, only 80% of grafts could be scanned successfully.

A landmark multi-centre study compared MRI to invasive coronary angiography in 109 patients using a volume-targeted coronary MRA protocol.[95] This technique is operator-dependent, requiring accurate localization of the coronary arteries and only limited access to the distal vessels and branches. The authors reported an overall accuracy of 72% in diagnosing significant CAD but 16% of coronary segments were not evaluable. All patients with left main or triple vessel disease were correctly identified by MRA.

With the advent of parallel imaging and steady-state free precession (SSFP), "whole heart MRA" with a single breath-hold became feasible.[96] This technique was less operator-dependent, and was found to have an improved overall accuracy of 89% when compared with invasive angiography.[97] A recent study comparing whole heart MRA to volume-targeted MRA using exogenous contrast found more visible segments and side branches with the whole heart MRA technique.[98] Typical spatial resolutions achievable with the whole heart technique are 0.7-0.8 mm in plane and 1-3mm through plane.[99]

Initial reports of imaging coronary arteries using high field 3T systems have been reported.[100, 101] Compared with traditional 1.5T systems, 3T can offer twice the signal-to-noise ratio, which can theoretically result in a four-fold reduction in scanning time. However, one problem with 3T scans can be reliable R-wave triggering, which may be overcome with sophisticated algorithms or T-wave triggering instead.

Despite these improvements in MRI technology, coronary MRA has not seen widespread clinical use. This is due, in part, to limited expert centres and limited access to MR systems. However, the main factor currently is the competition MRI faces from MDCT, which offers

superior spatial resolution, speed, diagnostic accuracy and widespread availability.[99, 102, 103] The 2006 multi-society appropriateness criteria[46] pertaining to coronary MRA recommends its use in:

1. Evaluation of suspected coronary anomalies
   The 2008 AHA committee on imaging recommends that MRA is preferred to MDCT due to radiation concerns[99]

2. Assessment of complex congenital heart disease, including anomalies of coronary circulation, great vessels, cardiac chambers and valves.

The guidelines state it is 'inappropriate' to use coronary MRA to evaluate symptomatic patients with intermediate pre-test probability of CAD, which contrasts with their recommendation for MDCT in the same group of patients. It was also deemed 'inappropriate' to use coronary MRA to evaluate CABGs in patients with symptoms.

Recommendations:

- **Coronary MRA may be used to evaluate suspected coronary anomalies or in complex congenital heart disease.**
- **Perhaps in a very select population where radiation is a concern (e.g. young women), coronary MRA may be used to exclude significant CAD in the proximal to mid-vessel level when performed in expert centres.**

SUMMARY

Noninvasive coronary imaging, and MDCT in particular, has advanced significantly since the last guidelines were published. Rapid development of technology accompanied by an explosion in research into MDCT have provided us with a clearer picture of its strengths and weaknesses. The appropriate indications have expanded, and a marked reduction in radiation exposure has fuelled a rush to adopt this new imaging modality. It is important that this emerging technology not be misused, and that consideration be given to other options when appropriate. Adequate training and accreditation is key to maintaining a high standard of the scans performed.

