

[ORIGINAL ARTICLE]

Improved Diagnostic Performance of New-generation 320-slice Computed Tomography with Forward-projected Model-based Iterative Reconstruction SoluTion for the Assessment of Late Enhancement in Left Ventricular Myocardium

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Abstract:

Objective Forward-projected Model-based Iterative Reconstruction SoluTion (FIRST) is a novel reconstruction method. We investigated the improvement in the diagnostic performance for the detection of abnormal late enhancement (LE) in left ventricular myocardium (LVM) using a new-generation 320-slice computed to-mography (CT) device with FIRST.

Methods This is a retrospective study that included 100 adult patients who underwent cardiac CT including a late phase scan and magnetic resonance imaging (MRI) within 3 months. The first 50 consecutive patients (first-generation group) underwent first-generation 320-slice CT without FIRST, and the next 50 consecutive patients (second-generation group) underwent second-generation 320-slice CT with FIRST. We compared the diagnostic performance of the first- and second-generation 320-slice CT with FIRST with MRI as a reference standard to detect LE in LVM.

Results In the patient-based analysis, the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of detection of LE on CT were 79%, 90%, 92%, 76%, and 84%, respectively, in the first-generation group and 97%, 84%, 91%, 94%, and 92%, respectively, in the second-generation group. The sensitivity was significantly higher in the second-generation group than in the first-generation group (p=0.049). In the segment-based analysis, the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of detection of LE on CT were 69%, 96%, 83%, 92%, and 90%, respectively, in the first-generation group and 87%, 94%, 84%, 95%, and 92%, respectively, in the second-generation group. The sensitivity and negative predictive value were significantly higher in the second-generation group than in the first-generation group (p<0.001 and p=0.016). The contrast-noise ratio was significantly higher in the second-generation group than in the first-generation group (p<0.001 and p=0.016). The contrast-noise ratio was significantly higher in the second-generation group than in the first-generation group than in the first-generation group (5.6±1.7 vs. 2.8± 1.1, p<0.001), and the radiation dose for the assessment of LE on CT was significantly higher in the first-generation group than in the first-generation group (4.7±2.7 mSv vs. 2.3±0.1 mSv, p<0.001).

Conclusion The diagnostic performance for the detection of LE in LVM significantly improved with the use of second-generation 320-slice CT and FIRST.

Key words: left ventricular myocardium, late enhancement, new generation computed tomography, Forwardprojected Model-based Iterative Reconstruction SoluTion (FIRST)

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Introduction

Late enhancement (LE) assessed by magnetic resonance imaging (MRI) represents myocardial damage (e.g., myocardial fibrosis) on pathology (1), which provides incremental value in addition to the left ventricular (LV) ejection fraction for predicting worse clinical outcomes in patients with ischemic and non-ischemic cardiomyopathy (2). Cardiac MRI is the gold-standard modality for evaluating LE (3) but is contraindicated for patients with old cardiovascular implantable electronic devices or claustrophobia.

Cardiac computed tomography (CT) is more commonly used in daily clinical practice than cardiac MRI (4) and can also evaluate LE (5). Thus, cardiac CT is a viable alternative to MRI for assessing LE, although recent guidelines do not recommend evaluating LE with CT due to the suboptimal diagnostic accuracy and lack of evidence (6). Forwardprojected Model-based Iterative Reconstruction SoluTion (FIRST), a recently developed imaging reconstruction technique, has been proposed for use with new-generation 320slice CT and can provide high-quality CT images even in a low-radiation scan setting (7). Furthermore, in addition to such improvements in the reconstruction technique, mechanical improvements have also been achieved with newgeneration 320-slice CT devices, as the maximum tube current and gantry rotation speed have been increased (8).

We previously reported on the improvement in the diagnostic performance of new-generation 320-slice CT with FIRST for detecting LE compared with previous settings (8). However, only patients with non-ischemic myocardial disease were included in that study, and the number of subjects who underwent CT examinations using new generation CT was small in that study (8).

The present study evaluated the improvement in the diagnostic performance of the new generation 320-slice CT with FIRST for detecting LE in LV myocardium (LVM) compared with previous settings in patients with various types of myocardial disease or cardiac tumors. We also explored the factors with a significant influence on the image quality of LE in new-generation 320-slice CT.

