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SHORT COMMUNICATION

Diagnostic accuracy of in-stent restenosis using model-based iterative reconstruction at coronary CT angiography: initial experience

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Objective: The purpose of our study was to compare the diagnostic performance of coronary CT angiography (CTA) subjected to model-based iterative reconstruction (IR) or hybrid IR to rule out coronary in-stent restenosis.

Methods: We enrolled 16 patients who harboured 22 coronary stents. They underwent coronary CTA on a 320-slice CT scanner. The images were reconstructed with hybrid IR (AIDR 3D) and model-based IR (FIRST) algorithms. We calculated the stent lumen attenuation increase ratio and measured the visible stent lumen diameter. Two blinded observers visually graded the likelihood of in-stent restenosis (lesions $\geq 50\%$) on hybrid IR and FIRST images.

Results: The stent lumen attenuation increase ratio on FIRST- was lower than on AIDR 3D images (0.20 vs 0.32). The ratio of the visible- compared to the true stent

lumen diameter was higher on FIRST- than AIDR 3D images (52.5 vs 47.5%). Invasive coronary angiography identified five stents (22.7%) with significant in-stent restenosis. The use of FIRST improved the sensitivity (60 vs 100%), positive (75.0 vs 83.3%) and negative predictive value (88.9 vs 100%) and the accuracy (86.4 vs 95.5%) for the detection of in-stent restenosis. Specificity was 94.1% for both reconstruction methods.

Conclusion: The model-based IR algorithm may improve diagnostic performance for the detection of in-stent restenosis.

Advances in knowledge: Compared to hybrid IR, the new model-based IR algorithm reduced blooming artefacts and improved the image quality. It can be expected to improve diagnostic performance for the detection of in-stent restenosis on coronary CTA images.

INTRODUCTION

Coronary CT angiography (CTA) is a suitable non-invasive imaging modality for patient follow-up after coronary artery stent implantation.¹ However, blooming artefacts from stent struts that arise from partial volume averaging and beam hardening limit the evaluation of the stent lumen;^{2–4} this complicates the identification of in-stent patency and in-stent restenosis.

Model-based iterative reconstruction (IR) is a new reconstruction algorithm. It repeats both back- and forward projections in the image-reconstruction process.^{5–7} It involves sophisticated modelling and has been shown to reduce blooming artefacts and to improve the image quality of coronary artery stent scans compared to hybrid IR.⁸

As, to the best of our knowledge, the diagnostic accuracy for the detection of in-stent restenosis has not been evaluated on model-based IR scans, we compared coronary CTA images acquired with hybrid- and model-based IR in patients with implanted coronary stents.

METHODS AND MATERIALS

Study population

Institutional review board approval was obtained for this retrospective study; patient informed consent was waived. We enrolled 16 consecutive patients (14 males, 2 females; median age 65 years, range 51–78 years) with 22 implanted coronary stents. They were referred for coronary CTA between July 2015 and August 2016 because of recurrent chest pain. Our exclusion criteria were renal insufficiency (estimated glomerular filtration rate <30 ml min⁻¹ per

1.73 m²), allergy to contrast agents, history of bypass grafting and potential pregnancy.

Coronary CTA and stress-rest myocardial perfusion scintigraphy were performed on all patients. Those who were suspected of myocardial ischaemia with stress-rest myocardial perfusion scintigraphy underwent invasive coronary angiography. The criterion for restenosis was significant in-stent restenosis with narrowing of the luminal diameter by 50% or more; for non-restenosis it was less than 50% stenosis on invasive coronary angiographs or negative findings on stress-rest myocardial perfusion scintigraphy. Consequently, 3 of 16 patients were classified as a non-restenosis group based on myocardial scintigraphy, and 13 of 16 patients underwent invasive coronary angiography. Based on the results of myocardial scintigraphy and invasive coronary angiography, 5 of the 22 stents (22.7%) revealed significant in-stent restenosis. Coronary CTA and invasive coronary angiography or stress-rest myocardial scintigraphy studies were performed within a 2-month period.

CT scanning

All CT scans were acquired on a 320-detector CT scanner (Aquilion ONE Vision, Toshiba Medical Systems Corp., Tokyo, Japan). Patients with a resting heart rate exceeding 65 beats per minute (bpm) received 20–40 mg of metoprolol (Seloken; AstraZeneca, Zoetermeer, Netherlands) perorally 60 min before the CT studies. All patients were given one dose of nitroglycerin (Myocor; Astellas Pharma, Tokyo, Japan) in the form of a sublingual spray (0.3 mg) approximately 5 min before the examination to dilate the coronary arteries. Using a dual shot injector (Nemoto Kyorindo, Tokyo, Japan), we delivered 210 mgI kg⁻¹ of non-ionic contrast material (Iomeprol, Iomeron 350 mgI ml⁻¹; Eisai, Tokyo, Japan) at a fixed duration of 10 s to all patients, followed by 20 ml of a 0.9% saline solution injected at the same flow rate as the contrast material.

