Feasibility of Four-Dimensional Similarity Filter For Radiation Dose Reduction in Dynamic Myocardial Computed Tomography Perfusion Imaging

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Research Article

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Abstract

Purpose: We aimed to evaluate the impact of four-dimensional noise reduction filtering using a similarity algorithm (4D-SF) on image noise during dynamic myocardial computed tomography perfusion (CTP) to simulate the reduction of radiation dose.

Methods: A total of 43 patients who underwent dynamic myocardial CTP using 320-row CT were included in the study. The original images were reconstructed using iterative reconstruction (IR); three different CTP datasets with simulated noise, which corresponded to 25%, 50%, and 75% reduction of the original dose (= 300mA), were reconstructed using a combination of IR and 4D-SF. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were assessed, and CT-derived myocardial blood flow (CT-MBF) was quantified. The results were compared between the original and simulated images with radiation dose reduction.

Results: The original, 25%-, 50%-, and 75%-dose reduced images with 4D-SF showed an SNR of 8.3 (6.5–10.2), 16.5 (11.9–21.7), 15.6 (11.0–20.1), and 12.8 (8.8–18.1) and a CNR of 4.4 (3.2–5.8), 6.7 (4.6–10.3), 6.6 (4.3–10.1), and 5.5 (3.5–9.1), respectively. Compared to the original images, the 25%-, 50%-, and 75%-dose reduced-simulated images showed significant improvement in both SNR and CNR with 4D-SF. There was no significant difference in CT-MBF between the original and 25%- or 50%-dose reduced-simulated images with 4D-SF, however, there was a significant difference in CT-MBF between the original and 75%-dose reduced-simulated images.

Conclusion: 4D-SF has the potential to reduce the radiation dose associated with dynamic myocardial CTP imaging by half, without impairing the robustness of MBF quantification.

Introduction

Assessment of myocardial ischemia is crucial for the management of coronary artery disease (CAD) [1, 2]. Coronary computed tomography angiography (CTA) is widely used for the assessment of coronary artery stenosis. However, CTA-based stenosis severity assessment still has some limitations in identifying hemodynamically significant CAD [3]. Myocardial computed tomography perfusion (CTP) imaging has emerged as one of the useful tools for myocardial perfusion imaging; dynamic CTP imaging allows for quantitative assessment of myocardial perfusion by quantifying hemodynamic parameters such as myocardial blood flow (MBF) [4, 5]. However, high radiation doses are inevitable with dynamic myocardial CTP imaging, because multiple scans are required during the first pass of contrast medium in the myocardium. The balance between the radiation dose and image quality should be considered in clinical practice [6].

The iterative reconstruction (IR) technique is an effective method for reducing image noise and radiation dose by combining the low-tube current scan [7]. However, the IR technique lacks temporal regularization in the time attenuation curve and impairs spatial resolution if the radiation dose is reduced excessively [8]. Therefore, other specific techniques are required for reducing the radiation dose associated with dynamic myocardial CTP imaging, while maintaining diagnostic image quality. A recent study has shown that a four-dimensional noise reduction filter using a similarity algorithm (four-dimensional similarity filter [4D-SF]) could be complementarily used with the IR technique to improve the image quality without altering the CT-MBF values [9], although several studies have investigated the image quality of dynamic myocardial CTP imaging using spatiotemporal noise reduction techniques [9-11]. However, the further feasibility of 4D-SF for radiation dose reduction associated with dynamic myocardial CTP imaging is not well discussed. This study aimed to evaluate the effects of 4D-SF on radiation dose reduction in dynamic myocardial CTP imaging.

Materials And Methods

Study population

The institutional ethics committee approved this retrospective observational study (registration number: 1910006) and waived the need for informed consent. We identified 50 patients from the clinical database who underwent stress dynamic CTP scanning for the assessment of CAD at the attending physician's discretion between September 2017 and September 2019. We excluded patients with (1) low left ventricular ejection fraction < 20%, (2) arrhythmia, (3) greater than first-degree atrioventricular block, or (4) inappropriate CTP data for CT-derived MBF quantification. Coronary artery stenosis of ≥ 50% on CTA was considered significant and was classified based on the three major coronary vessels; patients were assessed on a per-vessel basis. The radiation dose was calculated from the dose-length product in a dose report (conversion factor = 0.014) [12].

