Assessment of coronary artery remodelling by dual-source CT: a head-to-head comparison with intravascular ultrasound

Sören Gauss, Stephan Achenbach, Tobias Pflederer, Annika Schuhbäck, Werner G Daniel, Mohamed Marwan

ABSTRACT

Background While it is widely assumed that coronary CT angiography permits detection and quantification of ‘positive remodelling’ of coronary atherosclerotic lesions, there is a paucity of data comparing CT with established reference methods.

Objective To assess the accuracy of dual-source CT for detecting positive versus absent or negative coronary artery remodelling of coronary atherosclerotic lesions as compared with intravascular ultrasound (IVUS).

Methods The datasets were evaluated of 38 patients referred for invasive coronary angiography and in whom an IVUS study of one coronary vessel was performed. Coronary CT angiography was performed within 24 h before invasive coronary angiography. Using dual-source CT (Siemens Healthcare, Forchheim, Germany), a contrast-enhanced volume dataset was acquired (120 kV, 400 mA/rot, collimation 2×64×0.6 mm, 60–80 ml contrast agent, intravenous). IVUS was performed using a 40 MHz IVUS catheter (Atlantis, Boston Scientific Corporation, Natick, Massachusetts, USA) and motorised pullback at 0.5 mm/s. 48 corresponding non-calcified and partially calcified plaques within the coronary artery system were identified in both CT and IVUS using bifurcation points as fiducial markers. In CT datasets, multiplanar reconstructions orthogonal to the centre line of the coronary artery were rendered and cross-sectional vessel area measurements using CT compared with IVUS were performed.

Results CT classified 41 plaques as positively remodelled (RI≥1.05) and seven as having either absent or negative remodelling (RI<1.05). In IVUS, 29 plaques demonstrated positive remodelling, while 19 did not. Mean cross-sectional vessel area measurements by CT at the lesion and at the reference segment were 19±5 mm\(^2\) and 17±5 mm\(^2\), respectively. In IVUS, mean difference 1±2 mm\(^2\) and per 0.2±1 mm\(^2\), p<0.0001 and 0.8, respectively. The mean RI in CT was significantly larger than in IVUS (1.2±02 vs 1.1±0.2, p<0.0001). Correlation between CT and IVUS was higher for vessel area measurements (r>0.9, p<0.0001) than for remodelling indices (r=0.7, p<0.0001) with Bland–Altman analysis showing a systematic overestimation of vessel areas and RI in CT. Interobserver agreement was moderate for CT and IVUS measurements. Receiver operating characteristic curve analysis showed that a RI of 1.1 in CT identified positively remodelled plaques in IVUS with a sensitivity of 83% and a specificity of 78% (area under the curve=0.8, 95% CI 0.7 to 1.0). Using the standard cut-off point of 1.05 to identify positively remodelled plaques in CT resulted in a sensitivity of 100%, and a specificity of 45%.

Conclusion Coronary CT angiography allows analysis of coronary artery remodelling. The degree of positive remodelling is typically overestimated by CT. A threshold of 1.1 for the RI may be optimal to classify plaques as ‘positively remodelled’ in coronary CT angiography.

INTRODUCTION

The response of coronary arteries to atherosclerosis and plaque growth—whether with compensatory enlargement or shrinkage—is referred to as ‘coronary artery remodelling’. The assessment of compensatory enlargement or positive remodelling of coronary arteries has attracted a lot of attention owing to the propensity for positively remodelled coronary artery plaques to cause future cardiac events based on histopathological clinical studies. Intravascular ultrasound (IVUS) has been the preferred method for the assessment of coronary artery remodelling in vivo. Multi-detector CT is a non-invasive modality which can visualise the coronary artery lumen as well as coronary atherosclerotic plaque and has been extensively investigated. Furthermore, previous data on coronary vessel area measurements using CT compared with IVUS were promising.

It is widely assumed that coronary CT angiography permits detection and quantification of positive remodelling of coronary atherosclerotic lesions, yet there is a paucity of data to validate CT against established reference methods. Moreover, previous studies assessing coronary artery remodelling in CT were performed using older-generation scanners with limited temporal and spatial resolution. We assessed the accuracy of dual-source CT (DSCT) for detecting positive versus absent or negative coronary artery remodelling in patients with suspected coronary artery disease compared with IVUS.

