

Supplementary Tables**Supplementary Table S1.** CT scan parameters in our institution

CT Manufacturer and Model	GE Medical Systems (Discovery CT750HD/Revolution EVO); SIEMENS (SOMATOM Force)
Tube Voltage	90-140 KeV (median 120 keV)
Reconstruction thickness	Layer thickness: 1mm, 1.25mm, 1.5mm Layer spacing: 1mm, 1.25mm, 1.5mm
Matrix	512×512 pixels

Supplementary Table S2. 1223 radiomics features were extracted from pretreatment CECT imagesusing 3D slicer (V.5.2.2, <https://www.slicer.org>)

Feature Category	Feature Name	Number of features	Sum of features
Original shape features	1. Elongation	14	14
	2. Flatness		
	3. Least Axis Length		
	4. Major Axis Length		
	5. Maximum 2D Diameter Column		
	6. Maximum 2D Diameter Row		
	7. Maximum 2D Diameter Slice		
	8. Maximum 3D Diameter		
	9. Mesh Volume		
	10. Minor Axis Length		
	11. Sphericity		
	12. Surface Area		
	13. Surface Volume Ratio		
	14. Voxel Volume		
Original first-order features	1. The 10th percentile of X	18	93
	2. The 90th percentile of X		
	3. Energy		
	4. Entropy		
	5. Interquartile Range		
	6. Kurtosis		
	7. Maximum		
	8. Mean Absolute Deviation		
	9. Mean Intensity		
	10. Median Intensity		

			11. Minimum Intensity		
			12. Range		
			13. Robust Mean Absolute Deviation		
			14. Root Mean Squared		
			15. Skewness		
			16. Total Energy		
			17. Uniformity		
			18. Variance		
Original features	GLCM	texture	1. Autocorrelation	24	
			2. Cluster Prominence		
			3. Cluster Shade		
			4. Cluster Tendency		
			5. Contrast		
			6. Correlation		
			7. Difference Average		
			8. Difference Entropy		
			9. Difference Variance		
			10. ID (inverse difference)		
			11. IDM (inverse difference moment)		
			12. IDMN (inverse difference moment normalized)		
			13. IDN (inverse difference normalized)		
			14. IMC1 (informational measure of correlation 1)		
			15. IMC2 (informational measure of correlation 2)		
			16. Inverse Variance		
			17. Joint Average		
			18. Joint Energy		
			19. Joint Entropy		
			20. MCC		
			21. Maximum Probability		
			22. Sum Average		
			23. Sum Entropy		
			24. Sum Squares		
Original features	GLDM	texture	1. Dependence Entropy	14	
			2. Dependence Non-Uniformity		
			3. Dependence Non-Uniformity Normalized		
			4. Dependence Variance		
			5. Gray Level Non-Uniformity		
			6. Gray Level Variance		
			7. High Gray Level Emphasis		
			8. Large Dependence Emphasis		
			9. Large Dependence High Gray Level Emphasis		
			10. Large Dependence Low Gray Level Emphasis		

			11. Low Gray Level Emphasis		
			12. Small Dependence Emphasis		
			13. Small Dependence High Gray Level Emphasis		
			14. Small Dependence Low Gray Level Emphasis		
Original features	GLRLM	texture	1. Gray Level Non-Uniformity	16	
			2. Gray Level Non-Uniformity Normalized		
			3. Gray Level Variance		
			4. High Gray Level Run Emphasis		
			5. Long Run Emphasis		
			6. Long Run High Gray Level Emphasis		
			7. Long Run High Gray Level Emphasis		
			8. Low Gray Level Run Emphasis		
			9. Run Entropy		
			10. Run Length Non-Uniformity		
			11. Run Length Non-Uniformity Normalized		
			12. Run Percentage		
			13. Run Variance		
			14. Short Run Emphasis		
			15. Short Run High Gray Level Emphasis		
			16. Short Run Low Gray Level Emphasis		
Original features	GLSZM	texture	1. Gray Level Non-Uniformity	16	
			2. Gray Level Non-Uniformity Normalized		
			3. Gray Level Variance		
			4. High Gray Level Zone Emphasis		
			5. Large Area Emphasis		
			6. Large Area High Gray Level Emphasis		
			7. Large Area Low Gray Level Emphasis		
			8. Low Gray Level Zone Emphasis		
			9. Size Zone Non-Uniformity		
			10. Size Zone Non-Uniformity Normalized		
			11. Small Area Emphasis		
			12. Small Area High Gray Level Emphasis		
			13. Small Area Low Gray Level Emphasis		
			14. Zone Entropy		
			15. Zone Percentage		
			16. Zone Variance		
Original features	NGTDM	texture	1. Busyness	5	
			2. Coarseness		
			3. Complexity		
			4. Contrast		
			5. Strength		
LoG transform features			LoG-sigma-1.0mm-3D features	93	372
			LoG-sigma-1.5mm-3D features	93	

