AI-Based Early Detection of Lung Cancer: Imaging Analysis and Biomarker Discovery

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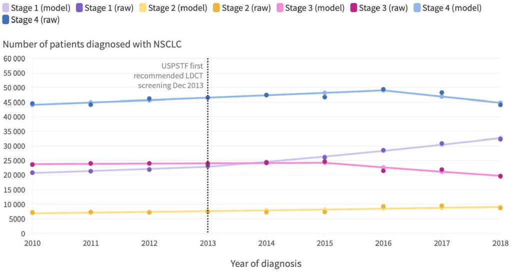
Contents

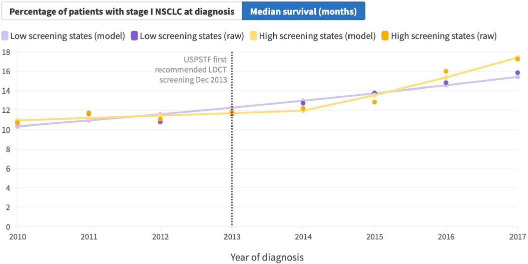
Integrating AI to improve precision in lung cancer care with applications in:

- **Early detection and screening**
- **Differentiation of benign vs. malignant lesions**
- **Prediction of future risk**

Importance of Early Detection

- US National Cancer Database and Surveillance and SEER program database



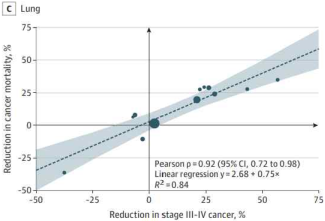


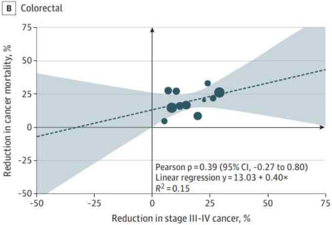
➔ **Favorable shift to higher incidence of stage I with decline in stage IV disease leading to improved mortality**

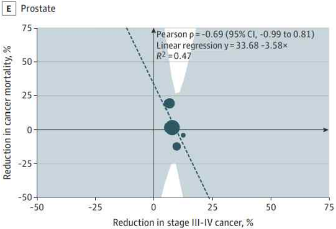
Potter et al. BMJ. 2022.

Reduction in Cancer Mortality and Incidence of Stage III-IV

- Potential major outcomes when designing RCTs to evaluate the benefit of cancer screening


C Lung


B Colorectal


E Prostate

➔ **Incidence of late-stage cancer may be suitable alternative end point to cancer-specific mortality only for certain cancer types**

Feng et al. JAMA. 2024.

Chest X-ray: Proved Ineffective for Lung Cancer Screening

- **Negative results from three large-scale randomized trials in 1970-1980**

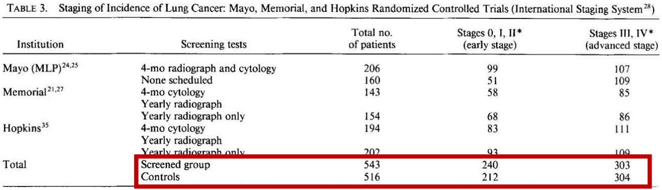


TABLE 3. Staging of Incidence of Lung Cancer: Mayo, Memorial, and Hopkins Randomized Controlled Trials (International Staging System[28])

Institution	Screening tests	Total no. of patients	Stages 0, I, II* (early stage)	Stages III, IV* (advanced stage)
Mayo (MLP)[24,25]	4-mo radiograph and cytology	206	99	107
	None scheduled	160	51	109
Memorial[21,27]	4-mo cytology Yearly radiograph	143	58	85
	Yearly radiograph only	154	68	86
Hopkins[35]	4-mo cytology Yearly radiograph	194	83	111
	Yearly radiograph only	202	93	109
Total	Screened group	543	240	303
	Controls	516	212	304

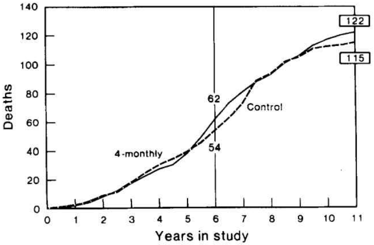
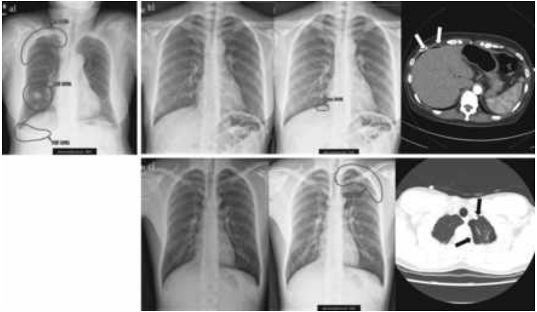


FIG. 8. Cumulative number of lung cancer deaths (includes postoperative deaths), Mayo Lung Project, by year in study; 4-monthly refers to group screened every 4 months (solid line), and control refers to control group (dashed line).

Fontana et al. Cancer. 1991.

Integration of AI into Modern Chest X-ray

-AI advancements to detect various lung abnormalities from a chest X-ray



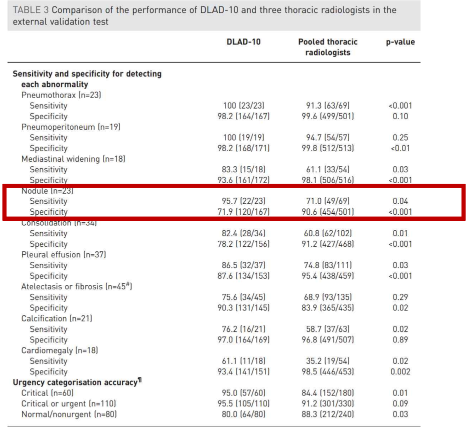


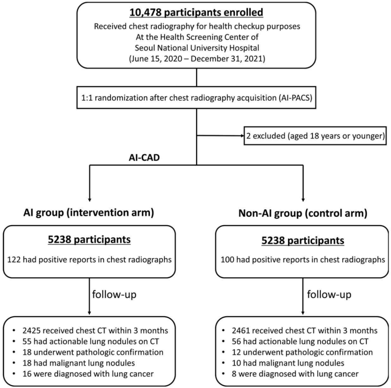
TABLE 3 Comparison of the performance of DLAD-10 and three thoracic radiologists in the external validation test

