Deep Learning for Diagnosis of Chronic Myocardial Infarction on Nonenhanced Cardiac Cine MRI

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See also the editorial by Leiner in this issue.

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Background: Renal impairment is common in patients with coronary artery disease and, if severe, late gadolinium enhancement (LGE) imaging for myocardial infarction (MI) evaluation cannot be performed.

Purpose: To develop a fully automatic framework for chronic MI delineation via deep learning on non–contrast material–enhanced cardiac cine MRI.

Materials and Methods: In this retrospective single-center study, a deep learning model was developed to extract motion features from the left ventricle and delineate MI regions on nonenhanced cardiac cine MRI collected between October 2015 and March 2017. Patients with chronic MI, as well as healthy control patients, had both nonenhanced cardiac cine (25 phases per cardiac cycle) and LGE MRI examinations. Eighty percent of MRI examinations were used for the training data set and 20% for the independent testing data set. Chronic MI regions on LGE MRI were defined as ground truth. Diagnostic performance was assessed by analysis of the area under the receiver operating characteristic curve (AUC). MI area and MI area percentage from nonenhanced cardiac cine and LGE MRI were compared by using the Pearson correlation, paired t test, and Bland-Altman analysis.

Results: Study participants included 212 patients with chronic MI (men, 171; age, 57.2 years ± 12.5) and 87 healthy control patients (men, 42; age, 43.3 years ± 15.5). Using the full cardiac cine MRI, the per-segment sensitivity and specificity for detecting chronic MI in the independent test set was 89.8% and 99.1%, respectively, with an AUC of 0.94. There were no differences between nonenhanced cardiac cine and LGE MRI analyses in number of MI segments (114 vs 127, respectively; \( P = .38 \)), per-patient MI area (6.2 cm\(^2\) vs 5.5 cm\(^2\); \( P = .27 \); correlation coefficient, \( r = .88 \)), and MI area percentage (21.5% ± 17.3 vs 18.5% ± 15.4; \( P = .17 \); correlation coefficient, \( r = .89 \)).

Conclusion: The proposed deep learning framework on nonenhanced cardiac cine MRI enables the confirmation (presence), detection (position), and delineation (transmurality and size) of chronic myocardial infarction. However, future larger-scale multicenter studies are required for a full validation.

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Diagnosis of chronic myocardial infarction (MI) is an important clinical task because the management of and treatment planning for patients is different for chronic MI versus acute MI (1,2). The extent of chronic MI, including location, size, and transmurality, provides rich information for patient diagnosis, prognosis, and therapy planning (3). Therefore, accurate delineation and comprehensive evaluation of chronic MI is of great clinical interest.

Late gadolinium enhancement (LGE) MRI has been established as the ground truth reference technique for chronic MI evaluation (4–6). However, including LGE MRI in the MRI examination extends the scanning duration and there are also growing concerns about its safety (7–9). While LGE MRI is contraindicated in patients with severe renal impairment, a recent study has also shown that gadolinium might deposit into the skin, dentate nucleus, and globus pallidus of patients with normal renal function (10). A reliable technique to detect and delineate MI without the need for gadolinium-based contrast agent would therefore be highly desirable.

T1 and T2 mapping techniques (11) are non–contrast material–enhanced approaches that show longer T1 and T2 relaxation times in acute MI compared with normal myocardium. In comparison, while T1 relaxation time is
Abbreviations
AUC = area under the receiver operating characteristic curve, CI = confidence interval, LGE = late gadolinium enhancement, MI = myocardial infarction

Summary
Deep learning on nonenhanced cardiac MRI data can detect the presence and extent of chronic myocardial infarction. This approach may have potential to reduce use of gadolinium contrast administration.

Key Points
- A deep learning method to identify myocardial infarction on nonenhanced cardiac cine MRI achieved good diagnostic performance for detecting chronic myocardial infarction (per-segment sensitivity, 90%; specificity, 99%; area under the receiver operating characteristic curve, 0.94).
- There was no difference between the area of chronic MI detected on nonenhanced cardiac cine MRI and ground truth defined by expert manual segmentation of late gadolinium enhancement MRI (per-patient myocardial infarction area, 6.2 cm² ± 2.8 vs 5.5 cm² ± 2.3, respectively; \( P = .27 \)).

Materials and Methods
This retrospective study was approved by our institutional review board in accordance with local ethics procedures. Further consent was waived with approval.

