Evidence based approach to incidentally detected subsolid pulmonary nodule

DM SEMINAR

July 27, 2018

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Outline

- Definitions
- Etiologies
- Risk evaluation
  - Clinical features
  - Radiology
- Approach
- Modifications: new guidelines
- Management

Incidentally detected parenchymal lesion

NODULE

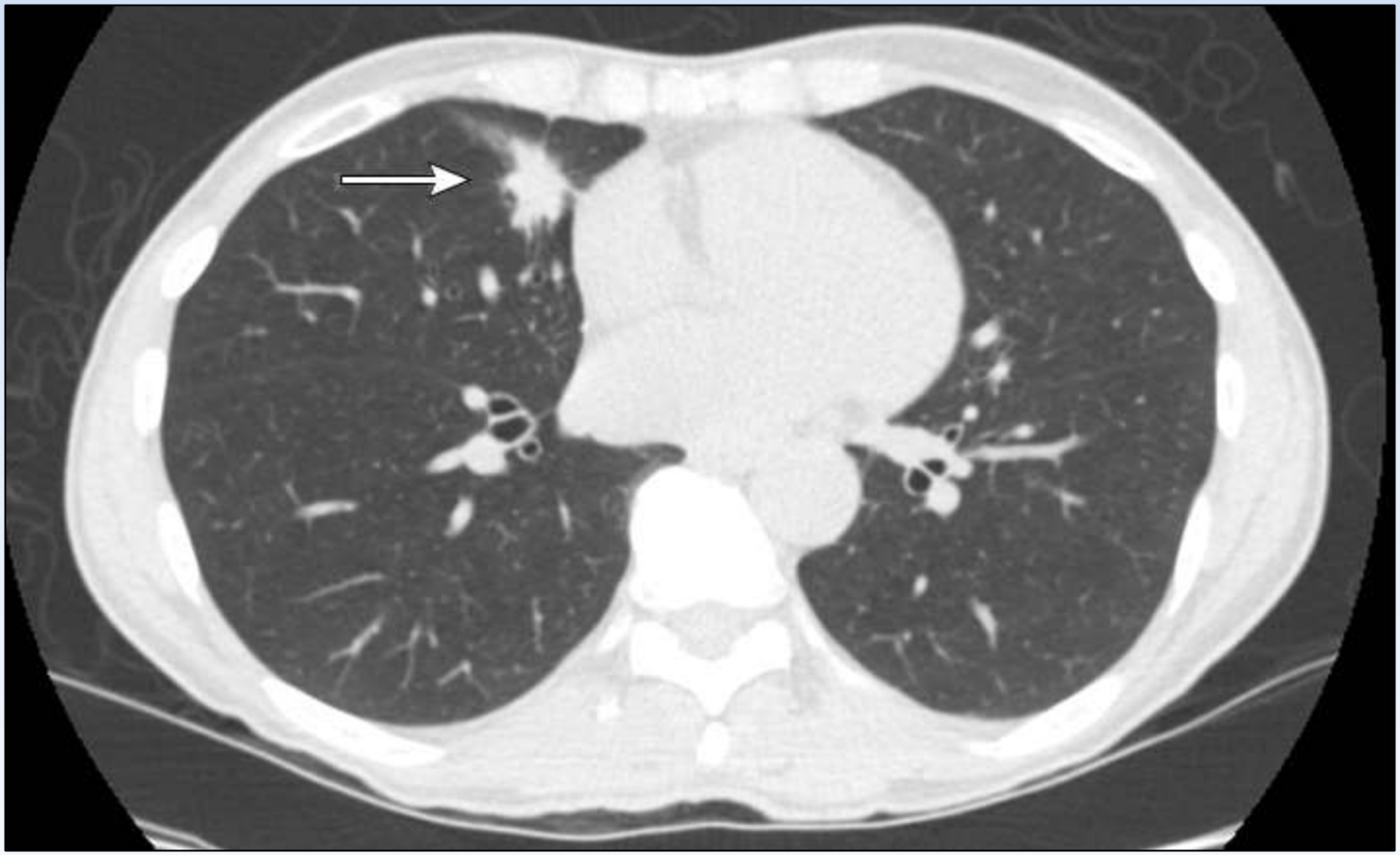
- **<30mm** in size
- Well defined
- Round, single
- Completely surrounded by normal lung parenchyma

MASS

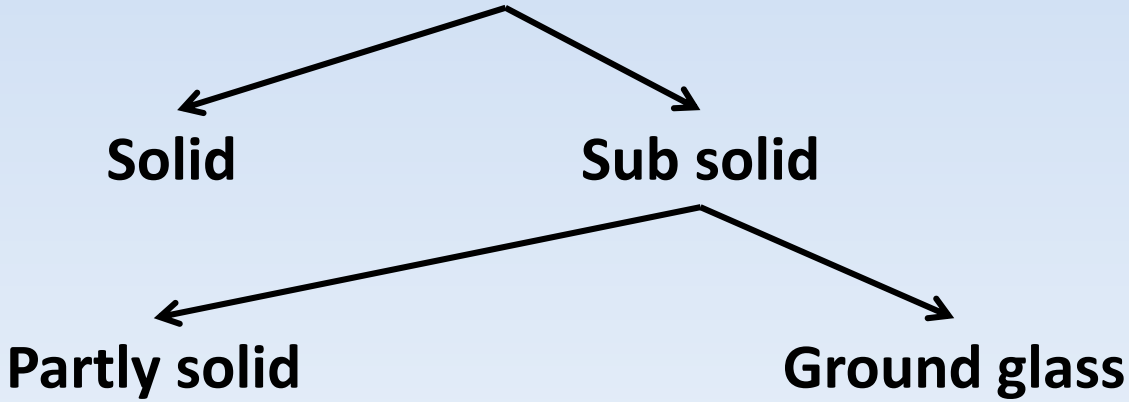
- **>30mm** in size

Solitary Pulmonary Nodule

Tan BB, et al. The solitary pulmonary nodule. Chest. 2003;123(1):89S-96S.



Pulmonary nodule-Definition,types



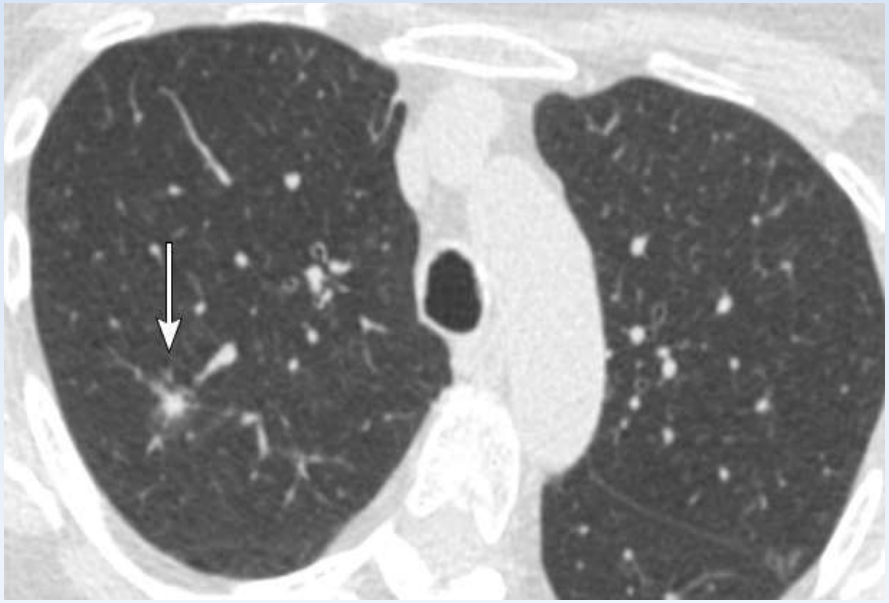
Solid nodule: completely obscures the entire lung parenchyma within it

Partly solid nodule: patches of parenchyma that are completely obscured

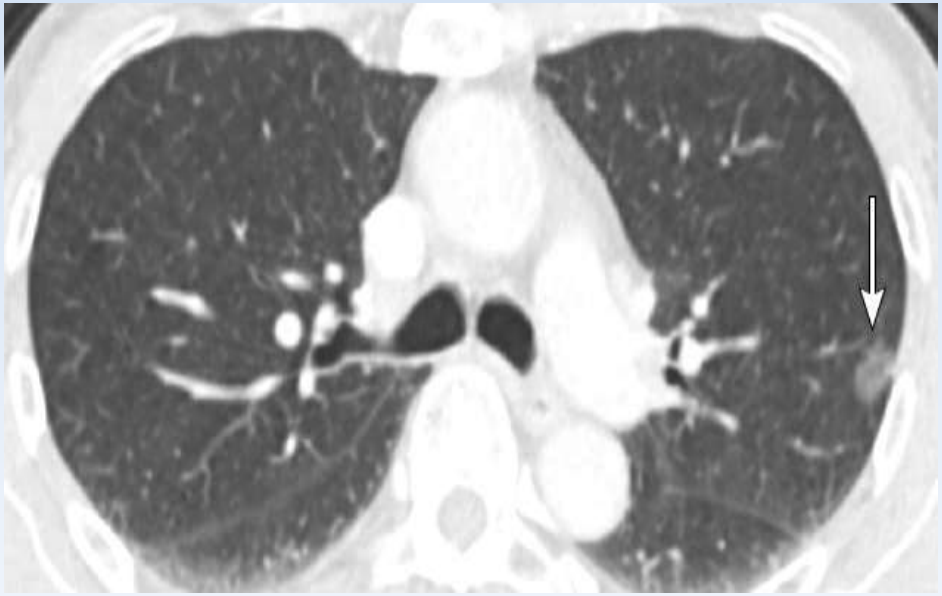
Ground glass nodule: NO patch of parenchyma that are completely obscured

