

Ni Yao¹, Yanhui Tian¹, Daniel Gama das Neves^{2,3}, Chen Zhao⁴, Claudio Tinoco Mesquita², Wolney de Andrade Martins^{3,5}, Alair Augusto Sarmet Moreira Damas dos Santos^{2,3}, Yanting Li¹, Chuang Han¹, Fubao Zhu¹, Neng Dai^{6,7}, Weihua Zhou^{4,8}

- ¹ Zhengzhou University of Light Industry, School of Computer Science and Technology, Zhengzhou, Henan, China
- ² Universidade Federal Fluminense, Department of Radiology, Rio de Janeiro State, Brazil
- ³ DASA Complexo Hospitalar de Niterói, Rio de Janeiro State, Brazil
- ⁴ Michigan Technological University, Department of Applied Computing, Houghton, MI, USA
- ⁵ Universidade Federal Fluminense, Department of Cardiology, Rio de Janeiro State, Brazil
- ⁶ Zhongshan Hospital, Fudan University, Shanghai Institute of Cardiovascular Diseases, Department of Cardiology, Shanghai, China
- ⁷ National Clinical Research Center for Interventional Medicine, Shanghai, China
- ⁸ Center for Biocomputing and Digital Health, Institute of Computing and Cybersystems, and Health Research Institute, Michigan Technological University, Houghton, MI, USA

INCREMENTAL VALUE OF RADIOMICS FEATURES OF EPICARDIAL ADIPOSE TISSUE FOR DETECTING THE SEVERITY OF COVID-19 INFECTION

ADDITIONAL MATERIALS

Supplementary Methods

Study Population

For the EAT extraction study, the heart contour of 47 subjects in Cohort 1 (27 mild and 20 severe COVID-19 cases) and 15 subjects in Cohort 2 (8 mild and 7 severe COVID-19 cases) was manually drawn by experienced operators on LabelMe (Version 4.5.9) and used to train the segmentation model. For the classification modeling phase of mild and severe cases, the EAT of the remaining 368 subjects from Cohort 1 and 85 subjects from Cohort 2 was extracted automatically using a trained deep learning model. 415 patients (371 mild cases and 44 severe cases) with confirmed COVID-19 from Cohort 1 were randomly divided into a derivation Cohort (n=290, 260 mild cases, 30 severe cases) and an internal validation cohort (n=125, 111 mild cases, 14 cases) (Figure 1). Each case contained its clinical information and a set of chest computed tomography (CT) images in Cohort 1. 100 patients (50 mild and 50 severe) from Cohort 2 were deemed as an external validation cohort (Figure 1). Each case contains a set of chest CT images in Cohort 2.

Supplementary Results

Patient characteristics

In the internal validation cohort, 14 (11.2%) patients were diagnosed with severe COVID-19. The mean age of mild and severe cases was 40.46 ± 15.23 yrs and 59.71 ± 14.46 yrs, respectively, and 59% (n=11) and 79% (n=14) were male, respectively (Table 1). There were no significant differences (p>0.05) in gender, white blood cell count, lactic acid, and creatinine.

Fifty patients (50%) were diagnosed with severe COVID-19 in the external validation cohort. The mean age of mild and severe cases was 46.22 ± 7.38 and 62.38 ± 16.14 yrs, respectively, and 56% (n=28) and 60% (n=30) were male, respectively. There were no significant differences (p>0.05) in gender.

Chest CT procedures

CT scans were performed using Toshiba Aquilion 64 CT scanner in Cohort 1. Image acquisition parameters consisted of 120 kV and 114.1 mAs. The thickness of the CT scanned slices was 5 mm, and the in-plane pixel size ranged from 0.579 mm to 0.935 mm. The number of chest CT slices for each patient ranged from 52 to 70. CT scans were performed using a Siemens Somatom Sensation 64 CT scanner in Cohort 2. Image acquisition parameters consisted of 120 kV and 94 mAs. The thickness of the CT scanned slices was 1 mm, and the in-plane pixel size ranged from 0.669 mm to 0.815 mm. The number of chest CT slices for each patient ranged from 300 to 370.

Due to the difference in CT data acquisition imaging between the two cohorts, the segmentation method was used to train the model in the two cohorts.

