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Lung Cancer Diagnosis for Primary Care

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Case 1

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In which of the following situations would the U.S. Preventive Services Task Force (USPSTF) recommend that M.B. be screened for lung cancer?

A. M.B. is 60 years of age, her diabetes is well controlled by diet, and she quit smoking 20 years ago.

B. M.B. is 60 years of age, her diabetes is well controlled by medications, and she quit smoking 10 years ago.

C. M.B. is 75 years of age, her diabetes is well controlled by medications, and she currently smokes.

D. M.B. is 78 years of age, her diabetes is poorly controlled, she has emphysema and heart failure with an ejection fraction of 30% and she currently smokes

Case 1

It is determined that M.B. should be screened for lung cancer. According to the USPSTF, which one of the following screening tests is recommended?

A. Annual chest radiography with sputum cytology.

B. Chest radiography and sputum cytology once every three years.

C. Annual low-dose computed tomography (CT).

D. Low-dose CT once every three years.

E. Annual magnetic resonance imaging.

Case 1

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Based on the USPSTF's findings, which one of the following statements about the potential benefits or harms of lung cancer screening is correct?

A. Annual screening can substantially lower lung cancer incidence in high-risk persons.

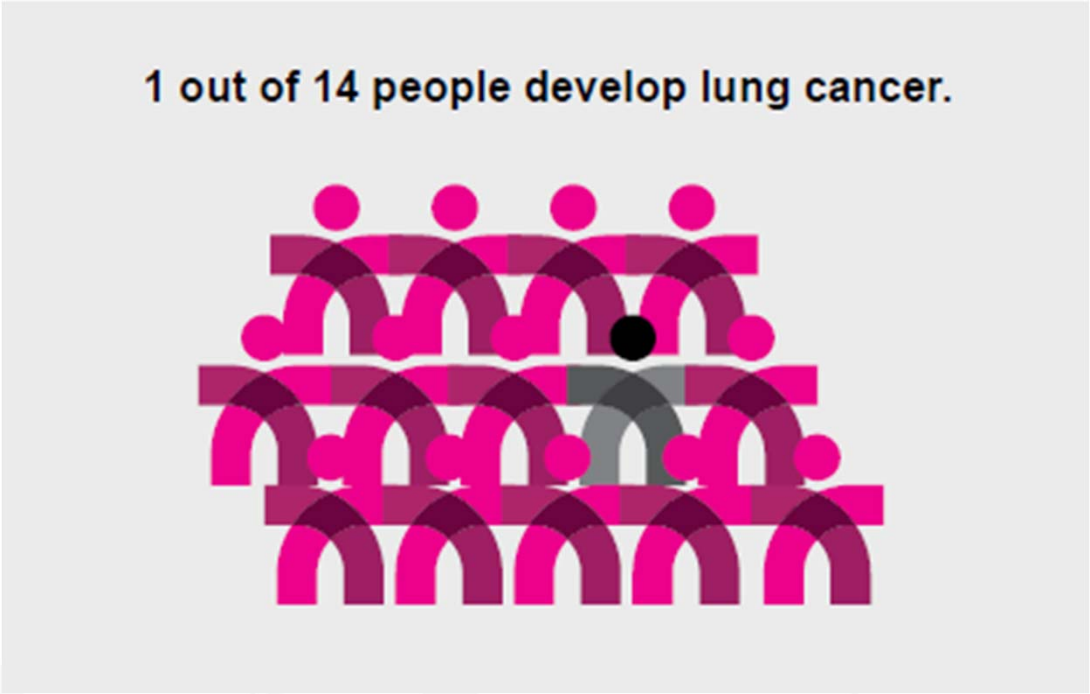
B. Annual screening can prevent a substantial number of lung cancer–related deaths in a defined population of high-risk persons.

C. Annual screening can prevent most lung cancer–related deaths.

D. There is a low likelihood of false-positive results; 95% of all positive results lead to a diagnosis of cancer.

E. Only 1% to 2% of screen-detected cancer cases are overdiagnosed.

Lung Cancer Facts



1. ACS Cancer Facts & Figures 2016
2. ALA Lung Cancer Fact Sheet
3. U.S. National Institutes of Health. National Cancer Institute. SEER Cancer Statistics Review, 1975-2014.

Leading Sites of New Cancer Cases and Deaths: 2016 Estimates

Estimated New Cases

Male	Female
Prostate 180,890 (21%)	Breast 246,660 (29%)
Lung & bronchus 117,920 (14%)	Lung & bronchus 106,470 (13%)
Colon & rectum 70,820 (8%)	Colon & rectum 63,670 (8%)
Urinary bladder 58,950 (7%)	Uterine corpus 60,050 (7%)
Melanoma of the skin 46,870 (6%)	Thyroid 49,350 (6%)
Non-Hodgkin lymphoma 40,170 (5%)	Non-Hodgkin lymphoma 32,410 (4%)
Kidney & renal pelvis 39,650 (5%)	Melanoma of the skin 29,510 (3%)
Oral cavity & pharynx 34,780 (4%)	Leukemia 26,050 (3%)
Leukemia 34,090 (4%)	Pancreas 25,400 (3%)
Liver & intrahepatic bile duct 28,410 (3%)	Kidney & renal pelvis 23,050 (3%)
All sites 841,390 (100%)	All sites 843,820 (100%)

Estimated Deaths

Male	Female
Lung & bronchus 85,920 (27%)	Lung & bronchus 72,160 (26%)
Prostate 26,120 (8%)	Breast 40,450 (14%)
Colon & rectum 26,020 (8%)	Colon & rectum 23,170 (8%)
Pancreas 21,450 (7%)	Pancreas 20,330 (7%)
Liver & intrahepatic bile duct 18,280 (6%)	Ovary 14,240 (5%)
Leukemia 14,130 (4%)	Uterine corpus 10,470 (4%)
Esophagus 12,720 (4%)	Leukemia 10,270 (4%)
Urinary bladder 11,820 (4%)	Liver & intrahepatic bile duct 8,890 (3%)
Non-Hodgkin lymphoma 11,520 (4%)	Non-Hodgkin lymphoma 8,630 (3%)
Brain & other nervous system 9,440 (3%)	Brain & other nervous system 6,610 (2%)
All sites 314,290 (100%)	All sites 281,400 (100%)

1. ACS Cancer Facts & Figures 2016
2. ALA Lung Cancer Fact Sheet
3. U.S. National Institutes of Health. National Cancer Institute. SEER Cancer Statistics Review, 1975-2013.

Why are we here?

Prevention is the most effective strategy for reducing the burden of lung cancer

For non-preventable lung cancers,

Early detection & screening is critical

IMPROVE PATIENT CARE • SAVE LIVES

Sense of Urgency

LUNG CANCER KILLS 433 PEOPLE EVERY DAY!

Patient Cohorts

SYMPTOMATIC PATIENTS

HIGH-RISK PATIENTS

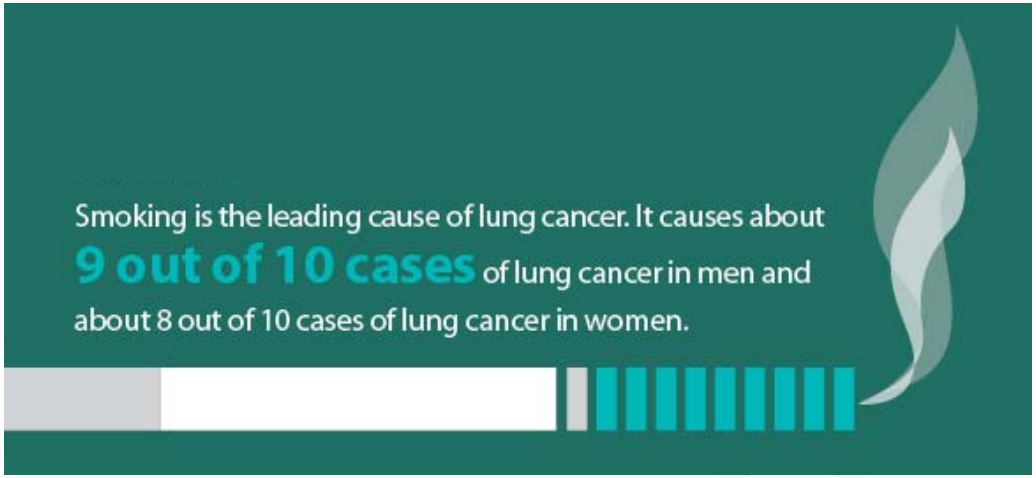
INCIDENTAL FINDINGS PATIENTS

Risk Factors

- Smoking
- Exposure to radon
- Exposure to other hazardous chemicals
  - Asbestos
  - Uranium
  - Arsenic
  - Cadmium
  - Chromium
  - Nickel
  - Some petroleum products
- Particle pollution
- Age
- Genetics: Personal or family history of lung cancer

1. ALA What Causes Lung Cancer
2. ACS Lung Cancer Risk Factors

Impact of Smoking



- Cigarette smoking is <u>by far</u> the most important risk factor for lung cancer
  - 80% of lung cancer deaths in women
  - 90% of lung cancer deaths in men
- Risk increases with both quantity and duration of smoking.

