Appendix 1

Deep learning (DL) models for myocardium segmentation on T2 maps

Automated analysis of T2 maps was performed by Myomics (Phantomics), which is a DL-based, automated cardiac magnetic resonance imaging (MRI) analysis software.

Dataset

Datasets were retrospectively collected from cardiac MRI examinations obtained from July 2017 to July 2020 in center 1 to develop a DL-based automated T2 map segmentation model. Data used for the validation set were excluded from the training/test dataset. All cardiac MRI examinations were acquired using a 3.0-T MRI system (Prisma^{fit}, Siemens Healthineers). Subsequently, the collected dataset was examined to ensure that the whole heart was represented in the T2 map. Data were anonymized by removing personally identifying information and keeping only the MRI acquisition parameters. T2 maps were acquired by the protocol for center 1. Finally, 586 patients were included. The dataset was randomly split into two groups for training and testing of the DL model at a ratio of 8:2 (23). The total number of images for the training set was 1,587 (527 cases), and for the testing set, it was 177 (59 cases).

Manual annotation and label data

Manually drawn annotation was needed as ground truth (GT) to train the convolutional neural network (CNN) model and evaluate the performance of the automated segmentation. Commercial software (cvi42, Circle Cardiovascular Imaging Inc.) was used for the annotation. Experienced researchers drew the contours along the boundary between the left ventricular (LV) endocardium and epicardium in each image. The endocardial contour was drawn to include the papillary muscle and trabeculations. Once the initial annotation was finished, all contours were reviewed by experienced cardiac radiologists and edited if necessary. The reviewed contours were converted to label images as the GT for the learning and evaluation process. The annotation software output consisted of contour indexes in XML format. The x and y coordinates were converted to a point in a two-dimensional (2D) matrix. The regions outside and inside of the endocardial contour were filled with ones. The final format of label data was a 2D mask image in which the myocardium was labeled as 1 and the background as 0.

Pre-processing

All T2 map images imported into DICOM format went through a series of image processing steps, including restoring the resolution, cropping of the center region, and intensity normalization to minimize variations in size, resolution, and signal intensity. Images that were interpolated to double size during reconstruction were resized to the original matrix size. Specifically, images were resampled based on voxel resolution and oversampling, utilizing information from DICOM tags. All images were transformed to 256×256 after resampling, and then, a 128×128 region was cropped as a region of interest (ROI) based on the center of the image. Signal intensity was normalized to values between 0 and 1. The label images underwent identical pre-processing.

Training the U-Net

A well-established CNN network, U-Net (24), was used to segment the myocardium from the T2 map images. *Figure 3* presents the network architecture of the 2D U-Net. The model has been trained to predict LV myocardium from the respective data. In training, data augmentation (rotation, flipping, and shifting) was applied to improve the performance and generalization of the model.

The models were constructed on the Keras DL library from Tensorflow (https://www.tensorflow.org/). Training and testing processes were implemented on an Ubuntu 18.04 system with an Intel® Xeon Silver 4116 CPU @ 2.10 GHz and Nvidia RTX 3090 graphics processing unit (GPU) (24 GB memory). An Adam optimizer with learning rate, 1.0E–04, $\beta1=0.9$, $\beta2=0.999$, and batch size =32 was used to compile models. A Rectified Linear Unit (ReLU) was used for the activation function in the convolution layers, except for the last layer (softmax layer, simple binary thresholding). A Dice loss function was employed in training the models. The network was trained for 200 epochs and took 4–5 hours with a single GPU.

Post-processing

After training, the model infers the probability map onto the testing group images. The probability map reveals the possibility that each pixel belongs to a myocardium region.

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Post-processing algorithms were applied to the probability map. First, the 2D predictions were rescaled to the original size and resolution. When multiple disconnected components were present in the prediction image after the rescaling procedure, the largest component was considered as the myocardial component was maintained in the probability map. The other disconnected components were considered noise and removed from the probability map.

Evaluation of the model

The Dice similarity coefficient (DSC) between the GT and prediction map was to evaluate the performance of the trained model. The DSC is defined as follows: given two sets, X and Y, DSC, $2|X \cap Y|/(|X| + |Y|)$. Prediction maps were generated using the test set by model inference and post-processing. The DSC of each image was calculated using the prediction map and GT. The mean DSC of the T2 segmentation model from the test set (177 images in 59 cases) was 0.836.

Automatic analysis and reporting

The measured myocardial T2 values were expressed as 16 American Heart Association segments in the form of a bull's eye map. For each slice, three reference points were utilized: the center of mass of the LV endocardial contour and two right ventricular insertion points (RVIPs). The generation of the bull's eye map was facilitated by a rule-based algorithm within the software. This algorithm automatically extracted the RVIP by employing binary masks of the LV myocardium and the right ventricular blood pool, which had been segmented using artificial intelligence techniques. By applying a polar coordinate transformation to these masks and utilizing the geometric information obtained from the transformed masks, the algorithm was able to detect the RVIP.

