Diagnostic Accuracy of Non-Invasive Coronary Angiography by Multi-Slice Computed Tomography

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Background The aim of this study was to compare the sensitivity and specificity of non-invasive coronary angiography using Multi-Slice Computed Tomography (MSCT) with invasive coronary angiography. Continuous technological advances in hardware acquisition and software processing are steadily improving its accuracy in the detection of coronary artery obstruction.

Methods **98** consecutive patients who underwent MSCT coronary angiography were subsequently studied by invasive coronary angiography. A total of ….. native main vessels, secondary branches and bypass grafts were analyzed by two sets of blinded observers. Lesions causing $\geq$ 50% stenosis were considered significant. CT angiography was performed with a 16 slice helical CT, with isotropic images, 0.5 x 0.5 x 0.5 cubic voxel, 400 msec gantry rotation, and retrospective EKG gating. Analysis was performed using 3D volume rendering with vessel probing, and standard axial, coronal and sagital Maximal Intensity Projection (MIP) views.

Results Compared with invasive digital angiography, coronary MSCT angiography of the main coronary arteries demonstrated a sensitivity of 97% and a specificity of 96%, with a positive predictive value of 89%, and a negative predictive value of 99%. Overall sensitivity and specificity for all coronary arteries, their branches and bypass grafts was 95% and 98% respectively; with a positive predictive value of 92%, and a negative predictive value of 99%, with a 95% confidence level. Non-assessability was at 2.1%.

Conclusions This data indicates that MSCT coronary angiography has reached a high sensitivity and specificity in the non-invasive diagnosis of coronary obstructive disease. This level of accuracy will likely impact on the use of diagnostic invasive coronary angiography.

Since 1999 Multi-Slice Computed Tomography (MSCT) has made significant technical advances allowing improvements in its temporal as well as its spatial resolution. Coronary angiography was not possible with a single slice CT, and the four slice detectors did not achieve enough resolution to provide diagnostic images of the coronary arteries in motion (1-21).

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With the advent of the 16-slice spiral CT, reduction of the slice thickness provided the spatial resolution needed, while the gantry's rotational speed increased the temporal resolution. Subsequently, several investigators, particularly from Europe, published their data (23, 24, 25, 32, 33, 34, and 35).

Further software enhancements were made with 3D volume rendering and vessel probing.

These advances increased the possibility to obtain diagnostic quality images of the coronary lesions.

Encouraged by these findings, and to assess our own accuracy, we attempted to evaluate our sensitivity and specificity by comparing MSCT coronary angiography (MSCTA) with the present standard digital invasive coronary angiography (ICA).

METHODS

Study Design. Included in the study were a total of 98 consecutive patients that had abnormal MSCTA findings, with lesions causing 50% stenosis and greater; these patients subsequently underwent conventional evaluation by ICA, for verification of degree of stenosis, and assessment for revascularisation. Forty-nine patients (57.0%) had angina pectoris, while thirty-seven others (43.0%), were asymptomatic, but had reversible myocardial perfusion defects on nuclear SPECT. Patients with atrial fibrillation were excluded because of EKG gating difficulties. Four patients with permanent pacers, set at 60 b/min, were included in the study. Those with impaired renal function and a creatinine value > 2.0 mg/dl were excluded. Those patients with allergy to contrast media were premedicated with a methylprednisolone pack and received an intravenous injection of 250 mg of hydrocortisone sodium succinate prior to the procedure. Metoprolol 50-100 mg was administered orally to eighteen patients (27.6%) with heart rates >60 b/min on arrival, one hour prior to procedure. Intravenous metoprolol, with 5 mg increments up to 15 mg, was given only as needed to lower heart rates below 60 b/min, prior to injection. Patients were monitored for approximately 90 minutes.

The patients signed an informed consent. The study was reviewed then approved by the Ethics Committee at the Rochester Medical Center and the Human Investigation Committee at Wayne State University.

