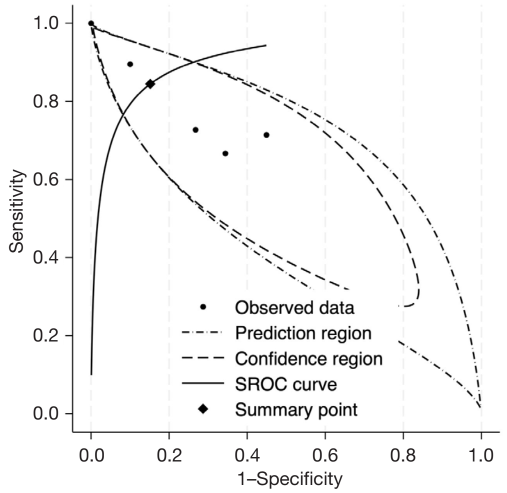

Figure S1 AUROC *ALK*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

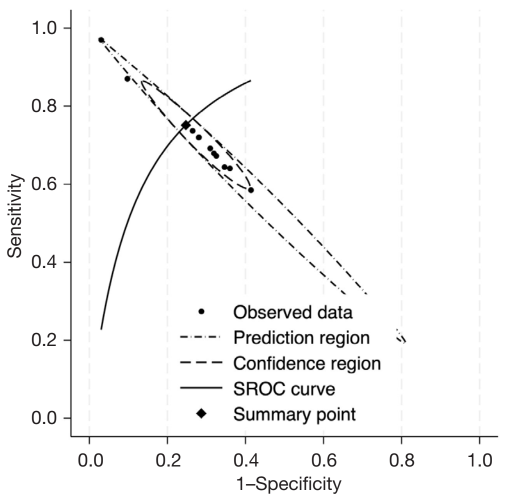

Figure S2 AUROC *TP53*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

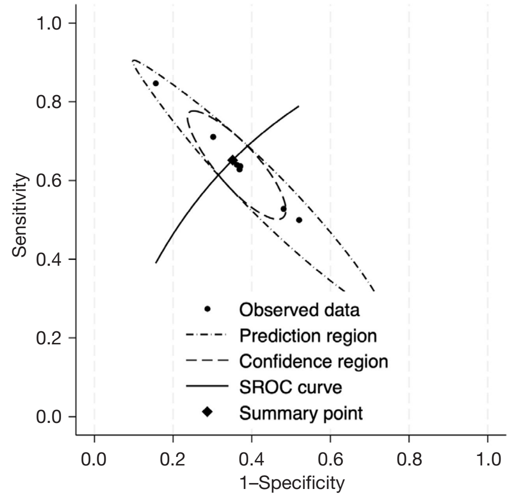

Figure S3 AUROC *STK11*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

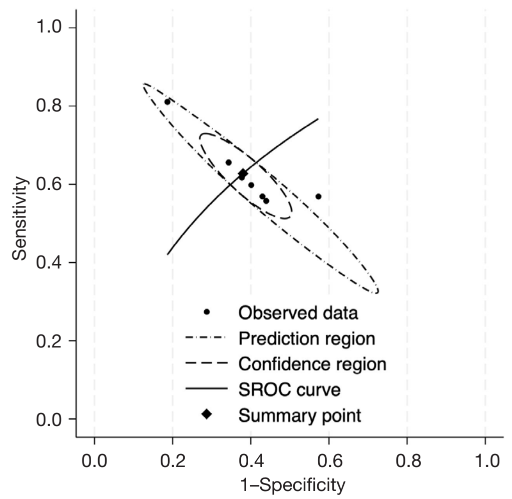

Figure S4 AUROC *KRAS*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

 https://dx.doi.org/10.21037/tlcr-2024-1196

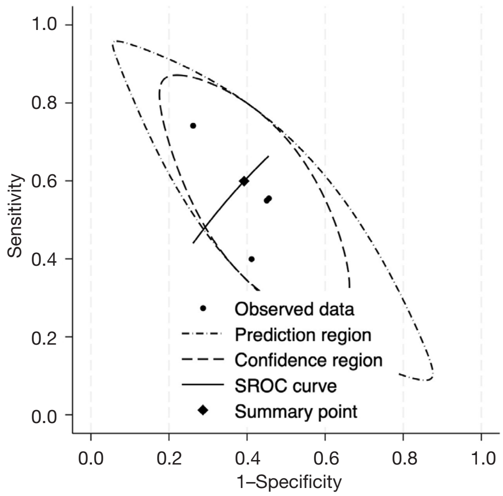