PATIENTS AND METHODS

From a registry of 68 patients, who underwent invasive coronary angiography with IVUS of at least one coronary vessel, and in whom coronary
CT angiography had been performed within 24 h before coronary angiography, datasets of 38 patients with either excellent or good image quality were included in the analysis. Thirty patients were excluded owing to suboptimal CT image quality (n=7), extensively calcified coronaries (n=9), absence of relevant plaque burden (n=9) or owing to a poor IVUS image quality (n=5). All patients had been referred for invasive coronary angiography and IVUS of at least one coronary vessel had been performed for clinical reasons. No patients with acute coronary syndromes were included in this study. All patients gave an informed consent and the study protocol was approved by the local ethics committee.

**DSCT examination**

All patients were in sinus rhythm at the time of CT data acquisition. Patients with a mean heart rate > 60 beats/min received 100 mg of atenolol orally 45–60 min before DSCT. If the mean heart rate remained > 60 beats/min at the time of scanning, up to four doses of metoprolol 5 mg were given intravenously. All patients received isosorbide dinitrate 0.8 mg sublingually before DSCT.

Coronary CT angiography was performed in all patients using DSCT (Definition, Siemens Medical Solutions, Forchheim, Germany) within 24 h before invasive coronary angiography. A contrast-enhanced volume dataset was acquired with retrospective ECG gating using tube current modulation. Acquisition parameters for CT angiography were 0.6 mm collimation, 530 ms rotation time, 120 kV tube voltage and a tube current of 400 mA. Scan direction was craniocaudal, and the scan volume ranged from the mid-pulmonary artery to below the diaphragmatic face of the heart. After placing an antecubital 18-G intravenous access, the contrast agent transit time of 6 ml/s using a dual-head power injector (CT Stellant, Medrad Inc, Indianola, Pennsylvania, USA). Contrast transit time was defined as the time between the start of contrast injection and maximum enhancement in the ascending aorta at the level of the coronary ostia. For angiographic CT data acquisition, a delay of 2 s longer than the contrast transit time was used to ensure adequate contrast enhancement of the coronary arteries. The volume of contrast agent injected for the scan depended on the estimated scan duration. Contrast was injected at a flow rate of 6 ml/s for the same duration as data acquisition, but for at least 10 s. Contrast injection was followed by a 50 ml saline chaser bolus (6 ml/s).

**CT image reconstruction**

Using a half-scan reconstruction algorithm (temporal resolution 83 ms), overlapping axial cross-sectional images with 0.75 mm slice thickness and 0.4 mm increment were reconstructed using a medium sharp convolution kernel (B26f). Using an internal algorithm, the scanner automatically suggested a best diastolic phase. If artefacts were still to be seen, further diastolic phases in 2% intervals of the cardiac cycle were reconstructed and then the diastolic phase reconstruction with minimal artefacts was evaluated.

**IVUS**

After intracoronary injection of 0.2 mg nitroglycerin, IVUS was performed using a 40 MHz IVUS catheter (Atlantis, Boston Scientific Corporation, Natick, Massachusetts, USA) and motorised pullback at 0.5 mm/s. Data were stored on DVD for further offline analysis.

**CT and IVUS image analysis**

Forty-eight exactly corresponding non-calcified or partially calcified plaques within the coronary artery system were identified by one observer in both DSCT and IVUS datasets using bifurcation points as fiducial markers. For each plaque, the site of maximum narrowing—as visually estimated—as well as a reference point proximal to the lesion were then identified in CT and IVUS and images were stored. For assessment of inter-observer variability, 15 consecutive lesions were then analysed by two observers in both modalities, otherwise for the remaining 33 lesions, analysis was performed by one independent observer in each modality. CT datasets were analysed on a dedicated workstation (Multimodality Workplace; Siemens Medical Solutions, Forchheim, Germany). Multiplanar reconstructions orthogonal to the centre line of the coronary artery were rendered and using a visually adjusted image display setting, cross-sectional vessel area was measured at the site of maximal narrowing as estimated visually (figures 1 and 2).

