CCS / CAR / CANM / CNCS / Can SCMR
Joint Position Statement on
Advanced Non-invasive Cardiac Imaging using
Positron Emission Tomography, Magnetic Resonance Imaging and
Multi-Detector Computed Tomographic Angiography
in the Diagnosis and Evaluation of Ischemic Heart Disease

Canadian Cardiovascular Society, Canadian Association of Radiologists
Canadian Association of Nuclear Medicine, Canadian Nuclear Cardiology Society, Canadian Society of Cardiac Magnetic Resonance

Primary Panel Members (Writing Team):
R.S.B. Beanlands, B.J.W. Chow, A. Dick, M.G. Friedrich,
K.Y. Gulenchyn, M. Kiess, H. Leong-Poi, R.M. Miller, G. Nichol

Secondary Panel Members:
M. Freeman, P. Bogaty, G. Honos, G. Hudon, G. Wisenberg

Also Assisting with Writing Team:
J. Van Berkom, K. Williams, K. Yoshinaga, J. Graham

Affiliations are noted in Appendix 1.

The costs associated with the literature search and teleconferencing were supported by the Canadian Cardiovascular Society (CCS) and the Canadian Association of Radiologists (CAR).
The conference held in Montreal in October 2005 was supported by the CCS, CAR and the Canadian Association of Nuclear Medicine (CANM).

Address for Correspondence:

Rob S.B. Beanlands MD
Professor of Medicine (Cardiology)/Radiology
Chief, Cardiac Imaging
University of Ottawa Heart Institute
40 Ruskin Street, Ottawa, Ontario (Canada) K1Y 4W7.

Abstract

Background: In decades, advanced imaging modalities with excellent diagnostic capabilities, have emerged. The aim of this position statement was to systematically review existing literature to define Canadian recommendations for their clinical use.

Methods: A systematic literature review to 2005 was conducted for positron emission tomography (PET), multi-detector CT angiography (MD-CTA) and magnetic resonance imaging (MRI) in ischemic heart disease. Papers meeting criteria were reviewed for accuracy, prognosis data and study quality. Recommendations were presented to a primary and secondary panel of experts where consensus was achieved.

Results: Indications for PET include detection of CAD with perfusion imaging, and viability using FDG to define LV function recovery and/or prognosis after revascularization (Class I). Detection of CAD in patients, vessel segments and grafts using CT angiography is considered Class IIA at the time of the literature review. Dobutamine MRI is 'Class I' for CAD detection and, along with late gadolinium enhancement (LGE) MRI, Class I for viability detection to predict LV function recovery. Imaging must be performed in institutions and interpreted by physicians with adequate experience and training.

Conclusions: Cardiac imaging using advanced modalities (PET, MD-CTA, MRI) is useful for CAD detection, viability definition and in some cases prognosis. These modalities complement the more wide-spread SPECT and echocardiography. Given the rapid evolution of technology, initial guidelines for clinical use will require regular updates. Evaluation of their integration in clinical practice should be ongoing. Optimal use will require proper training. *A joint effort among specialties is recommended to achieve these goals.*

Overview

Cardiovascular disease is the leading cause of mortality and a major cause of morbidity for Canadians. Non-invasive methods for diagnosis and risk stratification remain the cornerstone of management of patients with heart disease. Over the past few decades, advanced imaging modalities have emerged with excellent diagnostic capabilities. However these techniques are costly and require specific advanced training. While several professional organizations and governments have established recommendations for advanced imaging technologies, (1-4) Canadian recommendations had not previously been developed. The aim of this position statement is, therefore, to systematically review the existing literature so as to recommend indications for the clinical use of these modalities, and to define areas requiring further research and investigation.

The Canadian Cardiovascular Society (CCS), Canadian Association of Radiologists (CAR), Canadian Association of Nuclear Medicine (CANM), Canadian Nuclear Cardiology Society (CNCS), and the Canadian Society of Magnetic Resonance (CanSCMR) had each identified advanced cardiac imaging as a priority for assessment. Primary and secondary panels of experts and practitioners were assembled. (Appendix 1) Given the scope and timelines, it was agreed that this position paper would focus on ischemic heart disease (IHD) (detection, prognosis and viability), with future position statements and/or guidelines focusing on ventricular function and non-ischemic heart disease.

Methods

Search Method for Identification of Studies

A systematic literature review was conducted for the three imaging modalities: positron emission tomography (PET), magnetic resonance imaging (MRI) and multi-detector CT angiography (MD-CTA). Searches for each modality were divided into four categories: Coronary artery disease (CAD) and/or ischemia detection and diagnosis; CAD prognostication; myocardial viability detection; and viability prognostication. A systematic search of the literature, using validated BMJ filters for diagnosis and prognosis, was used to identify the best evidence for use of PET, computed tomography (CT) and MRI. A total of 3,655 references were reviewed. Databases searched were Medline (1966 to June 2005); Embase (1980 to June 2005); and Cochrane, Issue 3 2005; as well as other evidence based medicine (EBM) sites such as that of the Agency for Healthcare Research and Quality (AHRQ). Where a published meta-analysis existed, searches were started from this point forward. MRI was limited to 2004–2005, due to a meta-analysis by Danias, P (1991–Jan 2004 covered) (5). Searches for viability 'detection' using PET were limited to 2001–June 2005 (systematic review by Bax J ; covered up to 2001) (6) and prognosis using viability PET were limited to 2001–June 2005 (meta-analysis by Allman. (7))

For each topic, further exclusions such as size of study and method of imaging were added in areas where there were a very large number of studies. This allowed for practical and accurate review of the best work. Other studies that may have been missed by the systematic review were identified through cross-referencing of identified articles and literature review after June 2005. Lists of titles and abstracts that met search inclusion criteria were provided to the subgroups and reviewed to confirm that they met inclusion criteria. Full manuscripts that met inclusion criteria were circulated to the subgroup teams for review. The imaging subgroups updated literature beyond the primary search strategy time period when key references were identified that met inclusion criteria.

All members of the subgroup reviewed the papers for their specific modality. Sensitivity and specificity tables were completed. The study quality of each paper reviewed was assessed by subgroup members using the quality information questionnaires from the University of Alberta Evidence Based Medicine (EBM) Working Group: http://www.med.ualberta .ca/ebm/diagworksheet.htm; and http://www.med.ualberta.ca/ebm/prognosisworksheet.htm.

Based on the data review, preliminary draft recommendations were prepared and presented to the primary and secondary panels using the standard scoring methods adapted from previous guidelines on imaging from the American College of Cardiology (ACC), The American Heart Association (AHA) and the American Society of Nuclear Cardiology (ASNC). (Appendix 2) Following this, the recommendations were consolidated by the primary panel and circulated to the secondary panel for review and feedback. These recommendations and the document were then finalized by the panels and submitted to the executives of the participating organizations for approval.

Positron Emission Tomography

Given the large number of studies using PET, additional restrictions on search material were applied. For CAD detection, studies were excluded if they involved tracers other than Rb-82 and N-13–ammonia, applied flow quantification as the only method for defining disease, or involved fewer than 20 patients. For prognosis, only studies that considered PET findings in the prediction of outcomes were considered.

Detection and prognosis of coronary disease: Myocardial perfusion imaging (MPI) using Rb-82 or N-13-ammonia PET is a widely accepted technique. (1,2) Images are acquired at rest and during pharmacological stress. PET MPI has often been considered the most accurate non-invasive means for detecting functionally significant coronary disease. (1,2, 8-10) It is considered to be at least as accurate as single photon emission computed tomography (SPECT) MPI.

Diagnosis: Standard relative MPI uses perfusion radiotracer uptake relative to the maximum uptake in the heart to detect regional reductions. These defects in tracer uptake are indicative of functionally significant CAD. This principle is the same for PET and SPECT imaging. One advantage of PET MPI is the use of accurate and reliable attenuation correction that improves specificity and probably also sensitivity. This feature may be particularly relevant in patients with obesity or a body habitus prone to attenuation artifact. PET also provides high spatial resolution among nuclear imaging techniques. (11) Gating of PET MPI (and ^{18}F-fluorodeoxyglucose (FDG)) provides additional clinical information with respect to regional wall motion and left ventricular (LV) function. (2,12,13)

The mean sensitivity and specificity of MPI PET for detection of CAD are 89% and 89% with ranges from 83–100% and 73–100% respectively. (Table 1). (8,9,13-24) Comparison studies support that PET is at least as accurate as SPECT (8,9,14,20,25,26) and that disparate results are due to greater sensitivity and specificity of PET. (8,9,17,20,26,27) A recent study by Bateman et al. demonstrates superior diagnostic accuracy and normalcy rates for gated PET MPI compared to those of gated SPECT MPI ($p = 0.02$). (13) Recent advances in PET including PET/CT are currently being evaluated in multicentre studies such as the SPARC study. (28) The accuracy of PET for CAD detection has not been compared to that of CT or MRI.

In general the studies reviewed were considered to be of good quality, although some early studies did not report all the information now needed to assess quality. Most studies provided prospective evaluation, did not direct the gold standard procedure, and studied relevant patient populations. One study minimized bias by using a matched cohort design and random selection from an electronic database. (13) Most studies report blinded evaluation, but such information was not reported in one study, so blinded evaluation could not be confirmed. (15)

PET MPI and prognosis: A normal PET MPI indicates an excellent prognosis. Hard cardiac event rates range from 0.09% to 0.9% depending on the population and definition of normal. (29-31) These rates are comparable to those for SPECT MPI. (32,33) Patients with PET MPI defects have a worse prognosis for death (4.3% per year) (29) or hard events (7.0% per year with moderate to severe defects). (31) Recent data also indicate the prognostic value of PET MPI in specific populations with obesity or those referred after non-diagnostic ^{99m}Tc-SPECT MPI. (31) The prognostic value of PET/CT is being evaluated in the SPARC study. (28)

Table 2 summarizes the published data on prognosis. A study by MacIntyre et al., which evaluated the clinical outcome in patients with a negative thallium-201 SPECT study and positive PET MPI (26) is not included. This study did not consider the prognostic value of PET per se, although it did support the added value of PET over thallium-201 SPECT. Studies considering other outcomes such as restenosis post-PCI and risk assessment prior

to vascular surgery were not included in prognosis studies listed but are discussed below in 'Other Considerations'.

Exercise PET: (15-17, 34-38) This is feasible and combines the advantages of attenuation correction with the functional capacity data from exercise. There are disadvantages, however: the supine bicycle exercise done is prone to motion artifacts, while the treadmill, which is outside the camera, does not allow absolute flow quantification. Small studies support the accuracy of the method and its utility compared to pharmacological MPI with PET. (15-17, 34-38)

Quantification of myocardial blood flow is used to measure flow at rest and during stress. ^{13}N-ammonia and ^{15}O-water are well validated in this regard. (2, 39-41) ^{82}Rb has also been applied but requires a correction for its lower extraction fraction. (42,43) The advantage of flow quantification is that it provides a very sensitive means to evaluate and monitor therapies. It allows detection of early vascular and endothelial changes affecting flow before overt disease has developed and has the potential to define the hemodynamic significance of a stenosis (44) or balanced reductions in flow and flow reserve in patients with multivessel disease. (2,42) In these circumstances or in conditions which may affect the coronary microvasculature such as Syndrome X (2,45), there may be added value in the application of flow quantification, but clinical studies to evaluate this potential added value have been small and limited. In routine PET MPI, flow quantification is *not* required. Clinical application must be defined on a case by case basis.

Other considerations: ^{82}Rb PET MPI and the measurement of relative flow reserve have been applied and studied for the detection of restenosis six months following angioplasty. In 45 patients, the sensitivity and specificity of relative flow reserve measurements were 93% and 74% respectively. (46)

^{64}Cu-PTSM has also been shown to accurately detect coronary artery disease with sensitivity of 91% and normalcy rate of 100% among a group of 45 subjects. (47)

^{82}Rb PET MPI has also been applied for the prediction of peri-operative and late cardiac events in patients undergoing vascular surgery. In a study of 78 patients, most with intermediate risk factors for peri-operative events (diabetes, stable angina, compensated heart failure, prior myocardial infarction (MI)) (83% had >1 Eagle criteria), reversible ischemia on PET MPI had a 45% positive predictive value for post-operative events (unstable angina, MI, cardiac death) and a normal scan had a 92% negative predictive value. These are comparable to previous SPECT studies with the positive predictive value (PPV) range of 14–50% and negative predictive value (NPV) range of 85–100%. (1,48)

Myocardial Perfusion Imaging (MPI) using PET for Diagnosis and/or Risk Stratification of CAD

Recommendations

The interpretation of Cardiac PET MPI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Pharmacological MPI using PET for the diagnosis of CAD* and/or risk stratification of patients who
    a. have non-diagnostic non-invasive imaging tests or where such a test does not agree with clinical diagnosis (Level B evidence).
    b. may be prone to artifact that could lead to an equivocal other test, such as obese patients (Level B evidence);
    c. are unable to exercise or have left bundle branch block (LBBB) or ventricular pacing (Level B evidence).

Class IIa Indications

1. Pharmacological MPI using PET for the diagnosis of CAD* and/or risk stratification of patients who are able to exercise (Level B evidence);

2. For diagnosis and risk stratification of patients being considered for high-risk non-cardiac surgery who have intermediate clinical risk predictors; or have mild clinical risk predictors with poor functional capacity (<4 METS) (Level B/C evidence).

* Diagnosis is intended for patients with intermediate pretest likelihood of disease.

Class IIb Indications

1. Exercise PET using MPI for the diagnosis of CAD and/or risk stratification (Level B evidence);

2. Quantification of myocardial flow to determine the hemodynamic significance of a given coronary stenosis or to diagnose balanced multivessel disease (Level B/C evidence);

3. Quantification of myocardial flow to define impaired microvascular function (eg. Syndrome X) (Level B/C evidence).

Class III (no benefit or harmful)

1. Contraindications to all pharmacological agents (dipyridamole, adenosine, dobutamine);

2. Unstable pattern of ischemic chest pain;
3. Contraindications to radiation exposure.

Myocardial viability diagnosis: In addition to the exclusions noted above, additional restrictions were applied to FDG viability imaging studies. Excluded were studies with sample size ≤20; mean ejection fraction (EF) ≥ 40%; early post MI (≤10 days); LV recovery evaluation ≤ 8 weeks, or lack of LV recovery or outcome evaluation.

