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# Improvement of image quality on low-dose dynamic myocardial perfusion computed tomography with a novel 4-dimensional similarity filter

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**Abstract**

The aim of this study was to evaluate the effect of a novel 4-dimensional similarity filter (4DSF) on quantitative and qualitative parameters of low-dose dynamic myocardial computed tomography perfusion (CTP) images.

In this retrospective study, medical records of 32 patients with suspected or known coronary artery disease who underwent dynamic myocardial CTP at 80 kV were included. The 4DSF reduces noise by averaging voxels that have similar dynamic behavior after adaptive iterative dose reduction 3D (AIDR3D) and deformable image registration were applied. Qualitative (artefact, contour sharpness, and myocardial homogeneity [1 = poor; 2 = intermediate; 3 = good]) and quantitative measurement (standard deviation [SD] and signal-to-noise ratio [SNR]) were compared between the 4DSF and AIDR3D. Contrast-to-noise ratio (CNR) between ischemic and normal remote myocardium was also assessed using myocardial perfusion magnetic resonance imaging as the reference standard in seven patients.

The 4DSF was successfully applied to all the images. Improvement in subjective image quality yielded by 4DSF was higher than that yielded by AIDR3D (homogeneity, 1.0 [3 vs 2]; artefact, 1.5 [3 vs 1.5]; $P < .001$) in all patients. The 4DSF significantly decreased the SD by 59% (AIDR3D vs 4DSF: $33.5 \pm 0.4$ vs $13.8 \pm 0.4$, $P < .001$), increased the SNR by 134% (AIDR3D vs 4DSF: $4.4 \pm 0.2$ vs $10.3 \pm 0.2$, $P < .001$), and increased the CNR by 131% (AIDR3D vs 4DSF: $1.6 \pm 0.2$ vs $3.7 \pm 0.2$, $P < .001$).

The 4DSF improved the qualitative and quantitative parameters of low-dose dynamic myocardial CTP images.

**Abbreviations:** 4DSF = 4-dimensional similarity filter, AIDR3D = adaptive iterative dose reduction 3D, ATP = adenosine triphosphate, CNR = contrast-to-noise ratio, CTP = computed tomography perfusion, ECG = electrocardiography, HU = Hounsfield unit, IQR = interquartile range, LV = left ventricle, MDCT = multi-detector row computed tomography, MRI = magnetic resonance imaging, ROI = region of interest, SD = standard deviation, SNR = signal-to-noise ratio.

**Keywords:** dynamic myocardial computed tomography perfusion, four-dimensional similarity filter, ischaemic heart disease, noise reduction technique

## 1. Introduction

Myocardial computed tomography perfusion (CTP) with coronary CT angiography as a single modality can help diagnose functional myocardial ischemia in addition to coronary anatomical stenosis.[1] Compared to static CTP, dynamic CTP has more advantages, such as quantitative evaluation of absolute myocardial blood flow and coronary flow reserve and ability to capture the peak myocardial enhancement.[2] However, dynamic CTP is associated with a higher radiation dose. To solve this problem, dynamic low-dose CTP has been used.[3] However, the image noise would be increased at low dose.[3] Recently, iterative

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reconstruction methods such as adaptive iterative dose reduction 3D (AIDR3D; Canon Medical Systems, Otawara, Japan) have been adapted for noise reduction in dynamic CTP.[4–6] However, iterative reconstruction works for only spatial domain.

Although there were a few studies focusing on noise reduction method for dynamic CTP that works for the time domain,[7,8] most of these methods simply averaged temporally neighboring series. We applied a newly developed 4-dimensional similarity filter (4DSF), which uses per voxel-similarity within the 4D acquisition sequence to average identically perfused tissues, that is, showing similar time density curves to reduce image noise.

The purpose of this study was to compare the effects of the 4DSF and AIDR3D on quantitative and qualitative parameters of low-dose dynamic myocardial CTP image.