Patient Characteristics. The mean patient age was 69, including 58 males and 28 females. Thirteen patients had prior bypass surgery and four were permanently paced. All patients underwent coronary calcium scoring and angiography MSCTA first, followed by standard digital invasive coronary angiography (ICA).

MSCT Data Acquisition. A 16 slice Multi-row Detector was used (Aquilion, Toshiba America Medical Systems, Tustin, Ca), that provides true isotropic images. Acquiring isotropic volume data sets allows the resolution of axial images (X-Y plane) to be identical to that of the sagittal and coronal images (Z Plane), thus improving spatial resolution. A scout scan without contrast was used to measure coronary calcium scores using the Agatston equivalent scores for MSCT. The collimation was set at 16, providing 0.5 mm slices; the table feed was at 15mm/rotation, with a gantry rotation of 400 msec. The tube current was at 350 mAs, with 120kV Sure Start, a protocol developed by the manufacturer, detects the contrast enhancement in the region of interest (ROI), over the ascending aorta. It optimizes contrast use, while enhancing peak timing, and improving reproducibility. For automatic initiation of the scan and deployment of the Sure Start, a threshold of 100 Hounsfeld Units (HU) is entered, except for those with bypass, where it is set at 180 HU. The scanning area extends from the carina to the diaphragm. Data sets acquisition starts while the patients hold their breath

for 20-30 seconds: a single breath hold. A double barrel injector (Medrad, Inc. Indianola, PA) is used to inject 80-100 cc of non-ionic contrast media, Iohexol 350, at a rate of 4 ml/sec, followed by 50 cc of saline flush at the same rate.
All patients tolerated the procedure without significant adverse reactions. Flushing following contrast injection was common. Minor headaches and nausea were rarely reported. There was no evidence of associated arrhythmias, or hemodynamically significant hypotension during, and following the study.

CTA Interpretation. The images obtained by the scanner were EKG gated; retrospective reconstruction, from 60% to 80% of the preceding RR interval, was utilized to obtain multiple data sets. These were then forwarded to a separate workstation, the Vitrea (Vital Images, Plymouth, Minnesota), to load and visually determine the best quality data set, most suitable for interpretation (11,12,13,27); Processing with 3D Volume Rendering provides a good overview of the myocardium and vessels condition, and is not just an impressive artistic rendering. The Vessel Probe allows expansion throughout the artery, providing three-dimensional views of the vessel, including cross sections proximal and distal to the point of interest, see figure 1. The standard two-dimensional Maximal Intensity Projections (MIP) views with isotropic axial, coronal and sagittal images were also utilized, for precise assessment of the plaques and degree of obstruction. Further enhancement of vessel analysis is provided by the ability to obtain Curved and double oblique Multi-Planar Reformatting (MPR) images. The final diagnosis was based on the findings, after reviewing of all these images.

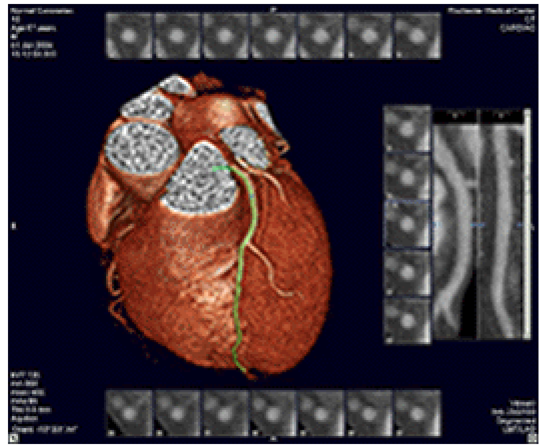


Figure 1.Volume Rendering in 3D, and Vessel Probing (green line), which visualizes the vessel lumen in coronal, sagittal and cross sectional views, proximal and distal to the point of interest (in blue). The patient presented with angina. All vessels were largely patent.