	LoG-sigma-2.0mm-3D features	93	744
	LoG-sigma-2.5mm-3D features	93	
Wavelet transform features	wavelet-LLH features	93	
	wavelet-LHL features	93	
	wavelet-LHH features	93	
	wavelet-HLL features	93	
	wavelet-HLH features	93	
	wavelet-HHL features	93	
	wavelet-HHH features	93	
	wavelet-LLL features	93	

Note: LoG transform features and Wavelet transform features both are obtained based on the transformation of the original first-order features and original texture features.

Abbreviations: CECT, contrast-enhanced computed tomography; GLCM, Gray Level Co-occurrence Matrix; GLDM, Gray Level Dependence Matrix; GLRLM, Gray Level Run Length Matrix; GLSZM, Gray Level Size Zone Matrix; NGTDM, Neighborhood Gray-tone Difference Matrix; LoG, Laplacian of Gaussian.

Supplementary Table S3. Tumor responses for patients with HCC receiving lenvatinib plus PD-1 inhibitors and interventional treatment according to mRECIST and RECIST 1.1 criteria

Tumor Response, n (%)	mRECIST (n=151)	RECIST 1.1 (n=151)
Complete response	3(2.0)	0(0.0)
Partial response	69(45.7)	55(36.4)
Stable disease	46(30.5)	57(37.7)
Progressive disease	33(21.8)	39(25.8)
Not evaluable	0(0.0)	0(0.0)
Objective response rate, n (%)	72(47.7)	55(36.4)
Disease control rate, n (%)	118(78.1)	112(74.2)
Conversion resection rate, n (%)	35(23.2)	35(23.2)

Abbreviations: uHCC, unresectable hepatocellular carcinoma.

Supplementary Table S4. Multivariable logistic regression analysis of the variables with statistical differences in univariate comparison in the training cohort

Variables	OR	OR lower 95% CI	OR upper 95% CI	P value
TBS grade	2.294	1.006	5.229	0.048
HBsAg	4.049	1.195	13.719	0.025

Abbreviations: TBS, tumor burden score; HBsAg, hepatitis B surface antigen; OR, odds ratio; CI, confidence interval.

Supplementary Table S5. The performance of clinical models constructed by nine ML classifiers for predicting the response to lenvatinib plus PD-1 inhibitors and interventional therapy in patients with unresectable HCC in the training and validation cohorts.

Model name	Cohort	ACC	AUC	95% CI	SEN	SPE	PPV	NPV	F1	Threshold
LR	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.624
LR	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.624
Naive Bayes	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.740
Naive Bayes	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.740
SVM	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.654
SVM	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.654
KNN	Training	0.594	0.514	0.406 - 0.622	0.922	0.448	0.560	0.765	0.696	0.600
KNN	Validation	0.440	0.413	0.275 - 0.551	0.952	0.105	0.426	0.667	0.588	0.400
RF	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.646
RF	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.646
Extra Trees	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.660
Extra Trees	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.660
LightGBM	Training	0.604	0.604	0.508 - 0.700	0.647	1.000	0.600	0.609	0.623	0.567
LightGBM	Validation	0.580	0.612	0.486 - 0.737	0.810	1.000	0.500	0.750	0.618	0.567
AdaBoost	Training	0.644	0.669	0.571 - 0.766	0.608	1.000	0.660	0.630	0.633	0.515
AdaBoost	Validation	0.580	0.585	0.442 - 0.728	0.714	1.000	0.500	0.700	0.588	0.515
MLP	Training	0.644	0.620	0.517 - 0.723	0.608	1.000	0.660	0.630	0.633	0.514
MLP	Validation	0.580	0.615	0.479 - 0.751	0.810	0.857	0.500	0.750	0.618	0.482

