# Current Management of the Incidental Nodule in Chest CT and the Need for Artificial Intelligence

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# Financial and Research Disclosures:

- Dr. David Yankelevitz is a named inventor on a number of patents and patent applications relating to the evaluation of diseases of the chest including measurement of nodules. Some of these, which are owned by Cornell Research Foundation (CRF) are non-exclusively licensed to General Electric. As an inventor of these patents, Dr. Yankelevitz is entitled to a share of any compensation which CRF may receive from its commercialization of these patents
- A shareholder in Accumetra LLC
- Medical Advisory Board Carestream Health
- Medical Advisory Board LungLife AI
- Medical Advisory Board Median Technology
- Medical Advisory Board and shareholder HeartLung
- Advisory Panel Pfizer

# Q: what is an incidental pulmonary nodule?

- An incidental pulmonary nodule (IPN) is a small, round or oval-shaped lesion in the lung that is found incidentally, usually during a chest imaging performed for another reason. IPNs are commonly found on CT scans, although they can also be identified on chest X-rays, MRI, or PET scans. IPNs can be benign or malignant, and their significance can range from being of no clinical significance to being a sign of lung cancer.
- It's important to note that not all IPNs are cancerous, many are benign, such as granulomas, hamartomas, and even hematomas, but some may be malignant such as primary lung cancer or metastasis from other primary site. And because of the potential for malignancy, the management and follow-up of IPNs is important. Due to the potential for malignancy, IPNs are typically followed with repeat imaging to monitor for growth, which can help to distinguish benign from malignant nodules.
- It is important to have a proper evaluation and management of IPNs, including a thorough patient history, physical examination, and appropriate imaging studies. The radiologist and pulmonologist in consultation with the patient will determine the best follow-up plan, which may include repeat imaging, biopsy, or other diagnostic tests.

# Q: how can artificial intelligence be used to manage incidental pulmonary nodules?

- Artificial intelligence (AI) can be used to assist in the management of incidental pulmonary nodules by analyzing medical images and providing automated recommendations for further testing and follow-up. This can include using deep learning algorithms to classify nodules as benign or malignant, determining their size and growth rate, and identifying any suspicious features. Additionally, AI can be used to help radiologists and other medical professionals evaluate and manage large numbers of pulmonary nodules more efficiently, potentially improving the accuracy and speed of diagnosis.
- AI can be used to help identify which nodules are most likely to be benign and which ones require further evaluation. This can be done by analyzing the characteristics of the nodules, such as their size, shape, and texture, as well as any associated changes in the surrounding lung tissue. AI can also be used to monitor the growth or shrinkage of nodules over time, which can help determine whether they are benign or malignant and whether they require further treatment. Additionally, AI can be used to analyze large

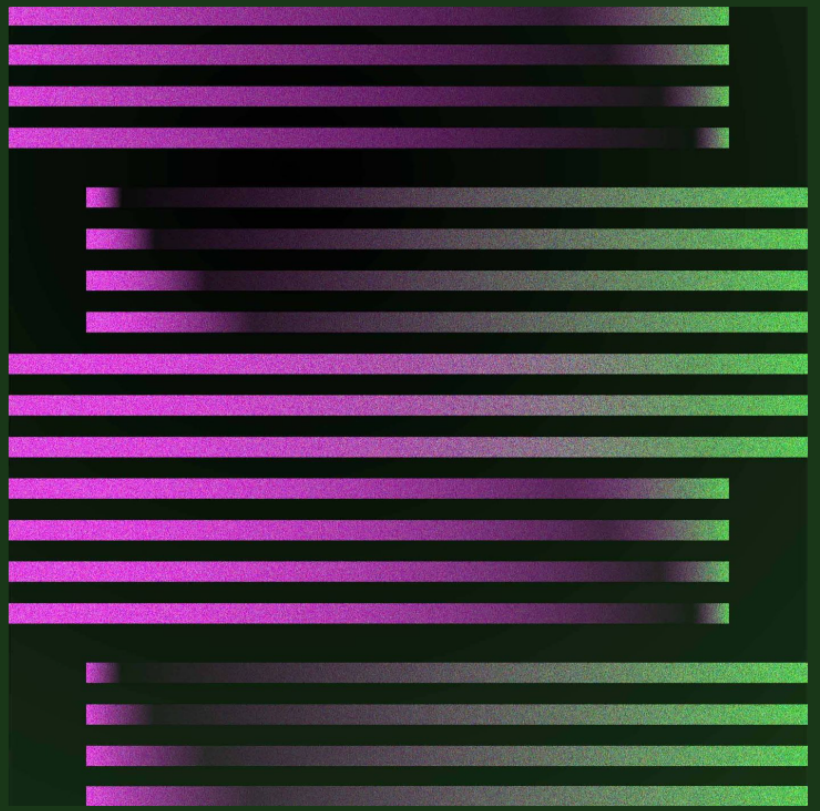
# Q: is AI better than humans at evaluating nodules?

