

Appendix 1

PyRadiomics settings were specified in the parameter file which used the default binWidths = 25 for the original image and the wavelet decomposition extraction. No kernel, image normalization or resampling options were used. Images were filtered through all the ["coif1"] wavelet decomposition levels (LLL, LLH, LHL, HLL, HLH, HHL, & HHH) with the default settings for 'start_level' and 'level'. For both the original and wavelet images the following feature classes were included: first order, shape, GLCM, GLRLM, GLSZM, GLDM, and NGTDM. Shape features were excluded in feature selection/reduction process since the whole lung was segmented.

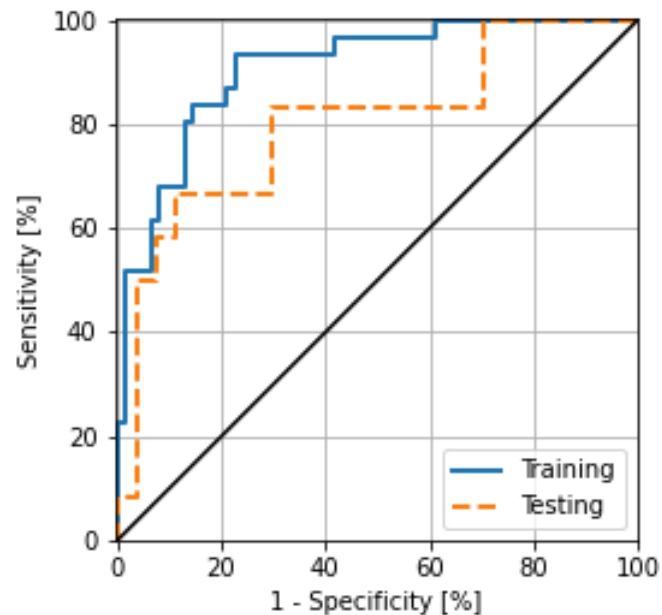


Figure S1 Area under the curve (AUC) performance results from the developed PFS prediction model using CT based radiomic features. PFS, progression-free survival.

Table S1 Programmed death ligand 1 (PD-L1) expression and acquisition results

	PFS		Pneumonitis	
	≤90 days PFS (cases)	>90 days PFS (controls)	Pneumonitis (cases)	No Pneumonitis (controls)
PD-L1 TPS (Biopsy) (<1%: 1-49%: ≥50%)	16:4:7	19:12:22	5:2:3	30:14:26
PD-L1 TPS (Cytology) (<1%: 1-49%: ≥50%)	6:2:2	12:11:8	0:4:0	18:9:10
PD-L1 TPS (All samples) (<1%: 1-49%: ≥50%: Unknown)	22:6:9:6	31:23:30:5	5:6:3:1	48:23:36:10
PD-L1 Assay (E1LN3:22C3:Unknown)	29:8:6	63:21:4	12:2:1	81:27:9

PFS, progression-free survival; SD, standard deviation.

Table S2 Pneumonitis clinical demographics

Parameter	All	Pneumonitis (cases)	No Pneumonitis (controls)	P value
N	132	15	117	-
Age, years (mean ± SD)	64.1±10.4	64.3±8.06	64.1±10.7	>0.9999
Sex (Male: Female)	67:65	5:10	62:55	0.1516
Race (White:African American/Black: Asian: Declined)	126:3:2:1	13:2:0:0	113:1:2:1	0.0220
Pack years (>20 yrs:<20 yrs:never smoker)	100:16:16	10:2:3	90:14:13	0.5851
Immunotherapy type (Pemb: Nivo: Avel)	97:30:5	8:6:1	89:24:4	0.1714
Programmed death ligand 1 (PD-L1) TPS (<1%:1-49%:≥50%:Unknown)	54:28:40:10	5:6:3:1	48:23:36:10	0.3507
Immunotherapy concurrent with chemotherapy (Yes:No)	28:104	3:12	25:92	0.9029
Lymphocyte count (per uL) (mean ± SD)	1,921±8,168	994.3±773.2	2,040±8,669	0.1390
Pneumonitis (Yes:No)	15:117	15:0	0:117	<0.0001
Line of treatment (Naïve:2nd Line:3rd Line:4th Line)	77:44:7:4	6:6:1:2	71:38:6:2	0.0661
Prior chest radiation (Yes:No)	54:78	9:6	45:72	0.1102
Days PFS (mean ± SD)	288.6±317.5	427.2±418.9	270.7±299.6	0.0405

PFS, progression-free survival; SD, standard deviation; Pemb, pembrolizumab; Nivo, nivolumab; Avel, avelumab.

Table S3 Feature reduction of selection results for pneumonitis prediction

Feature (mean ± SD)	PNEUMO_Radiomic + Clinical	PNEUMO_Radiomic	Pneumonitis	No Pneumonitis	P value
wavelet.HHH_glcm_ClusterProminence	X	X	0.9599±0.5444	0.9369±3.595	0.0001
original_glcm_ClusterShade	X	X	5106±3050	3899±1482	0.0409
wavelet.HLH_glcm_ClusterShade	X	X	0.8151±0.5282	0.2964±0.4593	0.0003
wavelet.LHH_firstorder_Mean	X	X	12.15±2.315	12.29±2.988	0.4995
HistoryofSystemicRadiation	X		9:6	45:72	0.1102
wavelet.HLH_gldm_SmallDependence-HighGrayLevelEmphasis	X	X	12.29±15.26	5.638±13.87	<0.0001
wavelet.LLH_glcm_Idmn	X	X	0.9959±0.0022	0.9966±0.0015	0.6182
wavelet.LHH_glrlm_GrayLevelVariance	X		6.551±1.636	4.492±1.692	<0.0001
Smoker	X		10:2:3	90:14:13	0.5851
wavelet.LHL_gldm_SmallDependenceEmphasis		X	0.0598±0.0187	0.0475±0.0189	0.0522
wavelet.HLH_glcm_InverseVariance		X	0.4729±0.0062	0.4756±0.0065	0.2118
wavelet.LHH_glcm_ClusterShade		X	0.7727±0.7312	0.1391±0.3272	<0.0001

Table S4 Performance results of pneumonitis prediction from developed models using image and/or clinical features

Pneumonitis prediction model	Training AUC (95% CI)	Testing AUC (95% CI)	Sensitivity	Specificity
Pneumo_Radiomic + Clinical (AUC-PR)	0.60 (0.42–0.78)	0.24 (0.11–0.37)	0.75	0.71
Pneumo_Radiomic (AUC-PR)	0.63 (0.5–0.76)	0.24 (0.03–0.45)	0.5	0.86
Pneumo_Clinical without PD-L1 (AUC-PR)	0.19 (0.14–0.24)	0.13 (0.03–0.23)	0.75	0.54
Pneumo_Clinical with PD-L1 (AUC-PR)	0.13 (–0.49–0.75)	0.10 (0.05–0.15)	0.25	0.74

AUC, area under the curve; PR, precision recall; PD-L1, programmed death ligand 1 expression.