Supplementary Discussion

EAT segmentation

A comparative test was conducted with a threedimensional V-Net [27] network to explore whether object detection combined with a two-dimensional network would enhance segmentation (Figure 3). The experimental results revealed that while the 3D network can avoid the need to select CT images by object detection, its accuracy in



Supplementary Table 1. Baseline characteristics of patients in the derivation and internal validation cohort with mild and severe COVID-19

Characteristics	Derivation Cohort			Internal Validation Cohort		
Characteristics	Mild	Severe	p	Mild	Severe	p
Age, yrs	39.98±15.39	59.23±14.86	<.001	40.46±15.23	59.71±14.46	<.001
Gender			59			15
Male	125 (48)	16 (53)		65 (59)	11 (79)	
Female	135 (52)	14 (47)		46 (41)	3 (21)	
Past cardiovascular disease	35 (13)	13 (43)	<.001	16 (14)	5 (36)	.045
Lactate dehydrogenase, (U/l)	219.37±61.10	346.47±142.47	<.001	220.29±83.26	326.29±102.63	<.001
NTPro-BNP, (pg/ml)	4.22±0.94	4.19±1.01	.84	4.26±0.83	3.71±0.62	.02
Creatine kinase isoenzymes, (ng/ml)	13.19±12.07	16.43±10.69	.16	12.61±4.66	12.91±2.37	.82
Hypertension,	31 (12)	9 (30)	.01	16(14)	5 (36)	.045
D-dimer, (ug/ml)	0.55±1.34	1.72±3.70	<.001	0.57±1.64	2.23±4.96	.01
White blood cell, (10 ⁹ /l)	5.55±1.90	5.37±1.94	.61	5.38±2.39	6.22±4.61	.29
Lymphocyte, (10 ⁹ /l)	1.44±0.60	1.02±0.41	<.001	1.45±0.49	0.93±0.61	<.001
Serum sodium, (mmol/l)	139.90±2.70	137.70±3.77	<.001	139.98±2.04	134.29±5.20	<.001
Urea, (mmol/l)	4.43±1.50	5.56±3.46	<.001	4.43±1.13	5.04±2.09	.09
PO2, (KPa)	14.34±4.34	9.94±4.94	<.001	14.68±4.75	13.45±5.51	.38
PCO2, (KPa)	5.43±0.45	5.49±0.89	.66	5.39±0.59	4.94±0.72	.01
PCT, (ng/ml)	0.04±0.03	0.18±0.39	<.001	0.04±0.04	0.16±0.18	<.001
APTT, (s)	38.57±6.35	42.06±6.57	.01	38.02±4.10	43.10±5.69	<.001
PT, (s)	13.38±1.10	13.62±0.83	.26	13.29±0.60	13.73±1.46	.04
Potassium, (mmol/l)	3.80±0.34	3.79±0.36	.89	3.83±0.34	3.58±0.43	.02
Lactic acid, (mmol/l)	1.26±1.20	1.37±1.03	.62	1.29±0.81	0.94±0.22	.11
HDL-C, (mmol/l)	29.23±3.90	28.46±3.77	.31	29.02±3.80	26.26±3.14	.01
eGFR, (ml/(min*1.73m ²))	117.13±25.09	106.31±29.54	.03	118.49±22.74	108.55±29.74	.14
Creatinine, (umol/l)	65.30±19.22	69.14±33.25	.35	64.35±14.09	70.31±21.95	.17
LDL-C, (mmol/l)	24.46±1.84	24.51±2.49	.89	24.37±1.77	24.56±2.44	.73
ALT, (U/l)	25.03±18.11	29.23±19.50	.24	29.72±22.25	36.08±35.10	.36
AST, (U/l)	24.61±19.05	37.50±25.24	<.001	24.56±12.24	37.51±23.90	<.001
Dyspnea	6(2)	2 (7)	.18	2 (2)	5 (36)	<.001
Diabetes	14 (5)	3 (10)	.31	4 (4)	3 (21)	.01
Antivirals	161 (56)	29 (97)	<.001	73 (66)	13 (93)	.04
Exudative lesions	50 (17)	10 (33)	.07	16 (14)	2 (14)	.99
CAD	5 (2)	4 (13)	<.001	0 (0)	0 (0)	-