Two blinded observers performed the interpretation of the MSCTA findings independently, and the final decision was reached by consensus. All the vessels, regardless of size, including the main coronary arteries, their secondary branches, and arterial as well as venous bypass grafts, were evaluated for degree of stenosis. Lesions causing ≥ 50% occlusion by visual observation were considered significant; patients having such lesions were referred for conventional ICA.

Digital Coronary Angiography. Digital invasive coronary angiography (ICA) was performed in the usual fashion, and considered as the standard for comparison. Three separate blinded angiographers, unaware of the MSCTA findings, evaluated the catheterization data independently, and decided, by consensus, on the final interpretation. The attending physician and the interventionist, based on the clinical data and the ICA findings, made the final therapeutic decisions.

Statistical Analysis. Statistical analyses for sensitivity, specificity, positive predictive values, negative predictive values and their associated confidence intervals were performed by an independent statistician, using SAS Version 8.2 (SAS Institute, Cary, N.C.) from data compiled and interpreted by the authors. The confidence level was 95%.

RESULTS

A total of 688 native primary vessels, secondary branches, and bypass grafts, were analyzed. Comparison of the MSCTA findings versus the ICA is summarized in table 1.

	1°	*2°*	*CABG*	*Total*
Sens	97.0	83.3	95.2	94.3
Spec	95.7	100	100	97.9
PPV	88.9	100	100	92.5
NPV	98.9	98.4	91.7	98.4

Table 1.Primary arteries include LMT, LAD, LCX and RCA. Secondary branches include Diagonals, Obtuse Marginals, Posterior Descending and Posterolaterals. CABG includes arterial and venous Bypass grafts.

For the primary arteries, comprising the left main trunk, the left anterior descending, the left circumflex, and the right coronary, the sensitivity was 97.0%, and the specificity 95.7%, with a positive predictive value of 89.9% and a negative predictive value of 98.9%. For the LMT, the sensitivity was 100%, and the specificity 98.2%, with a positive predictive value of 87.5%, and a negative predictive value of 100%.

(a)
(b)
(c)

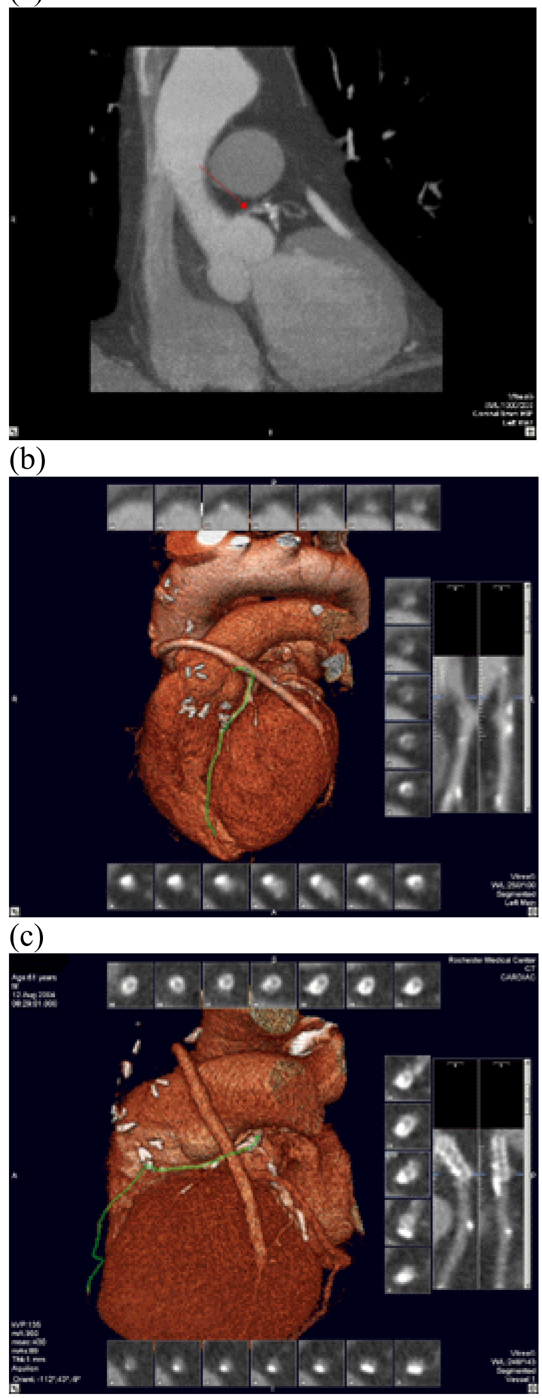
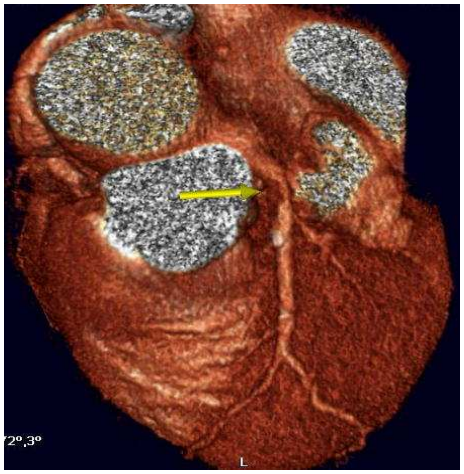