	DLAD-10	Pooled thoracic radiologists	p-value
Sensitivity and specificity for detecting each abnormality			
Pneumothorax (n=23)			
Sensitivity	100 (23/23)	91.3 (63/69)	<0.001
Specificity	98.2 (164/167)	99.6 (499/501)	0.10
Pneumoperitoneum (n=19)			
Sensitivity	100 (19/19)	94.7 (54/57)	0.25
Specificity	98.2 (168/171)	99.8 (512/513)	<0.01
Mediastinal widening (n=18)			
Sensitivity	83.3 (15/18)	61.1 (33/54)	0.03
Specificity	93.6 (161/172)	98.1 (506/516)	<0.001
Nodule (n=23)			
Sensitivity	95.7 (22/23)	71.0 (49/69)	0.04
Specificity	71.9 (120/167)	90.6 (454/501)	<0.001
Consolidation (n=34)			
Sensitivity	82.4 (28/34)	60.8 (62/102)	0.01
Specificity	78.2 (122/156)	91.2 (427/468)	<0.001
Pleural effusion (n=37)			
Sensitivity	86.5 (32/37)	74.8 (83/111)	0.03
Specificity	87.6 (134/153)	95.4 (438/459)	<0.001
Atelectasis or fibrosis (n=45[#])			
Sensitivity	75.6 (34/45)	68.9 (93/135)	0.29
Specificity	90.3 (131/145)	83.9 (365/435)	0.02
Calcification (n=21)			
Sensitivity	76.2 (16/21)	58.7 (37/63)	0.02
Specificity	97.0 (164/169)	96.8 (491/507)	0.89
Cardiomegaly (n=18)			
Sensitivity	61.1 (11/18)	35.2 (19/54)	0.02
Specificity	93.4 (141/151)	98.5 (446/453)	0.002
Urgency categorisation accuracy[¶]			
Critical (n=60)	95.0 (57/60)	84.4 (152/180)	0.01
Critical or urgent (n=110)	95.5 (105/110)	91.2 (301/330)	0.09
Normal/nonurgent (n=80)	80.0 (64/80)	88.3 (212/240)	0.03

Nam et al. Eur Resp J. 2021.

Implication of AI-Integrated Chest X-ray

- A randomized trial comparing AI and non-AI chest X-rays for nodule detection



10,478 participants enrolled
Received chest radiography for health checkup purposes
At the Health Screening Center of
Seoul National University Hospital
(June 15, 2020 – December 31, 2021)

1:1 randomization after chest radiography acquisition (AI-PACS)

2 excluded (aged 18 years or younger)

AI-CAD

AI group (intervention arm)

5238 participants

122 had positive reports in chest radiographs

follow-up

- 2425 received chest CT within 3 months
- 55 had actionable lung nodules on CT
- 18 underwent pathologic confirmation
- 18 had malignant lung nodules
- 16 were diagnosed with lung cancer

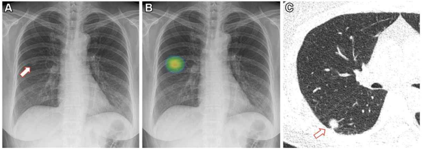
Non-AI group (control arm)

5238 participants

100 had positive reports in chest radiographs

follow-up

- 2461 received chest CT within 3 months
- 56 had actionable lung nodules on CT
- 12 underwent pathologic confirmation
- 10 had malignant lung nodules
- 8 were diagnosed with lung cancer



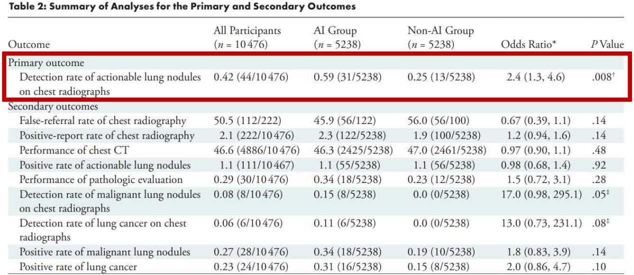


Table 2: Summary of Analyses for the Primary and Secondary Outcomes

Outcome	All Participants (*n* = 10 476)	AI Group (*n* = 5238)	Non-AI Group (*n* = 5238)	Odds Ratio*	*P* Value
Primary outcome					
Detection rate of actionable lung nodules on chest radiographs	0.42 (44/10 476)	0.59 (31/5238)	0.25 (13/5238)	2.4 (1.3, 4.6)	.008†
Secondary outcomes					
False-referral rate of chest radiography	50.5 (112/222)	45.9 (56/122)	56.0 (56/100)	0.67 (0.39, 1.1)	.14
Positive-report rate of chest radiography	2.1 (222/10 476)	2.3 (122/5238)	1.9 (100/5238)	1.2 (0.94, 1.6)	.14
Performance of chest CT	46.6 (4886/10 476)	46.3 (2425/5238)	47.0 (2461/5238)	0.97 (0.90, 1.1)	.48
Positive rate of actionable lung nodules	1.1 (111/10 467)	1.1 (55/5238)	1.1 (56/5238)	0.98 (0.68, 1.4)	.92
Performance of pathologic evaluation	0.29 (30/10 476)	0.34 (18/5238)	0.23 (12/5238)	1.5 (0.72, 3.1)	.28
Detection rate of malignant lung nodules on chest radiographs	0.08 (8/10 476)	0.15 (8/5238)	0.0 (0/5238)	17.0 (0.98, 295.1)	.05‡
Detection rate of lung cancer on chest radiographs	0.06 (6/10 476)	0.11 (6/5238)	0.0 (0/5238)	13.0 (0.73, 231.1)	.08‡
Positive rate of malignant lung nodules	0.27 (28/10 476)	0.34 (18/5238)	0.19 (10/5238)	1.8 (0.83, 3.9)	.14
Positive rate of lung cancer	0.23 (24/10 476)	0.31 (16/5238)	0.15 (8/5238)	2.0 (0.86, 4.7)	.10

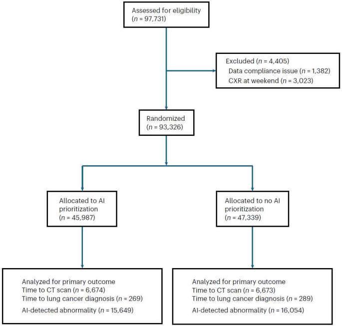
Nam et al. Radiology. 2023.

