Received:
19 July 2017

Revised:
05 October 2017

Accepted:
15 October 2017

<https://doi.org/10.1259/bjr.20170541>

Cite this article as:

Kai N, Oda S, Utsunomiya D, Nakaura T, Funama Y, Kidoh M, et al. Dual-region-of-interest bolus-tracking technique for coronary computed tomographic angiography on a 320-row scanner: reduction in the interpatient variability of arterial contrast enhancement. *Br J Radiol* 2018; **91**: 20170541.

FULL PAPER

Dual-region-of-interest bolus-tracking technique for coronary computed tomographic angiography on a 320-row scanner: reduction in the interpatient variability of arterial contrast enhancement

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Objective: We compared the effect of a dual-region-of-interest (ROI) bolus-tracking technique on interpatient variability of arterial contrast enhancement with that of the conventional bolus-tracking technique in coronary computed tomographic angiography (CTA) on a 320-row scanner.

Methods: This study included 100 patients who underwent coronary CTA using one of two protocols: (1) 50 patients underwent scanning using a conventional single-ROI bolus-tracking technique (P-single) with an ROI placed in the ascending aorta, and (2) 50 patients underwent scanning using a dual-ROI technique (P-dual) with two ROIs placed in the pulmonary trunk and the ascending aorta. CT attenuation in the ascending aorta and coronary arteries, and the

interpatient variability were compared between the two scanning protocols.

Results: The mean CT attenuation of the ascending aorta and coronary arteries tended to be higher for P-dual than for P-single, but the difference was not significant ($p = 0.08$ – 0.30). The interpatient variability of contrast enhancement (SD of the CT attenuation) was significantly smaller for P-dual than for P-single ($p < 0.01$).

Conclusion: The dual-ROI bolus-tracking technique can reduce interpatient variability of arterial contrast enhancement in coronary CTA on a 320-row scanner.

Advances in knowledge: The use of a dual-ROI bolus-tracking technique can provide sufficient and consistent arterial enhancement of coronary CTA.

INTRODUCTION

With the introduction of 64-row multidetector CT, coronary computed tomographic angiography (CTA) has become one of the most important diagnostic imaging modalities for evaluation of coronary artery diseases.^{1,2} During coronary CTA, sufficient vascular enhancement is essential for correct detection and evaluation of lesions in the coronary arteries.³ Previous studies have suggested that the target attenuation value of coronary arteries is ≥ 350 Hounsfield units (HU).^{4,5} A recent multi-centre and multivendor study by Hausleiter et al⁶ found that the mean attenuation value for diagnostic image quality was 412 ± 113 HU for the proximal coronary arteries. Thus, high coronary enhancement is important for precise assessment of coronary artery diseases in coronary CTA.

In coronary CTA, scan timing is commonly determined by using the bolus-tracking technique.⁷ In this technique, one region of interest (ROI) generally is placed on the ascending aorta with a threshold value of 100 to 200 HU, and 5–7 s after triggering, the coronary CTA scan is performed.⁸ Although this technique is used to optimize the scan timing, a wide range of interpatient variability of arterial contrast enhancement is still observed.⁸ To obtain sufficient arterial contrast enhancement with minimal interpatient variability, a dual-ROI bolus-tracking system is now available in a 320-row CT scanner. Using this technique, we can place two ROIs in different locations with different threshold values: the first ROI for the breath-hold command and the second ROI for scanning start. Because this technique can enable a substantially shorter scan delay

time than the conventional bolus-tracking technique, it may reduce interpatient variability of arterial contrast enhancement.

We hypothesized that use of a dual-ROI bolus-tracking system with placement of the first ROI (for the breath-hold command) in the pulmonary trunk and placement of the second ROI (for scanning start) in the ascending aorta would be effective for reducing interpatient variability of arterial contrast enhancement because of the shorter scan delay time than that of the conventional bolus-tracking system.

The purpose of this study was to investigate the effect of a dual-ROI bolus-tracking system on arterial contrast enhancement and interpatient variability in coronary CTA on a 320-row scanner.