Scan protocol of stress dynamic computed tomography perfusion (CTP)

Stress dynamic CTP was performed using a 320-row multi-detector CT system (Aquilion ONE GENESIS Edition, Canon Medical Systems Corporation, Otawara, Japan) as a part of the comprehensive cardiac CT protocol with a partial modification of the previous protocol [9]. The scan timing of dynamic CTP was independently optimized, with the timing bolus scan using a 20%-diluted contrast medium, to set at 6 s before the arrival of the contrast medium at the ascending aorta. Contrast medium (iopamidol, 370 mg iodine/mL; Bayer Yakuhin, Ltd., Osaka, Japan) and a saline chaser were administered at the same injection rate and volume as the timing bolus scan, 3 min after adenosine triphosphate loading (0.16 mg/kg/min). The stress dynamic CTP dataset was obtained using the prospective electrocardiogram-gated dynamic mode, targeting a phase of 45% of the RR interval. The scan parameters for CTP were as follows: tube voltage, 80 kVp; tube current, 300 mA; gantry rotation speed, 0.275 s/rotation; detector collimation, 320 × 0.50 mm; and effective coverage, 100 mm. Subsequently, coronary CTA and delayed-enhancement CT were performed at 10 min and 15 min after stress dynamic CTP, respectively.

Post-processing of dynamic myocardial CTP images

A 360° full-reconstruction algorithm, the adaptive iterative dose reduction in three-dimensional (3D) processing (AIDR 3D, FC03, strong), and the non-rigid registration algorithm for motion compensation were used for CTP image reconstruction. The trans-axial images in the dynamic CTP dataset were reconstructed with 1.0-mm slice thickness, as the original images. In addition, three other CTP datasets were generated by adding simulated noise corresponding to the dose reduction rate (presented as tube amplitude for the dose) through a statistical model tool including both quantum noise and electronic noise. These datasets had values with 25% (225 mA), 50% (150 mA), and 75% dose reductions (75 mA) from the original dose (300 mA) [13]. The image filtering process with 4D-SF was used after noise simulation processing (Figure 1). Finally, the four CTP datasets (original, 25%-, 50%-, and 75%-dose reduced-simulated images with 4D-SF) were evaluated using a dedicated workstation (Vitrea, Canon Medical Systems Corporation, Japan) for image quality and CT-MBF analyses.

Image quality analyses

Image quality analyses were performed for the four different CTP datasets using 5-mm-thick cardiac short-axis CTP images by *average* intensity projection reformat. An experienced radiologist (with 6 years of experience in cardiac imaging) selected a representative single phase (approximately 4 s after the time point of maximal enhancement in the ascending aorta) at the optimal phase for the assessment of myocardial ischemia from a series of dynamic CTP datasets, as previously described [14].

Regarding qualitative image quality, two radiologists (with 5 and 6 years of experience in cardiac imaging), who were blinded to all clinical and reconstruction information, independently evaluated the four different CTP datasets in random order in terms of the noise, contrast, and contour sharpness using a 5-grade scale (1, non-diagnostic; 2, fair; 3, moderate; 4, good; and 5, excellent) in the optimal window level/width settings for each case [15]. Discrepancies between the two observers were resolved by consensus.

Regarding quantitative image quality, the other experienced radiologist (with 6 years of experience in cardiac imaging) evaluated myocardial CT attenuation (Hounsfield unit) and the standard deviation (SD) by placing the regions of interest (ROIs) (100–150 mm^2) in the center of each myocardial segment based on a 16-segment model without the apex [16]. The ROI (50–100 mm^2) in the nearby skeletal muscle (latissimus dorsi, pectoralis, or intercostal) was defined as the reference tissue [15]. The signal-to-noise ratio (SNR) was calculated by dividing the myocardial CT attenuation of an ROI by the SD of the same ROI. The contrast-to-noise ratio (CNR) was calculated by dividing the difference in CT attenuation between the myocardium and reference tissue by the SD of the reference tissue [15].

Computed tomography-derived myocardial blood flow analyses

Two experienced radiologists (with 5 and 6 years of experience in cardiac imaging) analyzed myocardial peak CT attenuation, time to peak (TTP), and CT-MBF in the four different dynamic CTP datasets, independent of all the information. CT-MBF was semi-automatically quantified using the Renkin-Crone equation, validated with oxygen-15-labelled water positron emission tomography [17]. Global CT-MBF was defined as the mean of all 16 segmental values.

Statistical analyses

Continuous data are expressed as the mean (SD) or as the median (first quartile–third quartile) according to the distribution. Regarding the intra- and inter-observer agreements, Cohen kappa (k) statistics were used for the visual image quality scores, and intra-class correlation coefficients (ICC) were used for the quantitative CTP-derived quantitative parameters such as peak CT attenuation, TTP, and CT-MBF. Differences were compared between the original images and each simulated CTP image using the Dunnett test. In all tests, statistical significance was determined at $p < 0.05$. Statistical analyses were performed using JMP13 (SAS Institute, Cary, NC, USA).