REFERENCES

1. AIHW. Australia's health 2008. *Australian Institute of Health & Welfare*. 2008;5:173-259
2. Farrehi PM, Bernstein SJ, Rasak M, Dabbous SA, Stomel RJ, Eagle KA, Rubenfire M. Frequency of negative coronary arteriographic findings in patients with chest pain is related to community practice patterns. *Am J Manag Care*. 2002;8:643-648
3. Jong P, Mohammed S, Sternberg L. Sex differences in the features of coronary artery disease of patients undergoing coronary angiography. *Can J Cardiol*. 1996;12:671-677
4. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr., Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15:827-832
5. Achenbach S, Moshage W, Ropers D, Nossen J, Daniel WG. Value of electron-beam computed tomography for the noninvasive detection of high-grade coronary-artery stenoses and occlusions. *N Engl J Med*. 1998;339:1964-1971
6. Min JK, Swaminathan RV, Vass M, Gallagher S, Weinsaft JW. High-definition multidetector computed tomography for evaluation of coronary artery stents: Comparison to standard-definition 64-detector row computed tomography. *J Cardiovasc Comput Tomogr*. 2009;3:246-251
7. Flohr TG, McCollough CH, Bruder H, Petersilka M, Gruber K, Suss C, Grasruck M, Stierstorfer K, Krauss B, Raupach R, Primak AN, Kuttner A, Achenbach S, Becker C, Kopp A, Ohnesorge BM. First performance evaluation of a dual-source ct (dsct) system. *Eur Radiol*. 2006;16:256-268
8. Ropers U, Ropers D, Pflederer T, Anders K, Kuettner A, Stilianakis NI, Komatsu S, Kalender W, Bautz W, Daniel WG, Achenbach S. Influence of heart rate on the diagnostic accuracy of dual-source computed tomography coronary angiography. *J Am Coll Cardiol*. 2007;50:2393-2398
9. Wolak A, Gutstein A, Cheng VY, Suzuki Y, Thomson LE, Friedman J, Dey D, Hayes SW, Slomka PJ, Germano G, Berman DS. Dual-source coronary computed tomography angiography in patients with atrial fibrillation: Initial experience. *J Cardiovasc Comput Tomogr*. 2008;2:172-180
10. Achenbach S, Marwan M, Schepis T, Pflederer T, Bruder H, Allmendinger T, Petersilka M, Anders K, Lell M, Kuettner A, Ropers D, Daniel WG, Flohr T. High-pitch spiral acquisition: A new scan mode for coronary ct angiography. *J Cardiovasc Comput Tomogr*. 2009;3:117-121
11. Leschka S, Stolzmann P, Desbiolles L, Baumueller S, Goetti R, Schertler T, Scheffel H, Plass A, Falk V, Feuchtner G, Marincek B, Alkadhi H. Diagnostic accuracy of high-pitch dual-source ct for the assessment of coronary stenoses: First experience. *Eur Radiol*. 2009;19:2896-2903
12. Petersilka M, Bruder H, Krauss B, Stierstorfer K, Flohr TG. Technical principles of dual source ct. *Eur J Radiol*. 2008;68:362-368
13. Tran DN, Straka M, Roos JE, Napel S, Fleischmann D. Dual-energy ct discrimination of iodine and calcium: Experimental results and implications for lower extremity ct angiography. *Acad Radiol*. 2009;16:160-171
14. Hausleiter J, Meyer T, Hadamitzky M, Huber E, Zankl M, Martinoff S, Kastrati A, Schomig A. Radiation dose estimates from cardiac multislice computed tomography in daily practice: Impact of different scanning protocols on effective dose estimates. *Circulation*. 2006;113:1305-1310

