CLINICAL STUDY

Improved Diagnosis of Detection of Late Enhancement in Left Ventricular Myocardium Using 2nd Generation 320-Slice CT Reconstructed with FIRST in Non-Ischemic Cardiomyopathy

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Summary

Forward Projected Model-based Iterative Reconstruction Solution (FIRST) is a new reconstruction technique using CT, which provides successful reconstruction of high-quality CT images, especially in low contrast imaging. To evaluate improvements in the diagnostic accuracy of the detection of abnormal late enhancement (LE) in left-ventricular myocardium (LVM) using 2nd generation 320-slice CT with FIRST, we compared this modality with previous CT methods in patients with non-ischemic cardiomyopathy or a cardiac tumor.

This was a retrospective study of 88 patients (56 males; 57 ± 15 years) suspected of having non-ischemic myocardial disease or a cardiac tumor. The first 52 consecutive patients (Group 1) underwent 16-slice CT at 140 kV tube voltage and an average tube current of 337 ± 20 mA, and 1.5 T MRI. The next 18 patients (Group 2) underwent 1st generation 320-slice CT at 120 kV tube voltage and an average tube current of 255 ± 106 mA, and 1.5 T MRI; the remaining 18 patients (Group 3) underwent 2nd generation 320-slice CT with FIRST, at 80 kV tube voltage and a tube current of 800 mA, and 1.5T or 3T MRI.

On patient-based analysis, no significant differences were observed between the 3 groups. For segment-based analysis, the specificity and overall accuracy were significantly higher (both $P < 0.05$) in Group 3 than in Group 1. Positive predictive value (PPV) was significantly higher in Group 3 than in Groups 1 and 2.

The diagnostic accuracy of LE on CT for detecting myocardial fibrosis determined by late gadolinium-enhanced MRI was improved with the use of 2nd generation 320-slice CT with FIRST, in particular regarding specificity, PPV, and overall accuracy.

Key words: Magnetic resonance imaging

Forward Projected Model-based Iterative Reconstruction Solution (FIRST) is a new reconstruction technique incorporating a full iterative reconstruction algorithm and has recently become available using computed tomography (CT).1,2) This technique can provide successful reconstruction of high quality CT images, especially in low contrast imaging.

To evaluate improvements in diagnostic accuracy of the detection of abnormal late enhancement (LE) in left ventricular (LV) myocardium (LVM) using 2nd generation 320-slice CT with FIRST for detecting myocardial fibrosis determined by late gadolinium-enhanced T1 weighted magnetic resonance imaging (MRI), we compared this modality with previous CT methods in patients suspected of having non-ischemic myocardial disease or cardiac tumor, while regarding T1 weighted MRI as the gold standard.3-9)

Methods

Patient population: This was a retrospective study of 88 patients (56 males; mean age ± standard deviation 57 ± 15 years) suspected of having non-ischemic myocardial disease or a cardiac tumor who also underwent both late phase acquisition with electrocardiogram (ECG) gated CT and T1 weighted MRI to detect abnormal LE in LVM within 3 months.

Coronary arteries in all patients were evaluated by...
cardiac CT and either 1) no significant stenosis was observed in coronary arteries, or 2) significant coronary arterial stenosis was suspected on CT, although following invasive coronary angiography, no significant stenosis was observed. Thus, no patients exhibited significant stenosis on CT or invasive coronary angiography.

**CT protocol:** On all cardiac CT, all patients underwent late phase acquisitions at 6-8 minutes after injection of contrast, because there were some contrast defects in LVM or LV cavity; alternatively, abnormal structures such as a cardiac tumor were visualized in the early phase of acquisition.

The patients were classified into the following three groups.

The first 52 consecutive patients (Group 1) underwent 16-slice CT (Light Speed Ultra 16, GE Healthcare) reconstructed with filtered back projection (FBP) at retrospective ECG gated acquisition, 140 kV tube voltage and an average tube current of 337 ± 20 mA, and 1.5 tesla (T) MRI (Achieva, Philips).