Similarly, cross-sectional vessel area was determined at a reference segment without detectable plaque proximal to the lesion for each of the 48 plaques. In the absence of a segment free of plaque, the least diseased segment between the lesion and the coronary ostium or major bifurcation was used. IVUS datasets were viewed using a commercially available software package (iReview, Boston Scientific Corp, version 1.0.2544.18305). Cross-sectional vessel area was measured by tracing the external elastic membrane at the site of maximal luminal narrowing and in the proximal reference segment (figure 3). Similarly, in the absence of a segment free of plaque, the least diseased segment between the lesion and the coronary ostium or major bifurcation was used. The remodelling index (RI) was calculated in CT and IVUS datasets by dividing the vessel area at the site of maximal narrowing by the area of the reference segment. A previously suggested RI ≥ 1.05 was used to define plaques as positively remodelled.

**Figure 1** (A) Multiplanar reconstruction of the left anterior descending coronary artery (LAD) showing a non-calcified plaque in the proximal LAD just before the origin of a diagonal branch. (B) Intravascular ultrasound image of the same patient showing the same non-calcified plaque in the proximal LAD.
Statistical methods
Statistical analysis was done using SPSS for Windows release 18.0 (SPSS Inc). All data are expressed as mean±SD for continuous variables. Correlations were performed using Spearman’s correlation coefficient. Agreement was assessed using Bland–Altman analysis. Wilcoxon signed-rank test was used to compare non-parametric data. Receiver operating characteristic (ROC) curve analysis was performed to obtain the best cut-off point needed to define plaques as positively remodelled using IVUS as the ‘gold standard’.

RESULTS
Datasets of 38 patients (26 men, 59±10 years) were evaluated. The mean heart rate during CT examination was 58±7 bpm. Patient characteristics are shown in table 1. Forty-eight exactly corresponding non-calcified (n=37) and partially calcified (n=11) plaques in both IVUS and CT were assessed. The distribution of the studied plaques was as follows: 52 plaques in the left anterior descending coronary artery, 15 in the right coronary artery, 2 in the left main coronary artery and one in the left circumflex coronary artery. CT classified 41 plaques as positively remodelled (RI≥1.05) and seven as having either absent or negative remodelling (RI<1.05). In IVUS, 29 plaques were positively remodelled versus 19 with absent or negative remodelling. The mean cross-sectional vessel areas measured by CT at the site of the lesion with maximal narrowing and at the reference segment were 19±5 mm² and 17±5 mm², respectively versus 18±5 mm² and 17±5 mm² for IVUS (mean difference 1±2 mm² and −0.2±1 mm², p<0.0001 and 0.8, respectively). The mean RI in CT was 1.18±0.17 (range 0.85–1.69), whereas in IVUS the mean RI was 1.09±0.17 (range 0.78–1.62) (mean difference 0.1±0.1 mm², p<0.0001). The correlation between CT and IVUS was closer for vessel area measurements (r=0.9, p<0.0001) than for remodelling indices (r=0.7, p<0.0001) (figure 4). A Bland–Altman plot showed a better agreement between CT and IVUS for vessel area measurements at the

Figure 2 (A, B) Multiplanar reconstruction orthogonal to the centre line of the coronary artery is rendered for the same plaque shown in figure 1 at the site of maximal narrowing (A) and at a reference segment proximal to the lesion (B). (C, D) Manual tracing of the cross-sectional vessel area at the site of maximal narrowing (C) as well as at the reference segment (D).

Figure 3 (A, B). Intravascular ultrasound images corresponding to the plaque shown in figure 2 with manual tracing of the cross-sectional vessel area at the site of maximal narrowing (A) and at the reference segment (B).
reference segment than area measurements at the lesion site (mean difference –0.2 mm² vs 1.2 mm², 95% limits of agreement 2.8 to –3.1 mm² vs 4.6 to –2.3 mm², respectively) (figure 5).