15. Mowatt G, Cook JA, Hillis GS, Walker S, Fraser C, Jia X, Waugh N. 64-slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: Systematic review and meta-analysis. *Heart*. 2008;94:1386-1393
16. Hausleiter J, Meyer T, Hermann F, Hadamitzky M, Krebs M, Gerber TC, McCollough C, Martinoff S, Kastrati A, Schomig A, Achenbach S. Estimated radiation dose associated with cardiac ct angiography. *JAMA*. 2009;301:500-507
17. Hausleiter J, Bischoff B, Hein F, Meyer T, Hadamitzky M, Thierfelder C, Allmendinger T, Flohr TG, Schomig A, Martinoff S. Feasibility of dual-source cardiac ct angiography with high-pitch scan protocols. *J Cardiovasc Comput Tomogr*. 2009;3:236-242
18. Jakobs TF, Becker CR, Ohnesorge B, Flohr T, Suess C, Schoepf UJ, Reiser MF. Multislice helical ct of the heart with retrospective ecg gating: Reduction of radiation exposure by ecg-controlled tube current modulation. *Eur Radiol*. 2002;12:1081-1086
19. Maruyama T, Takada M, Hasuike T, Yoshikawa A, Namimatsu E, Yoshizumi T. Radiation dose reduction and coronary assessability of prospective electrocardiogram-gated computed tomography coronary angiography: Comparison with retrospective electrocardiogram-gated helical scan. *J Am Coll Cardiol*. 2008;52:1450-1455
20. Husmann L, Valenta I, Gaemperli O, Adda O, Treyer V, Wyss CA, Veit-Haibach P, Tatsugami F, von Schulthess GK, Kaufmann PA. Feasibility of low-dose coronary ct angiography: First experience with prospective ecg-gating. *Eur Heart J*. 2008;29:191-197
21. Arnoldi E, Johnson TR, Rist C, Wintersperger BJ, Sommer WH, Becker A, Becker CR, Reiser MF, Nikolaou K. Adequate image quality with reduced radiation dose in prospectively triggered coronary cta compared with retrospective techniques. *Eur Radiol*. 2009;19:2147-2155
22. Achenbach S, Marwan M, Ropers D, Schepis T, Pflederer T, Anders K, Kuettner A, Daniel WG, Uder M, Lell MM. Coronary computed tomography angiography with a consistent dose below 1 msv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J*. 2010;31:340-346
23. Bischoff B, Hein F, Meyer T, Krebs M, Hadamitzky M, Martinoff S, Schomig A, Hausleiter J. Comparison of sequential and helical scanning for radiation dose and image quality: Results of the prospective multicenter study on radiation dose estimates of cardiac ct angiography (protection) i study. *AJR Am J Roentgenol*. 2010;194:1495-1499
24. Raff GL, Chinnaiyan KM, Share DA, Goraya TY, Kazerooni EA, Moscucci M, Gentry RE, Abidov A. Radiation dose from cardiac computed tomography before and after implementation of radiation dose-reduction techniques. *JAMA*. 2009;301:2340-2348
25. Sun Z, Jiang W. Diagnostic value of multislice computed tomography angiography in coronary artery disease: A meta-analysis. *Eur J Radiol*. 2006;60:279-286
26. Vanhoenacker PK, Heijenbrok-Kal MH, Van Heste R, Decramer I, Van Hoe LR, Wijns W, Hunink MG. Diagnostic performance of multidetector ct angiography for assessment of coronary artery disease: Meta-analysis. *Radiology*. 2007;244:419-428
27. Hamon M, Morello R, Riddell JW. Coronary arteries: Diagnostic performance of 16- versus 64-section spiral ct compared with invasive coronary angiography--meta-analysis. *Radiology*. 2007;245:720-731
28. Hoffmann MH, Shi H, Schmitz BL, Schmid FT, Lieberknecht M, Schulze R, Ludwig B, Kroschel U, Jahnke N, Haerer W, Brambs HJ, Aschoff AJ. Noninvasive coronary angiography with multislice computed tomography. *JAMA*. 2005;293:2471-2478
29. Pannu HK, Jacobs JE, Lai S, Fishman EK. Coronary ct angiography with 64-mdct: Assessment of vessel visibility. *AJR Am J Roentgenol*. 2006;187:119-126

