Non-Invasive Coronary Angiography: CT and MR Techniques

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Background: Given the invasive nature and high costs of invasive coronary angiography, there is an increased interest in non-invasive methods to image the lumen of the coronary arteries. Non-invasive coronary angiography has made great strides over the last decade to become a clinically useful tool to augment conventional coronary angiography.

Objective: We sought to provide a comprehensive review of the literature relating to both electron beam angiography, magnetic resonance angiography and spiral computed tomography, currently the three most promising non-invasive methods to visualize obstructions in the coronary tree.

Results: Angiography and the general indications and uses are discussed. Three new methods to non-invasively image the coronary arteries are reviewed. Electron beam angiography provides an overall sensitivity of 86% and specificity of 91% for the 476 patients reported in these studies. Multi-row-detector spiral computed tomography data is limited, but overall sensitivity is 68% and specificity of 83%. Magnetic resonance angiography, using newer techniques, demonstrated a sensitivity of 71% and specificity of 82% in the 278 patients reported in these studies.

Conclusions: These techniques show great promise in their ability to non-invasively visualize the coronary segments. Given the current utility of these techniques, we can expect a rapid growth in both the knowledge and experience with non-invasive angiography, leading to a much wider clinical use of these modalities in visualizing the coronary lumens to evaluate obstructive coronary disease.

Over the past decade, great strides have been made in cardiac imaging. The ability to visualize the lumen of the coronary artery, has been at the forefront of these advances. Selective cardiac catheterization, the reference standard for visualization of coronary artery stenoses, is an invasive procedure with a significant cost and small procedure related morbidity and mortality. An alternative, less expensive, and non-invasive test for use as a diagnostic tool before possible intervention could have a major impact on health care practice and cost containment. Non-invasive coronary angiography, due to rapid coronary motion, limited arterial size and tortuous course, has been very challenging. This paper sought to review the benefits, risks and costs of invasive angiography to that of the three non-invasive methods with the greatest clinical experience, electron beam tomography (EBT), multi-row detector spiral computed tomography (MSCT) and magnetic resonance imaging (MRI).

Angiography

Visualization of the lumen of the coronary artery, to assess for the need for revascularization, is currently performed by injection of iodinated contrast directly into the coronary arteries.[1] Since the contrast resolution is limited with flouroscopy (the imaging method used during angiography), direct enhancement of the blood pool in the artery of interest is required. This requires direct arterial puncture with catheters advanced up the aorta (in a retrograde fashion). Conventional coronary angiography (CCA) further requires selective cannulation of the ostium of the left and right coronary arteries and, if present, each saphenous vein graft or internal mammary artery graft to obtain optimal selective contrast enhancement. Percutaneous or cutdown techniques, usually from the femoral or brachial artery, are used for insertion of special intravascular catheters. The purpose of coronary angiography is to define coronary anatomy and the degree of luminal obstruction of the coronary arteries.[1] Coronary angiography remains the standard for assessment of anatomic coronary disease. The limitations of this procedure include the risks (arterial puncture, iodinated contrast and radiation), the need for multiple staff members including a nurse, physician and technologists, and the costs incurred during the procedure and the ensuing observational period. Given these potential complications, the physician must make reasoned decisions on its use based on the anticipated clinical benefit versus the risks and costs of the procedure.

Risk of Invasive Angiography

The procedure is associated with a small but definable risk. A 1990 survey by the Society for Cardiac Angiography and Interventions indicated that the total risk of all major complications (including mortality) from coronary angiography is approximately 2%.[2] The most common risk is associated with arterial puncture and advancement of the catheter retrogradely up the aorta to the ostium of each coronary artery. This is required three or more times during a typical angiographic procedure. The catheter can dislodge aortic plaque, which can embolize, causing myocardial infarction or stroke. Furthermore, the arterial puncture can cause vessel damage, sometimes facilitating surgical repair. Serious bleeding and dissection of the wall of the artery are also rare but significant complications. Another risk of CCA is injection of iodinated dye (which is potentially renal toxic, and can also be associated with allergic reactions, including anaphalaxis). Once the catheters are removed from the artery, observation and patient immobility is usually required for several hours prior to patient ambulation. Newer techniques are now available to shorten this post-procedural observation period. In 1993, 1,800,000 cardiac catheterization procedures[3] were performed. Given the present trend of increased utilization, it is possible by 2010, annual use in the use will exceed 3,000,000 cardiac catheterizations.[4]

Costs

The 1992 mean charge for cardiac catheterization for inpatients younger than 65 years without a diagnosis of acute MI was $10,880, varying by state from a low of $6,400 in Maryland to $17,600 in California.[5] The physician charge made up 18% of the total, averaging $2,000 and varying from $1,300 in South Carolina to $2,550 in California.[6] Currently, non-invasive angiography is being offered for $1000-1750 (including physician interpretation) in different medical centers. Research on the cost-effectiveness of non-invasive coronary angiography is needed before the optimal use of this procedure in a wide range of clinical circumstances can be determined.

