폐결절 환자 진료하기

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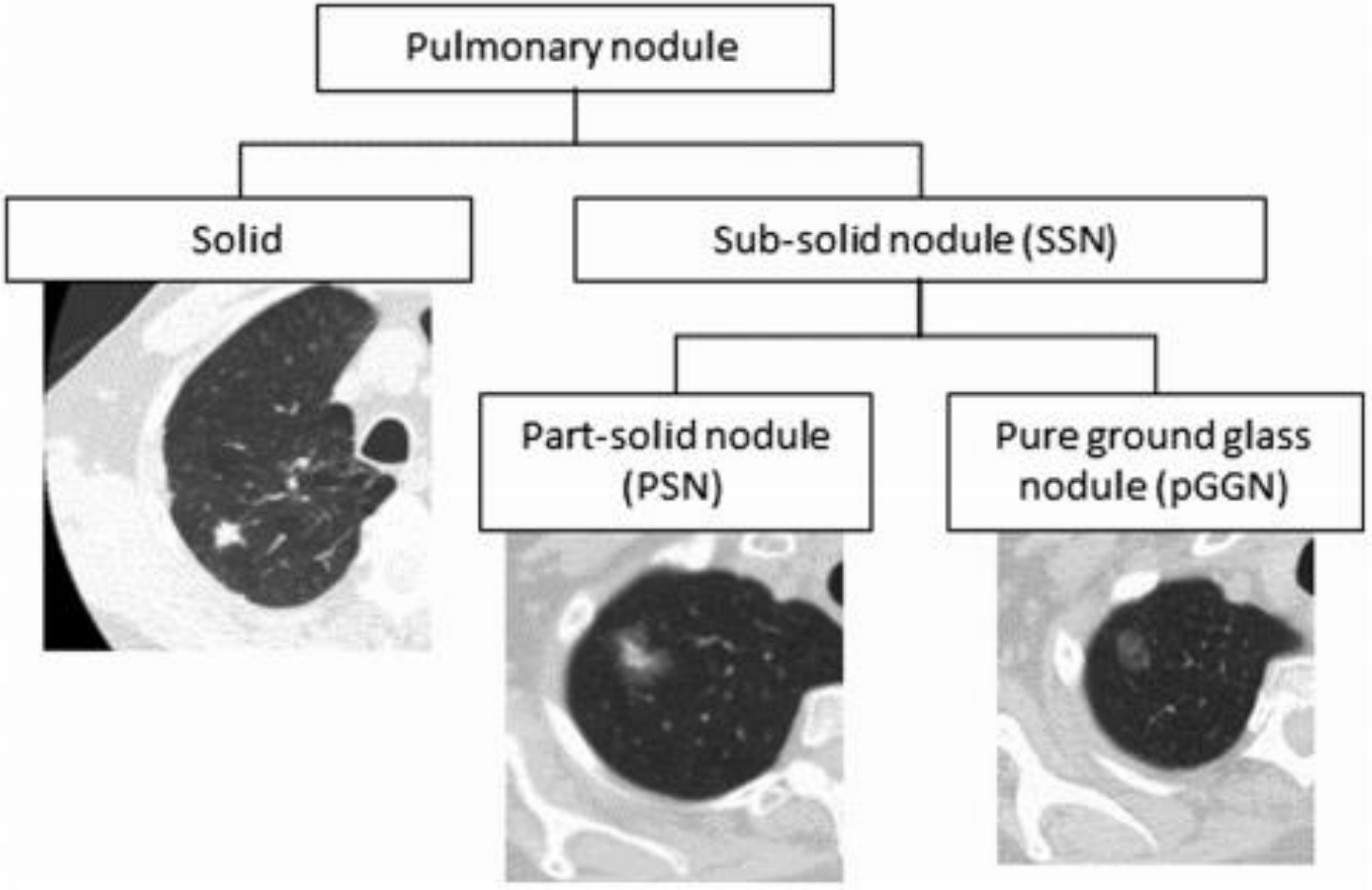
What is a pulmonary nodule?

- **Small (<3 cm), focal, distinct radiographic density**
- **Commonly encountered in clinical practice**
- **Incidence increasing with more use of CT**

- **Major routes of detection**

- Lung cancer screening
- Incidental
- During oncological follow up

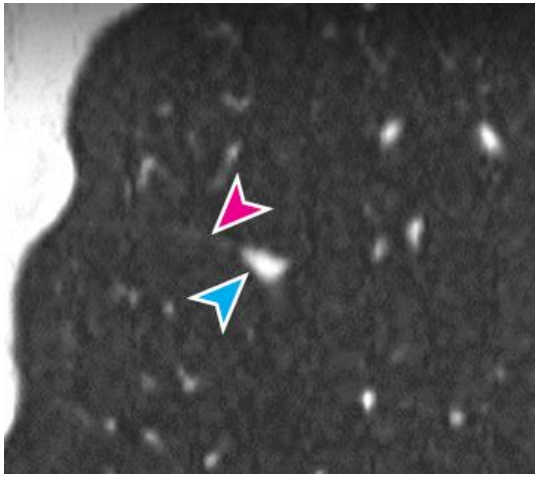
Classification of pulmonary nodules



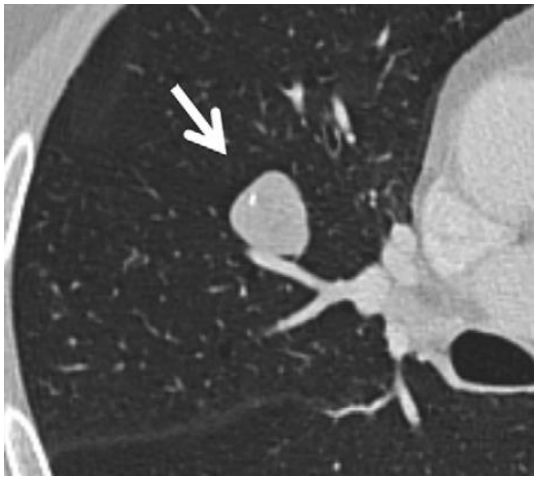
Baldwin et al. Thorax. 2015

Solid pulmonary nodules

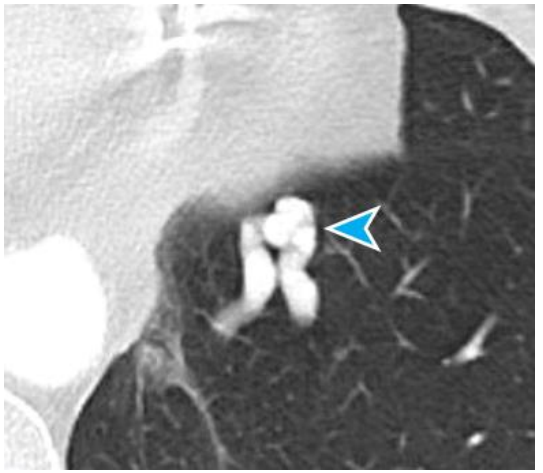
Calcified granuloma



Perifissural nodule



Hamartoma



Arteriovenous malformation

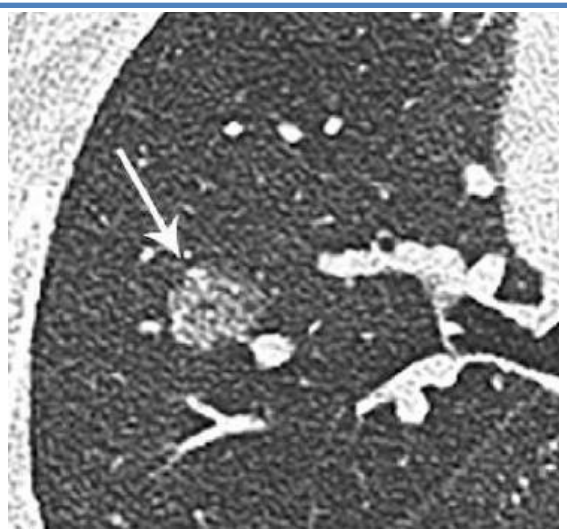
Mazzone et al. JAMA. 2022
MacMahon et al. Radiology. 2017

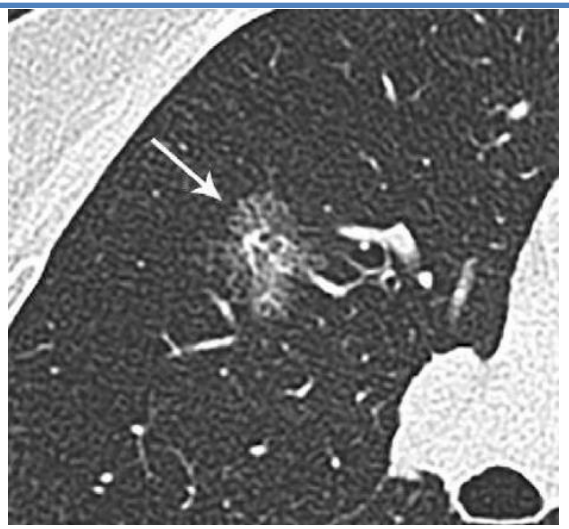
Solid pulmonary nodules with malignancy risk