AI-based Chest X-ray in the Lung Cancer Diagnostic Pathway

nature medicine

Article https://doi.org/10.1038/s41591-026-04253-5

AI-based chest X-ray prioritization in the lung cancer diagnostic pathway: the LungIMPACT randomized controlled trial



Assessed for eligibility (*n* = 97,731)

Excluded (*n* = 4,405)
- Data compliance issue (*n* = 1,382)
- CXR at weekend (*n* = 3,023)

Randomized (*n* = 93,326)

Allocated to AI prioritization (*n* = 45,987)

Allocated to no AI prioritization (*n* = 47,339)

Analyzed for primary outcome
Time to CT scan (*n* = 6,674)
Time to lung cancer diagnosis (*n* = 269)
AI-detected abnormality (*n* = 15,649)

Analyzed for primary outcome
Time to CT scan (*n* = 6,673)
Time to lung cancer diagnosis (*n* = 289)
AI-detected abnormality (*n* = 16,054)

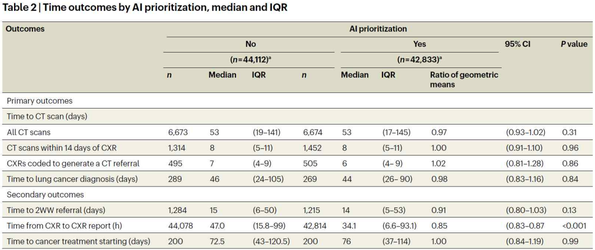
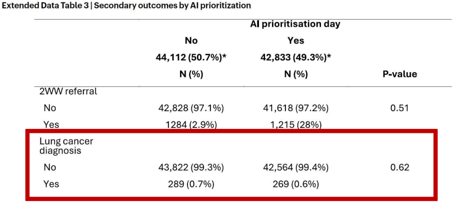


Table 2 | Time outcomes by AI prioritization, median and IQR

Outcomes	AI prioritization								
	No				Yes			95% CI	*P* value
	(*n*=44,112)[a]				(*n*=42,833)[a]				
	n	Median	IQR	*n*	Median	IQR	Ratio of geometric means		
Primary outcomes									
Time to CT scan (days)									
All CT scans	6,673	53	(19–141)	6,674	53	(17–145)	0.97	(0.93–1.02)	0.31
CT scans within 14 days of CXR	1,314	8	(5–11)	1,452	8	(5–11)	1.00	(0.91–1.10)	0.96
CXRs coded to generate a CT referral	495	7	(4–9)	505	6	(4– 9)	1.02	(0.81–1.28)	0.86
Time to lung cancer diagnosis (days)	289	46	(24–105)	269	44	(26– 90)	0.98	(0.83–1.16)	0.84
Secondary outcomes									
Time to 2WW referral (days)	1,284	15	(6–50)	1,215	14	(5–53)	0.91	(0.80–1.03)	0.13
Time from CXR to CXR report (h)	44,078	47.0	(15.8–99)	42,814	34.1	(6.6–93.1)	0.85	(0.83–0.87	<0.001
Time to cancer treatment starting (days)	200	72.5	(43–120.5)	200	76	(37–114)	1.00	(0.84–1.19)	0.99



Extended Data Table 3 | Secondary outcomes by AI prioritization

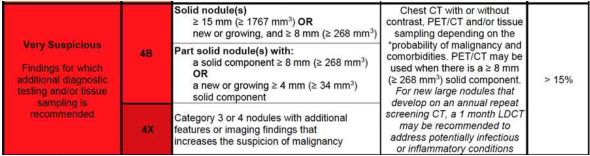
	AI prioritisation day		
	No	**Yes**	
	44,112 (50.7%)*	**42,833 (49.3%)***	
	N (%)	**N (%)**	**P-value**
2WW referral			
No	42,828 (97.1%)	41,618 (97.2%)	0.51
Yes	1284 (2.9%)	1,215 (28%)	
Lung cancer diagnosis			
No	43,822 (99.3%)	42,564 (99.4%)	0.62
Yes	289 (0.7%)	269 (0.6%)	

Woznitza et al. Nat Med. 2026.

LDCT: The Most Sensitive Modality to Detect Lung Cancer

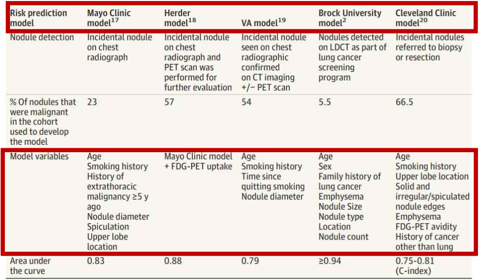
- **Excellent sensitivity, yet high false-positive rates**

-> Need better tools to better discriminate of detected nodules



Very Suspicious Findings for which additional diagnostic testing and/or tissue sampling is recommended	**4B**	**Solid nodule(s)** ≥ 15 mm (≥ 1767 mm^3) **OR** new or growing, and ≥ 8 mm (≥ 268 mm^3) **Part solid nodule(s) with:** a solid component ≥ 8 mm (≥ 268 mm^3) **OR** a new or growing ≥ 4 mm (≥ 34 mm^3) solid component	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm (≥ 268 mm^3) solid component. *For new large nodules that develop on an annual repeat screening CT, a 1 month LDCT may be recommended to address potentially infectious or inflammatory conditions*	> 15%
	4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy		