FDG PET imaging has long been regarded as the best standard for detection of viable recoverable myocardium. (2,49) In a comprehensive review of all prior viability studies, Bax et al. identified that FDG PET was the most sensitive method for predicting wall motion recovery while dobutamine echo was the most specific. (6) Few studies compared FDG imaging and dobutamine echo in more severe LV dysfunction, but a key finding in the study by Pagano et al. was the superiority of FDG PET over dobutamine echo in a group of 30 patients with very severe LV dysfunction (EF=23 $\pm$ 7) (PPV;NPV for FDG PET: 66;96%, dobutamine echo: 68;55%). This was even greater in the worst functioning (akinetic) segments (PPV;NPV for FDG PET: 80;94%; dobutamine echo: 73;41 %). (50) Comparison studies with MRI are even more limited (51) and have not compared prediction of LV function recovery.

Qualitative FDG PET imaging is used in conjunction with perfusion imaging to define perfusion defects with metabolic activity (PET mismatch indicating recoverable hibernating myocardium) or without metabolic activity ('PET match' indicating non-recoverable scar tissue); (2,52) or regions with maintained perfusion and metabolism in dysfunctional segments (chronic repetitive stunning with potential for recovery). (53,54). LV volume is also an important consideration as marked remodeling may prevent recovery of function even in the presence of viability. (55)

Quantification of FDG uptake applies Patlak graphical analysis of dynamic time-activity FDG data to determine the rate of uptake. This can be used to estimate exogenous myocardial glucose utilization (MGU). Maintained MGU indicates the presence of viable recoverable myocardium.

Both methods provide accurate means for predicting recovery of function after revascularization. (2,6,56,57) Recent data also indicate that PET-defined scar tissue and hibernating myocardium can be combined with clinical parameters to predict LV function recovery. (52) This approach is currently being evaluated in a randomized controlled trial (RCT). (58) Gating of FDG PET provides additional clinical information with respect to regional wall motion and LV function. (2,12)

From the studies included in this review, the sensitivity and specificity of FDG PET for LV function recovery are 91% and 61% respectively (see Table 3) (6,54,59-65) with ranges from 80–100% and 44–92%. These studies support the earlier meta-analysis indicating that FDG PET has a high level of sensitivity. Lower specificity likely relates to incomplete revascularization or failure to account for prolonged LV function recovery. (11,50,53)

The studies included in this review were gerenally considered to be of good quality, although some did not report some information needed to fully assess quality. It was sometimes difficult to identify the raw data to determine sensitivity and specificity. Although this was possible in most cases, occasionally it was not possible at all. (63) Most studies provided prospective evaluation, but it was sometimes unclear if revascularization was directed by the FDG PET imaging. Several studies focused on the most relevant patient population, i.e. those with IHD and severe LV dysfunction. Most studies reported blinded evaluation or used objective quantification methods. There was also variability in methods: for viability determination (mismatch vs % uptake of FDG); in follow-up duration; and in regional versus global LV recovery and analysis method. Regardless of the variability, there was consistent evidence to support the value of FDG imaging and in particular, the higher sensitivity of FDG PET over that of other methods. Thus, FDG PET has the potential to more definitively rule out viable myocardium when this is needed to select patients for revascularization.

Myocardial viability and prognosis: Table 4 outlines recent FDG PET studies that deal with prognosis. (7,66-74) Outcome data have consistently demonstrated that FDG PET defines viable myocardium in patients with LV dysfunction, and that these patients are at high risk for cardiac events including death, if they do not undergo timely revascularization. (71-75) Recent data support that early intervention in patients with viable myocardium can improve survival rates. (75) There is one small published randomized controlled trial comparing FDG PET with ^{99m}Tc-methoxyisobutyl isonitrile (MIBI) SPECT. Trends but no significant differences in outcomes were identified. However, in this study two-thirds of patients had mild-moderate LV dysfunction and were not representative of the population most likely to benefit from defining viable myocardium. (76) Prolonged delays to revascularization (mean >110 days) and technical comparison issues were the other limitations of this particular study. Ongoing RCTs are evaluating the utility of FDG PET in directing therapy in patients with severe LV dysfunction and IHD. These studies will help to further define the role of viability imaging in this patient population.

Many techniques are valuable in defining viable myocardium in patients with mild or moderate LV dysfunction. However, in patients with severe LV dysfunction, knowing the extent of scar tissue and hibernating myocardium (which can be defined using FDG PET), is often important in decision making for revascularization. (2,57) Fusion imaging of FDG PET with MRI or CT may provide even greater accuracy for detecting viable tissue, through combining the advantages of each technique.

Myocardial FDG PET Viability Imaging

Recommendations

The interpretation of FDG PET viability imaging should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. To define myocardial viability in patients with
    a. ischemic heart disease and severe LV dysfunction, to identify extent of recoverable myocardium and prognosis in patients being considered for revascularization or cardiac transplantation (Level B evidence);

    b. moderate to large fixed perfusion defects or with equivocal results on another viability test (Level B evidence).

Class IIa Indication

1. Moderate systolic LV dysfunction and IHD to identify the extent of recoverable viable myocardium and prognosis in patients being considered for revascularization or cardiac transplantation (Level B evidence).

Class III (no benefit or harmful)

a. Contraindications to insulin;
b. Severe untreated hypokalemia;
c. Contraindications to radiation exposure.

Computed Tomography Angiography

Detection of coronary artery disease: With the recent advances in the spatial and temporal resolution of multi-detector computed tomography (MDCT) scanners, cardiac CT angiography is feasible and is increasing in accuracy. Computed tomographic angiography (CTA) has the benefits of being a non-invasive modality with the potential of providing anatomical information with a very short imaging sequence (5–25 seconds). By obviating the need for arterial access and cannulation of the coronary arteries, CTA may avoid many of the risks associated with conventional invasive coronary angiography.

Computed tomographic angiography has been used to assess native coronary arteries, arterial and saphenous vein bypass grafts, coronary stents and anomalous coronary arteries. (77-82) Numerous studies have evaluated the accuracy of 16-slice MDCT with invasive coronary angiography (Table 5) (79,83-99) and have demonstrated good accuracy in coronary segments that can be evaluated (> 1.5 mm in diameter). The overall sensitivity and specificity for defining angiographic disease for 16-slice MDCT are 87% and 96% respectively. For detection of disease in patients, the sensitivity and specificity for detecting disease are 91% and 95% for 16-slice MDCT. More recently, the few studies using 64-slice MDCT have also demonstrated very good accuracy with a larger number of segments that could be evaluated than is the case using 16-slice MDCT (Table 6). (94,100-102)

Patients referred for coronary angiography are generally suspected of having obstructive CAD on the basis of the results of previous non-invasive investigations. This unavoidable bias in patient selection may result in the overestimation of CTA specificity (i.e., the underestimation of the false positive rate of CTA studies). However, the use of normal reference segments and vessels to determine vessel specificity suggests that any overestimation of specificity is probably small. The negative predictive value of CTA has consistently been excellent. CTA may therefore be most beneficial in patients for whom the diagnosis of obstructive CAD needs to be ruled out.

Cardiac motion and coronary calcification are two important limiting factors in the use of CTA. Accordingly, certain patients should not routinely undergo CTA such as those with irregular cardiac rhythms (e.g. atrial fibrillation, frequent extrasystoles), severe coronary calcification, an inability to perform sufficient breath-holds, and contraindications to intravenous contrast agents or to radiation exposure.

A recent meta-analysis of MDCT and MRI confirms the utility of CTA and also suggests that CT angiography has a significantly higher diagnostic accuracy than MRI for detection of significant CAD. (82) At this time, there is no data supporting the use of CTA for determining patient prognosis. The use of this diagnostic technique is the focus of current studies such as the SPARC trial (28) and will continue to be a focus of future investigation.

Ionizing radiation exposure with CT remains a concern. The estimated effective radiation dose with 16-slice CTA ranges from 7-15 mSv. (93,103,104) However, given the shorter imaging time of 64-slice MDCT, improved digital acquisitions systems and x-ray tube modulation, the radiation exposure associated with 64-slice MDCT is expected to be the same or slightly lower (4.8-14 mSv), although this remains to be confirmed by an independent source. The radiation dose of CTA appears to be similar to slightly higher than other traditional non-invasive modalities. Clinicians must continue to strive to minimize patient exposure to ionizing radiation. Future technological developments must be made without additional increases in patient radiation exposure.

As advances in CT hardware and software are made, Cardiac CT has the potential to improve cardiac patient care. Research is underway to investigate its utility in acquiring functional data such as the assessment of regional wall motion, estimation of ejection fraction and perfusion imaging.

Calcium scoring (with MDCT) is used to identify calcified plaque, which may have prognostic value but is beyond the scope of this evaluation. CTA also shows promise in the assessment of atherosclerotic plaque but remains a research tool.

Future Directions: Cardiac CT has promise in several areas pertinent to the assessment of patients with suspected or documented CAD. Ongoing research evaluates the ability of CT to assess coronary artery atherosclerotic plaque, (105,106) coronary stents, LV function, (107-109) myocardial perfusion (110) and/or myocardial viability. (111)

At the time of this review, there were limited data on 64-slice CTA, and the panel anticipates that these recommendations will require amendments as CTA continues to evolve.

CAD Detection with CT Angiography

Recommendations

The interpretation of cardiac CT and CTA should be carried out only by physicians and institutions with adequate training and experience.

Class I Indication

1. Assessment of anomalous coronary arteries (Level C evidence).

Class IIa Indications

1. 16- or 64-slice MDCT for patient diagnosis of significant coronary artery disease (≥ 50% diameter stenosis)(Level B evidence);
2. 16- or 64-slice MDCT for identification of coronary artery segments with significant stenosis (≥ 50% diameter stenosis) in coronary segments ≥ 1.5 mm in diameter (Level B evidence);
3. 16- and 64-slice MDCT for the assessment of graft patency (Level B evidence).

Class IIb Indication

1. 64-slice MDCT for the assessment of all coronary segments including those with vessel diameters < 1.5 mm (Level B evidence).

Class III (no benefit or harmful)

1. Diagnosis of CAD in patients with
    a. irregular dysrhythmias (atrial fibrillation, frequent extrasystoles);
    b. severe coronary calcification;
    c. inability to perform sufficient breath-holds;

d. renal failure or other contraindications to intravenous contrast agents;
e. contraindications to radiation exposure.

Magnetic Resonance Imaging

Cardiovascular magnetic resonance (CMR) imaging provides a very broad set of tools for diagnosis and prognosis in patients with coronary artery disease. The assessment of cardiac function, morphology and mass with CMR using 3D methods with no geometric assumptions has been extensively validated. These quantitative measurements have excellent inter-study reproducibility.

Detection of coronary artery disease: Several cardiac magnetic resonance (CMR) approaches are used to detect CAD. These include the direct visualization of the coronary artery lumen; visualization of ischemic myocardial injury (infarction); and detection of the effects of induced ischemia on wall motion, perfusion and coronary blood flow.

Coronary magnetic resonance angiography: Magnetic resonance angiography (MRA) and quantification of vascular flow is a common approach used in almost all vessels in the body except the coronaries. It remains technically challenging to image the coronary arteries with the temporal and spatial resolution necessary to predict > 50% stenoses. This is due to the size, tortuosity and, most importantly, complex motion of the coronary arteries during the cardiac cycle. Published data do not provide information on the diagnostic performance of recently modified 3D navigator techniques. In reported studies, the negative predictive value for coronary magnetic resonance angiography (CMRA) to exclude multi-vessel proximal obstructive CAD reached 81% in a recent multi-centre trial (112) but current techniques have not yet been shown to reproducibly predict diameter stenoses even in broad categories or adequately examined distal vessels. Three techniques have been extensively studied at 1.5 Tesla field strength: 2D breath held, 3D breath held, and 3D navigator. (112-138) The majority of these studies are performed without any magnetic resonance contrast agents. In two recent meta-analyses of 999 patients in 28 MRA studies, the positive and negative predictive values for detection of > 50% stenosis in interpretable segments were 65% and 90% respectively (Table 7). (5,82) If uninterpretable segments are included these values fall to 37% and 85% respectively. More recent work has been performed at 3 Tesla and yielded a sensitivity of 82% and a specificity of 89%. (114) Overall CMRA has a good diagnostic performance in all vessels except the circumflex coronary artery, which is likely due to its proximity to the adjacent blood pools of the left atrium and ventricle, and lower signal from its location which is often furthest from the receiver coil. False positive rates remain high. A review of the studies suggests that the greatest value of CMRA is with a negative study in a patient with low pretest probability of CAD. (5) Currently there are no clinically approved

truly intravascular magnetic resonance contrast agents that could increase the signal-to-noise ratio to such a level to permit improved coronary imaging. However, research is ongoing.

Coronary bypass graft patency has also been examined with CMR using MRA and MR flow measurement techniques. (139-150) While the positive predictive value for the detection of a patent bypass graft has been reported to be as high as 95%, limitations such as metallic clip artifacts reduce the negative predictive value to the 44% range. (150)

The course of anomalous coronary arteries which can induce ischemia, especially if the artery passes between the aorta and pulmonary artery, can be clearly delineated by CMR when compared to x-ray angiography. (151-154)

Stress wall motion: Using CMR, stress is induced pharmacologically, as physical exercise is difficult to perform within the magnet bore and often induces motion artifacts. Dobutamine stress-induced wall motion abnormalities are easily appreciated using the high quality imaging of CMR. This technique is well established and trials have shown it to be as good as or better than dobutamine stress echo in the diagnosis of CAD. Data from eight studies involving a total of 893 patients show an average sensitivity and specificity of 90% and 84% respectively (Table 8). (155-162) Objective quantification with techniques such as tagging, in which nulled signal lines deformation changes are recorded, adds to the sensitivity of the technique.

Stress perfusion: Myocardial perfusion can also be measured during stress (either with dobutamine or dipyridamole) following a first pass of an intravenous bolus of gadolinium contrast (0.1 mmol/kg) injected at 5-7 mL/s. The signal increase, as gadolinium washes into the myocardium, can be quantified as perfusion maps. Hypoperfused myocardial segments are seen as dark regions of low signal during first pass of the contrast. These techniques have been extensively studied and validated in animal models. Validation in human studies has also been performed with good correlation to x-ray angiography, PET and SPECT. Data from 11 studies involving a total of 647 patients show an average sensitivity and specificity of 84% and 86% respectively (Table 9). (162-172) Recently the MR-Impact study of 241 patients showed that first pass perfusion CMR was superior to SPECT in detecting CAD. Impaired subendocardial perfusion has also been demonstrated in metabolic syndrome. Newer non-contrast techniques to examine tissue oxygen levels such as T2* dependent effects in BOLD imaging hold promise but further investigation is needed.