The scan delay was determined with an automatic bolus tracking system (Real Prep Technique; Toshiba). The scan parameters were collimation 320 × 0.5 mm, rotation time 0.275 s, tube voltage 120 kV, tube current 540–750 mA, z-coverage 120–160 mm. All examinations were performed within a single heartbeat with prospective ECG-triggering. The phase window during which the patient was exposed was limited to 70–80% of the cardiac cycle for patients with a heart rate < 65 bpm and to 40–80% of the cardiac cycle for patients with a heart rate > 65 bpm.

All images were reconstructed with hybrid IR (adaptive iterative dose reduction 3D: AIDR 3D) using a medium sharp kernel (FC14) and with the model-based IR (forward projected model-based IR solution: FIRST). Axial images were reconstructed; the slice thickness and reconstruction interval were 0.5 and 0.25 mm, respectively. Reconstructed image data were transferred to a workstation (Virtual Place version 3.3; Aze, Tokyo, Japan) for post-processing. The effective radiation dose at coronary CTA was calculated as the product of the dose-length product multiplied by a conversion coefficient for the chest ($\kappa = 0.014 \text{ mSv mGy}^{-1} \text{ cm}^{-1}$).⁹

Quantitative analysis

One observer with 11 years of experience in cardiac radiology collected all measurements. All images were displayed with a fixed window level at 300 HU and a window width at 1200 HU. For quantitative analysis, we analysed the attenuation effects arising from the stent struts and measured the visible stent lumen diameter on AIDR 3D- and FIRST images. The image noise was recorded as the standard deviation of the attenuation value in a circular region of interest placed in the ascending aorta.

Attenuation effects elicited by stent struts

In each data set we measured the attenuation values inside the visible stent lumen at three stent sites (proximal, centre and distal) using a region of interest technique. We also measured the attenuation values inside the native coronary lumen at a site proximal to the stent. To assess the attenuation effects arising from metallic stent struts, stent lumen attenuation increase ratios (SAIRs) were calculated using the equation: $\text{SAIR} = (\text{in-stent attenuation} - \text{coronary lumen attenuation}) / \text{coronary lumen attenuation}$. The higher the value, the greater is the blooming effect from metallic stent struts and the poorer is the image quality.¹⁰

Visible stent lumen diameter

We measured the visible stent lumen diameter on AIDR 3D- and FIRST images at three different sites on the plane perpendicular to the long axis of the vessel. The mean value obtained for each stent was compared to the true diameter.

We categorized the evaluated stents depending on their material (Stainless steel or Cobalt–chromium alloy) or diameter (stent diameter of ≥ 3 or < 3 mm). The SAIR and the ratio of the visible-compared to the true stent lumen diameter in each category were compared on AIDR 3D- and FIRST images.

Qualitative analysis

Two observers with 5 and 11 years of experience in cardiac radiology, respectively, independently assessed the curved multi-planar reformations on the workstation. They were blinded to clinical information, the reconstruction method, and the results of invasive coronary angiography. Stents were visually evaluated using a 4-point score where 1 = no visible neointimal hyperplasia, 2 = non-occlusive neointimal hyperplasia (lumen reduction < 50%), 3 = in-stent restenosis (lumen reduction $\geq$ 50%) and 4 = in-stent occlusion (complete loss of attenuation inside the stent lumen). If their data analyses disagreed, final decisions were reached by consensus. Interobserver agreement in the qualitative evaluation was assessed with the Cohen kappa κ coefficient where a κ value of less than 0.20 = poor-, 0.21–0.40 = fair-, 0.41–0.60 = moderate-, 0.61–0.80 = substantial- and 0.81–1.00 = near perfect agreement.

The diagnostic accuracy of coronary CTA for detecting in-stent restenosis was analysed. The sensitivity, specificity, positive- and negative predictive value (PPV, NPV) and accuracy of coronary CTA for detecting in-stent restenosis were calculated on both AIDR 3D- and FIRST images. We also compared the ROC curves and the area under the curve obtained with the two reconstruction methods.