Current Uses

Despite these and other limitations, coronary angiography is the only method currently available for defining the details of the entire coronary endoluminal vascular anatomy, and it provides the reference standard against which other tests are compared. Coronary angiography is principally used in three clinical situations[7]: first, to determine the presence and extent of obstructive coronary artery disease (CAD) in a setting in which the diagnosis is uncertain and CAD cannot be reasonably excluded by noninvasive testing; second, to assess the feasibility and appropriateness of various forms of therapy, such as revascularization by percutaneous or surgical interventions; and finally, as a research tool for the assessment of treatment results and the progression or regression of coronary atherosclerosis. However, the 1999 guidelines concluded "in the absence of clinical indications, repeat angiography is both costly and potentially dangerous."[4] Although coronary lesions that reduce luminal diameter <50% are considered hemodynamically insignificant, they are not clinically benign. These lesions may progress either acutely or chronically, and patients with nonsignificant obstructions have significantly more cardiovascular events during follow-up than those with truly normal coronary angiograms.[8]

Potential Role of Non-Invasive Angiogram

While CCA remains the standard of reference for determining the severity of stenosis resulting from atherosclerosis in the coronary arteries, unfortunately, at least 20% of the clinically indicated diagnostic coronary angiographic procedures performed each year reveal no evidence of obstructive coronary artery stenosis, and therefore do not lead to further interventional procedures.[9] This problem may be two-fold in women. A recent report of 9,238 angiograms from five community hospitals demonstrated that 40.4% of women referred for angiography were found to have non-significant disease, nearly twice that of men.[10] Since most of the risk of conventional angiography revolves around the need for arterial access, including stroke, myocardial infarction, infection and bleeding, non-invasive methods, approached by intravenous administration of contrast (or no contrast at all), eliminate most of the risk associated with the procedure, including post-procedural observation periods, myocardial infarction, stroke, bleeding, arterial infection and vessel dissection.

Difficulties of Non-Invasive Angiography

Fluoroscopy, the method used to visualize the coronary artery lumen during angiography, has high temporal resolution, but low contrast resolution. Thus, it requires direct enhancement of the coronary artery blood pool to allow visualization of the lumen. Non-invasive angiography, without direct injection of contrast into the artery, requires increased spatial resolution to overcome the problems of loss of superb contrast enhancement and temporal resolution. Furthermore, rapid motion of the coronary arteries, complex and tortuous anatomy, as well as the small size of the vessels, all make non-invasive imaging challenging. All three techniques rely upon three-dimensional (3-D) reconstruction to assist with visualization. The CT techniques (EBT and MSCT), rely upon superior spatial resolution and a venous contrast injection. The venous contrast does not provide as robust an enhancement of the coronary arteries, since the contrast is diluted by mixing with the blood pool. Magnetic resonance imaging may utilize gadolinium, a non-iodinated contrast agent, to increase the identification of the lumen.

ELECTRON BEAM TOMOGRAPHY

Electron beam tomography with electrocardiographic (ECG) triggering has been used for detecting and quantifying coronary artery calcifications (CAC) for more than ten years.[11,12] EBT is established as the "gold standard" for CAC detection.[13] While CAC scores correlate well with the total atherosclerotic burden[14,15] and strongly predict future cardiac events,[16,17] the amount of CAC does not correlate well with the stenosis severity of a given lesion.[18] Thus, a high calcium score does not always impart a tight stenosis. While plaque burden itself is dangerous regardless of stenosis severity, use of calcium scanning for predicting the need for angioplasty or bypass surgery is limited.