Henschke CI et al. CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. AJR American journal of roentgenology. 2002;178(5):1053-7

PSN



GGN



Henschke CI et al. CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. AJR American journal of roentgenology. 2002;178(5):1053-7

Malignant
Bronchogenic carcinoma
Adenocarcinoma
Squamous cell carcinoma
Large cell carcinoma
Small cell carcinoma
Metastatic lesions
Breast
Head and neck
Melanoma
Colon
Kidney
Sarcoma
Germ cell tumor
Others
Pulmonary carcinoid
Extranodal lymphoma
Miscellaneous
Plasmacytoma
Schwannoma

Benign
Infectious granuloma
Histoplasmosis
Coccidioidomycosis
Tuberculosis
Atypical mycobacteria
Cryptococcosis
Blastomycosis
Other infections
Bacterial abscess
Dirofilaria immitis
Echinococcus cyst
Ascariasis
Pneumocystis jirovecii
Aspergillus
Benign neoplasms
Hamartoma
Lipoma
Fibroma
Neurofibroma
Leiomyoma
Angioma
Vascular
Arteriovenous malformation
Pulmonary varix
Hematoma
Pulmonary infarct
Developmental
Bronchogenic cyst
Inflammatory
Granulomatosis with polyangiitis (Wegener's)
Rheumatoid nodule
Sarcoidosis
Other

ORIGINAL ARTICLE

Probability of Cancer in Pulmonary Nodules Detected on First Screening CT

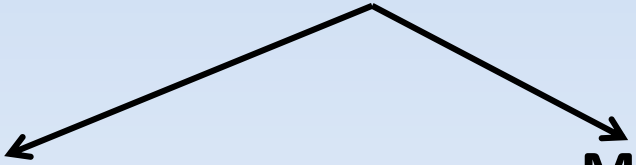
Annette McWilliams, M.B., Martin C. Tammemagi, Ph.D., John R. Mayo, M.D., Heidi Roberts, M.D., Geoffrey Liu, M.D., Kam Soghrati, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Simon Martel, M.D., Francis Laberge, M.D., Michel Gingras, M.D., Sukhinder Atkar-Khattra, B.Sc., Christine D. Berg, M.D., Ken Evans, M.D., Richard Finley, M.D., John Yee, M.D., John English, M.D., Paola Nasute, M.D., John Goffin, M.D., Serge Puksa, M.D., Lori Stewart, M.D., Scott Tsai, M.D., Michael R. Johnston, M.D., Daria Manos, M.D., Garth Nicholas, M.D., Glenwood D. Goss, M.D., Jean M. Seely, M.D., Kayvan Amjadi, M.D., Alain Tremblay, M.D.C.M., Paul Burrowes, M.D., Paul MacEachern, M.D., Rick Bhatia, M.D., Ming-Sound Tsao, M.D., and Stephen Lam, M.D.et al.

September 5, 2013
N Engl J Med 2013; 369:910-919
DOI: 10.1056/NEJMoa1214726

- Prospective study to follow up incidentally detected nodules
- Low dose CT used
- 2 cohorts (Pan Can & BCCA)
- Total of 2961 patients, 12029 nodules were followed up
- 144 (1%) were malignant

McWilliams A et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Common Etiologies



Benign

- Infectious granuloma (80%)
  - Tuberculosis
- Benign tumours
  - Hamartomas (10%)
- Vascular
  - Pulmonary AVMs
- Others
  - GPA, sarcoidosis, rh.arthritis

Malignant

- Primary lung cancer
  - Adenocarcinomas (50%)
  - Squamous cell CA (25%)
- Metastatic Carcinoma
  - Melanoma, sarcoma
  - Colon, breast, kidney
- Carcinoid

Subsolid nodule

Most common etiologies include

- Minimally invasive adenocarcinoma
- Adenocarcinoma insitu
- Atypical adenomatous hyperplasia

Kim HY, et al. Persistent pulmonary nodular ground-glass opacity at thin-section CT: histopathologic comparisons. Radiology. 2007;245(1):267-75

APPROACH AND EVALUATION

- Clinical features
- Radiology
- Risk assesment

Clinical risk factors

Age

- Probability of lung cancer rises as age increases
- Rare below 35yrs

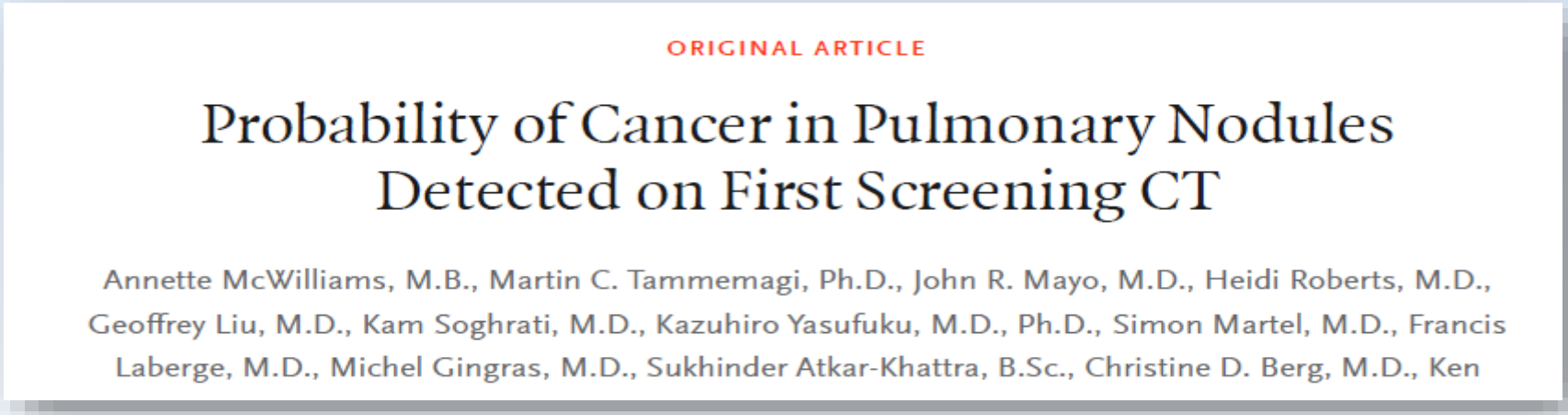
Table 2—*Relations of Age to Bronchogenic Carcinoma Appearing as Solitary Pulmonary Nodules*

Age Groups, yr.	Total Patients in Age Group	Bronchogenic Carcinomas	Carcinomas in Age Group, %
20-29	24	0	0
30-34	20	0	0
35-39	32	1	3.1
40-44	20	3	15.0
45-49	13	2	15.4
50-59	21	9	42.9
60-69	6	3	50
70-79	1	1	100
	137	19	

Trunk G, et al. The management and evaluation of the solitary pulmonary nodule. Chest. 1974;66(3):236-9

Female gender

- risk factor in the PanCan trial,
- Odds ratio of 1.8



ORIGINAL ARTICLE

Probability of Cancer in Pulmonary Nodules Detected on First Screening CT

Annette McWilliams, M.B., Martin C. Tammemagi, Ph.D., John R. Mayo, M.D., Heidi Roberts, M.D., Geoffrey Liu, M.D., Kam Soghrati, M.D., Kazuhiro Yasufuku, M.D., Ph.D., Simon Martel, M.D., Francis Laberge, M.D., Michel Gingras, M.D., Sukhinder Atkar-Khattra, B.Sc., Christine D. Berg, M.D., Ken

McWilliams A et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Family history

- risk factor for both smokers and those who never smoked
- overall relative risk of 1.5
- affected sibling: 1.8

Trunk G, et al. The management and evaluation of the solitary pulmonary nodule. Chest. 1974;66(3):236-9

Smoking and adeno CA

- Subsolid nodule (adeno CA) association with smoking is weak, not clearly established

- incidence of adenocarcinoma in non-smokers is increasing, with **young female non-smokers** being affected significantly more often than male non-smokers

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017.Radiology. 2017;284(1):228-43

Smoking and adeno CA

- Recent recommendations (2017) do not differentiate smokers and nonsmokers

- No sufficient evidence to use a different management guidelines for smokers till date

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017.Radiology. 2017;284(1):228-43

Risk factors in Radiology

Computed tomography

- Preferred for evaluation of a nodule for likelihood of malignancy

- Low dose radiation technique(1mSv)
- Thin collimation(1mm)
- Non contrast scans

CT follow up

- 10% patients develop new nodule that requires independent assessment

Swensen SJ, et al. CT screening for lung cancer: five-year prospective experience. Radiology. 2005;235(1):259-65

Nodule size

- size is an **independent predictor** for malignancy
- Dominant factor in management guidelines

• <5 mm	<1 percent
• 5 to 9 mm	2 to 6 percent
• 8 to 20 mm	18 percent
• >20 mm	>50 percent

McWilliams A et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Attenuation

- Solid nodule: more common
- Subsolid nodule: higher likelihood of malignancy

Henschke CI et al. CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. AJR American journal of roentgenology. 2002;178(5):1053-7

CT Screening for Lung Cancer: Frequency and Significance of Part-Solid and Nonsolid Nodules

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David F. Yankelevitz[1]
Rosna Mirtcheva[1]
Georgeann McGuinness[2]
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Olli S. Miettinen[3]
for the ELCAP Group

OBJECTIVE. In the Early Lung Cancer Action Project (ELCAP), we found not only solid but also part-solid and nonsolid nodules in patients at both baseline and repeat CT screening for lung cancer. We report the frequency and significance of part-solid and nonsolid nodules in comparison with solid nodules.