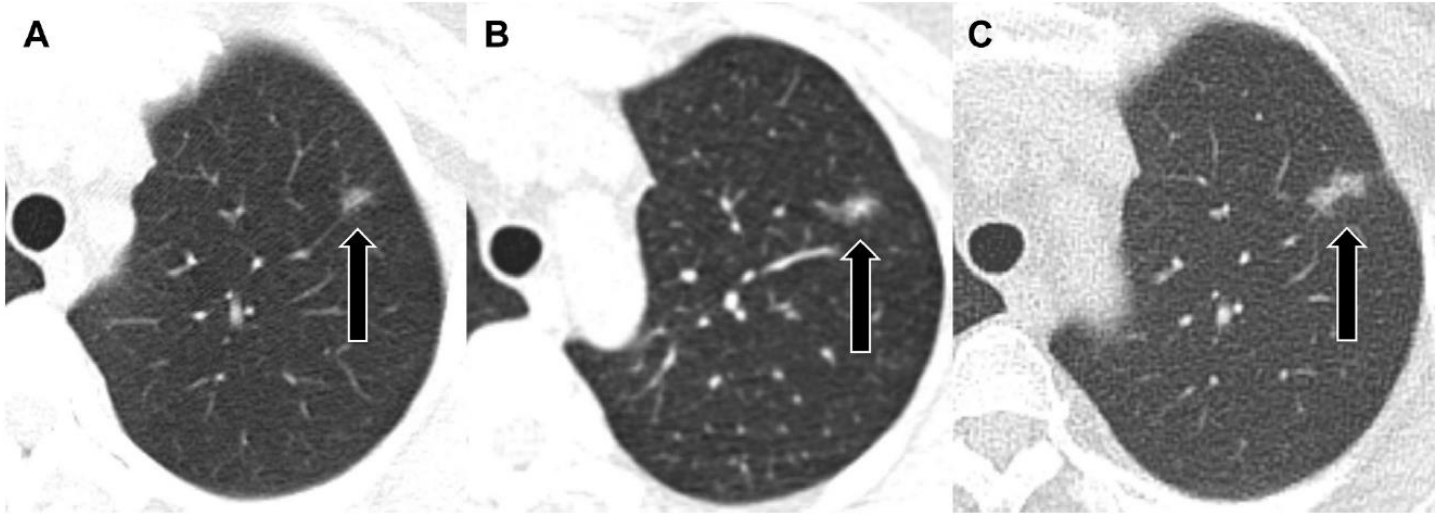
Parameter	Characteristics Associated With Malignant Nodules
Growth rate	Doubling time 20-400 d (< 100 d for most solid nodules); growth rate may be slower with ground-glass and subsolid nodules (> 200 d); very rapid doubling suggests an infectious or inflammatory cause
Location	Upper lobe is a more common site for malignant nodules, although the diagnostic significance of this finding is reduced in Asia due to the high prevalence of TB
Margins	Lobulated or speculated margins are strongly associated with malignancy; notches are commonly seen in adenocarcinomas with overt invasion
Cavitation	Malignant lesions are associated with irregular, thicker walls > 15 mm thick
Size	Probability of malignancy increases with size (nodules > 2 cm are more likely to be malignant, although smaller size does not exclude malignancy)
Calcification	Punctate and eccentric (evidence of necrosis within nodule) calcification may occur with malignancy
Other features	Vascular convergence, dilated bronchus leading into the nodule

MacMahon et al. Radiology. 2017
Bae et al. Chest. 2016

Subsolid pulmonary nodules







10 years of follow-up

Azour et al. Chest. 2021
Lee et al. J Thorac Oncol. 2019

Differential considerations for subsolid nodules

Primary Lung Adenocarcinoma	Nonprimary Lung Adenocarcinoma Etiologies
• Atypical adenomatous hyperplasia	• Transient infection (eg, aspergillosis, candidiasis)
• Adenocarcinoma in situ	• Transient inflammation
• Minimally invasive adenocarcinoma	• Focal interstitial fibrosis
• Invasive adenocarcinoma	• Organizing pneumonia
• Mucinous adenocarcinoma	• Eosinophilic pneumonia
	• Alveolar sarcoid
	• Drug reaction
	• Vasculitis (granulomatosis with polyangiitis)
	• Endometriosis
	• Mucosa associated lymphoid tissue (MALT) and lymphoproliferative disorders
	• Metastatic lesions (including melanoma; renal carcinoma; breast, GI, and pancreatic adenocarcinomas)

Azour et al. Chest. 2021

Nodules are commonly detected by screening

- **Results from LDCT screening trials**

Study	No. Randomized	Age (y): Mean ± SD or Median (IQR)	Male (%)	Pack-Years Median (IQR)	Active Smokers (%)	Positive Results[a] at T_0	Positive Results[a] by End of Screening Period	Lung Cancer Mortality RR (95% CI)
NLST[12,13]	53,454	61 ± 5	59	48 (27)	48.1	7,191 (27.3%)	10,287 (39.1%)	0.85 (0.75-0.96)
Depiscan[14]	765	56 (NR)	71	30 (NR)	64	24%	NR	NR
DANTE[15,16]	2,472	64.6 ± 3.5	100	45 (28.5)	56	199 (15.6%)	471 (37%)	1.01 (0.70-1.44)
DLCST[21]	4,104	58 ± 5	55	36 (13)	75.3	155 (7.6%)	241 (11.8%)	1.03 (CI 0.66-1.60)
NELSON[22,23]	15,822	59 (IQR: 6)	84	42 (19)	55	120 (1.6%)	2.0% (overall) 6.0% (at least 1 positive scan)	NR
ITALUNG[24-26]	3,206	61 ± 4	64	40 (NR)	66	426 (30.3%)	1,044 (46.1%)[b]	0.70 (0.48-1.04)
MILD[27-29]	4,099	Annual: 57 (NR) Biennial: 58 (NR)	Annual: 68 Biennial: 69	Annual: 39 (NR) Biennial: 39 (NR)	Annual: 69 Biennial: 68	Annual: 177 (14%) Biennial: 158 (15%)	NR	Annual: 2.48 (0.98-6.29) Biennial: 1.24 (0.42-3.70)
LUSI[30,31]	4,052	58 (IQR: 5)	66	36 (18)	61	451 (22.2%)	805 (39.7%)	NR
UKLS[32-34]	4,055	67 ± 4	75	NR	39	536 (26.9%)[c]	NR, single screen	NR
LSS[35,36]	3,318	NR	58	54 (NR)	57.9	340 (20.5%)	573 (34.5%)	NR

Mazzone et al. Chest. 2018

Screen-detected nodules

- **Lung-RADS 2022**

Size: mean diameter

Growth: increase of >1.5 mm (2 mm^3)