- Smoking
  - Cigarette smoking
  - Cigar & pipe smoking
  - Secondhand smoke
- Combined risk
  (*i.e.* smoking + asbestos)
- Smoking Cessation

1. ACS Cancer Facts & Figures 2016
2. ALA Lung Cancer Fact Sheet
3. Cancercenter.com
4. The Mesothelioma Center

Identifying Symptomatic Patients

- A cough that doesn't go away and gets worse over time
- A chronic cough or "smoker's cough"
- Hoarseness
- Constant chest pain
- Shortness of breath or wheezing
- Frequent lung infections such as bronchitis or pneumonia
- Coughing up blood
- Weight loss and loss of appetite
- Feeling tired or weak
- Infections such as bronchitis and pneumonia that don’t go away or keep coming back

1. ALA What are the symptoms of Lung Cancer
2. ACS Signs & Symptoms of Lung Cancer

Identifying High-risk Patients

Two identifiers:

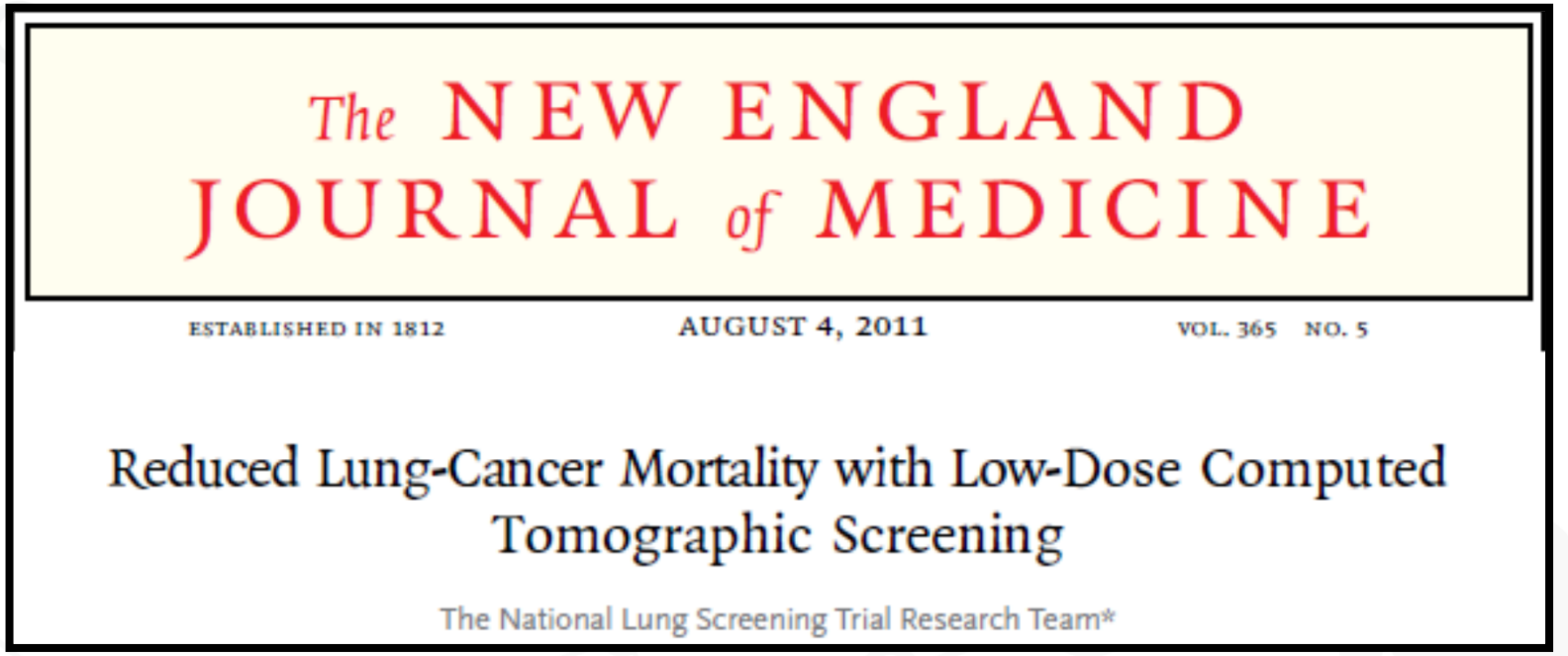
Age 55-74

30-pack year Smoking History

Primary Care Provider Role

- Know the risk factors
- Counsel on smoking cessation
- Critical role in identifying:
  - Symptomatic patients
  - High-risk patients

Screening for Lung Cancer
National Lung Screening Trial (NLST)



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

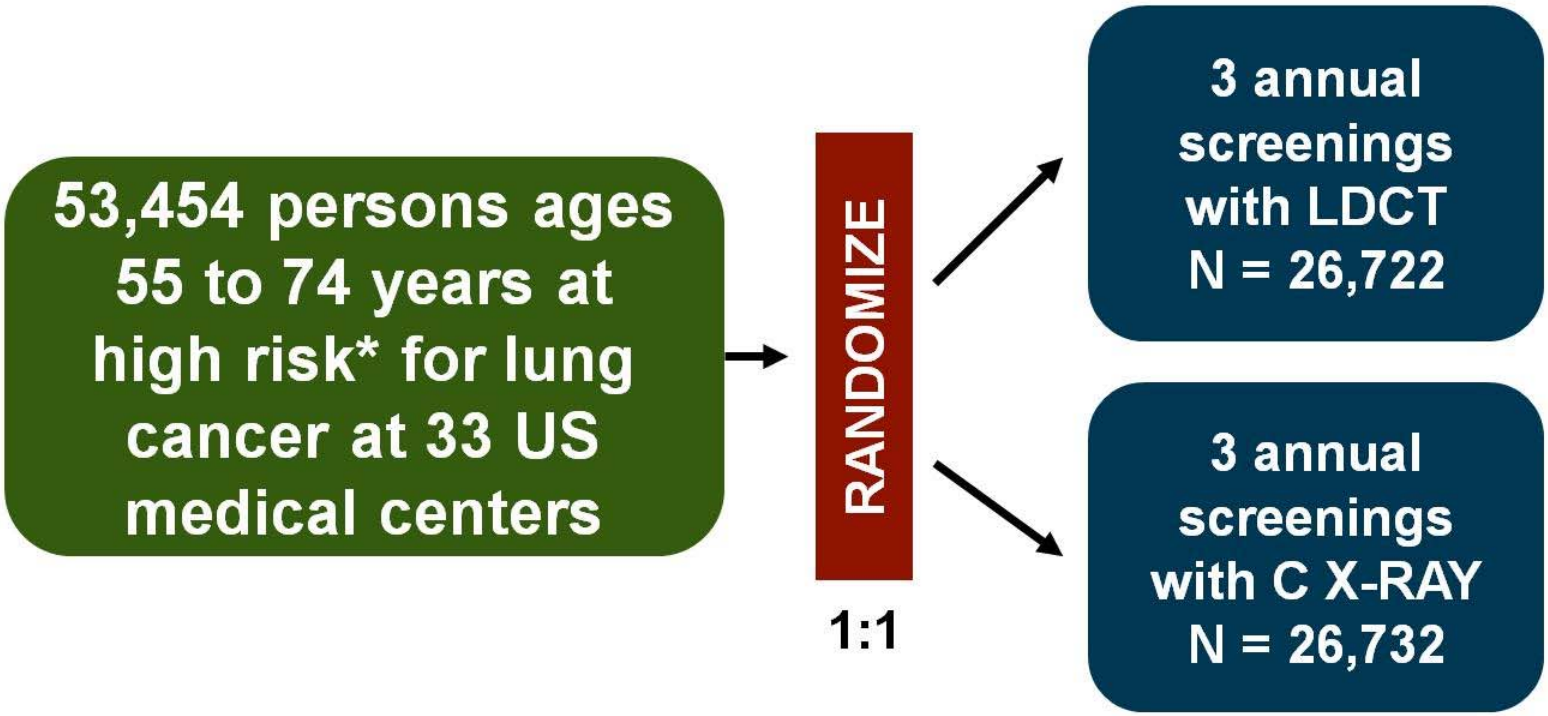
The National Lung Screening Trial Research Team*

20% fewer lung cancer deaths among 53,000 participants screened with low-dose helical (spiral) CT compared to those screened with chest X-rays.