- It is not accurate to say that AI is better than humans at evaluating pulmonary nodules, as both have their own strengths and limitations. AI algorithms can be trained on large datasets of medical images to identify patterns and characteristics that distinguish benign from malignant nodules, and can help to more efficiently and accurately evaluate large numbers of nodules. However, AI is not capable of the same level of visual perception and judgement as a human radiologist, who can take into account the patient's history, symptoms and other clinical information when interpreting the images.
- It is also worth noting that AI-algorithms performance can be affected by the quality of the training data, and the accuracy of the algorithm can be limited by the availability and quality of the data used to train it. Additionally, AI algorithms may not always agree with human experts and may not be able to explain the reasoning behind their predictions.
- Therefore, it is recommended to use AI as a tool to support radiologists and other medical professionals, rather than replacing them. AI-aided diagnosis should always be verified by a radiologist or pulmonologist, and it's important to keep in mind that it has limitations and is not a substitute for human expertise.

# ChatGPT: Optimizing Language Models for Dialogue

We've trained a model called ChatGPT which interacts in a conversational way. The dialogue format makes it possible for ChatGPT to answer followup questions, admit its mistakes, challenge incorrect premises, and reject inappropriate requests. ChatGPT is a sibling model to InstructGPT, which is trained to follow an instruction in a prompt and provide a detailed response.

TRY CHATGPT ↗



November 30, 2022
13 minute read

NORC at the University of Chicago

# Only 14% of Cancers Are Detected Through a Preventive Screening Test

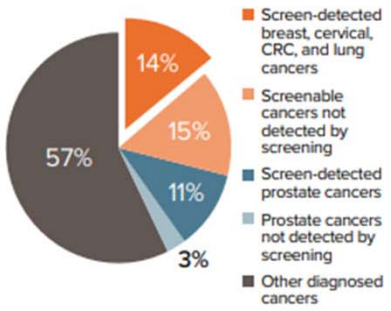
Improved cancer screening has the potential to detect cancers earlier, when treatment is more likely to improve outcomes and save lives. However, at present, only 14% of diagnosed cancers are detected by screening with a recommended screening test.

## Calculating Percent of Cancers Detected by Screening (PCDS)

Until now, the proportion of cancers detected each year by a preventive screening test has not been calculated. NORC at the University of Chicago developed a method to calculate this statistic, which we call the percent of cancers detected by screening (PCDS). We estimate PCDS using annual incidence data (National Cancer Institute), self-reported preventive screening data (National Health Information Survey), screening test efficacy (published literature), and state cancer statistics (Behavioral Risk Factor Surveillance System).

**TOTAL CANCERS IN THE UNITED STATES**

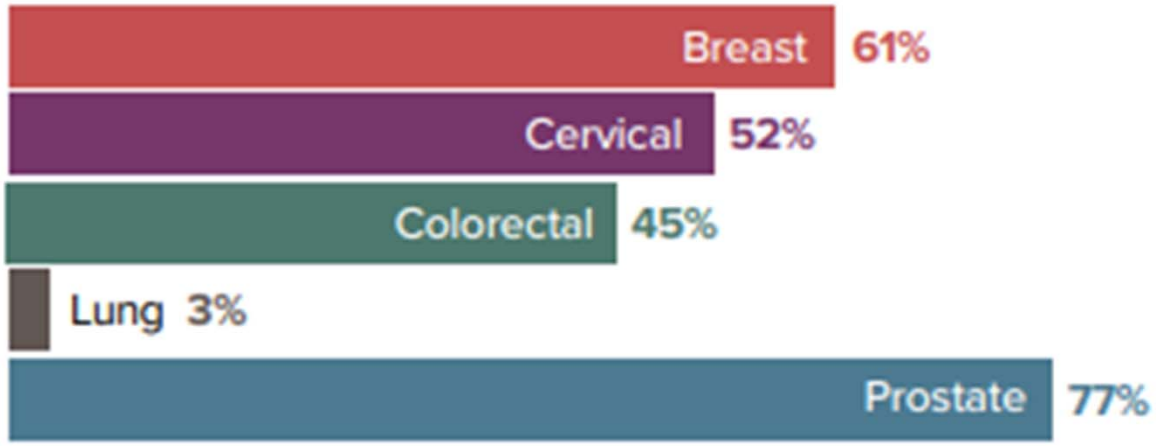
### Percent of Diagnosed Cancers Detected by Screening