Electron beam tomography appears well suited for imaging of the coronary artery. It has a unique combination of high temporal resolution (100 milliseconds per slice) and spatial resolutions (0.7x0.7x1.5mm),[13] allowing visualization of small lesions. Furthermore, ECG triggering allows image acquisition during the slow portion of coronary motion (diastole).[19,20] Contrast-enhanced electron beam angiography (EBA) is an emerging technology with the potential for obtaining essentially noninvasive coronary arteriograms (figures 1-3). Recent studies have reported contrast-enhanced, ECG-triggered, 3-D EBA for detecting and grading coronary stenosis.[21,22,23,24,25,26,27]

Coronary artery EBA, a noninvasive diagnostic procedure for demonstrating coronary artery anatomy, was first introduced in 1995.[21] Two studies[27, 28] confirmed that coronary EBA with 3D techniques could reveal the lumen of long segments of the major coronary arteries with high correlation to conventional selective coronary angiography (r=0.83).[28] More recently, researchers demonstrated that this modality could be used to identify significant coronary lumen narrowing (>50% stenosis) with the sensitivity of 74-92%, specificity of 79-100% and accuracy of 81.2-93.4% (see table 1). Summary data demonstrates an overall sensitivity of 86% and specificity of 91% for the 476 patients reported in these studies. Also, inter-observer reproducibility was found to be high (0.74-0.90 by Cohen's Kappa statistic).[25,26]

There is fair uniformity and imaging standards among EBA studies. The imaging procedure used by the above studies are all performed with similar imaging techniques. The studies were performed with a C-100 or C-150XLP electron beam CT scanner (Imatron, South San Francisco, California). ECG triggering is employed, so that each image is obtained at the same point in early diastole. Iodinated contrast is administered through an antecubital or jugular vein with an injection rate of 4 ml/sec and total volume of 120-160 ml. Forty to fifty images are obtained over a single breath hold, usually over 25-40 seconds. This entire protocol is performed within 15 minutes. The test is easy to perform, and interpretation can be made in minutes.

EBT Limitations

EBA studies had a technical success rate of 85-100% and 8-25% of coronary arteries were non-assessable (table 1). Impaired image quality, due to multiple image artifacts including coronary artery motion and breathing artifacts, limited its clinical use. In EBA studies, distal arteries are not as well visualized as the proximal segments. This is most likely due to the greater motion artifacts from cardiac pulsation and the partial volume effect (due to small vessel diameters) in distal epicardial vessels, as compared to the proximal segments.[23,25,29] The main determinant of false positive results for diagnosing ≥50% coronary luminal stenosis was small vessel size[21,29] and the diameter of stenotic segments tends to be underestimated by EBA.[23]

Several strides have been made over the last year to improve on image quality and interpretation of the EBA. Recent studies revealed that the ECG triggering at 80% of the R-R interval (late diastole) used in most prior studies might not be optimal for imaging of the coronary segments near the right or left atria, since atrial contraction during end-diastole causes rapid movement of the base of the heart.[25,30] It has been recently demonstrated that there is less coronary motion at 40% of the R-R interval (early diastole or end-systole),[31,32] which might significantly improve imaging. Improvements including more reliable ECG gating, use of different ECG triggers (40% instead of 80% of the R-R interval) as well as greater experience with this technique will continue to improve accuracy. Hardware improvements in the EBT scanner should also lead to higher accuracy. An available high-resolution detector system improves the spatial resolution by almost 40%, thus enabling improved imaging performance for future studies.[33] Currently, the high negative predictive values (95-98%) have demonstrated the ability of this tool to effectively 'rule out' the presence of obstructive CAD, potentially averting negative invasive coronary angiography in these patients.

EBA after Revascularization

EBA is a promising tool in the follow-up after coronary interventions, with the potential to replace some invasive catheterization procedures (figures 4-6). The most common clinical application of EBA is to evaluate patients with symptoms post-coronary artery bypass graft (CABG) surgery.[34] The utilization of EBA to detect the patency of CABG grafts has been reported as early as 1986.[35] Saphenous vein grafts (SVG), which are generally of large caliber and have little cardiac motion, are especially well suited for non-invasive imaging with EBA (figures 5-6). Flow studies demonstrate graft patency with sensitivities of 93% to 96% and specificities of 86% to 100%.[36,37,38,39] Using 3-D visualization in patients post-CABG demonstrated a sensitivity of 92-100% and specificity of 91-100% for establishing patency of SVG as compared to conventional coronary angiography.[34,40,41] The same studies demonstrated sensitivity and specificity for patency of left internal mammary of 80-100% and 82-100% respectively. Graft aneurysms have also been identified and reported using EBA techniques.[42,43] Percutaneous transluminal coronary angioplasty (PTCA) procedures are performed worldwide as one of the main methods for coronary artery stenosis treatment.[44] However, even with intra-coronary stents, restenosis (closure) of the site of angioplasty is still the greatest risk, which can lead to both myocardial infarction and death. Chest pain after stenting or angioplasty often requires visualization of the site of angioplasty to assess for early closure. A non-invasive method to visualize the site of angioplasty could potentially be used for less typical presentations of acute closure (no typical angina or ECG changes suggestive of ischemia). EBA has been shown to permit imaging of the coronary arteries and detecting high-grade restenosis after PTCA (figure 4). Achenbach et al.[45] reported 50 cases that had performed PTCA without coronary stent implantation. The sensitivity and specificity of EBA was 94% and 82%, respectively, to detect severe stenosis (≥70% stenosis).

