



# Non-Invasive CT / MRI Imaging: Current Status

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## ABSTRACT

Recent years have witnessed emergence of computed tomography (CT) and magnetic resonance imaging (MRI) as tools to obtain non-invasive coronary angiogram. MRI techniques initially showed promise in visualizing coronary arteries but have not matured really into a technique that offers sufficient clinical reliability.

With current CT techniques, which combine high speed and spatial resolution, the accuracy of CT coronary angiography for detection of coronary artery stenosis, appears promising enough to warrant pursuit of this application, though sensitivity is still not high enough for routine diagnostic requirements. The high negative predictive value of normal CT coronary angiogram may be useful for reliable exclusion of coronary artery stenosis. Use of contrast-enhanced CT/MR coronary angiography with further technical advances for detection, characterization and quantification of atherosclerotic plaques in coronary arteries is currently being investigated.

## INTRODUCTION

Conventional catheter based coronary angiography with selective intracoronary injection of contrast medium remains the undisputed standard of reference for luminal assessment of coronary arteries. Intracoronary ultrasound, Doppler, pressure measurements and various other applications have also been devised as adjunct to coronary angiography to further ascertain functional significance and hemodynamic consequences of obstructive coronary artery disease.

The greatest advantage of conventional angiography is high spatial resolution and the option of direct performance of interventions such as balloon dilatation or coronary stent placement. Despite minimal risk associated with the procedure, catheter-based selective coronary angiography remain an invasive procedure and few patients can have other complications associated with arterial puncture (haematomas, pseudoaneurysms), use of iodinated contrast (anaphylactic reaction, renal toxicity) and dislodgement of aortic plaque during catheter movement (causing stroke). One survey indicated total risk of all major complications (including mortality) from coronary angiography as 2%.<sup>1</sup>

So despite the clear diagnostic superiority of the procedure, substantial effort has been invested in the development of alternative, less expensive and non-invasive technique for visualization of coronary arteries which could have a major impact on healthcare practice and cost containment.

Several modalities such as electron beam computed tomography (EBCT), magnetic resonance imaging (MRI) and most recently

multi-slice spiral CT (MSCT) have been investigated. The scan characteristics and clinical experience with these techniques will be discussed.

## NON-INVASIVE ANGIOGRAPHY: A CHALLENGING TASK

Non-invasive imaging of coronary arteries has always been a challenging task. This, without direct injection of contrast into the artery, requires increased spatial resolution.

The small caliber and tortuous epicardial coronary vessels follow multiple non-linear courses around the heart and are in constant motion. The coronary arteries besides displacement due to cardiac contraction are also displaced by respiration.

To quantify stenosis in coronary vessels with diameter as small as 2 mm, the spatial resolution should be as low as 0.2 mm in all three dimensions. It may need to be further better, to differentiate the plaque components. The acquisition on reconstruction of images needs to be synchronized to the cardiac cycle and to the respiration.

There is small period during mid to end-diastolic phase, when coronary artery motion is relatively limited even though they are never completely immobile. The data acquisition or image reconstruction for coronary visualization should be restricted to this short period of relative immobility. This not only requires precise and consistent electrocardiogram (ECG) synchronization, the scan window should also be shortest possible to decrease chance of motion artifacts.

**Table 1: Comparison of Contrast-Enhanced Electron Beam CT and Invasive Coronary Angiography**

Author (Ref)	Number	Sensitivity	Specificity	Unevaluable
Achenbach <sup>25</sup>	125	92%	94%	25%
Budoff <sup>24</sup>	52	78%	91%	11%
Reddy <sup>21</sup>	23	88%	79%	8%
Rensing <sup>26</sup>	37	77%	94%	19%
Moshage <sup>67</sup>	118	90%	82%	24%
Achenbach <sup>68</sup>	36	92%	91%	20%