Figure 2: Visualization of soft plaques. **(a)** Post-bypass patient with exertional dyspnea found to have 80% soft plaque in the LMT by MSCTA. LIMA is closed. Patent SVG to OM **(b)** Vessel probing showed the lesion in all the views (blue point of interest). Note in white other calcified plaques. ICA confirmed the finding. **(c)** The lesion was successfully stented.

(a)



(b)

Figure 3. Soft plaque causing 80% obstruction in the proximal LAD. Seen (a) in volume rendering (b) in axial MIP images. The patient was asymptomatic, but had multiple risk factors, and a reversible antero-septal defect on his myocardial perfusion study.

For the LAD, the sensitivity was 100%, the specificity 85.7%, with a positive predictive value of 83.9%, and a negative predictive value of 100%.

For the LCX, the sensitivity was 91.7%, the specificity 100%, with a positive predictive value of 100%, and a negative predictive value of 97.1%.

For the RCA, the sensitivity was 94.4%, the specificity 97.8%, with a positive predictive value of 94.4%, and a negative predictive value of 97.8%.

When calculated for all the primary arteries combined, the sensitivity was 97.0%, the specificity 95.7%, with a positive predictive value of 88.9%, and a negative predictive value of 98.9%.

False positive interpretation on the MSCTA images of five of these vessels was attributed to heavy calcifications, particularly in the proximal LAD. The calcified plaques, in these arteries, showed no significant luminal narrowing on the invasive angiograms, consistent with arterial remodeling rather than obstruction. One false negative interpretation of a totally occluded RCA was due to retrograde filling by unusually large collaterals, documented on the ICA images.

The secondary branches included the diagonal branches of the LAD, the obtuse marginals of the LCX, the posterior descending branch of the RCA, and the postero-lateral branches. For statistical purposes, they were combined in the analysis. Their sensitivity by MSCTA compared to ICA was at 83.3%, their specificity at 100%, with a positive predictive value of 100%, and a negative predictive value of 98.4%. The lower sensitivity is likely due to the vessels smaller size, while the increased specificity is attributed to the lack of heavy calcium burden in these subsidiaries.

Thirteen patients, included in the study, had CABG; For the arterial and venous grafts combined, the sensitivity was 83.3%, with a specificity of 100%, with a positive predictive value of 100%, and a negative predictive value of 98.4%. Some striking illustrative examples are shown in figure 3.

One lesion, causing 70% obstruction in the proximal segment of the SVG to the RCA, was missed on the MSCTA, due to artifact caused by the proximity of the sternal wires from surgery.