MATERIALS AND METHODS. We reviewed all instances of a positive finding in patients at baseline (from one to six noncalcified nodules) and annual repeat screenings (from one to six newly detected noncalcified nodules with interim growth) to classify each of the nodules as solid, part-solid, or nonsolid. We defined a solid nodule as a nodule that completely obscures the entire lung parenchyma within it. Part-solid nodules are those having sections that are solid in this sense, and nonsolid nodules are those with no solid parts. Chi-square statistics were used to test for differences in the malignancy rates.

RESULTS. Among the 233 instances of positive results at baseline screening, 44 (19%) involved a part-solid or nonsolid largest nodule (16 part-solid and 28 nonsolid). Among these 44 cases of positive findings, malignancy was diagnosed in 15 (34%) as opposed to a 7% malignancy rate for solid nodules ($p = 0.000001$). The malignancy rate for part-solid nodules was 63% (10/16), and the rate for nonsolid nodules was 18% (5/28). Even after standardizing for nodule size, the malignancy rate was significantly higher for part-solid nodules than for either solid ones ($p = 0.004$) or nonsolid ones ($p = 0.03$). The malignancy type in the part-solid or nonsolid nodules was predominantly bronchioloalveolar carcinoma or adenocarcinoma with bronchioloalveolar features, contrasting with other subtypes of adenocarcinoma found in the solid nodules ($p = 0.0001$). At annual repeat screenings, only 30 instances of positive test results have been obtained; seven of these involved part-solid or nonsolid nodules.

CONCLUSION. In CT screening for lung cancer, the detected nodule commonly is either only part-solid or nonsolid, but such a nodule is more likely to be malignant than a solid one, even when nodule size is taken into account.

Location

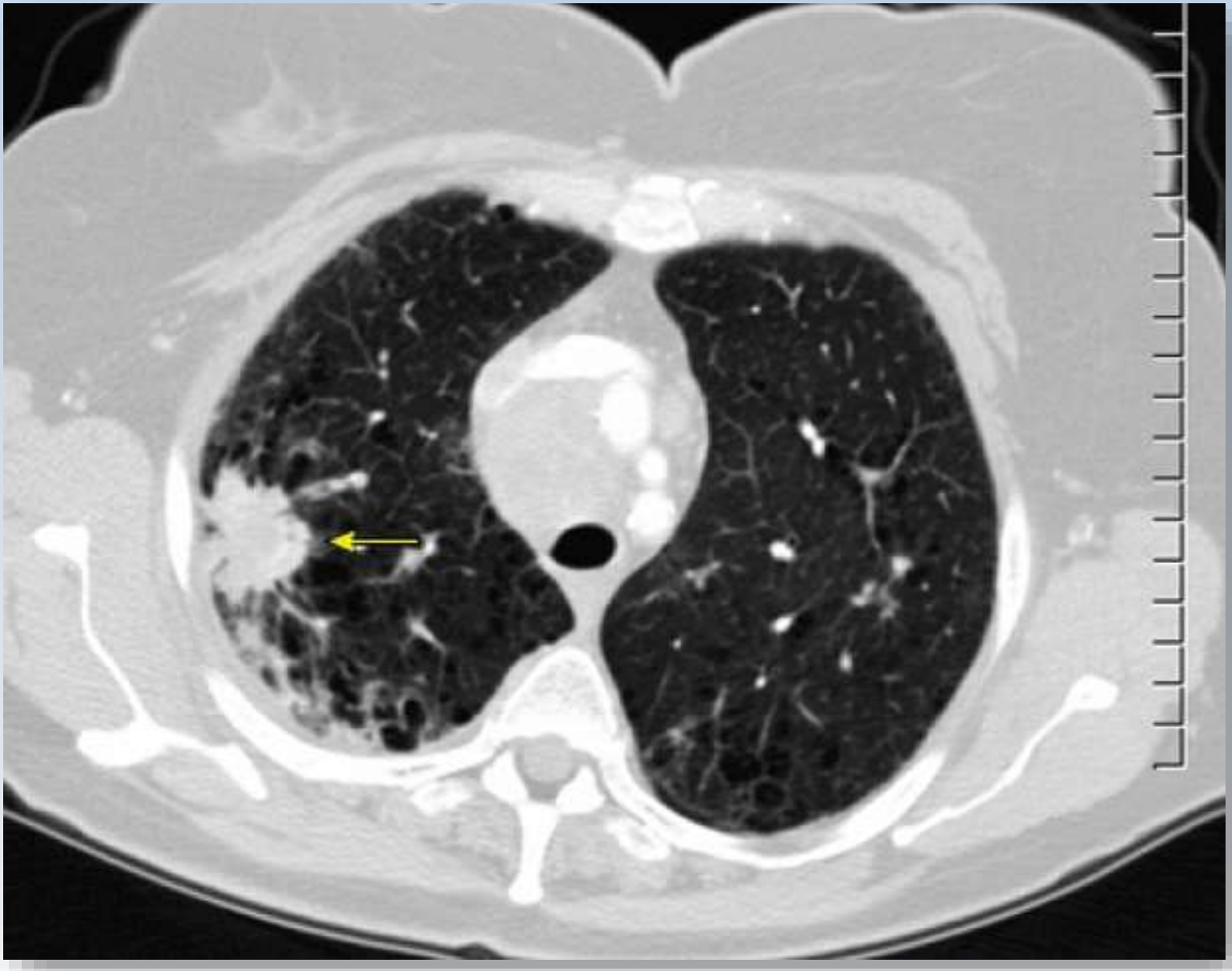
- **Upper lobe** nodules
- Risk factor for malignancy
- odds ratio of 2

Lindell RM,et al. Five-year lung cancer screening experience: CT appearance, growth rate, location, and histologic features of 61 lung cancers. Radiology. 2007;242(2):555-62
McWilliams A, et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Border

- Well defined smooth border : benign

- Malignant
  - **Spiculated:** growth of tumor cells along interstitium
  - **Lobulated:** differential growth rates within nodules



Spiculated border

- risk factor for malignancy
- odds ratio in the range of 2.2–2.5

McWilliams A et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Malignant versus Benign Nodules at CT Screening for Lung Cancer: Comparison of Thin-Section CT Findings[1]

PURPOSE: To evaluate thin-section computed tomographic (CT) characteristics of malignant nodules on the basis of overall appearance (pure ground-glass opacity [GGO], mixed GGO, or solid opacity) in comparison with the appearance of benign nodules.

MATERIALS AND METHODS: Institutional review board approval and patient consent were obtained. Follow-up diagnostic CT was performed in 747 suspicious pulmonary nodules detected at low-dose CT screening (17 892 examinations). Of 747 nodules, 222 were evaluated at thin-section CT (1-mm collimation), which included 59 cancers and 163 benign nodules (3–20 mm). Thin-section CT findings of malignant versus benign nodules with pure GGO (17 vs 12 lesions), mixed GGO (27 vs 29 lesions), or solid opacity (15 vs 122 lesions) were analyzed. Fisher exact test for independence was used to compare differences in shape, margin, and internal features between benign and malignant nodules. Positive predictive value (PPV) was analyzed when a category was significantly different from the others.

RESULTS: Among nodules with pure GGO, a round shape was found more frequently in malignant lesions (11 of 17, 65%) than in benign lesions (two of 12, 17%; $P = .02$; PPV, 85%); mixed GGO, a subtype with GGO in the periphery and a high-attenuation zone in the center, was seen much more often in malignant lesions (11 of 27, 41%) than in benign lesions (two of 29, 7%; $P = .004$; PPV, 85%). Among solid nodules, a polygonal shape or a smooth or somewhat smooth margin was present less frequently in malignant than in benign lesions (polygonal shape: 7% vs 38%, $P = .02$; smooth or somewhat smooth margin: 0% vs 63%, $P < .001$), and 98% (46 of 47) of polygonal nodules and 100% (77 of 77) of nodules with a smooth or somewhat smooth margin were benign.

CONCLUSION: Recognition of certain characteristics at thin-section CT can be helpful in differentiating small malignant nodules from benign nodules.

Number

- multiple nodules decreased the risk of malignancy

McWilliams A et al. Probability of cancer in pulmonary nodules detected on first screening CT. New England Journal of Medicine. 2013;369(10):910-9

Number

- increased risk of malignancy as the total nodule count increased from 1 to 4 but decreased risk in patients with 5 or more nodules

Peters R, et al. Prevalence of pulmonary multi-nodularity in CT lung cancer screening and lung cancer probability [abstr]. In: Radiological Society of North America Scientific Assembly and Annual Meeting Program. Oak Brook, Ill: Radiological Society of North America, 2015; 111.