## COMPUTED TOMOGRAPHY (CT)

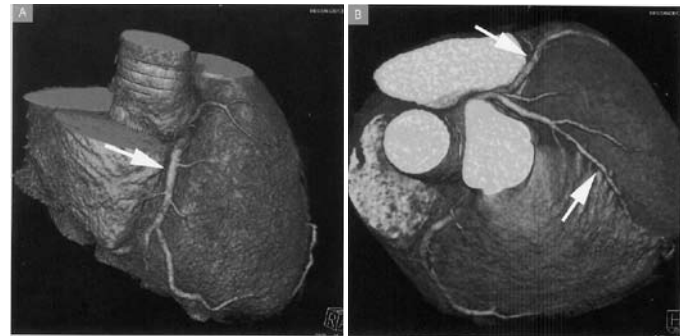
CT has already been used as an effective tool as premier non-invasive modality for vascular imaging of the thorax.<sup>2</sup> CT imaging of heart started to be considered as a reality with introduction of electron beam CT<sup>3</sup> and more recently, of multi-detector row CT<sup>4-6</sup> and with development of ECG-synchronized scanning and reconstruction techniques.<sup>7</sup> The real benefit of these modalities lies in fast volume coverage and high spatial and temporal resolution, which constitute the sine-quo-non for successful cardiac imaging.

## ELECTRON BEAM TOMOGRAPHY (EBCT)

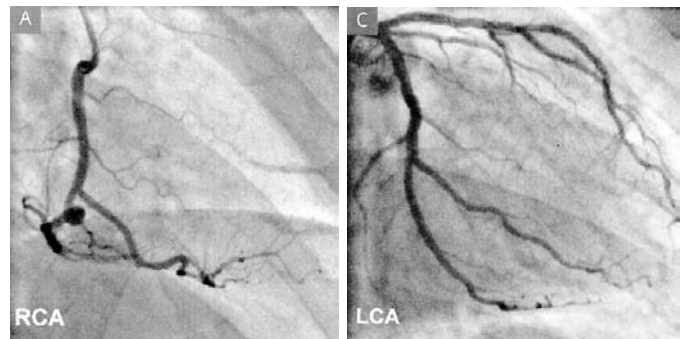
EBCT was introduced in 1983, and first angiographic experiences were published in 1995. The short scan time is accomplished by replacing the mechanically rotating X-ray tube with an electron gun, which (triggered by ECG) generates an electron beam that is guided along a 210° tungsten target ring in the gantry. X-rays are produced after the electrons strike the target ring and a collimated fan beam is passed through the patient in the gantry. A stationary 216° detector ring positioned opposite target rings acquires the data. Data for one tomogram can be collected in 50-100 milli seconds.

EBCT with ECG triggering has been 'gold standard' for detecting and quantifying coronary artery calcification (CAC) for more than 10 years.<sup>8,9</sup> While CAC scores correlate well with the total atherosclerotic burden<sup>10,11</sup> and strongly predict future cardiac events,<sup>12,13</sup> the amount of CAC does not correlate well with the stenosis severity of given lesion.<sup>14</sup>

By virtue of its high temporal resolution (100 msec/slice) and spatial resolution (0.7 x 0.7 x 1.5 mm)<sup>15</sup> which allows good visualization of small lesions, electron beam tomography seems suitable for coronary artery imaging. Further ECG triggering allows to acquire image during slow diastolic portion of coronary motion.<sup>16,17</sup> Contrast-enhanced electron beam angiography (EBA) is new technology, which has potential for obtaining non-invasive coronary angiogram. There are now various reports of contrast-enhanced, ECG triggered, 3D EBA for detecting and grading coronary stenosis.<sup>18-21</sup> Two studies found high correlation between conventional coronary angiography and 3D EBA technique in detecting the lumen of long segment of major coronary arteries.<sup>22,23</sup> In data comprising of 476 patients, this modality has been shown to detect significant coronary artery narrowing (> 50% stenosis) with sensitivity of 74 - 92%, specificity of 79 - 100% and accuracy of 81.2 - 93.4%.<sup>24,25</sup> The studies were carried out with C-100 or C-150 XLP electron beam CT scanner (Imatron, South San Francisco, California). Iodinated contrast (120 - 160 ml) at rate of 4 ml/sec is administered through an



**Fig. 1:** (a) MSCT 3-dimensional reconstruction of right coronary artery demonstrating absence of significant coronary artery stenosis (b) 3-dimensional reconstruction of the left coronary system again demonstrating absence of significant stenosis



**Fig. 2:** a, c Invasive angiogram in the same patient correlates with findings of MSCT non-invasive coronary angiogram.

antecubital or jugular vein. Forty-fifty images are acquired with ECG triggering over a single breathhold, over 25-40 seconds. Usually it takes 15 minutes to complete the entire protocol and its interpretation can be done within minutes (Table 1).

