APPENDICES

Appendix A: Eligibility Criteria

Table A1. Inclusion and exclusion criteria applied during study selection.

#	Inclusion Criteria	Exclusion Criteria
1	CT imaging as primary modality (single-modal or multimodal)	Focused exclusively on nodule detection, localisation, or segmentation where classification of malignancy or histological subtype is not a primary or secondary outcome, and no morphological feature analysis is reported
2	At least one deep learning method applied (CNN, ResNet, DenseNet, ViT, or hybrid)	Exclusively non-DL machine learning without any deep learning component
3	Lung cancer classification objective (malignancy, subtype, invasiveness, staging, or nodule characterisation)	Non-CT modalities only (PET, MRI, X-ray, pathology slide without CT)
4	Human subjects or human-derived CT datasets	Review articles, meta-analyses, editorials, letters, or conference abstracts without full methods
5	Peer-reviewed full-text articles in English	No quantitative performance metric reported
6	At least one quantitative performance metric reported (accuracy, AUC, sensitivity, specificity, F1-score, or precision)	Insufficient methodological detail for data extraction
7	Published from 2014 onwards (modern deep learning era)	Published before 2014
8	Sufficient methodological detail to enable data extraction	

Appendix B: Database Search Strings

PubMed/MEDLINE (executed 2026-07-05; n = 1,204)

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("Lung Neoplasms"[Mesh] OR "Solitary Pulmonary Nodule"[Mesh] OR "Multiple Pulmonary Nodules"[Mesh] OR lung cancer[tiab] OR lung neoplasm*[tiab] OR lung carcinoma[tiab] OR pulmonary nodule*[tiab] OR lung nodule*[tiab] OR pulmonary lesion*[tiab] OR NSCLC[tiab] OR non-small cell lung*[tiab] OR SCLC[tiab] OR adenocarcinoma[tiab] OR squamous cell carcinoma[tiab] OR pulmonary metastas*[tiab] OR lung metastas*[tiab] OR metastatic lung[tiab] OR secondary pulmonary[tiab] OR benign pulmonary[tiab] OR benign lung[tiab]) AND ("Tomography, X-Ray Computed"[Mesh] OR computed tomography[tiab] OR CT scan[tiab] OR chest CT[tiab] OR thoracic CT[tiab] OR low-dose CT[tiab] OR LDCT[tiab]) AND ("Deep Learning"[Mesh] OR "Neural Networks, Computer"[Mesh] OR deep learning[tiab] OR convolutional neural network*[tiab] OR CNN[tiab] OR neural network*[tiab] OR transfer learning[tiab] OR vision transformer*[tiab] OR ResNet[tiab] OR DenseNet[tiab] OR EfficientNet[tiab]) AND (classificat*[tiab] OR diagnos*[tiab] OR differentiat*[tiab] OR characteriz*[tiab] OR subtyp*[tiab]) AND (2014:2026[pdat]) AND (English[lang]) NOT (review[Publication Type] OR meta-analysis[Publication Type] OR editorial[Publication Type] OR comment[Publication Type])
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IEEE Xplore (executed 2026-07-05; n = 421)

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("Abstract":"lung cancer" OR "Abstract":"lung nodule" OR "Abstract":"pulmonary nodule" OR "Abstract":"pulmonary lesion" OR "Abstract":"NSCLC" OR "Abstract":"non-small cell lung cancer" OR "Abstract":"lung carcinoma" OR "Abstract":"pulmonary metastasis" OR "Abstract":"lung metastasis" OR "Abstract":"metastatic lung" OR "Abstract":"benign lung") AND ("Abstract":"computed tomography" OR "Abstract":"CT scan" OR "Abstract":"chest CT" OR "Abstract":"low-dose CT" OR "Abstract":"LDCT") AND ("Abstract":"deep learning" OR "Abstract":"convolutional neural network" OR
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"Abstract":"CNN" OR "Abstract":"ResNet" OR "Abstract":"DenseNet" OR
"Abstract":"transfer learning" OR "Abstract":"vision transformer") AND
("Abstract":"classification" OR "Abstract":"diagnosis" OR
"Abstract":"differentiation") | Filter: Year 2014-2026
```

Scopus (reference strategy; executed 2026-07-05; n = 3,781; Articles and Conference Papers, English)

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TITLE-ABS-KEY ( ( "lung cancer" OR "lung neoplasm*" OR "lung carcinoma" OR
"pulmonary nodule*" OR "lung nodule*" OR "pulmonary lesion*" OR "NSCLC" OR "non-
small cell lung" OR "SCLC" OR "adenocarcinoma" OR "squamous cell carcinoma" OR
"pulmonary metastas*" OR "lung metastas*" OR "metastatic lung" OR "secondary
pulmonary" OR "benign pulmonary" OR "benign lung" ) AND ( "computed tomography" OR
"CT scan" OR "chest CT" OR "thoracic CT" OR "low-dose CT" OR "LDCT" ) AND ( "deep
learning" OR "convolutional neural network" OR "CNN" OR "neural network" OR
"transfer learning" OR "vision transformer" OR "ResNet" OR "DenseNet" OR
"EfficientNet" ) AND ( "classification" OR "diagnosis" OR "differentiation" OR
"characterization" OR "subtyping" ) ) AND PUBYEAR > 2013 AND PUBYEAR < 2027 AND (
DOCTYPE ( ar ) OR DOCTYPE ( cp ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) )
```