Results

Study population

Among the 50 patients who underwent stress dynamic myocardial CTP, seven were excluded because of inappropriate CTP datasets due to insufficient breath-holding during the scan (n = 4) or beam-hardening artifacts (n = 3). Finally, 43 eligible patients were enrolled in the present study (Table 1). The median estimated radiation dose was 3.8 (3.3–4.2) mSv for the original dynamic myocardial CTP data acquisition.

Qualitative and quantitative image quality

The image quality results are shown in Table 2. Regarding qualitative image quality scores, the kappa values of intra- and inter-observer agreements were 0.92 and 0.88 for noise, 0.95 and 0.92 for contrast, and 0.86 and 0.91 for sharpness, respectively, indicating satisfactory reproducibility ($\kappa > 0.70$). Each of the dose reduced-simulated CTP images with 4D-SF had a significantly higher visual image quality score in terms of noise than the original images ($p < 0.001$). In contrast, those of the 75%-dose reduced-simulated CTP images with 4D-SF were significantly lower than those of the 50%-dose reduced-simulated CTP images ($p < 0.001$). No significant difference was observed in contrast and sharpness between the original and the four different simulated CTP images ($p = 0.057$ for contrast, $p = 0.134$ for sharpness).

Regarding quantitative image quality scores, all of the 4D-SF post-processed and dose reduced-simulated CTP images had significantly higher image quality scores in SNR and CNR than the original CTP images ($p < 0.001$, Figure 2a and 2b). In addition, the 4D-SF post-processed and 75%-dose reduced-simulated CTP images had significantly lower SNR and CNR than the 4D-SF post-processed and 25%- or 50%-dose reduced-simulated CTP images ($p < 0.001$ in each).

CTP-derived quantitative parameters

The results of the CTP-derived quantitative parameters are shown in Table 3. The myocardial peak CT attenuation and TTP were assessed using 10 randomly selected patients (160 myocardial segments) from the study population, and the ICCs were 0.95 for myocardial peak CT attenuation and 0.85 for TTP.

The myocardial peak CT attenuation in 75%-dose reduced-simulated images with 4D-SF was significantly lower than that in the original images ($p < 0.001$), however, those in 25%- or 50%-dose reduced-simulated images with 4D-SF were not significantly different from those in the original images ($p = 0.829$ and 0.595). No significant difference was observed in the TTP between original images and each dose reduced-simulated image with 4D-SF ($p = 0.431$, 0.6750, and 0.873).

The ICC for CT-MBF assessed using 10 randomly selected patients (160 myocardial segments) was 0.89. The CT-MBF in the original images was 2.10 (1.41–2.80) mL/g/min; those in 25%-, 50%-, and 75%-dose reduced-simulated images with 4D-SF were 2.08 (1.41–2.76), 2.07 (1.36–2.83), and 1.82 (0.98–2.64) mL/g/min, respectively (Figure 3). The CT-MBF in 75%-dose reduced-simulated images with 4D-SF was significantly lower than that in the original images ($p < 0.001$), however, those in 25%- or 50%-dose reduced-simulated images with 4D-SF were not significantly different from those in the original images ($p = 0.994$ and 0.993). A representative case is shown in Figure 4.

Discussion

In the present study, we showed that (1) 4D-SF could significantly improve qualitative and quantitative image quality in different dose-simulated CTP images, and (2) 4D-SF did not alter the CT-MBF values in 25- and 50%-dose reduced-simulated CTP images compared to the original images.

Dynamic myocardial CTP imaging can have a high diagnostic performance providing an incremental value to CTA for the detection of hemodynamically significant CAD assessed with invasive fractional flow reserve (FFR) [18, 19]. A recent prospective study by Li et al. has also shown that CTP outperformed CT-FFR in identifying hemodynamically significant CAD [20]. However, in dynamic CTP, a relatively high radiation dose remains a concern in the combined use of coronary CTA in clinical practice.

Low-tube voltage scanning is an effective method for radiation dose reduction. Although low-tube voltage scanning theoretically has the potential to improve the detectability of myocardial ischemia by increasing the image contrast between normal and ischemic myocardium, the diagnostic image quality is impaired by increasing image noise [21]. IR techniques reduce image noise and allow lower-tube voltage scans, which leads to further radiation dose reduction without impairing image quality [22]. However, IR has a limitation in radiation dose reduction, because of an over-smoothing effect associated with the left shift in spatial frequency curves toward lower frequencies if the radiation dose is reduced excessively [23]. A temporally undersampled scan is also useful for reducing the radiation dose in dynamic myocardial CTP imaging, although undersampling may impair the robustness of CT-MBF quantification [24].