The trial ended early due to promising results

N Engl J Med 2011; 365:395-409

NLST
Study Design

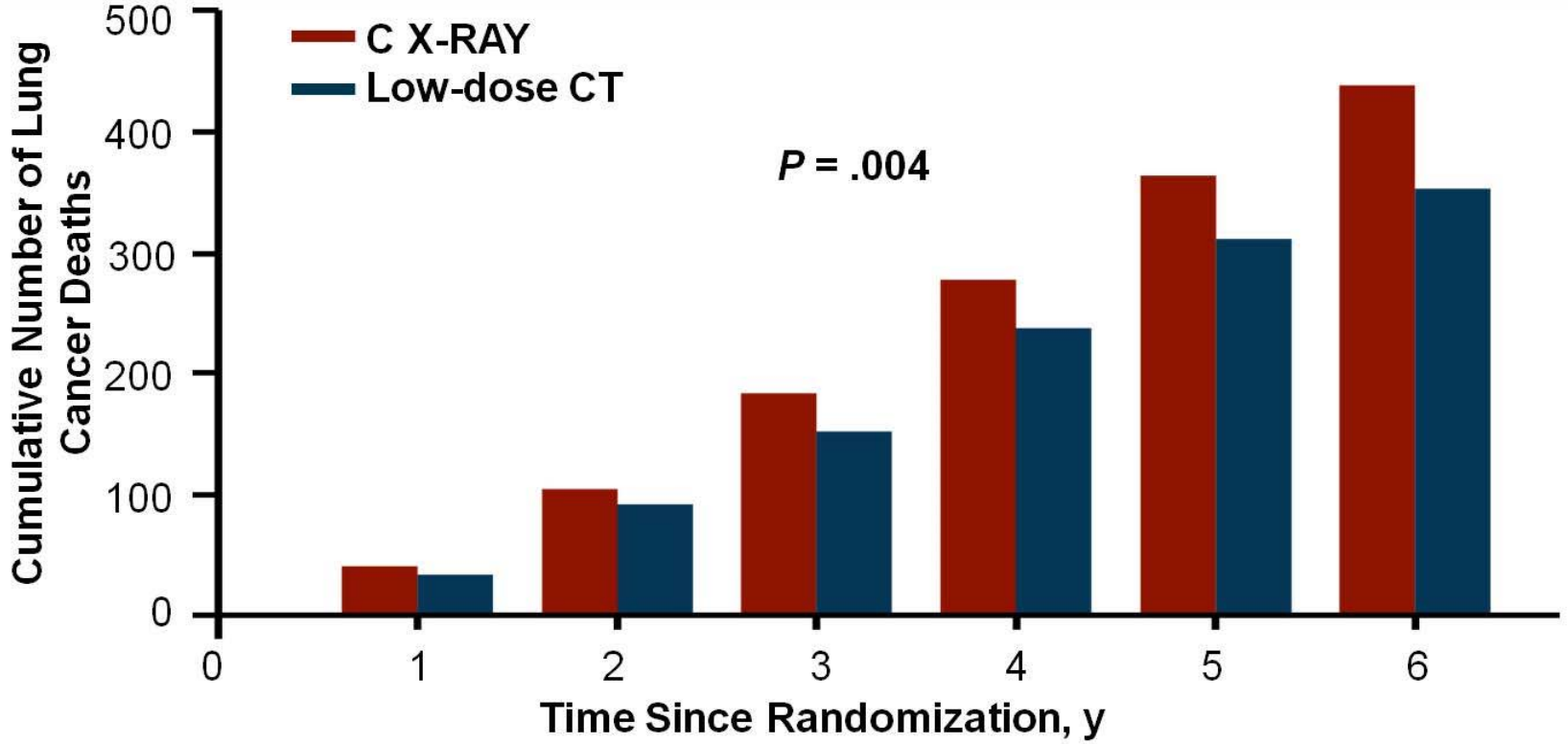


*High risk for lung cancer was defined as a 30-year or more history of cigarette smoking. If the patient was a former smoker, they must have quit smoking within the last 15 years.

National Lung Screening Trial Research Team, et al. *N Engl J Med*. 2011;365:395-409.[1]

NLST

Lung Cancer Mortality



- Positive screening rate for LDCT is 24.2%; for C X-RAY it is 6.9%
- 96.4% and 94.5% of the positive findings were false-positives in the LDCT and C X-RAY groups, respectively
- Lung cancer mortality was reduced by 20% in the LDCT group compared with the C X-RAY group.
- All-cause mortality was reduced by 6.9% in the LDCT group compared with the C X-RAY R group

National Lung Screening Trial Research Team, et al. *N Engl J Med*. 2011;365:395-409.[1]

United States Preventive Task Force (USPSTF) Screening Recommendation

- Age 55-80
- ≥ 30 pack-year smoking history
- Current smoker or quit within the last 15 years
- Able and willing to receive treatment
- Screening should be discontinued
  - Once a person has not smoked for 15 years
  - Develops health problem(s) that substantially limits life expectancy or the ability or willingness to have curative lung surgery

Lung Screening Programs
Requirements

Chart 6.1 Must-haves for screening sites

Follows an organized plan—a proven protocol—that is updated to include new technology and knowledge like that from NCCN
Has a high-quality screening program with enough staff and resources
Is accredited to do CT scans by a certifying organization, such as the American College of Radiology
Has scans read by an American Board of Radiology board-certified radiologist who's an expert in lung cancer screening
Has modern multislice CT equipment that does high-quality, low-dose, and non-contrast spiral CT
Is partnered with a health center that has: 1) experience and excellence in biopsy methods; 2) board-certified pulmonologists; and 3) board-certified thoracic surgeons who are experts in lung cancer

Case 2

- 58 year old male presented with dyspnea and dyspnea with exertion
- 40 pack year tobacco history, still smokes
- Father had lung lung cancer, age 68
- Hypertension
- ROS: chronic productive cough
- Exam: end expiratory wheezes

Case 2 Next Steps

- Treat exacerbation COPD
- PFT's
- Assess likelihood of lung cancer
- Manage pulmonary nodule

What are you going to tell the patient?

- A. You have a 5 mm nodule in the left lower lobe
- B. This might be cancer
- C. We want you to come back in 6 months
- D. We'll keep an eye on it
- E. A spot on the lung is always something to worry about. I don't want you to get frantic. We'll just take the test as we go along…

What's the Patient Thinking?

- What's a nodule? A "spot". A "shadow"
- What's the chances that it is cancer?
- If it's not cancer, what else are we considering?
- Is it serious?
- What should I expect? Will I be able to breathe? Will I have pain?
- How long do we watch?

Tell the Patient

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- 1. Estimate the risk of cancer
- 2. Must be verbal. A letter is not satisfactory.
- 3. Avoid minimizing or dismissive language
- 4. Give this high priority, answer all the questions
- 5. Provide details of the nodule, it's the size of a pea, etc.
- 6. Explain the evaluation or surveillance
- 7. Let the patient know what to expect and acknowledge their concerns

What is a Nodule?

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- Solitary Pulmonary Nodule (SPN) is a radiographic opacity < 3 cm with a least 2/3 of its margins surrounded by lung parenchyma
- This excludes lymph nodes, atelectasis, and post-obstructive pneumonia
- Establishing the etiology of a SPN assumes critical importance

SPN

- 150,00 per year
- CT imaging: 8% to 51%
- Prevalence of malignancy: 1.1% to 12%
- Accurate and timely diagnosis is important as treatment of early stage lung cancer provides the highest chance for cure.

Clinical Evaluation: History

- History of smoking
- History of prior malignancy
- History of interstitial Lung Disease
- Residence in or travel to areas endemic with fungal pathogens
- Prior CT scan or Chest radiograph

CT Scan

- Thin sections
- 1.5 mm
- Lung and mediastinal windows
- Contrast for mediastinal structures and nodule enhancement

Growth Rate

- Malignant nodules double in 20 to 400 days
- Volume of a sphere = $4\pi r^3/3$
- An increase in diameter of 26% represents a doubling in volume
- Example: 4mm nodule to 5mm is almost a doubling in volume
- A solid nodule which does not change in size over 2 years is considered benign

Size Matters

- Size trumps morphology: diameter and likelihood of cancer in screened smokers

- < 3 mm: 0.2%
- 4 – 7 mm 2.7%
- 8 – 30 mm 18%
- > 30 mm 99%

- Radiology 235:259, 2005

Benign patterns of calcifications

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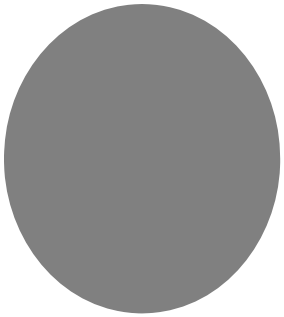
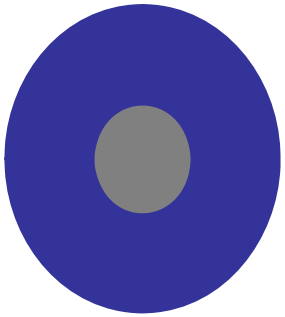
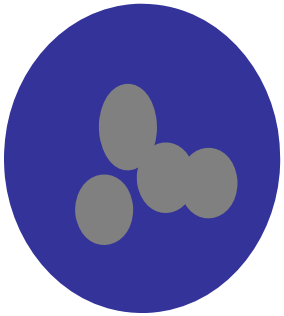


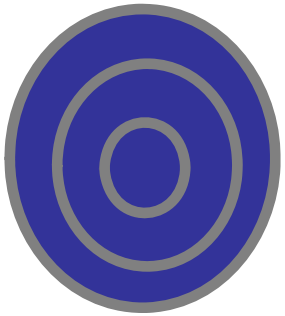
diffuse



central



popcorn



concentric

Indeterminate patters of calcification

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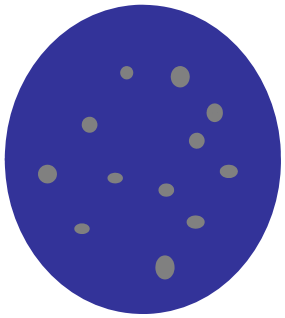
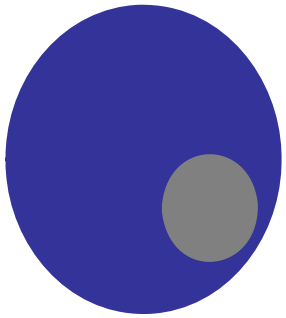
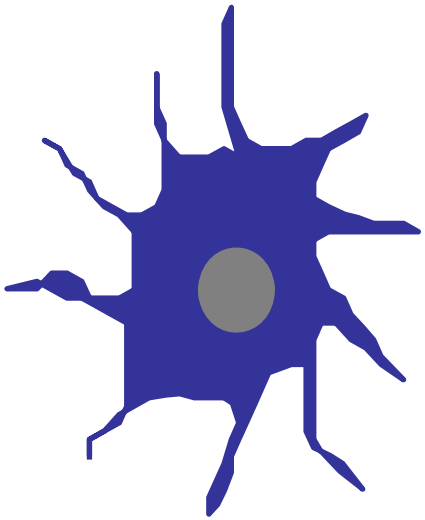