## Limitations

Despite good technical success rate, 8-25% of coronary arteries cannot be imaged with this modality. Its clinical use has been limited by impaired image quality due to multiple image artifacts including coronary artery motion and breathing artifacts. Further, distal coronary arteries are not as properly delineated as the proximal portion. Partial volume effect due to small vessel diameters and greater motion artifacts from cardiac pulsation in distal vessels is the most plausible explanation for this.<sup>20,24,26</sup> It has also been reported that EBA tends to underestimate the diameter of stenotic segments.

There is an ongoing effort to improve hardware in EBT scanner to get more accuracy.

This modality also holds promise particularly in follow up patients post-revascularization (surgical or catheter-based). To evaluate symptomatic patients post-CABG surgery is very important clinical application of EBA.<sup>27</sup> Saphenous vein grafts because of their large caliber and being little affected by cardiac motion are particularly well suited for imaging with EBA. EBA with 3D visualization established SVG patency with sensitivity of 92-100% and specificity of 91-100% when compared to conventional angiography.<sup>27-29</sup> Similar high patency rates have



**Fig. 3:** 68 years male patient with unstable angina, underwent non-invasive coronary angiogram (by MSCT) and then invasive coronary angiogram. Quantification of RCA stenosis was correlated well with both techniques. Patient underwent stenting to RCA. Depiction of RCA lesion by conventional coronary angiogram (A), image reconstruction by volume rendering technique on MSCT (B), and curved multiplanar reconstruction technique (C).

**Table 2: Comparison of Contrast-Enhanced Multislice Detector Spiral CT and Invasive Coronary Angiography**

Author (Ref)	Number	Sensitivity	Specificity	Unevaluable
Achenbach <sup>46</sup>	64	85%	76%	32%
Knez <sup>44</sup>	44	58%	91%	30%
Hong <sup>69</sup>	25	80%	76%	--
Giesler <sup>70</sup>	83	56%	86%	29%

been documented for LIMA conduit using imaging by EBA.<sup>28,29</sup> Graft aneurysms have also been identified with precision.<sup>30,31</sup>

Post-intracoronary stenting procedure, any of these non-invasive modalities (EBCT, MSCT, MRA) face problems in visualizing the coronary lumen through metal of stent, and this forms the potential limitation for clinical application of these techniques in studying this subset of patients. However, evaluating the flow distal to the stent and taking it as indicator of stent patency / stenosis,<sup>32-34</sup> is a possible solution to this problem. Pump et al detected significant in stent restenosis by EBA flow measurements with a sensitivity of 78% and specificity of 98%.<sup>35</sup>

### Current Clinical Uses

EBCT is well suited for assessment of congenital heart disease and coronary anomalies,<sup>36</sup> post-CABG and post-PTCA evaluation, to study myocardial mass, wall motion, and right and left ventricular ejection fraction.<sup>37,38</sup> As it has high negative predictive value, EBCT is useful in excluding obstructive CAD in patients with low probability of CAD.

Patients unable to breathhold for 25 seconds, those with significant arrhythmias and morbidly obese patients are poor candidates for EBA. Currently EBA has been approved for non-invasive coronary angiography by FDA.

### SPIRAL CT

In 1998, mechanical spiral CT systems with simultaneous acquisition by four detector rows and a minimum rotation time of 500 msec was introduced.<sup>4,6</sup> The strategy that has been

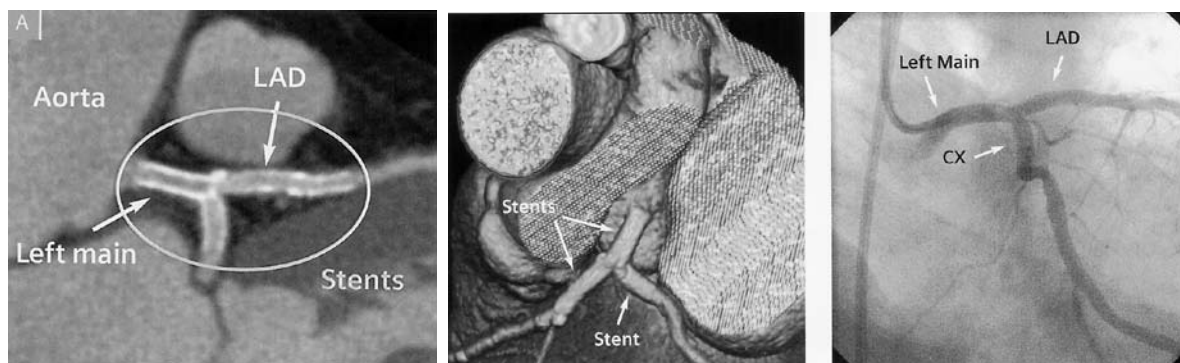
pursued since introduction of the first multidetector row CT scanner to further improve fast high resolution volume coverage is to increase the number of sections that are simultaneously acquired. So far, this has resulted in introduction of 8, 10, 16, 32, 40 and 64 detector row CT scanner with further reduced gantry radiation times.<sup>39</sup>