Intracoronary stenting is now increasingly used to decrease the restenosis rate of PTCA[46] and to avoid emergent complications, such as acute thrombus, coronary artery dissection, and even emergent CABG.[47] The ability to visualize the coronary lumen through the metal of the stent poses severe problems for EBA, MSCT and MRA. The widespread utilization of metal stents during revascularization procedures provides a major limitation for the clinical application of these techniques. One potential solution to the problem of visualizing the lumen within the stented region is to evaluate flow distal to the stent to assess for patency. EBA flow studies have been utilized to document flow distal to the respective stents to assess for stent patency and stenosis.[48,49,50,51] Pump et al reported a sensitivity of 78% (18 of 23 stenoses detected) and specificity of 98% (189 of 193 stents correctly judged to be free of stenosis) for the detection of significant in-stent restenosis by EBA flow measurements.

Current Clinical Uses

EBA is well suited for post-CABG and PTCA evaluation, pediatric applications, assessment of congenital heart disease and coronary anomalies,[52] and allows measurement of wall motion, myocardial mass as well as right and left ejection fractions during the EBA study.[53,54] Given the high negative predictive values, use in patients with lower probabilities of obstructive disease will allow physicians to exclude obstructive CAD. As compared with CCA, EBA is minimally invasive, has an extremely short acquisition time and markedly lower radiation dose.[55] Patients unable to breath-hold for 25 seconds, those with significant arrhythmias and morbidly obese patients are poor candidates for EBA. The Food and Drug Administration (FDA) has approved EBA for non-invasive coronary angiography.

SPIRAL CT

The 'need for speed' is essential to obtaining virtually motion-free images. The significantly improved temporal and spatial resolution of MSCT scanners opens up new possibilities for cardiac imaging. Due to high in-plane resolution and thin-slice collimation (up to 1.0 mm), high quality images can be obtained. However, as the mechanical detector head must rotate around the patient, no current CT can obtain a full rotation in less than 500 milliseconds, too slow to allow for motion free imaging of the coronary arteries.[56,57] The lack of sufficiently short image-acquisition time requires MSCT studies to obtain many more images (up to 400 images of the coronary tree are obtained), only utilizing a fraction of the obtained data for image reconstruction. Retrospective triggering, acquiring partial data on each scan, may allow shorter acquisition times, but require sophisticated postprocessing algorithms to reduce motion artifacts.[57] Several studies, published primarily in abstract form, are listed in table 2. Achenbach et al[57] reported the applicability and image quality of MSCT on 25 patients without coronary stenoses. This demonstrated that coronary arteries could be visualized over long segments. On average, 78% of the proximal and mid-segments could be visualized free of motion artifacts, and coronary diameters showed close correlation to quantitative coronary angiography (r=0.86).

A recent study described 44 patients who underwent MSCT angiography and traditional angiography. Evaluating all significant obstructions seen by conventional angiography, the overall sensitivity of MSCT in this study was 58%, which varied widely from vessel to vessel.[58] The left main coronary artery had a sensitivity of 100%, while stenoses in the circumflex had a sensitivity of only 44%. Given that patients with heart rates >70 beats per minute were excluded, and only proximal segments were analyzed, results in a general population should be anticipated to be lower.

Another study of 64 consecutive patients who underwent MSCT and coronary angiography was reported.[59] In this study, 68% of major coronary arteries could be evaluated. Similar to the previous study, 32 of 58 high-grade stenoses were detected (sensitivity 58%). In evaluable coronary arteries only, the sensitivity of lesions >50% was 85%, and specificity was 76%. However, all four major coronary arteries could be evaluated in only 30% of patients. In reference to this technique the authors note, "its clinical use may presently be limited due to degraded image quality in a substantial number of cases, mainly due to rapid coronary motion".

A recently presented abstract described 83 patients undergoing angiography and MSCT.[121] A total of 72 high grade stenoses were present, with 40 identified by MSCT (sensitivity of 56%). The specificity in this study was 86%. Of 332 coronary vessels, 235 (71%) could be evaluated. The authors concluded, "its (MSCT) clinical use may presently be limited due to degraded image quality in a substantial number of cases, mainly due to rapid coronary motion".