30. Stein PD, Yaekoub AY, Matta F, Sostman HD. 64-slice ct for diagnosis of coronary artery disease: A systematic review. *Am J Med*. 2008;121:715-725
31. 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;191:1667-1675
32. Abdulla J, Abildstrom SZ, Gotzsche O, Christensen E, Kober L, Torp-Pedersen C. 64-multislice detector computed tomography coronary angiography as potential alternative to conventional coronary angiography: A systematic review and meta-analysis. *Eur Heart J*. 2007;28:3042-3050
33. Meijboom WB, van Mieghem CA, Mollet NR, Pugliese F, Weustink AC, van Pelt N, Cademartiri F, Nieman K, Boersma E, de Jaegere P, Krestin GP, de Feyter PJ. 64-slice computed tomography coronary angiography in patients with high, intermediate, or low pretest probability of significant coronary artery disease. *J Am Coll Cardiol*. 2007;50:1469-1475
34. Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, Paul N, Clouse ME, Shapiro EP, Hoe J, Lardo AC, Bush DE, de Roos A, Cox C, Brinker J, Lima JA. Diagnostic performance of coronary angiography by 64-row ct. *N Engl J Med*. 2008;359:2324-2336
35. Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, Nieman K, van Werkhoven JM, Pundziute G, Weustink AC, de Vos AM, Pugliese F, Rensing B, Jukema JW, Bax JJ, Prokop M, Doevendans PA, Hunink MG, Krestin GP, de Feyter PJ. Diagnostic accuracy of 64-slice computed tomography coronary angiography: A prospective, multicenter, multivendor study. *J Am Coll Cardiol*. 2008;52:2135-2144
36. Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, Scherer M, Bellinger R, Martin A, Benton R, Delago A, Min JK. 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;52:1724-1732
37. Hadamitzky M, Freissmuth B, Meyer T, Hein F, Kastrati A, Martinoff S, Schomig A, Hausleiter J. Prognostic value of coronary computed tomographic angiography for prediction of cardiac events in patients with suspected coronary artery disease. *JACC Cardiovasc Imaging*. 2009;2:404-411
38. Fazel P, Peterman MA, Schussler JM. Three-year outcomes and cost analysis in patients receiving 64-slice computed tomographic coronary angiography for chest pain. *Am J Cardiol*. 2009;104:498-500
39. Kreisz FP, Merlin T, Moss J, Atherton J, Hiller JE, Gericke CA. The pre-test risk stratified cost-effectiveness of 64-slice computed tomography coronary angiography in the detection of significant obstructive coronary artery disease in patients otherwise referred to invasive coronary angiography. *Heart Lung Circ*. 2009;18:200-207
40. Cheng V, Gutstein A, Wolak A, Suzuki Y, Dey D, Gransar H, Thomson LE, Hayes SW, Friedman JD, Berman DS. Moving beyond binary grading of coronary arterial stenoses on coronary computed tomographic angiography: Insights for the imager and referring clinician. *JACC Cardiovasc Imaging*. 2008;1:460-471
41. Achenbach S, Moselewski F, Ropers D, Ferencik M, Hoffmann U, MacNeill B, Pohle K, Baum U, Anders K, Jang IK, Daniel WG, Brady TJ. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast-enhanced, submillimeter multidetector spiral computed tomography: A segment-based comparison with intravascular ultrasound. *Circulation*. 2004;109:14-17

42. Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, Wintersperger B, Reiser M, Becker CR, Steinbeck G, Boekstegers P. Quantification of obstructive and nonobstructive coronary lesions by 64-slice computed tomography: A comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol*. 2005;46:147-154
43. Leber AW, Becker A, Knez A, von Ziegler F, Sirol M, Nikolaou K, Ohnesorge B, Fayad ZA, Becker CR, Reiser M, Steinbeck G, Boekstegers P. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: A comparative study using intravascular ultrasound. *J Am Coll Cardiol*. 2006;47:672-677
44. Raff GL, Abidov A, Achenbach S, Berman DS, Boxt LM, Budoff MJ, Cheng V, DeFrance T, Hellinger JC, Karlsberg RP. Scct guidelines for the interpretation and reporting of coronary computed tomographic angiography. *J Cardiovasc Comput Tomogr*. 2009;3:122-136
45. Leber AW, Knez A, Becker A, Becker C, von Ziegler F, Nikolaou K, Rist C, Reiser M, White C, Steinbeck G, Boekstegers P. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: A comparative study with intracoronary ultrasound. *J Am Coll Cardiol*. 2004;43:1241-1247
46. Hendel RC, Patel MR, Kramer CM, Poon M, Carr JC, Gerstad NA, Gillam LD, Hodgson JM, Kim RJ, Lesser JR, Martin ET, Messer JV, Redberg RF, Rubin GD, Rumsfeld JS, Taylor AJ, Weigold WG, Woodard PK, Brindis RG, Douglas PS, Peterson ED, Wolk MJ, Allen JM. Accf/acr/scct/scmr/asnc/nasci/scai/sir 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: A report of the american college of cardiology foundation quality strategic directions committee appropriateness criteria working group, american college of radiology, society of cardiovascular computed tomography, society for cardiovascular magnetic resonance, american society of nuclear cardiology, north american society for cardiac imaging, society for cardiovascular angiography and interventions, and society of interventional radiology. *J Am Coll Cardiol*. 2006;48:1475-1497
47. Mark DB, Berman DS, Budoff MJ, Carr JJ, Gerber TC, Hecht HS, Hlatky MA, Hodgson JM, Lauer MS, Miller JM, Morin RL, Mukherjee D, Poon M, Rubin GD, Schwartz RS. Accf/acr/aha/nasci/saip/scai/scct 2010 expert consensus document on coronary computed tomographic angiography: A report of the american college of cardiology foundation task force on expert consensus documents. *Journal of the American College of Cardiology*. 2010;55:2663-2699
48. Meijboom WB, Mollet NR, Van Mieghem CA, Kluin J, Weustink AC, Pugliese F, Vourvouri E, Cademartiri F, Bogers AJ, Krestin GP, de Feyter PJ. Pre-operative computed tomography coronary angiography to detect significant coronary artery disease in patients referred for cardiac valve surgery. *J Am Coll Cardiol*. 2006;48:1658-1665
49. Ghostine S, Caussin C, Daoud B, Habis M, Perrier E, Pesenti-Rossi D, Sigal-Cinqualbre A, Angel CY, Lancelin B, Capderou A, Paul JF. Non-invasive detection of coronary artery disease in patients with left bundle branch block using 64-slice computed tomography. *J Am Coll Cardiol*. 2006;48:1929-1934
50. Andreini D, Pontone G, Pepi M, Ballerini G, Bartorelli AL, Magini A, Quaglia C, Nobili E, Agostoni P. Diagnostic accuracy of multidetector computed tomography coronary angiography in patients with dilated cardiomyopathy. *J Am Coll Cardiol*. 2007;49:2044-2050
51. Gregory SA, Ferencik M, Achenbach S, Yeh RW, Hoffmann U, Inglessis I, Cury RC, Nieman K, McNulty IA, Laffan JA, Pomerantsev EV, Brady TJ, Semigran MJ, Jang