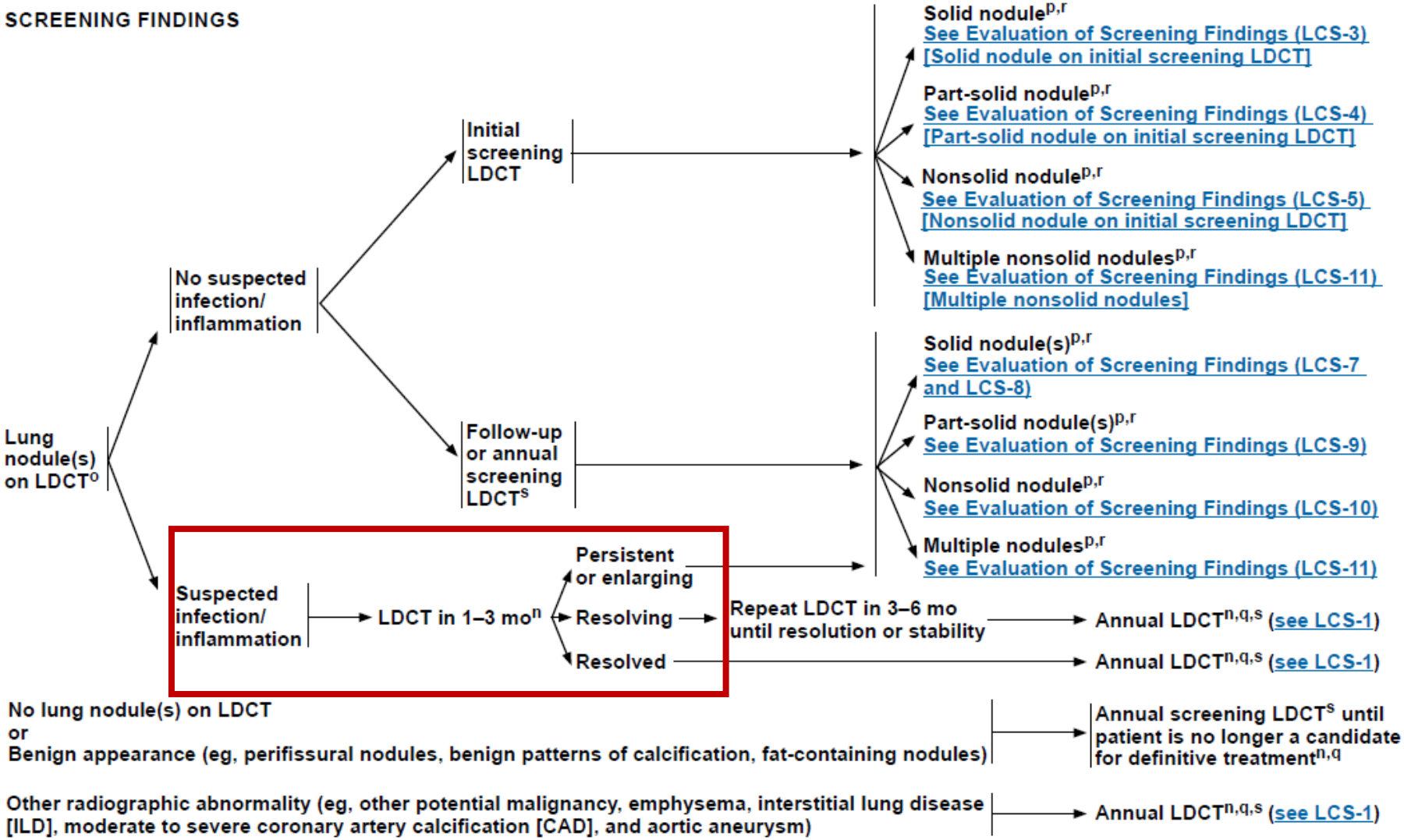
ACR American College of Radiology

Lung-RADS® v2022

Release Date: November 2022

Lung-RADS	Category Descriptor	Findings	Management
0	**Incomplete** Estimated Population Prevalence: ~ 1%	Prior chest CT examination being located for comparison (see note 9)	Comparison to prior chest CT;
		Part or all of lungs cannot be evaluated	Additional lung cancer screening CT imaging needed;
		Findings suggestive of an inflammatory or infectious process (see note 10)	1-3 month LDCT
1	**Negative** Estimated Population Prevalence: 39%	**No lung nodules OR** **Nodule with benign features:** • Complete, central, popcorn, or concentric ring calcifications **OR** • Fat-containing	12-month screening LDCT
2	**Benign** - Based on imaging features or indolent behavior Estimated Population	**Juxtapleural nodule:** • < 10 mm (524 mm^3) mean diameter at baseline or new **AND** • Solid; smooth margins; and oval, lentiform, or triangular shape	
		Solid nodule: • < 6 mm (< 113 mm^3) at baseline **OR** • New < 4 mm (< 34 mm^3)	
		Part solid nodule: • < 6 mm total mean diameter (< 113 mm^3) at baseline	
		Non solid nodule (GGN):	
4A	**Suspicious** Estimated Population Prevalence: 4%	**Solid nodule:** • ≥ 8 to < 15 mm (≥ 268 to < 1,767 mm^3) at baseline **OR** • Growing < 8 mm (< 268 mm^3) **OR** • New 6 to < 8 mm (113 to < 268 mm^3)	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm^3) solid nodule or solid component
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm^3) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm^3) at baseline **OR** • New or growing < 4 mm (< 34 mm^3) solid component	6-month LDCT
		Airway nodule, segmental or more proximal - at baseline (see note 11)	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst **OR** • Multilocular cyst at baseline **OR** • Thin- or thick-walled cyst that becomes multilocular	
4B	**Very Suspicious** Estimated Population Prevalence: 2%	**Airway nodule**, segmental or more proximal - stable or growing (see note 11)	Referral for further clinical evaluation
		Solid nodule: • ≥ 15 mm (≥ 1767 mm^3) at baseline **OR** • New or growing ≥ 8 mm (≥ 268 mm^3)	Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm^3) solid nodule or solid component; tissue sampling; and/or referral for further clinical evaluation Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)
		Part solid nodule: • Solid component ≥ 8 mm (≥ 268 mm^3) at baseline **OR** • New or growing ≥ 4 mm (≥ 34 mm^3) solid component	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst with growing wall thickness/nodularity **OR** • Growing multilocular cyst (mean diameter) **OR** • Multilocular cyst with increased loculation or new/increased opacity (nodular, ground glass, or consolidation)	
		Slow growing solid or part solid nodule that demonstrates growth over multiple screening exams (see note 8)	
4X	Estimated Population Prevalence: < 1%	Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)	As appropriate to the specific finding

NCCN guidelines for screen-detected nodules

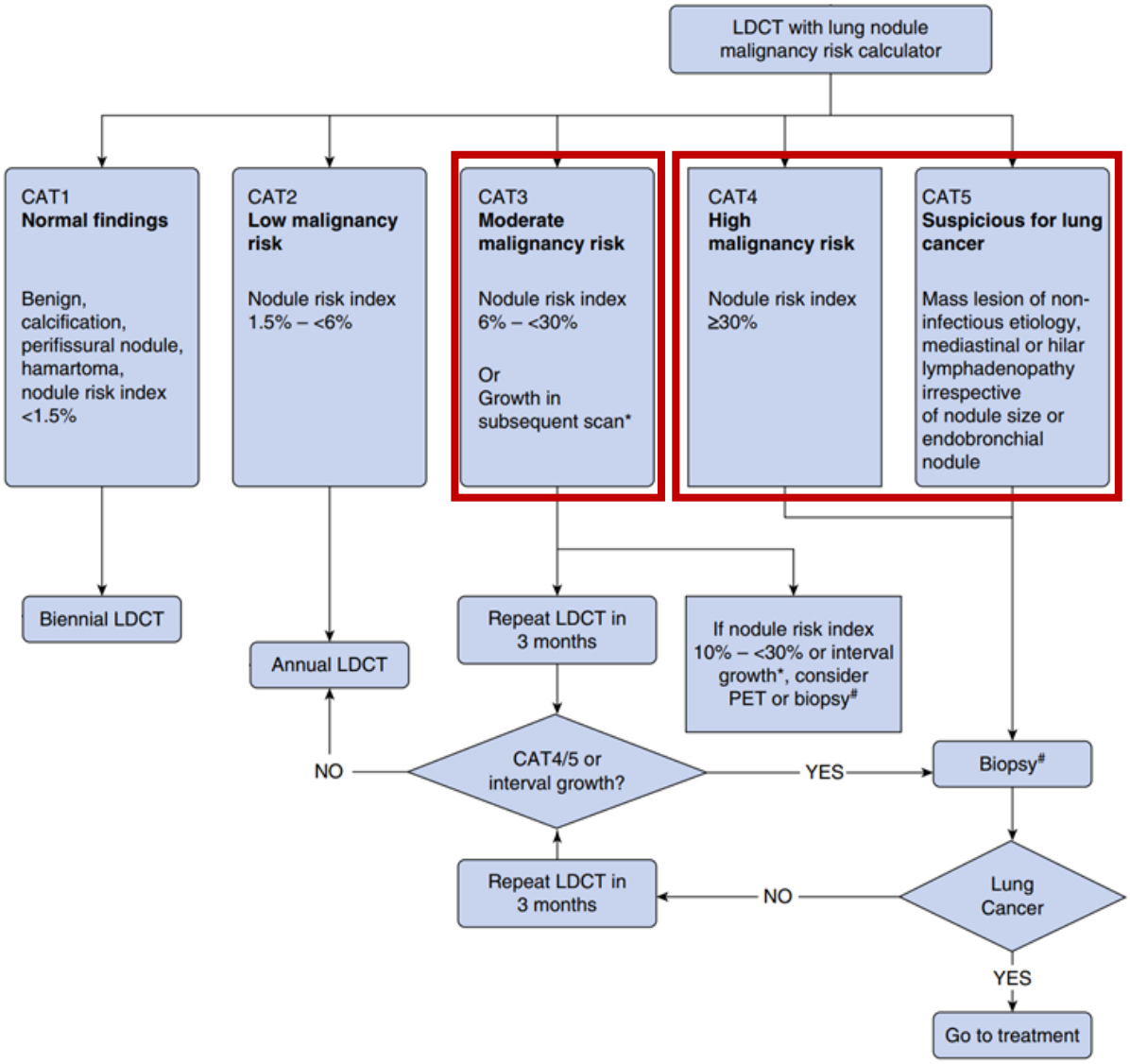


Management of screen-detected nodules

- **ILST protocol**

-Early recall for CAT3

-Diagnostic referral for CAT4/5



Lim et al. Ann Am Throac Soc. 2020

Incidence of incidentally detected nodules

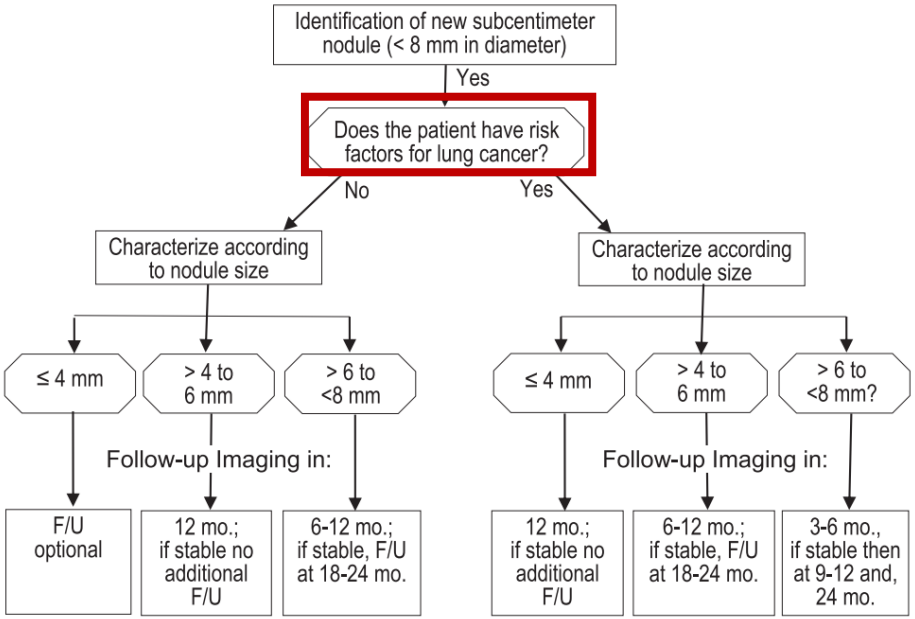
- **Frequency of chest CT imaging and positive scans**