<Lung-RADS classification>



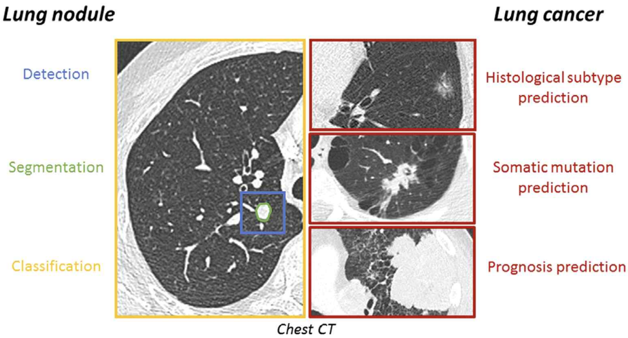
Risk prediction model	Mayo Clinic model[17]	Herder model[18]	VA model[19]	Brock University model[2]	Cleveland Clinic model[20]
Nodule detection	Incidental nodule on chest radiograph	Incidental nodule on chest radiograph and PET scan was performed for further evaluation	Incidental nodule seen on chest radiographic confirmed on CT imaging +/− PET scan	Nodules detected on LDCT as part of lung cancer screening program	Incidental nodules referred to biopsy or resection
% Of nodules that were malignant in the cohort used to develop the model	23	57	54	5.5	66.5
Model variables	Age Smoking history History of extrathoracic malignancy ≥5 y ago Nodule diameter Spiculation Upper lobe location	Mayo Clinic model + FDG-PET uptake	Age Smoking history Time since quitting smoking Nodule diameter	Age Sex Family history of lung cancer Emphysema Nodule Size Nodule type Location Nodule count	Age Smoking history Upper lobe location Solid and irregular/spiculated nodule edges Emphysema FDG-PET avidity History of cancer other than lung
Area under the curve	0.83	0.88	0.79	≥0.94	0.75-0.81 (C-index)

Mazzone et al. JAMA. 2022.

AI for Detection, Classification, and Discrimination

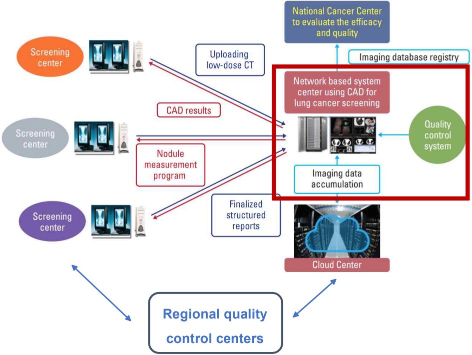
Lung Nodule Classification

- Radiomics based features
  - Morphological/shape feature
  - Texture features
  - Gray scale/histogram features
  - Gradient features
  - Spatial features
- Deep learning models
  - 3D Convolutional Neural Network (CNN)
  - Multi-view 2D CNN
  - 3D Deep Convolutional Neural Network (DCNN)
  - Neural Network Ensemble (NNE)
  - 3D Deep Convolutional Neural Network (DCNN)
  - Stacked Autoencoder (SAE)



Fahmy et al. Cancers. 2022.
de Margerie-Mellon et al. Diagnostic and Interventional Imaging. 2023.

AI-Supported National Lung Cancer Screening Program



National Cancer Center to evaluate the efficacy and quality

Imaging database registry

Screening center

Uploading low-dose CT

CAD results

Screening center

Nodule measurement program

Screening center

Finalized structured reports

Network based system center using CAD for lung cancer screening

Quality control system

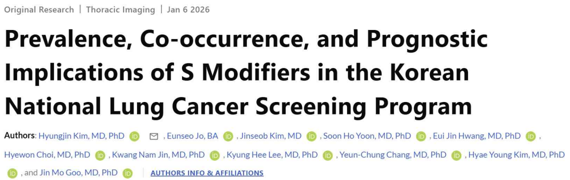
Imaging data accumulation

Cloud Center

Regional quality control centers

Lee et al. Cancer Res Treat. 2019.
Corelinesoft.inc.

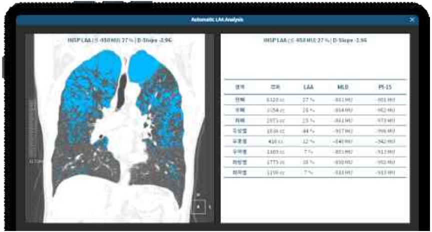
Detection of Other Important Findings

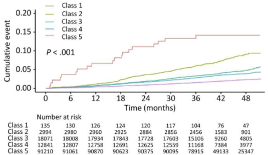


Original Research | Thoracic Imaging | Jan 6 2026

Prevalence, Co-occurrence, and Prognostic Implications of S Modifiers in the Korean National Lung Cancer Screening Program

Authors: Hyungjin Kim, MD, PhD , Eunseo Jo, BA , Jinseob Kim, MD , Soon Ho Yoon, MD, PhD , Eui Jin Hwang, MD, PhD , Hyewon Choi, MD, PhD , Kwang Nam Jin, MD, PhD , Kyung Hee Lee, MD, PhD , Yeun-Chung Chang, MD, PhD , Hyae Young Kim, MD, PhD , and Jin Mo Goo, MD, PhD | AUTHORS INFO & AFFILIATIONS





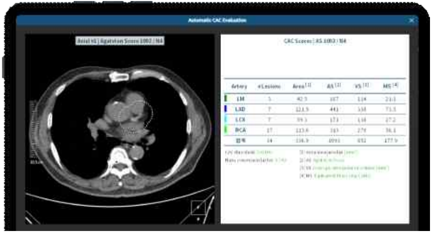
Number at risk

Class 1	135	130	126	124	120	117	104	76	47
Class 2	2994	2980	2960	2925	2884	2856	2456	1583	901
Class 3	18071	18008	17934	17843	17728	17603	15106	9260	4805
Class 4	12841	12807	12758	12691	12625	12559	11168	7384	3977
Class 5	91210	91061	90870	90623	90375	90095	78915	49133	25347

Class	Description
Class 1	Rare but high-risk S modifiers, including extrapulmonary malignancy, aortic aneurysm, or pleural or pericardial effusion
Class 2	Interstitial lung abnormalities, frequently occurring alongside coronary artery calcification and/or emphysema
Class 3	Coronary artery calcification, with some individuals also exhibiting emphysema
Class 4	Isolated emphysema
Class 5	No S modifiers and served as the reference group

- In 125,600 lung cancer screening participants, the most common S modifiers were coronary artery calcification (15%) and emphysema (14%)

- All 7 S modifiers were associated with increased mortality, ranging from emphysema (aHR, 1.15) to pleural/pericardial effusion (aHR, 8.28)

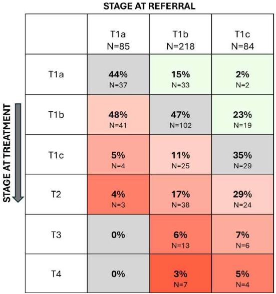


Kim et al. Radiology. 2025.