METHODS AND MATERIALS

Study population

The ethics committee of our hospital approved this retrospective study and waived individual informed patient consent. Between April 2013 and September 2013, 100 patients (45 females, 55 males; mean age, 66.4 ± 11.6 years; range, 20–88 years) who underwent coronary CTA were retrospectively collected in this study. All patients were suspected of, or had confirmed coronary artery disease, and were referred for coronary CTA for clinical reasons based on guidelines promulgated by the American College of Cardiology.⁹ The exclusion criteria were severe renal failure (estimated glomerular filtration rate of $< 30 \text{ ml min}^{-1}/1.73 \text{ m}^2$), atrial fibrillation, a history of coronary artery bypass grafting and heart failure (New York Heart Association Grades III–IV). The mean body weight of patients was $63.3 \pm 15.5 \text{ kg}$ (range, 33.0–82.5 kg) and their mean body mass index (BMI) was $24.7 \pm 3.5 \text{ kg m}^{-2}$ (range, 14.7–32.4 kg m^{-2}). 50 patients underwent scanning with a conventional single-ROI bolus-tracking technique (P-single) and 50 patients underwent scanning with a dual-ROI bolus-tracking technique (P-dual). We had changed our routine coronary CTA protocol from P-single to P-dual July 2013. The patients of the two groups were matched for sex and age. The patient characteristics are summarized in Table 1.

CT scanning and contrast infusion protocols

All patients were examined on a second-generation 320-row CT scanner (Aquilion ONE VISION, Toshiba, Otawara, Japan) by using prospective ECG-triggered axial scans. The parameters for coronary CTA imaging were a detector configuration of

$320 \times 0.5 \text{ mm}$ (detector collimation), slice thickness of 0.5 mm, section interval of 0.25 mm, gantry rotation time of 0.275 s and tube voltage of 120 kVp. The tube current was determined with automatic exposure control (SURE Exposure 3D, Toshiba Medical Systems) on the basis of the X-ray attenuation on anteroposterior and lateral scout images and the reconstruction kernel.¹⁰ The phase window was set at 70–80% of the R-R interval. If the baseline heart rate was $\geq 65 \text{ bpm}$, we intravenously injected the beta-blocker landiolol hydrochloride (6–12.5 mg, Corebeta; Ono Pharmaceutical, Osaka, Japan) 4–7 min before scanning, and/or administered metoprolol tartrate (20 mg, Lopressor; Novartis Pharma, Tokyo, Japan) orally 60 min before scanning. Each patient received nitroglycerin (0.3 mg, Nitrophen; Nippon Kayaku, Tokyo, Japan) sublingually 5 min before data acquisition, to dilate the coronary arteries. Using a dual-chamber power injector (Autoenhance A-250; Nemoto Kyorindo, Tokyo, Japan), we delivered iopamidol with an iodine concentration of 370 mg ml^{-1} (Iopamiron-370; Bayer HealthCare, Osaka, Japan) to each patient via a 20-gage catheter inserted into an antecubital vein. The amount of contrast media adjusted to the body weight of each patient [280 mg of iodine per kilogram of body weight (mgI kg^{-1})] was injected at a fixed injection duration of 10 s. We then injected 40 ml of a saline solution at the same rate as that of the contrast media. For the P-single group, the start time of data acquisition was determined by using a conventional single-ROI system with a trigger threshold of 150 HU in the ascending aorta, and data acquisition was started 7 s after triggering. For the P-dual group, the dual-ROI bolus-tracking system was used; the first ROI for the breath-hold command was placed in the pulmonary trunk, and the second ROI for scanning start was placed in the ascending aorta (Figures 1 and 2). The threshold values for the first and second ROIs were set at 200 and 300 HU, respectively. As soon as the first ROI reached the threshold (200 HU), the patient was instructed to take and hold a deep breath. Then, approximately 3 s after the second ROI reached the threshold (300 HU), a coronary CTA scan was performed automatically. We recorded the breath-holding time (the time between the end of voice instruction and the coronary CTA scan) in the P-single and P-dual groups. The CT images acquired from the two protocols were reconstructed using an adaptive iterative reconstruction algorithm (AIDR 3D; Toshiba Medical Systems, Otawara, Japan) and a medium cardiac kernel (FC14). The acquisition parameters for the two protocols are summarized in Table 2.