## Cancer Screening Tests

Regular screening is recommended[1] for breast, cervical, and colorectal cancers, as well as lung cancer screening for people who are at a high risk. Together, in 2017, these cancers made up 29% of all diagnosed cancers and 25% of all cancer deaths in the US.[2] Though not broadly recommended, prostate-specific antigen (PSA) tests can also screen for prostate cancer, which accounts for another 14% of all cancers in the US. The other 57% of cancers do not have recommended screening tests and account for 70% of cancer deaths in the US.

# Percent of Cancers Detected by Screening, by Cancer Type




| | | | | | |
|---|---|---|---|---|---|
| **NY** | 12.2% | 52.0% | 42.7% | 46.4% | 2.6% |
| **FL** | 16.2% | 77.0% | 43.0% | 56.9% | 1.9% |

CANCER

# Most People at Risk for Lung Cancer Never Get Screened: Here's How to Fix That

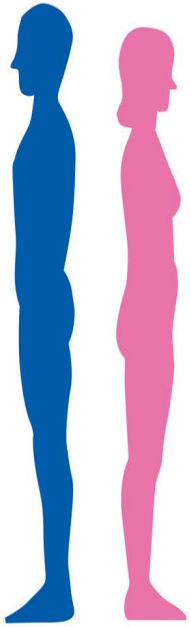
U.S. lung cancer screening guidelines miss people who have never smoked, as well as many women and Black people. Expanding outreach and eligibility could help

By Simar Bajaj on September 6, 2022

# Cancer statistics, 2022

**Estimated New Cases**

| Males | | | | Females | | |
|---|---|---|---|---|---|---|
| Prostate | 268,490 | 27% | | Breast | 287,850 | 31% |
| Lung & bronchus | 117,910 | 12% | | Lung & bronchus | 118,830 | 13% |
| Colon & rectum | 80,690 | 8% | | Colon & rectum | 70,340 | 8% |
| Urinary bladder | 61,700 | 6% | | Uterine corpus | 65,950 | 7% |
| Melanoma of the skin | 57,180 | 6% | | Melanoma of the skin | 42,600 | 5% |
| Kidney & renal pelvis | 50,290 | 5% | | Non-Hodgkin lymphoma | 36,350 | 4% |
| Non-Hodgkin lymphoma | 44,120 | 4% | | Thyroid | 31,940 | 3% |
| Oral cavity & pharynx | 38,700 | 4% | | Pancreas | 29,240 | 3% |
| Leukemia | 35,810 | 4% | | Kidney & renal pelvis | 28,710 | 3% |
| Pancreas | 32,970 | 3% | | Leukemia | 24,840 | 3% |
| **All Sites** | **983,160** | **100%** | | **All Sites** | **934,870** | **100%** |

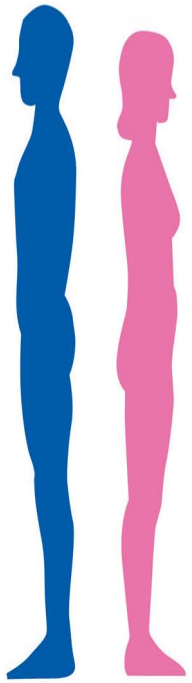


**CA A Cancer J Clinicians, Volume: 72, Issue: 1, Pages: 7-33, First published: 12 January 2022, DOI: (10.3322/caac.21708)**

# Cancer statistics, 2022

**Estimated Deaths**

| Males | | | Females | | |
|---|---|---|---|---|---|
| Lung & bronchus | 68,820 | 21% | Lung & bronchus | 61,360 | 21% |
| Prostate | 34,500 | 11% | Breast | 43,250 | 15% |
| Colon & rectum | 28,400 | 9% | Colon & rectum | 24,180 | 8% |
| Pancreas | 25,970 | 8% | Pancreas | 23,860 | 8% |
| Liver & intrahepatic bile duct | 20,420 | 6% | Ovary | 12,810 | 4% |
| Leukemia | 14,020 | 4% | Uterine corpus | 12,550 | 4% |
| Esophagus | 13,250 | 4% | Liver & intrahepatic bile duct | 10,100 | 4% |
| Urinary bladder | 12,120 | 4% | Leukemia | 9,980 | 3% |
| Non-Hodgkin lymphoma | 11,700 | 4% | Non-Hodgkin lymphoma | 8,550 | 3% |
| Brain & other nervous system | 10,710 | 3% | Brain & other nervous system | 7,570 | 3% |
| **All Sites** | **322,090** | **100%** | **All Sites** | **287,270** | **100%** |