4D-SF is a novel technique that can be combined with the IR technique; it allows for image quality improvement without impairing the robustness of CT-MBF quantification [9]. 4D-SF is dedicated for the post-processing of dynamic CTP data operating in the temporal domain; spatial resolution is maintained because 4D-SF does not apply any spatial filtering using neighborhood voxels. Thus, we applied 4D-SF after non-rigid registration algorithm for motion compensation in CTP image reconstruction. In the present study, 4D-SF could improve the qualitative and quantitative image quality in different dose reduced-simulated CTP images. However, the image quality (SNR and CNR) of myocardial CT attenuation in 75%-dose reduced-simulated images was significantly altered in comparison with the original images and resulted in the impairment of robust CT-MBF quantification, despite using 4D-SF.

In the present study, the radiation dose in dynamic myocardial CTP (3.8 [3.3–4.2] mSv]) was lower than that of previous studies [11, 18]. It is desirable to reduce the radiation dose as much as possible without impairing diagnostic image quality. The present results indicate that 50%-radiation dose reduced-simulated images with 4D-SF are feasible for dynamic myocardial CTP imaging, and the radiation dose can be reduced to approximately 2 mSv, which is one quarter of the mean radiation dose (9.45 mSv) used in previous studies [18]. 4D-SF has the potential to allow for dynamic myocardial CTP imaging with extremely low radiation dose (< 3 mSv) by combining low-tube voltage, low-tube current, and undersampled acquisition [24, 25]. Moreover, the post-processing of 4D-SF can be applied to dynamic myocardial CTP images in only 2 min using commercial software, substantially improving its availability in clinical practice [9].

This study has several limitations. First, it was a retrospective single-center study with a small sample size. Second, the capacity of 4D-SF may be affected by the patients' physiques and CAD severity. Third, 4D-SF could not be compared with the other post-processing techniques used for dynamic myocardial CTP [11, 25]. However, the strength of the 4D-SF lies in its commercial availability for routine clinical use. Finally, the impact of 4D-SF on the diagnostic performance for detecting myocardial ischemia was not evaluated because we focused on the effects on radiation dose reduction in the present study. Multicenter prospective trials are needed to evaluate the feasibility of dynamic myocardial CTP with 4D-SF in detecting myocardial ischemia.

In conclusion, 4D-SF is a promising method for achieving both the improvement of image quality and radiation dose reduction in dynamic myocardial CTP imaging. Future studies are required for evaluating the diagnostic performance of dynamic myocardial CTP imaging with an extremely low radiation dose, for detecting myocardial ischemia.

Declarations

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Authors' contributions:

Conceptualization: [Yuki Tanabe]; Methodology: [Yuta Yamamoto]; Software: [Shota Nakano]; Resources: [Teruyoshi Uetani, Shuntaro Ikeda]; Formal analysis and investigation: [Yuta Yamamoto, Shuhei Yamamoto];Validation: [Tomoyuki Kido]; Data curation: [Yuta Yamamoto]; Writing - original draft preparation: [Yuta Yamamoto]; Visualization: [Yuta Yamamoto, Tomoyuki Kido];Project administration: [Yuki Tanabe, Akira Kurata]; Writing - review and editing: [Yuki Tanabe, Akira Kurata]; Supervision: [Akira Kurata, Osamu Yamaguchi, Teruhito Kido]; Funding acquisition: [not applicable]. All authors read and approved the final manuscript.

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Availability of data and materials: Not applicable.

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Consent to participate: The institutional ethics committee waived the need for informed consent to participate due to the retrospective nature of the study.

Consent for publication: The authors affirm that human research participants provided informed consent for publication of the images in Figures 1 and 4. Patients signed informed consent regarding publishing their data and photographs.

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Tables

Table 1. Patient characteristics

Age (years)	68.4 (7.4)
Men (% of total)	32 (74%)
Body mass index (kg/m^2)	24.8 (3.3)
Coronary risk factors (n, %)	
Hypertension	29 (67%)
Dyslipidemia	21 (49%)
Diabetes mellitus	20 (47%)
Smoking habit	27 (63%)
Family history of CAD	12 (28%)
Chest pain (n, %)	29 (67%)

Data are expressed as the mean (standard derivation), or N (%). CAD, coronary artery disease.