## 2. Methods

### *2.1. Patients*

This was a retrospective and single-center study (Hokkaido University Hospital). Ethical approval was obtained from our institutional review board. The requirement for informed consent was waived because of the retrospective nature of the study. Thirty-five patients with confirmed or suspected coronary artery disease who underwent dynamic myocardial CTP at 80 kV from April 2015 to March 2017 were enrolled; patient inclusion and exclusion and patient preparation were performed as reported previously.[9] We excluded 3 patients who previously underwent coronary artery bypass grafting. Therefore, medical records of 32 patients were finally evaluated (aged 67.7±7.5 years). The patient characteristics are summarized in Table 1.

### *2.2. CT examination protocol*

All patients were scanned with 320-row MDCT (Aquilion ONE ViSION edition; Canon Medical Systems Corporation, Otawara, Japan). Dynamic CTP was performed with a tube potential of 80 kV, tube current of 120 mA at 75% R-R interval, and a rotation time of 0.275 seconds.

The protocols of CTP have been previously reported in detail.[9] In brief, with a continuous 6-minute infusion of adenosine triphosphate (ATP; 0.16 mg/kg/min), stress dynamic CTP imaging was performed for 25 seconds with 50 mL of an iodinated contrast agent (Iohexol, 350 mgI/mL, Daiichi Sankyo, Tokyo, Japan) and 30 mL of saline chaser (5.0 mL/s). After a 15-minute interval, rest CTP was performed in the same way as stress dynamic CTP was performed.

**Table 1**

**Patient characteristics.**

| | |
|---|---|
| No. of patients | 32 |
| Age | 67.7±7.5 |
| Male sex, n (%) | 18 (56) |
| Height, cm | 160.6±8.3 |
| Body weight, kg | 64.3 (53.9–71.0) |
| Body mass index | 25.1±3.6 |
| Hypertension, n (%) | 24 (75) |
| Hyperlipidemia, n (%) | 20 (63) |
| Diabetes mellitus, n (%) | 13 (40) |
| Current smoker, n (%) | 8 (25) |
| History of myocardial infarction, n (%) | 1 (3) |
| History of percutaneous catheter intervention, n (%) | 5 (16) |

Age, sex, and body mass index are expressed as mean±SD. Body weight is expressed as median (interquartile range). The remaining parameters were expressed as the number of patients (percentage).

Reconstruction was performed at 1-mm intervals using AIDR3D at strong level and beam-hardening correction as the standard dataset.

### *2.3. Four-dimensional similarity filter*

A dynamic myocardial computed tomography perfusion (CTP) dataset has a vast number of voxels. Each voxel has CT values which changes along time. Since 4DSF is particularly useful for spatially consistent data, motion compensation should be applied to create a dataset that is consistent beforehand. 4DSF needs a large number of voxels having a similar dynamic behavior. **x** and **y** are defined as voxel locations within the datasets. The number of phases is defined as **m** and the sampled phase is defined as **i**. **I(x, i)** is original CT value of a voxel. **Ii(x)** is CT value vector at location **x** excluding phase **i**:

$$\mathrm{Ii}(x) = (\mathrm{I}(\mathrm{x},\mathbf{1}), \mathrm{I}(\mathrm{x},\mathbf{2}), \ldots, \mathrm{I}(\mathrm{x}, i-\mathbf{1}), \mathrm{I}(\mathrm{x}, i+\mathbf{1}), \ldots, \mathrm{I}(\mathrm{x},\mathrm{m})).$$

**D(Ii(x), Ii(y))** is a distance between vectors **Ii(x)** and **Ii(y)**:

$$\mathrm{D}(\mathrm{Ii}(\mathrm{x}), \mathrm{Ii}(\mathrm{y})) = \sqrt{\sum\nolimits_{j=1, j\neq 1}^{m} [Ij(y) - Ij(x)]^2}$$

