Supplementary Table 1. Univariate logistic regression analysis of factors associated with non-diagnostic results in the validation cohort

			Univariate		
	Diagnostic (n = 98)	**Non-diagnostic (n = 28)**	***P* value**	**Odds ratio [95% CI]**	***P* value**
Age	69.2 ± 11.9	69.8 ± 10.8	0.925	1.005 [0.969–1.043]	0.788
Sex			0.072	2.345 [0.913–6.028]	0.077
Male	55 (56.1)	21 (75.0)			
Female	43 (43.9)	7 (25.0)			
COPD	6 (6.1)	2 (7.1)	1.000	1.179 [0.225–6.194]	0.845
No	92 (93.9)	26 (92.9)			
Myocardial infarction	7 (7.1)	1 (3.6)	0.683	0.481 [0.057–4.088]	0.503
No	91 (92.9)	27 (96.4)			
Cerebrovascular disease	5 (5.1)	3 (10.7)	0.375	2.232 [0.499–9.982]	0.293
No	93 (94.9)	25 (89.3)			
Size ≤ 1.5cm	6 (6.1)	7 (25.0)	0.004	5.111 [1.556–16.784]	0.007
> 1.5cm	92 (93.9)	21 (75.0)			
Lobe			0.819		0.824
Right upper lobe	25 (25.5)	5 (17.9)		**Reference**	
Right middle lobe	6 (6.1)	1 (3.6)		0.833 [0.082–8.519]	0.878
Right lower lobe	23 (23.5)	9 (32.1)		1.957 [0.571–6.702]	0.285
Left upper lobe	25 (25.5)	8 (28.6)		1.600 [0.460–5.570]	0.460
Left lower lobe	19 (19.4)	5 (17.9)		1.316 [0.332–5.207]	0.696
Location			0.089		0.127
Upper lung	26 (26.5)	2 (7.1)		0.202 [0.043–0.951]	0.043
Lower lung	30 (30.6)	10 (35.7)		0.875 [0.349–2.192]	0.776
Neither	42 (42.9)	16 (57.1)		**Reference**	
Morphology			0.001		0.002
Spiculated or lobulated	77 (78.6)	12 (42.9)		**Reference**	
Round or ovoid	10 (10.2)	7 (25.0)		4.492 [1.434–14.065]	0.010
Patchy	11 (11.2)	9 (32.1)		5.250 [1.800–15.314]	0.002
Nodule type			0.745	1.203 [0.395–3.659]	0.745
Solid	83 (84.7)	23 (82.1)			
Subsolid	15 (15.3)	5 (17.9)			
Internal low attenuation	25 (25.5)	19 (67.9)	< 0.001	6.164 [2.472–15.375]	< 0.001
No	73 (74.5)	9 (32.1)			
Cavitation	9 (9.2)	4 (14.3)	0.483	0.607 [0.172–2.141]	0.437
No	89 (90.8)	24 (85.7)			
Presence of atelectasis adjacent to the target lesion	17 (17.3)	10 (35.7)	0.037	2.647 [1.041–6.731]	0.041
No	81 (82.7)	18 (64.3)			
Open bronchus sign	18 (18.4)	2 (7.1)	0.240	2.925 [0.636–13.460]	0.168
No	80 (81.6)	26 (92.9)			
Distance from pleura to lesion	1.57 ± 1.59	1.31 ± 1.85	0.200	0.902 [0.688–1.183]	0.456
Distance from skin to lesion	5.25 ± 1.98	4.83 ± 2.18	0.266	0.900 [0.726–1.116]	0.338
Suggestive of pleural invasion	24 (24.5)	1 (3.6)	0.014	8.757 [1.129–67.909]	0.038
No	74 (75.5)	27 (96.4)			
Emphysema	29 (29.6)	13 (46.4)	0.096	2.062 [0.873–4.873]	0.099
No	69 (70.4)	15 (53.6)			
Needle traversal emphysema	5 (5.1)	2 (7.1)	0.651	1.431 [0.262–7.805]	0.679
No	93 (94.9)	26 (92.9)			
Accurate positioning of the biopsy needle tip	97 (99.0)	25 (89.3)	0.034	11.640 [1.161–116.737]	0.037
No	1 (1.0)	3 (10.7)			
Complication	34 (34.7)	8 (28.6)	0.544	1.328 [0.530–3.331]	0.545
No	64 (65.3)	20 (71.4)			
Parenchymal hemorrhage	32 (32.7)	8 (28.6)	0.682	1.212 [0.482–3.048]	0.683
No	66 (67.3)	20 (71.4)			

Data are presented as mean ± standard deviation or number (percentage), unless otherwise indicated. CI, confidence interval; COPD, chronic obstructive pulmonary disease.