IK. Comparison of sixty-four-slice multidetector computed tomographic coronary angiography to coronary angiography with intravascular ultrasound for the detection of transplant vasculopathy. *The American journal of cardiology*. 2006;98:877-884
52. Iyengar S, Feldman DS, Cooke GE, Leier CV, Raman SV. Detection of coronary artery disease in orthotopic heart transplant recipients with 64-detector row computed tomography angiography. *J Heart Lung Transplant*. 2006;25:1363-1366
53. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, Griffith JL, Selker HP. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med*. 2000;342:1163-1170
54. Kohn MA, Kwan E, Gupta M, Tabas JA. Prevalence of acute myocardial infarction and other serious diagnoses in patients presenting to an urban emergency department with chest pain. *J Emerg Med*. 2005;29:383-390
55. Hoffmann U, Nagurney JT, Moselewski F, Pena A, Ferencik M, Chae CU, Cury RC, Butler J, Abbara S, Brown DF, Manini A, Nichols JH, Achenbach S, Brady TJ. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. *Circulation*. 2006;114:2251-2260
56. Hoffmann U, Bamberg F, Chae CU, Nichols JH, Rogers IS, Seneviratne SK, Truong QA, Cury RC, Abbara S, Shapiro MD, Moloo J, Butler J, Ferencik M, Lee H, Jang IK, Parry BA, Brown DF, Udelson JE, Achenbach S, Brady TJ, Nagurney JT. Coronary computed tomography angiography for early triage of patients with acute chest pain: The romicat (rule out myocardial infarction using computer assisted tomography) trial. *J Am Coll Cardiol*. 2009;53:1642-1650
57. Rubinshtein R, Halon DA, Gaspar T, Jaffe R, Karkabi B, Flugelman MY, Kogan A, Shapira R, Peled N, Lewis BS. 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;115:1762-1768
58. 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. *Journal of the American College of Cardiology*. 2007;49:863-871
59. 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;49:125-136
60. Hansen M, Ginns J, Seneviratne S, Slaughter R, Premaranthe M, Samardhi H, Harker J, Lai T, Walters DL, Bett N. The value of dual-source 64-slice ct coronary angiography in the assessment of patients presenting to an acute chest pain service. *Heart Lung Circ*. 2010
61. White CS, Kuo D, Kelemen M, Jain V, Musk A, Zaidi E, Read K, Sliker C, Prasad R. Chest pain evaluation in the emergency department: Can mdct provide a comprehensive evaluation? *AJR Am J Roentgenol*. 2005;185:533-540
62. Schussler JM, Smith ER. Sixty-four-slice computed tomographic coronary angiography: Will the "triple rule out" change chest pain evaluation in the ed? *Am J Emerg Med*. 2007;25:367-375
63. Johnson TR, Nikolaou K, Wintersperger BJ, Knez A, Boekstegers P, Reiser MF, Becker CR. Ecg-gated 64-mdct angiography in the differential diagnosis of acute chest pain. *AJR Am J Roentgenol*. 2007;188:76-82
64. 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;71:92-99