4DSF searches the suitable voxel **I(y, i)** to make **D(Ii(x), Ii(y))** the smallest throughout the whole 3-dimensinal datasets, and then replace **I(x, i)** and **I(y, i)**. 4DSF repeats this process over and over and make the time-intensity curves smoother. The global search for similar voxels provides a more natural texture than local spatial filtering does. In addition, this method reduces motion artefacts and provides extremely stable images of anatomic structures across the whole dynamic acquisition. Because filtering mainly occurs in the temporal domain, spatial resolution is not reduced and the sharpness of tissue contour is preserved.[10]

4DSF can be applied by the specific software with these algorithm installed in the commercially available workstation (Vitrea; Canon Medical Systems Corporation, Otawara, Japan). 4DSF can be applied to each stress and rest CTP dataset, respectively.

In this study, 4DSF was additionally applied to the standard dynamic datasets with AIDR3D, which was applied to each of stress and rest dynamic 3D volume datasets. Deformable image registration was performed with Vitrea workstation before applying 4DSF.

### *2.4. Myocardial perfusion MRI acquisition*

Presence of myocardial ischemia was evaluated in 7 patients by myocardial perfusion MRI. All seven patients had myocardial ischemia with multivessel diseases.

Perfusion MRI was performed using a 3T whole-body scanner (Achieva Tx; Philips Medical Systems, Best, The Netherlands) with a 32-channel phased-array receiver torso-cardiac coil. The turbo field-echo technique with saturation recovery magnetization (slice thickness, 8 mm; field of view, 380 mm × 380 mm; matrix, 224 × 224) was used.

Stress myocardial perfusion MRI was performed as described previously.[11] In brief, perfusion MR images were obtained using ECG-triggered breath-hold technique in three short axes (basal, mid-ventricular, and apical). Three minutes after ATP infusion

(0.16 mg/kg/min), dynamic stress myocardial perfusion MRI was performed with 0.03 mmol/kg Gd-DTPA (Magnevist, Bayer, Wayne, NJ) and 20 mL saline chaser (4.0 mL/s). Rest myocardial perfusion MRI was also performed after stress myocardial perfusion MRI.

### 2.5. Qualitative analysis

The images were reformatted with short axes of the left ventricle (LV) at the basal, mid, and apical levels for each of the stress and rest CTP images at the peak enhancement of myocardium, with a slice thickness of 3 mm. Two independent readers (HK and TH; board certified radiologists) evaluated the image quality in a blinded, randomized fashion. They took a training course how to interpret dynamic myocardial CTP before the evaluation (the lecture about anatomy and image interpretation of dynamic CTP, and hands-on session using six datasets [stress and rest images] with three vessel territories for each basal, mid-ventricular and apical slice). Visual quality of each AIDR3D and 4DSF image belonging to the 32 patients was subjectively graded (artefacts for stress and rest, contour sharpness between LV cavity and myocardium, and myocardial homogeneity for rest images) for each of the 3 coronary territories on a 3-point scale (1 = poor, 2 = intermediate, 3 = good). Per-patient scores of the three vessel territories were averaged. The grades were averaged between readers for each measurement and patient. Inter-reader agreement was computed using kappa statistics.

### 2.6. Quantitative analysis

A radiologist (ST; 2 years of cardiac MRI experience) quantitatively assessed image quality using rest and stress images by measuring the image noise, signal-to-noise ratio (SNR), and contrast-to-noise ratio (CNR) between normal and ischemic myocardium (Fig. 1).

Regions of interest (ROI) were manually placed at each of the American Heart Association's (AHA) standard 16 myocardial segments (except for the apex) in each level (six 100 $mm^2$ ROIs at each basal and mid-ventricular segment, and 4 ROIs at apical segment) at the time of peak enhancement of the myocardium. SNR was evaluated using all 16 ROIs in rest CTP images and using ROIs without visible ischemia in stress CTP images. SNR was calculated as the mean attenuation of the normal myocardium divided by the SD value.

