

Radiomics-Based Outcome Prediction for Irinotecan-TACE in Colorectal Liver Metastases: Advanced Analysis from the Prospective CIREL Trial

ELECTRONIC SUPPLEMENTARY MATERIAL

Supplementary S1. Distribution of participating centers. Overview of the number of patients and lesions in the final included cohort (centers anonymized for GDPR), specifying which were assigned to the training and external validation sets.

Country	Center Name	Train/Test	Patients (n %)	Lesions (n %)
Portugal	CENTER 1	Train	6 (7.9%)	14 (8.0%)
Greece	CENTER 2	Train	5 (6.6%)	9 (5.1%)
North Macedonia	CENTER 3	Train	27 (35.5%)	62 (35.2%)
Hungary	CENTER 4	Train	21 (27.6%)	50 (28.4%)
Italy	CENTER 5	Train	2 (2.6%)	6 (3.4%)
Spain	CENTER 6	Train	1 (1.3%)	1 (0.6%)
Italy	CENTER 7	Train	1 (1.3%)	3 (1.7%)
Spain	CENTER 8	Test	2 (2.6%)	6 (3.4%)
Italy	CENTER 9	Test	10 (13.2%)	22 (12.5%)
Russia	CENTER 10	Test	1 (1.3%)	3 (1.7%)

Supplementary S2. CT image acquisition parameters. Summary of in-plane resolution, slice thickness, kVp, and scanner systems in the included cohort.

In-plane resolution (median IQR)	0.781 (0.706–0.872)
Slice thickness (median IQR)	3.0 (1.25–3.0)
kVp (median IQR)	120 (120–120)
CT scanners (n %)	
Ingenuity CT	16 (21.05%)
BrightSpeed	16 (21.05%)
SOMATOM Definition AS+	7 (9.21%)
LightSpeed VCT	5 (6.58%)
SOMATOM Definition Flash	5 (6.58%)
Brilliance 16P	5 (6.58%)
Aquilion	3 (3.95%)
SOMATOM go.Up	3 (3.95%)
Revolution EVO	3 (3.95%)
Brilliance 16	3 (3.95%)
Discovery IQ	2 (2.63%)
Asteion	1 (1.32%)
Brilliance 64	1 (1.32%)
Brilliance Big Bore	1 (1.32%)
SOMATOM go.Now	1 (1.32%)
LightSpeed RT16	1 (1.32%)
Emotion 16 (2007)	1 (1.32%)
Sensation Cardiac 64	1 (1.32%)
Discovery STE	1 (1.32%)

Supplementary S3. Radiomic feature extraction configuration. Detailed parameters for image pre-processing and radiomic feature extraction.

imageType:

Original:

binWidth: 5

Square:

binWidth: 1

SquareRoot:

binWidth: 14

Logarithm:

binWidth: 26

Exponential:

binWidth: 1

Gradient:

binWidth: 2

LoG:

binWidth: 2

sigma: [1.0, 2.0, 3.0, 4.0, 5.0] Wavelet: {}

LBP3D:

binWidth: 1.0

featureClass:

shape:

firstorder:

glcm:

- 'Autocorrelation'

- 'JointAverage'

- 'ClusterProminence'

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- 'ClusterShade'
- 'ClusterTendency'
- 'Contrast'
- 'Correlation'
- 'DifferenceAverage'
- 'DifferenceEntropy'
- 'DifferenceVariance'
- 'JointEnergy'
- 'JointEntropy'
- 'Imc1'
- 'Imc2'
- 'Idm'
- 'Idmn'
- 'Id'
- 'Idn'
- 'InverseVariance'
- 'MaximumProbability'
- 'SumEntropy'
- 'SumSquares'

glrlm:

glszm:

gldm:

ngtdm:

setting:

interpolator: 'sitkBSpline'

resampledPixelSpacing: [1, 1, 1]

padDistance: 10

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minimumROIDimensions: 2

minimumROISize: 1

correctMask: true

voxelArrayShift: 1000

label: 1

Supplementary S4. Expanded patient characteristics. Comparison of baseline laboratory-based values between training and external validation cohorts.