Myocardial viability: CMR employs two techniques to examine myocardial viability: Dobutamine stress MR (DSMR) to induce improvement of contractility of dysfunctional segments; and late gadolinium enhancement (LGE). DSMR has been shown to have similar or improved ability to predict contractile improvement post-

revascularization compared to that of dobutamine stress echo. Data from 14 studies involving a total of 569 patients demonstrate a sensitivity and specificity of 91% and 94% respectively (Table 10). (124,159,173-180)

LGE is a CMR technique to image non-viable/infarcted myocardium. The extravascular contrast agent gadolinium (0.1-0.2 mmol/kg) accumulates within infarcted tissue which has a larger extravascular space than does normal tissue. This accumulation leads to visualization of infarcted myocardium as areas with altered signal intensity in inversion recovery gradient echo sequences. This technique has been thoroughly validated in animals. LGE has been widely studied in humans. It shows good correlation with PET and superiority to SPECT in quantifying both viable and non-viable myocardium. Data from 13 studies involving a total of 357 patients reveal a sensitivity and specificity of 81% and 83% respectively for predicting recovery or lack of recovery of LV function (Table 11). (51,177,180-190) The transmurality of the infarct can also be determined, and this can be used to improve the ability of LGE to predict recovery after revascularization. In Kim et al. (181) for example, examination of severe hypokinetic, akinetic or dyskinetic segments with < 25% transmural LGE had a 79% chance of functional recovery after revascularization compared to a 6% chance of recovery if LGE showed > 50% transmurality. (181)

For both LGE MRI and dobutamine stress MRI for viability, the number of studies involving patients with more significant LV dysfunction (EF < 40%) is limited. Further studies continue to be needed in the patient population with severe LV dysfunction.

Currently, there are few studies evaluating the impact of DSMR and LGE CMR on cardiac outcomes, but several studies are currently underway. Outcome studies in patients with *severe* LV dysfunction are limited.

Evaluation of acute coronary syndromes: CMR has been used in the emergency room in the assessment of chest pain. CMR showed a sensitivity and specificity of 84% and 85% respectively for identifying patients with CAD. Multi-variate analysis including standard clinical tests (ECG, troponin, TIMI risk score) showed that CMR was the strongest predictor of CAD. CMR added diagnostic value over clinical parameters, including identification of enzyme-negative unstable angina. This promising data needs to be confirmed in other centres. CMR also identifies microvascular obstruction in acute MI. This is demonstrated early (1–2 minutes) after intravenous injection of gadolinium. At this timepoint, inversion recovery CMR shows areas within the MI with severely compromised perfusion as black, indicating areas with microvascular collapse. Microvascular obstruction detected by CMR has been linked to ventricular remodelling and adverse cardiovascular events. Finally, the transmural extent of late gadolinium-enhancement CMR predicts recovery of function following acute MI. CMR is effective in demonstrating the complications of acute MI, including ventricular aneurysm, pseudoaneurysms, ventricular septum perforation, and mitral regurgitation. Echocardiography may yield false

positive and false negative results when employed to look for LV thrombi in post-infarction patients. CMR is useful in this regard.

CAD Detection Using MRI

Recommendations

The interpretation of Cardiac MRI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Assessment of anomalous coronary arteries (Level C evidence);
2. Detection of coronary stenosis > 50%
    a. stress function with dobutamine (Level B evidence).

Class IIa Indication

1. Detection of coronary stenosis > 50%
    a. Stress First Pass Perfusion (Level B evidence).

Class IIb Indications

1. Detection of coronary stenosis > 50%
    a. Coronary MR angiography (Level B evidence);

2. Graft Patency
    a. Coronary MR angiography (Level C evidence).

Class III (no benefit or harmful)

1. contraindication to MRI;
2. contraindication to gadolinium contrast;
3. inability to perform sufficient breath-holds.

Myocardial Viability using MRI

Recommendations

The interpretation of Cardiac MRI should be carried out only by physicians and institutions with adequate training and experience.

Class I Indications

1. Assessment of myocardial viability in patients with LV dysfunction or akinetic segments for predicting recovery of ventricular function following revascularization

a. Late Gadolinium Enhancement (Level B evidence);
b. Dobutamine Stress Wall Motion (Level B evidence).

Class IIa Indications

1. Assessment of myocardial viability to determine prognosis following revascularization in patients with moderate/severe LV dysfunction

    a. late gadolinium enhancement (Level B/C evidence);

    b. dobutamine stress wall motion (Level B/C evidence).

Role of Echocardiography and SPECT Imaging (1,28,191-194)

Echocardiography remains an established imaging modality in patients with ischemic heart disease. The identification of segmental LV wall motion abnormalities, at rest or induced by exercise or pharmacologic (dobutamine or dipyridamole) stress, allows the detection of CAD and provides clinically useful prognostic data. dobutamine stress echocardiography has demonstrated utility in the detection of myocardial viability, and the prediction of recovery of function post-revascularization. Important advances in echocardiography have occurred over the past decade, with the aim of further improving the accuracy and reproducibility for CAD detection and prognostication. While a full discussion is beyond the scope of this current position statement, these advances have included, 1) real-time 3D echocardiography, enabling acquisition of 3D volume sets and off-line tomographic analysis, 2) techniques to quantify wall motion during stress echocardiography, including tissue Doppler, strain rate imaging and colour kinesis, and 3) the use of microbubble contrast agents for left ventricular opacification and myocardial perfusion. These ultrasound contrast agents are approved for use in Canada to improve LV endocardial border delineation, and have been demonstrated to increase the diagnostic accuracy and reproducibility of stress echocardiography, and reduce interobserver variability. Studies have now demonstrated the utility of contrast echocardiography to image myocardial perfusion at rest and during pharmacologic stress, allowing the simultaneous assessment of regional wall motion and perfusion, and potentially resulting in improved detection of CAD and myocardial viability.

Cardiac perfusion imaging using radioisotopes is a well-established technique that has been and continues to be the mainstay of noninvasive diagnosis and determination of prognosis for patients with coronary artery disease. It is a very robust technique that is widely available throughout the world. Myocardial perfusion imaging has excellent sensitivity and specificity for the detection of coronary artery disease. Over recent years, advances in radioisotopes, gating of images, and attenuation correction have significantly improved the sensitivity and specificity of the test. There is a vast literature (more than 50,000 patients) on the determination of prognosis for

patients in whom coronary artery disease is suspected. There are several advantages to using this technique. Standard protocols have been published, and acquisition of images is operator-independent. Large numbers of cardiologists, nuclear medicine physicians, and radiologists are able to interpret myocardial perfusion images. Training standards have been published in Canada and the United States. Appropriateness criteria have been published recently in the United States. Guidelines for the performance and use of radionuclide perfusion images have been published in the United States and are under development in Canada. Using tomographic imaging, left ventricular ejection fraction and volumes can be calculated, allowing simultaneous assessment of myocardial perfusion and function. Although perfusion imaging is usually performed in conjunction with stress testing (which adds prognostic value), it is possible to use pharmacological stress in patients who cannot exercise to their target heart rate. Myocardial perfusion images have the advantage of detecting physiology rather than anatomy. Many studies have shown the incremental value of physiological imaging over anatomical evaluation of coronary artery disease using coronary angiography. Myocardial perfusion imaging has also been very useful in special populations such as women and patients with diabetes.

The newest advances have been in instrumentation. Manufacturers have developed hybrid gamma cameras with CT. These hybrid devices have improved the specificity of perfusion imaging through the ability to do CT attenuation correction. However, newer cameras also have diagnostic CT scanners that can be used for calcium scoring and CT angiography, allowing an assessment of atherosclerosis rather than of just ischemia. Myocardial perfusion imaging will likely remain the standard for detection of coronary artery disease and for determining prognosis. The more advanced techniques discussed in this paper are very exciting developments. It will be important to develop pathways for the appropriate use of all the imaging techniques.

Due to their large clinical experience and ongoing advances in imaging technology, echocardiography and nuclear SPECT imaging will continue to play important first-line roles in the assessment of patients with CAD. As the advanced imaging techniques discussed in this position statement continue to develop, and as experience and long-term prognostic data grow, these newer modalities will likely play an ever-increasing role in the management of patients with ischemic heart disease. They serve as complementary tests when results of initial imaging tests are equivocal or non-diagnostic, and in some cases, first-line tests at sites with established expertise. Given that certain newer imaging modalities hold great promise for the non-invasive evaluation of the coronary tree, an approach combining a *functional* assessment of wall motion and perfusion, using nuclear SPECT, PET, echocardiographic or MRI techniques, with an *anatomical* assessment, with cardiac CT angiography or MRI, holds a certain appeal in the evaluation of patients with ischemic heart disease. New algorithms for patient evaluation will continue to evolve but will continue to involve SPECT and echocardiography.

Radiation Exposure

Table 12 lists the radiation exposure from common non-invasive radionuclide or x-ray based cardiac procedures. CT angiography appears comparable to other standard non-invasive imaging methods. (103, 194-197)

Cost Considerations:

Economic evaluation is an important consideration in the development of new technologies. In any cost-effectiveness analysis, it is important to determine the population under consideration, the intervention, the comparator or comparators, the perspective of the study, the outcomes and the costs involved. Analysis and modelling of the underlying processes involved also generally require some knowledge of factors (or covariates) that determine the costs and outcomes of the intervention.

For PET MPI imaging, cost data have been conflicting. In one study that compared PET to treadmill, SPECT MPI and coronary angiography, PET had the most favourable incremental cost-effectiveness ratio. (198) In another study that compared PET MPI, stress echocardiography, SPECT MPI, and coronary angiography, PET had the worst cost-effectiveness ratio. (199) However, these studies apply theoretical models that depend very much on the studies selected and clinical care assumptions. They do not consider evaluation in real patient populations, nor the impact of recent data on diagnostic accuracy or prognosis. They are also not valid in Canada where costs may be considerably lower in certain settings in which efficient practice considerations have been implemented. Despite these limitations, an evaluation regarding the 'selection of patients for angiography' suggested that PET and SPECT MPI are both cost-effective approaches in patients with intermediate pre-test likelihood of CAD. (200)

One study evaluated the incremental cost of FDG PET viability imaging in patients with ischemic heart disease and LV dysfunction. (201) Compared were coronary artery bypass grafting (CABG) for all patients, PET to select those with hibernating myocardium for grafting, and medical therapy for all patients. A health care perspective was used. Costs and outcomes were considered for one year from the time of initial treatment. The study concluded that FDG PET viability imaging was cost-effective in the selection of patients with LV dysfunction referred for CABG.

To our knowledge, no published studies have evaluated the incremental cost-effectiveness of MRI or CT angiography in patients with coronary artery disease. For new technologies such as CT angiography and fusion or hybrid imaging, there will need to be careful prospective consideration of costs in real patient populations.

Concluding Remarks

The recommendations in this position statement are based on the literature to 2005 and selected works published in early 2006. The best available evidence is combined with clinical expertise and opinion to determine the recommendations noted above.

The recommendations demand that any imaging technique be performed and interpreted in institutions and by physicians who have adequate experience and training.

It is anticipated that the availability of all these advanced imaging techniques will increase in Canada. This document serves as an initial guideline for clinical use. Given the rapid evolution of technologies and emerging literature, such recommendations will require regular updates; by the time this position statement is published, some of the recommendations may be outdated. Therefore, this position statement should be used as a guide and taken in the context of time and available data.

Future research and evaluation studies of diagnostic imaging would be helped by consistently reporting details of the patient population, methods of recruitment and blinded analysis. The gold standard method used for comparison should not be influenced by the test being evaluated. Studies should consider applicability and potential impact to patient management and outcome. Studies should consider criteria that have been developed and that are being applied to evaluate quality of data and evidence.

Imaging laboratories and facilities should engage in collection of patient registry data to allow characterization and improvement in appropriate utilization of these technologies for which access is currently limited.

Standardized reports appropriate for the specific technology should be developed and utilized across facilities. This combined with network integration of images may reduce the need for repeat testing.

Continued research will always be required to better characterize the utility, diagnostic and prognostic value of these tests. This will assist in the development of evidence-based patient care pathways and algorithms for an increasingly complex array of tests that are now available.

Finally, with the rapid emergence of these technologies, training guidelines are also needed. Imaging specialties and clinical specialties must further integrate their practices. This need must be transmitted to trainees who will become the experts to perform and interpret these tests in the future. A joint effort among specialties is recommended to achieve this goal.

Acknowledgements

The panel thanks Sherri Nipius for her excellent work in preparing the manuscript and organizing teleconferences and Linda Garrard, RN for organizing the panel meeting in Montreal. We also thank Holly Ananny, M.A. for her assistance in editing the manuscript.