65. Vrachliotis TG, Bis KG, Haidary A, Kosuri R, Balasubramaniam M, Gallagher M, Raff G, Ross M, O'Neil B, O'Neill W. Atypical chest pain: Coronary, aortic, and pulmonary vasculature enhancement at biphasic single-injection 64-section ct angiography. *Radiology*. 2007;243:368-376
66. Sommer WH, Schenzle JC, Becker CR, Nikolaou K, Graser A, Michalski G, Neumaier K, Reiser MF, Johnson TR. Saving dose in triple-rule-out computed tomography examination using a high-pitch dual spiral technique. *Invest Radiol*. 2010;45:64-71
67. Maintz D, Seifarth H, Raupach R, Flohr T, Rink M, Sommer T, Ozgun M, Heindel W, Fischbach R. 64-slice multidetector coronary ct angiography: In vitro evaluation of 68 different stents. *Eur Radiol*. 2006;16:818-826
68. Schuijf JD, Bax JJ, Jukema JW, Lamb HJ, Warda HM, Vliegen HW, de Roos A, van der Wall EE. Feasibility of assessment of coronary stent patency using 16-slice computed tomography. *Am J Cardiol*. 2004;94:427-430
69. Schroeder S, Achenbach S, Bengel F, Burgstahler C, Cademartiri F, de Feyter P, George R, Kaufmann P, Kopp AF, Knuuti J, Ropers D, Schuijf J, Tops LF, Bax JJ. Cardiac computed tomography: Indications, applications, limitations, and training requirements: Report of a writing group deployed by the working group nuclear cardiology and cardiac ct of the european society of cardiology and the european council of nuclear cardiology. *Eur Heart J*. 2008;29:531-556
70. Rixe J, Achenbach S, Ropers D, Baum U, Kuettner A, Ropers U, Bautz W, Daniel WG, Anders K. Assessment of coronary artery stent restenosis by 64-slice multi-detector computed tomography. *Eur Heart J*. 2006;27:2567-2572
71. Wykrzykowska JJ, Arbab-Zadeh A, Godoy G, Miller JM, Lin S, Vavere A, Paul N, Niinuma H, Hoe J, Brinker J, Khosa F, Sarwar S, Lima J, Clouse ME. Assessment of in-stent restenosis using 64-mdct: Analysis of the core-64 multicenter international trial. *AJR Am J Roentgenol*. 2010;194:85-92
72. Van Mieghem CA, Cademartiri F, Mollet NR, Malagutti P, Valgimigli M, Meijboom WB, Pugliese F, McFadden EP, Ligthart J, Runza G, Bruining N, Smits PC, Regar E, van der Giessen WJ, Sianos G, van Domburg R, de Jaegere P, Krestin GP, Serruys PW, de Feyter PJ. Multislice spiral computed tomography for the evaluation of stent patency after left main coronary artery stenting: A comparison with conventional coronary angiography and intravascular ultrasound. *Circulation*. 2006;114:645-653
73. Lau GT, Ridley LJ, Bannon PG, Wong LA, Trieu J, Brieger DB, Lowe HC, Freedman BS, Kritharides L. Lumen loss in the first year in saphenous vein grafts is predominantly a result of negative remodeling of the whole vessel rather than a result of changes in wall thickness. *Circulation*. 2006;114:I435-440
74. Martuscelli E, Romagnoli A, D'Eliseo A, Tomassini M, Razzini C, Sperandio M, Simonetti G, Romeo F, Mehta JL. Evaluation of venous and arterial conduit patency by 16-slice spiral computed tomography. *Circulation*. 2004;110:3234-3238
75. Schlosser T, Konorza T, Hunold P, Kuhl H, Schmermund A, Barkhausen J. Noninvasive visualization of coronary artery bypass grafts using 16-detector row computed tomography. *J Am Coll Cardiol*. 2004;44:1224-1229
76. Ropers D, Pohle FK, Kuettner A, Pflederer T, Anders K, Daniel WG, Bautz W, Baum U, Achenbach S. Diagnostic accuracy of noninvasive coronary angiography in patients after bypass surgery using 64-slice spiral computed tomography with 330-ms gantry rotation. *Circulation*. 2006;114:2334-2341; quiz 2334
77. Olivari Z, Rubartelli P, Piscione F, Ettori F, Fontanelli A, Salemme L, Giachero C, Di Mario C, Gabrielli G, Spedicato L, Bedogni F. Immediate results and one-year clinical outcome after percutaneous coronary interventions in chronic total occlusions: Data from a multicenter, prospective, observational study (toast-gise). *J Am Coll Cardiol*. 2003;41:1672-1678