Growth

- Defined as
  - Increase in size
  - Increase in attenuation
  - Increase in solid component
- Indication for biopsy/ resection during follow-up

In solid lesions, increase in size more than 2 mm

Bankier AA, et al. Recommendations for measuring pulmonary nodules at CT: a statement from the Fleischner Society. Radiology. 2017;285(2):584-600

Stable subsolid nodule

- Same size for 5 years
- Considered to be benign

2 years for solid nodule

- Longer volume doubling time than solid lesions
- Usually 3-5 years
- Longer follow-up is necessary

Hasegawa M, et al. Growth rate of small lung cancers detected on mass CT screening. The British journal of radiology. 2000;73(876):1252-9

The British Journal of Radiology, 73 (2000), 1252–1259

Growth rate of small lung cancers detected on mass CT screening

M HASEGAWA, MD, S SONE, MD, S TAKASHIMA, MD, F LI, MD, Z-G YANG, MD, Y MARUYAMA, MD and T WATANABE, MD

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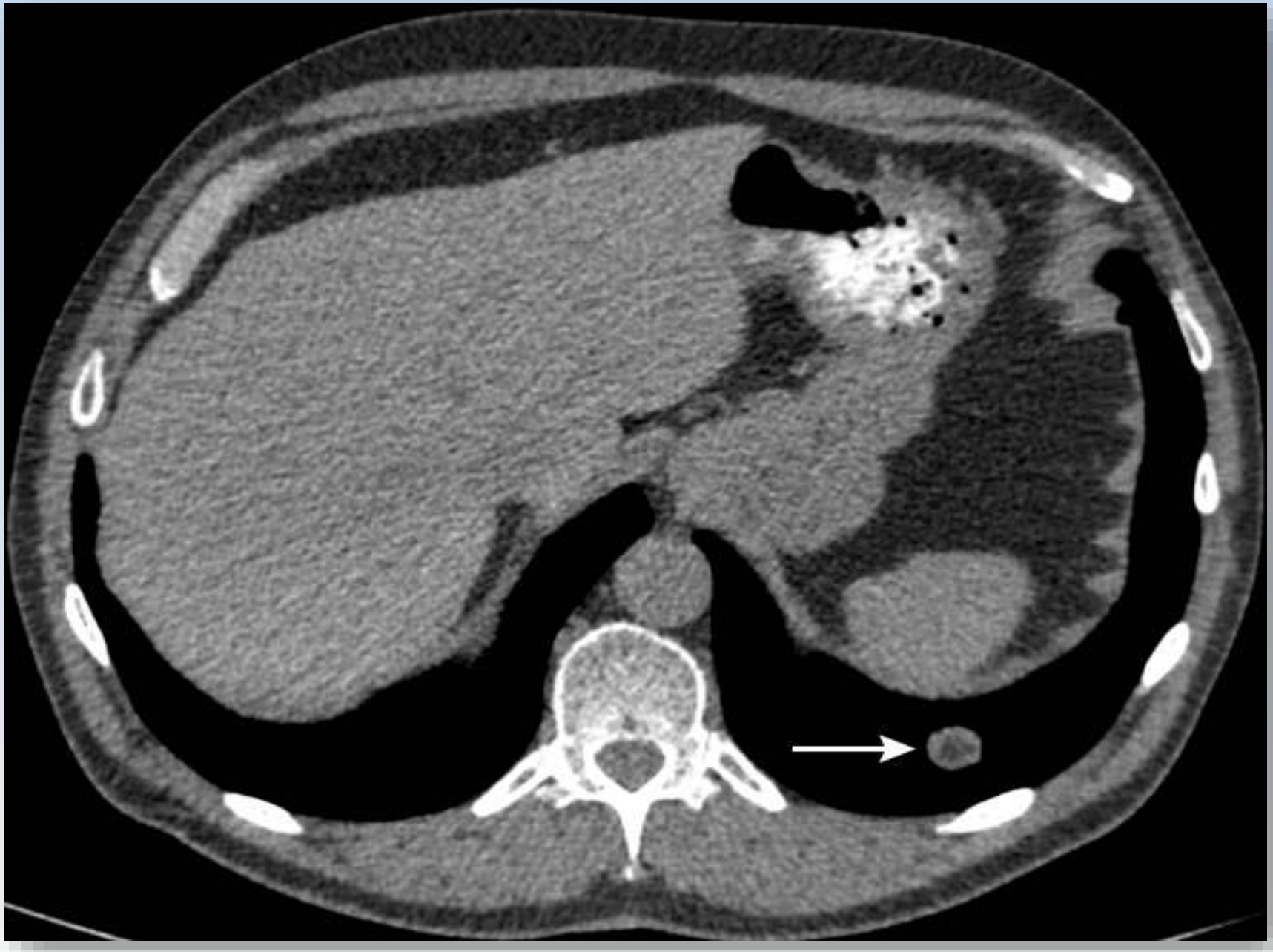
Abstract. CT has recently been used in mass screening for lung cancer. Small cancers have been identified but the growth characteristics of these lesions are not fully understood. We identified 82 primary cancers in our 3-year mass CT screening programme, of which 61 were examined in the present study. The volume doubling time (VDT) was calculated based on the exponential model using successive annual CT images or follow-up CT images. All cases were also examined in the hospital by high resolution CT (HRCT). Lesions were divided into three types based on HRCT characteristics: type G (n=19), ground glass opacity (GGO); type GS (n=19), focal GGO with a solid central component; and type S (n=23), solid nodule. 18 (95%) lesions of type G, 18 (95%) of type GS and 7 (30%) of type S were invisible on conventional chest radiographs. The mean size of the tumour was 10 mm, 11 mm and 16 mm for type G, type GS and type S, respectively. Most tumours (80%) were adenocarcinomas; 78% of these were GGO (type G and GS). Mean VDT values were 813 days, 457 days and 149 days for type G, type GS and type S, respectively; these are significantly different from each other (p<0.05). Our results show that annual mass screening CT for 3 successive years resulted in the identification of a large number of slowly growing adenocarcinomas that were not visible on chest radiographs.

Calcification / fat

- Presence of calcification or fat in the nodule suggests a benign etiology
- Sampling avoided

- Exceptions
  - Carcinoid
  - Mets from chondro/osteosarcomas



Emphysema

- presence of emphysema on a CT is an independent risk factor for lung cancer

- NLST trial shows
  - incidence of 25 cancer per 1000 screened patients with emphysema, compared with 7.5 in those without emphysema

de Torres JP, et al. Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest. Chest. 2007;132(6):1932-8

Fibrosis

- Pulmonary fibrosis (particularly IPF) is also an independent risk factor
- hazard ratio of 4.2 compared with emphysema alone

Kwak N, et al. Lung cancer risk among patients with combined pulmonary fibrosis and emphysema. Respiratory medicine. 2014;108(3):524-30

Role of CXR?

- insensitive for detection of small nodules most nodules less than 1 cm will not be seen
- Minimal increase in size of nodules not picked up

- Even though the radiation used in CT is higher than CXR, CT is the imaging modality of choice in evaluation and follow-up of pulmonary nodule
- CXR not to be used as it is insensitive

Bankier AA, et al. Recommendations for measuring pulmonary nodules at CT: a statement from the Fleischner Society. Radiology. 2017;285(2):584-600