Currently 16-row detector multislice scanner is considered most reliable non-invasive technique for visualizing coronary arteries.<sup>40,41</sup> The 16 slice CT scanner consists of single rotating X-ray tube generating a beam of photons that travel through the patient and then received by 16 rows of detectors thus effectively producing 16 slices for each X-ray tube rotation. This technique allows covering of whole heart, which usually is 12-14cm, in one breathhold of  $\pm$  20 seconds with slice thickness of 0.8 mm. The tube rotation time is 375 ms, which using a 180° data interpolation algorithm translates into temporal resolution of  $\pm$  190 ms.

X-ray contrast bolus (100-120 ml) is injected into brachial vein to improve the difference in the contrast between the blood filled coronary lumen and its adjacent structures (coronary wall and perivascular fat). In order to reduce the cardiac motion artifacts, reconstruction of coronary images is done from the data obtained by retrospective ECG gating during relative cardiac motion-free mid-diastolic phase.<sup>42</sup>

Basal heart rate of patient is aimed at < 70 bpm (of > 70 bpm, beta blocking agents used prior to scan). This is done to create a longer mid-diastolic motion-free period with view of compensating for relative long temporal resolution. Current multidetector row CT scanner provide in plane spatial resolution of 0.5 mm and effective through plane (Z axis) resolution of 0.6 - 0.8 mm.<sup>39</sup>

There are either scattered case reports or smaller studies in literature documenting the clinical applicability of this modality for non-invasive coronary angiography. A study by Achenbach et al<sup>43</sup> demonstrated that 78% of the proximal and mid segments could be visualized free of motion artifacts, and coronary



**Fig. 4:** Showing stent patency with non-invasive coronary angiogram by MSCT (A), (B) and by conventional coronary angiography (C)

diameters showed close correlation to quantitative coronary angiography.

Another study (44 patients), comparing MSCT with conventional angiography evaluated the sensitivity of MSCT in picking significant stenosis to be 58% which varied from vessel to vessel.<sup>44</sup> Left main coronary artery had sensitivity of 100%, while stenosis of left circumflex had sensitivity of only 44%. However in study by Nieman et al 100% of coronary artery segments were assessable and sensitivity (for > 50% stenosis) was 96% with specificity of 84% (Table 2).<sup>40</sup>

MSCT also allows identification of various plaque components such as fat, fibrous tissue or calcium. These different plaque components impart X-ray attenuation resulting in different CT densities thus establishing 'soft' plaque and hard plaque. However, future clinical studies are required to demonstrate the reproducibility of this technique and independent risk for adverse coronary events in various patient populations.

### MSCT Limitations

Since radiation is continuously applied while only a fraction of acquired data is utilized, high radiation doses (6-10 Rad/study) limit the clinical applicability of this modality.<sup>45</sup> These radiation doses are 2-3 times higher than can be expected for conventional angiography (3-4 Rads), and 5-10 fold higher than doses obtained for EBA (1-1.7 Rads).

Cardiac motion (HR > 60bpm) poses significant limitation to MSCT angiography. Achenbach in his study, demonstrated that sensitivity of MSCT (for significant stenosis) dropped from 90% with slow HR (< 60 bpm) to 52% for intermediate heart rates (61-90) to 0% for fast heart rates (> 90 bpm).<sup>46</sup> Current practice of slowing heart rate with beta-blockers might not be tolerated by many patients.

So far, the clinical applicability and accuracy of MSCT for detection of coronary artery stenosis have not been sufficiently validated.<sup>47</sup> Despite significant strides made by MSCT, further improvement in spatial / temporal resolution would make the imaging still better. MSCT has not yet been approved by FDA for non-invasive coronary angiography. New technical advances (especially 64 slice computed tomography), which are within reach, need to be implemented to make this technique clinically reliable.