Data are number (percentage) or mean±SD. ALT, alanine aminotransferase; APTT, activated partial thrombin time; AST, aspartate aminotransferase; CAD, coronary heart disease; eGFR, estimated glomerular filtration rate; HDL–C, high density liptein cholesterol; LDL–C, low density lipoprotein cholesterol; PCO2, partial pressure of carbon dioxide; PCT, procalcitonin; PO2, partial pressure of oxygen; NTPRO-BNP, NT pro B-type natriuretic peptide; PT, prothrombin time.

segmenting image details is not as high as that achieved after object detection using the 2D network. As a result, the 2D network was chosen over the 3D network. Hoori et al. [7] proposed an EAT segmentation method using the DeepLab-v³-plus technique. This method adds the learning of multiscale features to improve the segmentation performance. Commandeur et al. [8] combined pericardium detection to segment the EAT. However, these methods are segmented in CT slices containing the heart, and the CT slices that do not contain the heart still had to be manually removed. Our proposed method demonstrated superiority over existing methods in two cohorts, attributed to the influence of negative samples provided by the object detection module prior to segmentation, which improved segmentation accuracy.

Supplementary Table 2. Features used in diagnostic models. The F features were ranked according to the AUC in univariate analysis

Features of the source	Features			
EAT	original_glszm_ZoneEntropy			
Lung	original_firstorder_Kurtosis			
Lung	original_glszm_SmallAreaEmphasis			
EAT	original_firstorder_Skewness			
Lung	$original_glszm_Large Area Low Gray Level Emphasis$			
EAT	$original_glszm_Large Area Low Gray Level Emphasis$			
Lung	original_glcm_MaximalCorrelationCoefficient			
EAT	original_glszm_ZonePercentage			
Lung	original_ngtdm_Strength			
Lung	original_ngtdm_Complexity			