Patients
Detailed demographics and left ventricle volumetric data are summarized in Table 1. Between October 2015 and March 2017, 212 patients with chronic MI (based on clinical symptoms, electrocardiogram changes, and greater than twofold elevation of creatine kinase and/or positive troponin T) and 87 control patients (without negative LGE MRI) were selected from a single center for retrospective inclusion in our study (Fig 1, Appendix E1 [online]). Major exclusion criteria were acute MI, angina without MI, all kinds of nonischemic cardiomyopathy, cardiac neoplasm, valvular heart disease, congenital

differentiates regional myocardial morphology and cardiac wall motion abnormalities resulting from MI (18,19) on non–contrast-enhanced cardiac cine MRI, which is acquired as part of a standard cardiac MRI examination. However, only the presence and position information of the MI can be extracted from these examinations and these techniques may be further limited by the need for time-consuming processing after the examination.

We propose a fully automatic framework for chronic MI delineation via deep learning on nonenhanced cardiac cine MRI and assess its accuracy for identifying the presence, position, transmurality, and size of the MI without the need for gadolinium injection.

Table 1: Demographics of Patients and Control Patients with Left Ventricle Volumetric Data

| Characteristic                          | Patients with Chronic MI (n = 169) | Control Patients (n = 69) | \( P \) Value | Patients with Chronic MI (n = 43) | Control Patients (n = 18) | \( P \) Value |
|----------------------------------------|-----------------------------------|--------------------------|---------------|-----------------------------------|--------------------------|---------------|
| Male patient                           | 131 (77.5)                        | 33 (47.8)                | .001          | 40 (93.0)                         | 9 (50.0)                 | .001          |
| Age (y)*                               | 59.8 ± 11.1                       | 46.4 ± 15.3              | \(< .001\)    | 56.8 ± 11.0                       | 40.1 ± 13.5              | \(< .001\)    |
| Weight (kg)*                           | 76.6 ± 12.3                       | 77.8 ± 24.1              | .82           | 74.2 ± 12.0                       | 70.7 ± 8.8               | .26           |
| Height (cm)*                           | 169.2 ± 6.1                       | 165.1 ± 15.3             | .23           | 170.0 ± 7.0                       | 167.6 ± 8.3              | .58           |
| Left ventricular ejection fraction (%)*| 34.1 ± 17.8                       | 60.8 ± 8.4               | \(< .001\)    | 38.0 ± 18.4                       | 58.6 ± 8.0               | \(< .001\)    |
| Left ventricular end-diastolic volume index (mL/m²)* | 155.3 ± 89.0                | 89.0 ± 18.3              | \(< .001\)    | 132.6 ± 68.0                       | 90.2 ± 20.2              | \(< .001\)    |
| Left ventricular end-systolic volume index (mL/m²)* | 112.9 ± 88.9                | 36.6 ± 19.5              | \(< .001\)    | 88.9 ± 71.2                       | 35.4 ± 13.5              | \(< .001\)    |
| Stroke volume (mL)*                    | 43.9 ± 20.6                       | 57.8 ± 13.3              | \(< .001\)    | 41.2 ± 14.8                       | 58.5 ± 13.8              | \(< .001\)    |
| Cardiac output (L/min)*                | 3.5 ± 2.5                         | 4.4 ± 1.4                | .002          | 3.2 ± 1.5                         | 4.2 ± 1.2                | .001          |

Coronary risk factors

| Coronary risk factors | \( \chi^2 \) tests | \( t \) tests | \( \chi^2 \) tests | \( t \) tests |
|----------------------|------------------|---------------|------------------|---------------|
| Hypertension         | 86 (50.9)        | 19 (27.5)     | .001             | 18 (41.9)     | 5 (27.8)      | .31            |
| Diabetes             | 60 (35.5)        | 15 (21.7)     | .03              | 13 (30.2)     | 3 (16.7)      | .28            |
| Smoking              | 98 (58.0)        | 22 (31.9)     | \(< .001\)       | 17 (39.5)     | 3 (16.7)      | .09            |
| Dyslipidemia         | 43 (25.4)        | 5 (7.2)       | .001             | 17 (39.5)     | 4 (22.2)      | .20            |
| Family history       | 11 (6.5)         | 4 (5.8)       | .84              | 2 (4.7)       | 2 (11.1)      | .36            |

Note.—Unless otherwise indicated, data are medians. Data in parentheses are percentages. Independent \( t \) tests were used to compare the differences between two groups for continuous numerical variables. \( \chi^2 \) tests were used to compare the differences between two groups for sex and coronary risk factors. MI = myocardial infarction.