stippled



eccentric



inhomogeneous calcification of irregular nodule

Findings that suggest a benign lesion

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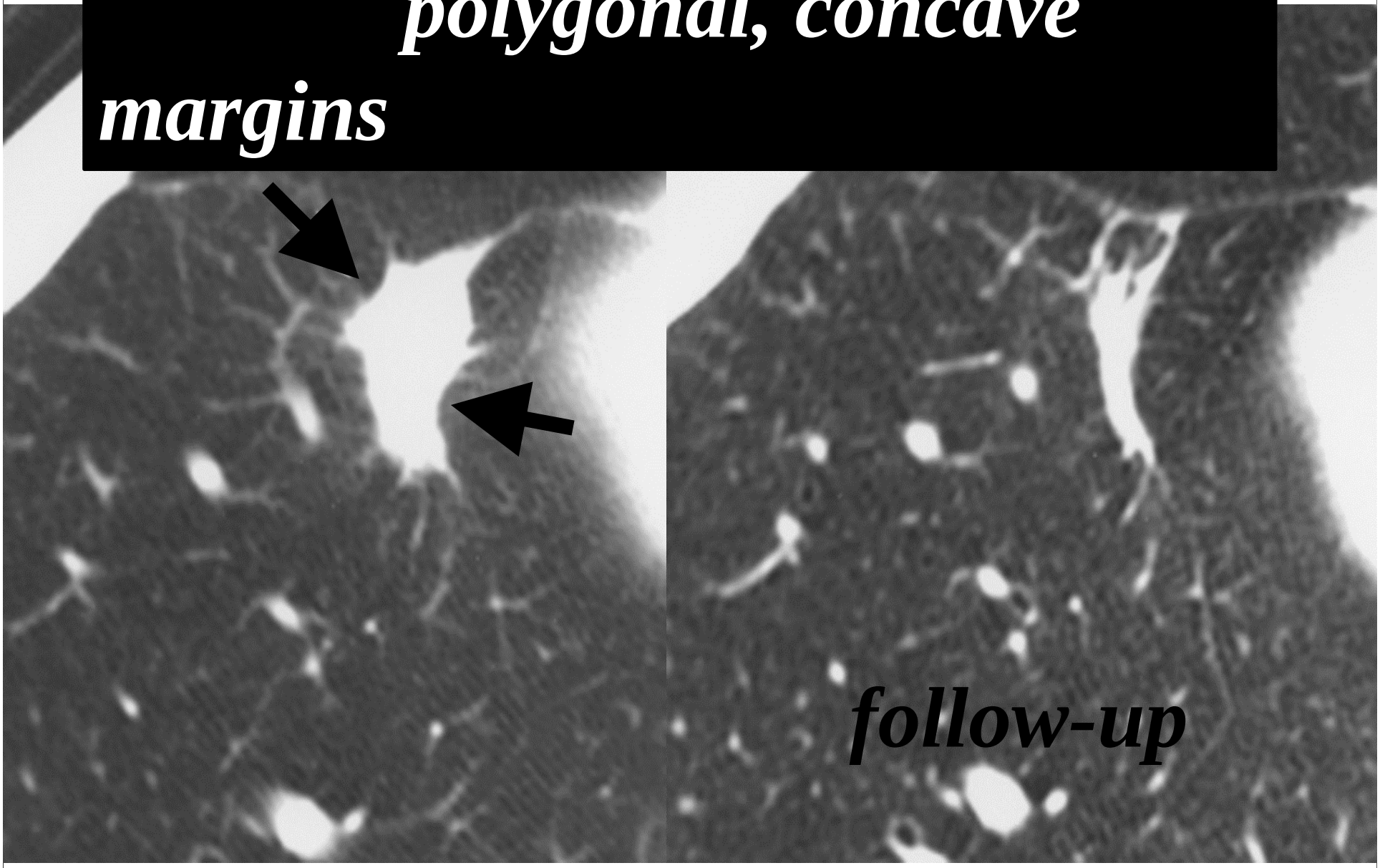
- **shape: oblong, polygonal, concave margins**
- **edge smooth**
- **subpleural location (attached to the pleura)**
- **satellite nodules**