CT radiation dose

To estimate the CT radiation dose, we recorded the volume CT dose index and the dose-length product for bolus-tracking and coronary CTA in each group. We also estimated the effective radiation dose exposure to the chest using the following equation¹¹:

$$\text{Effective radiation dose} = \text{dose} - \text{length product} \times 0.014$$

Data analysis

All images were reviewed and interpreted on PACS workstations with 1600×1200 matrix monitors (View R v. 1.09.15; Yokogawa Electronic, Tokyo, Japan). Available images included axial source images, and the image series acquired with the two protocols were intermixed. A cardiovascular radiologist, with 10 years of

Table 1. Patient demographics

	P-single (n = 50)	P-dual (n = 50)	p-value
Sex (male/female)	27/23	28/22	0.83
Age (years)	67.2 ± 11.4	66.7 ± 12.2	0.70
Body height (cm)	160.1 ± 11.4	157.8 ± 9.8	0.10
Body weight (kg)	62.3 ± 12.5	62.6 ± 10.7	0.74
Body mass index (kg m^{-2})	24.4 ± 3.4	25.2 ± 3.6	0.10
Heart rate (bpm)	57.3 ± 10.9	59.6 ± 8.5	0.50
Dose of contrast media (ml)	43.3 ± 6.6	44.6 ± 6.4	0.50

Note: Data presented as mean $\pm$ SD.

Figure 1. Axial locator image through the level of the pulmonary trunk and ascending aorta for a dual-region-of-interest (ROI) bolus-tracking technique. The first ROI for the breath-hold command was placed in the pulmonary trunk, and the second ROI was placed in the ascending aorta for scanning start.

experience with coronary CTA, performed all measurements, and was blinded to the specific protocol used and patient group. The CT attenuation for the ascending aorta was measured by using an ROI cursor (approximately 2.5 cm²) at the level where the left main artery (LMA) branches from the ascending aorta. Next, the attenuations for the proximal right coronary artery (RCA) and LMA were measured. A circular ROI was placed in a vascular area not so small as to be affected by pixel variability and not so large as to approach the edges of the vessel. Calcifications, coronary artery stents and soft plaques were carefully excluded from the ROI measurements. Two radiologists with 6 and 11 years of experience in coronary CTA, who were blinded to the scan protocols, assessed the images with respect to motion artefacts of the RCA, the left anterior coronary artery and the left circumflex coronary artery. The images were scored by consensus using a 4-point visual rating scale [4 (excellent) = no motion artefacts, useful diagnostic information; 3 (good) = some motion artefacts, sufficient diagnostic information; 2 (fair) = motion artefacts present, limited diagnostic information and 1 (poor) = too many motion artefacts, no diagnostic information].

Statistical analysis

All numeric values are reported as the mean $\pm$ SD. All quantitative data obtained in the P-single and P-dual groups were compared. Differences in the mean values between the two protocols with normally and non-normally distributed data were determined by performing the two-tailed independent *t*-test and the Mann–Whitney *U* test, respectively. We compared CT attenuation in the ascending aorta, proximal

Figure 2. Overview of a conventional single-region-of-interest (ROI) bolus-tracking protocol (P-single) and a dual-ROI bolus-tracking protocol (P-dual) for coronary computed tomographic angiography. For P-single, the scan timing was determined using a conventional single-ROI system with a trigger threshold of 150 HU in the ascending aorta, and data acquisition started 7 s after triggering. For P-dual, the first ROI was placed in the pulmonary trunk, and the second ROI was placed in the ascending aorta. The threshold values for the first and second ROI were set at 200 and 300 HU, respectively. As soon as the first ROI reached the threshold, the patient was instructed to take and hold a deep breath. Then, approximately 3 s after the second ROI reached the threshold, a coronary computed tomographic angiography scan was performed. HU, Hounsfield units.