The next 18 patients (Group 2) underwent 1st generation 320-slice CT (Aquilion one, Toshiba Medical) reconstructed with FBP at prospective ECG gated acquisition, 120 kV tube voltage and an average tube current of 255 ± 106 mA, and 1.5T MRI (Achieva, Philips).

The remaining 18 patients (Group 3) underwent 2nd generation 320-slice CT (Aquilion one VISION, Toshiba Medical) reconstructed with FIRST, at prospective ECG gated acquisition, 80 kV tube voltage and tube current of 800 mA, and 1.5T MRI (Achieva, or Ingenia, Philips) or 3T MRI (Ingenia, Philips).

Patient backgrounds and the details of CT scanning parameters for late phase acquisitions among the three groups are presented in Table I, II, respectively.

**Table I.** Patient Backgrounds

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 52)</th>
<th>Group 2 (n = 18)</th>
<th>Group 3 (n = 18)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57 ± 15</td>
<td>57 ± 15</td>
<td>59 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>Male</td>
<td>34 (65%)</td>
<td>9 (50%)</td>
<td>13 (65%)</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25 ± 3</td>
<td>22 ± 3</td>
<td>22 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>Interval between CT and MRI (days)</td>
<td>23 ± 18</td>
<td>30 ± 26</td>
<td>23 ± 25</td>
<td>NS</td>
</tr>
<tr>
<td>Prevalence of atrial fibrillation</td>
<td>6 (12%)</td>
<td>0 (0%)</td>
<td>4 (22%)</td>
<td>-</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
<td>14 (27%)</td>
<td>8 (44%)</td>
<td>4 (22%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac amyloidosis</td>
<td>3 (6%)</td>
<td>0 (0%)</td>
<td>1 (6%)</td>
<td>-</td>
</tr>
<tr>
<td>Cardiac sarcoidosis</td>
<td>3 (6%)*</td>
<td>2 (11%)</td>
<td>4 (22%)*</td>
<td>&lt; 0.05*</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td>2 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertensive heart disease</td>
<td>1 (2%)</td>
<td>1 (6%)</td>
<td>2 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac tumor</td>
<td>2 (4%)</td>
<td>1 (6%)</td>
<td>1 (6%)</td>
<td>NS</td>
</tr>
<tr>
<td>Unknown</td>
<td>16 (31%)</td>
<td>3 (17%)</td>
<td>2 (11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Others</td>
<td>9 (17%)</td>
<td>3 (17%)</td>
<td>2 (11%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*The percentage of cardiac sarcoidosis was significantly greater in Group 3 than Group 1 (P < 0.05).

**Table II.** Details of Computed Tomographic (CT) Scanning Parameters (for Late Phase Acquisition) among the 3 Groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 52)</th>
<th>Group 2 (n = 18)</th>
<th>Group 3 (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slice thickness</td>
<td>1.25 mm</td>
<td>0.5 mm</td>
<td>0.5 mm</td>
</tr>
<tr>
<td>ECG gating</td>
<td>Retrospective ECG gating</td>
<td>Prospective ECG gating</td>
<td>Prospective ECG gating</td>
</tr>
<tr>
<td>Speed of gantry rotation (seconds)</td>
<td>0.5</td>
<td>0.35</td>
<td>0.275-0.4</td>
</tr>
<tr>
<td>Tube voltage (kV)</td>
<td>140</td>
<td>120</td>
<td>80</td>
</tr>
<tr>
<td>Tube current (mA)</td>
<td>337 ± 20</td>
<td>255 ± 106</td>
<td>800</td>
</tr>
<tr>
<td>Amount of contrast media use (mL)</td>
<td>75-100</td>
<td>75-100</td>
<td>75-135</td>
</tr>
<tr>
<td>Image reconstruction</td>
<td>FBP</td>
<td>FBP</td>
<td>FIRST</td>
</tr>
</tbody>
</table>