Supplementary Figure 1. Feature importance scores

man adalars	ngtdm_Coarseness 0.258 firstorder_TotalEnergy		0.500		
ung_onginal ung_original	firstorder_Energy glszm_ZoneVariance		0.500		
lung_original	glrlm_RunLengthNonUniformity glszm_LargeAreaEmphasis		0.500 0.500		
lung_original	firstorder_Variance		0.500		
lung_original	gldm_GrayLevelNonUniformity glrlm_GrayLevelNonUniformity	200000000000000000000000000000000000000	0.500		
lung original	glszm_LargeAreaHighGrayLevel shape_VoxelVolume	Emphasis	0.500		
lung diagnos	tics_Mask-original_VoxelNum		0.500 0.500		
EAT original	firstorder_Energy firstorder_TotalEnergy		0.500		
	_shape_MeshVolume firstorder_RobustMeanAbsoluteC	eviation	0.500	0.581	
EAT original	firstorder InterquartileRange			0.607	
lung_original	glcm_Correlation glrlm_LowGrayLevelRunEmphas	is		0.621	
lung_original	firstorder_10Percentile gldm_LowGrayLevelEmphasis			0.623 0.623	
lung_original FAI_original	glszm_SmallAreaLowGrayLevelE	mphasis		0.626 0.645	
EAT original	ngtdm Coarseness			0.65	59
lung original	firstorder_Range _glcm_JointAverage			0.66	
lung original	glcm_SumAverage glrlm_HighGrayLevelRunEmpha glrlm_GrayLevelVariance	cic		0.66	
lung_original	glrlm_GrayLevelVariance			0.6	64
lung_original	gldm_HighGrayl evelEmphasis glcm_Autocorrelation			0.6	566 567
FAT_original_	gldm_LargeDependenceLowGray glrlm_ShortRunHighGrayLevelEr				567 568
lung_original	gldm_LargeDependenceHighGra	ayLevelEmphasis		0.	670
lung_original	_ngtdm_Busyness _glrlm_LongRunLowGrayLevelEm	phasis		0.	672 673
EAT_original_	firstorder_10Percentile				0.677 0.683
lung original	glrim_RunEntropy glszm_GrayLevelNonUniformity				0.684
lung_original	firstorder_Maximum _gldm_GrayLevelVariance				0.685 0.685
lung_original	gldm_SmallDependenceHighGra glszm_GrayLevelVariance	yLevelEmphasis			0.689 0.690
lung_original	_ngtdm_Complexity				0.691
EAT_original_	firstorder_RootMeanSquared glszm_SizeZoneNonUniformityNe	ormalized			0.692 0.694
EAT_original_	glszm_SmallAreaEmphasis firstorder_Mean				0.695
EAT_original_	gidm_DependenceVariance ngtdm_Strength				0.705
EAT original	glszm_GrayLevelNonUniformityN	lormalized			0.709
EAT original	shape Sphericity glcm Imc2				0.715 0.715
EAT_original_	firstorder_Median glcm_SumSquares				0.719
EAT_original_	glrlm_LongRunEmphasis				0.725
EAT_original_ EAT_original_	girim_RunVariance gidm_LargeDependenceEmphas	ls			0.725 0.725
lung_original	glcm_ldmn glrim_ShortRunEmphasis				0.726 0.730
EAT original	girim RunPercentage	anterior de la recon			0.731
EAT_original_ EAT_original_	glrim_RunLengthNonUniformityN gldm_DependenceNonUniformity	Normalized			0.733 0.733
EAT diagnost	ics_Mask-original_VolumeNum ngtdm_Busyness				0.733 0.734
lung_original	glcm_ClusterTendency				0.737
EAT_original_	_shape_SurfaceVolumeRatio gidm_SmailDependenceEmphas	ls			0.741 0.741
	firstorder_Median gldm_DependenceEntropy				0.742 0.742
EAT_original_	glszm_LargeAreaEmphasis				0.742
lung_original	glszm_ZoneVariance _firstorder_RootMeanSquared				0.743
	firstorder_Mean gldm_LargeDependenceLowGra	vLevelEmphasis			0.744
lung original	ngtdm Strength				0.747
lung original	glszm_ZonePercentage glcm_MCC				0.751
lung_original lung_original	alszm GrayLevelNonUniformity	Normalized			0.751 0.754
EAT_original_	giszm_LargeAreaLowGrayLevelE giszm_LargeAreaLowGrayLevelE	mphasis mohasis			0.759 0.763
EAT original	glcm ClusterShade				0.763
EAT original	firstorder_MeanAbsoluteDeviati firstorder_Skewness	on		_	0.768
lung original	glcm_ldn firstorder_90Percentile				0.772 0.778
lung_original	glcm_lmc2				0.778
ung_original ung original	glcm_DifferenceAverage				0.778 0.781
lung_original	glszm_ZoneEntropy glcm_DifferenceEntropy				0.786
lung original	glszm_ZonePercentage				0.790
lung_original lung original	glrim_RunEntropy gldm_SmallDependenceEmphas	ds.			0.791 0.791
lung original	girlm_LongRunEmphasis girlm_ShortRunEmphasis				0.795
lung_original	glrlm_RunPercentage				0.79
lung original lung original	gldm DependenceVariance gldm LargeDependenceEmphas	sis			0.79 0.79
lung original	glcm_SumEntropy glcm_JointFnergy				0.80
lung_original	glcm_MaximumProbability				0.80
lung_original lung_original	alem Idm				0.80
lung original	girlm_RunVariance ngtdm_Contrast				0.8 0.8
lung_original	_firstordet_InterquartileRange				0.8
iung_original lung_original	firstorder_Entropy _glcm_JaintEntropy				0.8 0.8
FAT original	glcm_faintEntropy gldm_DependenceEntropy glrlm_GrayLevelNonUniformityN	formalized			0.8
lung original	firstorder Uniformity				8.0
lung original	firstorder_RobustMeanAbsolutel glrlm_RunLengthNonUniformityl	Normalized			9.0 9.0
lung original	glszm SizeZoneNonUniformityN glszm SmallAreaEmphasis	ormalized			0.
lung original	glcm_InverseVariance				0
lung_original	gldm_DependenceNonUniformit firstorder_Skewness firstorder_Kurtosis	yNormalized			0
ung_original					

The left side of the bar shows the name of each feature, and the right side of the bar shows the importance score of the corresponding feature.

Notably, the operational time for segmenting and extracting EAT from a patient's chest CT data on a standard computer was less than 20 seconds, a significant reduction compared to the approximately 20 minutes required for manual extraction by a specialist. This efficiency improvement represents a substantial time-saving advantage, facilitating more convenient EAT extraction and meaningful research endeavors.

Limitations

Our study still has a few limitations. Firstly, in the segmentation model, two segmentation models need to be trained to complete the segmentation of the heart contour due to the imaging difference between the two centers' data. Secondly, the number of patients included in the study was relatively small.