There was a systematic overestimation of the vessel area at the lesion site in CT in comparison with IVUS, whereas for area measurements at the reference segment, a minimal trend towards underestimation was observed. Similarly, a Bland–Altman plot showed a moderate to good agreement between CT and IVUS for remodelling indices, with a systematic trend towards overestimation of the RI in CT versus IVUS (mean difference 0.1, 95% limits of agreement 0.3 to –0.2) (figure 6).

In order to assess interobserver agreement, 15 consecutive lesions were analysed by both observers in both modalities. There was no significant difference between both observers for cross-sectional vessel area measurements in CT and IVUS (at lesion or reference site, p > 0.1 for all). Bland–Altman plots showed moderate agreement between both observers for CT and IVUS measurements (figure 7). The mean difference for lesion area measurements was 0.3 mm² in CT vs. 0.4 mm² in IVUS (95% limits of agreement 3 to –2.5 mm² vs 2 to –2 mm², respectively). For reference area measurements, the mean difference between both observers was 0.4 mm² in CT vs 0.2 mm² in IVUS (95% limits of agreement 3 to –2 vs 2 to –2, respectively).

ROC curve analysis showed that a RI of 1.1 identified positively remodelled plaques in CT angiography with a sensitivity

### Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Age, years, mean±SD (range)</td>
<td>59±10 (34–87)</td>
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<tr>
<td>Heart rate, bpm, mean±SD (range)</td>
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</tr>
<tr>
<td>Male gender, n (%)</td>
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</tr>
<tr>
<td>BMI, mean±SD</td>
<td>26±7</td>
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<tr>
<td>History, n (%)</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>30 (79)</td>
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<tr>
<td>Diabetes</td>
<td>5 (13)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>29 (76)</td>
</tr>
<tr>
<td>Smoking</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>13 (34)</td>
</tr>
<tr>
<td>Effective radiation dose, mSv, mean±SD</td>
<td>9±3</td>
</tr>
</tbody>
</table>

BMI, body mass index; CAD, coronary artery disease.

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**Figure 4** Correlation plots for (A) CT vessel area measurements at the site of the lesion compared with intravascular ultrasound (IVUS); (B) CT vessel area measurements at reference site compared with IVUS; (C) remodelling indices in CT compared with IVUS. SEE, standard error of the estimate.
of 83% and a specificity of 78% (area under the curve = 0.8, 95% CI 0.7 to 1.0) (figure 8). When the standard cut-off point of 1.05 for the RI was used to identify positively remodelled plaques in CT, this resulted in a sensitivity of 100%, and a specificity of 45% as compared with IVUS.

**DISCUSSION**

The assessment of coronary artery remodelling using non-invasive imaging modalities is of potential clinical interest owing to the propensity of positively remodelled coronary atherosclerotic plaques to rupture and cause future cardiac events. This information can affect risk stratification and subsequent treatment decisions. Previous CT studies looking at the morphology of culprit lesions in patients presenting with acute coronary syndromes have shown that positive remodelling is characteristic of such lesions. In a prospective study, Motoyama et al. recently showed that patients with atherosclerotic plaques which displayed both positive remodelling and low attenuation areas in CT angiography are at high risk of developing acute coronary syndromes. All the more surprising is the fact that there is a paucity of data concerning

![Figure 5](image_url)  
**Figure 5** (A, B) Bland–Altman plots for the agreement between CT and intravascular ultrasound (IVUS) for vessel area measurement at the site of the lesion (A) and at the reference segment (B) (mean difference 1.2 ± 2 mm² and −0.2 ± 1 mm², respectively, 95% limits of agreement 4.6 to −2.3 mm² and 2.8 to −3.1 mm², respectively).

![Figure 6](image_url)  
**Figure 6** Bland–Altman plot for the agreement between CT and intravascular ultrasound (IVUS) for remodelling indices (mean difference 0.1 ± 0.1, 95% limits of agreement 0.3 to −0.2).