Management Beyond Detection Matters More

Low-dose CT for lung cancer screening in a high-risk population (SUMMIT): a prospective, longitudinal cohort study

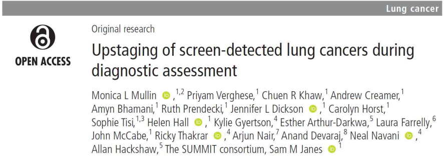
Amyn Bhamani, Andrew Creamer*, Priyam Verghese, Ruth Prendecki, Carolyn Horst, Sophie Tisi, Helen Hall, Chuen Ryan Khaw, Monica Mullin, John McCabe, Kylie Gyertson, Vicky Bowyer, Dominique Arancon, Jeannie Eng, Fanta Bojang, Claire Levermore, Anne-Marie Hacker, Esther Arthur-Darkwa, Laura Farrelly, Anant Patel, Sara Lock, Alan Shaw, Rajesh Banka, Angshu Bhowmik, Ugo Ekeowa, Zaheer Mangera, Christopher Valerio, William M Ricketts, Ali Mohammed, Terry O'Shaughnessy, Neal Navani, Samantha L Quaife, Arjun Nair, Anand Devaraj, SUMMIT consortium†, Jennifer L Dickson, Allan Hackshaw, Sam M Janes*



STAGE AT REFERRAL

STAGE AT TREATMENT

	T1a N=85	T1b N=218	T1c N=84
T1a	**44%** N=37	**15%** N=33	**2%** N=2
T1b	**48%** N=41	**47%** N=102	**23%** N=19
T1c	**5%** N=4	**11%** N=25	**35%** N=29
T2	**4%** N=3	**17%** N=38	**29%** N=24
T3	**0%**	**6%** N=13	**7%** N=6
T4	**0%**	**3%** N=7	**5%** N=4



Lung cancer

OPEN ACCESS

Original research

Upstaging of screen-detected lung cancers during diagnostic assessment

Monica L Mullin ,[1,2] Priyam Verghese,[1] Chuen R Khaw,[1] Andrew Creamer,[1] Amyn Bhamani,[1] Ruth Prendecki,[1] Jennifer L Dickson ,[1] Carolyn Horst,[1] Sophie Tisi,[1,3] Helen Hall ,[1] Kylie Gyertson,[4] Esther Arthur-Darkwa,[5] Laura Farrelly,[6] John McCabe,[1] Ricky Thakrar ,[4] Arjun Nair,[7] Anand Devaraj,[8] Neal Navani ,[4] Allan Hackshaw,[5] The SUMMIT consortium, Sam M Janes ,[1]

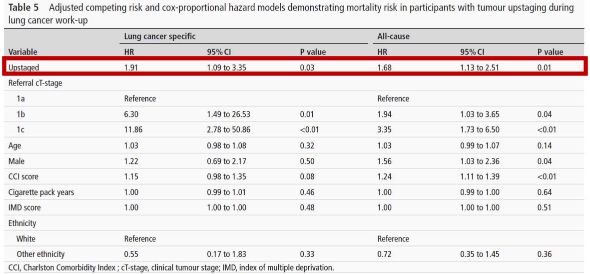


Table 5 Adjusted competing risk and cox-proportional hazard models demonstrating mortality risk in participants with tumour upstaging during lung cancer work-up

	Lung cancer specific			All-cause		
Variable	HR	95% CI	P value	HR	95% CI	P value
Upstaged	1.91	1.09 to 3.35	0.03	1.68	1.13 to 2.51	0.01
Referral cT-stage						
1a	Reference			Reference		
1b	6.30	1.49 to 26.53	0.01	1.94	1.03 to 3.65	0.04
1c	11.86	2.78 to 50.86	<0.01	3.35	1.73 to 6.50	<0.01
Age	1.03	0.98 to 1.08	0.32	1.03	0.99 to 1.07	0.14
Male	1.22	0.69 to 2.17	0.50	1.56	1.03 to 2.36	0.04
CCI score	1.15	0.98 to 1.35	0.08	1.24	1.11 to 1.39	<0.01
Cigarette pack years	1.00	0.99 to 1.01	0.46	1.00	0.99 to 1.00	0.64
IMD score	1.00	1.00 to 1.00	0.48	1.00	1.00 to 1.00	0.51
Ethnicity						
White	Reference			Reference		
Other ethnicity	0.55	0.17 to 1.83	0.33	0.72	0.35 to 1.45	0.36

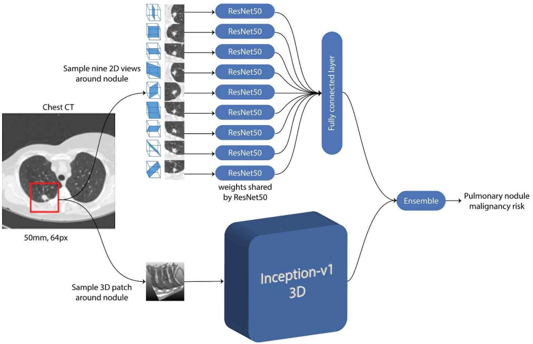
CCI, Charlston Comorbidity Index ; cT-stage, clinical tumour stage; IMD, index of multiple deprivation.