References

1. *Klocke F, Baird M, Bateman T, et al. ACC/AHA/ASNC Guidelines for the Clincial Use of Cardiac Radionuclide Imaging. J Am Coll Cardiol. 2003;42:1-69.*
2. *Schelbert H, Beanlands R, Bengel F, et al. PET myocardial perfusion and glucose metabolism imaging: Part 2-Guidelines for interpretation and reporting. J Nucl Cardiol. 2003;10:557-71.*
3. *Underwood R, Bax JJ, vom Dahl J, et al. Imaging techniques for the assessment of myocardial hibernation. Report of a Study Group of the European Society of Cardiology. Eur Heart J. 2004;25:815-836.*
4. *Pennell D, Sechtem UP, Higgins CB, et al. Clinical indication for cardiovascular magnetic resonance (CMR): Consensus Panel report. Eur Heart J. 2004;25:1940-65.*
5. *Danias P, Roussakis A, Ioannidis J. Diagnostic performance of coronary magnetic resonance angiography as compared against conventional X-ray angiography: A meta-analysis. J Am Coll Cardiol. 2004;44:1867-76.*
6. *Bax JJ, Poldermans D, Elhendy A, Boersma E, Rahimtoola S. Sensitivity, specificity, and predictive accuracies of various noninvasive techniques for detecting hibernating myocardium. Curr Probl Cardiol. 2001;26:141-86.*
7. *Allman KC, Shaw L, Hachamovitch R, Udelson J. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. J Am Coll Cardiol. 2002;39:1151-8.*
8. *Go R, Marwick T, MacIntyre W, et al. A prospective comparison of rubidium-82 PET and thallium-201 SPECT myocardial perfusion imaging utilizing a single dipyridamole stress in the diagnosis of coronary artery disease. J Nucl Med. 1990;31:1899-905.*
9. *Stewart R, Schwaiger M, Molina E, et al. Comparison of rubidium-82 positron emission tomography and thallium-201 SPECT imaging for detection of coronary artery disease. Am J Cardiol. 1991;67:1303-10.*
10. *Tamaki N, Ruddy T, deKemp R, Beanlands R. Evaluation of Myocardial Perfusion. In: R W, ed. Principles and Practice of Positron Emission Tomography. In Press ed; 2002.*
11. *Bax JJ, Beanlands R, Klocke F, et al. Diagnostic and clinical perspectives of fusion imaging in cardiology: Is the total greater than the sum of its parts? Heart. 2006;Dec 2005.*
12. *Saab G, de Kemp R, Ukkonen H, Ruddy T, Germano G, Beanlands R. Gated 19-Fluorine Fluorodeoxyglucose Positron Emission Tomography: Determination of Global and Regional Left Ventricular Function and Myocardial Tissue Characterization. J Nucl Cardiol. 2003;10:297-303.*
13. *Bateman T, Heller G, McGhie A, et al. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: Comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol. 2006;13:24-33.*
14. *Schelbert HR, Wisenberg G, Phelps ME, Gould KL, Henze E, Hoffman EJ, Gomes A, Kuhl DE. Noninvasive assessment of coronary stenoses by myocardial imaging during pharmacologic coronary vasocilation. VI. Detection of coronary artery disease in human beings with intravenous N-13 ammonia and positron computed tomography. Am J Cardiol. 1982;49:1197-207.*
15. *Tamaki N, Yonekura Y, Senda M, et al. Myocardial positron computed tomography with 13N-ammonia at rest and during exercise. Eur J Nucl Med. 1985;11:246-51.*

16. *Yonekura Y, Tamaki N, Senda M, et al. Detection of coronary artery disease with 13N - ammonia and high resolution positron emission computed tomography. Am Heart J. 1987;113:645-54.*
17. *Tamaki N, Yonekura K, Yamashita K, et al. Relation of Left Ventricular Perfusion and Wall Motion with Metabolic Activity in Persistent Defects on Thallium-201 Tomography in Healed Myocardial Infarction. Am J Cardiol. 1988;62:202-208.*
18. *Gould K, Goldstein R, Mullani N, et al. Noninvasive assessment of coronary stenoses by myocardial perfusion imaging during pharmacologic coronary vasodilation. VIII. Clinical feasibility of positron cardiac imaging without a cyclotron using generator-produced rubidium-82. J Am Coll Cardiol. 1986;7:775-89.*
19. *Demer L, Gould K, Goldstein R, et al. Assessment of coronary artery disease severity by positron emission tomography. Comparison with quantitative arteriography in 193 patients. Circulation. 1989;79:825-35.*
20. *Marwick T, Nemec J, Stewart W, Salcedo E. Diagnosis of coronary artery disease using exercise echocardiography and positron emission tomography: Comparison and analysis of discrepant results. J Am Soc Echocardiogr. 1992;5:231-8.*
21. *Grover-McKay M, Ratib O, Schwaiger M, et al. Detection of coronary artery disease with positron emission tomography and rubidium 82. Am Heart J. 1992;123:646-52.*
22. *Laubenbacher C, Rothley J, Sitomer J, et al. An automated analysis program for the evaluation of cardiac PET studies: initial results in the detection and localization of coronary artery disease using nitrogen-13-ammonia. J Nucl Med. 1993;34:968-78.*
23. *Williams B, Mullani N, Jansen D, Anderson B. A retrospective study of the diagnostic accuracy of a community hospital-based PET center for the detection of coronary artery disease using rubidium-82. J Nucl Med. 1994;35:2586-92.*
24. *Simone G, Mullani N, Page D, Anderson BS. Utilization statistics and diagnostic accuracy of a nonhospital-based positron emission tomography center for the detection of coronary artery disease using rubidium-82. Am J Physiol Imag. 1992;7:203-9.*
25. *Tamaki N, Yonekura Y, Senda M, et al. Value and limitation of stress thallium-201 single photon emission computed tomography: Comparison with nitrogen-13 ammonia positron tomography. J Nucl Med. 1988;29:1181-8.*
26. *MacIntyre W, Go R, King J, et al. Clinical outcome of cardiac patients with negative thallium-201 SPECT and positive rubidium-82 PET myocardial perfusion imaging. J Nucl Med. 1993;34:400-4.*
27. *Schelbert HR, Buxton D. Insights into coronary artery disease gained from metabolic imaging. Circulation. 1988;78:496-505.*
28. *Di Carli M, Hachamovitch R. Should PET replace SPECT for evaluating CAD? The end of the beginning. J Nucl Cardiol. 2006;13:2-7.*
29. *Marwick T, Shan K, Patel S, Go R, Lauer M. Incremental value of rubidium-82 positron emission tomography for prognostic assessment of known or suspected coronary artery disease. Am J Cardiol. 1997;80:865-70.*
30. *Chow B, Wong J, Yoshinaga K, et al. Prognostic significance of dipyridamole-induced ST depression in patients with normal 82Rb PET myocardial perfusion imaging. J Nucl Med. 2005;46:1095-101.*
31. *Yoshinaga K, Chow B, deKemp R, et al. What is the prognostic value with rubidium-82 perfusion positron emission tomography imaging? J Am Coll Cardiol. 2006;In Press.*
32. *Iskander S, Iskandrian AE. Risk assessment using single-photon emission computed tomographic technetium-99m sestamibi imaging. J Am Coll Cardiol. 1998;32:57-62.*

33. *Hachamovitch R, Berman DS, Shaw L, et al. Incremental prognostic value of myocardial perfusion single photo emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation. 1998;97:535-43.*
34. *Abramson B, Ruddy TD, deKemp R, Laramee L, Marquis J-F, Beanlands R. Stress perfusion/metabolism imaging: A pilot study for a potential new approach to the diagnosis of coronary disease in women. J Nucl Cardiol. 2000;7:205-212.*
35. *Chow B, Ananthasubramaniam K, deKemp R, Dalipaj M, Beanlands R, Ruddy T. Comparison of treadmill exercise versus dipyridamole stress with myocardial perfusion imaging using 82Rb positron emission tomography. J Am Coll Cardiol. 2005;45:1227-34.*
36. *Chow B, Beanlands R, Lee A, J D, deKemp R, Alkahatani A, Ruddy T. Treadmill exercise produces larger perfusion defects than dipyridamole stress N-13 ammonia positron emission tomography. J Am Coll Cardiol. 2006;47:411-16.*
37. *Krivokapich J, Smith GT, Sung-Cheung H, et al. 13-N ammonia myocardial imaging at rest and with exercise in normal volunteers; Quantification of absolute myocardial perfusion with dynamic positron emission tomography. Circulation. 1989;80:1328-1337.*
38. *Wyss C, Koepfli P, Mikolajczyk K, Burger C, von Schulthess G, Kaufmann P. Bicycle exercise stress in PET for assessment of coronary flow reserve: repeatability and comparison with adenosine stress. J Nucl Med. 2003;44:146-54.*
39. *Schelbert H, Phelps M, Huang S-C, et al. N-13 ammonia as an indicator of myocardial blood flow. Circulation. 1981;63:1259-1271.*
40. *Muzik O, Duvernoy C, Beanlands RSB, et al. Assessment of diagnostic performance of quantitative flow measurements in normal subjects and patients with angiographically documented coronary artery disease by means of nitrogen-13 ammonia and positron emission tomography. J Am Coll Cardiol. 1998;31:534-540.*
41. *Walsh MN, Bergmann SR, Steele R, et al. Delineation of impaired regional myocardial perfusion by positron emission tomography with H2(15)O. Circulation. 1988;78:612-20.*
42. *Parkash R, deKemp RA, Ruddy TD, et al. Potential utility of rubidium 82 PET quantification in patients with 3-vessel coronary artery disease. J Nucl Cardiol. 2004;11:440-9.*
43. *Yoshida K, Mullani N, Gould LK. Coronary flow and flow reserve by PET simplified for clinical applications using Rubidium-82 or Nitrogen-13-Ammonia. J Nucl Med. 1996;37:1701-1712.*
44. *Uren NG, Melin JA, De Bruyne B, Wijins W, Baudhuin T, Camici PG. Relation between myocardial blood flow and the severity of coronary artery stenosis. N Engl J Med. 1994;330:1782-1788.*
45. *Geltman EM, Hennes GC, Senneff MJ, Sobel BE, Bergmann SR. Increased myocardial perfusion at rest and diminished perfusion reserve in patients with angina and angiographically normal coronary arteries. J Am Coll Cardiol. 1990;16:586-595.*
46. *Schelbert HR, Wisenberg G, Phelps ME, et al. Serial myocardial perfusion imaging with dipyridamole and rubidium-82 to assess restenosis after angioplasty. J Nucl Med. 1995;36:1553-1560.*
47. *Wallhaus TR, Taylor M, DeGrado TR, et al. Myocardial free fatty acid and glucose use after carvedilol treatment in patients with congestive heart failure. Circulation. 2001;103:2441-6.*
48. *Marwick T, Shan K, Go R, MacIntyre W, Lauer M. Use of positron emission tomography for prediction of perioperative and late cardiac events before vascular surgery. Am Heart J. 1995;130:1196-202.*

49. *Camici P, Ferrannini E, Opie LH. Myocardial metabolism in ischemic heart disease: basic principles and application to imaging by positron emission tomography. Progress in Cardiovascular Diseases. 1989;XXXII:217-238.*
50. *Pagano D, Bonser R, Townend J, Ordoubadi F, Lorenzoni R, Camici P. Predictive value of dobutamine echocardiography and positron emission tomography in identifying hibernating myocardium in patients with postischaemic heart failure. Heart. 1998;79:281-288.*
51. *Klein C, Nekolla S, Bengel F, et al. Assessment of myocardial viability with contrast-enhanced magnetic resonance imaging: Comparison with positron emission tomography. Circulation. 2002;105:162-7.*
52. *Beanlands R, Ruddy T, deKemp R, et al. Positron Emission Tomography and Recovery Following Revascularization (PARR-1): The Importance of Scar and the Development of a Prediction Rule for the Degree of Recovery of Left Ventricular Function. J Am Coll Cardiol. 2002;40:1735-1743.*
53. *Haas F, Augustin N, Holper K, et al. Time course and extent of improvement of dysfunctioning myocardium in patients with coronary artery disease and severely depressed left ventricular function after revascularization: Correlation with positron emission tomographic findings. J Am Coll Cardiol. 2000;36:1927-34.*
54. *Bax JJ, Visser F, Poldermans D, et al.. Time course of functional recovery of stunned and hibernating segments after surgical revascularization. Circulation. 2001;104:1314-1318.*
55. *Bax JJ, van der Wall E, Harbinson M. Radionuclide techniques for the assessment of myocardial viability and hibernation. Heart. 2004;90:v26-v33.*
56. *Tillisch J, Brunken R, Marshall R, et al. Reversibility of cardiac wall-motion abnormalities predicted by positron tomography. N Engl J Med. 1986;314:884-888.*
57. *Pagano D, Townend J, Littler W, Horton R, Camici P, Bonser R. Coronary Artery Bypass Surgery as Treatment for Ischemic Heart Failure: The Predictive Value of Viability Assessment with quantitative Positron Emission Tomography for Symptomatic and Functional Outcome. J Thorac Cardiovasc Surg. 1998;115:791-799.*
58. *Beanlands R, Nichol G, Ruddy TD, et al. Evaluation of outcome and cost-effectiveness using an FDG PET-guided approach to management of patients with coronary disease and severe left ventricular dysfunction (PARR-2): rationale, design, and methods. Control Clin Trials. 2003;24:776-94.*
59. *Barrington S, Chambers J, Hallett W, O'Doherty M, Roxburgh J, Nunan T. Comparison of sestamibi, thallium, echocardiography and PET for the detection of hibernating myocardium. Eur J Nucl Med Mol Imaging. 2004;31:355-61.*
60. *Bax JJ, Fath-Ordoubadi F, Boersma E, Wijns W, Camici PG. Accuracy of PET in predicting recovery after revascularization in patients with chronic ischaemic dysfunction: Head-to-head comparison between blood flow, glucose utilisation and water-perfusable tissue fraction. Eur J Nucl Med Mol Imaging. 2002;29:721-7.*
61. *Bax JJ, Maddahi J, Poldermans D, et al. Preoperative comparison of different noninvasive strategies for predicting improvement in left ventricular function after coronary artery bypass grafting. Am J Cardiol. 2003;92:1-4.*
62. *Gerber B, Ordoubadi F, Wijns W, et al. Positron emission tomography using (18)F-fluoro-deoxyglucose and euglycaemic hyperinsulinaemic glucose clamp: optimal criteria for the prediction of recovery of post-ischaemic left ventricular dysfunction. Results from the European Community Concerted Action Multicenter study on use of (18)F-fluoro-deoxyglucose Positron Emission Tomography for the Detection of Myocardial Viability. Eur Heart J. 2001;2001:1691-701.*