RCA and LMA between the two protocol groups. To assess the interpatient variability of the contrast enhancement, we compared the SD of the CT attenuation between the two

Table 2. Imaging and contrast media parameters of the two protocols

	P-single	P-dual
Detector collimation (mm)	320 $\times$ 0.5	
Tube voltage (kVp)	120	
Tube current ^a (mA)	200–450	
Gantry rotation time (s)	0.275	
Contrast material dose (mgI/kg)	280	
Injection duration (s)	10	
Bolus-tracking threshold (HU)		
Pulmonary trunk	NA	200
Ascending aorta	150	300
Section/interval thickness (mm)	0.5/0.25	
Image reconstruction	AIDR-3D	
Reconstruction kernel	FC14	

AIDR-3D, adaptive iterative reconstruction algorithm.

^aThe tube current was determined using automatic exposure control.

Table 3. Mean and interpatient variability of the CT attenuation

	P-single	P-dual	<i>p</i> -value
Mean CT attenuation (HU)			
Ascending aorta	438.2	462.0	0.08
Left main artery	448.6	461.9	0.31
Proximal right coronary artery	423.3	445.9	0.09
Interpatient variability ^a (HU)			
Ascending aorta	80.3	50.8	<0.01
Left main artery	78.0	47.8	<0.01
Proximal right coronary artery	83.9	38.4	<0.01

^aInterpatient variability of the contrast enhancement was determined by the SD of the mean CT attenuation.

groups by using the Levene test. Bayesian analysis was used to assess the post-test probability of achieving optimal contrast enhancement (> 350 HU in the ascending aorta) by using the two bolus-tracking systems in the assumptive general population ($n = 100,000$). Differences of $p < 0.05$ indicated statistical significance. Statistical analysis was performed using an Excel statistics software package for Microsoft Windows (BellCurve for Excel; SSRI, Tokyo, Japan) and the free statistical software “R” (R, v. 2.6.1; The R Project for Statistical Computing; <http://www.r-project.org/>).

RESULTS

There were no statistically significant differences in the patients' sex, age, body weight, BMI, heart rate during CT acquisition and dose of contrast media between the two protocol groups (Table 1). The mean and interpatient variabilities of the CT attenuations for the ascending aorta, proximal RCA and LMA are shown in Table 3.

Although the mean attenuations in the ascending aorta, proximal RCA and LMA were slightly higher in the P-dual group, the differences were not significant (ascending aorta, $p = 0.08$; proximal RCA, $p = 0.09$; and LMA, $p = 0.31$). The SDs of the mean attenuations in the ascending aorta, proximal RCA and LMA were statistically significantly smaller in the P-dual group than in the P-single group (ascending aorta, $p < 0.01$; proximal RCA, $p < 0.01$; and LMA, $p < 0.01$). Our Bayesian analysis indicated that when P-dual was used, the pre-test probability of achieving optimal contrast enhancement (> 350 HU in the ascending aorta) was $98.2 \pm 0.4\%$, whereas it was $85.9 \pm 7.7\%$ when P-single was used (Figure 3).

Mean breath-holding time was significantly longer in the P-dual group than in the P-single group (10.1 ± 2.2 s vs 5.2 ± 0.6 s, respectively; $p < 0.01$). There was no significant difference between the P-single and P-dual groups with respect to visual scores for motion artefact for any of the coronary arteries. The mean effective radiation doses during bolus-tracking for the P-single and P-dual groups were 0.2 ± 0.1 and 0.4 ± 0.1 mSv, respectively; the between-group difference was statistically significant. There was no significant difference between the two protocols with respect

Figure 3. The graph shows the results of the Bayesian analysis for the predicted probability distribution of achieving optimal contrast enhancement (> 350 HU in the ascending aorta) using a conventional single-region-of-interest bolus-tracking protocol (P-single) and a dual-region-of-interest bolus-tracking protocol (P-dual). The pre-test probabilities of achieving optimal contrast enhancement were $98.2 \pm 0.4\%$ for P-dual and $85.9 \pm 7.7\%$ for P-single. HU, Hounsfield units.

to the mean effective radiation dose during coronary CTA and total scans (coronary CTA, 3.4 ± 1.1 vs 3.0 ± 1.4 mSv, $p = 0.20$; total, 3.6 ± 1.6 vs 3.4 ± 1.4 mSv, $p = 0.45$) (Table 4).