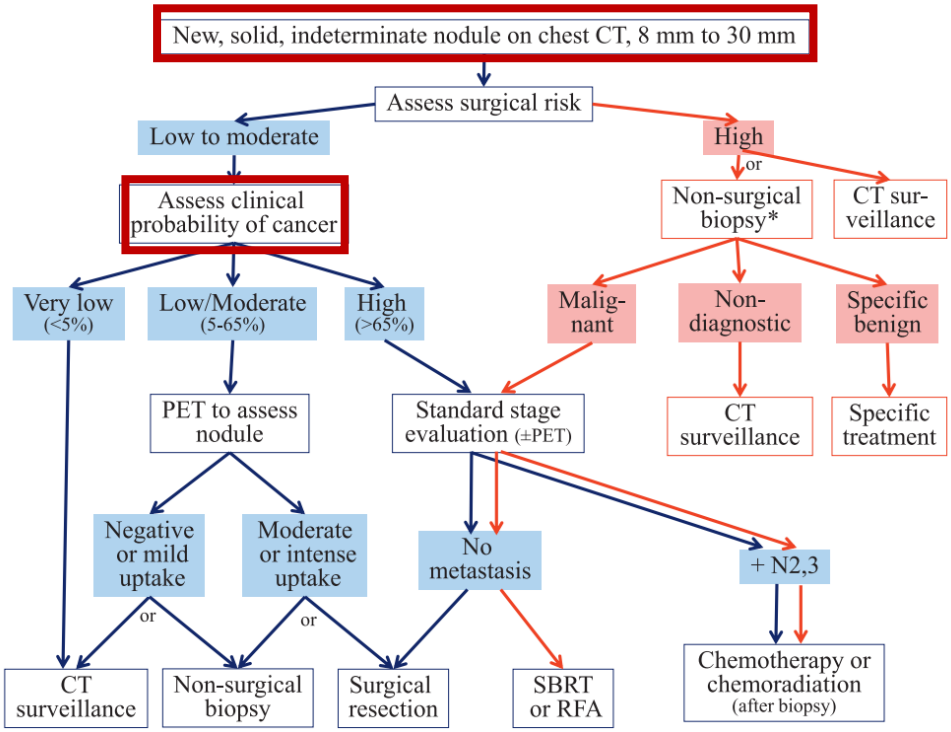
Year	Total Members (*N*)	Chest CT Scans Performed (*n*)	Positive Chest CT Scans [*n (% of Scans)*]	Time at Risk for Scanning* (*Person-Years*)	Chest CT Scans Performed† [*Rate per 1,000 Person-Years (95% CI)*]	Positive CT Scans† [*Rate per 1,000 Person-Years (95% CI)*]
2006	2,623,719	46,663	11,172 (23.9)	2,288,046	20.4 (20.2 –20.6)	4.9 (4.8–5.0)
2007	2,673,078	50,571	13,645 (27.0)	2,342,118	21.6 (21.4–21.8)	5.8 (5.7–5.9)
2008	2,672,351	55,264	15,171 (27.5)	2,369,685	23.3 (23.1–23.5)	6.4 (6.3–6.5)
2009	2,663,055	60,430	17,250 (28.5)	2,375,472	25.4 (25.2, 25.6)	7.3 (7.2–7.4)
2010	2,698,679	63,036	19,420 (30.8)	2,412,059	26.1 (25.9–26.3)	8.1 (7.9–8.2)
2011	2,822,145	68,411	20,346 (29.7)	2,540,580	26.9 (26.7–27.1)	8.0 (7.9–8.1)
2012	2,916,094	71,206	21,766 (30.6)	2,635,220	27.0 (26.8–27.2)	8.3 (8.2–8.4)
2006–2012 Total‡	19,069,121	415,581	118,770 (28.6)	16,963,179	24.5 (24.4–24.6)	7.0 (7.0–7.0)

Gould et al. Am J Respir Crit Care Med. 2015

Management of incidentally detected nodules

- **ACCP guidelines (2013)**

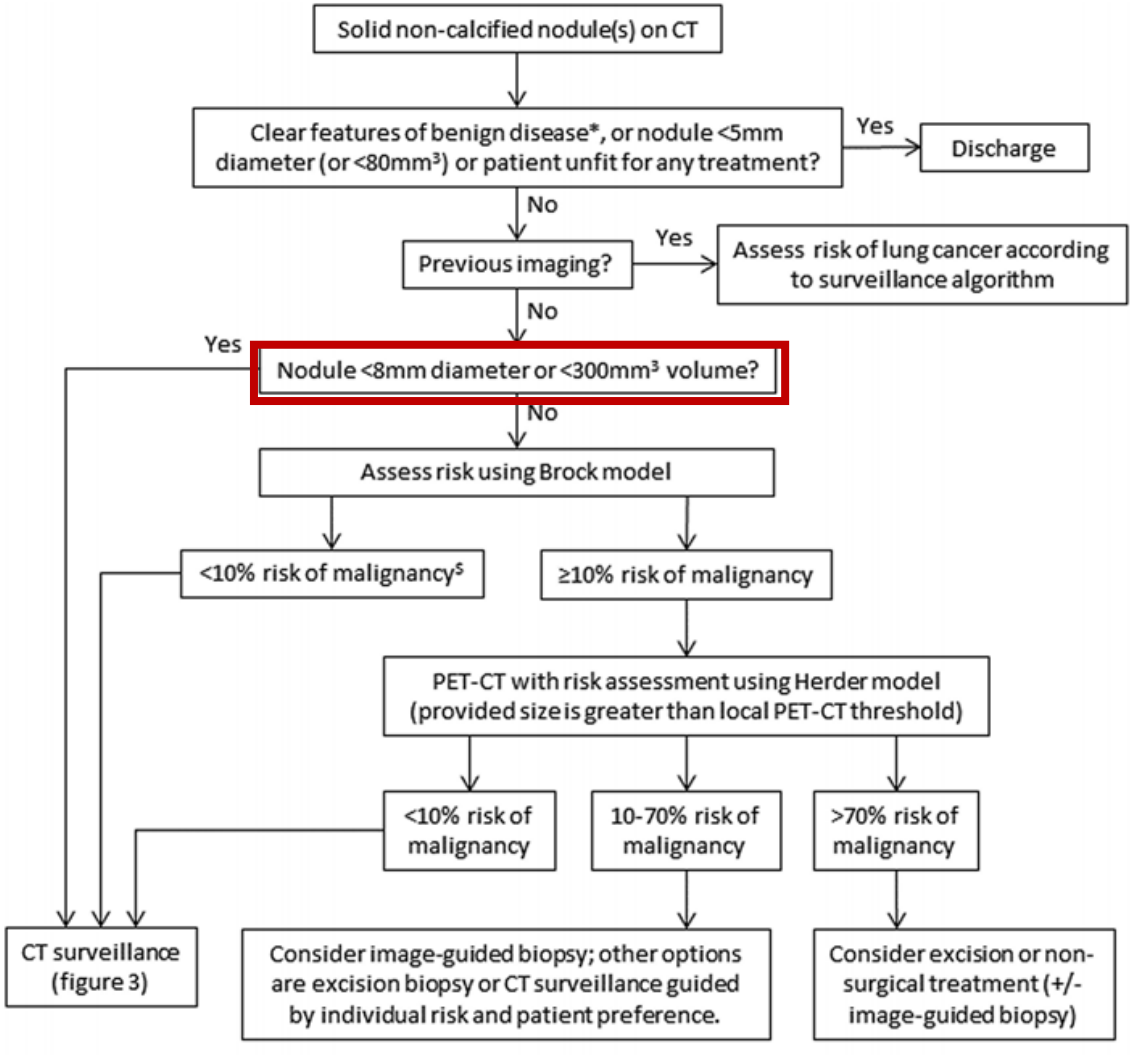




Gould et al. Chest. 2013

Incidentally detected nodules

- **BTS guidelines (2015)**



Baldwin et al. Thorax. 2015

Risk prediction for malignancy

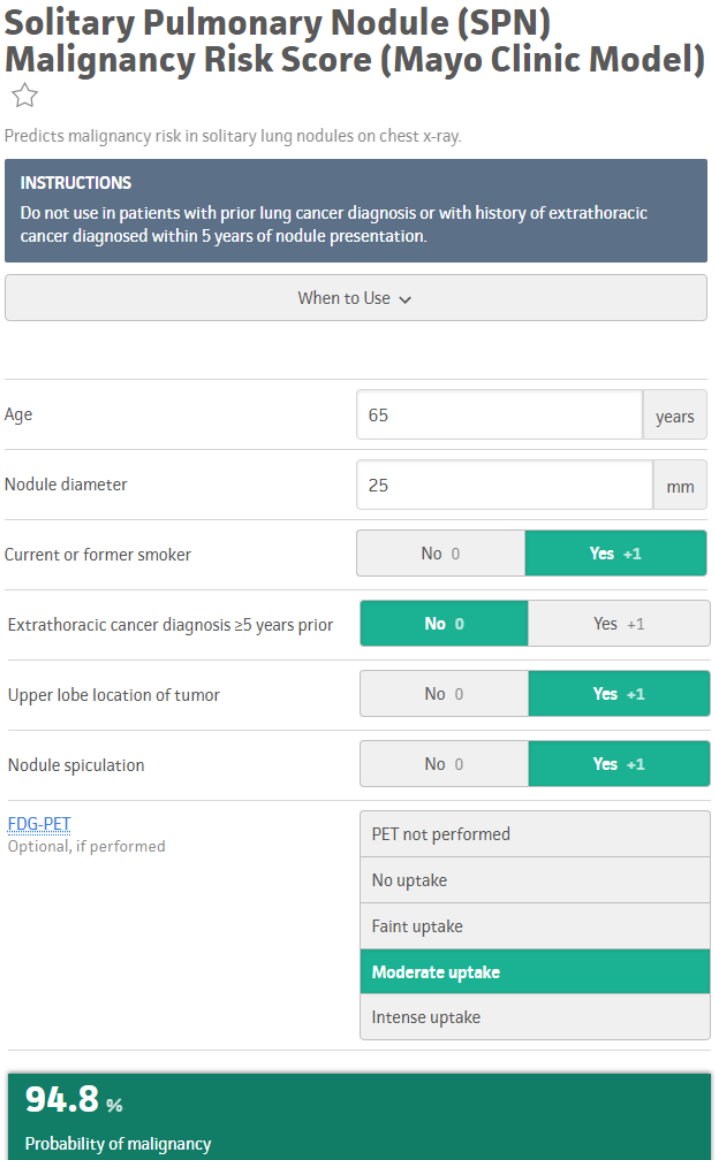
Risk prediction model	Mayo Clinic model[17]	Herder model[18]	VA model[19]	Brock University model[2]	Cleveland Clinic model[20]
Nodule detection	Incidental nodule on chest radiograph	Incidental nodule on chest radiograph and PET scan was performed for further evaluation	Incidental nodule seen on chest 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