Table 1. Quantitative image quality parameters at different stent diameters

	AIDR 3D	FIRST
SAIR		
Stent diameter of ≥ 3 mm ($n = 13$)	0.28 (0.06–0.43)	0.18 (0.03–0.36)
Stent diameter of < 3 mm ($n = 9$)	0.40 (0.02–0.83)	0.24 (0.01–0.62)
Overall ($n = 22$)	0.32 (0.02–0.83)	0.20 (0.01–0.62)
Visible diameter (%)		
Stent diameter of ≥ 3 mm ($n = 13$)	50.8 (45.0–57.5)	54.8 (50.0–65.0)
Stent diameter of < 3 mm ($n = 9$)	45.2 (32.0–76.4)	51.1 (37.1–80.0)
Overall ($n = 22$)	47.5 (32.0–76.4)	52.5 (37.1–80.0)

AIDR 3D, adaptive iterative dose reduction 3D; FIRST, forward projected model-based iterative reconstruction solution; SAIR, stent lumen attenuation increase ratio.

RESULTS

We examined 22 stents in 16 patients; 11 had one-, 4 had two- and 1 had three stents. The labelled stent diameter was 2.5 mm ($n = 6$), 2.75 mm ($n = 3$), 3.0 mm ($n = 4$), 3.5 mm ($n = 6$) and 4.0 mm ($n = 3$); the stent length ranged from 12 to 33 mm.

CT scans were acquired without complications in all 16 patients. The mean body mass index of our patients was 24.9 ± 2.7 (range 21.1–29.1); their mean heart rate during scanning was 55.7 ± 6.0 bpm (range 46–69 bpm). The mean DLP and the effective radiation dose were 295.1 ± 41.3 mGy $\times$ cm and 4.1 ± 0.6 mSv, respectively. The mean time required for reconstruction with AIDR 3D and FIRST was 20 and 205 s, respectively.

Quantitative image quality parameters

The quantitative image quality parameters at different stent materials or diameters are shown in [Tables 1 and 2](#). The attenuation effects arising from stent struts were lower on FIRST- than AIDR 3D images regardless of stent material or diameter. Also, the ratio of the visible- compared to the true stent lumen diameter was higher on FIRST- than AIDR 3D images regardless of stent material or diameter. The image noise on images reconstructed with FIRST- (22.6 ± 2.8 HU) was slightly lower than on AIDR 3D images (25.4 ± 3.3 HU).

Visual evaluation

The diagnostic performance for the detection of in-stent restenosis on AIDR 3D- and FIRST images is shown in [Table 3](#). The sensitivity, specificity, PPV, NPV and accuracy for AIDR 3D were 60, 94.1, 75.0, 88.9 and 86.4%, respectively. For FIRST they were 100, 94.1, 83.3, 100.0 and 95.5%, respectively. The area under the curve value was slightly higher with FIRST than AIDR 3D (0.97 vs 0.77). There was substantial interobserver agreement with respect to the overall image quality ($\kappa = 0.79$). A representative case is shown in [Figures 1 and 2](#).

DISCUSSION

Ours is the first study to evaluate the diagnostic performance of coronary CTA scans reconstructed with model-based IR for the detection of in-stent restenosis. We found that the model-based IR algorithm reduced the attenuation effects arising from stent struts and improved the diagnostic performance for the detection of in-stent restenosis.

Despite the increased temporal- and spatial resolution of CT scanners, blooming artefacts from stent struts limit the evaluation of the stent lumen.¹¹ These artefacts are primarily attributable to partial volume averaging and to beam hardening that limit the identification of in-stent patency and in-stent restenosis.¹²

Table 2. Quantitative image quality parameters at different stent materials

	AIDR 3D	FIRST
SAIR		
Stainless steel ($n = 14$)	0.41 (0.02–0.83)	0.24 (0.01–0.62)
Cobalt-chromium alloy ($n = 8$)	0.27 (0.06–0.43)	0.18 (0.03–0.40)
Overall ($n = 22$)	0.32 (0.02–0.83)	0.20 (0.01–0.62)
Visible diameter (%)		
Stainless steel ($n = 14$)	40.5 (32.0–47.5)	46.4 (37.1–53.3)
Cobalt-chromium alloy ($n = 8$)	57.7 (50.0–76.4)	61.3 (51.4–80.0)
Overall ($n = 22$)	47.5 (32.0–76.4)	52.5 (37.1–80.0)

AIDR 3D, adaptive iterative dose reduction 3D; FIRST, forward projected model-based iterative reconstruction solution; SAIR, stent lumen attenuation increase ratio.

Table 3. Diagnostic performance in the detection of in-stent restenosis on AIDR 3D and FIRST images

	AIDR 3D	FIRST
Sensitivity (%)	3/5 (60.0)	5/5 (100.0)
Specificity (%)	16/17 (94.1)	16/17 (94.1)
PPV (%)	3/4 (75.0)	5/6 (83.3)
NPV (%)	16/18 (88.9)	16/16 (100.0)
Accuracy (%)	19/22 (86.4)	21/22 (95.5)

AIDR 3D, adaptive iterative dose reduction 3D; FIRST, forward projected model-based iterative reconstruction solution; NPV, negative predictive value; PPV, positive predictive value.