Slice thickness ranged from 1.25 mm (Group 1) to 0.5 mm (Groups 2 and 3). Electrocardiogram (ECG) gating acquisition method ranged from retrospective ECG gating (Group 1) to prospective ECG gating (Groups 2 and 3) to reduce radiation dose exposure. Tube voltage was reduced from 140 kV (Group 1), to 120 kV (Group 2), to 80 kV (Group 3) and conversely to reduce image noise, tube current was increased to 800 mA in Group 3. Furthermore, to reduce image noise, FIRST was used for image reconstruction in Group 3. As the degree of late enhancement on CT images depends upon the total amount of contrast material, even though 320-slice CT was used, if renal function was preserved, 75-135 mL of iodinated contrast material was used in Group 3. FBP and FIRST indicate Filtered Back Projection and Forward Projected Model-based Iterative Reconstruction SoluTion, respectively.
I n tH e a r tJ

Advance Publication 3LATE ENHANCEMENT USING 320 SLICE CT WITH FIRST

Figure 1. Comparison of typical late enhancement (LE) images of computed tomography (CT) and magnetic resonance images (MRI). Case 1 with hypertrophic cardiomyopathy. Multiplanar reconstruction CT and MRI of long axis of left ventricle (LV). CT was acquired with 2nd generation 320-slice CT and reconstructed with FIRST (Group 3). T1 weighted 1.5T MRI was also acquired. In both images, multiple LEs were observed (arrows) to be widely distributed, ranging from the apical portion to the anterior and inferior wall of LV in both cases. FIRST indicates Forward Projected Model-based Iterative Reconstruction Solution; and LA, left atrium.

In all groups, the amount of contrast medium was 75-135 mL (most frequently 100 mL) depending upon renal function and the main objective.

In all groups, contrast injection was performed using a triple injection protocol as follows: During the first phase we injected 50-70 mL of undiluted contrast agent (1st phase), followed by 40 mL of a 50/50 saline/contrast material mixture (2nd phase) and finally 30 mL of pure saline (3rd phase).

Radiation dose for late phase acquisition was estimated to be 1) approximately 3-5 mSv in Group 1 (retropective ECG gating with tube voltage 140 mV, tube current 250-300 mA and slice thickness 1.25 mm), 2) approximately 1-3 mSv in Group 2 (prospective ECG gating with tube voltage 120 mV, tube current 580 mA and slice thickness 0.5 mm), 3) approximately 1-2 mSv in Group 3 (prospective ECG gating with tube voltage 80 mV, tube current maximum 800 mA and slice thickness 0.5 mm).

To control patient heart rates, beta blockers (propranolol in Group 1) (metoprolol in Group 2), (metoprolol and/or landiolol hydrochloride in Group 3), were used if patient heart rates were greater than 65 beats per minute and there were no contraindications for beta blockers; as a result, patient heart rates were controlled to less than 65 beats per minute in most cases.

In a patient-based analysis, if LE in LVM were detected in at least one lesion at any point in LVM both by CT and MRI, these findings were considered as concordant even when CT and MRI revealed LE in different LV myocardial lesions.

The LVM was divided into 17 segments, as defined by the American Heart Association and in a segment-based analysis, if LE in LVM both on CT and MRI are detected at corresponding sites, the CT and MRI findings are regarded as concordant at these lesions.

This study was approved by the ethical committee of Chiba University Hospital and was carried out in accordance with the Declaration of Helsinki.

Statistical analysis: All quantitative data are expressed as the mean ± standard deviation. For all analyses, \( P < 0.05 \) was considered to be statistically significant.

Quantitative data among the 3 groups (= Group 1-3) were compared using the Tukey-Kramer method (SPSS software, version 17.0, SPSS, Inc.)

The percentage of background disease and diagnostic accuracy were compared using hypothesis testing for the difference in population proportions (Excel statistics, Esumi).