Figure S5 AUROC *FAT1*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

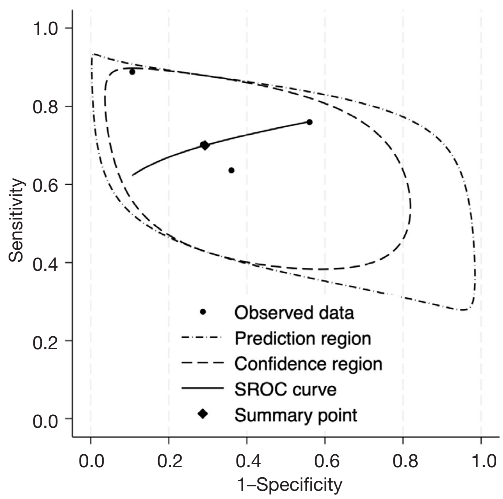

Figure S6 AUROC TMB. AUROC, area under the roc curve; TMB, tumor mutational burden; SROC, summary receiver operating characteristic.

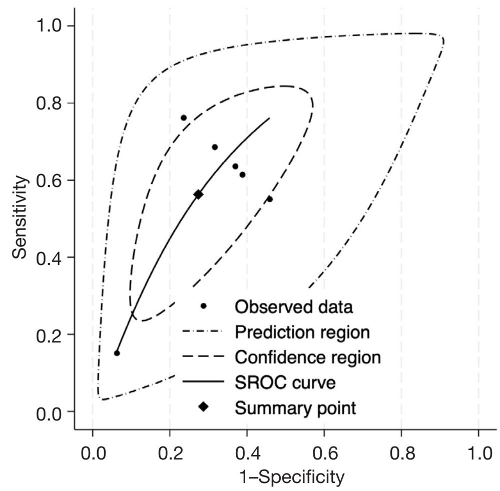

Figure S7 AUROC *KEAP1*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic.

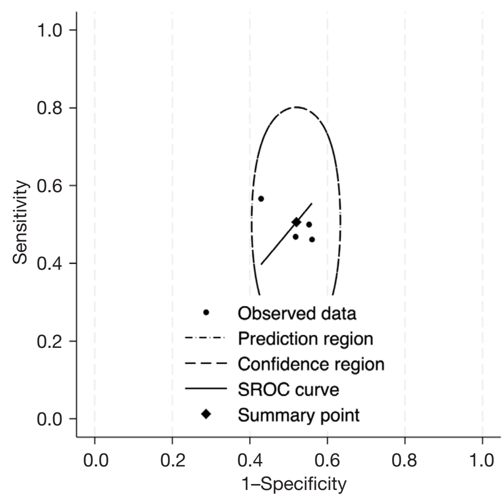

Figure S8 AUROC *BRAF*. AUROC, area under the roc curve; SROC, summary receiver operating characteristic