* Data are mean ± SD.
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**Imaging Protocol**

Cardiac MRI was performed using a 3-T MRI system (Verio; Siemens, Erlangen, Germany). Retrospectively gated balanced steady-state free-precession nonenhanced cardiac cine images with 25 reconstructed phases were acquired (repetition time msec/echo time msec, 3.36/1.47; field of view, 286 × 340 mm²; matrix, 216 × 256; average temporal resolution, ~40 msec) during repeated breath holds in short-axis views covering the whole left ventricle.

LGE MRI was performed in the same orientations and with the same section thickness using a two-dimensional segmented fast low-angle shot phase-sensitive inversion recovery sequence (4.09/1.56; field of view, 284 × 350 mm²; matrix, 163 × 256) 10 minutes after intravenous injection of gadolinium-based contrast agent (Magnevist, 0.2 mmol/kg; Bayer Healthcare, Berlin, Germany).

Full details of both protocols are given in Appendix E1 (online).

**Ground Truth Definition**

**Data standardization and left ventricle localization.**—Images from nonenhanced cardiac cine and LGE MRI were cropped automatically into 64 × 64 pixels (pixel size, 1.46 × 1.46 mm²), which included the full left ventricle area. Sections beyond the most base and apex regions were excluded manually.

**Endocardial and epicardial contours delineation.**—Endocardial and epicardial contours were manually delineated on the LGE MRI by a radiologist (N.Z., with 7 years of experience in cardiovascular MRI) after rigid registration (21) of the end-diastole phase of the cine and LGE images. Following visual inspection and assessment by mutual information, any residual registration errors were corrected using a diffeomorphic image registration technique (22) with parameterized deformation fields.

**MI delineation.**—MI was manually outlined on the LGE images by the same radiologist (N.Z.) after appropriate setting of the display window level and width. Microvascular obstructions were included in the MI regions.

All manual segmentations (epicardial and endocardial contours and MI) were reviewed by another expert (L.X., with 10 years of experience in cardiovascular MRI) and in cases of disagreement, a consensus was reached. The MI area percentage (23) was calculated as (MI pixels/left ventricle myocardium pixels) × 100%.

**Segment model.**—A 16-segment model proposed by the American Heart Association was used, in which the apex was...
Deep Learning

Our deep learning model extracts representative local and global motion features in nonenhanced cardiac cine MRI and relates them to LGE images (details in Appendix E1 [on-
Once the model is trained, predictions of MI location, size, and transmurality can be made without LGE images. The deep learning framework consists of (Fig 2): (a) a localization deep network for detecting the left ventricle; (b) a motion feature extraction component incorporating local motion features extracted from a recurrent neural network and global motion features derived using an advanced optical flow method; and (c) a fully connected discriminative network (26) that distinguishes MI from normal myocardium. The deep motion networks output a probability map, which has stored the version we used to achieve the current reported results.

### Experimental Settings
The performance of our trained deep learning model was evaluated using independent testing, that is, a data set was not used for model development (external validation as mentioned in Park et al [28]). The 299 participants were randomly divided 80:20 into training data sets (169 patients with chronic MI, 69 control patients) and independent testing data sets (43 patients with chronic MI, 18 control patients). Basal, midcavity, and apical sections were analyzed in each participant, resulting in a total of 3808 segments for training and 976 segments for independent testing.

In addition, 10-fold cross-validation (29,30) on the whole data sets (with 299 participants) was performed to further confirm the effectiveness of our proposed deep learning model (details and secondary results are shown in Appendix E1 [online]).

| Groups Compared | Sensitivity | Specificity | AUC |
|-----------------|-------------|-------------|-----|
| Overall MI segments (single phase) vs overall MI segments (full 25 phases) | <.001 | <.001 | <.001 |
| Overall MI segments (single phase) vs overall subendocardial MI segments (full 25 phases) | <.001 | <.001 | <.001 |
| Overall MI segments (single phase) vs overall transmural MI segments (full 25 phases) | <.001 | <.001 | <.001 |
| Overall MI segments (full 25 phases) vs overall subendocardial MI segments (full 25 phases) | .17 | .66 | .29 |
| Overall MI segments (full 25 phases) vs overall transmural MI segments (full 25 phases) | .29 | .35 | .27 |
| Overall subendocardial MI segments (full 25 phases) vs overall transmural MI segments (full 25 phases) | .03 | .61 | .09 |

Note.—Data are percentages. Data in parentheses are raw data (number of segments or sections) used to calculate percentages. Data in brackets are 95% confidence intervals. If more than half of the pixels in a segment were MI positive, then that segment was MI positive. AUC = area under the receiver operating characteristic curve, MI = myocardial infarction.
Statistical Analysis
Statistical analysis was performed using SPSS 23.0 (SPSS, Chicago, Ill). Independent t tests and χ² tests were used to compare differences between two groups for continuous and dichotomous variables, respectively.