Results

Typical images of LE on CT and MRI at sites corresponding to each other are presented in Figures 1-4. LE on CT and MRI was detected in 45 (51%) and 43 (48%) patients, respectively.

On patient-based analysis, sensitivity, specificity, positive and negative predictive values (PPV and NPV), and overall accuracy of detection of LE on CT compared to MRI were detected in 92, 89, 88, 92, and 90% respectively, in Group 1, 89, 89, 89, 89, and 89% respectively, in Group 2, and 100, 89, 90, 100, and 94% respectively, in Group 3. No significant differences were observed among the 3 groups. In a patient-based analysis, there were no patients who exhibited LE both on CT and MRI but in whom there were no lesions which exhibited LE in both CT and MRI simultaneously at the corresponding site.

In a segment-based analysis, LE on CT and MRI was detected on 257 and 256 segments, respectively, among a total of 1496 segments. Sensitivity, specificity, PPV, NPV, and overall accuracy of detection of LE on CT compared
Figure 2. Comparison of typical late enhancement (LE) images of computed tomography (CT) and magnetic resonance images (MRI). Case 2 with cardiac sarcoidosis. Multiplanar reconstruction CT and T1 weighted 1.5 Tesla MRI of long axis of left ventricle (LV). CT was acquired with 16-slice CT and reconstructed with Filtered Back Projection (Group 1). In both images, massive LE was observed (arrows) from the thickened basal portion to inferior wall of LV, in both cases. LA indicates left atrium.

Figure 3. Comparison of typical late enhancement (LE) images of computed tomography (CT) and magnetic resonance images (MRI). Case 3 with cardiac amyloidosis. Multiplanar reconstruction CT and T1 weighted 1.5 Tesla MRI of short axis of left ventricle (LV). CT was acquired with 1st generation 320-slice CT and reconstructed with Filtered Back Projection (Group 2). In both images, diffuse LEs were observed (arrows) in endocardial portion of thickened LV wall. LEs were more remarkable and wider in area in CT than MRI. RV indicates right ventricle.

to MRI were 65, 92, 68, 91, and 87%, respectively (Group 1), 67, 94, 66, 95, and 91% respectively (Group 2), and 73, 97, 85, 95, and 93%, respectively (Group 3). Specificity and overall accuracy were significantly higher (both \( P < 0.05 \)) in Group 3 than in Group 1. PPV was significantly higher in Group 3 than in Group 1 and 2.

**Discussion**

We have previously evaluated the diagnostic accuracy of 16-slice CT for the detection of LE in LVM compared with MRI in patients with various myocardial diseases.\(^{11} \) The sensitivity, specificity, PPV, NPV, and overall accuracy for detection of LE on CT in comparison with MRI were 90, 89, 89, 89 and 89%, respectively, on patient-based analysis, and 67, 92, 68, 91 and 87%, respectively, on segment-based analysis. From this analysis we concluded that compared with MRI, the diagnostic accuracy of CT for evaluation of LE in LVM in such patients was relatively higher on patient-based analysis, but was limited on segment-based analysis.

Advances in CT have been dramatic and the numbers of detector rows employed have increased from 4 in 1998, to 16 in 2002,\(^{11} \) 64 in 2004,\(^{12,13} \) and to 320 currently.\(^{14,16} \) In parallel, the maximum rotation speed has increased from 0.5 seconds per rotation (4 - 16-slice CT) to 0.35 seconds (1st generation 320-slice CT)\(^{14,15} \) and 0.275 seconds (2nd generation 320-slice CT)\(^{16} \) in Toshiba Medical
Comparison of typical late enhancement (LE) images of computed tomography (CT) and magnetic resonance images (MRI). Case 4 with unknown etiology. Axial source CT and T1 weighted 3 Tesla MRI at LV inflow level. CT was acquired with 2nd generation 320-slice CT and reconstructed with FIRST (Group 3). In both images, massive LE was observed (arrows) in LV lateral wall in both cases. FIRST indicates Forward Projected Model-based Iterative Reconstruction SoluTion; RV, right ventricle; RA, right atrium; and LA, left atrium.