Chest tomosynthesis

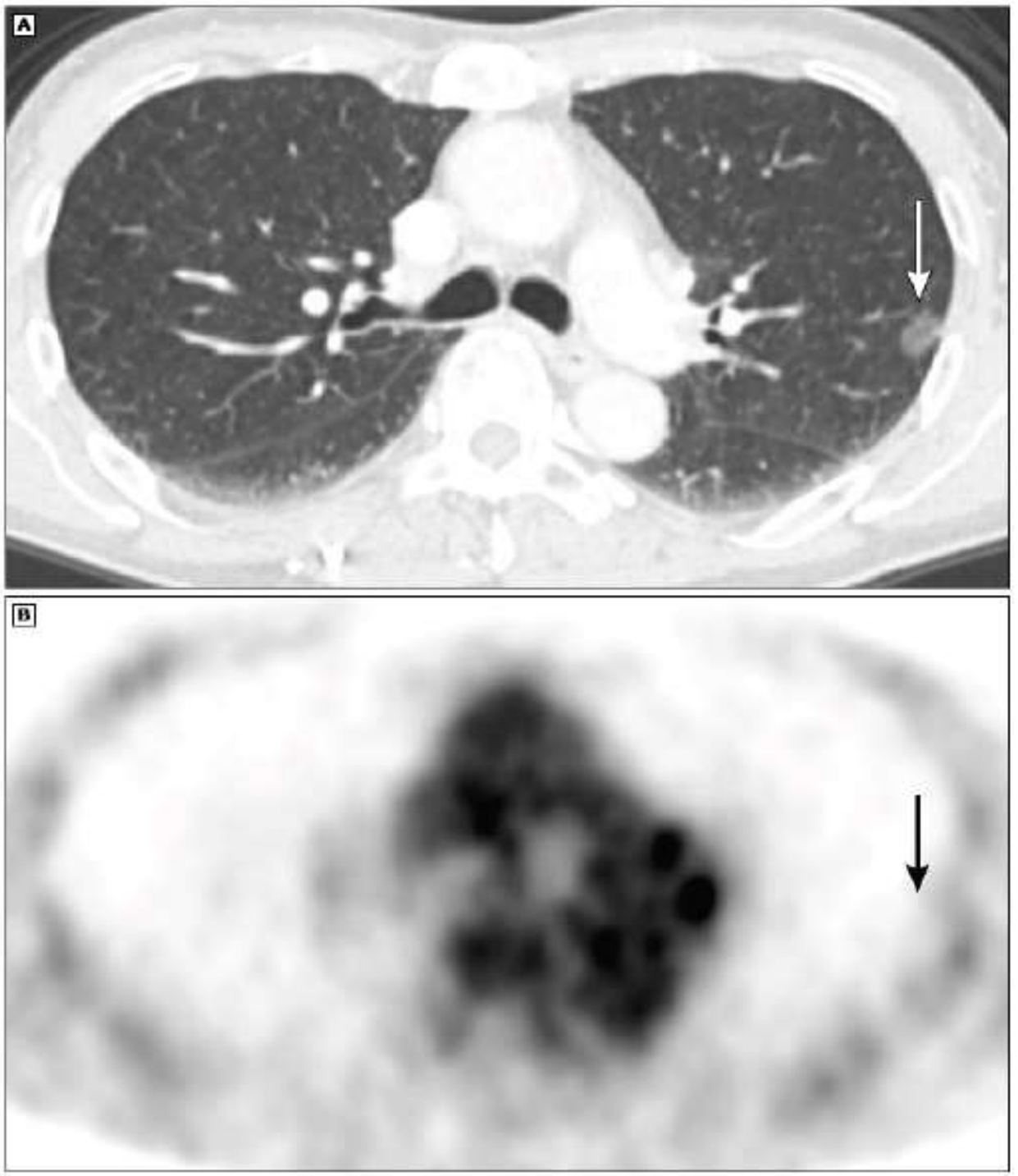
- Lower radiation dose (10-fold lower- 0.15mSv)
- not widely available
- more sensitive than CXR but less sensitive than CT
- half of nodules measuring ≥6 mm on CT are detected
- Not recommended as primary modality of imaging in pulmonary nodule

Meltzer C, et al. Detection and characterization of solid pulmonary nodules at digital chest tomosynthesis: data from a cohort of the pilot Swedish Cardiopulmonary Bioimage Study. Radiology. 2018;287(3):1018-27

FDG PET/CT

- Poor characterization of subsolid nodules
- Sensitivity: 10%
- Specificity: 20% for detecting malignancy in a ground-glass nodule

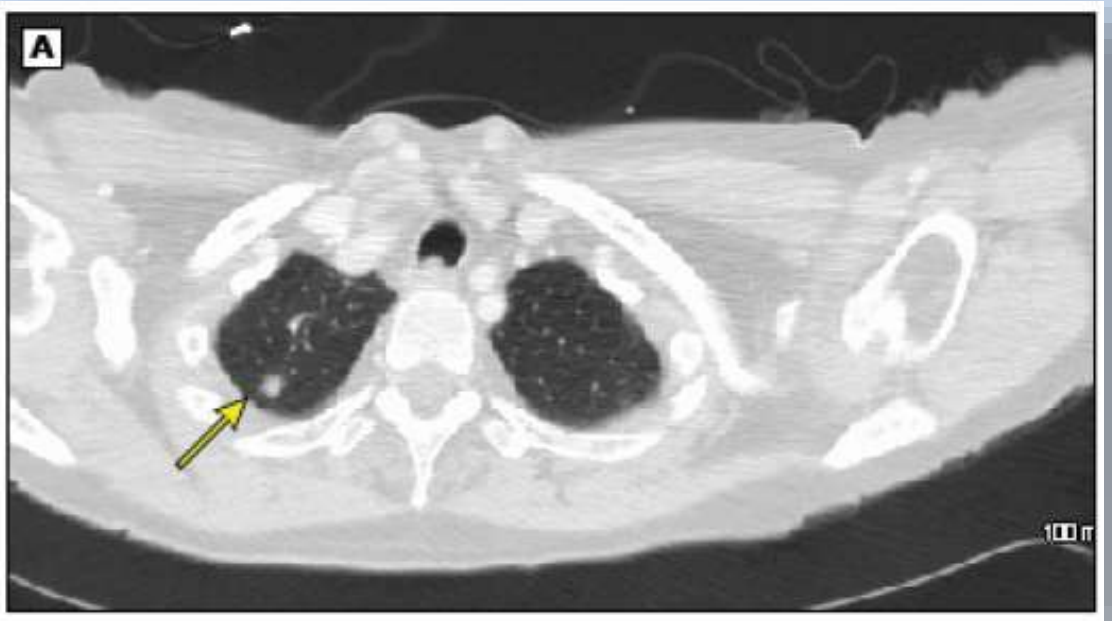
Nomori H, et al. Evaluation of F-18 fluorodeoxyglucose (FDG) PET scanning for pulmonary nodules less than 3 cm in diameter, with special reference to the CT images. Lung cancer. 2004;45(1):19-27


A
B

PET in solid nodule?

- Recommended for evaluation in solid nodules
- Helps in differentiating malignant nodules which are >8mm in size (SUVmax 2.5)
- Sensitivity 89%, specificity 75%
- Solid nodules measuring >8 mm that are not FDG-avid are likely to be benign
- used to evaluate for metastases and to select the safest target for biopsy

Deppen SA, et al. Accuracy of FDG-PET to diagnose lung cancer in areas with infectious lung disease: a meta-analysis. Jama. 2014;312(12):1227-36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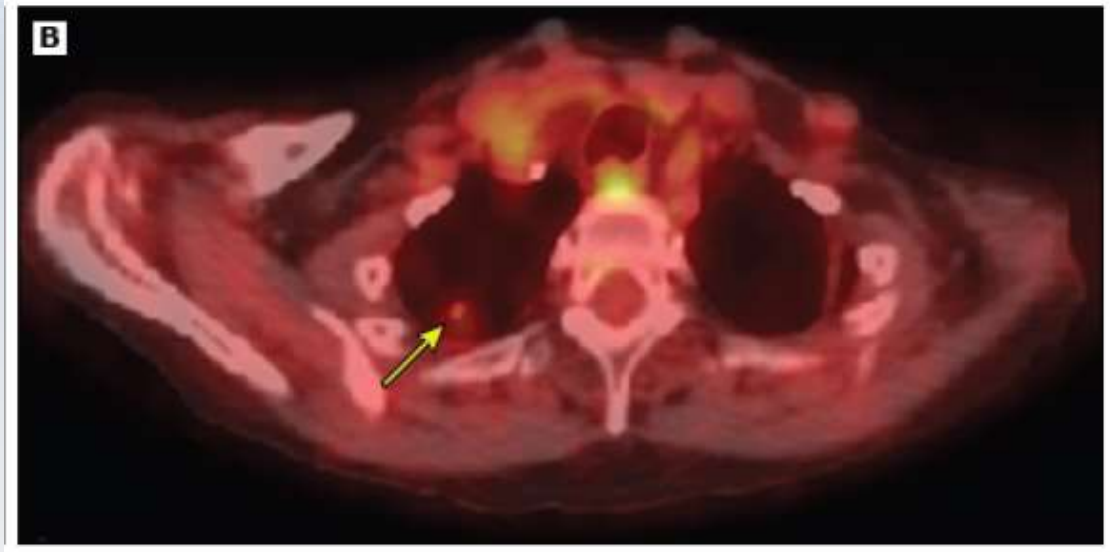
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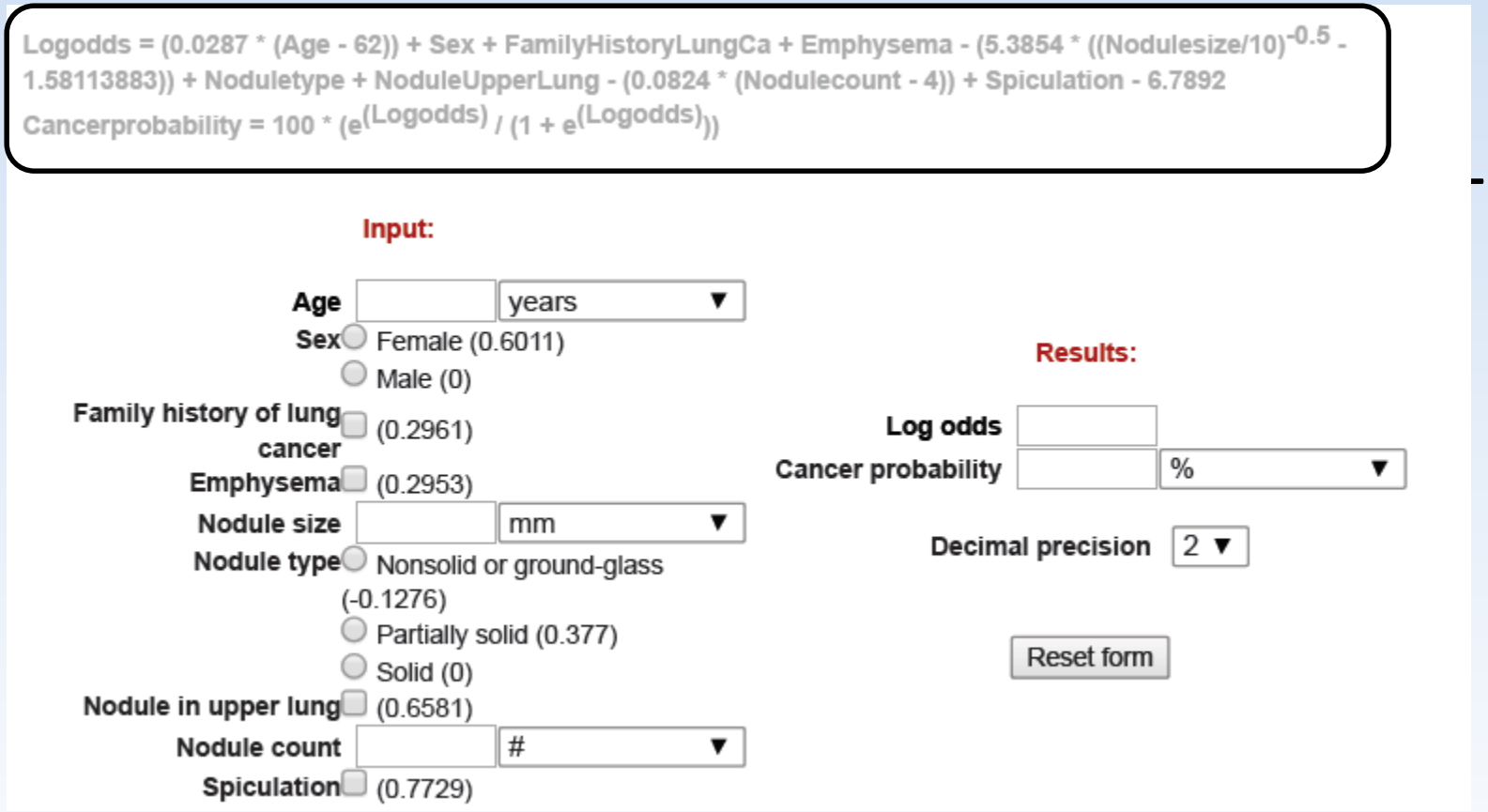
Risk evaluation