Semantic Scholar / Elicit (executed 2026-07-05; n = 1,000, retrieval capped at 1,000), natural-language query: "Deep learning models classifying lung lesions on CT images as primary lung cancer, pulmonary metastasis, or benign using morphological features (shape, margin, texture, density), and their classification performance."

PubMed via Semantic Scholar/Elicit (n = 27 included after full-text screening)

AI-assisted screening performed using Elicit platform with predefined eligibility thresholds. Search query: "deep learning CT lung cancer classification morphological features". Results screened against predefined PICOS criteria.

Appendix C: Per-Study Quality Appraisal and Study Characteristics

Table A2. Per-study QUADAS-2 risk-of-bias and applicability judgements for the 27 included studies (RoB = risk of bias).

#	Study	Patient selection (RoB)	Index test (RoB)	Reference standard (RoB)	Flow & timing (RoB)	Overall RoB	Applic.: Patient selection	Applic.: Index test	Applic.: Reference standard
1	1. Li L (2023)	High	High	Low	Low	High	High	Low	Low
2	2. Liu Y (2024)	Unclear	Low	Low	Low	Unclear	High	Low	Low
3	3. Xiao (2025)	Unclear	Unclear	Low	Unclear	Unclear	High	Low	Low
4	4. Gong (2025)	High	Unclear	Unclear	Unclear	High	High	Low	Unclear
5	5. Gao (CRC) (2026)	High	Low	High	High	High	High	Low	High
6	6. Gao S (n.d.)	Unclear	High	Low	Unclear	High	Low	Low	Low
7	7. Nishio (2018)	High	Unclear	Unclear	Unclear	High	Low	Low	Unclear
8	8. Li R (2023)	Unclear	High	Low	Low	High	High	Low	Low
9	9. Piskorski (2025)	High	Unclear	Unclear	High	High	High	Low	Unclear
10	10. Yang (2023)	High	Low	Low	Unclear	High	High	Low	Low
11	11. He (2026)	Unclear	Unclear	Low	Low	Unclear	High	Low	Low
12	12. Nady (2026)	Unclear	Unclear	High	Unclear	High	Low	Low	High
13	13. Paul (2018)	High	High	Unclear	Unclear	High	Low	Low	Low
14	14. Huang J (2024)	High	High	Low	High	High	High	Low	Low
15	15. Safta (2024)	Unclear	Low	High	Unclear	High	Low	Low	High
16	16. Song (2024)	Unclear	Low	Unclear	Unclear	Unclear	High	Low	Unclear
17	17. Esha (2024)	High	High	High	Unclear	High	High	Low	High
18	18. Lin (2021)	High	High	Low	Low	High	High	Low	Low
19	19. EL-Bana (2020)	Unclear	Low	High	High	High	Low	Low	High

20	20. Zhang (2019)	Unclear	High	High	Unclear	High	Low	Low	High
21	21. Wang (2022)	Unclear	Low	Low	Low	Unclear	Low	Low	Low
22	22. Liufu (n.d.)	Unclear	High	Unclear	High	High	High	Low	Unclear
23	23. Venugopal (n.d.)	Unclear	Unclear	High	High	High	Low	Low	High
24	24. Li K (2021)	High	High	Low	Low	High	High	Low	Low
25	25. Zhu (2026)	Unclear	Low	Low	Low	Unclear	High	Low	Low
26	26. Zhao (n.d.)	Unclear	High	High	Unclear	High	Low	Low	High
27	27. Huang Y (2025)	Unclear	Low	Unclear	Unclear	Unclear	Low	Low	Unclear

Table A3. Per-study CLAIM adherence and key reporting items for the 27 included studies.