Diagnostic accuracy of late enhancement (LE) on computed tomography (CT) compared with magnetic resonance images (MRI) as gold standard; a patient based analysis. Sensitivity, specificity, positive and negative predictive values (PPV and NPV), and overall accuracy of detection of LE on CT against that on MRI were 92, 89, 88, 92, and 90% in Group 1, 89, 89, 89, 89 and 89% in Group 2, and 100, 89, 90, 100, and 94%, respectively, in Group 3. No significant differences were observed among the 3 groups. Group 1 (n = 52): Underwent 16-slice CT with retrospective electrocardiogram (ECG) gated acquisition, 140 kV tube voltage and an average tube current of 337 ± 20 mA, and 1.5 T MRI. Group 2 (n = 18): Underwent 1st generation 320-slice CT with prospective ECG gated acquisition, 120 kV tube voltage, and an average tube current of 255 ± 106 mA, and 1.5 T MRI. Group 3 (n = 18): Underwent 2nd generation 320-slice CT with FIRST, at prospective ECG gated acquisition, 80 kV tube voltage and a tube current of 800 mA, and 1.5 T MRI or 3T MRI. FIRST indicates Forward Projected Model-based Iterative Reconstruction SoluTion.
Products alone.

However, to improve low contrast CT image quality in cases such as detection of LE in LVM, low tube voltage acquisition is preferable. Nonetheless, under conditions of low tube voltage, the total radiation dose is not sufficient to obtain good quality images and image noise can occur. To overcome this problem, it is necessary to increase tube current as much as possible; however, total radiation dose is often still not sufficient to obtain good quality images, especially in patients who are obese or who have large body size.

Adaptive iterative dose reduction 3D (AIDR 3D) for image reconstruction is a next generation candidate method designed to improve image quality under conditions of low radiation dose.\(^\text{15}\) We have previously reported in a mock phantom study, that when physicians evaluate the patency of a coronary arterial lumen surrounded by a XIENCE stent (XIENCE Prime, Abbot) \(< 3 \text{ mm diameter using 1st generation 320-slice CT under pulsation at 60 beats per minute, weak, mild AIDR 3D), or no AIDR 3D should be used for image reconstruction.}\(^\text{15}\)

FIRST is categorized as a fully iterative reconstruction algorithm. Yasaka, et al reported that the metal artefact index in FIRST was significantly improved compared with AIDR 3D.\(^\text{21}\) Therefore, using FIRST, the quality of images with low tube voltage and maximum tube current may be furthermore improved over usage of AIDR 3D.

In this study involving segment-based analysis, the specificity and overall accuracies were significantly higher (both \(P < 0.05\)) in Group 3 than in Group 1. PPV was significantly higher in Group 3 than in Groups 1 and 2 (both \(P < 0.05\)). Group 1 \((n = 52)\): Underwent 16-slice CT with retrospective electrocardiogram (ECG) gated acquisition, 140 kV tube voltage and an average tube current of \(337 \pm 20\ \text{mA}\), and 1.5 T MRI. Group 2 \((n = 18)\): Underwent 1st generation 320-slice CT with prospective ECG gated acquisition, 120 kV tube voltage, and an average tube current of \(255 \pm 106\ \text{mA}\), and 1.5T MRI. Group 3 \((n = 18)\): Underwent 2nd generation 320-slice CT with FIRST, at prospective ECG gated acquisition, 80 kV tube voltage and a tube current of 800 mA, and 1.5T MRI. FIRST indicates Forward Projected Model-based Iterative Reconstruction Solution.