Abbreviations: ML, machine learning; LR, logistic regression; SVM, support vector machine; KNN, k-nearest neighbor; RF, random forest; LightGBM, light gradient boosting machine; AdaBoost, adaptive boosting; MLP, multilayer perceptron; ACC, accuracy; AUC, area under the receiver operating curve; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Supplementary Table S6. Pre-scores of predict models between non-response group and response group in training and validation cohorts

Cohort	Model	Non-responders	Responders	P value
Training cohort (N=101)	Clinical Model	0.450(0.373,0.624)	0.624(0.450,0.624)	0.002
	Radiomics Model	0.329(0.150,0.430)	0.729(0.502,0.867)	<0.001
	Combined Model	0.175(0.034,0.341)	0.909(0.568,0.976)	<0.001
Validation cohort (N=50)	Clinical Model	0.624(0.450,0.624)	0.624(0.450,0.624)	0.243
	Radiomics Model	0.395(0.285,0.522)	0.620(0.561,0.761)	<0.001
	Combined Model	0.113(0.029,0.393)	0.701(0.515,0.922)	<0.001

Note: Values refer to median (interquartile range).

Supplementary Table S7. The performance of radiomics models constructed by nine ML classifiers for predicting the response to lenvatinib plus PD-1 inhibitors and interventional therapy for patients with unresectable HCC in the training and validation cohorts.

Model name	Cohort	ACC	AUC	95% CI	SEN	SPE	PPV	NPV	F1	Threshold
LR	Training	0.703	0.775	0.686 - 0.864	0.529	0.880	0.818	0.647	0.643	0.648
LR	Validation	0.780	0.808	0.685 - 0.931	0.524	0.966	0.917	0.737	0.667	0.670
Naive Bayes	Training	0.703	0.737	0.641 - 0.834	0.549	0.860	0.800	0.652	0.651	0.823
Naive Bayes	Validation	0.760	0.833	0.723 - 0.942	1.000	0.586	0.636	1.000	0.778	0.547
SVM	Training	0.772	0.867	0.800 - 0.933	0.627	0.920	0.889	0.708	0.736	0.530
SVM	Validation	0.800	0.817	0.695 - 0.939	0.571	0.966	0.923	0.757	0.706	0.540

KNN	Training	0.703	0.805	0.727 - 0.883	0.490	0.920	0.862	0.639	0.625	0.800
KNN	Validation	0.700	0.711	0.567 - 0.855	0.429	0.897	0.750	0.684	0.545	0.800
RF	Training	0.782	0.855	0.783 - 0.926	0.843	0.720	0.754	0.818	0.796	0.417
RF	Validation	0.740	0.800	0.675 - 0.926	0.952	0.607	0.625	0.944	0.755	0.417
Extra Trees	Training	0.891	0.959	0.927 - 0.991	0.902	0.880	0.885	0.898	0.893	0.494
Extra Trees	Validation	0.740	0.839	0.731 - 0.947	0.952	0.586	0.625	0.944	0.755	0.499
LightGBM	Training	0.842	0.911	0.858 - 0.965	0.882	0.800	0.818	0.870	0.849	0.485
LightGBM	Validation	0.720	0.752	0.613 - 0.891	0.762	0.690	0.640	0.800	0.696	0.542
AdaBoost	Training	0.832	0.918	0.867 - 0.968	0.961	0.700	0.766	0.946	0.852	0.487
AdaBoost	Validation	0.640	0.706	0.563 - 0.849	0.857	0.483	0.545	0.824	0.667	0.495
MLP	Training	0.832	0.900	0.842 - 0.958	0.686	0.980	0.972	0.754	0.805	0.607
MLP	Validation	0.820	0.893	0.804 - 0.982	0.952	0.724	0.714	0.955	0.816	0.490

Abbreviations: ML, machine learning; LR, logistic regression; SVM, support vector machine; KNN, k-nearest neighbor; RF, random forest; LightGBM, light gradient boosting machine; AdaBoost, adaptive boosting; MLP, multilayer perceptron; ACC, accuracy; AUC, area under the receiver operating curve; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Supplementary Table S8. The comparison of the performance of different prediction models using Delong test in the training and validation cohorts.