78. Sathe S, Alt C, Black A, Manolas E, Warren R, Valentine P. Initial and long-term results of percutaneous transluminal balloon angioplasty for chronic total occlusions: An analysis of 184 procedures. *Aust N Z J Med*. 1994;24:277-281
79. Saito S, Tanaka S, Hiroe Y, Miyashita Y, Takahashi S, Satake S, Tanaka K. Angioplasty for chronic total occlusion by using tapered-tip guidewires. *Catheter Cardiovasc Interv*. 2003;59:305-311
80. Mollet NR, Hoye A, Lemos PA, Cademartiri F, Sianos G, McFadden EP, Krestin GP, Serruys PW, de Feyter PJ. Value of preprocedure multislice computed tomographic coronary angiography to predict the outcome of percutaneous recanalization of chronic total occlusions. *The American journal of cardiology*. 2005;95:240-243
81. Soon KH, Cox N, Wong A, Chaitowitz I, Macgregor L, Santos PT, Selvanayagam JB, Farouque HM, Rametta S, Bell KW, Lim YL. Ct coronary angiography predicts the outcome of percutaneous coronary intervention of chronic total occlusion. *J Interv Cardiol*. 2007;20:359-366
82. Garcia-Garcia HM, van Mieghem CA, Gonzalo N, Meijboom WB, Weustink AC, Onuma Y, Mollet NR, Schultz CJ, Meliga E, van der Ent M, Sianos G, Goedhart D, den Boer A, de Feyter P, Serruys PW. Computed tomography in total coronary occlusions (ctto registry): Radiation exposure and predictors of successful percutaneous intervention. *EuroIntervention*. 2009;4:607-616
83. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with framingham score for risk prediction in asymptomatic individuals. *JAMA*. 2004;291:210-215
84. Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, c-reactive protein, and atherosclerotic cardiovascular disease events: The st. Francis heart study. *Journal of the American College of Cardiology*. 2005;46:158-165
85. Budoff MJ, Cohen MC, Garcia MJ, Hodgson JM, Hundley WG, Lima JA, Manning WJ, Pohost GM, Raggi PM, Rodgers GP, Rumberger JA, Taylor AJ, Creager MA, Hirshfeld JW, Jr., Lorell BH, Merli G, Tracy CM, Weitz HH. Accf/aha clinical competence statement on cardiac imaging with computed tomography and magnetic resonance: A report of the american college of cardiology foundation/american heart association/american college of physicians task force on clinical competence and training. *J Am Coll Cardiol*. 2005;46:383-402
86. Abbara S, Arbab-Zadeh A, Callister TQ, Desai MY, Mamuya W, Thomson L, Weigold WG. Scct guidelines for performance of coronary computed tomographic angiography: A report of the society of cardiovascular computed tomography guidelines committee. *J Cardiovasc Comput Tomogr*. 2009;3:190-204
87. Edelman RR, Manning WJ, Burstein D, Paulin S. Coronary arteries: Breath-hold mr angiography. *Radiology*. 1991;181:641-643
88. Manning WJ, Li W, Edelman RR. A preliminary report comparing magnetic resonance coronary angiography with conventional angiography. *N Engl J Med*. 1993;328:828-832
89. Botnar RM, Stuber M, Danias PG, Kissinger KV, Manning WJ. Improved coronary artery definition with t2-weighted, free-breathing, three-dimensional coronary mra. *Circulation*. 1999;99:3139-3148
90. Fayad ZA, Fuster V, Fallon JT, Jayasundera T, Worthley SG, Helft G, Aguinaldo JG, Badimon JJ, Sharma SK. Noninvasive in vivo human coronary artery lumen and wall imaging using black-blood magnetic resonance imaging. *Circulation*. 2000;102:506-510
91. Maintz D, Aepfelbacher FC, Kissinger KV, Botnar RM, Danias PG, Heindel W, Manning WJ, Stuber M. Coronary mr angiography: Comparison of quantitative and qualitative data from four techniques. *AJR Am J Roentgenol*. 2004;182:515-521