#	Study	CLAIM adherence (%)	Rating	External validation	Partition (train/val/test) reported	Metric uncertainty (CI/SE) reported	Clinician comparison	Reference standard
1	1. Li L (2023)	83	High	No	Yes	Yes	No	Histopathology
2	2. Liu Y (2024)	83	High	Yes	Yes	No	No	Histopathology
3	3. Xiao (2025)	83	High	Yes	No	Yes	No	Histopathology
4	4. Gong (2025)	75	High	No	Yes	No	No	Histopathology
5	5. Gao (CRC) (2026)	92	High	Yes	No	Yes	Yes	Histopathology
6	6. Gao S (n.d.)	83	High	No	No	Yes	Yes	Histopathology
7	7. Nishio (2018)	67	Moderate	No	No	No	No	Histopathology
8	8. Li R (2023)	83	High	No	Yes	Yes	No	Histopathology
9	9. Piskorski (2025)	75	High	No	No	Yes	No	Histopathology
10	10. Yang (2023)	92	High	Yes	Yes	No	Yes	Histopathology
11	11. He (2026)	92	High	No	Yes	Yes	Yes	Histopathology
12	12. Nady (2026)	75	High	No	No	Yes	Yes	Radiologist reference
13	13. Paul (2018)	83	High	No	Yes	Yes	No	Histopathology
14	14. Huang J (2024)	92	High	Yes	No	Yes	Yes	Histopathology
15	15. Safta (2024)	67	Moderate	No	No	No	Yes	Radiologist reference
16	16. Song (2024)	92	High	Yes	Yes	Yes	No	Histopathology
17	17. Esha (2024)	58	Moderate	No	No	No	No	Radiologist reference
18	18. Lin (2021)	92	High	No	Yes	Yes	Yes	Histopathology
19	19. EL-Bana (2020)	92	High	Yes	Yes	Yes	No	Histopathology
20	20. Zhang (2019)	67	Moderate	No	Yes	No	No	Radiologist reference
21	21. Wang (2022)	83	High	No	Yes	Yes	No	Histopathology
22	22. Liufu (n.d.)	83	High	No	Yes	Yes	No	Histopathology
23	23. Venugopal (n.d.)	75	High	Yes	No	No	Yes	Radiologist reference
24	24. Li K (2021)	75	High	No	No	No	Yes	Histopathology
25	25. Zhu (2026)	92	High	Yes	No	Yes	Yes	Histopathology
26	26. Zhao (n.d.)	75	High	No	Yes	Yes	No	Radiologist reference
27	27. Huang Y (2025)	83	High	Yes	No	Yes	No	Histopathology

Table A4. Characteristics of the 27 included studies: population and setting, sample size and class composition, reference standard, model, input dimensionality, ImageNet transfer learning, external validation, and headline performance. NR = not reported.