Xu et al, Radiology 250; 264, 2009

Li et al, Radiology 233; 793, 2004

Takashima et al. AJR 2003; 180:1255

polygonal, concave margins

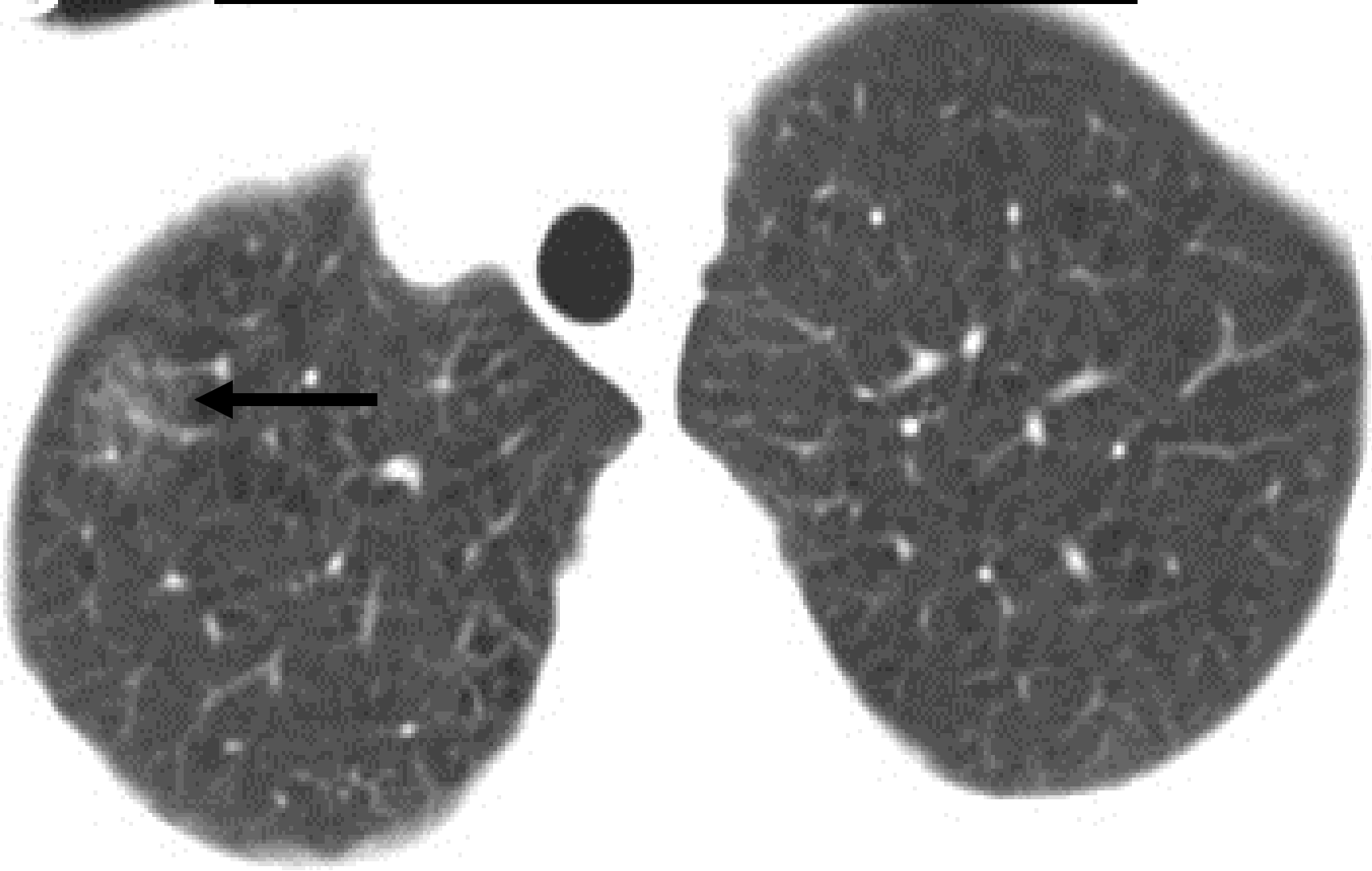


Takashima et al. AJR 2003; 180:12

Ground Glass Opacities

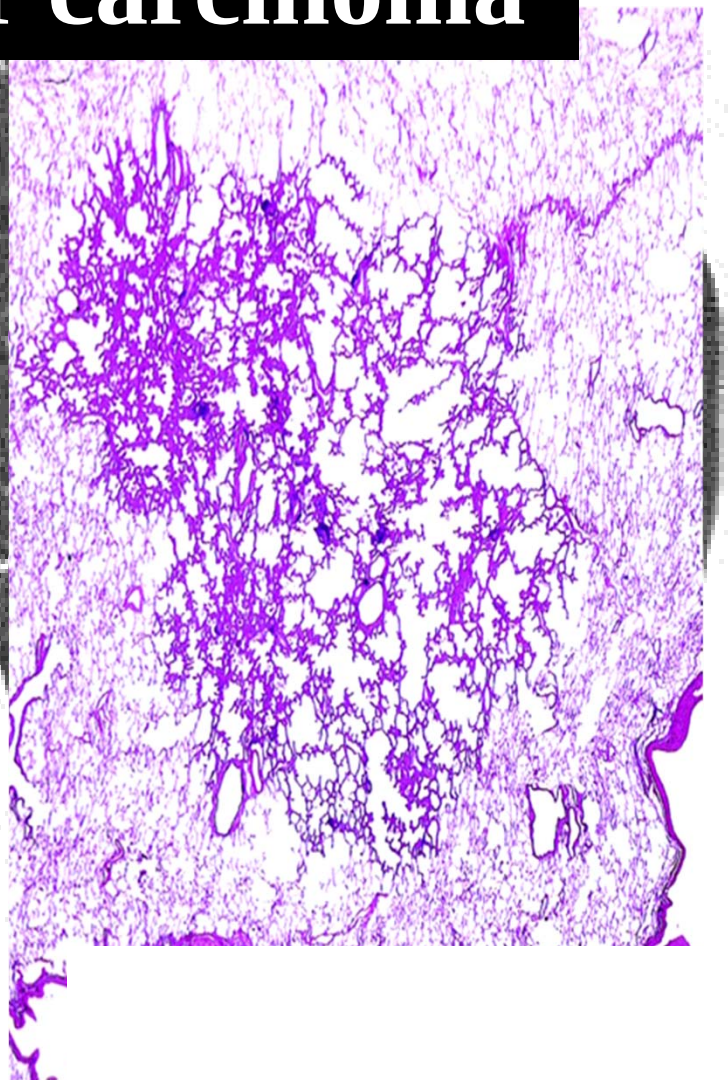
- Subsolid nodule = pure GGO
- Partly solid GGN: focal nodular area of increased attenuation
- Semi-solid GGN: may represent a histologic spectrum of adenocarcinoma
- Atypical adenomatous hyperplasia → adenocarcinoma in situ →minimally invasive adenocarcinoma →lepidic predominant adenocarcinoma

Ground-glass opacity



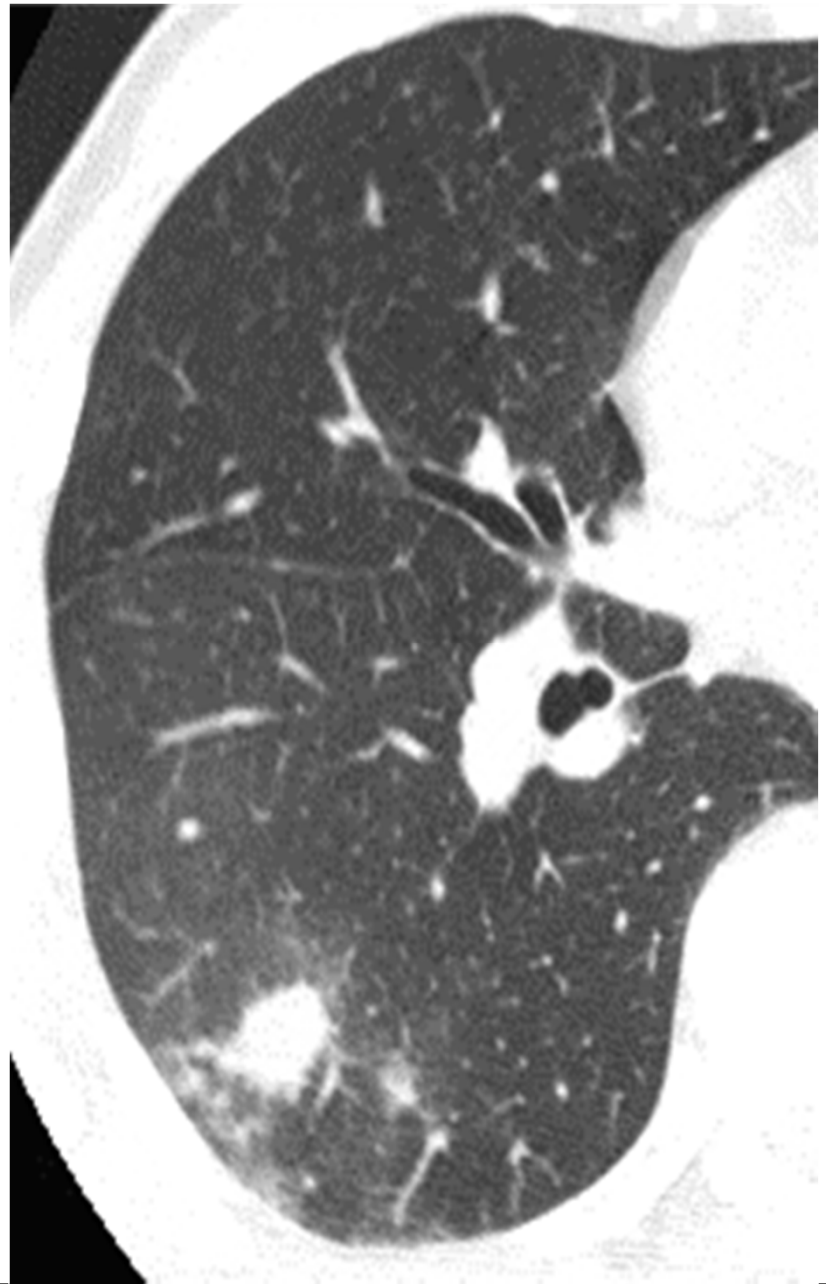
5 mm, standard algorithm

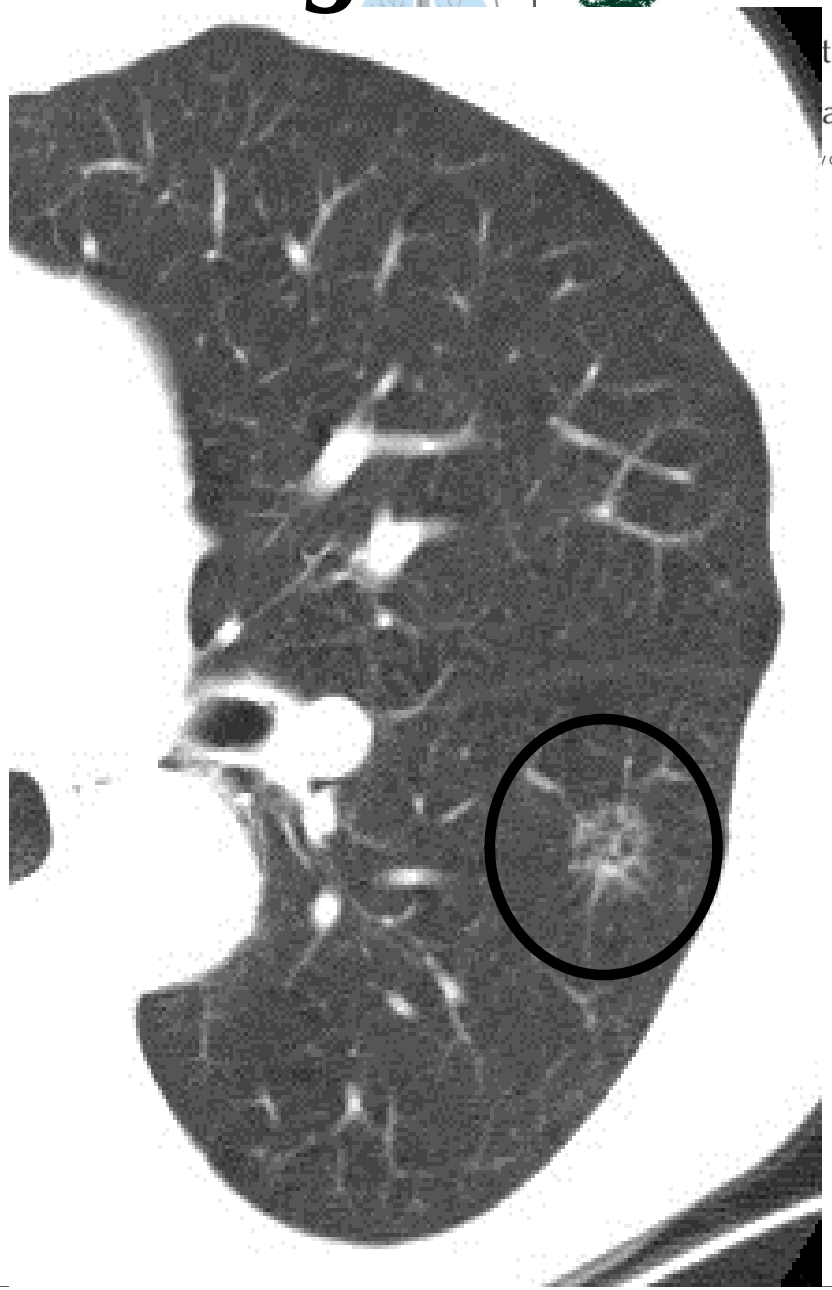
Ground-glass opacity bronchioloalveolar carcinoma



Shimizu et al. Chest 2005, 127:8

Which nodule is Malignant?