Using manually delineated LGE images as the ground truth, sensitivity and specificity of the delineated MI derived from non-enhanced cardiac cine images with our deep learning framework were calculated. We also performed analysis of the area under the receiver operating characteristic curve (AUC).

MI area and MI area percentage at the segmental level were normally distributed (Kolmogorov–Smirnoff test) and differences from ground truth were assessed using paired t testing, Pearson correlation, and Bland-Altman analyses. Differences between count variables (per segment, per section, and per patient) were assessed by using the McNemar test. A two-sided P value less than .05 was considered to indicate a statistically significant difference.

Results
Study Population Characteristics
No significant differences were found in weight and height between patients with chronic MI and control patients (training data sets, P = .82 and P = .23; independent testing data sets, P = .26 and P = .58). Table 1 and Table E1 (online) show that men were more common in the chronic MI cohort than in the control cohort (training data sets, 131 of 169 [77.5%] vs 33 of 69 [47.8%], respectively [P = .001]; independent testing data sets, 40 of 43 [93.0%] vs nine of 18 [50.0%], respectively [P = .001]). Patients with chronic MI were also older than control patients (Table 1) and had poorer cardiac function (eg, cardiac output: training data sets, 3.5 L/min ± 2.5 vs 4.4 L/min ± 1.4, respectively [P = .002]; independent testing data sets, 3.2 L/min ± 1.5 vs 4.2 L/min ± 1.2, respectively [P = .001]). In addition, we found that with similar weight and height, the left ventricle chamber was dilated for the patients with chronic MI (left ventricular end-diastolic volume index: training data sets, 155.3 mL/m² ± 89.0 vs 89.0 mL/m² ± 18.3, respectively [P < .001]; independent testing data sets, 132.6 mL/m² ± 68.0 vs 90.2 mL/m² ± 20.2, respectively [P = .001]).

Computational Time
The parameters of our deep learning implementation are summarized in Figure E1 (online). The training time of our deep learning on the entire 238 data sets is 373 minutes (~1.6 minutes per data set). In the test phase, the computational time is 191 seconds for one MRI data set and about 8 seconds for one MRI section.

Independent Testing on Single End-Diastolic Phase and Full Nonenhanced Cardiac Cine Images
The quantitative results of using our deep learning framework on single end-diastolic and full nonenhanced cardiac cine image data sets are summarized in Tables 2 and 3. As expected, the
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Figure 4: Area under the receiver operating characteristic curve (AUC) (with the zoomed-in upper left corner) shows the diagnostic performance of the myocardial infarction (MI) detected with our deep learning framework in the independent testing data: A, for all MI segments; B, for the subendocardial MI; and C, for the transmural MI (lower right panel).

By using the full nonenhanced cardiac cine image data, the overall sensitivity and specificity for the detection of MI segments were almost all higher than 90%, with the exceptions being sensitivity for detection of subendocardial MI (36 of 44 [81.8%]; 95% confidence interval [CI]: 66.8%, 91.3%) and sensitivity for detection of all MI (114 of 127 [89.8%]; 95% CI: 82.8%, 94.2%). Results were similar for basal, midcavity, and apical sections. There were no MI segments found in control patients. In addition, the Dice score between the MI segmentation from nonenhanced cardiac cine MRI and the ground truth segmentation in the independent testing data sets was 86.1% ± 5.7.

Correlation with Manual Segmentation

Table 4: Comparison of Per-Segment Results (in Independent Testing Data Sets) for Deep Learning on Full Nonenhanced Cardiac Cine Images versus Ground Truth Delineated Manually on LGE Images

| Type of MI Segment | Deep Learning | LGE | P Value (LGE vs Deep Learning) |
|--------------------|--------------|-----|--------------------------------|
| Overall            | 114          | 127 | .38                            |
| Apical sections    | 27           | 31  | .68                            |
| Midcavity sections | 45           | 49  | 1.00                           |
| Basal sections     | 42           | 47  | .72                            |
| Subendocardial     | 36           | 44  | 1.00                           |
| Apical sections    | 9            | 12  | 1.00                           |
| Midcavity sections | 13           | 16  | 1.00                           |
| Basal sections     | 14           | 16  | 1.00                           |
| Transmural         | 78           | 83  | .75                            |
| Apical sections    | 18           | 19  | .48                            |
| Midcavity sections | 32           | 33  | 1.00                           |
| Basal sections     | 28           | 31  | .69                            |

Note.—LGE = late gadolinium enhancement, MI = myocardial infarction. Agreement of count variables was assessed by the McNemar test.
or greater, which shows the robustness of the developed deep learning framework.