EBT Versus MSCT

The difference in image acquisition time has lead to marked differences between EBT and spiral CT in regards to CAC scores, with inter-test variability between 40-91% reported.[60,61,62] A recent comparison study in 70 patients undergoing both EBT and spiral CT concluded, "spiral CT has not yet proved to be a feasible alternative to electron-beam CT for coronary artery calcium quantification."[63] The lower temporal resolution leads to a lower sensitivity and accuracy for diagnosing coronary calcium, and these differences are also be encountered with 3-D coronary angiography (where motion free images are required to visualize the coronary arteries without major image artifacts).

In the only direct comparison between MSCT and EBA, MSCT [69] displayed a worse signal-to-noise ratio(10.4 vs. 14.0, $p < 0.001$) meaning that the MSCT image had more noise as compared to EBA. Furthermore, MSCT was affected significantly more severely by motion artifact than EBT (17% of vessel segments vs. 8% of vessel segments, $p < 0.01$).[64] When evaluating coronary vessels without significant motion artifacts, EBA was able to visualize a significantly greater portion of the coronary tree without motion artifacts than MSCT (94!10 vs 77!15%, $p<0.01$). Cumulative data is presented in Table 2.

MSCT Limitations

Since radiation is continuously applied while only a fraction of the acquired data is utilized, high radiation doses (doses of 6-10 rad/study) limit the clinical applicability of this modality. [55,69,60,65,66] In females, the effective radiation doses is another 25% higher than in males (WinDose 2.0a, Scanditronix Wellhofer, Bartlett TN), raising the mean dose from 8 Rads in men to 10 Rads per study in women.[67] These radiation doses are two to three times higher than can be expected for conventional angiography (3-4 Rads), and 5-10 fold higher than doses obtained during EBA (1-1.7 Rads).[4,65]

The need to image in phases of slow coronary artery motion, which progressively shorten with faster heart rates, poses a significant obstacle to this modality.[68] MSCT angiography has noted significant limitations due to cardiac motion have been seen with heart rates >60 beats per minute.[69] One evaluation demonstrated that stenosis detection dropped from 90% with slow heart rates (<60 bpm) to 52% for intermediate heart rates (61-90) to 0% for fast heart rates (>90 bpm) with MSCT.[59] Current research practice is to inject beta-blockers to slow the heart rate prior to imaging, to increase the length of diastole and slow cardiac motion. However, slowing heart rates with beta blockers may pose increased risk, in the form of transient bradycardias and heartblock, with potential serious adverse events. So far, the clinical applicability and accuracy of MSCT for the detection of coronary artery stenoses have not been sufficiently validated.[70] Vigorous research is now underway to improve this methodology (reduce motion artifacts and radiation dose) and more data should be available in the near future. MSCT has not yet obtained FDA approval for non-invasive coronary angiography.

Magnetic resonance angiography (MRA)

MRA provides excellent soft tissue contrast, has inherent 3-D capabilities, and allows acquisition in any anatomic plane. Furthermore, MRA does not expose the patient to radiation, nor iodinated contrast, making this the safest of the current non-invasive modalities, with the exception of those patients with pacemakers, implantable defibrillators or recent stent placement. MRA of the coronary arteries became possible in 1991 with the development of a new group of fast MR imaging sequences.[71,72] The new MRI techniques may also allow quantification of velocity and flow in coronary arteries. MR imaging has proved successful in producing angiograms of peripheral vascular anatomy and abnormalities.[73] Recent advances in fast MR imaging have allowed for compensation of coronary and respiratory motion.[74,75,76,77] However, limitations in spatial and temporal resolution makes visualizing coronary artery lumens more difficult (figure 8-9).

Several generations of coronary MRA techniques have since been described (Table 3). All techniques use ECG-triggering. First generation breathhold techniques, as described in 1991, acquire one 2-D image per breathhold, however, their clinical usefulness was severely limited.[78,79,80,81,82,83] The second generation techniques use respiratory gating or triggering and are referred to as "non-breathholding" or "free-breathing" techniques, as they do not require breathholding during image acquisition.[84,85] Although initial implementations were somewhat unreliable, dramatic improvements have since been made. Third generation techniques allow 3D volume acquisitions in a single breathhold, in combination with real-time interactive slice positioning, appears very promising. Real-time slice positioning, and higher-resolution acquisition schemes, such as spiral MRA, can further improve and facilitate the use of these coronary MR angiographic techniques. [86,87,88,89,90,91,92,93,94,95,96,97] (figure 7-8). The newest versions are now being tested which will allow 3D volume acquisitions in one breathhold and /or real-time interactive slice positioning (figure 9) [98,99,100,101,102]. In addition the use of MR contrast agents appears to further improve some techniques.[103,104]