Brock model calculator

	A	B	C	D	E	F
1	**Probability calculator estimating a pulmonary nodule being lung cancer.***			Version Tammemagi V1-2SEP13		
2	**Model: Full with spiculation.**					
3	**Instructions: In column B enter the values for the variable listed in column A. Ignore columns C through F.**					
4	**A**	**B**	C	D	E	F
5	**Variables**	**Enter Values**	**Transformation**	**Transfomed value**	**Beta coefficients**	**Calculated value**
6	Age (years)	64	-62	2	0.0286687	0.0573
7	Sex (Male=0, Female=1)	0			0.6010727	0.0000
8	Family history of lung cancer (No=0, Yes=1)	1			0.296109	0.2961
9	Emphysema (No=0, Yes=1)	1			0.2953112	0.2953
10	Nodule size (in millimeters)	25.0		-0.9487	-5.385484	5.1091
11	Nodule type (choose only one from this category)					
12	Groundglass/nonsolid (No=0, Yes=1)	0			-0.1276173	0.0000
13	Semisolid/part-solid (No=0, Yes=1)	0			0.3769578	0.0000
14	Solid [referent group](No=0, Yes=1)	1			0	0.0000
15	Upper lobe location (No=0, Yes=1)	1			0.6581383	0.6581
16	Spiculation (No=0, Yes=1)	1			0.7729335	0.7729
17	Nodule count (number of nodules detected on screen)	3	-4	-1	-0.0824156	0.0824
18	Model constant (do not change)					-6.78917
19					xb =	0.482194
20						
21					**Probability that nodule is lung cancer ** =**	**0.618**
22	* Reference: McWilliams A, Tammemagi M, Mayo J, Roberts H, Liu G, Soghrati K, Yasufuku K, Martel S, Laberge F. et al. Probability of cancer in pulmonary nodules detected on first screening computed tomography. New England Journal of Medicine 2013;369;10.					
23	** This is the probability that a nodule of this type and with these patient demographics & history would be diagnosable as cancer during standard follow-up monitoring for 2 to 4 yrs.					
24	Please send comments or issues with the calculator to martin.tammemagi@brocku.ca					
25						

Mayo clinic model



Fleischner society guidelines (2017)

A: Solid Nodules*

Nodule Type	Size <6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

Nodule Type	Size <6 mm (<100 mm³)	≥6 mm (>100 mm³)	Comments
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C).
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

MacMahon et al. Radiology. 2017

Optimal management: solid nodules

Nodule Dimensions	The Fleischner Society [19]	American College of Chest Physicians [24]	British Thoracic Society [25]	Lung CT Screening Reporting and Data System * [26]
<6 mm	LR, no FU HR, 12 mo FU	LR, ≤4 mm no FU LR, >4–6 mm or HR, ≤4 mm, 12 mo FUHR, >4–6 mm, 6–12 mo FU	<5 mm, no FU5–6 mm, 12–24 mo FU	<6 mm, AS (cat 2)
≥6 mm to 8 mm	LR and HR, 6–12 mo FU, then re-evaluate	LR, 6–12 mo FU HR, 3–6 mo FU	3 mo FU then 12 mo FU	≥6 mm or new nodules 4–6 mm, 6 mo LDCT (cat 3)
≥8 mm	CT or PET/CT at 3 mo	<5% risk, 3 mo FU; 5–65% risk, PET/CT and/or biopsy; >65% risk, treatment	<10% risk, surveillance; >10% risk, PET/CT or consider resection	8–15 mm, 3 mo LDCT (cat 4A) >15 mm (cat 4B)

Guerrini et al. Int J Envrion Res Public Health. 2022

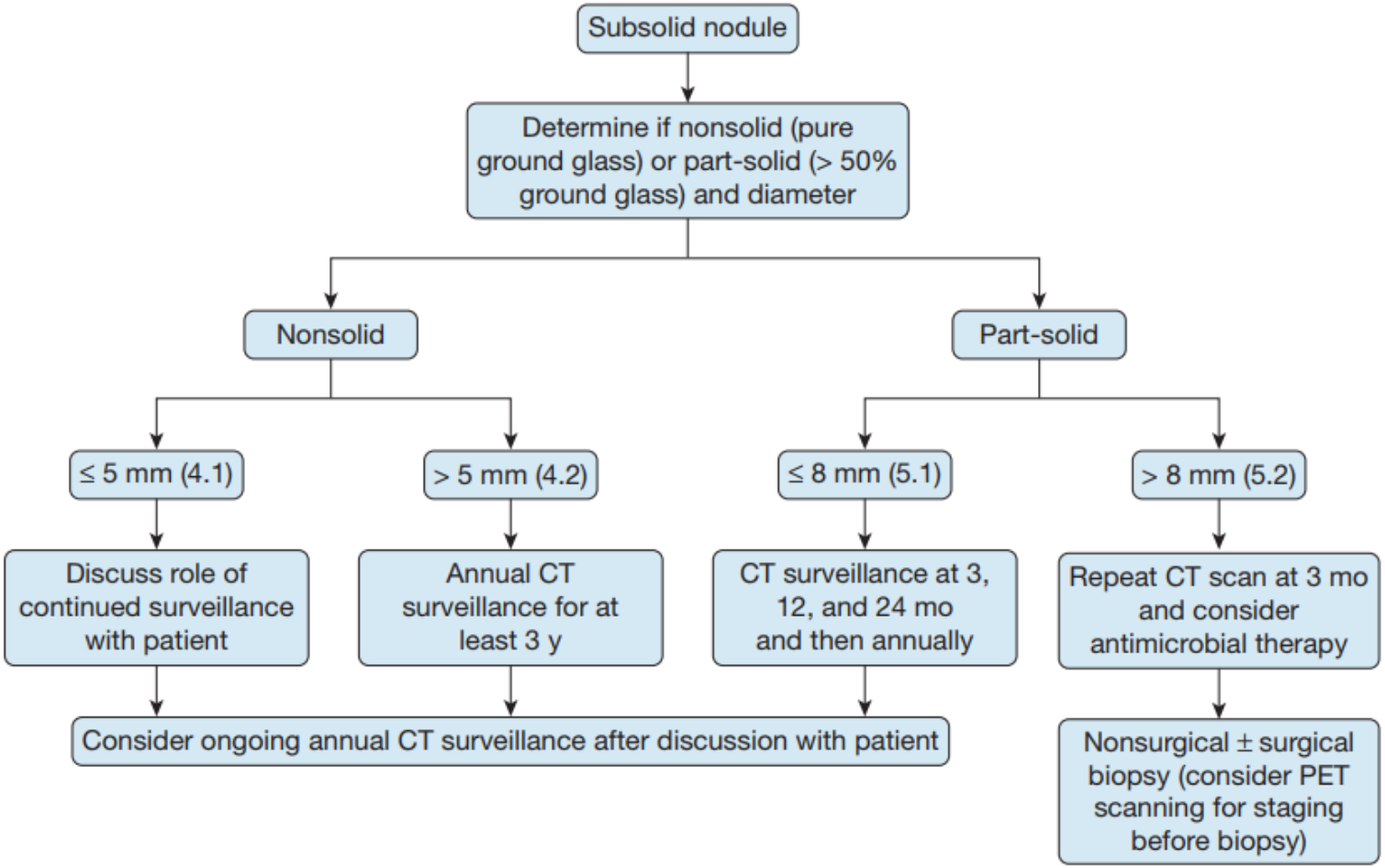
Guidelines for subsolid nodule management

