

## Multi-slice Computed Tomography versus Invasive Coronary Angiography in Symptomatic Patients Post Percutaneous Coronary Interventions

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**Abstract: Objectives:** This study sought to evaluate the diagnostic accuracy of 64-slice multi-slice computed tomography (MSCT) for the assessment of in-stent stenosis using conventional coronary angiography as the reference standard. **Background:** Although promising results have been obtained using 64-slice computed tomography for the detection of coronary artery stenosis in native coronary arteries, as compared with previous-generation of MSCT scanners, but data on the evaluation of coronary stents are scarce. **Methods:** In 48 patients (42 [88%] male, ages 55± 11 years) with previous stent (≥ 2.5 mm diameter) implantation (n = 90), 64-slice MSCT angiography using either Definition dual-source 64-slice, Siemens, [n=14] or Aquilion 64-slice, Toshiba Medical Systems, [n=34]) was performed. At each center, coronary stents were evaluated by 2 experienced observers and evaluated for the presence of significant (≥50%) in-stent restenosis. Quantitative coronary angiography served as the standard of reference. **Results:** A total of 11 (12%) stented segments were excluded because of poor image quality. In the interpretable stents, 24 of the 79 (30.4%) evaluated stents were significantly stenosed, of which 18 were correctly detected by 64- Slice MSCT. Accordingly, sensitivity, specificity, and positive and negative predictive value to identify in-stent re-stenosis in interpretable stents were 75%, 95%, 86% and 90%, respectively. **Conclusions:** In selected patients, ISR can be evaluated with 64-slice MSCT with good diagnostic accuracy. In particular, a high negative predictive value of 90% which indicating that 64-slice MSCT may be most valuable as a noninvasive method of excluding in-stent restenosis.

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### 1. Introduction

Coronary stents implantation was established as a golden method for treating patients with coronary artery disease (1, 2). Though, conventional coronary angiography is still the domain of the assessment of 'in-stent' restenosis in symptomatic patients with previously stents implantation, but it has many limitations because of its invasiveness and high medical expense (3). Thus, a non-invasive alternative to assess the patency of the stented arterial segment would be highly desirable.

The multi-slice computed tomography (MSCT) is emerging technique that provides a non invasive tool to assess stents patency in patients undergoing stent implantation, however, the application of MSCT Faced a lot of difficulties when initially performed on four-slice multi-detector CT scanners, because of limited spatial and temporal resolution and long acquisition times that required intolerably long breath-holds.(4)

With the continuous evolution, Sixteen-slice scanners produced revolutionary improvement in MSCT technique, with increasing numbers of detector rows, Sixty four slice scanners were building on the improvement seen with sixteen slices CT

scanners, they now provide Coronary arterial images with markedly improved temporal and spatial resolution able to perform reliable cardiac imaging not only independent of the heart rate, but also without the compromises of beta blockers or multi-segment reconstruction, so. It constitutes a promising new concept for cardiac CT as compared to earlier scanner generations. (5, 6)

Although promising results have been obtained using multi-slice computed tomography for the detection of coronary artery stenosis in native coronary arteries (10) but evaluation of metallic stents was not been promising (11, 12), while substantial improvement in image quality and diagnostic accuracy observed with 16-slice as compared to 4-slice MSCT systems, however still relatively high numbers of stents with inadequate image quality were reported. In particular, stents with thicker struts or smaller diameters tended to suffer from degraded image quality. Since 64-slice MSCT systems became available, studies evaluating coronary stent in vitro suggest further improvement in image quality promising a new concept for cardiac CT as compared to earlier scanner generations (13).

The purpose of the present study was to assess the diagnostic performance of 64-slice multi-detector computed tomography for the evaluation of coronary stent stenosis and occlusion by using conventional coronary angiography as the reference standard.

## 2. Methods

**Study population.** The study group consisted of 48 patients who had previously undergone percutaneous coronary angioplasty with stent placement. Patients were referred for conventional coronary angiography; Referral of patients for invasive coronary angiography was based on the presence of symptoms of ischemia, in addition, 64- slice coronary angiography was done before invasive coronary angiography as a tool for non-invasive evaluation of the coronary stents, and there were no coronary events in between the two studies. Exclusion criteria were the following: 1) atrial fibrillation, 2) renal insufficiency (serum creatinine >1.6), 3) known allergy to iodine contrast media, all participating patients gave informed consent.