Table 2. Qualitative and quantitative image quality scores in dynamic myocardial CTP with 4D-SF

	Qualitative image quality			Quantitative image quality	
	Noise	Contrast	Sharpness	SNR	CNR
Original image	3.63 (0.49)	4.74 (0.44)	4.70 (0.51)	8.3 (6.5–10.2)	4.4 (3.2–5.8)
25%-dose reduction + 4D-SF	4.98 (0.15)*	4.86 (0.35)	4.65 (0.53)	16.5 (11.9–21.7)*	6.7 (4.6–10.3)*
50%-dose reduction + 4D-SF	4.98 (0.15)*	4.84 (0.37)	4.60 (0.54)	15.6 (11.0–20.8)*	6.6 (4.3–10.1)*
75%-dose reduction + 4D-SF	4.56 (0.55)*†	4.58 (0.63)	4.56 (0.55)	12.8 (8.8–18.1)*†	5.5 (3.5–9.1)*†

Data are expressed as the mean (standard deviation) or median (interquartile range)

*$p < 0.001$, vs. original CTP images; †$p < 0.001$, with 75%- vs. 50%-radiation dose CTP image + 4D-SF. CTP, computed tomography perfusion; 4D-SF, four-dimensional similarity filter; SNR, signal-to-noise ratio; CNR, contrast-to-noise ratio.

Table 3. Myocardial peak CT attenuation, TTP, and CT-MBF in dynamic myocardial CTP with 4D-SF

	Peak CT attenuation (HU)	TTP (s)	CT-MBF (mL/g/min)
Original image	120.5 (16.5)	17.7 (2.9)	2.10 (1.41–2.80)
25%-dose reduction + 4D-SF	119.5 (17.1)	18.0 (3.1)	2.08 (1.41–2.76)
50%-dose reduction + 4D-SF	118.7 (18.0)	18.0 (3.0)	2.07 (1.36–2.83)
75%-dose reduction + 4D-SF	113.3 (22.6)*	17.8 (3.1)	1.82 (0.98–2.64)*

Data are expressed as the mean (standard derivation). *$p < 0.05$ vs. original CTP images. CT, computed tomography; TTP, time to peak; CT-MBF, computed tomography-derived myocardial blood flow; CTP, computed tomography perfusion; 4D-SF, four-dimensional similarity filter; HU, Hounsfield unit.