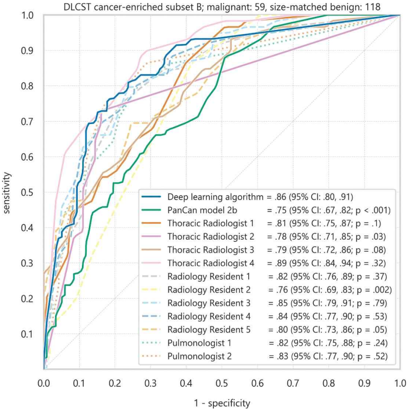
- 43% (165/390) of patients experienced tumour upstaging between referral and treatment decision

Bhamani et al. Lancet Oncol. 2025.
Mullin et al. Thorax. 2026.

Radiomics for Better Discrimination

-Developed with 16,077 nodules (1,249 malignant) collected -from the NLST





Venkadesh et al. Radiology. 2021.

AI-Integrated Novel Biomarkers for Nodule Risk Stratification

The CANDLE Project

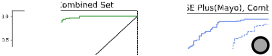
High-risk subjects for lung cancer

Low-dose Chest CT

Indeterminate nodule

Risk Assessment of Malignancy

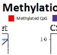
Clinical & CT factors such as Brock model



RCTs	LC mortality	Positive rate of baseline CT	False positive rate
NLST	HR 0.80	27%	96%
NELSON	HR 0.76	22%*	96%*

*Since 'medium-sized nodules' require additional CT scan, these were included in the initial test positive rate and false positive rate. HR, hazard ratio; LC, lung cancer

(1)*NEJM.* 2011;365(5):395-409. (2)*NEJM.* 2020;382(6):503-13. (3)*Am J Respir Crit Care Med.* 2018;197(9):1220-3. This figure has been designed using images from Flaticon.com

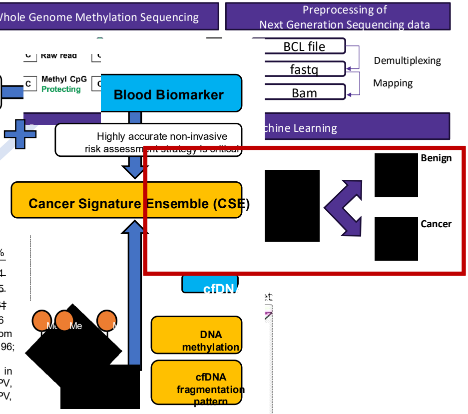


Brock model accuracy for identifying LC†

Model probability thresholds	10%	20%
Sensitivity	0.71	0.61
Specificity	0.79	0.85
PPV	0.25‡	0.28‡
NPV	0.97	0.96

†Secondary analysis of data from the NLST: >8 mm nodule, n=2196; lung cancer, n= 193

‡At low prevalence of cancer in the sample, PPV were poor. PPV, positive predictive value; NPV, negative predictive value



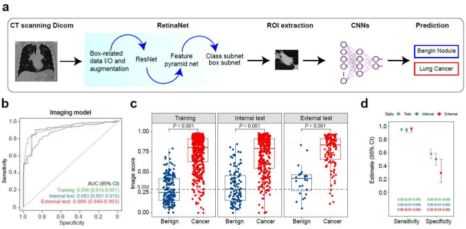
100% - Specificity(%)

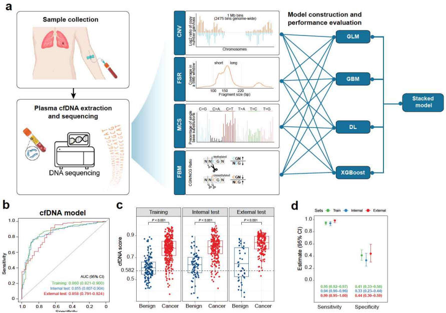
100% - Specificity(%)

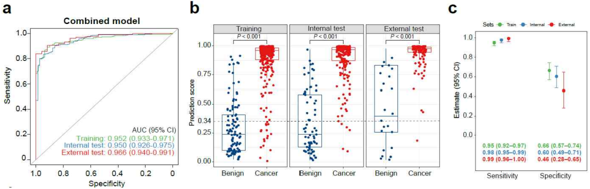
100% - Specificity(%)

Unpublished data

AI-Based Multimodal Prediction Tools



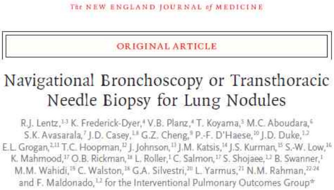




Wang et al. Lancet Reg Health West Pac. 2025.

Earlier and More Accurate Diagnosis of Smaller Nodules

- Advanced technologies for biopsy and pathologic diagnosis

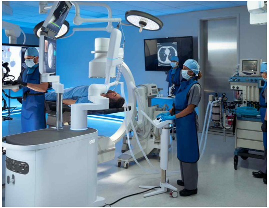


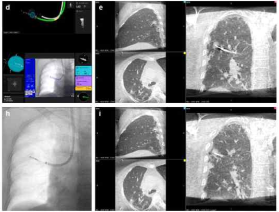
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Navigational Bronchoscopy or Transthoracic Needle Biopsy for Lung Nodules

R.J. Lentz,[1-3] K. Frederick-Dyer,[4] V.B. Planz,[4] T. Koyama,[5] M.C. Aboudara,[6] S.K. Avasarala,[7] J.D. Casey,[1,8] G.Z. Cheng,[9] P.-F. D'Haese,[10] J.D. Duke,[1,2] E.L. Grogan,[2,11] T.C. Hoopman,[12] J. Johnson,[13] J.M. Katsis,[14] J.S. Kurman,[15] S.-W. Low,[16] K. Mahmood,[17] O.B. Rickman,[18] L. Roller,[1] C. Salmon,[17] S. Shojaee,[1,2] B. Swanner,[1] M.M. Wahidi,[19] C. Walston,[18] G.A. Silvestri,[20] L. Yarmus,[21] N.M. Rahman,[22-24] and F. Maldonado,[1,2] for the Interventional Pulmonary Outcomes Group*





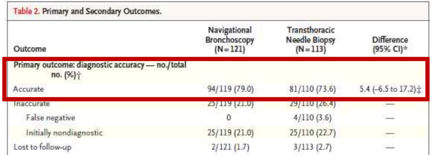


Table 2. Primary and Secondary Outcomes.