Variable	Incidental SSNs				Screen-Detected SSNs	
	ACCP, 2013[4]	British Thoracic Society, 2015[6]	CHEST Clinical Practice Consensus Guidelines for Asia, 2016[5]	Fleischner Society, 2017[7]	American College of Radiology, Lung-RADS,[a] 2019[8]	National Comprehensive Cancer Network, 2020[9]
Population for which guidelines applicable	• Individuals with SSNs	• Adults aged ≥ 18 y with SSNs	• Individuals with SSNs	• Age ≥ 35 y • No active malignancy • Non-immunocompromised	• Eligibility age 55 y • Upper age limit 77 y per Centers for Medicare & Medicaid Services; 80 y per US Preventive Services Task Force • No active symptoms of lung cancer • ≥ 30 pack year history • Current smoker or quit within 15 y	High-risk individuals: • Age 55-74 y and ≥ 30 pack year history, cessation < 15 y; or • Age ≥ 50 y and ≥ 20 pack years and additional factors that elevate risk ≥ 1.3%
SSNs warranting imaging follow-up	• GGN > 5 mm • PSN of any size; PSN > 15 mm may proceed directly to PET, nonsurgical biopsy, and/or surgical resection	• SSN ≥ 5 mm	• GGN > 5 mm; consider annual surveillance for nodules ≤ 5 mm following discussion with patient • PSN of any size	• SSN (GGN or PSN) ≥ 6 mm; may consider follow-up at 2 and 4 y for a suspicious GGN < 6 mm • Multiplicity of SSNs at baseline	• Annual surveillance implied by screening program enrollment	• Annual surveillance implied

Azour et al. Chest. 2021

Optimal management: subsolid nodules

- **Consensus guideline for Asia**



Bae et al. Chest. 2016

Considerations in Asia

- **Risk caused by high levels of air pollution**
- **High incidence of adenocarcinomas in female nonsmokers**
- **High prevalence of infectious pulmonary nodules**

-> Less reliance on non-Asian based risk calculators

-> Less reliance on PET

-> Greater use of nonsurgical biopsy

Bae et al. Chest. 2016

Baseline and new nodules – solid

- New solid nodules detected at interval screening have a high probability of malignancy even at a small size

	Second screening round (lung cancer/ total nodules)	Third screening round (lung cancer/total nodules)	Second and third screening rounds (lung cancer/ total nodules)	Lung cancer probability (95% CI)
New solid nodules	13/452 (3%)	35/679 (5%)	48/1131 (4%)	4·2% (3·2–5·6)
<25 mm³	1/160 (1%)	1/216 (<1%)	2/376 (1%)	0·5% (0·0–2·0)
25 to <50 mm³	3/104 (3%)	4/154 (3%)	7/258 (3%)	2·7% (1·2–5·6)
50 to <100 mm³	2/72 (3%)	4/113 (4%)	6/185 (3%)	3·2% (1·3–7·1)
100 to <200 mm³	2/46 (4%)	2/85 (2%)	4/131 (3%)	3·1% (0·9–7·8)
200 to <300 mm³	2/19 (11%)	4/31 (13%)	6/50 (12%)	12·0% (5·2–24·2)
300 to <400 mm³	0/14	2/18 (11%)	2/32 (6%)	6·3% (0·7–21·2)
400 to <500 mm³	0/8	3/20 (15%)	3/28 (11%)	10·7% (2·9–28·0)
≥500 mm³	3/29 (10%)	15/42 (36%)	18/71 (25%)	25·4% (16·6–36·6)
Cutoff values				
<27 mm³	1/180 (1%)	1/237 (<1%)	2/417 (<1%)	0·5% (0·0–1·9)
27 to <206 mm³	7/206 (3%)	10/336 (3%)	17/542 (3%)	3·1% (1·9–5·0)
≥206 mm³	5/66 (8%)	24/106 (23%)	29/172 (17%)	16·9% (12·0–23·2)

Data are n/N (%), unless otherwise specified. Exact volume measurement was not available for 89 benign nodules and two cancers, and they were not included in the calculations.

Table 3: **Volume at first detection and lung cancer probability of new solid nodules (N=1131; 1083 benign nodules and 48 lung cancer nodules)**

Walter et al. Lancet Oncol. 2016

Baseline and new nodules – subsolid

Frequency of Nonsolid Nodules and Diagnoses of Lung Cancer Identified in 2392 of 57 496 Participants at Baseline CT Screening according to Size of Largest Nonsolid Nodule

Parameter	Diameter of Largest Nodule					
	<6 mm	6–9 mm	10–14 mm	15–30 mm	≥31mm	Total
Resolved or decreased	341	177	70	39	1	628
Lung cancer	0	0	0	0	0	0
Stable or growth	1063	439	164	92	6	1764
Pathologic diagnosis						
Lung cancer	9	20	27	15	2	73
AAH, ABP*	2	3	0	0	0	5
Nonmalignant diagnosis	1	1	1	1	0	4
Total	1404	616	234	131	7	2392

Frequency of Nonsolid Nodules and Diagnoses of Lung Cancer Identified in 485 of 64 677 Annual Repeat Screenings according to Size of Largest Nonsolid Nodule

Parameter	Diameter of Largest Nodule					
	<6 mm	6–9 mm	10–14 mm	15–30 mm	≥31 mm	Total
Resolved or decreased	125	113	53	28	3	322
Lung cancer	0	0	0	0	0	0
Stable or growth	89	42	29	3	0	163
Pathologic diagnosis						
Lung cancer	2	4	5	0	0	11
AAH, ABP*	0	1	1	0	0	2
Nonmalignant diagnoses	0	1	1	0	0	2
Total	214	155	82	31	3	485

Newly seen nonsolid decrease more frequently (322/485, 66%)

than those seen at baseline screening (628/2392, 26%)

Yankelevitz et al. Radiology. 2015

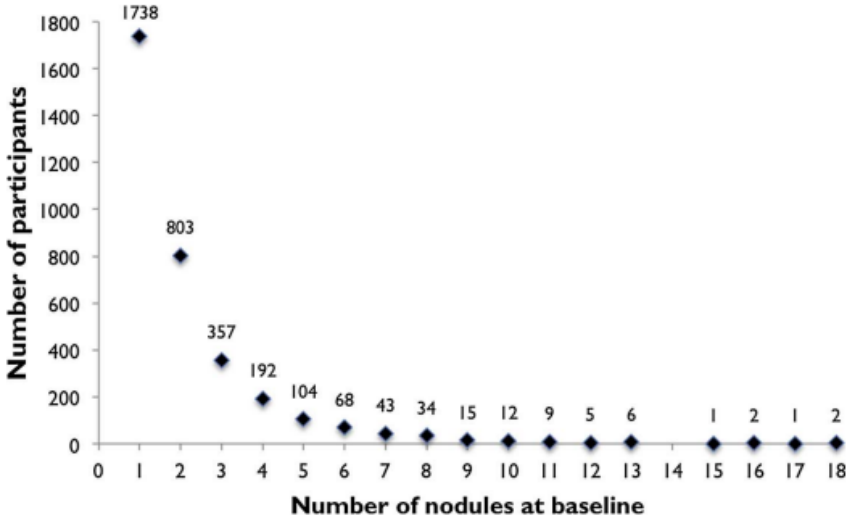
Multiple nodules

Data from the NELSON trial

- Among screenees with a positive nodule, 48.5% had multiple nodules

- Multiplicity did not affect lung cancer probability

- Each nodule should be assessed separately



Nodule Count	Participants	Total Cancer	Lung cancer probability	95% CI	Baseline Cancer	Lung cancer probability Baseline
1 Nodule	1746	62	3.6%	2.8–4.6%	30	1.7%
2 Nodules	800	33	4.1%	2.9–5.8%	17	2.1%
3 Nodules	354	17	4.8%	2.9–7.7%	6	1.7%
4 Nodules	191	12	6.3%	3.4–11.0%	7	4.2%
> 4 Nodules	301	10	3.3%	1.7–6.2%	6	2.0%
Total	*3392*	*134*	*4.1%*	*3.4–4.8%*	*66*	*2.0%*

Heavelmans et al. Lung Cancer. 2017

Multiple subsolid lung cancers

In cases of malignancy

- **Most multifocal nodules are synchronous primary adenocarcinomas**
- **Each nodule should be evaluated individually**

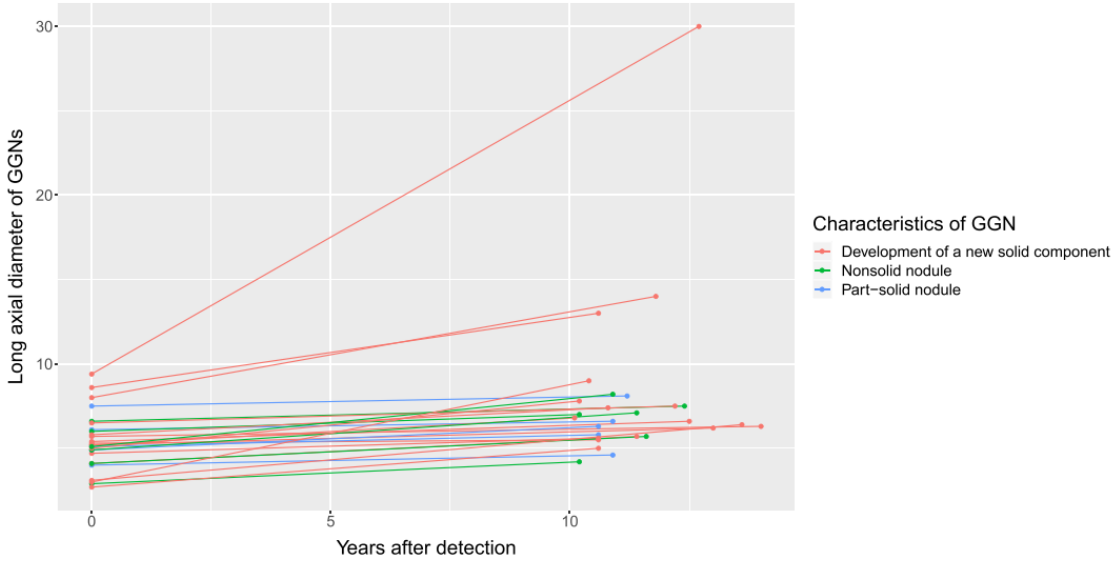
TABLE 3. Summary of *EGFR* and *K-ras* Gene Combinations in the Multiple GGOs