Figures

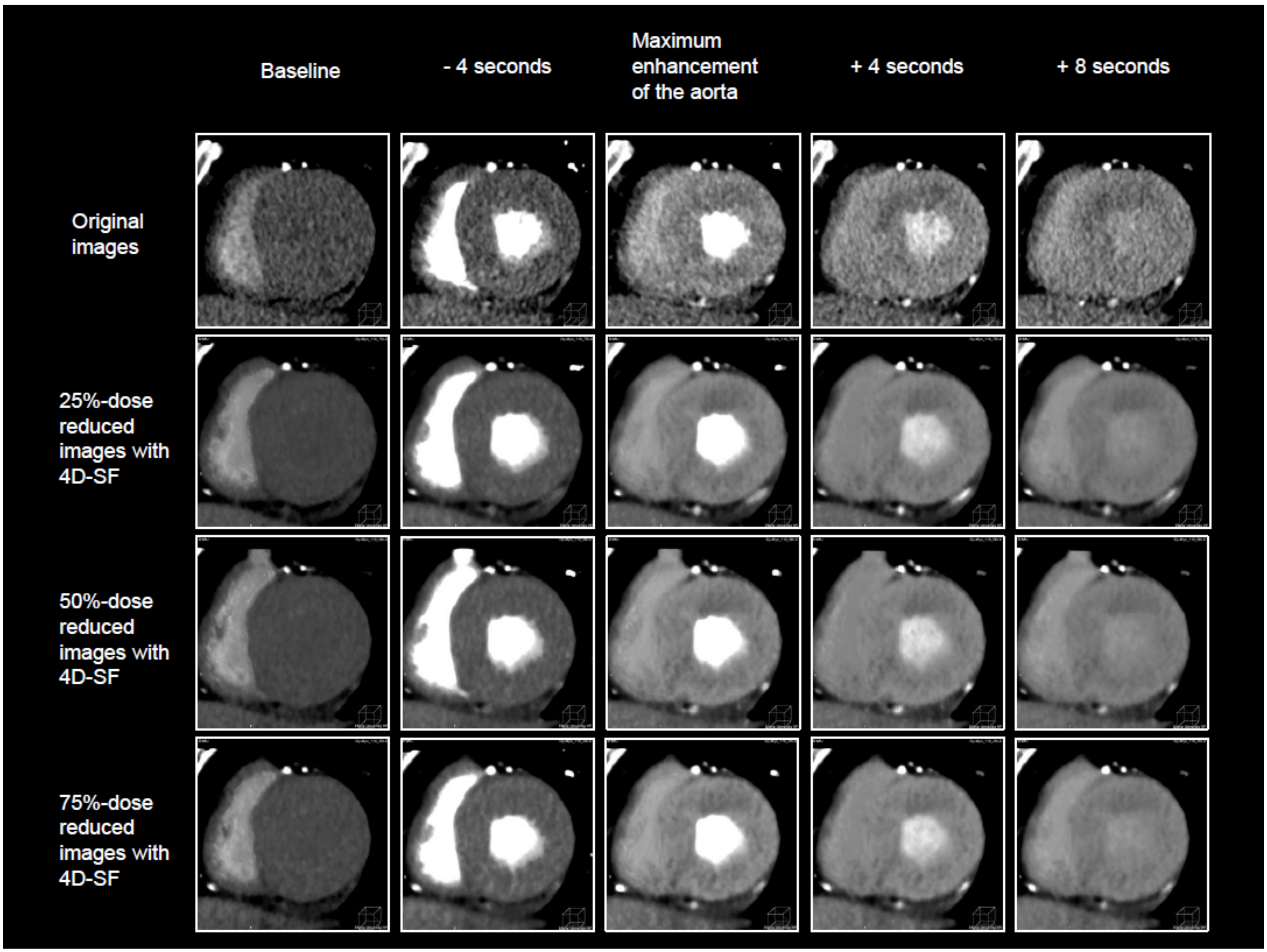

Figure 1

Post-processing of dynamic myocardial CTP images Dynamic CTP images were reconstructed with AIDR 3D and the non-rigid registration algorithm, as the original images. Three other CTP datasets were generated by adding simulated noise corresponding to the dose reduction rate (25%-, 50%-, and 75%-dose reduced-simulated images). The image filtering process with 4D-SF was used after noise simulation processing CTP, computed tomography perfusion; AIDR 3D, adaptive iterative dose reduction 3D; 4D-SF, four-dimensional similarity filter

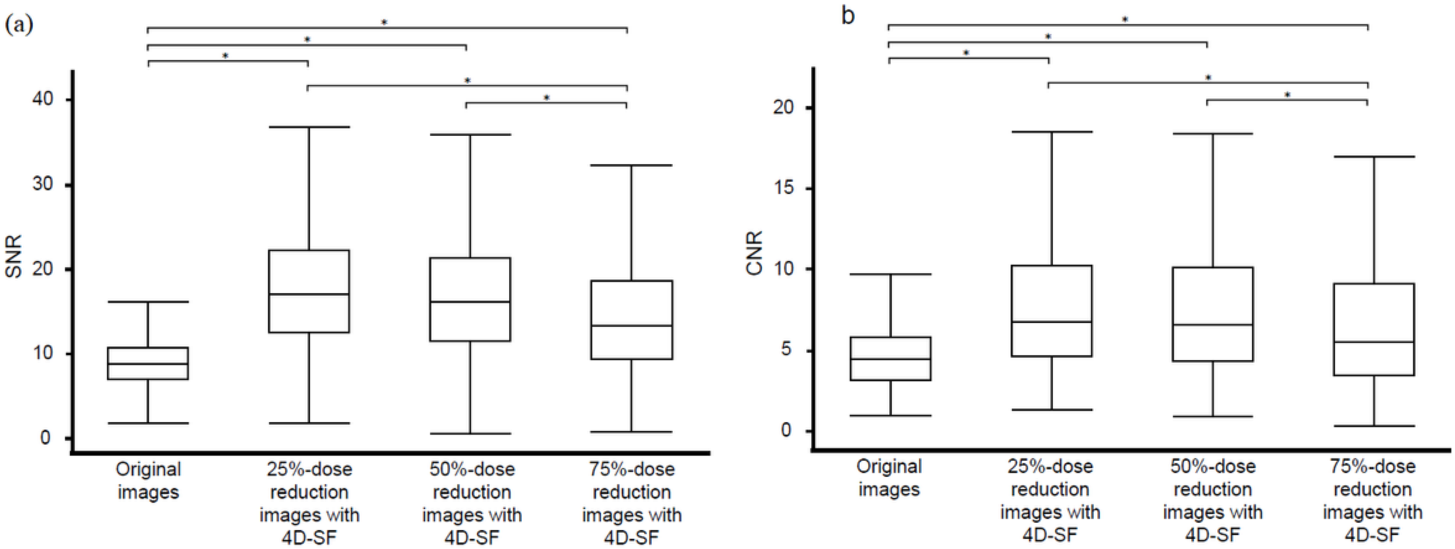

Figure 2

SNR (a) and CNR (b) in original CTP and 25%-, 50%, and 75%-dose reduced images with 4D-SF 4D-SF results in a significant improvement in the SNR and CNR of myocardial CTP images despite dose reduction. Both SNR and CNR were significantly lower in 75%-dose reduced images with 4D-SF than in 25%- and 50%-dose reduced images with 4D-SF SNR, signal-to-noise ratio; CNR, contrast-to-noise ratio; CTP, computed tomography perfusion; 4D-SF, four-dimensional similarity filter. *p < 0.001