The RCA could not be assessed in two of the four patients with permanent pace makers, due to blooming effect. This constitutes a clear limitation when performing MSCTA in such patients.

The percentage of non-assessability was relatively low at 2.1%, and primarily attributed to motion artifacts, and heavy calcifications, as illustrated in figure 4.

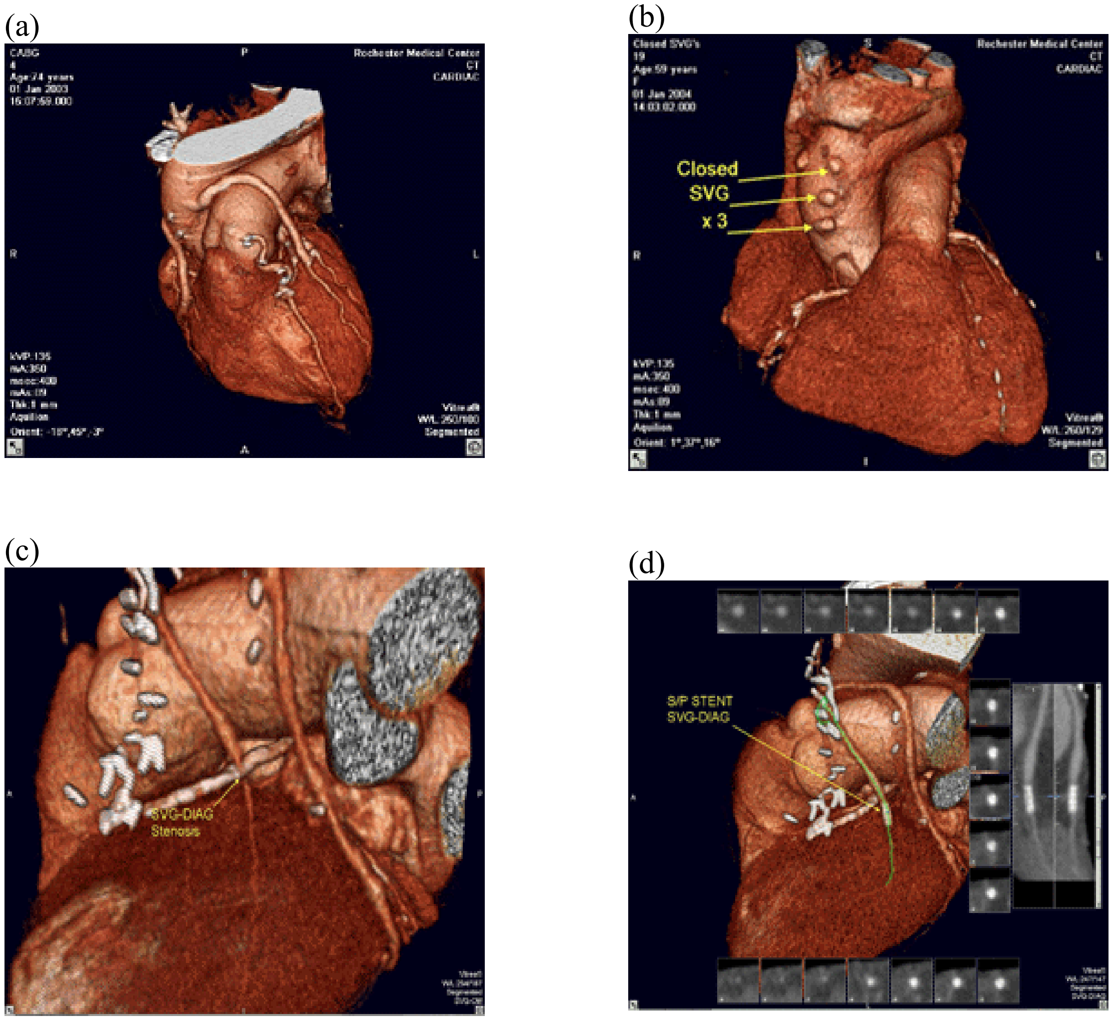
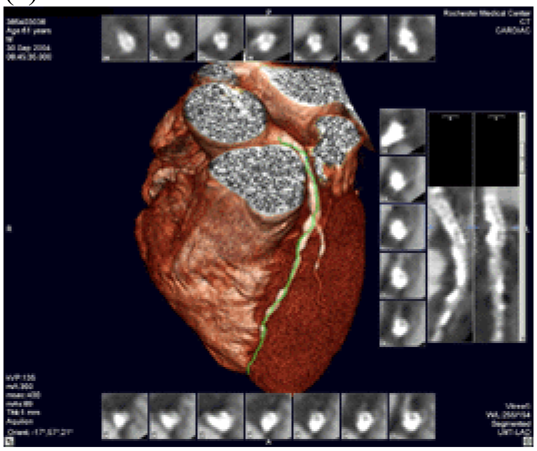
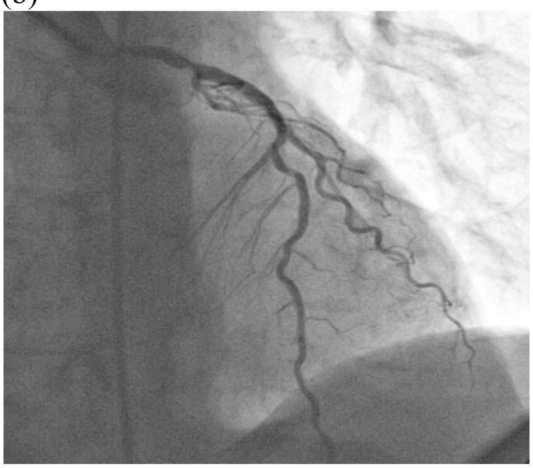