https://dx.doi.org/10.21037/tlcr-2024-1196

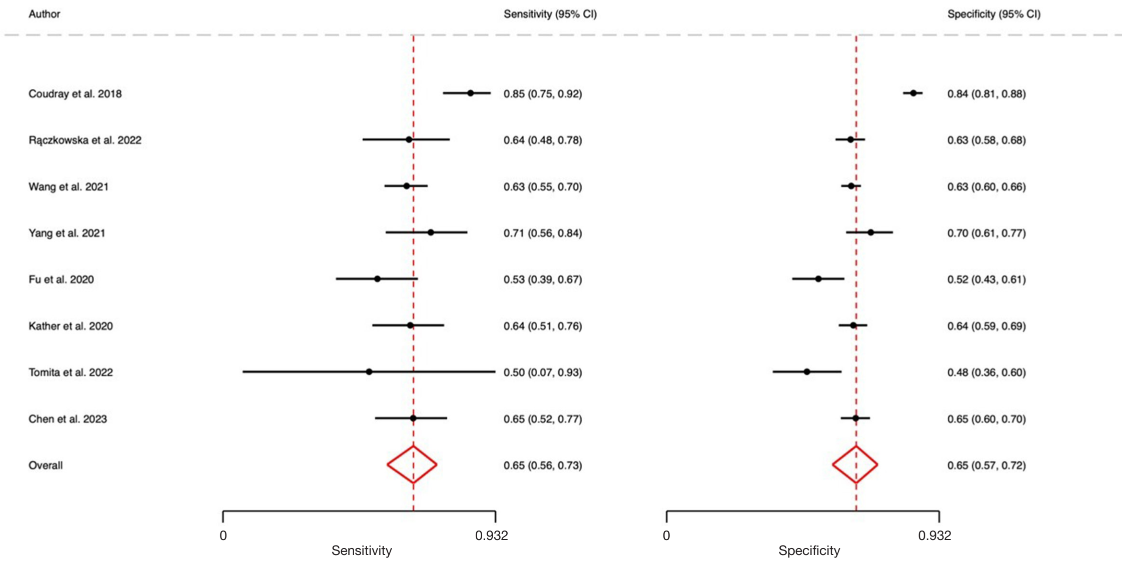

Figure S9 *STK11* meta-analysis. CI, confidence interval.

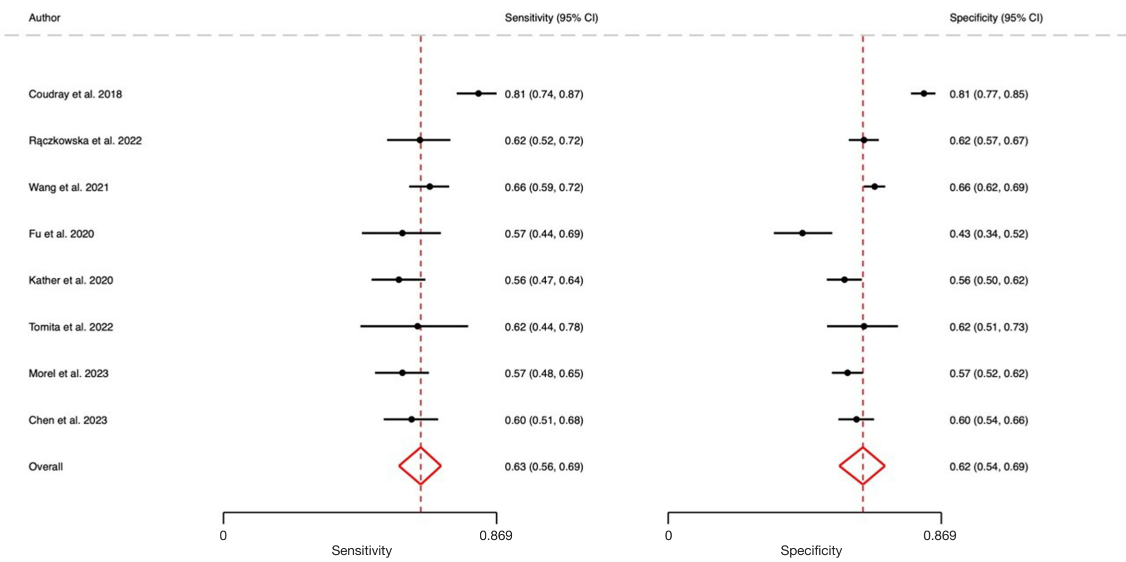

Figure S10 *KRAS* meta-analysis. CI, confidence interval.