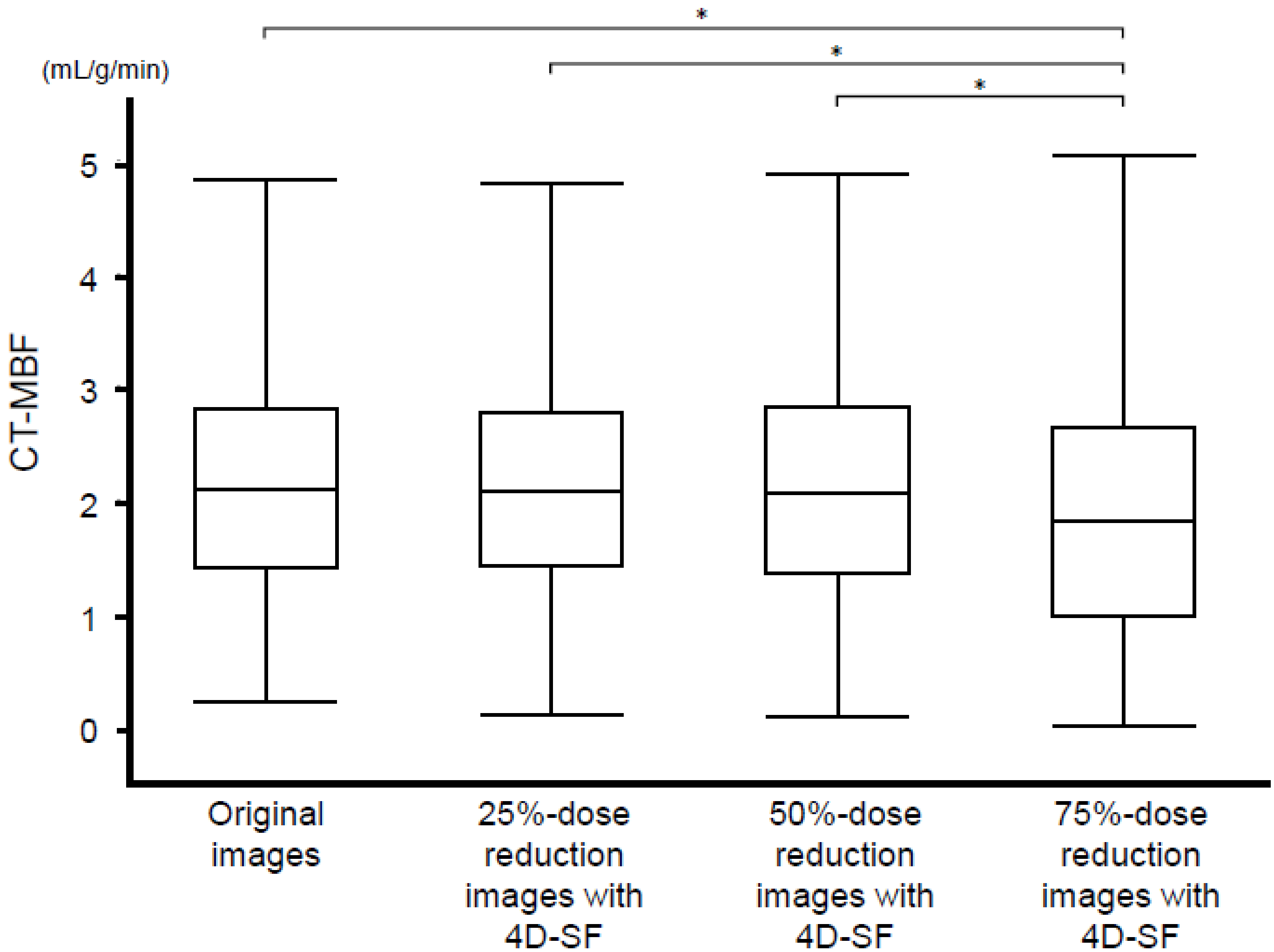

Figure 3

The CT-MBF in original CTP and 25%-, 50%, and 75%-dose reduced images with 4D-SF 4D-SF did not alter the quantification of CT-MBF in the simulated CTP images with 25% and 50% dose reduction. The CT-MBF in 75%-dose reduced images with 4D-SF was significantly lower than that in the original and 25%- and 50%-dose reduced images with 4D-SF CT-MBF, computed tomography-derived myocardial blood flow; CTP, computed tomography perfusion; 4D-SF, four-dimensional similarity filter. *p < 0.05