Figure 4: Bypass grafts visualization. Volume rendered images of bypass grafts are striking in quality and diagnostic power. **(a)** Patient with patent LIMA, SVG to PDA, and SVG with bridging to D1 and D2. **(b)** Totally occluded saphenous vein grafts with three stumps noted on the ascending aorta. **(c)** Totally closed LIMA and LAD in a patient with large antero–apical aneurysm. SVG to D1 shows subtotal occlusion prior to anastomosis with D1 **(d)** Vessel probing of SVG to D1 after stenting demonstrates patency.

(a)



(b)



(c)

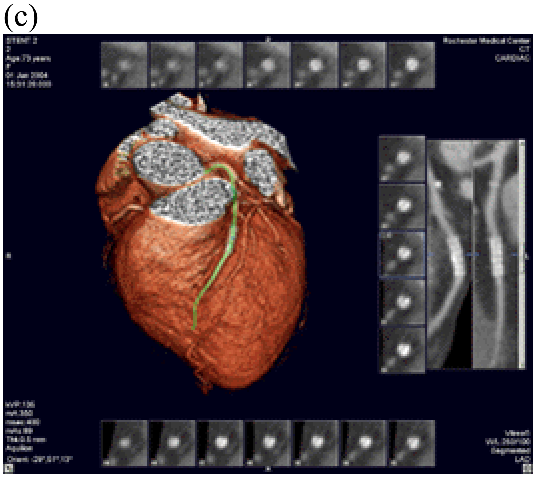


Figure 5. Heavy calcifications. Calcifications could lead to misinterpretation of luminal obstruction. **(a)** The LMT and ostial LAD could not be assessed by MSCTA. **(b)** 90% underlying stenosis was seen on ICA, and was successfully stented. **(c)** On the other hand, intracoronary stents are becoming easily accessible. This patient had post-stenting angina; MSCTA shows a patent stent, with no obstruction.