https://dx.doi.org/10.21037/tlcr-2024-1196

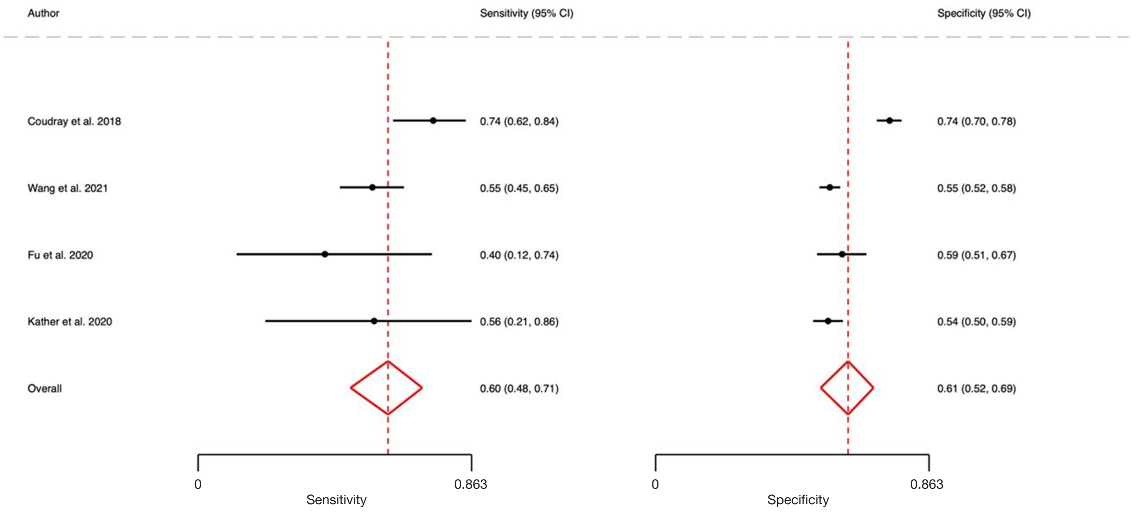

Figure S11 *FAT1* meta-analysis. CI, confidence interval.

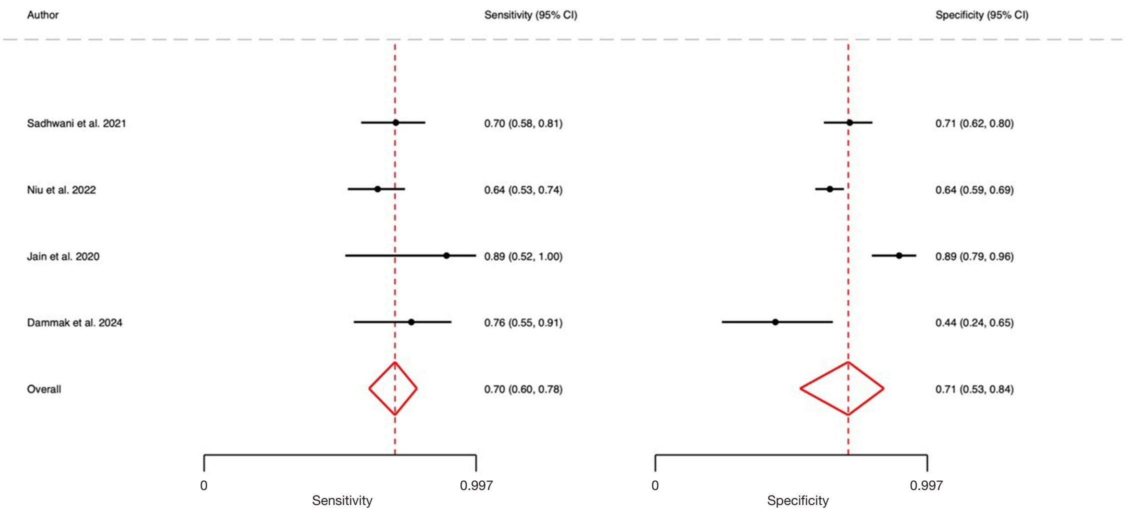

Figure S12 TMB meta-analysis. CI, confidence interval; TMB, tumor mutational burden.