2-dimensional magnetic resonance coronary angiography (first and second generation techniques)

The breath-hold 2-dimensional technique represented the first attempt at high-resolution imaging of the coronary arteries.[78] A breath-hold lasting 16 heartbeats could produce a single image (table 3). However, multiple breathholds were necessary to cover all parts of the coronary artery tree, and the exact reproduction of the level of inspiration required extremely good collaboration of the patient and caused problems in up to 44% of all subjects. Also, the selection of proper images required constant input of an experienced investigator throughout the imaging procedure, which typically lasted between 45 and 60 minutes.[79] Other limitations of the technique included difficulties in distinguishing veins or pericardial structures from coronary arteries, poor visualization of the left main coronary artery and impaired image quality due to ghosting, ringing and blurring.[80] While an early study with MR angiography yielded favorable results,[79] multiple subsequent studies could not reproduce the promising results obtained in these initial reports[74,80,81,82,83] (table 3).

3-dimensional respiratory gated Magnetic Resonance Coronary Angiography Techniques (third generation techniques)

Many problems of two-dimensional MR coronary angiography can be overcome with the acquisition of a 3-D data set ("volume data set"). A contiguous data set can be acquired independently of operator input, and it permits sophisticated post-processing techniques including 3-D reconstructions[86,87,88] which may facilitate image evaluation. To compensate for the long acquisition time necessary to collect the large amount of data required for imaging of the complete cardiac volume, a number of free-breathing techniques have been developed[89,90] (figures 7-8). A number of clinical studies have compared the results obtained by these 3D respiratory gated MR coronary angiography techniques to conventional invasive coronary angiography.[91,92,93,94] Accuracy varies widely from study to study (sensitivity: 38-83%, specificity: 57-95%) even when the exams of subjects with poor image quality are excluded (table 4). Summary data reveals a sensitivity of 71% and specificity of 82% in the 278 patients reported in these studies. However, a major problem of *retrospective* respiratory gating is the fact that parts of the data necessary to reconstruct the images may not be available in the desired end-expiratory position. In order to fill these gaps it becomes necessary to include measurements which were not made during the ideal respiratory phase, and that may lead to decreased image quality. Therefore, attempts have been made to use prospective gating[98] or to "re-register" the volume according to the respiratory shift indicated by the diaphragm position.[99] However, these approaches to respiratory gated imaging have not been evaluated in large comparative studies.

Limitations

The combination of temporal and spatial resolution currently available with MRA is limited. For MRA, the spatial resolution is inversely proportional to the temporal resolution. Currently used protocols use temporal resolution of approximately 125 msec, and spatial resolution of 1.2x1.2x2.0 mm (table 5). In addition, a relatively low contrast-to-noise ratio, movement artifacts and decreased image quality on the 3-D datasets often prevent adequate visualization of the coronary vessels with the current technology.[70] Other limitations are due to calcifications, metal artifacts, thickened pericardium and small pericardial fluid collections, which can mimic the signal void of blood flow.[41] Finally, patients with claustrophobia, recently implanted stents or other metallic objects, pacemakers and implantable defibrillators cannot undergo this procedure.

R*ecent Developments*

To overcome the difficulties associated even with 3-dimensional navigator-echo-based image acquisition techniques for coronary MRA, a number of new imaging protocols have been developed. Major aim of these approaches was to increase the signal-to-noise ratio of the coronary artery through the injection of contrast agent (figure 9). Initial reports of such techniques have been published and demonstrated promising results[100,103,104,102] A second approach is to use new contrast agents which remain in the intravascular space long enough to achieve signal enhancement during the longer acquisition times necessary for non-breathhold imaging sequences.[105,106] Another aspect in the investigation of coronary arteries by MRI is the analysis of coronary artery flow using phase difference imaging which demonstrates sufficient accuracy in comparison to invasive Doppler flow measurements.[107,108] Such studies have been used to assess coronary stents which, due to metal artifacts, cannot be directly visualized by coronary MRA.[109] MRI, by use of both flow modes and 3D reconstruction, can also visualize CABG patency with high accuracy. Studies demonstrate a diagnostic sensitivity of 93-98% and specificity of 85-97% for saphenous vein grafts.[110,111]