63. *Korosoglou G, Hansen A, Hoffend J, et al. Comparison of real-time myocardial contrast echocardiography for the assessment of myocardial viability with fluorodeoxyglucose-18 positron emission tomography and dobutamine stress echocardiography. Am J Cardiol. 2004;94:570-6.*
64. *Nowak B, Schaefer W, Koch K-C, et al. Assessment of myocardial viability in dysfunctional myocardium by resting myocardial blood flow determined with oxygen 15 water PET. J Nucl Cardiol. 2003;10:34-45.*
65. *Wiggers H, Egeblad H, Nielsen T, Botker H. Prediction of reversible myocardial dysfunction by positron emission tomography, low-dose dobutamine echocardiography, resting ECG, and exercise testing. Cardiology. 2001;96:32-7.*
66. *Zhang X, Liu X, Wu Q, et al. Clinical outcome of patients with previous myocardial infarction and left ventricular dysfunction assessed with myocardial (99m)Tc-MIBI SPECT and (18)F-FDG PET. J Nucl Med. 2001;42:1166-73.*
67. *Sawada S, Hamoui O, Barclay J, et al. Usefulness of positron emission tomography in predicting long-term outcome in patients with diabetes mellitus and ishemic left ventricular dysfunction. Am J Cardiol. 2005;96:2-8.*
68. *Santana C, Shaw L, Garcia E, et al. Incremental prognostic value of left ventricular function by myocadial ECG-gated FDG PET imaging in patients with ischemic cardiomyopathy. J Nucl Cardiol. 2004;11:542-50.*
69. *Rohatgi R, Epstein S, Henriquez J, et al. Utility of positron emission tomography in predicting cardiac events and survival in patients with coronary artery disease and severe left ventricular dysfunction. Am J Cardiol. 2001;87.*
70. *Desideri A, Cortigiani L, Christen A, et al. The extent of perfusion-F18-fluorodeoxyglucose positron emission tomography mismatch determines mortality in medically treated patients with chronic ischemic left ventricular dysfunction. J Am Coll Cardiol. 2005;46:1264-1269.*
71. *Eitzman D, Al-Aouar Z, Kanter HL, et al. Clinical outcome of patients with advanced coronary artery disease after viability studies with positron emission tomography. J Am Coll Cardiol. 1992;20:559-565.*
72. *Di Carli MF, Davidson M, Little R, et al. Value of metabolic imaging with positron emission tomography for evaluating prognosis in patients with coronary artery disease and left ventricular dysfunction. Am J Cardiol. 1994;73:527-533.*
73. *Lee KS, Marwick TH, Cook SA, et al. Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction: Relative efficacy of medical therapy and revascularization. Circulation. 1995;90:2687-2694.*
74. *Beanlands RS, Hendry PJ, Masters RG, deKemp RA, Woodend K, Ruddy TD. Delay in revascularization is associated with increased mortality rate in patients with severe left ventricular dysfunction and viable myocardium on fluorine 18-fluorodeoxyglucose positron emission tomography imaging. Circulation. 1998;98:II51-6.*
75. *Tarakji K, Brunken RC, McCarthy PM, et al. Myocardial viability testing and the effect of early intervention in patients with advanced left ventricular systolic dysfunction. Circulation. 2006;113:230-7.*
76. *Siebelink H-M, Blanksma PK, Crijns H, et al. No Difference in Cardiac Event-Free Survival Between Positron Emission Tomography-Guided and Single-Photon Emission computed Tomography-Guided Management. J Am Coll Cardiol. 2001;37:81-88.*
77. *Chow B, Hoffman U, Nieman K. Computed tomographic coronary angiography: An alternative to invasive coronary angiography. Can J Cardiol. 2005;21:933-940.*

78. *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;44:1224-9.*
79. *Schuijf J, Bax JJ, Salm L, et al. Noninvasive coronary imaging and assessment of left ventricular function using 16-slice computed tomography. Am J Cardiol. 2005;95:571-4.*
80. *Schmitt R, Froehner S, Brunn J, et al. Congenital anomalies of the coronary arteries: Imaging with contrast-enhanced, multidetector computed tomography. European Radiology. 2005;15:1110-21.*
81. *Shi H, Aschoff A, Brambs H, Hoffmann M. Multislice CT imaging of anomalous coronary arteries. European Radiology. 2004;14:2172-81.*
82. *Schuijf J, Bax JJ, Shaw L, et al. Meta-analysis of comparative diagnostic performance of magnetic resonance imaging and multislice computed tomography for noninvasive coronary angiography. Am Heart J. 2006;151:404-11.*
83. *Nieman K, Cademartiri F, Lemos P, Raajmakers R, Pattynama P, de Feyter P. Reliable noninvasive coronary angiography with fast submillimeter multislice spiral computed tomography. Circulation. 2002;106:2051-4.*
84. *Mollet N, Cademartiri F, Nieman K, et al. Multislice spiral computed tomography coronary angiography in patients with stable angina pectoris. J Am Coll Cardiol. 2004;43:2265-70.*
85. *Martuscelli E, Romagnoli A, D'Eliseo A, et al . Accuracy of thin-slice computed tomography in the detection of coronary angiography. Eur Heart J. 2004;25:1043-8.*
86. *Hoffmann U, Moselewski F, Cury R, et al. Predictive value of 16-slice multidetector spiral computed tomography to detect significant obstructive coronary artery disease in patients at high risk for coronary artery disease: patient- versus segment-based analysis. Circulation. 2004;110:2638-43.*
87. *Cademartiri F, Runza G, Marano R, et al. Diagnostic accuracy of 16-row multislice CT angiography in the evaluation of coronary segments. Radiologia Medica. 2005;109:91-7.*
88. *Cademartiri F, Marano R, Luccichenti G, et al. Image assessment with multislice CT coronary angiography. Radiologia Medica. 2005;109:198-207.*
89. *Dorgelo J, Willems T, Geluk C, van Ooijen P, Zijlstra F, Oudkerk M. Multidetector computed tomography-guided treatment strategy in patients with non-ST elevation acute coronary syndromes: A pilot study. European Radiology. 2005;15:708-13.*
90. *Morgan-Hughes G, Roobottom C, Owens P, Marshall A. Highly accurate coronary angiography with submillimetre, 16-slice computed tomography. Heart. 2005;91:308-13.*
91. *Heuschmid M, Kuettner A, Schroeder S, et al. ECG-gated 16-MDCT of the coronary arteries: assessment of image quality and accuracy in detecting stenoses. Am J Roentgenol. 2005;184:1413-9.*
92. *Hoffmann M, Shi H, Schmitz B, et al. Noninvasive coronary angiography with multislice computed tomography. JAMA. 2005;203.*
93. *Kefer J, Coche E, Legros G, et al. Head-to-head comparison of three-dimensional navigator-gated magnetic resonance imaging and 16-slice computed tomography to detect coronary artery stenosis in patients. J Am Coll Cardiol. 2005;46:92-100.*
94. *Mollet N, Cademartiri F, Krestin G, et al. Improved diagnostic accuracy with 16-row multi-slice computed tomography coronary angiography. J Am Coll Cardiol. 2005;45:128-32.*
95. *Kuettner A, Beck T, Drosch T, et al. Diagnostic accuracy of noninvasive coronary imaging using 16-detector slice spiral computed tomography with 188 ms temporal resolution. J Am Coll Cardiol. 2005;45:123-7.*
96. *Achenbach S, Ropers D, Pohle F-K, et al. Detection of coronary artery stenoses using multi-detector CT with 16 x 0.75 collimation and 375 ms rotation. Eur Heart J. 2005;26:1978-86.*

97. Aviram G, Finkelstein A, Herz I, et al. Clinical value of 16-slice multi-detector CT compared to invasive coronary angiography. Int J Cardiovasc Intvent. 2005;2005:21-8.
98. Burgstahler C, Beck T, Kuettner A, et al. Image quality and diagnostic accuracy of 16-slice multidetector spiral computed tomography for the detection of coronary artery disease in elderly patients. J Comput Assist Tomogr. 2005;29:734-8.
99. Kuettner A, Beck T, Drosch T, et al. Image quality and diagnostic accuracy of non-invasive coronary imaging with 16-detector slice sprial computed tomography with 188 ms temporal resolution. Heart. 2005;91:938-41.
100. Raff G, Gallagher M, O'Neill W, Goldstein J. Diagnostic accuracy of noninvasive coronary angiography using 64-slice spiral computed tomography. J Am Coll Cardiol. 2005;2005:552-7.
101. Leber A, Knez A, von Z, et al. 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;46:147-54.
102. Leschka S, Alkadhi H, Plass A, et al. Accuracy of MSCT coronary angiography with 64-slice technology: first experience. Eur Heart J. 2005;15:1482-7.
103. Thompson R, Cullom S. Issues regarding radiation dosage of cardiac nuclear and radiography procedures. J Nucl Cardiol. 2006;23:19-23.
104. Mollet N, Cademartiri F, Van Mieghem C, et al. High-resolution sprial computed tomography coronary angiography in patients referred for diagnostic conventional coronary angiography. Circulation. 2005;112:2318-23.
105. Leber A, Knez A, Becker A, et al. Visualising noncalcified coronary plaques by CT. Int J Cardiovasc Imag. 2005;21:55-61.
106. Leber A, Becker A, Knez A, et al.. 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;47:672-7.
Multi-detector row CT of left ventricular function with dedicated analysis software versus MR imaging: Initial experience. Radiology. 2003;230:403-10.
108. Grude M, Juergens K, Wichter T, et al. Evaluation of global left ventricular myocardial function with electrocardiogram-gated multidetector computed tomography: Comparison with magnetic resonance imaging. Invest Radiol. 2003;38:653-61.
109. Halliburton S, Petersilka M, Schvartzman P, Obuchowski N, White R. Evaluation of left ventricular dysfunction using multiphasic reconstructions of coronary multi-slice computed tomography data in patients with chronic ischemic heart disease: Validation against cine magnetic resonance imaging. Int J Cardiovasc Imag. 2003;19:73-83.
110. Hoffmann U, Millea R, Enzweiler C, et al. Acute myocardial infarction: Contrast-enhanced multi-detector row CT in a porcine model. Radiology. 2004;231:697-701.
111. Nikolaou K, Sanz J, Poon M, et al. Assessment of myocardial perfusion and viability from routine contrast-enhanced 16-detector-row computed tomography of the heart: preliminary results. Eur Radiol. 2005;15:864-871.
112. Kim W, Danias P, Stuber M, et al. Coronary magnetic resonance angiography for the detection of coronary stenoses. N Eng J Med. 2001;345:1863-9.
113. Bogaert J, Kuzo R, Dymarkowski S, Beckers R, Piessens J, Rademakers FE. Coronary artery imaging with real-time navigator three-dimensional turbo-field-echo MR coronary angiography: initial experience. Radiology. 2003;226:707-16.
114. Sommer T, Hackenbroch M, Hofer U, et al. Coronary MR angiography at 3.0 T versus that at 1.5 T: Initial results in patients suspected of having coronary artery disease. Radiology. 2005;234:718-25.

115. *Muller F, Fleisch M. Recurrent coronary artery stenosis: Assessment with three-dimensional MR imaging. Journal of Magnetic Resonance Imaging. 2004;20:383-9.*
116. *Gerber B, Coche E, Pasquet A, et al. Coronary artery stenosis: Direct comparison of four-section multi-detector row CT and 3D navigator MR imaging for detection -- Initial results. Radiology. 2005;234:98-108.*
117. *Jahnke C, Paetsch I, Schnackenburg B et al. Coronary MR angiography with steady-state free precession: individually adapted breath-hold technique versus free-breathing technique. Radiology. 2004;232:669-76.*
118. *Ikonen A, Manninen H, Vainio P, et al. Three-dimensional respiratory-gated coronary MR angiography with reference to X-ray coronary angiography. Acta Radiol. 2003;44:583-9.*
119. *Kessler W, Laub G, Achenbach S, Ropers D, Moshage W, Daniel WG. Coronary arteries: MR angiography with fast contrast-enhanced three-dimensional breath-hold imaging--initial experience. Radiology. 1999;210:566-72.*
120. *Muller MF, Fleisch M, Kroeker R, Chatterjee T, Meier B, Vock P. Proximal coronary artery stenosis: three-dimensional MRI with fat saturation and navigator echo. J Magn Reson Imaging. 1997;7:644-51.*
121. *Plein S, Ridgway JP, Jones TR, Bloomer TN, Sivananthan MN. Coronary artery disease: assessment with a comprehensive MR imaging protocol--initial results. Radiology. 2002;225:300-7.*
122. *Post J, van Rossum AC, Hofman MB, Valk J, Visser CA. Three-dimensional respiratory-gate MR angiography of coronary arteries: comparison with conventional coronary angiography. Am J Roentgenol. 1996;166:1399-404.*
123. *Regenfus M, Ropers D, Achenbach S, et al. Comparison of contrast-enhanced breath-hold and free-breathing respiratory-gated imaging in three-dimensional magnetic ressonance coronary angiography. Am J Cardiol. 2002;90:725-30.*
124. *Sandstede JJ, Bertsch G, Beer M, et al. Detection of myocardial viability by low-dose dobutamine Cine MR imaging. Magnetic Resonance Imaging. 1999;17:1437-43.*
125. *Sardanelli F, Molinari G, Zandrino F, Balbi M. Three-dimensional, navigator-echo MR coronary angiography in detecting stenoses of major epicardial vessels, with conventional coronary angiography as the standard of reference. Radiology. 2000;214:808-14.*
126. *van Geuns R, de Bruin HG, Rensing BJ, et al. Magnetic resonance imaging of the coronary arteries: clinical results from three dimensional evaluation of a respiratory gated technique. Heart. 1999;82:515-9.*
127. *Watanabe Y, Nagayama M, Amoh Y, et al. High-resolution selective three-dimensional magnetic resonance coronary angiography with navigator-echo technique: segment-by-segment evaluation of coronary artery stenosis. J Magn Reson Imaging. 2002;16:238-45.*
128. *Weber C, Steiner P, Sinkus R, Dill T, Bornert P, Adam G. Correlation of 3D MR coronary angiography with selective coronary angiography: feasibility of the motion-adapted gating technique. Eur Radiol. 2002;12:718-26.*
129. *Wittlinger T, Voigtlander T, Rohr M, et al. Magnetic resonance imaging of coronary artery occlusions in the navigator technique. Int J Cardiovasc Imag. 2002;18:203-11; discussion 213-5.*
130. *Woodard P, Li D, Haacke EM, et al. Detection of coronary stenoses on source and projection images using three-dimensional MR angiography with retrospective respiratory gating: preliminary experience. Am J Roentgenol. 1998;170:883-8.*
131. *van Geuns R-J M, Oudkerk M, Rensing BJWM, et al. Comparison of coronary imaging between magnetic resonace imaging and electron beam computed tomography. Am J Cardiol. 2002;90:58-63.*