Table 4 summarizes the comparative results between our deep learning framework and LGE in the independent testing data sets (per segment) for all MIs and for transmural and subendocardial MI subgroups, with no significant differences. Table 5 summarizes the per-patient and per-section results, respectively. Ten-fold cross-validation showed very similar per-segment, per-section, and per-patient results (Tables E2 and E3 in Appendix [online]).

Pearson correlation and Bland-Altman analyses for MI area and MI area percentage are shown in Figure 5 (per-section results) with correlation coefficients of 0.94 and 0.95, respectively. The corresponding biases (limits of agreement) are $-0.2 \text{ cm}^2$ ($-0.72 \text{ cm}^2$, $0.32 \text{ cm}^2$) and $-1.2\%$ ($-13\%$, $11\%$). Two example images—one with good correlation and one with poorer correlation—are also shown. Per-patient results in Figure 6 also show strong correlations of the MI area and MI area percentage (correlation coefficients, 0.88 for MI area and 0.89 for MI area percentage) measured from nonenhanced cardiac cine MRI and the manual delineated ground truth from the LGE MRI.

**Discussion**

In our study, we developed a fully automatic deep learning framework to detect chronic myocardial infarction (MI) in nonenhanced cardiac cine images based on extracted motion features. Using an independent testing data set, the Dice score $(86.1\% \pm 5.7\%)$ and correlations (per-patient MI area, $6.2 \text{ cm}^2 \pm 2.8$ vs $5.5 \text{ cm}^2 \pm 2.3$ [$P = .27$; $r = 0.88$] and per-patient MI area percentage, $21.5\% \pm 17.3$ vs $18.5\% \pm 15.4$ [$P = .17$; $r = 0.89$]) between chronic MI segmented from nonenhanced cardiac cine images and that manually delineated on LGE images show that our deep learning approach is able to detect the...
Our framework only requires nonenhanced cardiac cine images, which are routinely acquired as part of a cardiac examination for function assessment. Other approaches using nonenhanced cardiac cine MRI combined with tagging and/or feature-tracking techniques have also differentiated established or chronic MI from healthy remote myocardium. However, while Ogawa et al (19) showed that MI presence and position could be assessed using both feature tracking and myocardial tagging, the sensitivity and specificity for detecting MI segments were low (feature tracking: sensitivity, 72%; specificity, 71%; tagging technique: sensitivity, 71%; specificity, 75%). Fent et al (34) also reported that feature tracking could identify prior MI but the AUC was low (0.66 [95% CI: 0.54, 0.79], \( P = .012 \)).

The feasibility of \( T_{1w} \) cardiac MRI (35,36) for nonenhanced detection of chronic MI has also been shown but the contrast-to-noise ratio between healthy tissue and MI is low and further sequence developments are required. More recently, texture analysis has been investigated for detecting subacute and chronic MI from nonenhanced cardiac cine; sensitivity of 86% and specificity of 82% was obtained by Bessler et al (37) and overall AUC of 0.85 was achieved by Larroza et al (38).

Our study has a number of limitations: (a) It is a proof-of-concept study using retrospective data from a single vendor.
Our independent testing data set was small, consisting of 43 patients with chronic MI and 18 control patients (20% of all patients). Our ground truth endocardium, epicardium, and MI delineations were performed manually by a single expert due to limited resources. These were then reviewed by a second expert who either ratified the first expert’s segmentation or made minor modifications (by consensus following joint discussion). As such, we are unable to provide interrater agreement. It should also be noted that for our study, any microvascular obstructions were included in the MI regions, although this may affect the motion features (39). For the single-phase method, we only tested an end-diastolic phase but an end-systolic phase may have performed better. However, this is not due to any inherent limitations in the methodology itself but reflects the fact that the LGE data that we had available to train the model was acquired in end diastole. We have not assessed how the number of cardiac phases in the cine study affects diagnostic accuracy of the technique.

In conclusion, a robust deep learning framework for using nonenhanced cardiac cine MRI to infer the likely location, extent, and transmurality of myocardial infarction (MI) has been described, which can be readily expanded to future prospective studies. Future larger-scale studies with data from multiple sites are required for a full validation of our deep learning framework. These would also allow the accuracy of MI prediction to be determined for different myocardial segments with different motion characteristics. Further comparison with microvascular obstructions excluding data and texture analysis will be investigated in future work.
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