No. of Lesion	*n*	Case No.
Identical combination (*n*= 6)		
EGFR and K-*ras* wild type	6	5, 8, 9, 14, 19, 22
Different combination (*n*= 18)		
EGFR exon19 del and wild type	9	1, 2, 6, 10Ð12, 15, 20, 24
EGFR exon19 del/K-*ras*PM (G12V) and wild type	1	13
EGFR exon19 del and exon 21PM(L858R)	4	4, 7, 21, 23
EGFR exon19 del/exon18 PM (F712L) and wild type	1	3
EGFR exon 21 PM (L858R) and wild type	1	18
EGFR exon 21 PM (L858R) and exon 18/21 PM (G724S/L861Q)	1	17
K-ras mutation and wild type	1	16

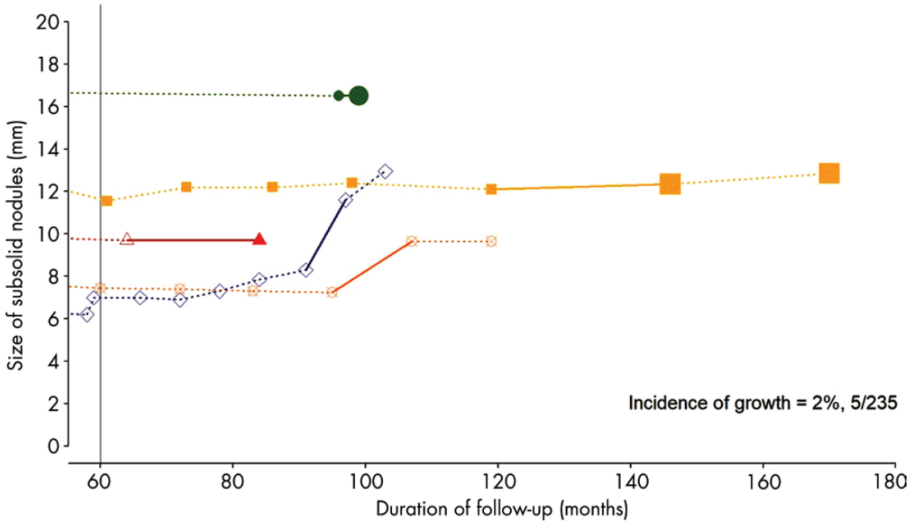
Chung et al. J Thorac Oncol. 2009

Follow up duration for subsolid nodules

- **Growth detected in 13% of subsolid nodules stable for the initial 5 years**

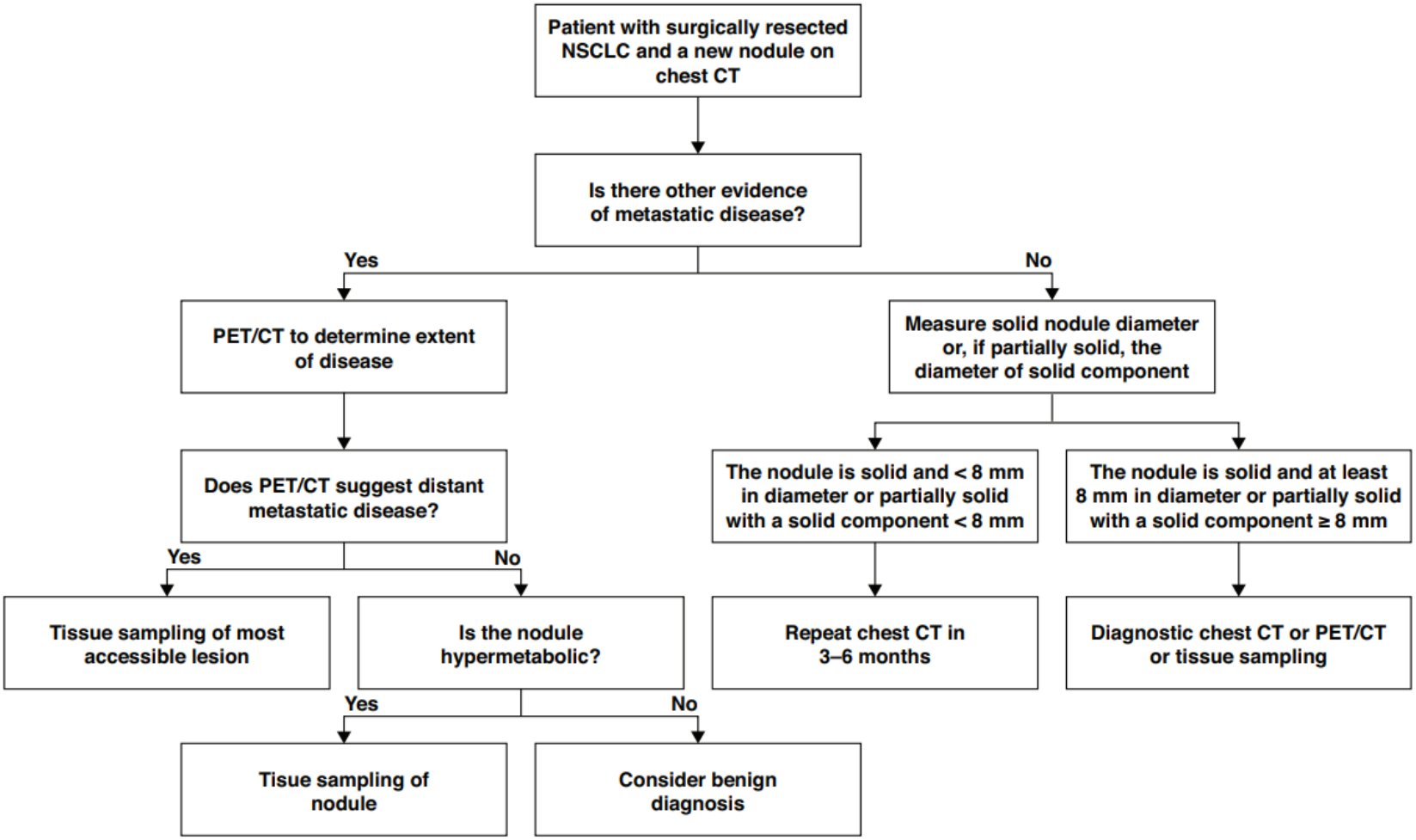


- **2% of subsolid pulmonary nodules ≥6mm grew after 5 years of stability**



Lee et al. J Thorac Oncol. 2019
Lee et al. Radiology. 2020

Nodules detected on oncologic follow up



Araujo-Filho et al. AJR. 2021

Diagnostic tissue sampling

- **Nonsurgical biopsy**

- Transthoracic needle biopsy
- Conventional bronchoscopy and EBUS -> **Not optimal for peripheral nodules**
- Advanced image-guided bronchoscopy

- **Surgical biopsy**

- Sublobar resection with VATS or RATS preferred

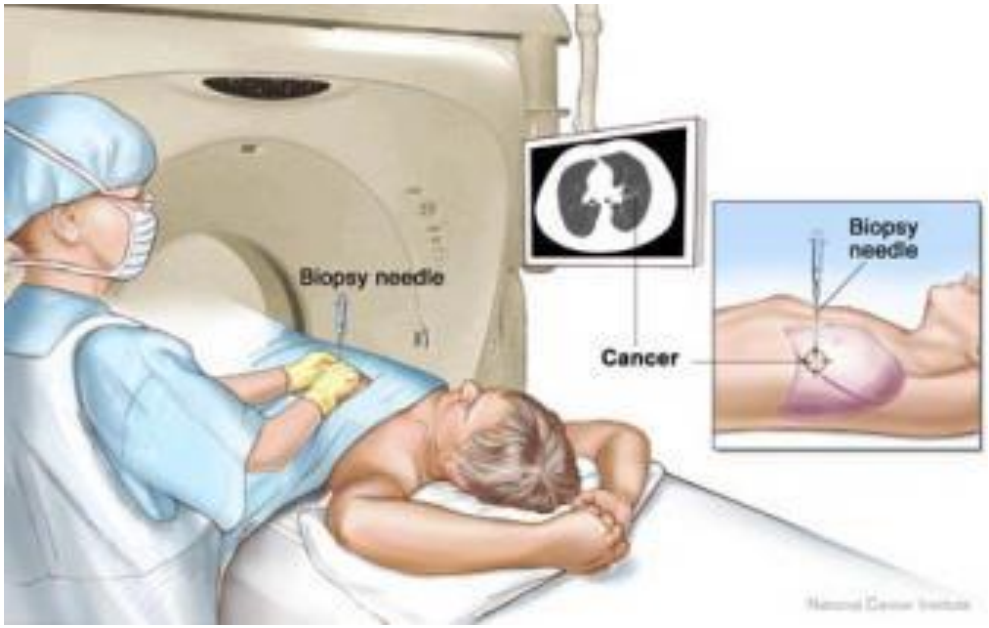
Sensitivity of flexible bronchoscopy for peripheral lung lesions

