

Appendix 1 The Rad-score formula

$$\begin{aligned} \text{Rad-score} = & 1.031 \times \text{original_firstorder10Percentile} + \\ & 0.294 \times \text{original_firstorder_Median} + \\ & 0.010 \times \text{original_glrlm_ShortRunHighGrayLevelEmphasis} + \\ & -0.011 \times \text{log.sigma.1.0.mm.3D_ngtdm_Busyness} + \\ & -0.074 \times \text{wavelet.LHL_gldm_GrayLevelNonUniformity} \end{aligned}$$

Table S1 CT scanning parameters

CT scanner	CT 256	CT 128	CT 64	CT 64	CT 64	CT 16
Scanner model	Brilliance iCT 256	Somatom Definition Flash	Somatom Sensation 64	Discovery 750	LightSpeed VCT	Brilliance 16
Manufacturer	Philips	Siemens	Siemens	General Electric	General Electric	Philips
Gantry rotation time (s)	0.5	0.28	0.5	0.5	0.5	0.5
Tube voltage (kV)	120	120	120	120	120	120
Tube current	250 mAs	Ref. 200 mAs	200 mAs	200–400 mAs (automatic tube current modulation)	200 mAs	200 mAs
Detector collimation (mm)	0.625	0.6	0.6	0.625	0.625	0.75
Matrix	512×512	512×512	512×512	512×512	512×512	512×512
Pitch	0.915	1.0	1.0	1.375	0.984	1
Slice thickness (mm)	5	5	5	5	5	5

Table S2 Baseline data of patients in the training cohort and validation cohort

Characteristics	Training cohort (n=351)	Validation cohort (n=150)	P value
Age, year, median (range)	61.00 (53.00–63.00)	61.00 (51.00–64.25)	0.253
Maximum diameter, mm, median (range)	21.00 (14.00–32.00)	24.00 (14.75–31.25)	0.643
CEA, ng/mL, median (range)	2.04 (1.02–4.58)	1.81 (1.09–4.86)	0.879
CA125, U/mL, median (range)	10.74 (7.79–18.32)	11.06 (8.00–17.69)	0.733
CYFRA21-1, ng/mL, median (range)	2.41 (1.84–3.47)	2.44 (1.82–3.64)	0.758
ALP, U/L, median (range)	68.00 (56.00–82.00)	69.00 (55.00–84.25)	0.730
Gender (male/female)	156/195	59/91	0.290
Smoking history (yes/no)	100/251	44/106	0.914
Ki-67 ($\leq 5\%$ / $> 5\%$)	150/201	67/83	0.689
EGFR (mutant/wild)	147/204	67/83	0.564
Location (peripheral/central)	332/19	144/6	0.506
Shape (regular/irregular)	89/262	31/119	0.260
Edge (clear/vague)	198/153	74/76	0.145
Lobulation (yes/no)	211/140	95/55	0.496
Spiculation (yes/no)	116/235	55/95	0.434
Cavity (yes/no)	7/344	8/142	0.085
Vacuole (yes/no)	47/304	21/129	0.855
Air bronchogram (yes/no)	77/274	42/108	0.144
Pleural traction (yes/no)	187/164	93/57	0.072
Pleural thickening (yes/no)	34/317	15/135	0.914
Pleural effusion (yes/no)	33/318	9/141	0.208
Vessel convergence (yes/no)	57/294	35/115	0.060
Morphology (solid/mixed/ground-glass)	219/65/67	93/23/34	0.528
Stage (I/II/III/IV)	236/37/38/40	97/9/25/19	0.421

CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CYFRA21-1, cytokeratin-19-fragment; ALP, alkaline phosphatase; EGFR, epidermal growth factor receptor.

Table S3 The results of multivariate analysis

Characteristics	OR (95% CI)	P value
Maximum diameter	0.990 (0.956–1.024)	0.544
CEA	0.999 (0.994–1.005)	0.760
CA125	1.002 (0.997–1.008)	0.389
CYFRA21-1	1.211 (1.073–1.367)	0.002
ALP	0.995 (0.980–1.011)	0.545
Gender	0.601 (0.250–1.443)	0.254
Smoking history	0.307 (0.091–1.033)	0.057
Ki-67	26.444 (2.554–273.831)	0.006
Location	1.809 (0.390–8.383)	0.449
Edge	9.752 (3.407–27.913)	<0.001
Lobulation	4.308 (1.225–15.143)	0.023
Spiculation	1.597 (0.646–3.944)	0.310
Air bronchogram	1.679 (0.619–4.553)	0.309
Pleural traction	2.219 (0.843–5.840)	0.107
Pleural thickening	1.145 (0.326–4.014)	0.833
Pleural effusion	1.874 (0.433–8.116)	0.401
Vessel convergence	1.536 (0.556–4.249)	0.408
Morphology	1.268 (0.427–3.761)	0.669
Stage	2.637 (1.687–4.124)	<0.001

CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CYFRA21-1, cytokeratin-19-fragment; ALP, alkaline phosphatase; OR, odds ratio; CI, confidence interval.

Table S4 Results of the DeLong test of the model

Models	Training cohort		Validation cohort	
	Z value	P value	Z value	P value
Clinical model vs. radiomics model	0.943	0.346	0.387	0.699
Clinical model vs. combined model	0.246	0.806	0.954	0.340
Radiomics model vs. combined model	2.138	0.033*	1.479	0.139

*, statistically significant differences.