Earlier, 7.3–9.2% of coronary stents could not be evaluated due to severe blooming artefacts^{3,4} that may result in false-positive findings of in-stent restenosis or the overestimation of lesion severity. Consequently, a novel reconstruction method that improved the image quality was needed for the evaluation of coronary stents.

IR algorithms can be classified into two types: hybrid IR and model-based IR.^{5,7} The former applies some noise reduction techniques in sinograms and image spaces. The image noise is lower and streak artefacts are fewer with hybrid IR than conventional filtered back projection.^{13,14} Model-based IR involves an IR algorithm in the true sense; it repeats both back and forward projections in the image-reconstruction process until differences between the original- and the forward projection data are minimal.^{5–7} Thus, the image noise or sharpness of model-based IR images depends on the convergence condition of each IR algorithm. Currently available model-based IRs include Veo (GE Healthcare), IMR (Philips Healthcare) and FIRST (Toshiba Medical Systems). Their advantage is a higher spatial resolution than on images reconstructed with conventional FBP or hybrid IR.^{5,7} Recently, the effect of a model-based IR on the image quality of coronary artery stents has been reported;⁸ the stent strut was sharper and the attenuation effects arising from stent struts were lower on model-based- than hybrid IR images. This resulted in better image quality.

The SAIR, introduced as a marker for blooming artefacts from stent struts on CT images,¹⁰ was lower on FIRST- than AIDR 3D images. Also, the ratio of the visible- compared to the true stent lumen diameter was higher on FIRST- than AIDR 3D images. Consequently, the diagnostic performance for the detection of in-stent restenosis was improved on FIRST images. In our study, all stents with in-stent restenosis were correctly identified on FIRST images; no stents with in-stent restenosis were missed. The high sensitivity on FIRST image implies that this technique is unlikely to miss severe in-stent restenosis. The NPV on FIRST images was 100%, suggesting that this IR algorithm is particularly useful for the exclusion of significant in-stent restenosis. de Graaf *et al*¹⁵ reported that the diagnostic accuracy for detecting coronary in-stent restenosis was high on their 320-detector CT scanner; however, the PPV for the assessment of significant in-stent restenosis was relatively low (65%) by stent-based analysis and remains an important limitation of coronary CTA. As the PPV was relatively high in our study (AIDR 3D = 75.0%, FIRST = 83.3%), we suggest that the IR algorithm helped to improve the PPV for stent evaluation.

The stent material and diameter are typically considered to be a major factor in terms of diagnostic accuracy and lumen visibility, therefore, we categorized the evaluated stents depending on their material (Stainless steel or Cobalt–chromium alloy) or diameter (stent diameter of ≥ 3 or < 3 mm). In our study, the use of FIRST had the same effects on the SAIR and the ratio of the visible- compared to the true stent lumen diameter regardless of stent material or diameter. Detection or exclusion of in-stent restenosis would also be dependent on the stent material or diameter, but sufficient evaluation of the difference in accuracy based on their material or diameter would be difficult in this study because of the small number of patients.

Our study has some limitations. First, the small number of patients limits the informational value of our findings. Studies on larger patient populations are underway to confirm our preliminary results. Second, we served invasive coronary angiography as the standard of reference, but 3 of 16 patients were classified as a non-restenosis group based on myocardial scintigraphy.

Figure 1. Examples of a true negative result on both AIDR 3D- (a) and FIRST (b) images. A 67-year-old male with neointimal hyperplasia in the stent placed in the proximal segment of the right coronary artery. On the FIRST image the blooming artefacts observed on the AIDR 3D image are reduced and neointimal hyperplasia (arrow) is more clearly visualized. The invasive coronary angiogram (c) shows neointimal hyperplasia as an irregular contour along the stent lumen but no significant stenosis (arrow).

Figure 2. Examples of a false negative result on an AIDR 3D (a) image that was a true positive result on a FIRST (b) image. A 77-year-old male with in-stent restenosis in the proximal segment of the left anterior descending artery. A filling defect in the proximal part of the stent (arrow) is clearly visualized on the FIRST- but not the AIDR 3D image. The invasive coronary angiogram (c) shows in-stent restenosis in the stent located in the proximal left anterior descending artery (arrow).

Third, although both readers were blinded to the reconstruction method used (AIDR 3D or FIRST), it may have been obvious due to major differences in the image characteristics. Lastly, we investigated the effect of IR algorithms on an instrument from a specific CT vendor. The effect of IR algorithms on scanners provided by different vendors may be different.

In conclusion, the model-based IR algorithm may improve diagnostic performance for the detection of in-stent restenosis.

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