In segments with visible ischemia, as determined by stress perfusion MRI, CNR was calculated as the difference in CT attenuation between the hypoperfused and remote myocardium, divided by the SD value of the remote myocardium.

Among the 14 myocardial datasets (7 datasets each for stress and rest CTP), 1 stress dataset was excluded because of excessive motion artefacts, and a total of 6 segments were excluded owing to beam-hardening or streak artefacts. Therefore, a total of 202 segments were included. The image noise was assessed with 154 segments (110 segments in rest CTP datasets and 44 segments in stress CTP datasets). CNR was assessed with 48 segments in stress CTP datasets. The number of patients and segments in MRI datasets are summarized in Fig. 2.

### 2.7. Statistical analysis

All data are expressed as mean ± SD except for body weight. Because body weight was not normally distributed, it is expressed as median and interquartile range (IQR). Normal distribution was assessed using the Shapiro-Wilk test. Qualitative scores were statistically compared using the paired Wilcoxon rank sum test. Kappa statistics were computed to assess inter-reader agreement in the qualitative scores. Quantitative value was statistically assessed with Student *t* test. All statistical analyses were performed using JMP14. Differences were considered to be statistically significant when *P* values were <.05.

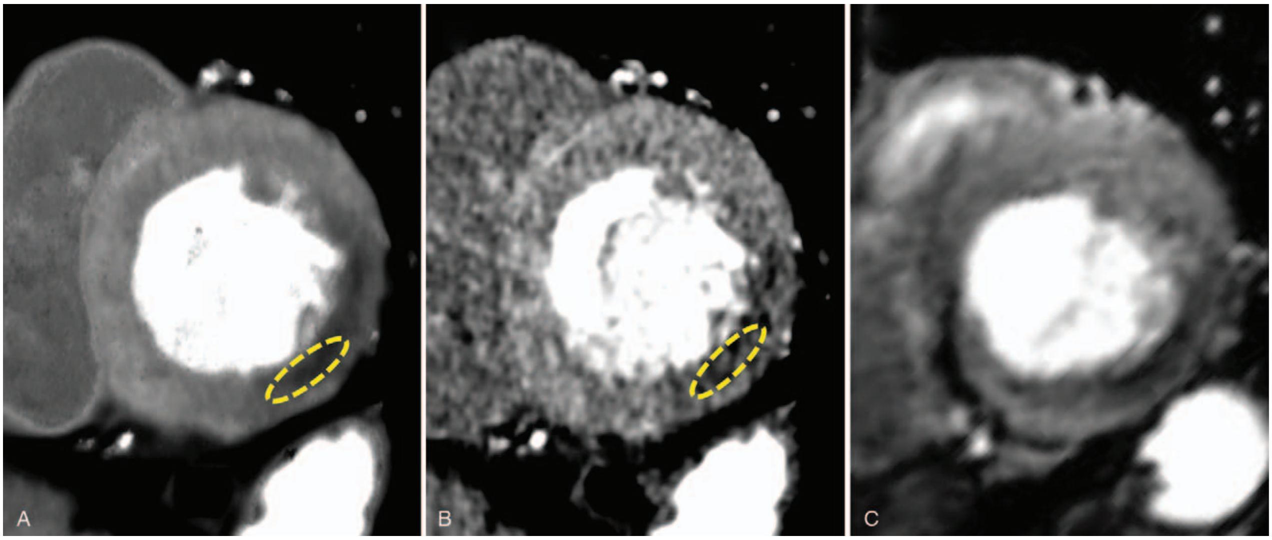

**Figure 1.** A case of a man in his 70s with severe stenosis in the left circumflex artery. The clarity of ischemia at the lateral wall in the basal level is higher with 4-dimensional similarity filter (4DSF) (A) than with adaptive iterative dose reduction 3D (AIDR3D) (B), because of less image noise; corresponding stress myocardial perfusion MR image (C) for reference. For example, the region of interest in the American Heart Association segment 5 is placed as shown in (A, B) for the calculation of contrast-to-noise ratio. In this case, visual image quality scores (artefacts, contour sharpness, myocardial homogeneity) of 4DSF were (3, 3, 3) (A) and the scores of AIDR3D were (2, 3, 2) (B).