92. Stuber M, Botnar RM, Kissinger KV, Manning WJ. Free-breathing black-blood coronary mr angiography: Initial results. *Radiology*. 2001;219:278-283
93. Aurigemma GP, Reichek N, Axel L, Schiebler M, Harris C, Kressel HY. Noninvasive determination of coronary artery bypass graft patency by cine magnetic resonance imaging. *Circulation*. 1989;80:1595-1602
94. Langerak SE, Vliegen HW, Jukema JW, Kunz P, Zwinderman AH, Lamb HJ, van der Wall EE, de Roos A. Value of magnetic resonance imaging for the noninvasive detection of stenosis in coronary artery bypass grafts and recipient coronary arteries. *Circulation*. 2003;107:1502-1508
95. Kim WY, Danias PG, Stuber M, Flamm SD, Plein S, Nagel E, Langerak SE, Weber OM, Pedersen EM, Schmidt M, Botnar RM, Manning WJ. Coronary magnetic resonance angiography for the detection of coronary stenoses. *N Engl J Med*. 2001;345:1863-1869
96. Weber OM, Martin AJ, Higgins CB. Whole-heart steady-state free precession coronary artery magnetic resonance angiography. *Magn Reson Med*. 2003;50:1223-1228
97. Jahnke C, Paetsch I, Nehrke K, Schnackenburg B, Gebker R, Fleck E, Nagel E. Rapid and complete coronary arterial tree visualization with magnetic resonance imaging: Feasibility and diagnostic performance. *Eur Heart J*. 2005;26:2313-2319
98. Tang L, Merkle N, Schar M, Korosoglou G, Solaiyappan M, Hombach V, Stuber M. Volume-targeted and whole-heart coronary magnetic resonance angiography using an intravascular contrast agent. *J Magn Reson Imaging*. 2009;30:1191-1196
99. Bluemke DA, Achenbach S, Budoff M, Gerber TC, Gersh B, Hillis LD, Hundley WG, Manning WJ, Printz BF, Stuber M, Woodard PK. Noninvasive coronary artery imaging: Magnetic resonance angiography and multidetector computed tomography angiography: A scientific statement from the american heart association committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. *Circulation*. 2008;118:586-606
100. Gharib AM, Herzka DA, Ustun AO, Desai MY, Locklin J, Pettigrew RI, Stuber M. Coronary mr angiography at 3t during diastole and systole. *J Magn Reson Imaging*. 2007;26:921-926
101. Stuber M, Botnar RM, Fischer SE, Lamerichs R, Smink J, Harvey P, Manning WJ. Preliminary report on in vivo coronary mra at 3 tesla in humans. *Magn Reson Med*. 2002;48:425-429
102. Schuetz GM, Zacharopoulou NM, Schlattmann P, Dewey M. Meta-analysis: Noninvasive coronary angiography using computed tomography versus magnetic resonance imaging. *Ann Intern Med*. 2010;152:167-177
103. Schuijf JD, Bax JJ, Shaw LJ, de Roos A, Lamb HJ, van der Wall EE, Wijns W. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. *Am Heart J*. 2006;151:404-411