DISCUSSION

The data shown above leads to the conclusion that non-invasive coronary angiography, using the 16-slice CT, has made significant improvements, yielding high sensitivity and specificity, when compared to conventional invasive coronary angiography.

Other means to evaluate non-invasively coronary artery obstruction, such as Magnetic Resonance Angiography (MRA) and Electron Beam Tomography (EBT), are not the subject of this study, which is limited to Multi- Row Detectors CT.

The initial studies with the 4 slice row detectors (7,8,15,16,19) showed a sensitivity of 52-81%. Despite a high specificity of 84-97%, it was felt that the 4 slice MSCT was not sufficiently adequate to assess coronary obstructive lesions. The rate of non-assesability, 12-30% depending on the author, and the extent of misregistration artifacts were very significant.

With the 16-slice row detectors, the slice thickness was significantly reduced, allowing for improved spatial resolution. The gantry rotation speed was also increased, which enhanced the temporal resolution. The use of such advancements by Nieman et al. (23), Ropers et al. (30), Schlosser et al. (32), and Kuettner et al. (33) improved the sensitivity of the MSCT images, allowing for more accurate results. Nieman and Ropers restricted their study to vessels measuring $\geq$ 1.5 and 2.0 mm respectively. Schlosser evaluated bypass grafts only, while Kuettner used coronary calcium scoring threshold to improve the sensitivity and specificity of MSCT angiography.

Encouraged by these reports, we studied our own accuracy, and slightly widened the scope for patient selection. This decision was made, due to our experience and the technical advances mentioned in our methodologies, often not used by the other investigators. Their equipment used twelve out of the sixteen row detectors for simultaneous acquisition for cardiac protocols; the images were not isotropic; the slice thickness was only at 0.75-1.5mm compared to ours at 0.5 mm; and gantry rotation was 500ms, slower compared to ours at 400 msec. So we studied not only the patients' main native vessels, but added their branches without size restriction, and included patients with permanent pacemakers, as well as those with bypass grafts (18%). We did not set a coronary calcium scoring threshold for inclusion. We attempted to maintain heart rates below 60 beats/min to improve image quality (5,6,7,12,13,28).

Despite these additions, the overall sensitivity of MSCTA for the detection of significant coronary lesions was 94%, the specificity 98%, with a positive predictive value of 93%, and a negative predictive value of 98.4%, with a confidence level of 95%. These results would have been even higher, had we included patients with normal coronaries, or with mild obstruction on MSCTA. We felt it unethical to catheterize such patients with clear-cut findings. None of these patients had a coronary event during the study period.

The rate of non-assessability at 2.1% is similar to what other investigators have found.

The presence of heavy calcifications, arrhythmias and the blooming artifacts caused by pacing wires remain as major limitations. Their presence requires resorting to conventional angiography.

Radiation remains a concern, but a limited one, as the ECG-controlled tube current modulation allows significant dose reductions (36,37). Radiation estimation varies widely depending on how it is calculated, but remains significantly lesser than during conventional coronary angiography (38).

CONCLUSION

Our findings in this cohort of patients indicate that the accuracy of MSCTA is high. With advances in technology, the sensitivity and specificity of MSCTA have significantly improved, providing accurate diagnostic studies.

Most recently, Mollet (34) and Kuettner (35), using a faster gantry rotation than the one used in their previous studies, reported similar accurate diagnostic yields to those presented here.

Because of these consistent results, MSCT coronary angiography should no longer be considered a research tool; it appears ready for appropriate use in the diagnosis of coronary artery disease, keeping in mind its limitations.

It is the authors' opinion that this data will, in all likelihood, increase the use of MSCT coronary angiography. Its results are now useful in clinical decision-making; and would likely limit some unnecessary and costly diagnostic invasive procedures. MSCT coronary angiography has fewer risks; therefore, patient safety is increased. The 99% negative predictive value, alone, ought to decrease, at least, the current number of normal invasive coronary angiograms.

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