https://dx.doi.org/10.21037/tlcr-2024-1196

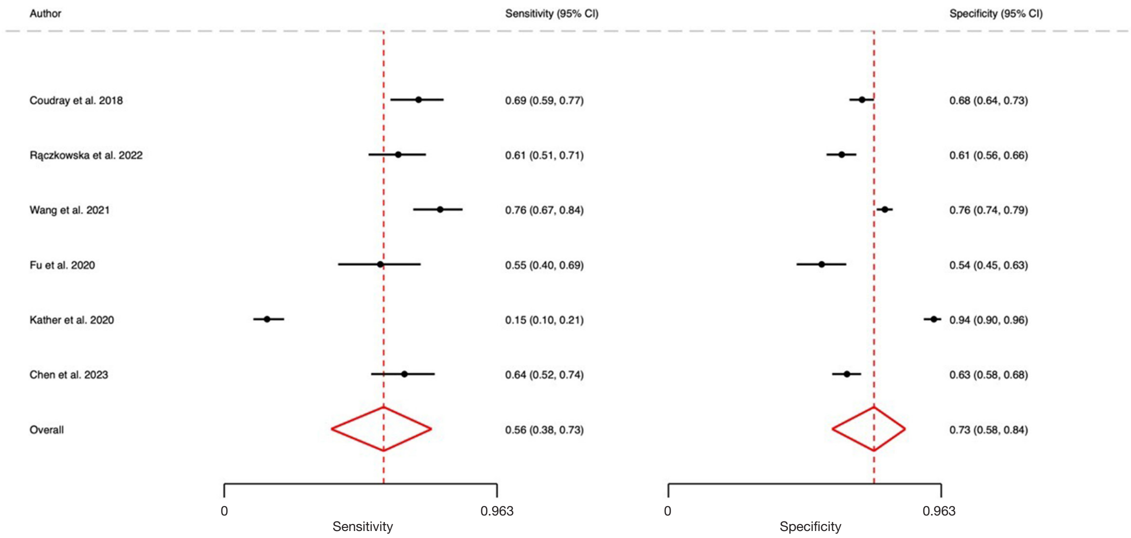

Figure S13 *KEAP1* meta-analysis. CI, confidence interval.