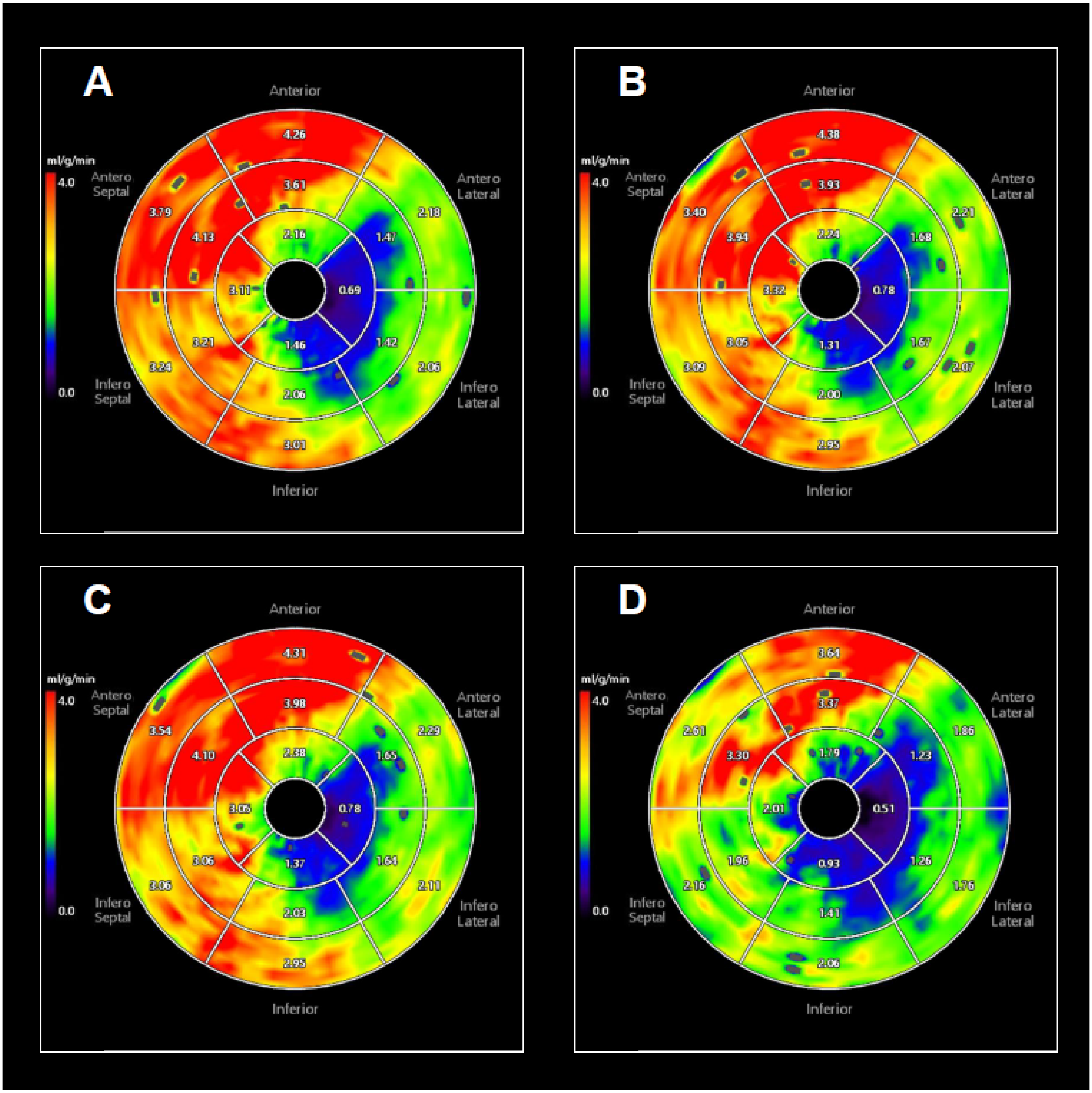

Figure 4

CT-MBF in original CTP images (a) and 25%- (b), 50%- (c), and 75%- (d) dose reduced images with 4D-SF A 73-year-old man with severe stenosis in the left circumflex coronary artery territory. The mean value of CT-MBF in 75%-dose reduced images with 4D-SF (1.91 mL/g/min) was lower than that in the original and 25%- and 50%-dose reduced images (2.53, 2.53, and 2.56 mL/g/min, respectively) CT-MBF, computed tomography-derived myocardial blood flow; CTP, computed tomography perfusion; 4D-SF, four-dimensional similarity filter