PET Scan

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- Combined PET-CT correlates results from 2 modalities
- Glucose analog tagged with positron-emitting isotope fluorine(FDG)
- Reveals aspects of tumor function and metabolism
- Metabolic activity quantitated using Standard Uptake Value (SUV) Mean value > 2.5

Case 2 PET

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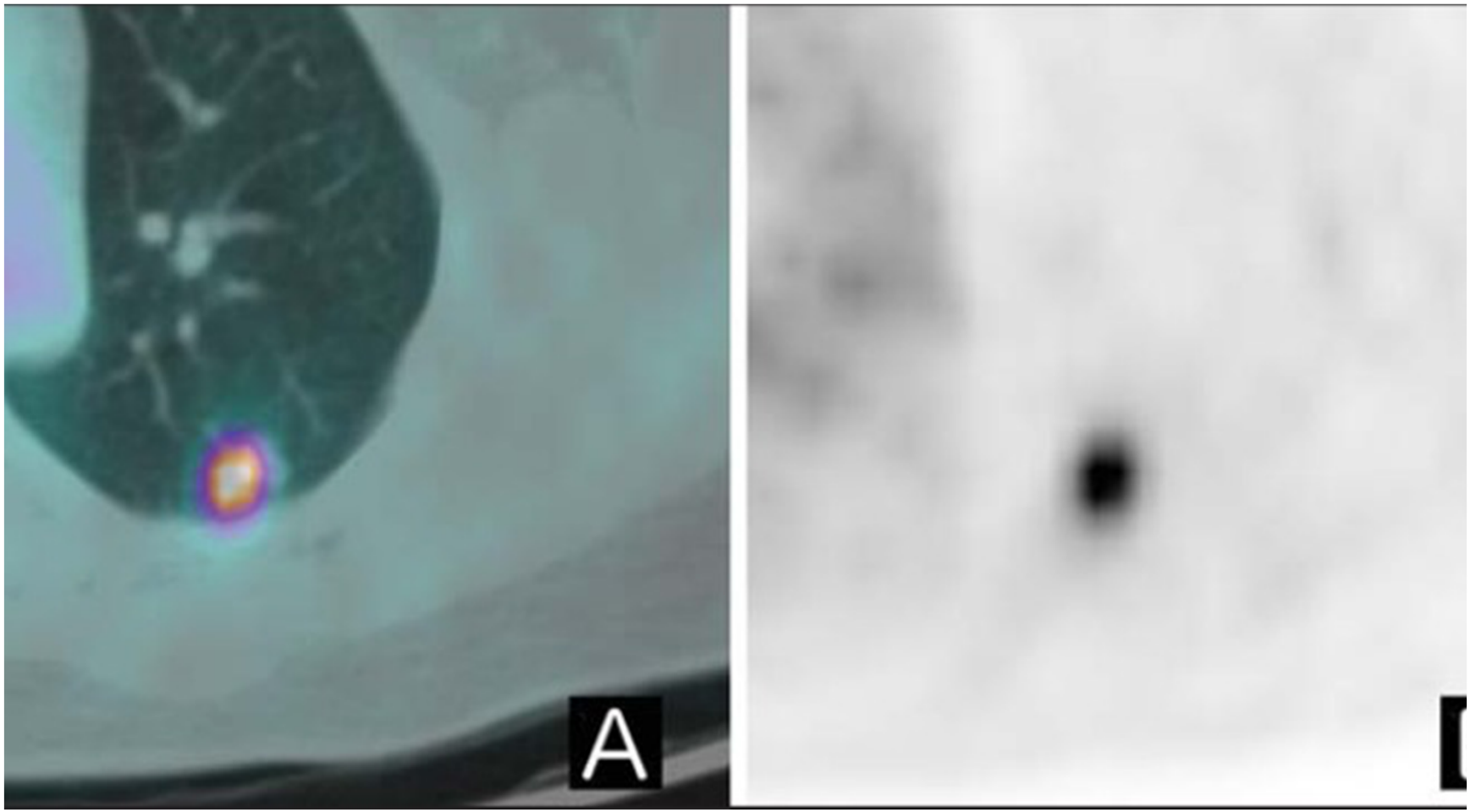

Pulmonary nodules: FDG-PET diagnosis

Gould et al. JAMA 2001; 285:914

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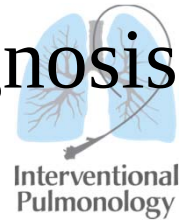
- **meta-analysis of 40 studies with 1474 nodules**
- **SUV 2.5**
- **sensitivity 97%; specificity 78%; accuracy 90%**

Pulmonary nodules: FDG-PET diagnosis

Bryant et al. Ann Thorac Surg 2006; 82:1016



- **625 patients**
- **433 diagnosed with cancer**
- **false negatives:**
  - **» 11/23 (48%) Lepidic predominant adeocarcinoma**
  - **» 8/234 (3%) adenocarcinoma**
  - **» 4/14 (29%) carcinoid**
  - **» 2/8 (25%) renal cell metastases**

Pulmonary nodules: FDG-PET diagnosis

Nomori et al. Lung Cancer 2004; 45:19

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- **136 nodules < 3 cm; 81 malignant**
- **all 20 < 1 cm (8 malignant) were negative on PET**
- **101 solid nodules 1-3 cm (63 malignant) sensitivity 90%, specificity 71%**
- **15 ground-glass nodules 1-3 cm (10 malignant) sensitivity 10%, specificity 20%**

Solitary Pulmonary Nodule Calculator

http://www.chestx-ray.com/SPN/SPNProb.html

Google

Probability of Malignancy in SPN: Logistic Regression

Compare the above result to this method derived from multivariate logistic regression in 629 patients (65% benign, 23% malignant, 12% indeterminate). The equation is based on 3 clinical and 3 radiographic variables.

$$\text{Probability of Malignancy} = e^x(1 + e^x)$$

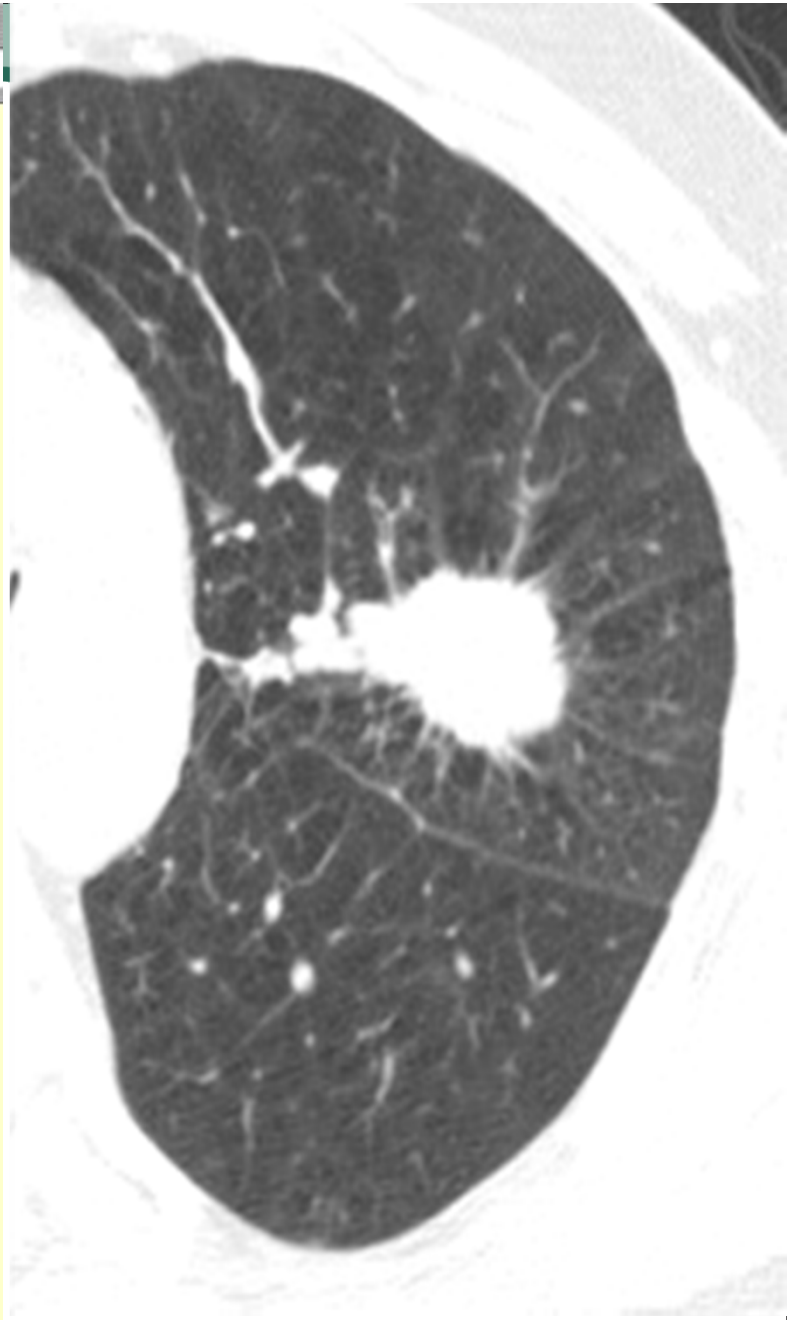
where x = -6.8272 + (0.0391 * Age) + (0.7917 * Cigarettes) + (1.3388 * Cancer) + (0.1274 * Diameter) + (1.0407 * Spiculation) + (0.7838 * Upper).

Note: this equation is not applicable to patients with a diagnosis of cancer that has been made within the previous 5 years or to patients with previous lung cancer.