#	Study	Task	Population / setting	N (class composition)	Reference standard	Model	Input	ImageNet TL	Ext. val.	Headline performance
9	Nishio (2018)	Benign / primary / metastatic (3-class)	Private single-centre	1236 pts (412 benign / 571 primary / 253 met)	Histopathology	VGG-16 CNN	2D	Yes	No	Acc 68.0%
10	Paul (2018)	Benign vs malignant	NLST (public)	237 cases	Histopathology	CNN (VGG) + radiomics	2D	Yes	No	Acc 76.8%; AUC 0.87
11	Zhang (2019)	Benign vs malignant	LUNA16 / LIDC-IDRI (public)	1004 nodules (450 malignant / 554 benign)	Radiologist	3D dual-path (ResNeXt+DenseNet)	3D	No	No	Acc 93.8%; AUC 0.97
12	El-Bana (2020)	Benign vs malignant	LUNA16 + Kaggle DSB17 (public)	888 / 1397 scans	Histopathology	DeepLabV3+ / Faster R-CNN	2D	Yes	Yes	Acc 95.7%; Sens 96.4 / Spec 99.4
13	Venugopal (n.d.)	Benign vs malignant	NLST + LIDC (public)	103 test cases	Radiologist	3D residual-CNN ensemble	3D	No	Yes	Acc 85%; Sens 70.3 / Spec 75
14	Lin (2021)	Granuloma vs cancer	Private single-centre	915 pts (603 cancer / 312 benign)	Histopathology	3D CNN + radiomics	3D	No	No	Acc 84.8%; AUC 0.91; Sens 87.6 / Spec 79.1
15	Li K (2021)	Adeno / other malignancy / metastasis / benign (4-class)	Private single-centre	486 lesions (55 met)	Histopathology	3D DenseNet / ResNet-34	3D	No	No	Acc 81.1%
16	Wang (2022)	Benign vs malignant (+subtype)	Private single-centre	8950 lesions (2211 benign)	Histopathology	3D-ResNet (multi-task)	3D	No	No	Acc 83.3%; AUC 0.85
17	Li L (2023)	Metastatic (BCLM) vs primary	Private single-centre	100 pts (60 met / 40 primary)	Histopathology	ResNet18 + radiomics	Multi-channel	No	No	Acc 92%; AUC 0.91; Sens 82.5 / Spec 88.3
18	Li R (2023)	Adenocarcinoma subtyping (IAC/MIA/AIS)	Private (2 centres)	338 nodules (193 MIA / 86 IAC / 59 AIS)	Histopathology	CNN + GNN (ResNet28+GIN)	2D	No	No	Acc 66.3%; AUC 0.76
19	Yang (2023)	Subtyping (AAH-AIS / MIA / ADC)	LUNA16 + private	1479 nodules	Histopathology	MVCS + 3D-ResNet	3D	No	Yes	Acc 85%
20	Liu Y (2024)	Metastasis vs hamartoma	Private (2 centres)	341 (120 met / 221 benign)	Histopathology	3D-ResNet + clinical / radiomics	3D	No	Yes	Acc 94.8%; AUC 0.94; Sens 87.2 / Spec 93.5
21	Gao S (n.d.)	Benign vs malignant	Private single-centre	570 subjects	Histopathology	3D DenseNet (IRCL)	3D	No	No	Acc 92.1%; AUC 0.92
22	Huang J (2024)	PEH vs other pulmonary disease	Private + literature cases	96 pts	Histopathology	ResNet-18	2D	No	Yes	Acc 74%; AUC 0.71
23	Safta (2024)	Benign vs malignant	LIDC-IDRI (public)	822 nodules (331 benign)	Radiologist	3D-CNN + engineered features	3D	No	No	Acc 97.8%; AUC 0.99; Sens 98.1 / Spec 94.7
24	Song (2024)	Distal metastasis (present / absent)	Private (2 centres)	674 (143 met)	Histopathology	NAS custom ensemble	3D	No	Yes	AUC 0.78
25	Esha (2024)	Benign / primary / metastatic (3-class)	LIDC-IDRI (public)	135 nodules	Radiologist	MVSA-CNN (attention)	Multi-view	No	No	Acc 97.1%; Sens 96.3 / Spec 97.5
26	Xiao (2025)	Benign vs malignant (IPN)	Private tertiary centre	321 IPNs (26 met / 295 primary / 125 benign)	Histopathology	DenseNet CNN	NR	No	Yes	AUC 0.75
27	Gong (2025)	Metastasis present / absent (ACC)	Private single-centre	130 (41 met / 89 no-met)	Histopathology	3D-ResNet + radiomics	3D	No	No	Acc 85%; AUC 0.87
28	Piskorski (2025)	Risk stratification (3 levels)	Private single-centre	422 lesions (105 malignant)	Histopathology	CNN (NLST-pretrained)	NR	No	No	Acc 93%; AUC 0.93
29	Zhao (n.d.)	Benign vs malignant	LUNA16 (public)	888 scans	Radiologist	Multi-scale CNN + ViT (MSTD)	2D	No	No	Acc 94.5%; AUC 0.98; Sens 91.1 / Spec 96.5
30	Huang Y (2025)	Benign vs malignant	Private single-centre	435 (241 benign / 194 malignant)	Histopathology	ViT + CNN hybrid	NR	No	Yes	Acc 91%; AUC 0.93
31	Gao X (2026)	Metastasis vs benign (CRC)	Private (3 centres)	2670 (1335 met / 1335 benign)	Histopathology	3D-ResNet18	3D	No	Yes	Acc 96.4%; AUC 0.95; Sens 89.6 / Spec 88.8
32	He (2026)	Invasiveness (pre-invasive vs invasive GGN)	Private single-centre	517 (204 pre-invasive / 313 invasive)	Histopathology	ResNet-101 + radiomics	2D	Yes	No	Acc 76.9%; AUC 0.87
33	Nady (2026)	Cancer vs non-cancer	Data Science Bowl 2017 (public)	790 pts / 30,020 images	Radiologist	CoAtNet (CNN + attention)	2D	No	No	Acc 99.9%; AUC 0.96; Sens 99.8 / Spec 100

34	Liufu (2026)	MPLC / IPM / benign (3-class)	Private single-centre	260 pts (81 IPM / 83 MPLC / 96 benign)	Histopathology	MambaOut-Kobe (state-space)	2D	Yes	No	Acc 82.9%; AUC 0.95; Sens 81.9 / Spec 91.4
35	Zhu (2026)	Benign vs malignant	Private (9 hospitals) + NLST	463 primary / 222 benign	Histopathology	ViT + CNN + GCN (DeepFAN)	3D	No	Yes	Acc 89.7%; AUC 0.95; Sens 95.3 / Spec 73.3