Materials and Methods

Patient population

This is a retrospective study enrolling 100 adult patients who underwent electrocardiogram (ECG)-gated cardiac CT including late-phase scans and cardiac MRI including cardiac-gated T1-weighted sequences to detect abnormal LE in LVM within a 3-month interval, and who did not undergo open heart surgery between the performance of the two cardiac imaging tests. Informed consent was obtained from all patients. Patients were classified into either the first- (n=50) or second- (n=50) generation group. In the first-generation group, 50 consecutive patients underwent both first-

generation 320-slice CT (Aquilion One; Cannon Medical Systems, Otawara, Japan) and 1.5-T cardiac MRI (Achieva; Philips Medical Systems, Best, the Netherlands) from December 2008 to October 2010 at Chiba University Hospital. The late-phase CT images were reconstructed with filtered back projection at prospective ECG-gated acquisition.

The second-generation group included 50 consecutive patients who underwent both second-generation 320-slice CT (Aquilion one ViSION Edition; Cannon Medical Systems, Otawara, Japan) using the new image reconstruction technique FIRST and 3.0-T cardiac MRI (Ingenia; Philips Medical Systems) from February 2016 to October 2017 at Chiba University Hospital.

The ethics committee of Chiba University approved this study.

CT protocol

On cardiac CT, all patients underwent early-phase acquisitions at 30 to 40 seconds after the injection of contrast media for the evaluation of coronary artery stenosis in the early-phase CT images. They also underwent late-phase acquisitions at about 6 to 8 minutes after the injection of contrast (without additional contrast injection), as contrast defects in the LVM or cardiac lumen were suspected in the early-phase images and myocardial damage or luminal thrombus were suspected (5, 8, 9). The slice thickness was 0.5 mm, and the prospective ECG gating acquisition was selected in both groups to reduce the radiation dose. The tube voltage was decreased from 120 kV to 80 or 100 kV from the first- to the second-generation group, while the tube current was increased from 248±86 mA to 803±19 mA for image noise reduction. FIRST, which is a novel image reconstruction technique, was used for additional noise reduction of CT images only in the second-generation group (7).

In brief, 100 mL of iodine contrast media was injected in each case, but the amount of contrast media was modified based on the body weight or renal function of each case. The CT scanning parameters for late-phase acquisitions in the two groups are summarized in Table 1. The radiation dose of scanning for late enhancement was calculated from the dose-length product in a dose report in both groups (conversion factor 0.014) (10).

MRI protocol

During the MRI examination, patients were placed in the supine position in a clinical 1.5- or 3.0-T MRI machine with 5-channel cardiac or dS Torso coils around the chest. All MR images were obtained with ECG gating and during repeated breath-holds (11). Surface-coil intensity correction was performed for cine MR and MR for LE. Cine MR images were acquired with a steady-state free precession sequence. After acquiring cine MR images on the two- and four-chamber long-axis views, we obtained short-axis cine MR images for LE were acquired 10 to 15 minutes after intravenous administration of 0.15 mmol/kg of gadolinium contrast

	First-generation Group (n=50)	Second-generation Group (n=50)	p value
Slice thickness	0.5mm	0.5mm	-
ECG gating	Prospective ECG gating	Prospective ECG gating	-
Speed of gantry rotation (sec)	0.352±0.008	0.351±0.031	0.98
Tube voltage (kV)	120	81±5	<0.001
Tube current (mA)	248±86	803±19	<0.001
Amount of iodine dose for contrast per body weight (mg/kg)	608±164	635±170	0.42
Image reconstruction	FBP	FIRST	-

 Table 1. Details of Computed Tomographic Scanning Parameters for Late-phase Acquisition.

FBP: filtered back projection, FIRST: Forward-projected Model-based Iterative Reconstruction SoluTion

agent. An inversion-recovery prepared, T1-weighted, 3D gradient-echo sequence was used to obtain MR images for LE in the same planes as cine images. The inversion time was adjusted to minimize the signal from the normal myocardium in each patient, by using a look-locker sequence to find a null point of normal myocardium. The typical inversion time for LE MR ranged from 230 to 330 ms. Imaging data were analyzed on workstations (Ziostation 2; Ziosoft, Tokyo, Japan), as we previously reported (11).