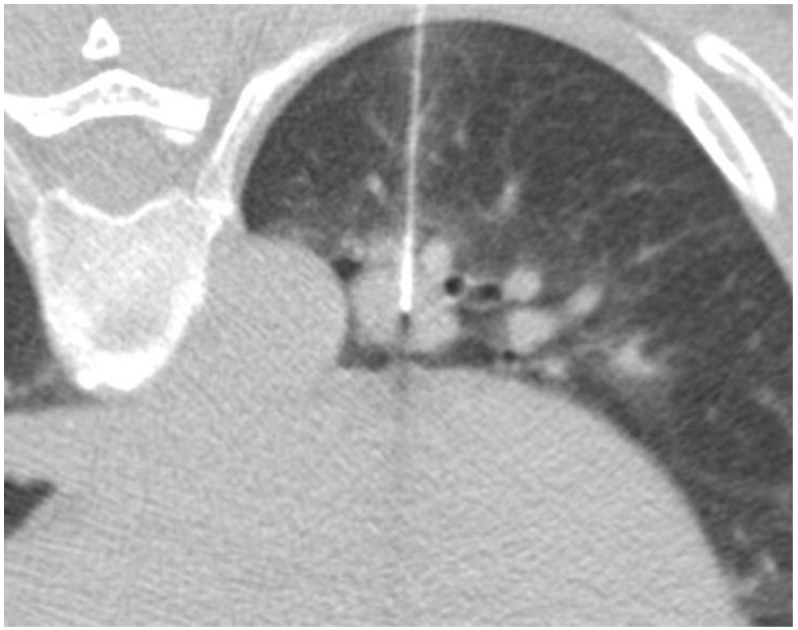
All Methods:		< 2 cm LESION				> 2 cm LESION			
First Author	**Year**	**N**	**Pos**	**Neg**	**Sens**	**N**	**Pos**	**Neg**	**Sens**
Gasparini[110]	1995	195	82	113	**42**	300	169	131	**56**
Hattori[76]	1971	17	13	4	**76**	182	150	32	**82**
Baaklini[88]	2000	16	4	12	**25**	135	93	42	**69**
Wallace[122]	1982	65	3	62	**5**	78	24	54	**31**
Bandoh[130]	2003	25	8	17	**32**	72	50	22	**69**
Radke[106]	1979	21	6	15	**29**	76	49	27	**64**
Naidich[121]	1988	15	4	11	**27**	46	26	20	**57**
Trkanjec[129]	2003	17	9	8	**53**	33	27	6	**82**
McDougall[105]	1981	9	1	8	**11**	36	21	15	**58**
Stringfield[107]	1977	3	1	2	**33**	26	13	13	**50**
Summary		383	131	252	**34**	984	622	362	**63**

Rivera et al. Chest. 2013

Transthoracic needle biopsy

- **Conducted under local anesthesia**
- **High diagnostic yield > 90%**
- **Notable rate of complications (pneumothorax rate =~ 20%)**
- **Lower diagnostic yield for smaller nodules**



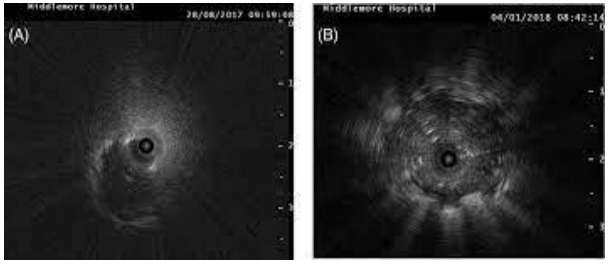


National Cancer Institute
Lee et al. Radiology. 2019

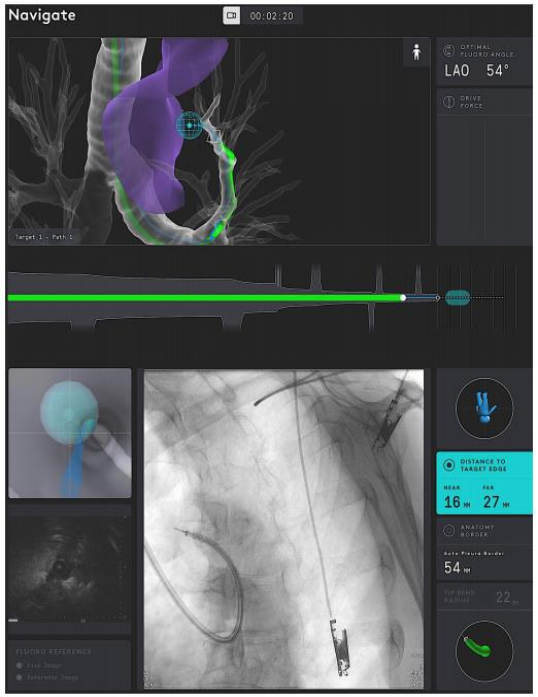
Advanced guided bronchoscopy

- **Moderate sedation or general anesthesia**
- **Diagnostic yield of 70-80%**
- **Lower risk of complications (pneumothorax rate <5%)**
- **Lower diagnostic yield for smaller nodules without bronchus sign**

Electromagnetic Navigation Bronchoscopy



Radial EBUS

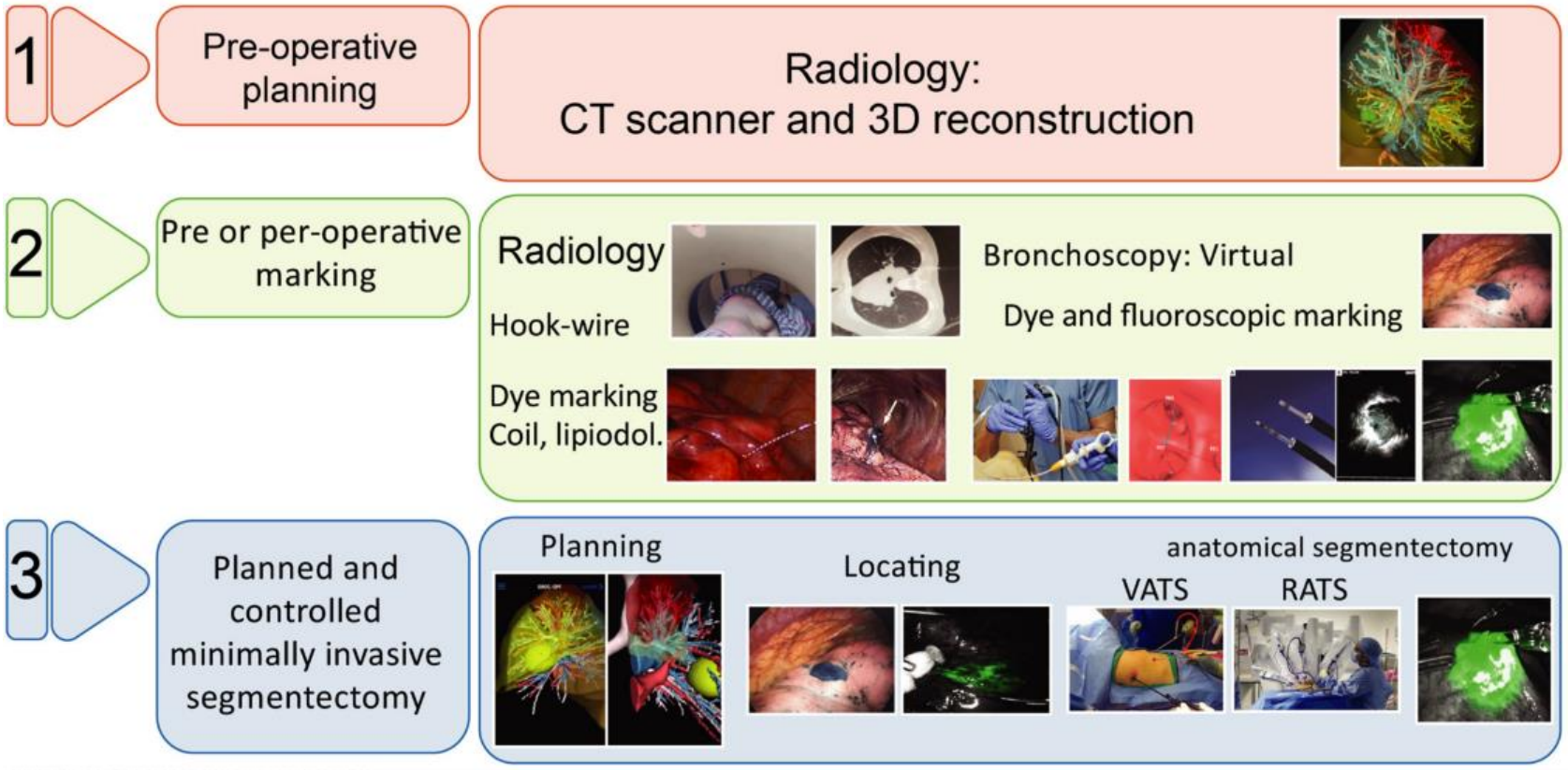


Robot-assisted (shape sensing)

Kemp. Respiration. 2020
Simoff et al. BMC Pulm Med 2021

Surgical biopsy

- **Provided definitive diagnosis and management**
- **Risks of physical complications and deterioration of lung function**
- **Possibility of unnecessary surgery for benign nodules**



Montagne et al. Cancers (Basel). 2021

Take home

- **Lung nodules** are increasingly detected and the burden is projected to rise with more use of **CT imaging** and implementation of **lung cancer screening**

- **Different types of nodules** can be detected in **different situations**, requiring **individualized management** and use of various guidelines

- **Invasive diagnosis** of a nodule should be guided by the **probability of malignancy**, expected **yield and safety** of testing, and **patient preference**

Thank you for your attention

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