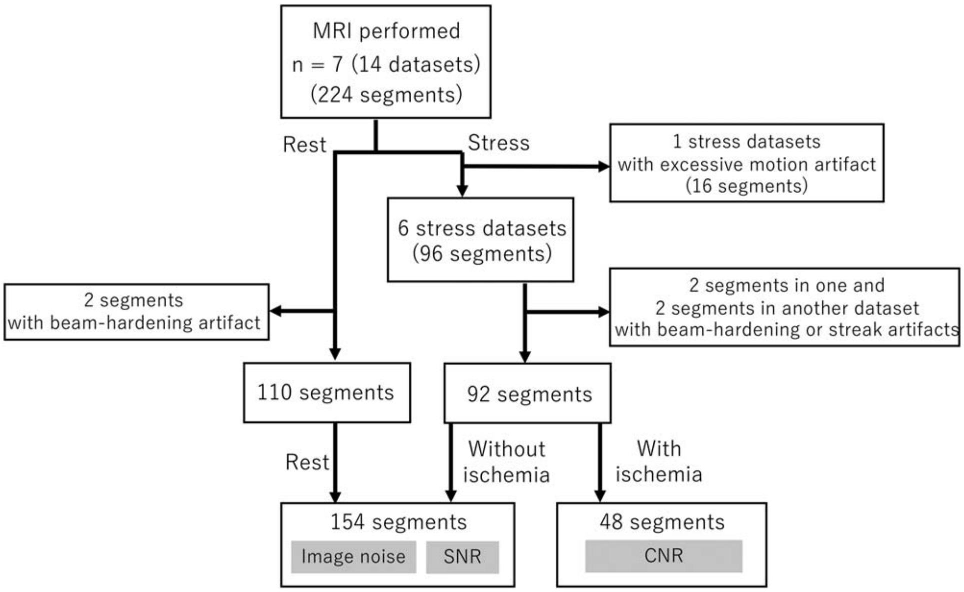

**Figure 2.** Enrolment of magnetic resonance imaging datasets. CNR = contrast-to-noise ratio, SNR = signal-to-noise ratio.

## 3. Results

The 4DSF was successfully applied to the CTP images of all 32 patients. There were no specific artefacts or technical errors in process.

### 3.1. Qualitative analysis

There were no significant differences in the scores among the 3 coronary vessel territories. Improvement in subjective image quality yielded by using 4DSF was higher than that yielded by using AIDR3D (homogeneity, 1.0 (3.0 vs 2.0); artefacts, 1.5 (3.0 vs 1.5); $P < .001$) in all images. Sharpness score was either equal or improved in all images (Fig. 3). The kappa value was moderate (kappa = 0.54 [95% confidence interval, CI: 0.48–0.59]).

### 3.2. Quantitative analysis

The 4DSF significantly decreased the mean image noise in all segments by 59% (4DSF vs AIDR3D: 13.8 ± 0.4 vs 33.5 ± 0.4, $P < .001$) and increased the SNR by 134% (4DSF vs AIDR3D: 10.3 ± 0.2 vs 4.4 ± 0.2, $P < .001$). The difference in CT values between normal and ischemic myocardium was 51.8 ± 21.0 HU with 4DSF and 52.2 ± 24.4 HU with AIDR3D. The 4DSF increased the CNR by 131% (4DSF vs AIDR3D: 3.7 ± 0.2 vs 1.6 ± 0.2, $P < .001$) (Fig. 4).