**Scan protocol and image reconstruction.** All patients were instructed to remain fasting for about four hours before doing the scan, Thirteen patients (27%) had a prescan heart rate >65 beats/min, and were given a single oral dose of 100 mg Atenolol 1 h before the examination in the absence of contraindications.

The full procedure was explained to the patient, breathing exercise was done to make sure the patient can hold his breath adequately, an intra-venous (IV) access was secured (an 18 G cannula), followed by IV saline injection to make sure of the patency of the line and to make sure there were no extravasations, the scans were performed using two 64-slice scanners (Definition dual-source 64-slice, Siemens, [n=14] and Aquilion 64-slice, Toshiba Medical Systems, [n=34]), a topogram of the chest was done on which the attempted scan volume was planned, the contrast media was then injected using the dual head injector, followed by a 50 ml of saline chaser. The injection rate was set at 5 ml/sec for both the contrast and the saline. The contrast used was a non ionic iso-osmolar iodine containing contrast (Scanlux, 370). The volume of the contrast was determined based on the calculated scan time, e.g. for a 12 seconds scan a 70 ml of contrast was administered ( $12\text{ s} \times 5\text{ ml/s} + 10\text{ ml}$ ).

Twelve seconds after starting the contrast injection, serial axial scans were taken at the base of the heart where the Hounsfield units (HU) were calculated at the ROI. The scans were taken every two second (bolus-tracking technique), when the attenuation reaches 120 HU in the region of interest the cardiac scan was started automatically, the

contrast enhanced cardiac scans were performed by spiral retrospectively ECG gated scans. The scans were acquired with a collimated slice thickness of 0.5 mm, 64 slices per gantry rotation (64X0.5). The scan pitch was 2. The gantry rotation speed was 400 msec. The scan was also acquired during a single deep breath hold. The tube voltage was set at 120 Kv and the tube current was set at a range of 400-480 mAs, where higher doses were given to obese patients.

Axial slices were reconstructed from the acquired MSCT data with the use of segmented or half reconstruction algorithms. Image data sets were reconstructed during the mid-to-end diastolic phase, during which coronary artery displacement is relatively small, with reconstruction window positions starting at 400 ms before the next R wave and/or at 75% of the R-to-R interval. If indicated, additional temporal window positions were explored, including the end-systolic phase to obtain images with least motion arte-facts.

The data sets were reconstructed at effective section thickness of 1.0mm (thin section), and reconstruction increment was 0.5 mm. Two sets of CT images were reconstructed with convolution during image data post processing: One set with a medium-smooth kernel and the other with a sharp kernel. Images generated with the sharp kernel are useful in general for visualizing fine details in high-contrast materials (metals used in stents), whereas images generated with the smooth kernel generally are used for delineating low-contrast objects such as blood vessels.

**MSCT image interpretation.** The data sets were then displayed and analyzed using several modes of presentation (axial images, MPR, oblique MPR, curved MPR, MIP as well as VRT formats), Image noise was measured by calculating the standard deviation of the mean CT attenuation in the ascending aorta. To improve the delineation of the stents, the images were displayed in a zoom mode with the window level at 200 HU and with window width ranging from 700 to 2000 HU. We found that the combination of a 200-HU window level with 1500-HU window width provided a better visualization of stents with respect to both in-stent luminal dimension and stent strut contrast enhancement. Thus, the data obtained in this setting were used for further analysis.

First, each individual stent was assigned an image quality score of: 1 (un-interpretable, no diagnosis possible), 2 (moderate image quality, minor or moderate artifacts present but diagnosis possible) or 3 (good image quality, no artifacts) as previously described. (14)

In-stent luminal diameter and coronary artery lumen 5.00 mm proximal and distal to the stent were

measured by using electronic calipers. At each site, measurements were made on transverse images of three adjacent sections; the presence of more than 50% reduction of lumen diameter is a significant restenosis. (15)

In cases of extensive calcification attached to the stent or if the axis of the stent was neither perpendicular nor parallel to the imaging plane, the measurements were performed on the MPR images that showed a longitudinal view of the stent. scans were analyzed by two observers experienced in cardiac MDCT.