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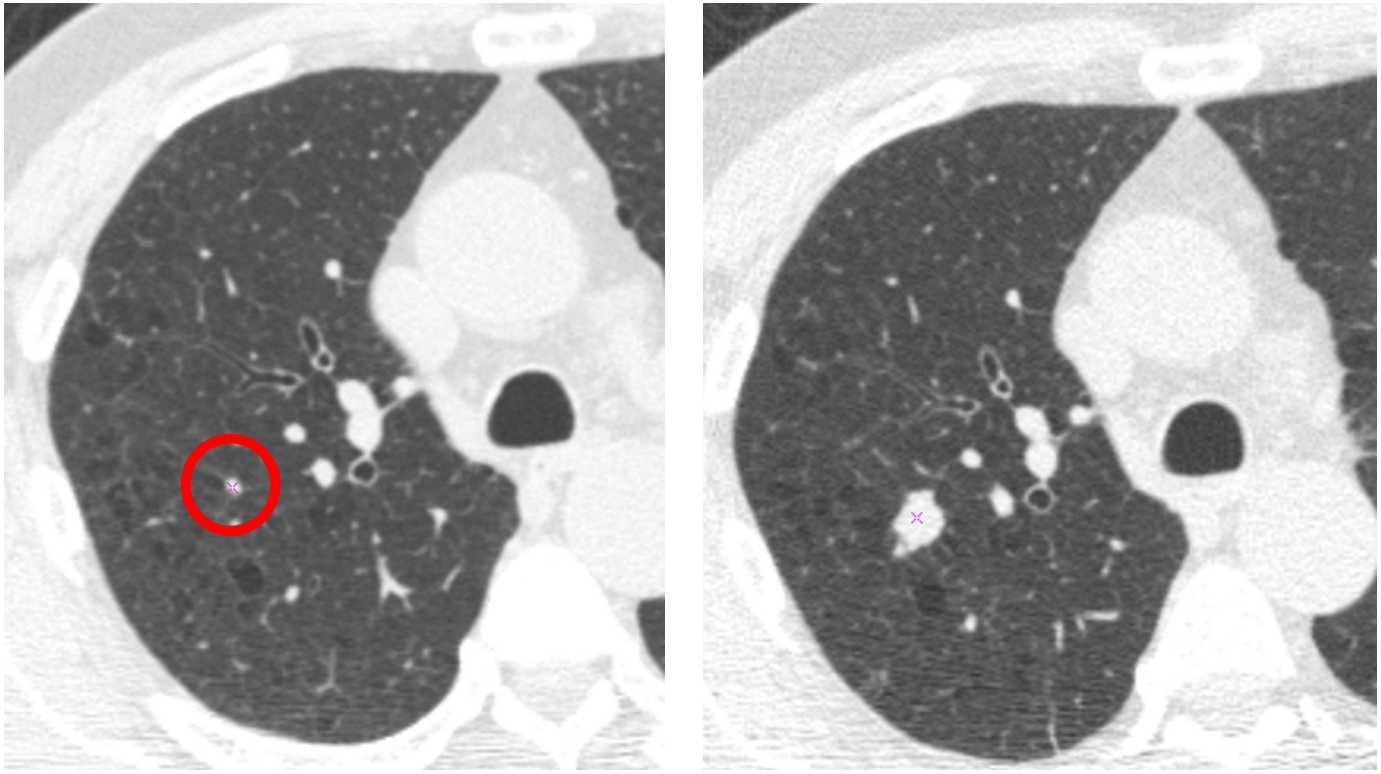
# Nodule Prevalence

- 1950's, 0.2% of CXRs
- Over 1.5 million/year in United States
- Chest CT approximately 30%
- Baseline screening studies, > 50%