## 4. Discussion

Our study applied the novel 4DSF method to low-dose dynamic myocardial CTP images. The 4DSF improved visual homogeneity

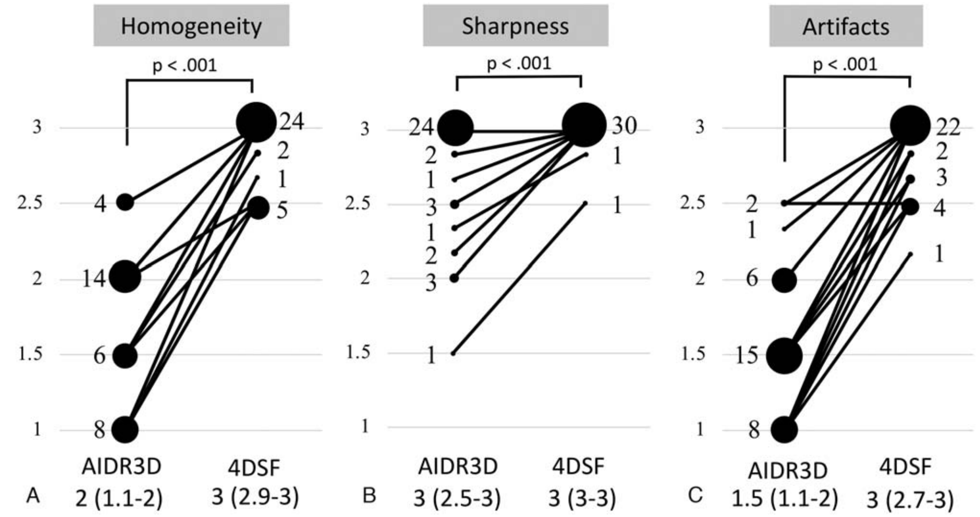

**Figure 3.** Paired plots of qualitative scores. The numbers of patients are indicated beside the dots. The dots' sizes correlate with the number of patients. The 4DSF significantly improved homogeneity and artefact scores (all, $P < .001$), relative to AIDR3D (A, C). The average of sharpness score was equal but statistically improved ($P < .001$) between 2 reconstructions (B). The scores were expressed as median (IQR). 4DSF = 4-dimensional similarity filter, AIDR3D = adaptive iterative dose reduction 3D.

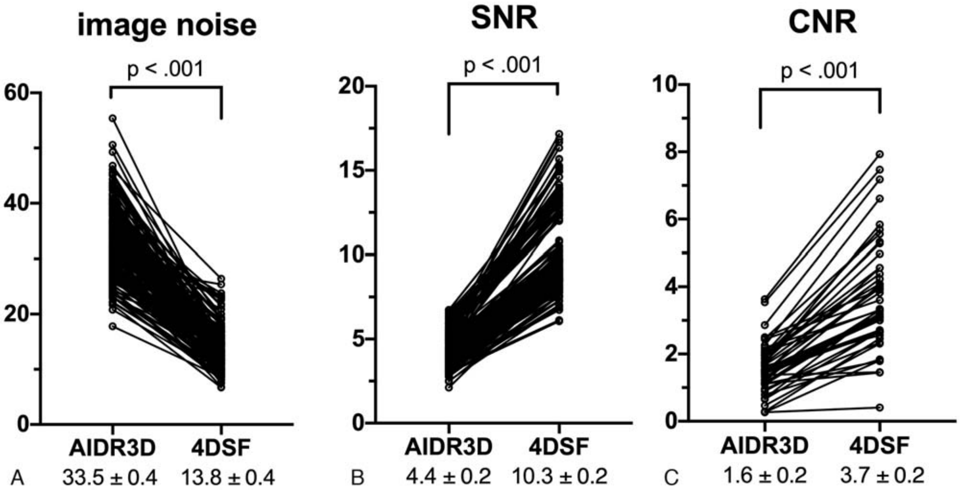

**Figure 4.** The paired comparison plots of image noise, SNR, and CNR. The mean image noise with the 4DSF was significantly lower than that with AIDR3D ($P < .001$) (A). SNR with the 4DSF was significantly higher than that with AIDR3D ($P < .001$) (B). CNR with the 4DSF was significantly higher than that with AIDR3D ($P < .001$) (C). The scores were expressed as mean ± SD. 4DSF = 4-dimensional similarity filter, AIDR3D = adaptive iterative dose reduction 3D, CNR = contrast-to-noise ratio, SNR = signal-to-noise ratio.