132. Manning W, Li W, Edelman R. A preliminary report comparing magnetic resonance coronary angiography with conventional angiography. N Eng J Med. 1993;328:828-32.
133. Mohiaddin RH, Bogren HG, Laxim F, et al. Magnetic resonance coronary angiography in heart transplant recipients. Coronary Artery Disease. 1996;7:591-7.
134. Pennel DJ, Keegan J, Firmin DN, Gatehouse PD, Underwood SR, Longmore DB. Magnetic resonance imaging of coronary arteries: technique and preliminary results. Br Heart J. 1993;70:315-26.
135. Pennell DJ, Bogren HG, Keegan J, Firmin DN, Underwood SR. Assessment of coronary artery stenosis by magnetic resonance imaging. Heart. 1996;75:172-33.
136. Post JC, van Rossum AC, Hofman MB, de Cock CC, Valk J, Visser CA. Clinical utility of two-dimensional magnetic resonance angiography in detecting coronary artery disease. Eur Heart J. 1997;18:426-33.
137. Regenfus M, Ropers D, Achenbach S, et al. Noninvasive detection of coronary artery stenosis using contrast-enhanced three-dimensional breath-hold magnetic resonance coronary angiography. J Am Coll Cardiol. 2000;36:44-50.
138. van Geuns RJ, Wielopolski PA, de Bruin HG, et al. MR coronary angiography with breath-hold targeted volumes: preliminary clinical results. Radiology. 2000;217:270-7.
139. White R, Caputo G, Mark A, Modin G, Higgins C. Coronary artery bypass graft patency: Noninvasive evaluation with MR imaging. Radiology. 1987;164:681-6.
140. Rubinstein R, Askenase A, Thickman D, Feldman M, Agarwal J, Helfant R. Magnetic resonance imaging to evaluate patency of aortocoronary bypass grafts. Circulation. 1987;76:786-91.
141. Jenkins J, Love H, Foster C, Isherwood I, Rowlands D. Detection of coronary artery bypass graft patency as assessed by magnetic resonance imaging. Br J Radiol. 1988;61:2-4.
142. Frija G, Schouman-Claeys E, Lacombe P, Bismuth V, Ollivier J. Detection of coronary artery bypass graft patency as assessed by magnetic resonance imaging. J Comput Assist Tomogr. 1989;13:226-32.
143. White R, Pflugfelder P, Lipton M, Higgins C. Coronary artery bypass grafts: Evaluation of patency as assessed by magnetic resonance imaging. Am J Roentgenol. 1988;150:1271-4.
144. Aurigemma G, Reichek N, Axel I, Schiebler M, Harris C, Kressel H. Noninvasive determination of coronary artery bypass graft patency by cine magnetic resonance imaging. Circulation. 1989;80:1595-602.
145. Galjee M, van Rossum A, Doesburg T, van Eenige M, Visser CA. Value of magnetic resonance imaging in assessing patency and function of coronary artery bypass grafts. An angiographically controlled study. Circulation. 1996;93:660-6.
146. Hoogendoorn L, Pattynama P, Buis B, van der Geest R, van der Wall E, de Roos A. Noninvasive evaluation of aortocoronary bypass grafts with magnetic resonance flow mapping. Am J Cardiol. 1995;75:845-8.
147. Wintersperger B, Engelmann M, von Smekal A, et al. Patency of coronary bypass grafts: Assessment with breath-hold contrast-enhanced MR angiography--value of a non-electrocardiographically triggered technique. Radiology. 1998;208:345-51.
148. Kalden P, Kreitner K, Wittlinger T, et al. Assessment of coronary artery bypass grafts: value of different breath-hold MR imaging techniques. Am J Roentgenol. 1999;172:1359-64.
149. Bedaux W, Hofman M, Vyt S, Bronzwaer J, Visser CA, van Rossum A. Assessment of coronary artery bypass graft disease using cardiovascular magnetic resonance determination of flow reserve. J Am Coll Cardiol. 2002;40:1848-55.

150. *Bunce N, Lorenz C, John A, Lesser J, Mohjaddin R, Pennell D. Coronary artery bypass graft patency: Assessment with true AST imaging with steady-state precession versus gadolinium-enhanced MR angiography. Radiology. 2003;227:440-6.*
151. *Bunce N, Lorenz C, Keegan J, et al. Coronary artery anomalies: Assessment with free-breathing three-dimensional coronary MR angiography. Radiology. 2003;227:201-8.*
152. *Varghese A, Keegan J, Pennell D. Cardiovascular magnetic resonance of anomalous coronary arteries. Coronary Artery Disease. 2005;16:355-64.*
153. *McConnell M, Ganz P, Selwyn AP, Li W, Edelman R, Manning W. Identification of anomalous coronary arteries and their anatomic course by magnetic resonance coronary angiography. Circulation. 1995;92:3158-62.*
154. *Post J, van Rossum A, Bronzwaer J, et al. Magnetic resonance angiography of anomalous coronary arteries. A new gold standard for delineating the proximal course? Circulation. 1995;92:3163-71.*
155. *van Rugge FP, van der Wall EE, Spanjersberg SJ et al. Magnetic resonance imaging during dobutamine stress for detection and localization of coronary artery disease. Quantitative wall motion analysis using a modification of the centerline method. Circulation. 1994;90:127-38.*
156. *Nagel E, Lehmkuhl HG, Bocksch W, et al. Noninvasive diagnosis of ischemia-induced wall motion abnormlities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. Circulation. 1999;99:763-70.*
157. *Hundley WG, Hamilton CA, Thomas MS, et al. Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. Circulation. 1999;100:1697-702.*
158. *Schalla S, Klein C, Paetsch I, et al. Real-time MR image acquisition during high-dose dobutamine hydrochloride stress for detecting left ventricular wall-motion abnormalities in patients with coronary arterial disease. Radiology. 2002;224:845-51.*
159. *van Dijkman P, Kuijpers D, Blom B, van H. Dobutamine stress magnetic resonance imaging: A valuable method in the noninvasive diagnosis of ischemic heart disease. Journal of Electrocardiology. 2002;35:57-9.*
160. *Kuijpers D, Ho K, van Dijkman P, Vliegenthart R, Oudkerk M. Dobutamine cardiovascular magnetic resonance for the detection of myocardial ischemia with the use of myocardial tagging. Circulation. 2003;107:1592-7.*
161. *Wahl A, Paetsch I, Roethemeyer S, Klein C, Fleck E, Nagel E. High-dose dobutamine-atropine stress cardiovascular MR imaging after coronary revascularization in patients with wall motion abnormalities at rest. Radiology. 2004;233:210-6.*
162. *Paetsch I, Jahnke C, Wahl A, et al. Comparison of dobutamine stress magnetic resonance, adenosine stress magnetic resonance and adenosine stress magnetic resonance perfusion. Circulation. 2004;110:835-42.*
163. *Al-Saadi N, Nagel E, Gross M, et al. Noninvasive detection of myocardial ischemia from perfusion reserve based on cardiovascular magnetic resonance. Circulation. 2000;101:1379-83.*
164. *Schwitter J, Nanz D, Kneifel S, et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation. 2001;103:2230-5.*
165. *Al-Saadi N, Gross M, Paetsch I, et al. Dobutamine induced myocardial perfusion reserve index with cardiovascular MR in patients with coronary artery disease. Journal of Cardiovascular Magnetic Resonance. 2002;4:471-80.*

166. *Ibrahim T, Nekolla SG, Schreiber K, et al. Assessment of coronary flow reserve: Comparison between contrast-enhanced magnetic resonance imaging and positron emission tomography. J Am Coll Cardiol. 2002;39:864-70.*
167. *Nagel E, Klein C, Paetsch I, et al. Magnetic resonance perfusion measurements for the noninvasive detection of coronary artery disease. Circulation. 2003;108:432-7.*
168. *Plein S, Greenwood J, Ridgway J, Cranny G, Ball S, Sivananthan M. Assessment of non-St-segment elevation acute coronary syndromes with cardiac magnetic resonance imaging. J Am Coll Cardiol. 2004;44:2173-81.*
169. *Kawase Y, Nishimoto M, Hato K, Okajima K, Yoshikawa J. Assessment of coronary artery disease with nicorandil stress magnetic resonance imaging. Osaka City Medical Journal. 2004;50:87-94.*
170. *Wolff S, Schwitter J, Coulden R, et al. Myocardial first-pass perfusion magnetic resonance imaging: A multicenter dose-ranging study. Circulation. 2004;110:732-7.*
171. *Plein S, Radjenovic A, Ridgway J, et al. Coronary artery disease: Myocardial perfusion MR imaging with sensitivity encoding versus conventional angiography. Radiology. 2005;235:423-30.*
172. *Giang TH, Nanz D, Coulden R, et al. Detection of coronary artery disease by magnetic resonance myocardial perfusion imaging with various contrast medium doses: First European multi-centre experience. Eur Heart J. 2004;25:1657-65.*
173. *Dendale P, Franken PR, Holman E, Avenarius J, van der Wall EE, de Roos A. Validation of low-dose dobutamine magnetic resonance imaging for assessment of myocardial viability after infarction by serial imaging. Am J Cardiol. 2998;82:375-7.*
174. *Baer F, Theissen P, Crnac J, et al. Head to head comparison of dobutamine-transoesophageal echocardiography and dobutamine-magnetic resonance imaging for the prediction of left ventricular functional recovery in patients with chronic coronary artery disease. Eur Heart J. 2000;21:981-91.*
175. *Trent R, Waiter G, Hillis G, McKiddle F, Redpath T, Walton S. Dobutamine magnetic resonance imaging as a predictor of myocardial functional recovery after revascularisation. Heart. 2000;83:40-6.*
176. *Kramer C, Malkowski M, Mankad S, Theobald T, Pakstis D, Rogers WJ. Magnetic resonance tagging and echocardiographic response to dobutamine and functional improvement after reperfused myocardial infarction. Am Heart J. 2002;143:1046-51.*
177. *Motoyasu M, Sakuma H, Ichikawa Y, et al. Predication of regional functional recovery after acute myocardial infarction with low dose dobutamine stress cine MR imaging and contrast enhanced MR imaging. Journal of Cardiovascular Magnetic Resonance. 2003;5:563-74.*
178. *Schmidt M, Voth E, Schneider C, et al. F-18-FDG uptake is a reliable predictor of functional recovery of akinetic but viable infarct regions as defined by magnetic resonance imaging before and after revascularization. Magnetic Resonance Imaging. 2004;22:229-36.*
179. *Uemura S, Sakuma H, Motoyasu M, et al. Thallium-201 SPECT and low-dose dobutamine stress cine MRI for predicting functional recovery of regional myocardial contraction in patients with myocardial infarction. Journal of Cardiovascular Magnetic Resonance. 2004;6:697-707.*
180. *Gutberlet M, Frohlich M, Mehl S, et al. Myocardial viability assessment in patients with highly impaired left ventricular function: Comparison of delayed enhancement, dobutamine stress MRI, end-diastolic wall thickness, and TI201-SPECT with functional recovery after revascularization. Eur Radiol. 2005;15:872-80.*
181. *Kim R, Wu E, Rafael A, et al. The use of contrast enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med. 2000;343:1445-53.*

182. *Sandstede J, Lipke C, Beer M, et al. Analysis of first-pass and delayed contrast-enhancement patterns of dysfunctional myocardium on MR imaging: Use in the prediction of myocardial viability. Am J Roentgenol. 2000;174:1737-40.*
183. *Choi K, Kim R, Gubernikoff G, Vargas J, Parker M, Judd R. Transmural extent of acute myocardial infarction predicts long-term improvement in contractile function. Circulation. 2001;104:1101-7.*
184. *Gerber B, Garot J, Bluemke D, Wu K, Lima J. Accuracy of contrast-enhanced magnetic resonance imaging in predicting improvement of regional myocardial function in patients after acute myocardial infarction. Circulation. 2002;106:1083-9.*
185. *Beek A, Kuhl H, Bondarenko O, et al. Delayed contrast-enhanced magnetic resonance imaging for the prediction of regional functional improvement after acute myocardial infarction. J Am Coll Cardiol. 2003;42:895-901.*
186. *Kitagawa K, Sakuma H, Hirano T, Okamoto S, Makino K, Takeda K. Acute myocardial infarction: Myocardial viability assessment in patients early thereafter comparison of contrast-enhanced MR imaging with resting (201)TI SPECT. Single photon emission computed tomography. Radiology. 2003;226:138-44.*
187. *Kuhl H, Beek A, van der Weerdt A, et al. Myocardial viability in chronic ischemic heart disease: Comparison of contrast-enhanced magnetic resonance imaging with (18)F-fluorodeoxyglucose positron emission tomography. J Am Coll Cardiol. 2003;41:1341-8.*
188. *Schvartzman P, Srichai M, Grimm R, et al. Nonstess delayed-enhancement magnetic resonance imaging of the myocardium predicts improvement of function after revascularization for chronic ischemic heart disease with left ventricular dysfunction. Am Heart J. 2003;146:535-41.*
189. *Selvanayagam J, Kardos A, Francis J, et al. Value of delayed-enhancement cardiovascular magnetic resonance imaging in predicting myocardial viability after surgical revascularization. Circulation. 2004;110:1535-41.*
190. *Van Hoe L, Vanderheyden M. Ischemic cardiomyopathy: Value of different MRI techniques for prediction of functional recovery after revascularization. Am J Roentgenol. 2004;182:95-100.*
191. *Armstrong WF, Zoghbi W. Stress echocardiography. Current methodology and clinical applications. J Am Coll Cardiol. 2005;45:1739-47.*
192. *Tsutsui J, Kusler M, Porter T. Intravenous myocardial contrast echocardiography for the diagnosis of coronary artery disease. Curr Opin Cardiol. 2005;20:381-385.*
193. *Mulvagh S, DeMaria A, Feinstein S, et al. Contrast Echocardiography: Current and Future Applications. J Am Soc Echocardiogr. 2000;13:331-42.*
194. *Borges-Neto S, Fiacro E, Groch M, et al. Update Imaging Guidelines for Nuclear Cardiology Procedures. Part 1. J Nucl Cardiol. 2001;8:G3-G84.*
195. *Bacharach SL, Bax JJ, Case J, Delbeke D, Kurdziel K, Martin WH, Patterson R. PET Myocardial Glucose Metabolism and Perfusion Imaging: Part 1 - Guidelines for Patient Preparation and Data Acquisition. J Nucl Cardiol. 2003;10:543-56.*
196. *ICRP Publication 53: Radiation Dose to Patients From Radiopharmaceuticals, 53. Annals of the IRCP; Vol 18/1-4. ISBN:0-08-035591-9. Elsevier, 1998.*
197. *Coles D, Smail M, Negus I, et al. Comparison of radiation doses from multislice computed tomography coronary angiography and conventional diagnostic angiography. J Am Coll Cardiol. 2006;47:1840-5.*
198. *Patterson RE, Eisner RL, Horowitz SF. Comparison of cost-effectiveness and utility of exercise ECG, single photon emission computed tomography, positron emission tomography*

and coronary angiography for diagnosis of cornary artery disease. Circulation. 1995;91:54-65.