	Total cohort	Training set	External validation	p
Serum creatinase (median IQR)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	0.9 (0.8-1.0)	0.195
Alanine aminotransferase (median IQR)	27.0 (19.0-36.0)	29.0 (19.2-36.0)	23.0 (15.0-27.0)	0.170
Aspartate transaminase (median IQR)	31.0 (25.0-43.0)	31.0 (25.0-46.8)	29.0 (25.0-34.0)	0.556
Lactate dehydrogenase (median IQR)	229.5 (177.5-353.2)	242.0 (201.5-384.0)	163.0 (101.0-208.0)	<0.001
Alkaline phosphatase (median IQR)	130.0 (96.2-188.0)	142.0 (101.0-200.0)	77.0 (69.0-130.0)	0.007
Neutrophil count (median IQR)	4.6 (3.6-6.0)	4.7 (3.8-6.0)	4.3 (3.0-7.0)	0.591
Platelet count (median IQR)	207.0 (158.5-256.8)	207.0 (158.0-254.0)	217.0 (160.0-260.0)	0.907
Bilirubin (median IQR)	8.1 (1.0-12.5)	9.3 (4.5-12.9)	1.0 (0.7-1.1)	0.002
Carcinoembryonic antigen (median IQR)	64.3 (19.2-265.8)	71.8 (20.0-279.2)	46.6 (19.0-197.0)	0.842
Mismatch repair status (n %)				
pMMR	14 (18.4%)	14 (22.2%)	0 (0.0%)	0.124
dMMR	2 (2.6%)	2 (3.2%)	0 (0.0%)	
Missing	60 (78.9%)	47 (74.6%)	13 (100.0%)	

Supplementary S5. Final feature sets for imaging and clinical-lab models. The general radiomic signature, intensity features, and clinical-laboratory variables were included in the final machine learning models.

General radiomic signature	Intensity features	Clinical-lab features
original_firstorder_Maximum	original_firstorder_10Percentile	Gender
original_glcml_ClusterProminence	original_firstorder_90Percentile	Age
square_glszm_GrayLevelVariance	original_firstorder_Energy	ECOG performance
square_ngtdm_Strength	original_firstorder_Entropy	Dominant lobe affected
squareroot_firstorder_Kurtosis	original_firstorder_InterquartileRange	Synchronous vs. Metachronous
squareroot_glcml_ClusterProminence	original_firstorder_Kurtosis	Serum creatinase
logarithm_firstorder_Kurtosis	original_firstorder_Maximum	ALT
logarithm_firstorder_Range	original_firstorder_MeanAbsoluteDeviation	AST
logarithm_firstorder_Skewness	original_firstorder_Mean	LDH
logarithm_glcml_Autocorrelation	original_firstorder_Median	Alkaline phosphatase
logarithm_glrml_LowGrayLevelRunEmphasis	original_firstorder_Minimum	Neutrophils
exponential_glrml_ShortRunLowGrayLevelEmphasis	original_firstorder_Range	Platelets
exponential_glszm_SmallAreaHighGrayLevelEmphasis	original_firstorder_RobustMeanAbsoluteDeviation	CEA
exponential_gldm_DependenceVariance	original_firstorder_RootMeanSquared	RAS mutation
log-sigma-1-0-mm-3D_gldm_LargeDependenceLowGrayLevelEmphasis	original_firstorder_Skewness	BRAF mutation
log-sigma-2-0-mm-3D_firstorder_Mean	original_firstorder_TotalEnergy	Bilirubin
log-sigma-2-0-mm-3D_firstorder_Skewness	original_firstorder_Uniformity	MMR status
log-sigma-2-0-mm-3D_glcml_Correlation	original_firstorder_Variance	
log-sigma-2-0-mm-3D_glcml_Imc1		
log-sigma-3-0-mm-3D_firstorder_10Percentile		
log-sigma-3-0-mm-3D_firstorder_Median		
log-sigma-3-0-mm-3D_firstorder_Skewness		

log-sigma-3-0-mm-3D_glcml_ClusterShade		
log-sigma-3-0-mm-3D_glcml_Imc2		
log-sigma-4-0-mm-3D_firstorder_Median		
log-sigma-4-0-mm-3D_glcml_ClusterShade		
wavelet-LLH_glcml_ClusterShade		
wavelet- LLH_glszm_SmallAreaLowGrayLevelEmphasis		
wavelet- LHL_glrIm_LongRunLowGrayLevelEmphasis		
wavelet-LHL_glrIm_LowGrayLevelRunEmphasis		
wavelet-LHH_glcml_ClusterShade		
wavelet- LHH_glszm_SmallAreaLowGrayLevelEmphasis		
wavelet- HLL_glrIm_LongRunLowGrayLevelEmphasis		
wavelet-HLH_firstorder_Mean		
wavelet-HHH_firstorder_Mean		
wavelet-HHH_firstorder_Median		
wavelet- LLL_glrIm_ShortRunHighGrayLevelEmphasis		
lbp-3D-m1_firstorder_Maximum		
lbp-3D-m1_firstorder_Minimum		