Image analyses

LE was defined as lesions with elevated CT attenuation, relative to the remainder of the myocardium, within the LVM in the late-contrast-phase CT images (8). The LVM was divided into 17 segments according to the American Heart Association definition (12), and LE was assessed on a patient and segment basis. In the patient-based analysis, the subjects were categorized as having LE when LE was observed for at least one lesion in the LVM. In the segmentbased analysis, the segment was considered concordant when LE was detected at corresponding sites on both CT and MRI. The presence of LE on CT and MRI in all cases was evaluated by an experienced observer (H.T.), and those in the first 20 cases in both generation groups were evaluated by another experienced observer (M.U.). The interobserver variability was evaluated in those 20 cases in each group.

In addition, the contrast-to-noise ratio (CNR) was defined as in a previous study (slightly modified) (13) and calculated in the cases with LE on both CT and MRI. CT values were measured by tracing regions of interest (ROIs) on CT images, and the size of the ROIs were 50 mm² for measuring normal LVM and 10 mm² for measuring LE (Fig. 1). "Contrast" was defined as the difference in the mean CT value between the LE and normal LVM, and "noise" was defined as the standard deviation of the normal LVM. Finally, the CNR was calculated by dividing the "contrast" by the "noise" in each case (13) and then was compared between the first- and second-generation groups to assess the image quality. The correlation of the CNR and the amount of iodinate dose of contrast medium per body weight or body mass index (BMI) was also evaluated. The primary endpoint of the present study was the comparison of the patient - and segment-based diagnostic performance of the first - and second-generation CT findings with MRI as a reference standard to detect LE in LVM.

Statistical analyses

Statistical analyses were carried out using the software packages (SPSS software, version 17.0; IBM SPSS, Chicago, USA). All quantitative data are expressed as the mean ±standard deviation and were compared using an independent t-test. Qualitative data, including the distribution of the causative diseases and diagnostic accuracy, were compared using the chi-square test (if any expected count is less than 5, Fisher's exact test was used). Inter-observer variability was evaluated by kappa statistics and compared using the chi-square test (if any expected count is less than 5, Fisher's exact test was used). The relationship between variables was analyzed using Pearson's correlation coefficient. p<0.05 was considered statistically significant.

Results

The details of CT scanning parameters for late-phase acquisition are shown in Table 1. The tube current was significantly higher in the second-generation group than in the first-generation group (803 ± 19 vs. 248 ± 86 mA, p<0.001), but the tube voltage was significantly lower in the secondgeneration group than in the first-generation group (81 ± 5 vs. 120 kV, p<0.001). The speed of gantry rotation and the iodine dose of contrast medium per body weight were not significantly different between the two groups.

The patient characteristics are shown in Table 2. There was no significant difference in the distribution of the background disease between the two groups (Table 2). Four and five patients in the first- and second-generation group had ischemic cardiomyopathy. Typical images of LE in LVM on CT and MRI in the first- and second-generation groups are shown in Figs. 2 and 3. The inter-observer agreement assessed by kappa statistics between 2 independent observers was 0.83 in the first-generation group and 0.79 in the second-generation group, with no significant difference (p= 0.44). The CNR was negatively correlated with the BMI (r



Figure 1. Measurement of contrast noise ratio of CT image. Contrast on CT was defined as the CT value of LE (ROI 10 mm²) in LVM minus the CT value of normal LVM (ROI 50 mm²), and noise on CT was defined as the standard deviation of the CT value of normal LVM. The diagnostic accuracy of LE on LVM, contrast-to-noise ratio, and inter-observer agreement on CT were compared between the two groups. LV: left ventricle, RV: right ventricle, LE: late enhancement, ROI: region of interest, LVM: left ventricular myocardium