199. Garber AM, Solomon NA. Cost-Effectiveness of Alternative Test Strategies for the Diagnosis of Coronary Artery Disease. Ann Intern Med. 1999;130:719-728.

200. Maddahi J, Gambhir SS. Cost-effective selection of patients for coronary angiography. J Nucl Cardiol. 1997;4:S141-S151.

201. Jacklin P, Barrington S, Roxburgh J, et al. Cost-effectiveness of preoperative positron emission tomography in ischemic heart disease. Ann Thorac Surg. 2002;73:1403-9.

Table 1: PET CAD DIAGNOSIS

Author	Year	Number	Stress	Tracer	Reference CAG	Sensitivity +ve test	Sensitivity Pt. w. CAD	Sensitivity %	Specificity -ve test	Specificity Pt. w.o. CAD	Specificity %
Schelbert HR	1982	45	dipyridamole	$^{13}NH_3$	>50%	31	32	97%	13	13	100%
Tamaki N	1985	25	exercise	$^{13}NH_3$	N/R	18	19	95%	6	6	100%
Yonekura Y	1987	50	exercise	$^{13}NH_3$	>75%	37	38	97%	12	12	100%
Tamaki N	1988	51	exercise	$^{13}NH_3$	>50%	47	48	98%	3	3	100%
Gould L (@)	1986	50	dipyridamole	$^{82}Rb/^{13}NH_3$	QCA SFR < 3	21	22	95%	9	9	100%
Demer L (@)	1989	193	dipyridamole	$^{82}Rb/^{13}NH_3$	QCA SFR < 4	126	152	83%	39	41	95%
Go RT	1990	202	dipyridamole	82Rb	>50%	142	152	93%	39	50	78%
Stewart RE	1991	81	dipyridamole	^{82}Rb	QCA >50%*	50	60	83%	18	21	86%
Marwick T	1992	74	dipyridamole	^{82}Rb	>50%	63	70	90%	4	4	100%
Grover McKay	1992	31	dipyridamole	^{82}Rb	>50%	16	16	100%	11	15	73%
Laubenbacher	1993	34	dipyridamole/adenosine	$^{13}NH_3$	QCA >50%*	14	16	88%	15	18	83%
Bateman TM†	2006	112	dipyridamole	^{82}Rb	>50%*	64	74	86%	38	38	100%
Williams BR**	1994	287	dipyridamole	^{82}Rb	>67%	88	101	87%	99	112	88%
Simone GL**	1992	225	dipyridamole	^{82}Rb	>67%	**	**	83%	**	**	91%
Totals + Weighted Mean		**1460**				**696**	**778**	**89%**	**297**	**333**	**89%**
Weighted Mean excluding R/S						**544**	**603**	**90%**	**160**	**183**	**87%**
Non-weighted Mean								**91%**			**91%**

@ - Study reported that 50 pts in Gould et al 1986 were included. Thus Gould et al not included in mean calculations.
** - Retrospective study; MPI influenced CAG decision; mixed patient and region method for sensitivity / specificity; patients with disease could not be easily determined in one study.
* - Other cut-offs reported; >50% noted here
† - Electronic database, matched cohort design; values derived from reported population, sensitivity and specificity.

N/R = Not reported
R/S = Retrospective
CAG = Coronary Angiogram
QCA = Quantitative Coronary Angiography
SFR = Stenosis Flow Reserve Based on QCA Data

Table 2: PET CAD PROGNOSIS

Author	Year	Patient Number	Stress	Tracer	Outcomes	Follow-up Time (years)	Normal Scan- Annual Event Rate (%/yr)		Abnormal Scan- Annual Event Rate (%/yr)	
							Hard Events	Total Events	Hard Events	Total Events
Yoshinaga	2004	367	dipyridamole	^{82}Rb	death,MI,Rev,Hosp	3.1	0.4	1.7	mild: 2.3 mod/sev: 7.0	mild: 12.9 mod/sev: 13.2
Chow	2005	629	dipyridamole	^{82}Rb	death,MI,Rev,CAG	2.3	0.09	0.98		ECG +ve Normal MP: 1.9
Marwick T	1997	581	dipyridamole	^{82}Rb	death,MI,Rev,UAP	3.4	0.9	4	4	7
Marwick T	1995	Prediction of peri-operative and late cardiac events before vascular surgery*								
MacIntrye	1993	Outcomes in patients with False Negative Thallium-201 SPECT*								

MI = Myocardial Infarction
Rev = Revascularization
CAG = Coronary Angiogram
UAP = Unstable Angina

* See text for details

TABLE 3: PET VIABILITY DIAGNOSIS (EF < 40%)

Author	Year	Number	EF(%)	Tracer	Reference Method	Sensitivity +ve test	Sensitivity Patient/segments with recovery	Sensitivity %	Specificity -ve test	Specificity Patient/segments. without recovery	Specificity %
Bax (meta-analysis) 20 studies	2001	598	36±8	^{18}FDG	WM/EF F/U 4.1m	751	807	93%	417	725	58%
Barrington†	2004	25	36	$^{13}NH_3/^{18}$FDG uptake+MM	WM 8m F/U	6	6	100%	23	25	92%
Bax, Visser*	2001	47	30	^{201}Tl/^{18}FDG SPT MM	WM + EF 3-6m F/U	18	21	86%	24	26	92%
Bax, Fath-Ordoubadi*	2002	34	32	$^{13}NH_3/^{18}$FDG MRGR>60%	WM + EF 4-6m F/U	10	10	100%	17	24	71%
Bax, Maddahi*	2003	47	30	^{18}FDG SPT uptake	EF 6m F/U	17	19	89%	24	28	86%
Gerber*†	2001	178	38	^{18}FDG-MGU %uptake	EF 4-6m F/U	65	82	79%	49	89	55%
Kosoroglou	2004	41	31	MIBI/FDG uptake	WM 3-6m F/U	**	**	90%	**	**	44%
Nowak	2003	42	38	TF/FDG MM	WM F/U 6-17m	32	40	80%	23	32	72%
Wiggers*	2001	35	35	^{15}O-H_2O $^{13}NH_3/^{18}$FDG uptake+MM	Pt WM F/U 6.1m	14	14	100%	14	21	67%
Totals + Wt'd Mean		**1047**	**33.8**			**913**	**999**	**91%**	**591**	**970**	**61%**
Mean weighted by number of patients								**90%**			**61%**

* = EF recovery used or patient based recovery
† = Values derived from sensitivity, specificity and other values provided.
** = Not reported and cannot be easily determined from data presented
WM = Wall Motion
SPT = SPECT
MM = Mismatch
MRGR = Metabolic Rate of Glucose (Relative)
TF = Tetrafosmin

Table 4: PET VIABILITY PROGNOSIS (EF < 40%)

Citation		Patient Population			Test Method	Mortality Rates			
Author	Year	N	EF	mean FU (months)	Tracer	Viab +ve Rev +ve	Viab +ve Rev -ve	Viab -ve Rev +ve	Viab -ve Rev -ve
Allman (meta-anal)†	2002	3088	32	25	Tl/DE/FDG	3.2%	16.0%	7.7%	6.2%
Allman(PET)†		1029	35	24	perfusion/FDG	6.0%	21.0%	7.0%	8.0%
Eitzman	1993	82	33	12	Rb-NH3/FDG	3.8%	33.3%*	0.0%	8.3%
Di Carli	1994	93	25	14	NH3/FDG	11.5%	23.5%*	5.9%	18.2%
Lee	1994	129	37	17	Rb /FDG	8.2%	14.3%*	5.3%	12.5%
Beanlands	1998	85	26	17	MIBI/FDG	3.2%	28.6%††	-	18.8%
Zhang	2001	123	35	37	MIBI/FDG	0.0%	26.7%**	8.0%	3.8%
Rohatgi	2001	99	22	25	NH3/FDG	0.0%	34.5%**	0.0%	15.2%
Santana	2004	90	26	22	G-Rb/FDG	NR	NR€	NR	NR
Dessideri€€	2005	261	29	34	NH3/FDG	14.5%	28.3%**	10.3%	21.5%
Sawada†††	2005	61	29	48	NH3/FDG	47.4%	83.3%**	57.1%	43.8%
TOTALS/mean €€€		**933**	**30**	**26**		**9.4%**	**30.9%¶**	**11.8%**	**17.7%**

† Meta-analysis of 24 viability studies; rates reported are for all studies in line 1; line 2 is data for 11 FDG PET studies: 7 of which reported outcomes; 4 of which compared event rates in subgroups and had EF<40%; table data derived from reported values and estimated for 1 year follow-up based on rates and mean follow-up reported.

* p <0.05 Viab +ve, rev -ve vs rev +ve for total cardiac event rates.

** p <0.05 Viab +ve, rev -ve vs rev +ve (also vs other groups (Allman, 2002; Zhang 2002)).

†† p<0.05 delayed vs early revasculuarization

€ Values not reported: 11% survival benefit with revascularization in patients with viability and LV remodeling (EDV>260).

€€ Values determined from reported percentages.

††† Pts with Diabetes; LV dysfunction and CAD

€€€ Totals/mean include 8 studies with reported values. Does not include meta-analysis

¶ p <0.05 vs other groups using a Fisher's exact test.

Tl = Thallium-201
DE = Dobutamine Echo
FDG = F-18 Fluorodeoxyglucose
Viab = Viability
Rev = Revascularization

Table 5: 16-SLICE MDCT

	Yr	N Seg	Segment Analysis	Sen	Sp	Patient Analysis	Sen	Sp	Accuracy
Nieman	2002	58	≥ 2 mm	95(82/86)	86(125/145)		100(50/50)	88(7/8)	98% (57/58)
Mollet	2004	128	≥ 2 mm	92(216/234)	95(1092/1150)		100(106/106)	86(18/21)	98% (124/127)
Kuettner	2004	58	ALL	72(54/75)	97(679/700)				97% (58/60)
Martuscelli	2004	61	>1.5 mm	89(83/93)	98(511/520)				
Hoffmann U	2004	33	ALL	70(30/43)	94(371/393)		86 (19/22)	82(9/11)	85% (28/33)
Cademartiniri	2005	40	≥ 2mm	96(88/92)	96(322/336)				
Cademartiniri	2005	60	≥ 2mm	93(93/100)	97(557/572)				
Doregelo	2005	22	≥ 2mm	94(30/32)	96 (216/225)				
Morgan-Hughes	2005	57	ALL	83(75/90)	97(566/585)		100(32/32)	96(24/25)	98% (56/57)
Heuschmid	2005	37	ALL	59(22/37)	96(329/343)				97% (36/37)
Hoffman M	2005	103	≥ 1.5 mm	95(149/157)	98(1117/1139)		96(55/58)	84(38/45)	90% (93/103)
Kefer	2005	52	≥ 1.5 mm	82(64/78)	79(293/369)		92	67	
Schuijf	2005	31	≥ 2mm	93(53/57)	96(179/186)		95(20/21)	80(8/10)	90% (28/31)
Mollet	2005	51	≥ 2mm	95(61/64)	98(537/546)		100(31/31)	85(17/20)	94% (48/51)
Kuettner	2005	72	ALL	82(96/117)	98(804/819)				90% (65/72)
Achenbach	2005	50	≥ 1.5 mm	94(50/53)	96(559/582)		100(25/25)	83(19/23)	92% (44/48)
Aviram	2005	22	> 1.5 mm	86(24/28)	98(255/260)				
Burgstahler	2005	117	ALL	84(294/348)	97(1105/1134)				
Kuettner	2005	124	ALL	85(304/359)	98(1172/1201)		85	98	92% (110/120)
Weight Mean				87(1868/2143)	96(10789/11205)		98(352/359)	86%(140/163)	

Table 6: 64-SLICE MDCT

Author	Yr	N	Segment Analysis	Sen	Sp	Patient Analysis	Sen	Sp	Accuracy
Raff	2005	70	ALL	86(79/92)	95(802/843)		95(38/40)	90(27/30)	93%(65/70)
Leber	2005	55	ALL	79(52/66)	73(29/40)		88(22/25)		
Leshcka	2005	67	≥ 1.5 mm	94(165/176)	97(805/829)		100(47/47)	100(20/20)	100%(67/67)
Mollet	2005	52	ALL	99 (93/94)	95(601/631)		100 (38/38)	92 (12/13)	98%(51/52)
Weighted Mean				91 (389/428)	95(2237/2343)		97(145/150)	94(59/63)	