Outcome	Navigational Bronchoscopy (N=121)	Transthoracic Needle Biopsy (N=113)	Difference (95% CI)*
Primary outcome: diagnostic accuracy — no./total no. (%)†			
Accurate	94/119 (79.0)	81/110 (73.6)	5.4 (−6.5 to 17.2)‡
Inaccurate	25/119 (21.0)	29/110 (26.4)	—
False negative	0	4/110 (3.6)	—
Initially nondiagnostic	25/119 (21.0)	25/110 (22.7)	—
Lost to follow-up	2/121 (1.7)	3/113 (2.7)	—

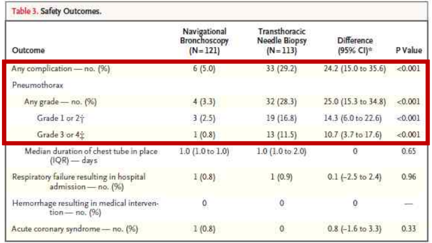
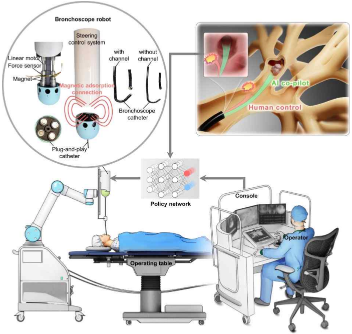


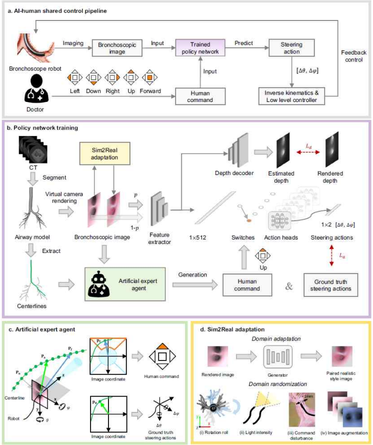
Table 3. Safety Outcomes.

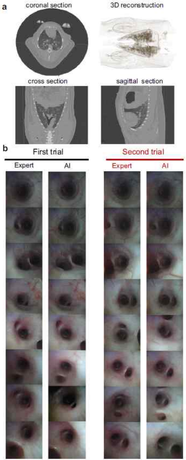
Outcome	Navigational Bronchoscopy (N=121)	Transthoracic Needle Biopsy (N=113)	Difference (95% CI)*	P Value
Any complication — no. (%)	6 (5.0)	33 (29.2)	24.2 (15.0 to 35.6)	<0.001
Pneumothorax				
Any grade — no. (%)	4 (3.3)	32 (28.3)	25.0 (15.3 to 34.8)	<0.001
Grade 1 or 2†	3 (2.5)	19 (16.8)	14.3 (6.0 to 22.6)	<0.001
Grade 3 or 4‡	1 (0.8)	13 (11.5)	10.7 (3.7 to 17.6)	<0.001
Median duration of chest tube in place (IQR) — days	1.0 (1.0 to 1.0)	1.0 (1.0 to 2.0)	0	0.65
Respiratory failure resulting in hospital admission — no. (%)	1 (0.8)	1 (0.9)	0.1 (−2.5 to 2.4)	0.96
Hemorrhage resulting in medical intervention — no. (%)	0	0	0	—
Acute coronary syndrome — no. (%)	1 (0.8)	0	0.8 (−1.6 to 3.3)	0.33

Lentz et al. N Eng J Med. 2025.

AI for Modern Bronchoscopy

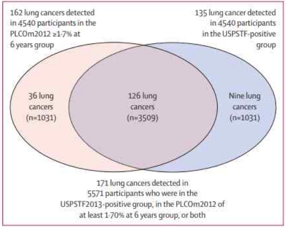


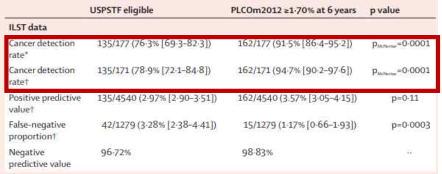




Zhang et al. Nat Comm. 2024.

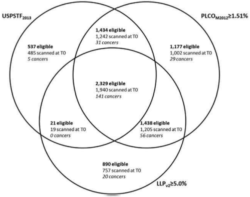
Risk Modelling for Future Lung Cancer Prediction

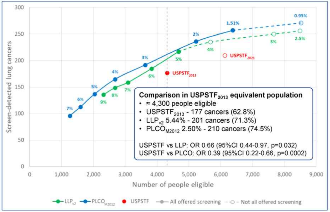




	USPSTF eligible	PLCOm2012 ≥1·70% at 6 years	p value
ILST data			
Cancer detection rate*	135/177 (76·3% [69·3–82·3])	162/177 (91·5% [86·4–95·2])	$p_{McNemar}$=0·0001
Cancer detection rate†	135/171 (78·9% [72·1–84·8])	162/171 (94·7% [90·2–97·6])	$p_{McNemar}$=0·0001
Positive predictive value†	135/4540 (2·97% [2·90–3·51])	162/4540 (3·57% [3·05–4·15])	p=0·11
False-negative proportion†	42/1279 (3·28% [2·38–4·41])	15/1279 (1·17% [0·66–1·93])	p=0·0003
Negative predictive value	96·72%	98·83%	..