References

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Table S1 Acquisition parameters for T2 mapping sequences

Parameters	Center 1	Center 2
Pulse sequence	T2-prepared, single-shot TrueFISP	T2-prepared, single-shot turbo flash
Thickness (mm)	8	8
TR/TE (ms)	175.89/1.33	230.9/1.25
Flip angle (°)	12	12
Bandwidth (Hz/px)	1,200	1,184
Matrix	192×132	192×144
Field of view (mm)	380×380	380×380
GRAPPA factor	2	2
TR preparation time (ms)	0, 30, 55	0, 35, 55

TrueFISP, true fast imaging with steady-state precession; TR, repetition time; TE, echo time; GRAPPA, generalized autocalibrating partial parallel acquisition.

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Table S2 Clinical characteristics of the normal group and myocarditis group

Characteristics	Total (n=83)	Center 1 (n=60)			Center 2 (n=23)		
		Normal (n=29)	Myocarditis (n=31)	P value	Normal (n=13)	Myocarditis (n=10)	P value
Sex, n (%)				0.464			0.002
Male	41 (49.4)	13 (44.8)	11 (35.5)		13 (100.0)	4 (40.0)	
Female	42 (50.6)	16 (55.2)	20 (64.5)		0 (0)	6 (60.0)	
Age (years), mean ± SD	41.7±15.8	48.0±15.2	41.6±16.9.	0.129	33.5±8.4	34.3±14.9	0.866
BMI (kg/m^2), mean ± SD	23.2±3.6	22.7±2.6	23.0±4.5	0.770	24.8±2.9	22.9±3.3	0.157

BMI, body mass index; SD, standard deviation.

Table S3 Cardiac MRI results of myocarditis group

Variables	Center 1 (n=31)	Center 2 (n=10)
Left ventricular ejection fraction (%)	48.8±14.3	46.4±14.6
Abnormality in T2-weighted imaging	N/A	10 (100.0)
Elevated native T1 value	31 (100.0)	10 (100.0)
Elevated extracellular fraction	31 (100.0)	10 (100.0)
Presence of late gadolinium enhancement	31 (100.0)	9 (90.0)
Pattern of late gadolinium enhancement	Subepicardial 23, mesocardial 9, subendocardial 7, transmural 3, patchy 3	Subepicardial 5, mesocardial 1, subendocardial 2, transmural 3
Presence of pericardial effusion	27 (87.1)	5 (50.0)
Presence of pleural effusion	11 (35.5)	4 (40.0)

Unless indicated, data are presented as the number of subjects (percentage) or mean ± SD. MRI, magnetic resonance imaging; N/A, not available; SD, standard deviation.

Table S4 Reference T2 values (ms) in the normal group

Group	Base		Mid		Apex	
	Mean (SD)	Upper limit	Mean (SD)	Upper limit	Mean (SD)	Upper limit
Center 1	39.88 (2.15)	44.18	41.81 (3.33)	48.46	44.65 (4.39)	53.42
Center 2	39.67 (2.55)	44.76	40.42 (3.12)	46.66	41.54 (3.24)	48.02
Total	39.82 (2.28)	44.37	41.37 (3.32)	48.01	43.66 (4.30)	52.27

SD, standard deviation.

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Table S5 Number of myocardial segments or patients with elevated T2 values using automated measurements

Automated	Basal		Mid		Apex		Per patient	
	T2 high	Total	T2 high	Total	T2 high	Total	T2 high	Total
Center 1								
Normal	19	170	12	169	9	111	17	29
Myocarditis	116	180	77	180	18	124	27	31
Center 2								
Normal	16	78	9	78	9	52	7	13
Myocarditis	34	54	21	54	9	36	9	10
Total								
Normal	35	248	21	247	18	163	24	42
Myocarditis	150	234	98	234	27	160	36	41

17 segments in 2 subjects were excluded due to segmentation failures, and 25 segments in 4 subjects were excluded due to poor quality images with severe artifacts.

Table S6 Number of myocardial segments or patients with elevated T2 values using reference measurements

Reference	Basal		Mid		Apex		Per patient	
	T2 high	Total	T2 high	Total	T2 high	Total	T2 high	Total
Center 1								
Normal	5	170	6	169	4	112	11	29
Myocarditis	107	180	68	180	18	124	27	31
Center 2								
Normal	3	78	3	78	2	52	3	13
Myocarditis	29	60	17	60	10	40	9	10
Total								
Normal	8	248	9	247	6	164	14	42
Myocarditis	136	240	85	240	28	164	36	41

25 segments in 4 subjects were excluded due to poor quality images with severe artifacts.

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