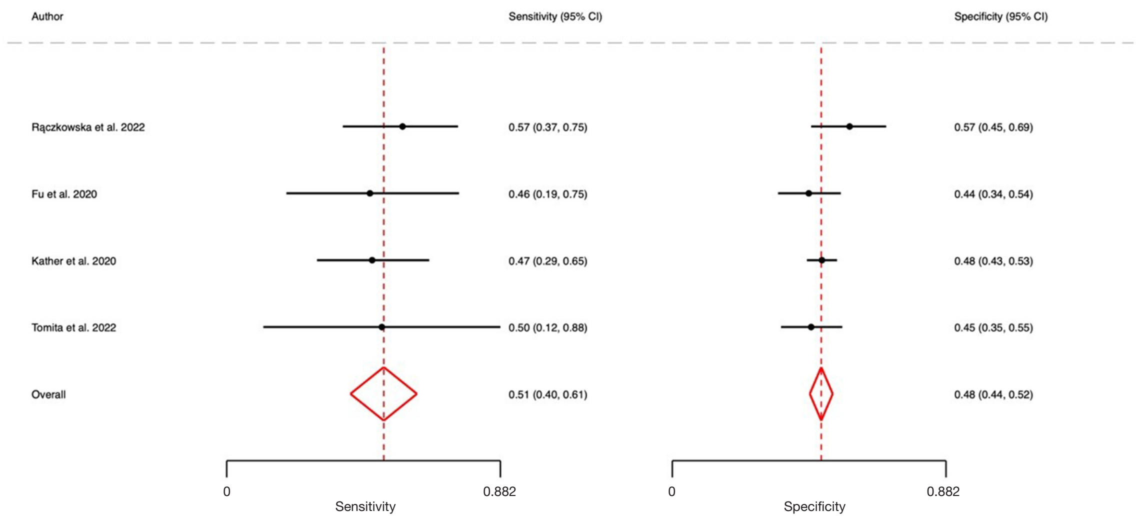

Figure S14 *BRAF* meta-analysis. CI, confidence interval.

Table S1 Search strategy used in this review

Database searched	Search terms used
MEDLINE; LILACS; Web of Science; Embase; Cochrane	((non-small cell lung carcinoma) OR (non-small cell lung cancer) OR (adenocarcinoma) OR (squamous cell carcinoma) OR (pulmonary neoplasms) OR (lung cancer)) AND ((ERBB-1) OR (epidermal growth factor receptor) OR (EGFR) OR (RFCE) OR (KRAS) OR (anaplastic lymphoma kinase) OR (ALK) OR (ALK kinase) OR (NPM-ALK) OR (ALK receptor tyrosine kinase) OR (RET) OR (proto-oncogene c-ret) OR (c-ret protein) OR (methionine-arnt ligase) OR (methionyl-tRNA synthetase) OR (MET) OR (ROS1) OR (ERBB-2 receptor) OR (proto-oncogene HER2 protein) OR (protein c-ERBB-2) OR (HER2*) OR (HER-2*) OR (ERBB2) OR (ERBB-2) OR (ERB2) OR (ERB-2) OR (proto-oncogene B-RAF) OR (BRAF) OR (NTRK) OR (PIK3CA) OR (MAP kinase kinase 1) OR (PD-L1) OR (immune checkpoint inhibitors)) AND ((digital pathology) OR (digital image analysis) OR (artificial intelligence) OR (ai) OR (deep learning) OR (computer-assisted diagnosis) OR (computer-aided diagnosis) OR (Machine Learning) OR (Neural network) OR algorithm))

https://dx.doi.org/10.21037/tlcr-2024-1196

Table S2 Assessment of the quality of evidence and risk of bias for each study using the criteria of the checklist for Artificial Intelligence in Medical Imaging (CLAIM) 2024 update