**Invasive coronary angiography.** Conventional coronary angiography was performed with standard Judkins technique with access via the femoral and evaluated by a reviewer blinded to the MSCT results with the use of quantitative coronary angiography systems, assessment of the stented segment as well as its proximal and distal (5.00 mm) Lumina and percentage diameter reduction was determined. An in-stent lumen diameter narrowing  $\geq 50\%$  in diameter (up to in-stent occlusion) was defined as a significant restenosis, measurements on conventional angiograms served as the reference standard for in-stent luminal measurements on CT images. (16)

#### Statistical analysis:

Data entry and analysis were accomplished with the aid of computer's SPSS program version 17. The results were represented in tabular forms and charts then interpreted. Mean, standard deviation, range, frequency and percentage were used as descriptive statistics. Chi square test and paired t-test were used as tests of significance, the significant was adjusted when  $P < 0.05$ , Sensitivity, specificity, positive and negative predictive values for the detection of in-stent restenosis were calculated

### 3. Results

**Patient characteristics.** In total, 48 patients 42, (88%) males, there mean ages  $55 \pm 8$ , Baseline characteristics of the study population are provided in Table 1. The average time interval between stent implantation and 64-slice MSCT coronary angiography was  $20 \pm 16$  months. 64-slice MSCT and conventional angiography were performed within 1 month of each other; MSCT was always performed first. The sites of stents implantation were: right coronary artery in 18 stents (22.8%), left main coronary artery in 2 stents (2.5%), left anterior descending coronary artery in 40 stents (50.6%), left Circumflex coronary artery in 15 stents (19 %) and saphenous venous grafts in 4 stents (5.1%).

The site of stent implantation was: right coronary artery in 55 (28.6%), left main coronary artery in 11 (5.7%), left anterior descending coronary artery in 113 (58.9%), and left circumflex coronary

artery in 13 (6.8%). The average stent diameter was  $4.2 \pm 1$  mm (range from 2.5 to 4.5 mm), whereas the mean stent length  $20 \pm 10$  (ranged from 12 to 33 mm).

Six different stents types were evaluated, 72 stents (93%) were drug-eluting stents (Taxus, Boston Scientific, [n = 51]). (Cypher, Cordis Corp., Johnson & Johnson, [n = 18]) (Xience, Abbott Corporation, [n = 3]). (Endeavour, Medtronic, Minneapolis, Minn [n = 2]). In addition to 5 stents (7%) were non drug-eluting (Zeta, Abbott Corporation, [n = 2]) (Express, Cordis Corporation, [n = 3]).

**Coronary stent analysis.** In a total of 90 coronary stents, 79 stents (88%) were available for evaluation in the study, whereas 11 stents (12%) were considered un-interpretable because of residual motion and high-density artifacts, they were excluded, stents number per patient were ranged from 1 to 5 stents.

Significant ISR (non occlusive ISR and total stent occlusions) were detected in 24 stents (30.4%) as determined by conventional angiography, 18 stents of them (22.8%) were correctly identified by MSCT (figure 31, 32), while the remaining 6 stents were misdiagnosed by MSCT. Stent Patency was detected in 55 stents (69.6%) as determined by conventional angiography, 52 stents of them (94%) were correctly identified by MSCT (figure 33, 34), while the remaining 3 stents (6%) were misdiagnosed by MSCT. Accordingly, the overall sensitivity, specificity and positive and negative predictive value of MSCT to detect significant in-stent restenosis were 75%, 95%, 86% and 90% respectively, where as overall accuracy is 89%.

In sub-analysis, overall false diagnosis by MSCT were detected in 9 stents, there were an influence of stent size on false diagnosis of MSCT where 3 stent with false positive have size  $\leq 3$ mm and all 6 stent with false negative have size  $> 3$ mm ( $P < 0.05$ )

The accuracy of MSCT was increased in assessment of proximally located stent versus non proximally located stents, sensitivity and specificity 82% and 97% versus 69 and 92 respectively, with  $P > 0.05$ .

All stents with false positive (3 stents) had thicker struts while all stent with false negative had thin struts, where  $P < 0.05$ .

Per-vessel analysis: revealed stent location at LCX is associated with poor assessment and worst accuracy than other arteries, in total 40 stents at LAD, The incidence of significant in-stent restenosis was 30% (12 of 40), as determined by conventional angiography, 9 stents of them were correctly identified by MSCT, while the incidence of stent patency was 70% (28 of 40), as determined by conventional angiography, 25 stents of them were

correctly identified by MSCT. On the other hand, in total 15 stents at LCX, The incidence of significant in-stent restenosis was 40% (6 of 15), as determined by conventional angiography, 4 stents of them were correctly identified by MSCT, while the incidence of stent patency was 60% (9 of 15), as determined by conventional angiography, 7 stents of them were correctly identified by MSCT. Accordingly, the overall sensitivity and specificity for LAD, RCA and LCX were 75%, 89%, 100%, 86%, 67%, 78%, respectively.