Table 7: MR ANGIOGRAPHY

Year / Author	Patients (n)	Assessable % (Number of Segments)	Sensitivity % (Number of Segments)	Specificity % (Number of Segments)	PPV % (95% CI)	NPV % (95% CI)
2D breath hold						
1993 Manning	39	98 (147/150)	90 (47/52)	92 (87/95)		
1993 Pennell	7	NA	83 (5/6)	NA		
1996 Mohiaddin	16	90 (43/48)	56 (5/9)	82 (28/34)		
1996 Pennell	39	NA	85 (47/55)	NA		
1997 Post	35	89 (125/140)	63 (22/35)	89 (80/90)		
Total	136				84 (78-90)	86 (82-91)
Weighted mean		93 (315/338)	80 (126/157)	**89 (195/219)**		
3D breath hold						
1999 Kessler	6	NA	60 (3/5)	NA		
2000 van Geuns	38	69 (187/272)	68 (21/31)	97 (151/156)		
2000 Regenfus	50	77 (268/350)	86 (48/56)	91 (193/212)		
2002 Regenfus	32	76 (171/224)	87 (26/30)	91 (129/141)		
2004 Jahnke	40	45 (143/320)	63 (12/19)	82 (102/124)		
Total	166				65 (58-72)	95 (93-97)
Weighted mean		66 (769/1166)	78 (110/141)	**91 (575/633)**		
3D navigator						
1996 Post	20	96 (77/80)	38 (8/21)	95 (53/56)		
1997 Muller	35	NA	83 (45/54)	94 (115/122)		
1997 Kessler	73	52 (236/455)	65 (28/43)	88 (169/193)		
1998 Woodard	10	NA	70 (7/10)	NA		
1999 Sandstede	30	77 (92/120)	81 (30/37)	89 (49/55)		
1999 van Geuns	32	74 (151/203)	50 (13/26)	91 (114/125)		
1999 Kessler	6	NA	60 (3/5)	NA		
2000 Sardanelli	42	86 (234/273)	82 (55/67)	89 (149/167)		
2001 Kim	109	86 (374/434)	83 (78/94)	73 (204/280)		
2002 Plein	10	93 (37/40)	88 (15/17)	85 (17/20)		
2002 Weber	11	70 (62/88)	88 (14/16)	93 (43/46)		
2002 Wittlinger	25	85 (102/120)	75 (18/24)	100 (78/78)		
2002 Regenfus	32	69 (155/224)	60 (15/25)	88 (115/130)		
2002 Watanabe	12	70 (49/70)	80 (12/15)	85 (29/34)		
2002 van Geuns	27	69 (139/201)	46 (12/26)	90 (102/113)		
2003 Bogaert	21	72 (134/186)	56 (15/27)	83 (89/107)		
2003 Ikonen	69	84 (233/276)	75 (64/85)	62 (92/148)		
2004 Jahnke	40	79 (254/320)	72 (26/36)	92 (200/218)		
2005 Gerber	27	100 (294/294)	62 (36/58)	84 (198/236)		
2004 Muller	30	100 (221/221)	85 (35/41)	84 (151/180)		
2005 Sommer	18	87 (109/126)	82 (14/17)	88 (80/91)		
Total	679				61 (58-64)	91 (90-92)
Weighted mean		82 (2953/3731)	73 (543/744)	85 (2047/2399)		
					65 (62-68)	90 (89-91)
TOTAL for 1.5 T	981			87(2600/2997)		
Weighted mean		83 (3441/4147)	72 (749/1043)			
3T						
2005 Sommer	18	86 (108/126)	82 (14/17)	**89 (80/90)**		

Adapted from Schuijf J et al. Meta-analysis of comparative diagnostic performance of magnetic resonane imaging and multislice computed tomography for noninvasive coronary angiography. *Am Heart J*. 2006;151:404-11.

Table 8: DOBUTAMINE STRESS MR CAD DIAGNOSIS - RESULTS TABLE

Author	Year	Number	Max Dose (µg/kg/min)	Reference	Sensitivity			Specificity		
					+ve test	Pt. w. CAD	% (DSE)	-ve test	Pt. w.o. CAD	%
van Rugge	1994	39	20	CAG ≥50%	30	33	91	5	6	83
Nagel	1999	172	40+1mg Atropine	CAG ≥50%	94	109	86 (74*)	60	70	86(70*)
Hundley	1999	41**	40+1mg Atropine	CAG ≥50%	37	41	90	5	6	83
Schalla	2002	22	40+1mg Atropine	QCA ≥75%	14	16	88	5	6	83
van Dijkaman†	2002	95	40	CAG ≥50%	41	42	98	NA	NA	NA
Kuijpers†	2003	194	40	CAG ≥50%	65	68	96	NA	NA	NA
Wahl	2004	151	40+2mg Atropine	QCA ≥50%	101	113	89	32	38	84
Paetsch	2004	79	40+2mg Atropine	QCA ≥50%	47	53	89	21	26	80
Totals + Weighted Mean		**893**			**429**	**475**	**90**	**128**	**152**	**84**

* - Values for dobutamine stress echo
** - Total patients in study 153, only 41 patients underwent coronary angiogram which are shown in this analysis
† - Only patients with positive dobutamine stress MR underwent coronary angiogram
CAG = Coronary angiogram
QCA = Quantitative coronary angiography
DSE = Dobutamine stress echo

Table 9: MRI FIRST PASS PERFUSION CAD DIAGNOSIS - RESULTS TABLE

Author	Year	Number	Stress Agent	Reference	Sensitivity			Specificity		
					+ve test	Pt. w. CAD	%	-ve test	Pt. w.o. CAD	%
Al-Saadi	2000	34	Dipyridamole	CAG ≥75%	26	29	90	4	5	83
Schwitter	2001	48	Dipyridamole	CAG ≥75%, PET*	32	37	87(91**)	9	11	85(94**)
Al-Saadi	2002	27	Dobutamine	QCA ≥75%	19	23	81%	3	4	73%
Ibrahim†	2002	39	Adenosine	QCA ≥75%, PET*	17	25	69(86**)	12	14	89(86**)
Nagel	2003	84	Adenosine	CAG ≥75%	38	43	88	37	41	90
Paetsch	2004	79	Adenosine	QCA ≥50%	48	53	91	16	26	62
Plein	2004	68	Adenosine	CAG ≥70%	54	56	96	10	12	83
Kawase	2004	50	Nicorandil	CAG ≥75%	31	33	94	16	17	94
Wolff°	2004	75	Adenosine	QCA ≥70%	11	37	93	29	38	75
Plein	2005	92	Adenosine	CAG ≥70%	52	59	88	27	33	82
Giang#°	2004	51	Adensosine	QCA ≥50%	31	33	93	14	18	75
Totals + Weighted Mean		**647**			**359**	**428**	**84**	**177**	**219**	**81**

* - ^{13}N-ammonia
** - Comparison to second reference
† - Comparison to normal controls
# - Gadolinum dose finding study; results reported for two highest doses (0.10 and 0.15 mmol/kg)
° - Multi-centre trial
CAG = Coronary angiogram
QCA = Quantitative coronary angiography

Table 10: DOBUTAMINE STRESS MR VIABILITY DIAGNOSIS – RESULTS TABLE

Author	Year	Number	EF(%)	Other Reference	Reference Method	Sensitivity +ve test	Sensitivity Pt. w. recovery	Sensitivity %	Specificity -ve test	Specificity Pt. w.o. recovery	Specificity %
Dendale	1998	28	45±12		WM/EF 3-4m F/U	9	10	90	11	14	79
Sandstede	1999	25			WM/EF 6m F/U	13	17	77	12	12	100
Baer	2000	103	39±13	TEE	WM/EF 4.9m F/U	24	28	86	22	24	92
Trent	2000	25	54±15		WM/EF 4m F/U	6	6	100	23	25	92%
van Dijkman	2002	95	30		WM + EF 17m F/U	38	39	97	NA*	NA*	NA*
Kramer	2002	22	46±10	DSE	WM + EF 2m F/U	CT	CT	86**	CT	CT	69**
Motoyasu	2003	23	51	LGE	WM 3-11m F/U	CT	CT	89**	CT	CT	80**
Schmidt	2004	40	42±10	FDG PET (F-18)	WM 4-6m F/U	24	25	96	15	13	87
Uemura	2004	20	50	SPECT (Tl^{201})	WM 4m F/U	CT	CT	89**	CT	CT	89**
Gutberlet	2005	20	27±9	SPECT (Tl^{201}), LGE	WM + EF 6m F/U	CT	CT	88**	CT	CT	90**
Totals + Wt'd Mean		**401**				**114**	**125**	**91**	**83**	**88**	**94**
Mean weighted by number of patients											

* Patients without evidence of viability by DSMR were not revascularized
* * Reported by segment
CT = Cannot tell from data presented
TEE = Transoesophageal echocardiolgraphy
DSE = Dobutamine stress echocardiography
LGE = Late gadolinium enhancement

TABLE 11: LATE GADOLINIUM ENHANCEMENT MR VIABILITY DIAGNOSIS – RESULTS TABLE

Author	Year	Number	EF(%)	Other Reference	Reference Method	Sensitivity			Specificity		
						+ve test*	Segment w. recovery	%	-ve test**	Segment w.o. recovery	%
Kim	2000	50	43±13		WM/EF 3m F/U	329	256	78	124†	110†	98†
Sandstede	2000	12	CT		WM 3m F/U	47	39	83	26	25	96
Choi	2001	24	CT		WM 2-3m F/U	275	213	77	64	61	95
Gerber	2002	20	CT		WM 7m F/U	170	109	64	219	179	82
Klein	2002	31	28±9	^{18}FDG PET	PET	NA	NA	83	NA	NA	88
Beek	2003	30	51		WM/EF 2-4m F/U	151	119	79	35º	31º	89
Kitagawa	2003	22		SPECT (^{201}TI)	WM 2-4m F/U	196	192	98	68	51	75
Kuhl	2003	26	31±11	^{18}FDG PET, SPECT	PET	NA	NA	96	NA	NA	84
Motoyasu	2003	23	51	DSMR	WM 3-11m F/U	175	146	83	103	74	72
Schvartzman	2003	29	28±10		WM/EF 3-8m F/U	44	36	82	33	27	82
Selvanayagam	2004	52	62±11		WM/EF 5m F/U	190	156	82	88	71	81
Van Hoe	2004	18		DSMR	WM 7-11m F/U	61	56	92	24º	22º	92º
Gutberlet	2005	20	27±9	SPECT (TI^{201}), DSMR	WM + EF 6m F/U	CT	CT	99	CT	CT	94
Totals + Wt'd Mean **Mean weighted by number of segments**		**357**				**1638**	**1322**	**81**	**784**	**651**	**83**

Table 12: RADIATION

Modality	Radiation Source	Total Dose (mCi)	Radiation Dose (mSv)
SPECT MPI (1 day protocol)	Tc-99m	32-40	9.2-11.4
SPECT MPI (2 day protocol)	Tc-99m	50	14.8
SPECT MPI	Tl-201	2.5-3.0	15.7-18.9
PET MPI	Rb-82		
Camera (3D BGO)		20-40	3.6-7.1
Camera (2D BGO/LSO/GSO and 3D LSO/GSO)		60-120	10.6-21.2
PET MPI	N-13 ammonia	20-40	2.0-4.0
PET FDG		5-15	5.0-15.0 mSv
PET Viability			
Camera (3D BGO)	Rb-82/FDG	10-20/10	6.8-18.6
Camera (2D BGO/LSO/GSO and 3D LSO/GSO)	Rb-82/FDG	30-60/10	10.3-25.6
	N-13/FDG	10-20/10	6.0-17.0
CT (16-slice MDCT)	x-ray		7-15
CT (64-slice MDCT)	x-ray		5-15
Invasive Coronary Angiography	x-ray		2.1-2.5
MRI	N/A		N/A

CT - Computed tomography
SPECT - Single photon emission tomography
MPI - Myocardial perfusion imaging
PET - Positron emission tomography
RB-82 - Rubidium -82
FDG - Fluorodeoxyglucose
MRI - Magnetic resonance imaging

Appendix 1:

NAME	EXPERTISE	INSTITUTION	MEMBERSHIP AFFILIATIONS
Primary Panel Members (Writing Team)			
BEANLANDS, Dr. Rob S.B.	Cardiology, PET, Nuclear Cardiology	University of Ottawa Heart Institute	CCS, CNCS, CANM
CHOW, Dr. Benjamin J.W.	Cardiology, CT Angiography, PET, Nuclear Cardiology	University of Ottawa Heart Institute	CCS, CNCS
DICK, Dr. Alexander	Cardiology, Cardiac MRI	Sunnybrook & Women's College HSC University of Toronto	CCS, CanSCMR
FRIEDRICH, Dr. Matthias G.	Cardiology, Cardiac MRI	Foothills Medical Centre, University of Calgary	CCS, CanSCMR*
GULENCHYN, Dr. Karen	Nuclear Medicine, PET	Hamilton HSC, McMaster University	Chair-Standards of Practice (2005-06) CANM*, CNCS*
KIESS, Dr. Marla	Cardiology, Nuclear Cardiology	St.Paul's Hospital , University of British Columbia	CCS, CNCS*
LEONG-POI, Dr. Howard	Cardiology, Echocardiography	St. Michael's Hospital, University of Toronto	CCS
MILLER, Dr. Robert M.	Radiology, CT, MRI	Halifax Infirmary, Dalhousie University	CAR*
NICHOL, Dr. Graham	Clinical Epidemiology, Cost Analysis	Harborview Prehospital & Clinical Trial Center University of Washington	CCS
Secondary Panel Members:			
FREEMAN, Dr. Michael	Cardiology, Nuclear Cardiology	St. Michael's Hospital, University of Toronto	CCS, CNCS
BOGATY, Dr. Peter	Cardiology	Quebec Heart Institute, Universite Laval	CCS
HONOS, Dr. George	Cardiology, Echocardiography	SMBD Jewish General Hospital, McGill University	CCS*
HUDON, Dr. Gilles	Radiology	Montreal Heart Institute, Universite de Montreal	CAR
WISENBERG, Dr. Gerald	Cardiology, Cardiac Imaging (MRI, PET)	London HSC, University of Western Ontario	CCS, CNCS*
Also Assisting with Writing Team			
VAN BERKOM, Judith	Information Specialist	Children's Hospital of Eastern Ontario, University of Ottawa	
WILLIAMS, Kathryn	Biostatistician	University of Ottawa Heart Institute	
YOSHINAGA, Dr. Keiichiro	PET/Nuclear Cardiology Fellow	University of Ottawa Heart Institute	
GRAHAM, Dr. John	MRI Fellow	Sunnybrook & Women's College HSC, University of Toronto	

**Current Executive*

Appendix 2:

The ACC/AHA Classifications I, II, and III are used to summarize indications as follows:

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and /or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/ efficacy is less well established by evidence/ opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/ effective and in some cases may be harmful.

Levels of evidence for individual class assignments are designated as:

A = Data derived from randomized clinical trials

B = Data derived from a single randomized trial, or from nonrandomized studies

C = Consensus opinion of experts

Techniques considered investigational are not further classified.

In considering the use of a specific technique in individual patients, the following factors are important:

1) The quality of the available laboratory and equipment used for performing the study and the quality, expertise, and experience of the professional and technical staff performing and interpreting the study.

2) The sensitivity, specificity, and predictive accuracy of the technique.

3) The cost and accuracy of the technique compared with that of other diagnostic procedures.

4) The effect of positive or negative results on subsequent clinical decision making.

(*Klocke FJ et al. ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging. JACC 2003;42(7):1-69*)