EBA versus MRA

In a recent study of 105 patients post-PTCA, EBA revealed significantly higher sensitivity (93%), specificity (65%), positive and negative predictive values than MRA (navigator-echo-based respiratory gated sequences, sensitivity 67%, specificity 49%) for the detection of high-grade restenosis after PTCA.[112] A second study of 27 patients undergoing EBA, MRA and conventional angiography was recently reported. The sensitivity of EBA for significant stenosis was significantly better (77% versus 54% for MRA, $p<0.05$). Specificity was high for both EBA and MRA (95% versus 91%, p=n.s.). EBA visualized more segments of the coronary arteries than MRA (82% versus 74%, p<0.0%) and had higher in plane spatial resolution (EBA 0.7X0.7 mm versus 1.9x1.25x2.0 mm for MRA).[113]

Clinical Applications

Although the role of coronary artery MRA for stenosis detection has not yet been established, coronary MRA has already been very successful in the detection of coronary artery variants, and the imaging of coronary stents and bypass grafts. Current clinical applications are limited to anomalous coronary artery evaluation[114,115] and post-CABG evaluation. The clinical role of MR coronary angiography still needs to be established.[116,117] Spatial and temporal resolution are constantly improving and, in selected cases under non-clinical conditions, MR even permits imaging of the coronary vessel wall.[76] Multiple new techniques (including new coils, contrast agents and acquisition methodology) are currently being developed and should continue to improve upon the current state.

CONCLUSIONS

EBA, MSCT and MRI coronary angiography are rapidly developing techniques and currently not an alternative to conventional coronary angiography in all cases (Table 6). EBA is currently used clinically in certain centers. Selective use might prove both cost effective and provide a safer, less-invasive method for patients. These non-invasive techniques have potential capabilities of assessing perfusion and coronary flow in addition to coronary anatomy, and thus may provide a comprehensive cardiac evaluation.

Successful development of a non-invasive angiogram with consistently high sensitivity and specificity for obstructive CAD would greatly reduce the cost and also the morbidity and mortality currently associated with conventional coronary arteriography. The replacement of some of these invasive procedures by non-invasive means would be very desirable. Some potential uses include: following the non-diagnostic stress test; for those persons with intermediate likelihood of CAD (where the step to coronary angiography might be premature); for symptomatic persons post-PTCA and possibly post-stent; evaluating graft patency post CABG, and for early detection of obstructive CAD in the high-risk person. EBA, MSCT and MRI must prove to be accurate and interpretable in most vessels prior to their widespread implementation in clinical practice. Given the current utility of these techniques, we can expect a rapid growth in both the knowledge and experience with non-invasive angiography, leading to a much wider clinical use of these new techniques in visualizing the coronary lumens to evaluate obstructive coronary disease.

Table 1: Comparisons of contrast-enhanced electron beam CT and invasive coronary angiography

AUTHOR (REF)	NUMBER	SENSITIVITY	SPECIFICITY	UNEVALUABLE
Achenbach[26]	125	92%	94%	25%
Budoff[25]	52	78%	91%	11%
Moshage[21]	20	74%	100%	--
Reddy[24]	23	88%	79%	8%
Rensing[29]	37	77%	94%	19%
Schmermund[30]	28	83%	91%	12%
Nakanishi[118]	37	74%	94%	12%
Moshage[101]	118	90%	82%	24%
Achenbach[119]	36	92%	91%	20%
SUMMARY	476	86%	91%	18%

Table 2: Comparisons of contrast-enhanced multirow detector spiral CT and invasive coronary angiography

AUTHOR (REF)	NUMBER	SENSITIVITY	SPECIFICITY	UNEVALUABLE
Achenbach[59]	64	85%	76%	32%
Knez[58]	44	58%	91%	30%
Hong[120]	25	80%	76%	
Giesler[121]	83	56%	86%	29%
SUMMARY	216	68%	83%	30%

Table 3: Coronary MR Angiography technique classification, as proposed by Duerinckx[71] and Wielopolski[75]

Coronary MR Angiography techniques		
Generation	**Principle**	**Pros and Cons**
First	One slice per breathhold	2D; spatial registration problems; available on all commercial scanners
Second	Free-breathing	3D and high resolution; but long acquisition times (up to 45 minutes)
Third	3D volume in a single breathhold	3D and low spatial resolution; shorter acquisition times

Table 4: Sensitivity and specificity for the detection of coronary artery stenoses by 2-dimensional breathhold (first generation) magnetic resonance coronary angiography in comparison to conventional invasive coronary angiography.