Reference:

Swensen SJ, Silverstein MD, Ilstrup DM, Schleck CD, Edell ES. The probability of malignancy in solitary pulmonary nodules. Application to small radiologically indeterminate nodules. Arch Intern Med 1997; 157:849-855.
[Related Records]

Age (yrs):	62
SPN diameter (mm):	25
Edge:	Spiculated
Previous Malignancy:	No Hx Malignancy
Smoking:	Smoker or Former Smoker
Location:	Upper lobe
Calculate Probability of Malignancy	
The Probability of Malignancy is:	80
Reset	



Schultz. Thorax 2008; 63:3

Probability of Cancer in Pulmonary Nodules NEJM 369; 10, September 5 2013

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- Predictors of cancer model
- Older age
- Female sex
- Family history of lung cancer
- Emphysema
- Larger nodule size
- Location of nodule in the upper lobe
- Part-solid nodule type
- Lower nodule count
- Spiculation

Pulmonary Nodule Risk for Cancer Predictor

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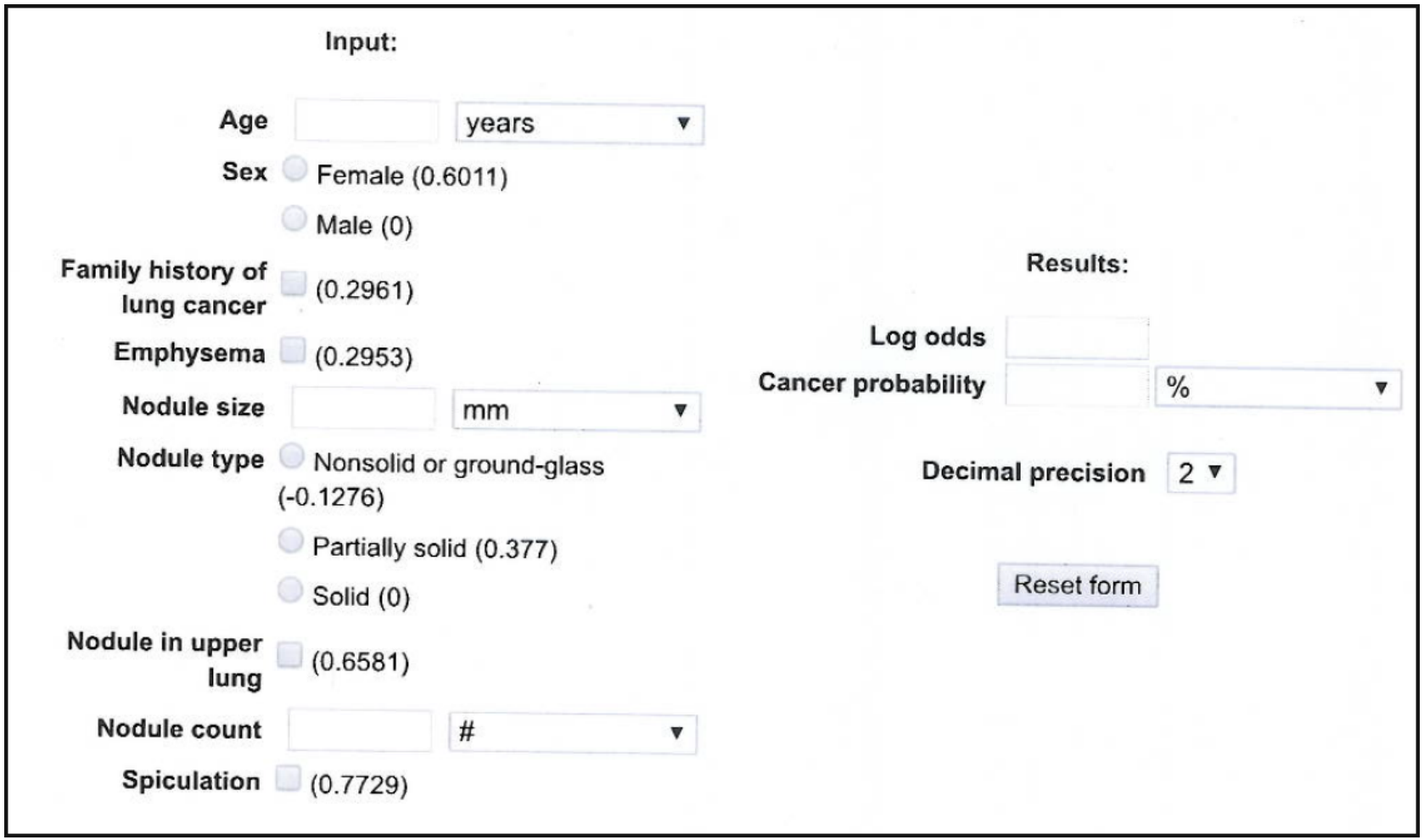
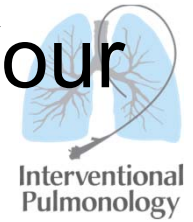


Algorithmic Approach to SPN

- Review previous imaging
- Solid or subsolid
- Solid nodules < 8 mm can be followed
- Solid nodules > 8mm need pretest probability for cancer
- Pretest probability < 5%, follow
- Pretest probability > 60% needs tissue diagnosis
- Intermediate range: PET

Where Do You Compare With Your Peers?



- Annals of the American Thoracic Society, January 2018
- An Assessment of Primary Care and Pulmonary Provider Perspectives on Lung Cancer Screening

Primary Provider Perspective On Lung Cancer Screening

- 196 participants
- 80% primary care
- 41% University or affiliated clinics
- 47% county hospital based clinics

- 74% endorsed screening effectiveness
- Key barriers: inadequate time (36%), inadequate staffing (36%), patients have too many other illnesses to address (38%)
- Decision aids were important, at point of referral, to facilitate screening
- Point-of-care referral materials may be helpful in reducing knowledge gaps and clinical burden of referral.

Lung Cancer Screening Recommendation

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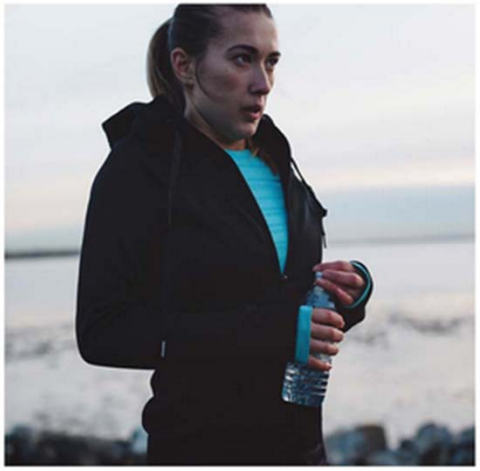
RISK CRITERIA	USPSTF	CMS	NCCN
Age	55-80	55-77	55
Pack-year Smoking History	≥ 30	≥ 30	≥ 30
Status	Current smoker or quit within the last 15 years	Current smoker or quit within the last 15 years	Current smoker or quit within the last 15 years
Other	Able and willing to receive treatment	Shared decision making	Shared decision making
Discontinuation Guidelines	Age 80 Once a person has not smoked for 15 years Develops health problem(s) that substantially limits life expectancy or the ability or willingness to have curative lung surgery	Age 77	N/A

AMERICAN LUNG ASSOCIATION.

LUNG FORCE




LIGHT
PROG.
SNAP

Monarch Peripheral Bronchoscopy Animation

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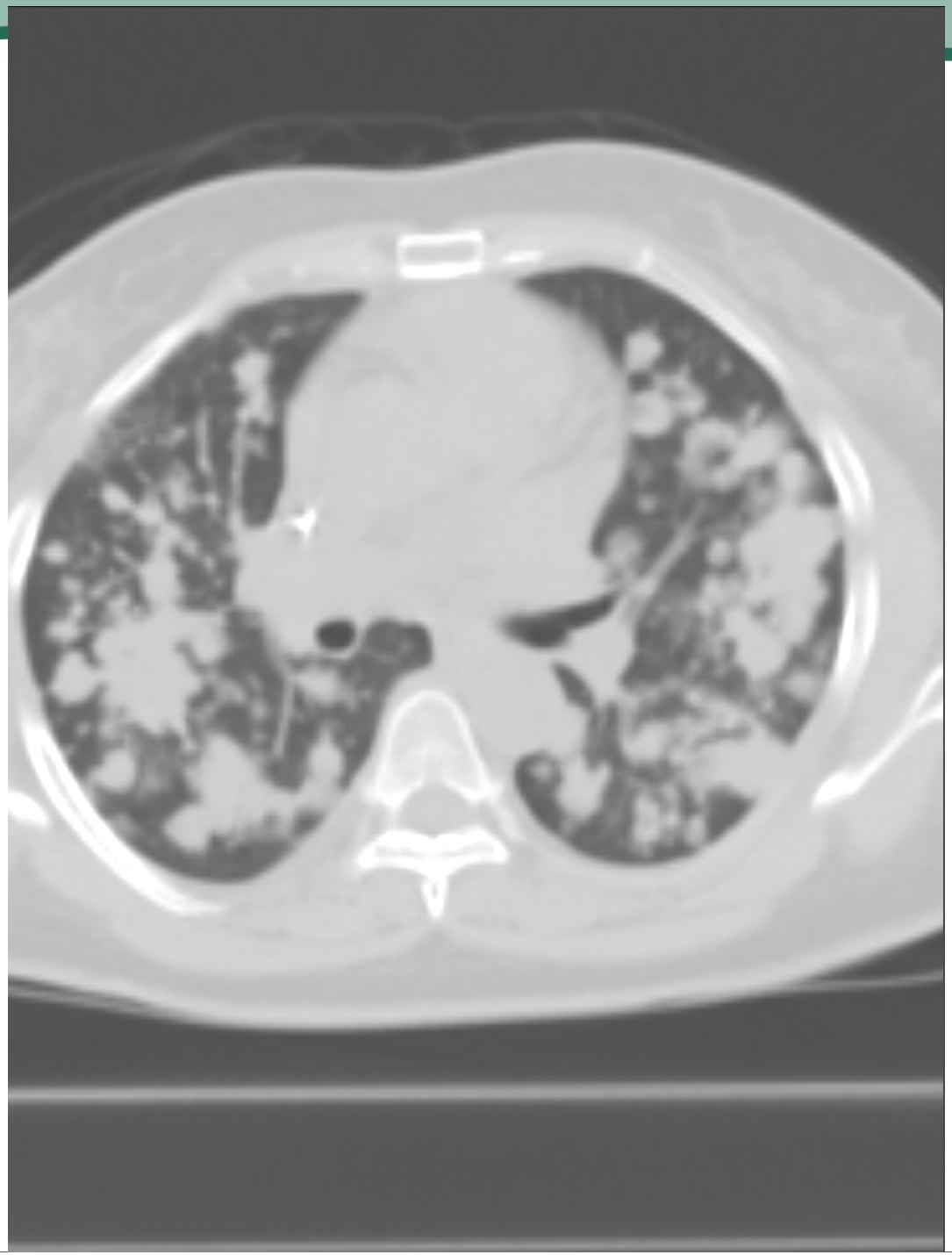
- https://vimeo.com/266186220