Cohort	Model comparison	P value
Training cohort	Clinical Model vs. Radiomics Model	<0.001
	Clinical Model vs. Combined Model	<0.001
	Radiomics Model vs. Combined Model	0.112
Validation cohort	Clinical Model vs. Radiomics Model	<0.001
	Clinical Model vs. Combined Model	<0.001
	Radiomics Model vs. Combined Model	0.907

Supplementary Table S9. The relative HRs with 95% CIs, cut-off points, C-indexes and corresponding 95% CIs of Radiomics model, and Combined model in predicting PFS for training and validation cohorts.

Cohort	Model	PFS Prediction					
		Cut-off point	HR	HR 95% CI	P value	C-index ±SE	C-index 95% CI
Training cohort	Radiomics model	0.499	1.913	[1.121 - 3.265]	0.016	0.593±0.034	[0.526 - 0.660]
	Combined model	0.715	2.160	[1.264 - 3.690]	0.007	0.602±0.031	[0.541 - 0.663]
Validation cohort	Radiomics model	0.484	2.347	[1.095 - 5.031]	0.012	0.632±0.046	[0.542 - 0.722]
	Combined model	0.337	2.033	[0.965 - 4.285]	0.039	0.616±0.047	[0.524 - 0.708]

Abbreviations: HR, hazard ratio; PFS, progression-free survival; CI, confidence interval.

Supplementary Table S10. The relative HRs with 95% CIs, cut-off points, C-indexes and corresponding 95% CIs of Radiomics model, and Combined model in predicting OS for training and validation cohorts.

Cohort	Model	OS Prediction					
		Cut-off point	HR	HR 95% CI	P value	C-index ±SE	C-index 95% CI
Training cohort	Radiomics model	0.554	4.252	[2.051 - 8.816]	0.001	0.643±0.040	[0.565 - 0.721]
	Combined model	0.589	3.314	[1.600 - 6.865]	0.003	0.630±0.043	[0.546 - 0.714]
Validation cohort	Radiomics model	0.484	2.592	[1.050 - 6.394]	0.019	0.622±0.058	[0.508 - 0.736]
	Combined model	0.337	2.181	[0.903 - 5.266]	0.062	0.607±0.058	[0.493 - 0.721]

Abbreviations: HR, hazard ratio; OS, overall survival; CI, confidence interval.

Supplementary Table S11. The detailed information of PFS prediction for Radiomics model and Combined model between high- and low-risk groups in the training and validation sets

Value	Radiomics model		Radiomics model		Combined model		Combined model	
	Training set		Validation set		Training set		Validation set	
	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
n	46	55	29	21	37	64	28	22
events	20	34	14	16	15	39	14	16
Median PFS	NA	12.0	NA	5.0	NA	12.0	16.0	5.0
Median PFS, 95%CI	NA	5.8-18.2	NA	3.2-6.8	NA	7.8-16.2	10.5-21.5	3.2-6.8
6 months PFS rate, %	84.8	61.8	72.4	38.1	89.2	62.4	71.4	40.9
12 months PFS rate, %	61.1	44.8	60.2	25.5	66.6	43.2	58.6	29.1

Abbreviations: PFS, progression-free survival; CI, confidence interval.

Supplementary Table S12. The detailed information of OS prediction for Radiomics model and Combined model between high- and low-risk groups in the training and validation sets

Value	Radiomics model		Radiomics model		Combined model		Combined model	
	Training set		Validation set		Training set		Validation set	
	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
n	40	61	29	21	45	56	28	22
events	5	24	9	12	7	22	9	12
Median OS	NA	17.0	NA	12.0	NA	17.0	NA	3.7
Median OS, 95%CI	NA	NA	NA	5.2-18.8	NA	13.0-21.0	NA	7.8-22.2
6 months OS rate, %	100.0	90.1	84.5	76.2	100.0	89.2	83.9	77.3
12 months OS rate, %	86.5	68.9	78.6	49.4	82.8	71.0	77.8	51.9

Abbreviations: OS, overall survival; CI, confidence interval.