DISCUSSION

Our results demonstrated that the use of a dual-ROI bolus-tracking technique yielded sufficient and more consistent aortic and coronary arterial enhancement with reduced interpatient variability than the protocol involving a conventional single-ROI bolus-tracking technique at coronary CTA on a 320-row scanner. This finding is of practical importance because sufficient and consistent coronary arterial enhancement could provide stable diagnostic performance of coronary CTA in evaluating stenotic severity and characterization of coronary plaque, which are significantly affected by coronary lumen attenuation.

In coronary CTA, high and consistent vascular enhancement is a prerequisite for sufficient evaluation,^{3,12,13} and an optimal enhancement value in the coronary arteries is considered to be 300–350 HU.⁴ A recent study that evaluated the arterial contrast enhancement and image quality of coronary CTA indicated that the target attenuation value of the proximal coronary artery required for diagnostic image quality was 390–500 HU.¹⁴ Cademartiri et al³ investigated the relationship between intracoronary attenuation and the diagnostic accuracy of coronary CTA for detection of clinically significant stenosis, and reported that greater intracoronary attenuation led to higher diagnostic accuracy for detection of coronary artery stenosis; the sensitivities were 90 and 93%, and the specificities were 95 and 97%, for the low-attenuation group (233 ± 29 HU) and the high-attenuation group (371 ± 39 HU), respectively. In the present study,

Table 4. Breath-holding time, motion artefact score and radiation dose

	P-single	P-dual	<i>p</i> -value
Breath-holding time (s)	5.2 ± 0.6	10.1 ± 2.2	<0.01
Motion artefact score ^a			
Right coronary artery	3.9 ± 0.4	3.9 ± 0.4	0.86
Left anterior coronary artery	3.9 ± 0.3	3.9 ± 0.3	0.86
Left circumflex coronary artery	3.7 ± 0.6	3.8 ± 0.4	0.54
Radiation dose (mSv)			
Bolus-tracking	0.2 ± 0.1	0.4 ± 0.1	<0.01
Coronary CTA	3.4 ± 1.1	3.0 ± 1.4	0.20
Total	3.6 ± 1.6	3.4 ± 1.4	0.45

CTA, computed tomographic angiography.

Note: Data presented as mean ± SD.

^aA 4-point visual rating scale was used for assessment of motion artefacts.

Bayesian analysis showed that if a dual-ROI bolus-tracking technique was applied, the pre-test probability of achieving optimal contrast enhancement (> 350 HU in the ascending aorta) was 98.2 ± 0.4%, whereas it was 85.9 ± 7.7% if a conventional single-ROI bolus-tracking technique was used. The use of the dual-ROI bolus-tracking technique may provide more precise evaluation of coronary artery diseases.

In coronary CTA performed on a 320-row scanner, it has been reported that the optimal duration for the injection of contrast material is the sum of the scan delay time from triggering at bolus-tracking (6–7 s) and the time necessary for scanning the whole heart (1–3 s), and the use of 245 to 280 mgI kg⁻¹ of contrast media is feasible for sufficient coronary arterial enhancement.¹⁵ In this study, all patients received 280 mgI kg⁻¹ of contrast media injected at 10 s in both groups. On the other hand, Bae et al¹⁶ reported that a patient's cardiovascular circulation critically affects the time to peak contrast enhancement. Therefore, even if the weight-adapted contrast media dose protocol with the conventional bolus-tracking technique is used, a wide range of interpatient variability for arterial contrast enhancement is still observed.