My Patient

Interventional Pulmonology

Cancer Treatment Centers of America®

Winning the fight against cancer, every day.®



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Genomic Test Results

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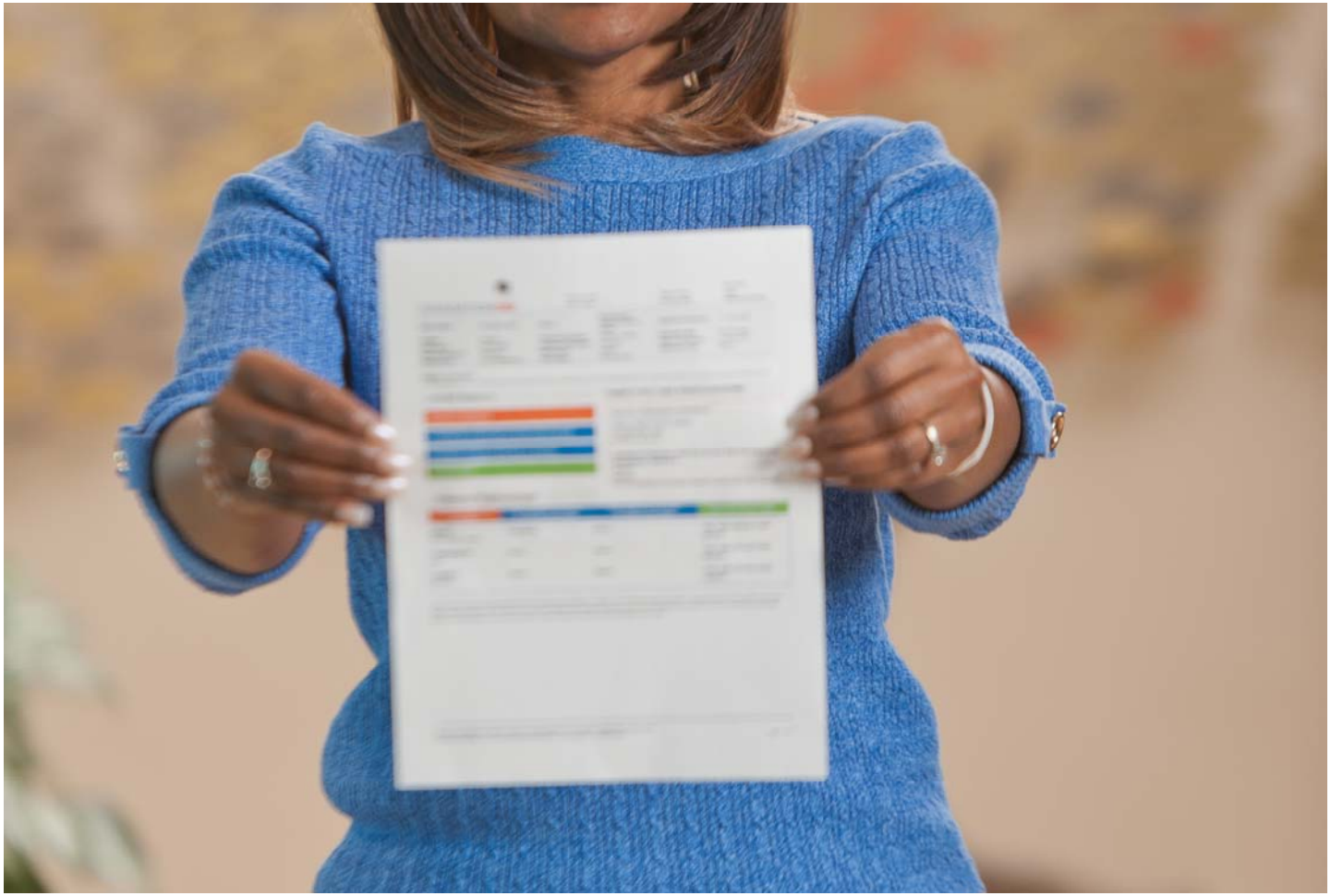

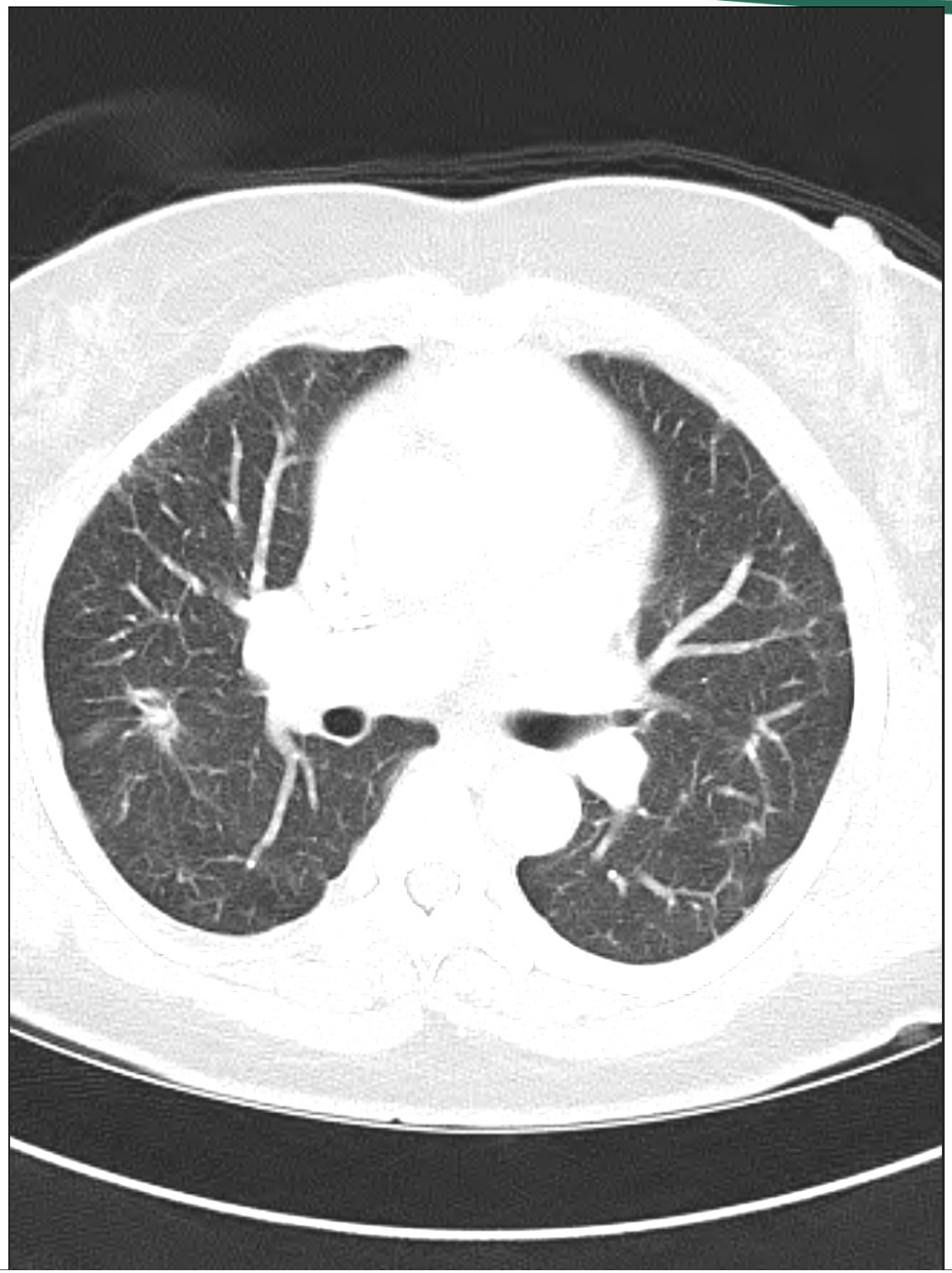

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Questions?

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