- Clinical and radiological features
- Predictive models and calculators

Brock University cancer prediction equation

- $Logodds = (0.0287 * (Age - 62)) + Sex + FamilyHistoryLungCa + Emphysema - (5.3854 * ((Nodulesize/10)^{-0.5} - 1.58113883)) + Noduletype + NoduleUpperLung - (0.0824 * (Nodulecount - 4)) + Spiculation - 6.7892$

  $Cancerprobability = 100 * (e^{(Logodds)} / (1 + e^{(Logodds)}))$



McWilliams A, et al. Probability of cancer in pulmonary nodules detected on first screening CT. N Engl J Med. 2013 Sep 5;369(10):910

Probability

- Low <5 percent
- Intermediate 5 to 65 percent
- High >65 percent

McWilliams A, et al. Probability of cancer in pulmonary nodules detected on first screening CT. N Engl J Med. 2013 Sep 5;369(10):910

Why to evaluate risk?

- Lesion>3cm : high risk➔ resection
- Lesion<6mm: low risk➔ followed up with CT

- Role in deciding the management of those lesions which fall in between(indeterminate nodule)

- Assessing the pretest probability of the lesion being malignant

Why to evaluate risk?

- Achieve a balance between
  - Life saving benefits of detecting resectable lung cancer
  - Avoiding morbidity associated with procedure/intervention

Its role in subsolid nodules

- Used in individualizing the approach to a particular patient (clinical judgement)
- Not used in the flow chart recommended by the guidelines
- Used to categorize the solid nodule >8mm into low, intermediate and high risk and followed up, FDGPET/CT, biopsy are done respectively

Whereas in a solid nodule

Guidelines recommend its use in flow chart

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

Used only for

- **Incidentally** detected nodules
- Age >35yrs
- No symptoms/signs attributable to lesion
- Baseline risk of lung CA equivalent to general population

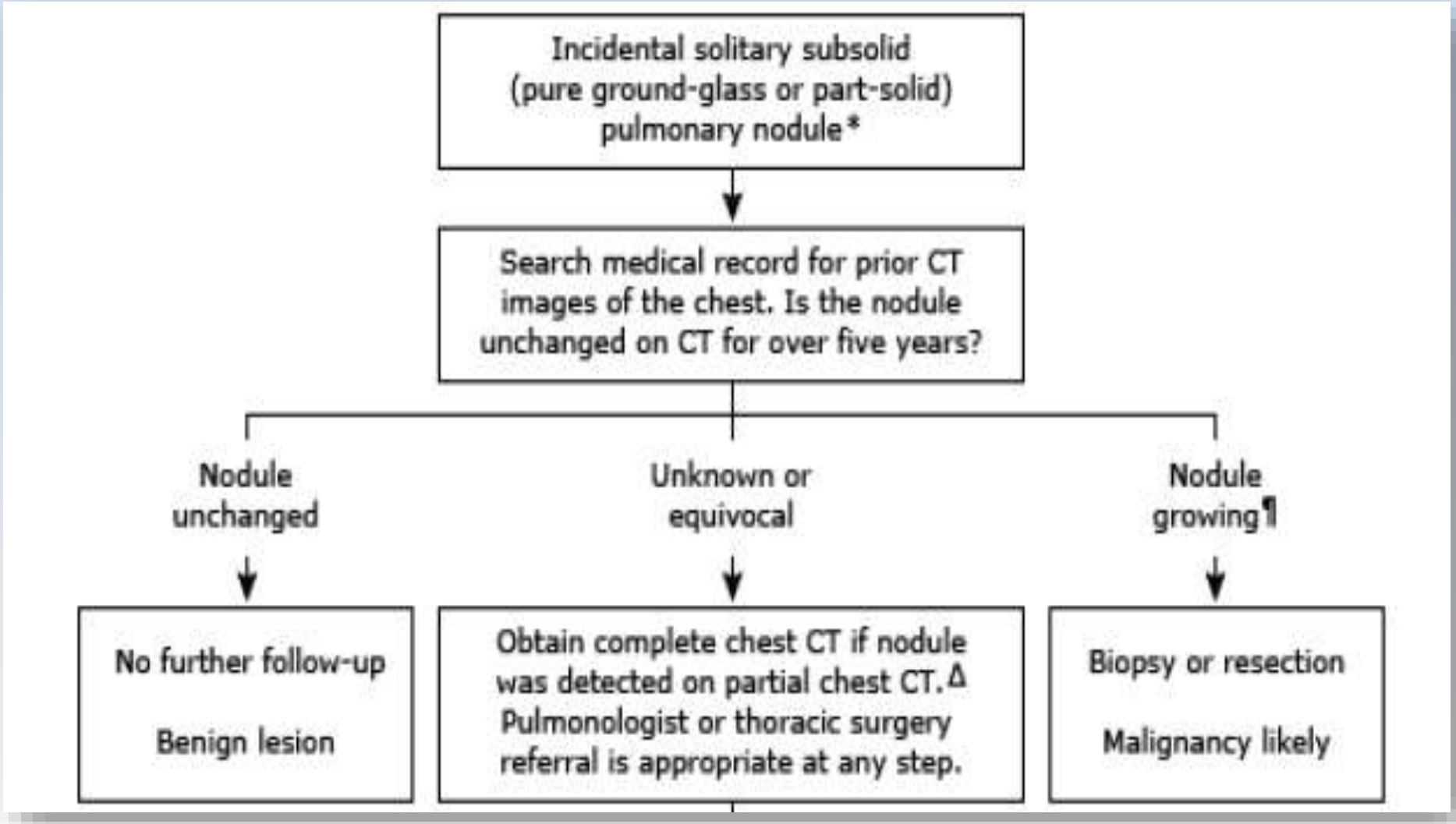
MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

Exclusion

- Immunocompromised pts
- k/c/o malignancy
- Symptomatic due to lesion
- In whom screening for lung cancer is done

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

Preliminary requirement



Principles of follow-up

- Stable nodule on follow up does not need any intervention
- Resolution of nodule doesnot need followup CT
- Any growth in the size of nodule on follow up CT warrants histological diagnosis