![Figure 7](image_url)  
**Figure 7** (A, B) Bland–Altman plots for agreement between both readers for CT lesion area measurements (A) and reference area measurement (B) (mean difference 0.3 ± 1 mm² and 0.4 ± 1 mm², respectively, 95% limits of agreement 3 to −2.5 mm² and 3 to −2 mm², respectively). (C, D) Bland–Altman plots for agreement between both readers for intravascular ultrasound (IVUS) lesion area measurements (C) and reference area measurement (D) (mean difference 0.4 ± 1 mm² and 0.2 ± 1 mm², respectively, 95% limits of agreement 2 to −2 mm² for both measurements).
Figure 8 Receiver operating characteristic curve for identification of positively remodelled plaques in CT using different remodeling indices (area under the curve \( AUC \) 0.8, 95% CI 0.7 to 1).

the accuracy of identifying the extent of coronary remodelling in CT angiography.\(^5\)

We analysed 48 non-calcified and partially calcified coronary atherosclerotic plaques in 38 patients using contrast-enhanced DSCT and IVUS. The reproducibility of vessel area measurements using contrast-enhanced CT angiography compared with IVUS has been recently assessed by our research group.\(^4\) In CT, 41 plaques were classified as positively remodelled (RI≥1.05). Of these 41 plaques, IVUS identified only 29 plaques as positively remodelled (RI≥1.05). The mean vessel area at the site of maximal narrowing was significantly higher in CT than with IVUS with a systematic trend towards overestimation in CT. The mean vessel area at the reference segment was not significantly different in both modalities with a higher mean RI in CT versus IVUS (1.2±0.2 vs 1.1±0.2, respectively, p<0.0001). These results are partly in line with an earlier study by Achenbach et al\(^5\) where coronary artery remodelling was assessed using 16-slice multidetector CT, and validated by IVUS in a subset of 13 patients. In their study, the mean vessel area was similarly higher in CT than in IVUS (20±7 mm\(^2\) vs 18±8 mm\(^2\)). The correlation between CT and IVUS for the RI was similar in our study and theirs (r=0.7 vs 0.8, respectively). Similarly, Moselewski et al\(^5\) compared cross-sectional vessel area in 16-slice CT and IVUS. They observed a systematic overestimation of vessel area in CT with a mean difference of 0.9±4.0 mm\(^2\) as compared with IVUS. It is worth mentioning that the agreement between CT and IVUS measurements in our study is slightly better than the agreement reported in the Moselewski study. This can be probably explained by the different technology used in both studies. Temporal and spatial resolutions were higher in our study, and so was soft tissue contrast, with resulting effects on image quality.

Typically, a cut-off value of 1.05 is used for the RI to define plaques as ‘positively remodelled’.\(^5\) However, using ROC-curve analysis, we found that a cut-off RI≥1.1 allowed better distinction of positively remodelled plaques in CT (area under the curve=0.8, 95% CI 0.7 to 1). Specificity was 78% compared with a specificity of 45% using the standard cut-off RI of 1.05, yet sensitivity declined from 100% to 85%.

There are several limitations to be acknowledged. Only selected datasets of excellent or good image quality were included in this analysis, apart from the relative small sample size. Moreover, for determining the RI, we used the vessel diameter at the site of maximal narrowing and not at the site of maximal vessel area. There is no consensus as to which approach predicts better results. Furthermore, all vessel areas, whether at the lesion or reference site, were determined by manual tracing. Finally, it should be mentioned that the ultimate goal of atherosclerotic lesion analysis by CT is the identification of ‘vulnerable plaques’, and the quantification of positive remodelling is only a surrogate marker. The optimal validation of any approach would therefore be the comparison with outcome data. However, large patients groups and long follow-up would be required.

In summary, our study demonstrates that vessel area measurements in the presence of plaque tend to be overestimated in CT as compared with IVUS, and hence a RI with a slightly higher cut-off value of 1.1 should potentially be adopted to accurately classify plaques as positively remodelled in CT angiography.

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**Competing interests** SA received research support from Siemens and Bayer Schering Pharma.

**Patient consent** Obtained.

**Ethics approval** This study was conducted with the approval of the local ethics committee.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**REFERENCES**


22. Ropers D, Rix E, Anders K, et al. Usefulness of multidetector row spiral computed tomography with 64 x 0.6-mm collimation and 330-ms rotation for the noninvasive detection of significant coronary artery stenoses. J Am Cardiol 2006;97:343—8.
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