Author	Patients	Sensi-tivity	Speci-ficity	Spatial Resolution (mm)	Temporal Resolution (ms)
Manning[79]	39	90%	92%	1.4x0.9x5.0	80-104
Pennell[81]	39	85%	-	1.6x0.8x5.0	126
Post[82]	35	40-63%	89-97%	1.8x1.0x4.0	88-113
Mohiaddin[83]	16	56%	82%	1.6x0.8x4.0	126
Duerinckx[74]	21	63%	-	1.0x2.0x5.0	117

Table 5: Detection of coronary artery stenoses: comparison of the sensitivity and specificity of navigator-echo based respiratory gated and breathhold (third generation) 3-dimensional magnetic resonance coronary angiography to conventional invasive coronary angiography.

Author	Patients	Sensitivity	Specificity	Spatial Resolution (mm)	Temporal Resolution (ms)
Post 91	20	38%	95%	1.2x2.3x2.1	260
Woodard 92	10	70%	-	1.2x2.0x3.0	-
Kessler 93	73	65%	88%	1.2x1.2x2.0	125
Müller 94	30	83%	94%	1.2x1.2x2.0	125
Sandstede 95	30	81%	89%	1.2x1.2x2.0	230
Van Geuns113	27	54%	91%	1.95x1.25x2.0	-
Regenfus[122]	50	94%	57%	1.4x1.25x1.5	294
Van Geuns102	38	68%	97%	1.9x1.25x1.5	-
TOTAL	278	71%	82%	-	-

Table 6. Strengths and Weaknesses of Each of the Three non-invasive angiography techniques. (Bolded terms demonstrate relative strength)

ELECTRON BEAM ANGIOGRAPHY	MULTI-SLICE COMPUTED TOMOGRAPHY	MAGNETIC RESONANCE ANGIOGRAPHY
FDA Approved	Not FDA Approved	Not FDA Approved
Limited availability	**Equipment Widely Available**	**Equipment widely available**
Standardized Protocol	Protocols under development	Protocols under development
Requires Iodinated Contrast and Radiation	Requires Iodinated Contrast and Radiation	**No Iodinated contrast or radiation required**
Multiple Studies Reported	Limited Studies Reported	**Multiple Studies Reported**
Consistent Results across different laboratories	Limited experience	Varied results in different laboratories

Figure Legends:

1. Electron beam angiogram of a person with abnormal nuclear scan (reversible anterior defect). The three-dimensional reconstruction reveals normal epicardial arteries. This volume rendered image reveals the left anterior descending (L), Circumflex (C) and Right Coronary artery (white arrow). Multiple such images, from different angles, are examined for full visualization of the coronary tree.
2. Electron beam angiogram of the distal coronary arteries. While the distal right coronary can only be visualized 80% of the time by this technique, this image demonstrates the posterolateral marginal branch (PLMB) and posterior descending arteries (PDA). Image courtesy of Dr. Beh, Kuala Lumpur, Malaysia.
3. Electron beam angiogram of the circumflex distribution. This image demonstrates a normal circumflex and large obtuse marginal. Image courtesy of Dr. Beh, Kuala Lumpur, Malaysia.
4. Electron beam angiogram taken after symptoms of chest discomfort status post percutaneous coronary angioplasty with stenting of the left anterior artery. The image reveals a restenosis (white arrow) of the LAD.
5. Electron beam angiogram of a person 8 years post coronary bypass surgery. The Left Internal Mammary graft is widely patent, inserting into the left anterior descending artery (white arrowheads). The distal artery is well seen and patent, with minimal distal disease. There are two closed saphenous vein grafts (black arrowheads). There are two patent saphenous vein grafts (white arrows), one to a diagonal and one to an obtuse marginal. The right coronary artery has a 100% mid-vessel stenosis (black arrow).
6. Electron beam angiogram of a person 22 years after coronary bypass surgery. A saphenous vein graft is widely patent (white arrow), inserting into the left anterior descending artery, just after a high grade stenosis in the native coronary (white arrowhead). The distal artery is well seen and patent, extending around the apex of te heart. Three saphenous vein grafts are closed proximally (black arrowheads).
7. Navigator-echo-based, non-contrast enhanced magnetic resonance coronary angiography (A) in a patient with a stenosis of the left anterior descending coronary artery (arrows). (B) Corresponding invasive coronary angiogram of that patient

8. 3-dimensional surface reconstruction of normal coronary arteries obtained by navigator-echo based 3D magnetic resonance coronary angiography.
9. MR coronary angiogram of the right coronary artery obtained in a single breathhold. A stenosis of the right coronary artery can be seen (arrow, A). (B) corresponding invasive coronary angiogram which also demonstrates the stenosis.

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