Table 2.	Patient	Characteristics.
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	First-generation Group (n=50)	Second-generation Group (n=50)	p value
Age	57±14	58±13	0.36
Male	28 (56%)	29 (58%)	0.84
Body Mass Index (BMI) (kg/m ²)	23±5	24±5	0.41
Interval between CT and MRI (days)	29±21	21±24	0.07
Hypertrophic Cardiomyopathy	15 (30%)	9 (18%)	0.16
Cardiac sarcoidosis	5 (10%)	9 (18%)	0.25
Dilated cardiomyopathy	5 (10%)	7 (14%)	0.54
Ischemic cardiomyopathy	4 (8%)	5 (10%)	1.00
Collagen disease	4 (8%)	2 (4%)	0.68
Myocarditis	4 (8%)	0 (0%)	0.12
Hypertensive heart disease	2 (4%)	3 (6%)	1.00
Cardiac tumor	2 (4%)	1 (2%)	1.00
Valvular disease	1 (2%)	2 (4%)	1.00
Cardiac amyloidosis	1 (2%)	2 (4%)	1.00
Pericarditis	1 (2%)	1 (2%)	1.00
Shunt disease	1 (2%)	0 (0%)	1.00
Fabry disease	1 (2%)	0 (0%)	1.00
Drug induced cardiomyopathy	1 (2%)	0 (0%)	1.00
POEMS syndrome	1 (2%)	0 (0%)	1.00
Myopathy	1 (2%)	0 (0%)	1.00
Muscle dystrophy	0 (0%)	1 (2%)	1.00
Tachy-induced cardiomyopathy	0 (0%)	1 (2%)	1.00
Takotsubo cardiomyopathy	0 (0%)	1 (2%)	1.00
Sigmoid septum	0 (0%)	1 (2%)	1.00
Unknown	1 (2%)	5 (10%)	0.20
Radiation dose (mSv)	4.7±2.7	2.3±0.1	< 0.001

POEMS: polyneuropathy, organomegaly, endocrinopathy, M-protein, and skin changes syndrome

=-0.46, p=0.011) significantly in the second-generation group but not significantly in the first-generation group (r= -0.16, p=0.47). The CNR was also positively correlated with the iodine dose of contrast medium per body weight (r=

0.46, p=0.011) in the second-generation group but not significantly in the first-generation group (r=0.29, p=0.18). The CNR was significantly higher in the second-generation than in the first-generation group (5.6 ± 1.7 vs. 2.8 ± 1.1 , p<0.001).



Figure 2. Representative images of late enhancement in the first-generation group. (A) and (B) are CT and MRI images of a case with Fabry disease. (C) and (D) are CT and MRI images of a case with dilated cardiomyopathy. Arrows indicate late enhancement in left ventricular myocardium. CT images were acquired with first-generation 320-slice CT and reconstructed with filtered back projection. LV: left ventricle, RV: right ventricle

The radiation dose on scanning for LE was 4.7 ± 2.7 mSv in the first-generation group and 2.3 ± 0.1 mSv in the second-generation group, being significantly smaller in the second-than in the first-generation group (p<0.001) (Table 2).

The patient-based analysis

In the patient-based analysis, LE on CT and MRI was detected in 25 (50%) and 29 (58%) subjects in the firstgeneration group, respectively, and 33 (66%) and 31 (62%) subjects in the second-generation group, respectively. No significant difference of the percentages of patients with LE on MRI was observed between the 2 groups (p=0.68). The sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and overall accuracy of detection of LE on CT compared to MRI as a reference standard were 79%, 90%, 92%, 76%, and 84% in the first-generation group, respectively, and 97%, 84%, 91%, 94%, and 92% in the second-generation group, respectively (Fig. 4). The sensitivity was significantly higher in the second-generation group than in the first-generation group (p=0.049).

The segment-based analysis

In the segment-based analysis, LE on CT and MRI was detected in 150 and 181 segments in the first-generation group, respectively, and 231 and 225 segments in the second-generation group, respectively, among a total of 850 segments in each group. The sensitivity, specificity, PPV,

NPV, and overall accuracy of detection of LE on CT compared to MRI were 69%, 96%, 83%, 92%, and 90% in the first-generation group, respectively, and 87%, 94%, 84%, 95%, and 92% in the second-generation group, respectively (Fig. 5). The sensitivity and NPV were significantly higher in the second-generation group than in the first-generation group (p<0.001, p=0.016).