Title	Criteria																																												
Article	Identification as a study of AI methodology specifying the category of technology used (e.g., deep learning)	Summary of study design methods results and conclusions	Scientific and/or clinical background including the intended use and role of the AI approach	Study aims objectives and hypotheses	Prospective or retrospective study	Study goal	Data sources	Inclusion and exclusion criteria	Data preprocessing	Selection of data subsets	De-identification methods	How missing data were handled	Image acquisition protocol	Definition of method(s) used to obtain reference standard	Rationale for choosing the reference standard	Source of reference standard annotations	Annotation of test set	Measures of inter- and intrarater variability of features described by the annotators	How data were assigned to partitions	Level at which partitions are disjoint	Intended sample size	Detailed description of model	Software libraries frameworks and packages	Initialization of model parameters	Details of training approach	Method of selecting the final model	Ensembling techniques	Metrics of model performance	Statistical measures of significance and uncertainty	Robustness or sensitivity analysis	Methods for explainability or interpretability	Evaluation on internal data	Testing on external data	Clinical trial registration	Numbers of patients or examinations included and excluded	Demographic and clinical characteristics of cases in each partition	Performance metrics and measures of statistical uncertainty	Estimates of diagnostic performance and their precision	Failure analysis of incorrectly classified cases	Study limitations	Implications for practice including intended use and/or clinical role	Provide a reference to the full study protocol or to additional technical details	Statement about the availability of software trained model and/or data	Sources of funding and other support role of funders	Total	%
Artificial Intelligence-Powered Prediction of ALK Gene Rearrangement in Patients With Non-Small-Cell Lung Cancer	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	41	93,18
Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	41	93,18
Comparative Analysis of Machine Learning Approaches to Classify Tumor Mutation Burden in Lung Adenocarcinoma Using Histopathology Images.	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	42	95,45
Deep Learning-Based Tumor Microenvironment Segmentation Is Predictive of Tumor Mutations and Patient Survival in Non-Small-Cell Lung Cancer	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	42	95,45
Direct identification of ALK and ROS1 fusions in non-small cell lung cancer from hematoxylin and eosin-stained slides using deep learning algorithms	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	41	93,18
HEAL: An Automated Deep Learning Framework for Cancer Histopathology Image Analysis	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	40	90,91
Machine learning-based gene alteration prediction model for primary lung cancer using cytologic images	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	40	90,91
Multi-Field-of-View Deep Learning Model Predicts Nonsmall Cell Lung Cancer Programmed Death-Ligand 1 Status from Whole-Slide Hematoxylin and Eosin Images	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	41	93,18
Predicting EGFR Mutational Status from Pathology Images Using a Real-World Dataset	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	42	95,45
Predicting oncogene mutations of lung cancer using deep learning and histopathologic features on whole-slide images	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	41	93,18
Predicting Tumor Mutational Burden from Lung Adenocarcinoma Histopathological Images Using Deep Learning.	1	1	1	1	0	1	1	1	1	1	1	0	1	0	0	1	1	0	1	0	1	1	1	1	1	1	0	1	1	1	0	1	1	NA	1	1	1	1	0	1	1	1	1	1	34	77,27
Prediction of Target-Drug Therapy by Identifying Gene Mutations in Lung Cancer with Histopathological Stained Image and Deep Learning Techniques	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	0	1	1	1	1	NA	1	1	1	1	0	1	1	1	1	1	37	84,09
Preliminary evaluation of deep learning for first-line diagnostic prediction of tumor mutational status *	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	0	1	0	1	1	1	1	1	1	1	1	0	0	0	1	0	NA	1	1	1	1	0	1	1	1	1	1	35	79,55
Using Deep Learning to Predict Tumor Mutational Burden from Scans of H&E-Stained Multicenter Slides of Lung Squamous Cell Carcinoma **	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	0	1	0	NA	1	1	1	1	0	1	1	1	1	1	37	84,09
Prediction of Epidermal Growth Factor Receptor Mutation Subtypes in NoneSmall Cell Lung Cancer From Hematoxylin and EosineStained Slides Using Deep Learning	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	1	0	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1	NA	1	1	1	1	0	1	1	0	0	1	35	79,55
Pan-cancer image-based detection of clinically actionable genetic alterations	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	0	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	38	86,36
Predicting tumour mutational burden from histopathological images using multiscale deep learning	1	1	1	1	0	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	39	88,64
Pan-cancer computational histopathology reveals mutations, tumor composition and prognosis	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	42	95,45
Deep learning-based cross-classifications reveal conserved spatial behaviors within tumor histological images	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	41	93,18
Identification and Validation of Efficacy of Immunological Therapy for Lung Cancer From Histopathological Images Based on Deep Learning	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	42	95,45
Optimization of deep learning models for the prediction of gene mutations using unsupervised clustering	1	1	1	1	0	1	1	NA	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	NA	1	1	1	1	1		NA	1	2	1	1	1	1	1	1	2	1	42	95,45
Deep learning using histological images for gene mutation prediction in lung cancer: a multicentre retrospective study	1	1	1	1	0	1	1	NA	1	1	1	1	1	1	1	1	1	2	1	1	1	1	1	1	1	1	NA	1	1	1	1	1		NA	1	2	1	1	1	1	1	1	2	1	42	95,45