With respect to the determination of scan timing, two standard synchronization methods, bolus-tracking and test injection techniques, are commonly used in clinical settings. Cadernartiri et al⁷ compared test injection and bolus-tracking techniques in coronary CTA using a 16-row CT scanner and found that the bolus-tracking technique yielded more stability and higher enhancement than that by the test injection. However, the scan delay time from triggering in the conventional bolus-tracking system is relatively long (6–7 s). The long scan delay time causes interpatient variability of the arterial contrast enhancement. The advantage of the use of the dual-ROI bolus-tracking system is that the scan delay time can be shortened (approximately 3 s) by instructing the patient to take a breath and hold it before the scan start triggering using the first ROI placed in the pulmonary trunk, which enables the threshold value of the ROI for scan start (the second ROI is placed in the ascending aorta) to be set higher

(300 HU) than in the conventional single-ROI bolus-tracking system (150 HU). These advantages are thought to contribute to CT scans being performed near the peak enhancement and to making it possible to obtain more consistent arterial enhancement, which results in reduced interpatient variability of the arterial contrast enhancement. In fact, previous investigations that have used the same contrast media injection and dual-ROI bolus-tracking protocol as ours suggested that it is technically feasible to obtain sufficient arterial contrast enhancement in coronary CTA.¹⁷

Tatsugami et al¹⁸ evaluated the effect of a dual-ROI bolus-tracking system on interpatient variability of arterial enhancement. They placed the two ROIs in the ascending aorta and set the first and second threshold values at 100 and 300 HU, respectively; they concluded that the use of a dual-ROI bolus-tracking technique could reduce interpatient variability more than that by a conventional single-ROI technique. Although our results are similar to those reported by Tatsugami et al, when using their method (two ROIs in the ascending aorta), the patient's heart rate during scanning may be unstable because the time between the breath-hold command and scanning is so short that it may cause motion artefacts. It may also cause blurring of coronary arteries on CTA images in some patients because of incomplete breath-holding (presumably as the patient's chests and diaphragms were still moving).

This study had some limitations. First, we did not evaluate the diagnostic performance of our two protocols for detecting coronary stenosis by correlation of our imaging findings with the results of coronary catheterization because the incidence of coronary stenosis was too low in our patients, and we had no reference standard for most of their lesions. Rather, we focused on comparing the arterial contrast enhancement and variability of coronary CTA images obtained using P-single and P-dual methods. Second, the study population was small, and our techniques must be rigorously evaluated in large-scale prospective studies. Third, the body size of the Japanese patients recruited in this study (mean BMI, 24.7 ± 3.5 kg m⁻²; range, 14.7–32.4 kg m²) was smaller than those of North American and European individuals. Further studies are required to determine whether our results are applicable to larger-sized patients. Fourth, we did not enrol heart failure patients in this study because the breath-hold time during coronary CTA could be longer in patients with reduced cardiac output under a dual-ROI bolus-tracking protocol, which might result in poor coronary CTA imaging because of inappropriate breath-holding. In such patients, conventional single-ROI bolus-tracking or test injection techniques may be helpful for determining the scan timing. We actually make the patients practice breath-holding for the required length of time prior to scanning in our routine practice and use a conventional single-ROI bolus-tracking for patients who show poor capacity for breath-holding. Fifth, only the 120-kVp coronary CTA protocol was evaluated in this study. The low-tube voltage (100-kVp) protocols that are recommended for non-obese patients and that help reduce radiation exposure and contrast material dose were not employed. To evaluate the effect of the dual-ROI bolus-tracking technique on interpatient

variability of arterial contrast enhancement, we standardized all the scan parameters (including tube voltage) except the bolus-tracking techniques in this study. Lastly, all patients and coronary CTA examinations in this study originated from a single institution. Multicentre prospective clinical trials are required to validate our data.

CONCLUSION

The use of a dual-ROI bolus-tracking technique can provide sufficient and consistent arterial enhancement of coronary CTA on a 320-row scanner and may contribute to stable diagnostic performance of coronary CTA in evaluating stenotic severity and characterization of coronary plaque.

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