Discussion

The present study showed that the diagnostic performance of the detection of LE on CT was better in the secondgeneration group than in the first-generation group in a segment-based analysis, especially concerning the sensitivity and NPV. In the patient-based analysis, the sensitivity of detecting LE on CT was also higher in the second-generation group than in the first-generation group. In addition, the CNR in the second-generation group was significantly higher than that in the first-generation group and was positively correlated with the iodine dose of contrast medium per body weight while negatively correlated with the BMI in both groups.

Clinical perspective of an LE analysis using CT

Cardiac MRI is the gold-standard modality for evaluating LE (3), which is clinically useful for not only diagnosing various types of myocardial diseases (14) but also assessing



Figure 3. Representative images of late enhancement in the second-generation group. (A) and (B) are CT and MRI images of a case with myocardial disease of unknown etiology. (C) and (D) are CT and MRI images of a case with hypertrophic cardiomyopathy. Arrows indicate late enhancement in left ventricular myocardium. CT images were acquired second-generation 320-slice CT and reconstructed with Forward-projected Model-based Iterative Reconstruction SoluTion. LV: left ventricle, RV: right ventricle



Figure 4. Diagnostic performance of late enhancement on computed tomography compared with magnetic resonance images as the gold standard: A patient-based analysis. NPV: negative predictive value, PPV: positive predictive value



Figure 5. Diagnostic performance of late enhancement on computed tomography compared with magnetic resonance images as the gold standard: A segment-based analysis. NPV: negative predictive value, PPV: positive predictive value

the risks of adverse cardiac events (2). However, the number of cardiac MRI procedures performed each year is only onetenth of the cardiac CT procedures performed (4). MRI is also contraindicated for patients with old cardiovascular implantable electronic devices or claustrophobia. In addition, it is often difficult to obtain clear LE images on MRI in cases with arrhythmia, such as atrial fibrillation or frequent ventricular premature beats, whereas 320-slice CT can perform imaging without severe motion artifacts in these arrhythmic cases (15). Therefore, 320-slice CT is a potential alternative to MRI for evaluating LE in daily clinical practice. Candidates for trans-catheter aortic valve implantation (TAVI) are also good candidates for LE assessment on CT, as CT screening just before TAVI is necessary, and the assessment of myocardial damage is clinically important for these patients. They are also relatively old, and the negative effects of CT radiation are relatively small (16).

We previously evaluated the diagnostic performance of 16-slice CT for the detection of LE compared with MRI as a reference standard in patients with various types of myocardial disease (11). The sensitivity, specificity, and overall accuracy were 90%, 89%, and 89%, respectively, in a patient-based analysis and 67%, 92%, and 87%, respectively, in a segment-based analysis (11). We concluded that the diagnostic performance of 16-slice CT for the evaluation of LE was relatively high in the patient-based analysis but was limited in the segment-based analysis (11). Subsequently, we also reported improved the diagnostic performance of the detection of LE on CT in a segment-based analysis using first- and second-generation 320-slice CT compared to 16slice CT, although the difference in the diagnostic accuracy between the groups receiving 320-slice CT with and without FIRST was not significant, probably due to the small number of subjects included (8).

The present study, which focused on a head-to-head comparison of first- and second-generation 320-slice CT, indicated the better diagnostic performance in second-generation CT with FIRST. However, it was recently reported that a new dual-energy technique with cardiac CT had a high diagnostic performance for detecting LE with a sensitivity of 97.1% and specificity of 88.9% in a patient-based analysis and sensitivity of 92% and specificity of 98% in a segmentbased analysis (17). Further studies are therefore warranted to optimize the technique for detecting LE using cardiac CT.

Two different observers evaluated LE on CT in 20 cases in both the first- and second-generation groups in the present study. The inter-observer agreement assessed by kappa statistics was 0.83 in the first-generation group and 0.79 in the second-generation group. The inter-observer agreement in our previous study using 16 slice-CT was 0.83 (11). The inter-observer agreement was not improved in the current generation settings with 320-slice CT, which we primarily attributed to the difference in background cardiac diseases of the patients and the relatively high agreement in all groups.