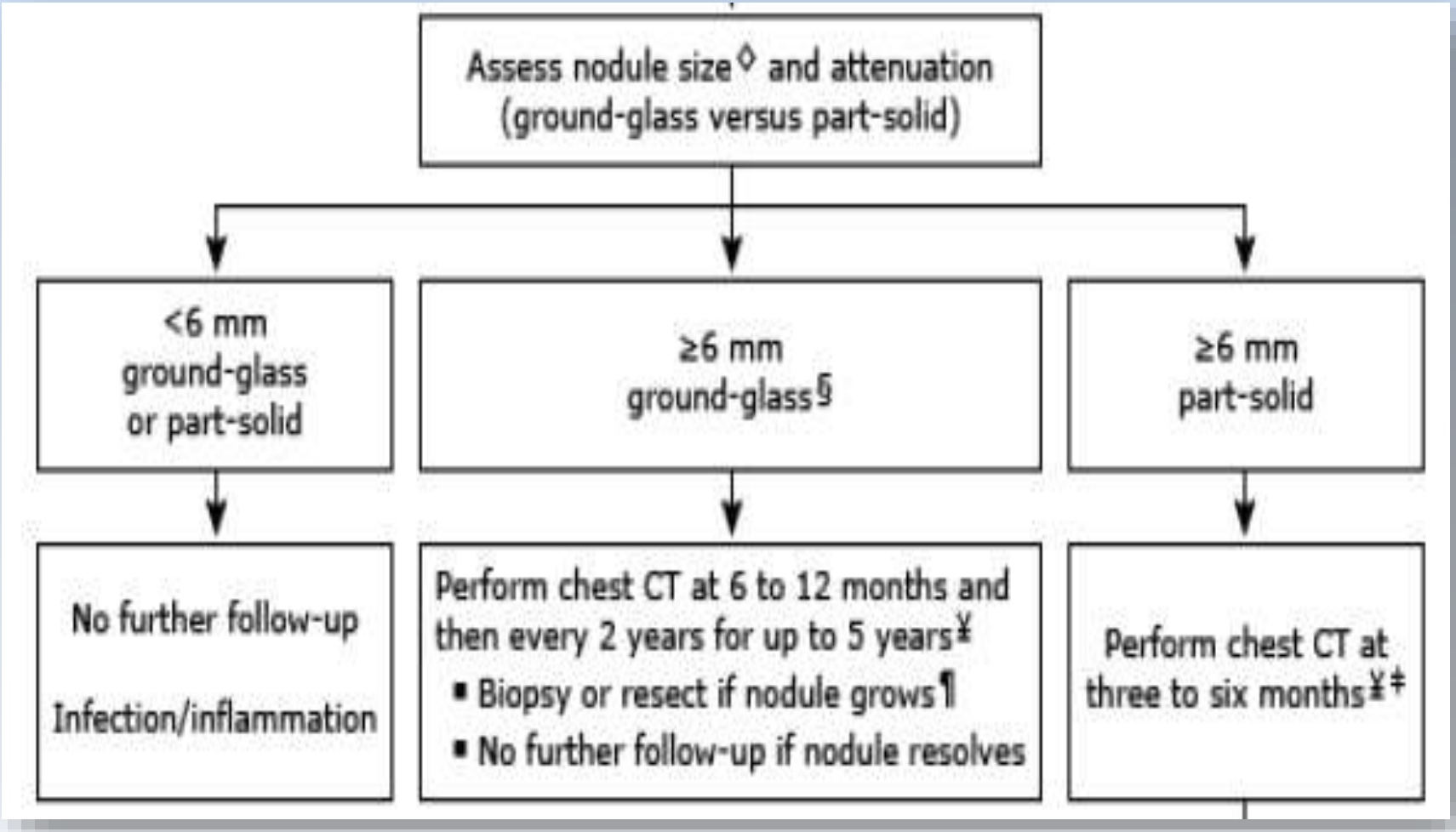
- For pure ground-glass nodules smaller than 6 mm in diameter, **no routine follow-up** is recommended (grade 1B; strong recommendation, moderate-quality evidence)**.**

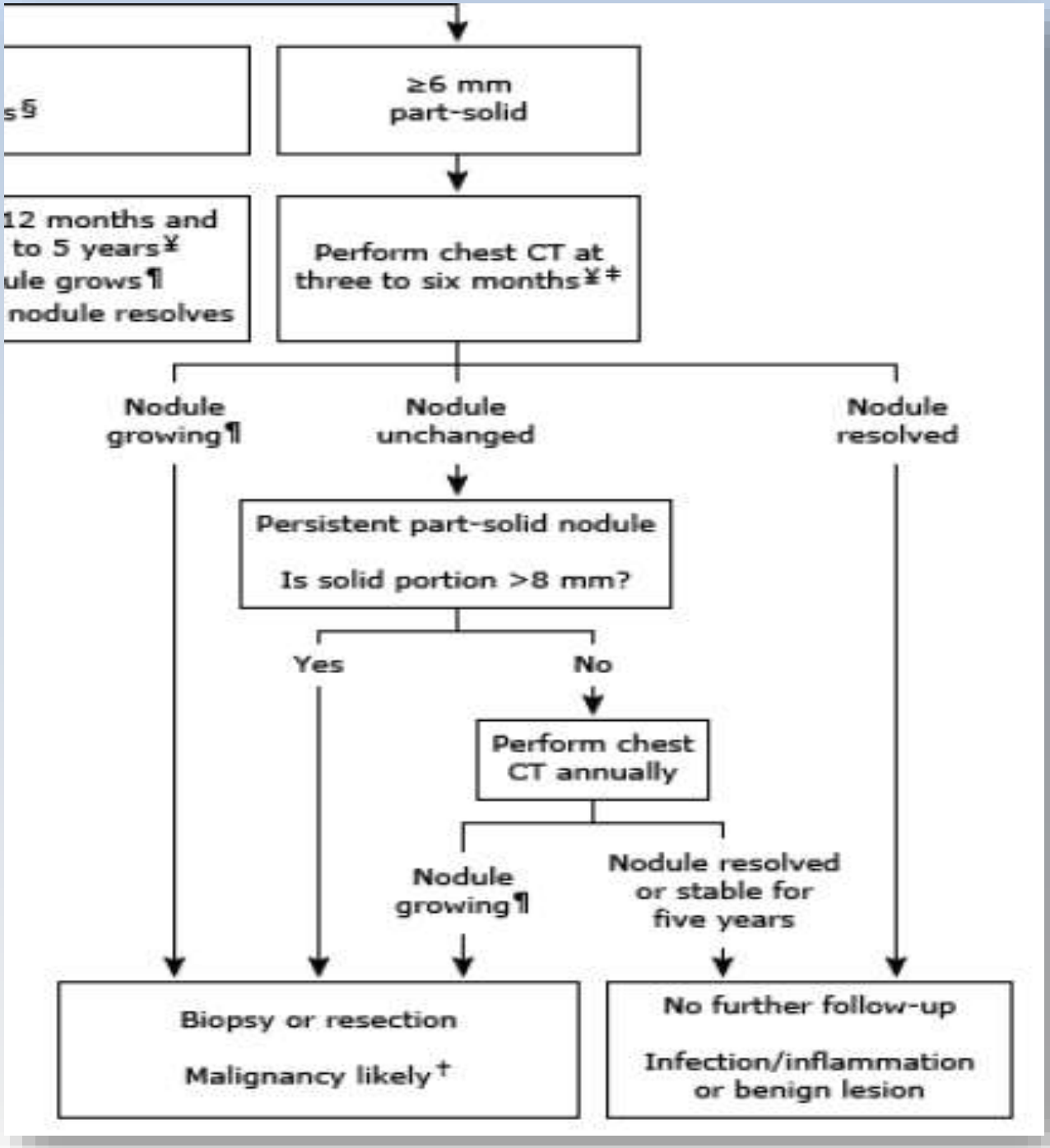
- For pure ground-glass nodules 6 mm or larger, follow-up scanning is recommended at **6–12 months** and then **every 2 years thereafter until 5 years** (grade 1B; strong recommendation, moderate-quality evidence).

- For solitary partsolid nodules smaller than 6 mm, **no routine follow-up** is recommended (grade 1C; strong recommendation, low- or very-low-quality evidence)

- For solitary part-solid nodules 6 mm or larger with a solid component less than 6 mm in diameter**, follow-up is recommended at 3–6 months** and then annually for a minimum of 5 years
- For solitary part-solid nodules with a solid component 8 mm or larger, a short-term follow-up **CT scan at 3–6 months** should be considered. In high risk nodules with FDG avid, **biopsy or resection** are recommended (grade 1B; strong recommendation, moderate quality evidence).

Nodule type and size (mm)	Recommendation
Solitary pure ground-glass	
<6	No routine follow-up.
≥6	CT at 6 to 12 months to confirm persistence. If unchanged, then CT every two years until five years. Growing nodules should undergo histologic sampling.*
Solitary part-solid	
<6	No routine follow-up.
≥6	CT at three to six months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for five years. Nodules with solid component >8 mm or growing nodules should undergo histologic sampling.*


Assess nodule size◊ and attenuation (ground-glass versus part-solid)
<6 mm ground-glass or part-solid
≥6 mm ground-glass§
≥6 mm part-solid
No further follow-up
Infection/inflammation
Perform chest CT at 6 to 12 months and then every 2 years for up to 5 years¥
Biopsy or resect if nodule grows¶
No further follow-up if nodule resolves
Perform chest CT at three to six months¥‡


s§
≥6 mm
part-solid
12 months and
to 5 years¥
ule grows¶
nodule resolves
Perform chest CT at
three to six months¥‡
Nodule
growing¶
Nodule
unchanged
Nodule
resolved
Persistent part-solid nodule
Is solid portion >8 mm?
Yes
No
Perform chest
CT annually
Nodule
growing¶
Nodule resolved
or stable for
five years
Biopsy or resection
Malignancy likely†
No further follow-up
Infection/inflammation
or benign lesion

New modifications in 2017 guidelines?