CABG<sub>3</sub> coronary artery bypass grafts; LAD<sub>3</sub> left anterior descending coronary artery; LCX<sub>3</sub> left circumflex coronary artery; LM<sub>3</sub> left main coronary artery; RCA; right coronary artery. SVG; Savenous vein graft.

Table No.1	Demographic and Angiographic Characteristics of Patients (n = 48) N (%)
Male	42 (88%)
Type II DM	28 (58%)
HTN	32 (67%)
Smoking	26 (54%)
Dyslipidemia	35 (73%)
CABG	10 (21%)
Stent location	
RCA	18 (22.8%)
LM	2 (2.5%)
LAD	40 (50.6%)
LCX	15 (19%)
SVG	4 (5.1%)

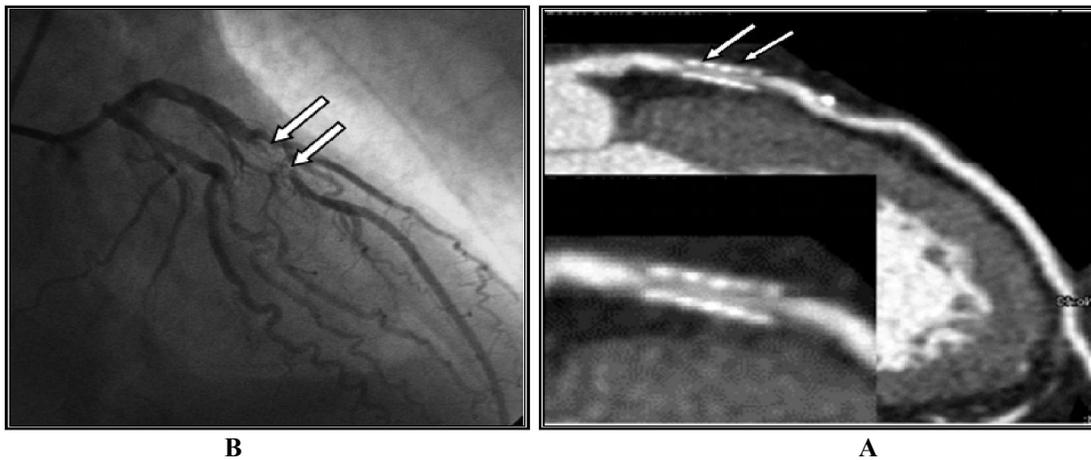


Figure 1: (A). MSCT image with curved MPR view of LAD showing proximal stent with significant ISR. (B) Conventional angiographic view that confirmed significant ISR in proximal LAD (Patient no, 11, true positive result)

Table 2	Stents Locations			Per-Vessel Analysis		
	Total	Proximal	Non proximal	LAD	LCX	RCA
Sensitivity	75%	82%	69%	75%	67%	100%
Specificity	95%	97%	92%	89%	78%	86%
PPV	86%	90%	82%	75%	67%	67%
NPV	90%	93%	86%	89%	78%	100%

PPV; Positive predictive value, NPV; Negative predictive value, LAD; left anterior descending coronary artery; LCX; left circumflex coronary artery; RCA; right coronary artery.

**4. Discussion:**

In the present study sensitivity, specificity and PPV and NPV of respectively 75%, 95%, 86, 90 were observed for non invasive detection of in-stent restenosis, denoting that 64-slice MSCT still challenging for the detection of stent occlusion and in-stent restenosis. Our current observations compared favourably with the previous study of Rist *et al.* (17) in evaluating the accuracy of 64-slice CT to assess significant ISR in 25 patients with 46 stents.

He observed 75% sensitivity and 92% specificity in detecting in stent restenosis, these results were further underlined by Carbone *et al.* (18)

However, higher sensitivity and accuracy were reported in the study of Chung *et al.* (19) on 60 patients with 91 stents, in stents that could be assessed [n=58], sensitivity, specificity, PPV and NPV were 90.0%, 73.5%, 58.1%, and 94.7%, respectively, for detection of significant ISR. Further excellent diagnostic accuracy of 64-slice CT were

reported by Martuscelli *et al.* (20) also found an excellent diagnostic accuracy of 64-slice CT to detected significant ISR in his study on 213 patients with 321 stents, however, ISR were detected only in

27 stent, thus, sensitivity, specificity, and PPV and NPV of 64- slice MSCT were 96%, 99%, 93%, and 99%.