Figure 6. Diagnostic accuracy of late enhancement (LE) on computed tomography (CT) compared with magnetic resonance images (MRI) as gold standard; a segment based analysis. The left ventricular myocardium (LVM) was divided into 17 segments, as defined by the American Heart Association.\(^\text{10}\) Sensitivity, specificity, positive and negative predictive values (PPV and NPV), and overall accuracy of detection of LE on CT against that on MRI were 65, 92, 68, 91, and 87\% (Group 1), 67, 94, 73, 95, and 91\% (Group 2), and 73, 97, 84, 95, and 93\%, respectively (Group 3). Specificity and overall accuracy were significantly improved (both \(P < 0.05\)) in Group 3 than in Group 1. PPV was significantly higher in Group 3 than in Groups 1 and 2 (both \(P < 0.05\)). Group 1 \((n = 52)\): Underwent 16-slice CT with retrospective electrocardiogram (ECG) gated acquisition, 140 kV tube voltage and an average tube current of \(337 \pm 20\ \text{mA}\), and 1.5 T MRI. Group 2 \((n = 18)\): Underwent 1st generation 320-slice CT with FIRST, at prospective ECG gated acquisition, 120 kV tube voltage, and an average tube current of \(255 \pm 106\ \text{mA}\), and 1.5T MRI. Group 3 \((n = 18)\): Underwent 2nd generation 320-slice CT with FIRST, at prospective ECG gated acquisition, 80 kV tube voltage and a tube current of 800 mA, and 1.5T MRI. FIRST indicates Forward Projected Model-based Iterative Reconstruction Solution.
lence of AF did not have an impact on impairing cardiac image quality in Groups 2 and 3.

Inter-observer Variability of Detection of LE on CT and on MRI in Segment-based Analysis: We have previously demonstrated inter-observer agreement in the detection of LE on 16 slice CT, in which LE was evaluated using segment-based analysis. In such analysis, the 17-LV myocardial segments model described by the American Heart Association was used, as in this study. Inter-observer agreement for detection of LE on CT was 0.71 (kappa coefficient), and was significantly lower than that on MRI (0.82) using segment-based analysis (P < 0.05).

Actual images of LE were dramatically improved in 320 slice CT over 16 slice CT as presented in Figures 1-4; thus, we speculated that inter-observer agreement for detection of LE on 320 slice CT, especially 2nd generation with FIRST, was improved over that on 16 slice CT (0.71).

Study limitations: This was a non-randomized single study with a small number of patients. It was a qualitative rather than a quantitative study designed to evaluate detection of LE on CT and MRI, and inter-observer variabilities of detection of LE on CT or on MRI in each group were not performed. The presence of LE both on CT and MRI indicate not only myocardial fibrosis, but also edema due to inflammation. The latter may occur in active phase cardiac sarcoidosis or acute myocarditis. We have previously determined optimal periods for (18) F-fluorodeoxyglucose positron emission tomography examination in subjects with suspected acute myocarditis; we compared these with endomyocardial biopsy and concluded that acquisition timing may influence the detection of edema due to inflammation. The time interval between onset of diseases and CT and MRI was difficult to determine accurately.

In Group 3, the detectability of 1.5T and 3T MRI may have differed which could have influenced the results of this study.

To evaluate the effect of FIRST compared with FBP, the same raw data may be reconstructed with both FIRST and FBP; comparisons can then be made of the detection of LE on CT reconstructed with FIRST and those reconstructed with FBP, with reference to those on MRI; this approach has the potential to be the new gold standard in the future.

In order to compare the diagnostic values of various LE CT generations for detecting myocardial fibrosis, we should have assessed whether the area under the curves of receiver operating characteristic analysis was statistically different among the 3 LE CT generations.

Conclusion

The diagnostic accuracy of LE on CT for detecting myocardial fibrosis determined by late gadolinium-enhanced MRI was improved with the use of 2nd generation 320-slice CT with FIRST, in particular regarding specificity, PPV, and overall accuracy.

Disclosures

Conflicts of interest: There is no conflict of interest to declare.

References