- For pure ground-glass nodules smaller than 6 mm in diameter, **no routine follow-up** is recommended

- In case of nodule being suspicious for malignancy or with risk factors, then an option of 2 and 4 year follow up can be made

Kakinuma R, et al. Solitary pure ground-glass nodules 5 mm or smaller: frequency of growth. Radiology 2015;276(3):873–882.

Solitary Pure Ground-Glass Nodules 5 mm or Smaller: Frequency of Growth[1]

Purpose: To clarify the percentage of solitary pure ground-glass nodules (SPGGNs) 5 mm or smaller that grow and develop into invasive adenocarcinomas.

Materials and Methods: This study was approved by the institutional review board, and informed consent was obtained from all people who were screened. From February 2004 through December 2007, 7294 participants underwent screening for lung cancer with computed tomographic (CT) imaging. The nodule database was reviewed to identify SPGGNs 5 mm or smaller. Growth of the SPGGNs was evaluated as of March 31, 2013. In cases of pathologic analysis–proven adenocarcinomas that developed from SPGGNs 5 mm or smaller, solid components were evaluated. Percentages, 95% confidence intervals, and means were calculated.

Results: At baseline screening, 438 SPGGNs 5 mm or smaller were identified, and during the study period one SPGGN 5 mm or smaller developed de novo. Of the 439 SPGGNs, 394 were stable and 45 (10.3% [95% confidence interval: 7.5%, 13.7%]), including newly developed SPGGN, grew. Of the 45 SPGGNs that grew, 0.9% (four of 439 [95% confidence interval: 0.3%, 2.3%]) developed into adenocarcinomas (two minimally invasive [including the newly developed SPGGN] and two invasive). The mean period between baseline CT screening and the appearance of solid components in the four adenocarcinomas was 3.6 years.

Conclusion: Of SPGGNs 5 mm or smaller, approximately 10% will grow and 1% will develop into invasive adenocarcinomas or minimally invasive adenocarcinomas. SPGGNs 5 mm or smaller should be rescanned 3.5 years later to look for development of a solid component.

- For pure ground-glass nodules 6 mm or larger, follow-up scanning is recommended at **6–12 months**

- The previous recommendation of initial follow-up at **3 months** has been changed to follow-up at **6–12 months** because earlier follow-up is unlikely to affect the outcome of these characteristically indolent lesions.

Naidich DP, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. Radiology. 2013;266(1):304-17

New modifications in 2017 guidelines?

- Recommended **follow-up intervals are now given as a range** rather than as a precise time period to give radiologists, clinicians, and patients greater discretion to accommodate individual risk factors and preferences

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

Multiple nodules

Multiple	
<6	CT at three to six months. If stable, no routine follow-up.
≥6	CT at three to six months. If stable, subsequent evaluation is based on the most suspicious nodule (largest nodule for pure ground-glass and largest solid component for part-solid).

MacMahon H, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology. 2017;284(1):228-43

- Most of the incidentally detected multiple nodules are benign, resolution usually occurs within 3-6months,
- follow-up CT will help to avoid unnecessary sampling and assessment of resolution of subclinical pathology

Lung cancer screening?

- Every nodule must be evaluated
- Cutoff of 20mm used instead of 6mm

- <20mm→CT f/u q 1year
- >20mm→CT f/u q 6 month

Naidich DP, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. Radiology. 2013;266(1):304-17

Management

Excisional surgical biopsy

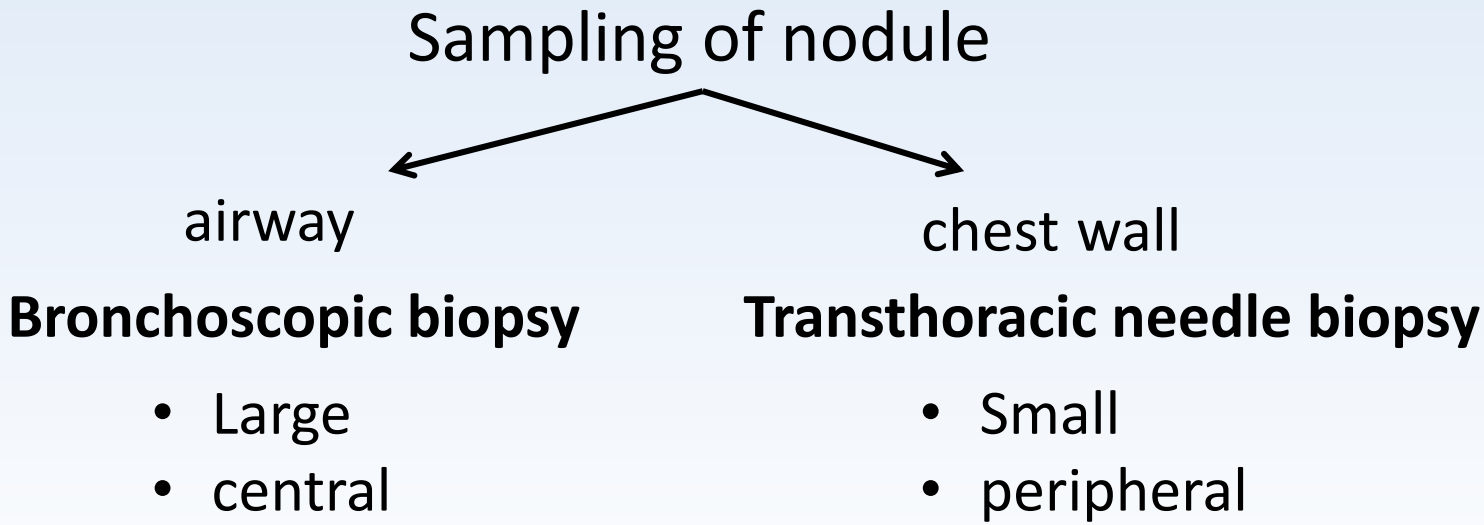
- Gold standard
- Diagnostic and therapeutic strategy
- 2 types
  - Open
  - VATS guided
- Diagnostic wedge resection by VATS(preferred, safe procedure)

- Intraoperative frozen section analysis
- If positive, converted into VATS lobectomy with mediastinal lymph node sampling
- 50% required thoracotomy for complete resection and staging

Allen M, et al. Video-assisted thoracoscopic stapled wedge excision for indeterminate pulmonary nodules. The Journal of thoracic and cardiovascular surgery. 1993;106(6):1048-52

Non surgical biopsy

- Preferred in
  - Intermediate risk
  - High risk non surgical candidates



Transthoracic needle biopsy

- Under CT guidance
- Sensitivity >90%
- Specificity >99%
- Yield >90%

} nodules 1cm

- However, the rates of nondiagnostic biopsy do increase for nodules measuring ≤6 mm

Lee SM, et al. C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of lung nodules: clinical experience in 1108 patients. Radiology. 2013;271(1):291-300

- Complications
  - Pneumothorax (10-17%)
  - Hemoptysis (1-7%)

Lee SM, et al. C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of lung nodules: clinical experience in 1108 patients. Radiology. 2013;271(1):291-300

Conventional TBLB

- Sensitivity 65 to 88 percent
- highest sensitivity for large, central lesions
- lower rates for peripheral nodules
  - >2 cm: 63 percent
  - <2 cm: 34 percent

Rivera MP, et al. Establishing the diagnosis of lung cancer: Diagnosis and management of lung cancer: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5):e142S-e65S

Radial EBUS TBLB

- Sensitivity of 73-85% (larger central lesions)
- 70% if nodule <20mm
- 56% for peripheral nodules

EBUS TBB vs TBB

Chest. 2005 Nov;128(5):3551-7.

ELSEVIER FULL-TEXT ARTICLE

Endobronchial ultrasound-driven biopsy in the diagnosis of peripheral lung lesions.

Paone G[1], Nicastri E, Lucantoni G, Dello Iacono R, Battistoni P, D'Angeli AL, Galluccio G.

Author information

Abstract

STUDY OBJECTIVES: The aim of our study was to compare the diagnostic yield of two bronchoscopic procedures: endobronchial ultrasound-driven transbronchial biopsy (EBUS-TBB) and transbronchial biopsy (TBB) in peripheral pulmonary lesions.

- Sensitivity 79% vs 55%
- Lesion >3cm : no significant difference
- <3cm: considerable fall in sensitivity of TBB(31%)
- EBUS TBB had similar sensitivity

Paone G, et al. Endobronchial ultrasound-driven biopsy in the diagnosis of peripheral lung lesions. Chest. 2005;128(5):3551-7

Navigational bronchoscopy

- Using the CT guidance and electromagnetic radiation in navigation of bronchoscope to target small peripheral nodules

- Planning phase
  - Preprocedure CT done
  - 3D reconstruction of airways
  - Target located
  - Plan the approach

- Navigation phase
  - Software hybridises the CT images and realtime bronchoscope images
  - Navigation of scanner probe and working channel to target
  - Locking at target and sampling of nodule

- Diagnostic yield: 70%
- Significantly higher than traditional bronchoscopy
- Increased as lesion size increased

Wang Memoli JS, et al. Meta-analysis of guided bronchoscopy for the evaluation of the pulmonary nodule. Chest. 2012 Aug;142(2):385-93

Take home message

- Subsolid: more malignant, low growth rate
- Risk factor assessment
- CXR , PET has not role in f/u
- Individualizing the approach
- Radial EBUS and navigation Bronchoscopy: better options

THANK YOU