of myocardial attenuation and reduced artefacts in dynamic CTP images. Moreover, the 4DSF significantly decreased the mean image noise and increased SNR and CNR.

Myocardial CTP images have a poorer CNR than MR perfusion images do.[12] The difference in CT value between ischemic and normal remote myocardium is small, (approximately 20 HU at 100 kV).[13,14] In our study, the difference in CT value between ischemic and normal myocardium, obtained by using both the methods, was relatively high (AIDR3D, 53.6 HU; 4DSF, 51.1 HU) owing to low-dose protocol with 80 kV. Moreover, our study showed the 4DSF decreased image noise by 59% and increased CNR by 131% (4DSF vs AIDR3D: 33.5 vs 13.8 and 3.7 vs 1.6, respectively). Therefore, the 4DSF would facilitate better visualization of ischemia. Regarding subjective evaluation, myocardial homogeneity, contour sharpness, and artefacts were improved by the 4DSF.

For dynamic CTP, there were several techniques to reduce image noise, which were divided into the approaches to improve sinogram data or to improve reconstructed CT images using various filters. Iterative reconstruction technologies such as AIDR3D improve sinogram data and were generally used for noise reduction in dynamic myocardial CTP images.[5] It is effective for spatial denoising. However, it does not ensure temporal smoothness. On the other hands, noise reduction filters used for spatial denoising and temporal smoothness. Some previously reported noise reduction methods, regarding temporal domain, used temporal information to average voxels in the temporally neighbor series alone.[7,8,15] A modified simple linear iterative clustering algorithm with robust perfusion quantification (SLICR) employed temporal voxels' similarity of dynamic myocardial CTP.[16] SLICR generates super-voxels of tissues with similar hemodynamic properties on the basis of both spatial and temporal feature distances from the targeted voxel. Although SLICR is useful for calculating quantitative myocardial blood flow (MBF) or generating MBF map, generating super-voxel with SLICR leads to loss of spatial resolution. The 4DSF is unique voxel-wise algorithm that results in potent noise reduction without losing spatial resolution or temporal information. Another voxel-wise technique for high resolution myocardial CTP has been presented that combines temporal filtering with principle component analysis.[17] In their study, image noise was reduced by 34% (SD: 21.4 vs 14.1) and SNR was increased by 47% (3.6 vs 5.3).[17] We did not compare these methods and 4DSF directly; however, their results were similar to our study. For dynamic CTP, the algorithm with temporal domain would be effective for image noise reduction.

Our study had several limitations. First, we included a small number of patients who were confirmed to have myocardial ischemia with MRI, which allowed the presentation of descriptive statistics alone. Second, this study did not compare the absolute MBF between AIDR3D and the 4DSF. We have previously established the algorithm and validated the absolute MBF values with AIDR3D compared to $^{15}$O-water PET.[9,18] Since 4DSF reduced image noise, it would be expected to improve the algorithm. Further investigations must be performed to study the effect of 4DSF on the absolute myocardial blood flow.

In conclusion, the 4DSF improved the qualitative and quantitative parameters of low-dose dynamic myocardial CTP. The improvement in CNR suggests that 4DSF facilitates better visualization of myocardial ischemia in dynamic myocardial CTP images.

## Author contributions

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**Writing – original draft:** Satonori Tsuneta, Noriko Oyama-Manabe.
**Writing – review & editing:** Noriko Oyama-Manabe.

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