Palmisano reported that the diagnostic accuracy of LE on CT depended on the experience of the reader, but the experience of the two readers in the present study was similar, and both had sufficient experience to evaluate LE on CT (18).

Important role of FIRST and a high tube current for improving the CNR

Low-tube-voltage acquisition should be performed for higher CT values of iodine contrast; however, the image noise also increases due to an insufficient radiation dose with low-tube-voltage acquisition (19). To increase the image quality without increasing the image noise on CT, a higher iodine dose of contrast medium, the FIRST technique, and a higher tube current must be applied to compensate for the low tube voltage. A higher tube current and the use of the FIRST technique can be performed with newgeneration 320-slice CT, and this combination of techniques leads to an improvement in the image quality of late-phase acquisition and the diagnostic accuracy of LE in LVM on CT.

We did not compare the CT reconstruction techniques of FBP and FIRST in the same case because the purpose of this study was to assess the improvement achieved with new-generation 320 slice CT with FIRST. A low tube voltage was used to obtain a high CNR even though the CT images might be noisy in the second-generation group because the image noise would be decreased by the increased tube current and FIRST technique, so it would not be meaningful to compare these reconstruction techniques in the same case. The FIRST technique as well as a higher tube current in new-generation CT were equally important for improving the diagnostic accuracy of LE on CT.

The higher CNR can reportedly increase the diagnostic performance of LE detection on CT (15). In the present study, the CNR was higher in the second-generation group than in the first-generation group (5.6±1.7 vs. 2.8±1.1, p< 0.001). The higher CNR in the second-generation group can therefore explain the improved diagnostic performance. The CNR was positively correlated with the iodine dose of contrast medium per body weight and was negatively correlated with the BMI, especially in the second-generation group. Based on these results, a higher image quality of LE on CT can be expected in cases with a low BMI and high iodine dose of contrast medium. However, patients with heart failure often show renal dysfunction, so we decreased the amount of contrast medium in those cases. Therefore, we cannot expect a high image quality for LE on CT in cases with renal dysfunction and obesity.

Tanabe et al. previously reported the utility of the iterative reconstruction technique for increasing the CNR and improving the diagnostic performance of LE on CT in cases with old myocardial infarction, and we further determined its utility in cases with other myocardial diseases as well (20).

Radiation dose of LE on CT

The radiation dose of cardiac CT decreased following the introduction of new-generation CT, and the radiation dose was <1 mSv when using second-generation 320-slice CT with prospective ECG-gated scanning in a recent study (21). The radiation dose for evaluating LE on second-generation 320-slice CT in the present study was similar to that in the previous study on cardiac CT, and even the dose on first-generation 320-slice CT was similar to that with chest CT (22). Therefore, additional radiation is no longer an ob-

stacle hindering the use of CT for the detection of LE.

The image quality and diagnostic accuracy have also been improved recently, so the use of CT for evaluating LE should be considered in cases suspected of having myocardial diseases based on the presence of LV wall thinning or low CT attenuation in LVM in early-phase images obtained mainly for the evaluation of coronary artery stenosis.

Study limitations

Several limitations associated with the present study warrant mention. This is a retrospective study with a small number of patients. The presence of LE on both CT and MRI can indicate not only myocardial fibrosis (6) but also edema due to inflammation (23, 24). Some patients who had inflammation cardiac diseases (e.g., cardiac sarcoidosis) were included in this study. However, there was no significant difference of the background myocardial diseases between the two groups. This might have influenced the results to some degree, because the intervals between CT and MRI differed among the patients, although there was no marked difference in the intervals between the first- and second-generation groups. The detectability of 1.5-T and 3.0-T MRI for LE may differ, which could have influenced the results of this study. However, the assessment of LE on MRI has already been recognized as the gold standard for the detection of myocardial fibrosis, even when using 1.5-T MRI, so we feel that any difference in the detectability of the different scanners would be negligible (2).

Conclusion

The diagnostic performance of the detection of LE in LVM on CT compared to MRI was improved for second-generation 320-slice CT with FIRST.

The authors state that they have no Conflict of Interest (COI).

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