## MAGNETIC RESONANCE ANGIOGRAPHY (MRA)

MRI is a tomographic imaging technique based on magnetic characteristics of tissues and molecules within a magnetic field. The first reports of MR coronary angiography came in 1991<sup>48,49</sup> with the development of a new group of fast MR imaging sequences. The new MRI techniques allow quantification of velocity and flow in coronary arteries. Recent advances in fast MR imaging have also allowed for compensation of coronary and respiratory motion.<sup>50-53</sup>

Currently, data acquisition for MR coronary angiogram is done as 2 ways: 1. Entire cardiac volume is scanned in a long respiratory gated session (> 10 min) 2. Smaller targeted volumetric sections are acquired, with a slightly lower resolution but within a single breathhold. The synchronization to the cardiac cycle is done by prospective ECG triggering. The further enhancement of image signal from coronary lumen can be done by use of flow-dependant MR acquisition sequences or by injection of MR-specific contrast agents.

Third generation MR techniques with 3D volume acquisition in single breathhold, in combination with real time interactive slice positioning appears very promising. This technique and higher resolution acquisition schemes such as spiral MRA, can further facilitate use of coronary MR angiographic techniques.<sup>54-57</sup>

In one study, sensitivity and specificity of MRA for detection of high grade coronary stenosis was found to be 54% and 91% respectively. MRA was able to visualize 74% segments of coronary arteries.<sup>58</sup> MRI, by use of both flow modes and 3D reconstruction can also visualize graft patency with high accuracy, with sensitivity of 93-98% and specificity of 85-97%.<sup>59,60</sup> Further, multicontrast MRI has been able to distinguish various plaque components.<sup>52</sup> MRI is also considered good modality in calculating cardiac cavity volumes, myocardial mass, stroke volumes and ejection fraction. Assessment of contraction LV function is accurate, highly reproducible and therefore often regarded as the gold standard (Table 3).

### Limitations

The combination of temporal and spatial resolution (125 msec and 1.2 x 1.2 x 2.0 mm respectively) currently available with MRA is still limited. There are other difficulties like low contrast to noise ratio, movement artifacts and reduced image quality on 3D data sets preventing proper visualization of coronary vessels.<sup>47</sup>

**Table 3: 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
Kessler <sup>71</sup>	73	65%	88%
Sandstede <sup>72</sup>	30	81%	89%
Regenfus <sup>73</sup>	50	94%	57%
Van Geuns <sup>74</sup>	38	68%	97%

The structures like thickened pericardium, small pericardial effusions, calcifications and metal artifacts can mimic the signal void of blood flow and may pose problems.<sup>29</sup> Lastly patients with pacemakers, implantable defibrillators, recently implanted stents and patients with claustrophobia cannot undergo this procedure.

New imaging protocols associated with 3D navigator echo-based image acquisition techniques for coronary MRA have been developed. Initial reports with this technique are encouraging.<sup>61,62</sup> Another approach in improving MR coronary imaging is by using new blood pool contrast agents, which remain in intravascular space long enough to achieve enhanced signal during non-breathholding long image acquisition times.

### Current clinical applications

The clinical role of MR coronary angiography still needs to be established.<sup>63,64</sup> Current clinical applications are limited to anomalous coronary artery evaluation<sup>65,66</sup> and post-CABG evaluation (Table 4).

### CONCLUSION

Non-invasive coronary angiography is rapidly evolving but currently not an alternative to conventional coronary angiography in all cases. Some of the potential indications where non-invasive coronary angiogram can be obtained are:

1. Following non-diagnostic stress test
2. For those persons with low / intermediate likelihood of CAD (where invasive coronary angiography might be premature)
3. For symptomatic patients, post-PTCA and possibly post-stent.
4. Evaluating graft patency for CABG.
5. For early detection of obstructive CAD in high risk person.

Given the current status of these techniques (EBA, MSCT, MRA) and amount of effort put in this field, we do expect that rapid growth and refinement in these modalities might lead to successful development of non-invasive coronary angiogram to diagnose obstructive CAD with consistent high sensitivity/specificity and may become an alternative to conventional coronary angiography in future.

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**Table 4: Strengths and Weaknesses of Each of The Three Non-invasive Angiography Techniques**

Electron Beam Angiography	Multi-slice Computed Tomography	Magnetic Resonance Angiography
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 and radiation required
Multiple studies reported, consistent results	Limited studies reported	Multiple studies reported, varied results
FDA approved	Not FDA approved	Not FDA approved

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