Supplementary Table 2. Bootstrap internal validation and sensitivity analysis for the scoring system

(a) Bootstrap optimism-corrected performance (1,000 resamples of the training cohort)

Performance measure	**Value**
Apparent AUC, training cohort	0.731 (95% CI, 0.674–0.789)
Mean optimism	0.039
Optimism-corrected AUC	0.692
Optimism-corrected calibration slope	0.79

(b) Frequency of retention in the final model across 1,000 bootstrap resamples

Variable	Selection frequency (%)
Inaccurate needle tip positioning*	76.8
Absence of pleural invasion*	60.8
Lesion size ≤ 1.5 cm*	59.8
Patchy morphology*	51.2
Atelectasis adjacent to the target lesion*	49.7
Myocardial infarction	27.3
Cerebrovascular disease	11.3
Open bronchus sign	11.1
Male sex	10.9
All other candidate variables	≤ 4.0

(c) Sensitivity analysis: scoring system rederived after omitting absence of pleural invasion

	Four-predictor score	Full scoring system
AUC, training cohort	0.689 (0.619–0.752)	0.731 (0.674–0.789)
AUC, validation cohort	0.729 (0.617–0.831)	0.769 (0.669–0.869)

In each bootstrap resample, the entire model-development process (univariate screening, backward stepwise elimination, Firth penalized logistic regression, and weight assignment) was repeated. Optimism was the difference between performance in the bootstrap sample and in the original training cohort. *Predictors included in the final scoring system. In the sensitivity analysis, all four retained predictors were kept in the rederived score. AUC, area under the receiver operating characteristic curve; CI, confidence interval.

Supplementary Table 3. Diagnostic methods and presence of internal low attenuation according to final diagnosis among diagnostic benign and malignant lesions in the training cohort

		Malignancy (n = 254)	**Benign (n = 31)**	***P* value**
Diagnostic methods	Histopathology	254 (100.0)	15 (48.4)	< 0.001
	Microbiology	0 (0.0)	16 (51.6)	
Internal low attenuation	Yes	80 (31.5)	19 (61.3)	0.001
	No	174 (68.5)	12 (38.7)	

Supplementary Table 4. Presence and extent of internal low attenuation according to diagnostic method in benign lesions of the training cohort

Diagnostic methods/internal low attenuation	**Histopathology (n = 15)**	**Microbiology (n = 16)**	***P* value**
Yes	5 (33.3)	14 (87.5)	0.003
No	10 (66.7)	2 (12.5)	
< 30 %	3 (20.0)	3 (18.8)	0.008
30–50 %	1 (6.7)	3 (18.8)	
> 50 %	1 (6.7)	8 (50.0)	
No	10 (66.7)	2 (12.5)	

Supplementary Table 5. Post-hoc analysis of non-diagnostic results according to the relationship between the target lesion and the pleura

Lesion–pleura relationship	**Training cohort**	**Validation cohort**
Abutting the pleura	32/136 (23.5)	15/50 (30.0)
Not abutting the pleura	41/222 (18.5)	13/76 (17.1)
P value	0.249	0.089
Among lesions abutting the pleura		
With CT findings suggestive of pleural invasion	1/42 (2.4)	1/24 (4.2)
Without CT findings suggestive of pleural invasion	31/94 (33.0)	14/26 (53.8)
P value	< 0.001	< 0.001

Data are presented as the number of non-diagnostic results/total number of lesions (percentage). Lesions were classified as abutting the pleura when the distance from the pleura to the lesion was 0 cm. Groups were compared using Pearson's chi-squared test for lesions abutting vs. not abutting the pleura, and Fisher's exact test for the comparison within lesions abutting the pleura. CT, computed tomography.

Supplementary Table 6. Post-hoc comparison of patient and lesion characteristics according to the presence of emphysema in the training cohort

Characteristic	**Emphysema (n = 123)**	**No emphysema (n = 235)**	***P* value**
Age (years)	71.3 ± 10.5	67.8 ± 12.6	0.011
Male sex	113 (91.9)	106 (45.1)	< 0.001
Malignant final diagnosis	104 (84.6)	174 (74.0)	0.024
Lesion size ≤ 1.5 cm	8 (6.5)	32 (13.6)	0.051
Patchy morphology	27 (22.0)	39 (16.6)	0.251
Subsolid lesion	8 (6.5)	43 (18.3)	0.002
Internal low attenuation	56 (45.5)	69 (29.4)	0.003
Cavitation	17 (13.8)	19 (8.1)	0.097
Presence of atelectasis adjacent to the target lesion	21 (17.1)	42 (17.9)	0.885
Distance from pleura to lesion (cm)	1.19 ± 1.46	1.67 ± 1.76	0.011
Distance from skin to lesion (cm)	4.58 ± 1.96	5.46 ± 3.36	0.002
Suggestive of pleural invasion	26 (21.1)	20 (8.5)	0.001
Inaccurate needle tip positioning	13 (10.6)	15 (6.4)	0.213
Non-diagnostic result	17 (13.8)	56 (23.8)	0.027

Data are presented as mean ± standard deviation or number (percentage). Categorical variables were compared using Fisher's exact test and continuous variables using Mann-Whitney U test.