International Lung Screening Trial





Comparison in $USPSTF_{2013}$ equivalent population

- ≈ 4,300 people eligible
- $USPSTF_{2013}$ - 177 cancers (62.8%)
- LLP_{v2} 5.44% - 201 cancers (71.3%)
- $PLCO_{M2012}$ 2.50% - 210 cancers (74.5%)

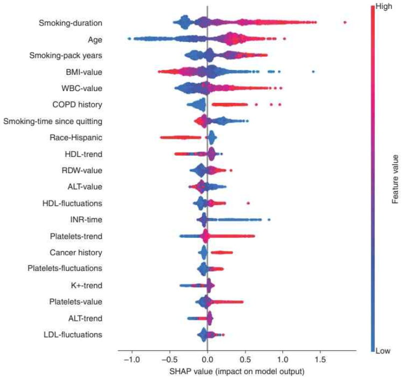
USPSTF vs LLP: OR 0.66 (95%CI 0.44-0.97, p=0.032)
USPSTF vs PLCO: OR 0.39 (95%CI 0.22-0.66, p=0.0002)

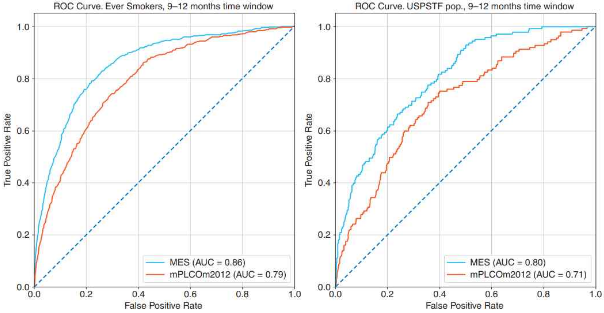
Yorkshire Lung Screening Trial

Tammemagi et al. Lancet Oncol. 2022.
Gabe et al. J Thorac Oncol. 2025.

Integration of AI on Risk-Modelling

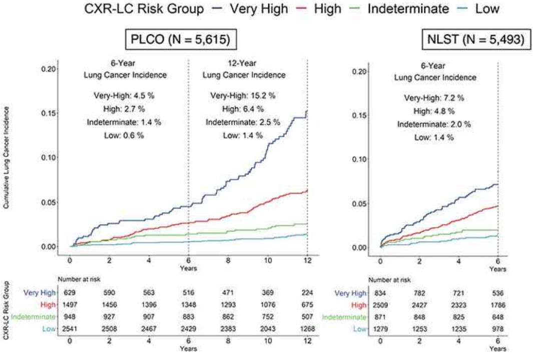
- Comparison of XGBoost vs. PLCOm2012 in a cohort of 6,505 of lung cancer cases and 189,597 controls

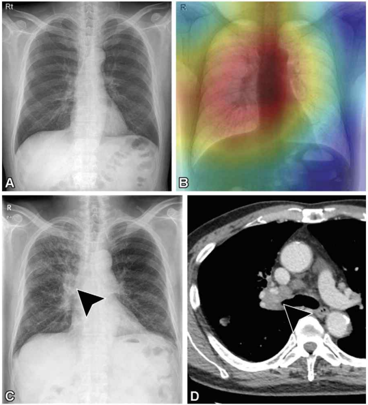




Gould et al. Am J Respir Crit Care Med 2021.

AI for Predicting Future Risk Using Chest X-ray





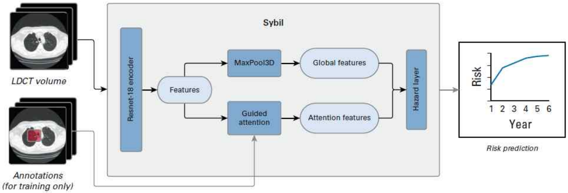
Lu et al. Ann Intern Med. 2020.
Lee et al. Radiology. 2023.

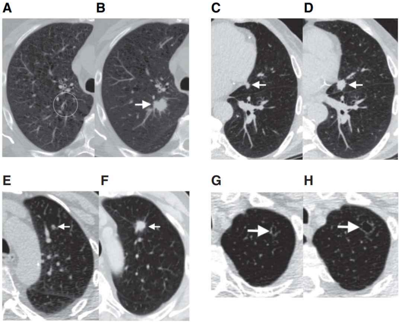
Predicting Future Lung Cancer From an LDCT Scan

- **Sybil: A Deep Learning Risk-Prediction Model Based on LDCT**

  -> Predicts an individual's future lung cancer risk up to 6 years from a single screening LDCT

  Irrelevant of demographic or clinical characteristics

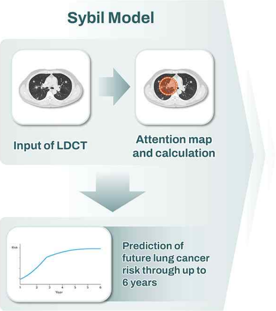




Mikhael et al. J Clin Oncol. 2023.

Implications with Considerations of Region-Specific Needs

- **Performance in an Asian Cohort (Korea) of 21,087 Individuals Who Underwent Self-Initiated Screening**



Sybil Model

Input of LDCT

Attention map and calculation

Prediction of future lung cancer risk through up to 6 years

Performance by smoking-related risk profile

- ≥ 20 PYs
- < 20 PYs or unknown PYs
- No smoking history

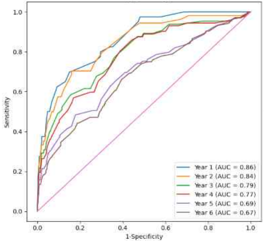
Performance by demographic and region-specific features

- Sex
- Family history of lung cancer
- Granulomatous sequelae
- Subsolid nodules

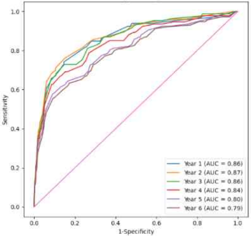
Comparison with Lung-RADS for short-term performance metrics

- To assess the complementary and synergistic value

≥ 20 PY smoking history



Individuals who have never smoked



Implications

➔ Identify at-risk groups that currently excluded from LCS eligibility criteria

➔ Identify true low-risk individuals that could be guided to discontinue screening

Kim et al. Unpublished data.

Summary/Take Home

- AI can significantly **enhance and support early detection, nodule discrimination, and prediction of future lung cancer risk** by providing adjunctive information and greater precision

- Implications can vary depending on the **clinical setting** and the **context** in which they are applied, making a **clear understanding of the intended purpose** essential

- Incorporating **region- and population-specific features** could further enhance the **clinical utility** of AI and **broaden its applicability across global settings**

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