**Figure 2: (A) MSCT image with curved MPR view of LCX showing patent stent implanted at mid segments (arrow).**

**(B) Conventional angiographic view confirmed patency of mid LCX stents (arrow). (Patient no, 38, true negative result)**

By the analysis of 14 studies comparing 64-slice CT angiography with conventional coronary angiography for the detection of coronary in-stent restenosis, A meta-analysis of Sun Z and Almutairi (21) were estimates the sensitivity and specificity of 90% and 91% respectively based on assessable segments.

During MSCT imaging, visualization of stents is particularly challenging because of the metallic struts resulting in blooming artifacts. Accordingly, the stent wall appears enlarged on the MSCT images, which in turn affects the capability to visualize the in-stent lumen. The extent of this artefact depends on the material and design of the stent, with more severe artifacts in stents with high metal content. Although this effect is of minor or no importance in large vessels, such as the aorta and its abdominal branches, it can considerably impair the visualization of the lumen in smaller vessels such as the coronary arteries as reported in the study of Maintz *et al.* (22).

Not surprisingly, therefore, visualization of stent lumen could not be achieved in preliminary investigations using 4-slice MSCT scanners in the study of kruger *et al.* (23).

The prevalence of non-evaluable stents (12%, 11 from 90) was acceptable in contrast to rate of ( 2.6 to 23.5) reported by meta-analysis Andreini *et al.* ( 24) on 24 study.

In The current study, accuracy of MSCT is affected by stent size and struts thickness; thinner and wider stents were associated by high accuracy, as reported in the study of Cademartiri *et al.* (25)

Post processing was an important part of our study. We used an edge-enhancing high spatial resolution kernel for reconstruction. Because this kernel yields fewer blooming artifacts, artificial lumen narrowing and intraluminal attenuation changes caused by such artefacts would be minimized. Therefore, edge-enhancing kernels can allow better visualization of the stents, even though image noise will increase as compared with image noise produced by standard kernels. Seifarth *et al.* (26), compared the effect of different reconstruction kernels and a noise-reducing post processing filter on the delineation of coronary artery stents and noticed that the visible lumen diameter was significantly greater in edge-enhancing high spatial resolution kernel post processed images.

remarkable increase in sensitivity and specificity of MSCT in detecting significant ISR in proximal coronary artery compared to non proximal segments (82%, 97%, versus 69%, 92% respectively), agreed with data reported by Chabbert *et al.* (27), on 121 patient with 131 stents located in proximal coronary segments, when he reported excellent results with sensitivity of 93%, however it's

not statistically significant in the current study, which may be explained by limited number of stent.

In the current study, stents implanted in LCX have the worst accuracy in comparison to LAD and RCA, as reported by Chung *et al.* (28) in his study of 91 stent to determined factors affecting the ability of 64-multislice MSCT to detect, assess, and concluded that evaluation of stents by 64-MSCT is not recommended in stents with diameters of  $\leq 2.75$  mm or stents located at the left circumflex coronary artery.

High negative predictive value (90%) was observed in this study, underlining the potential of MSCT as a non invasive technique to rule out the presence of in-stent restenosis, This concept is consistent with the findings addressed by Kumbhani *et al.* (29). who performed a meta-analysis including 14 studies with 895 patients and ensures the value of the MSCT as a rule out modality.

#### Study limitations.

Several limitations should be addressed. **1)** - The overall rate of stents with a significant ISR was relatively low, (24 of 79, 30.4%). This low rate of restenosis was below our assumptions for the statistical power of calculation. **2)** - The presence of non evaluable stents which affected the diagnostic value of MSCT in studies included it in analysis, making the MSCT a suitable non invasive procedure in selected population only. **3)** - As reported previously with MSCT coronary angiography, only patients with regular and low heart rate were included in the study. Accordingly, the results of the present study may not apply to the general population, as patients with atrial fibrillation were excluded. **4)** - several disadvantages inherent to the technique itself, including the high radiation exposure (15 to 20 mSv) and the use of iodinated contrast, which remain a matter of concern for routine use of this technique. (15). **5)** - an important limitation of MSCT remains the fact that only anatomical information is obtained, whereas the presence or absence of ischemia cannot be established from the MSCT images. Accordingly, in patients with significant restenosis, functional testing remains mandatory to determine further management.(15)

#### Conclusions

The detection of ISR by MSCT is possible with an accuracy that could justify its clinical application, the relatively high rate of non-evaluable stents does not allow its use in all patients, in particular, 64-slice CT is useful for non-invasive exclusion of ISR, and therefore, we can avoid invasive coronary angiography in a considerable number of patients.

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