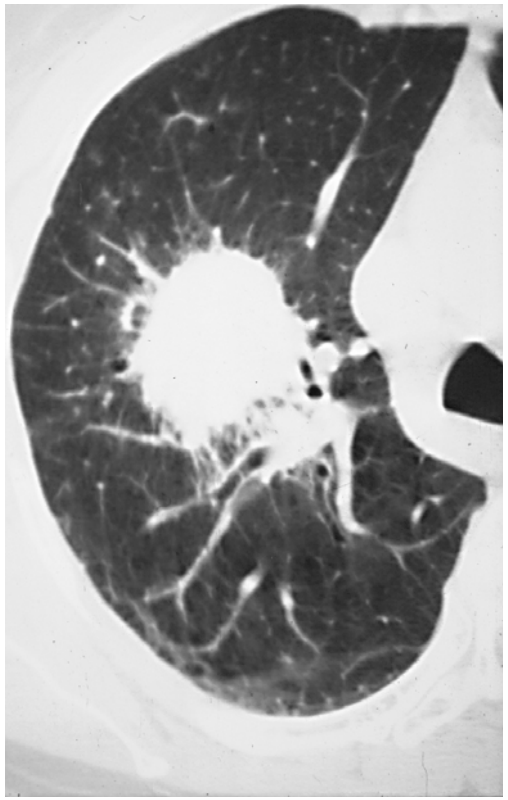
Gould M. AJRCC 2015

# One Year Later



Adenosquamous carcinoma

# Large Solid Nodule



Journal of Health Economics and Outcomes Research

Methodology and Health Care Policy

# No Apparent Workup for most new Indeterminate Pulmonary Nodules in US Commercially-Insured Patients

Bruce S. Pyenson[1*], Carol M. Bazell[1], Michael J. Bellanich[1], Melissa A. Caplen[1], Javier J. Zulueta[2,3]

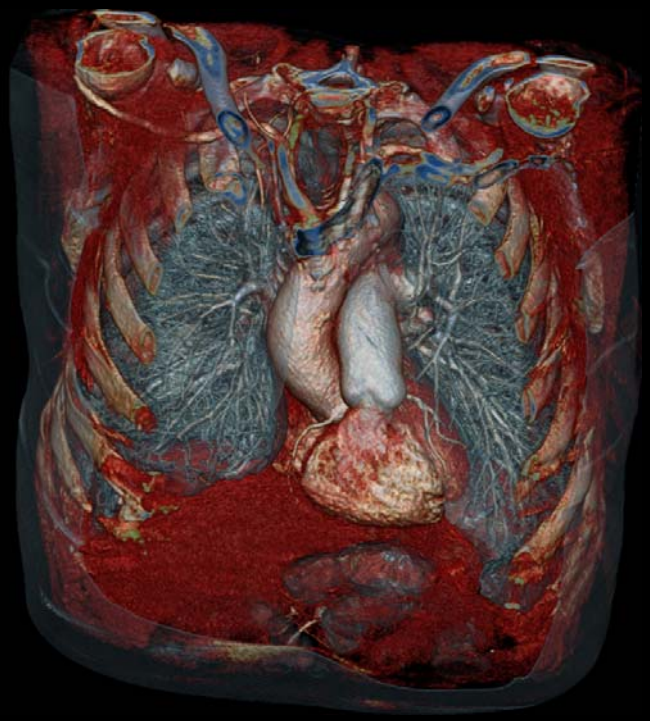
**Conclusions:** The majority of commercially-insured members with newly identified IPNs do not appear to have any guideline-recommended workup, despite a low incremental cost of such workup services on a population basis.

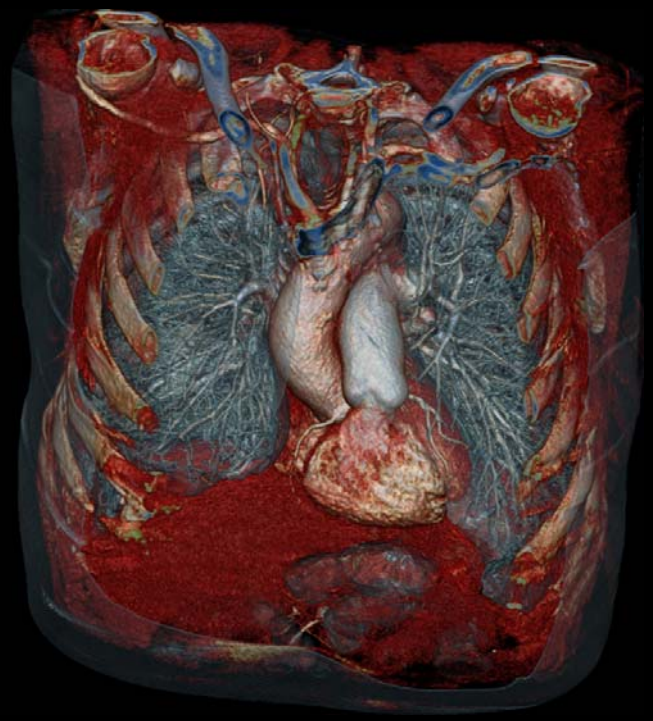
JHEOR: 2019

SOMATOM Definition Flash
Split-second thorax

SIEMENS

- **Conventional**



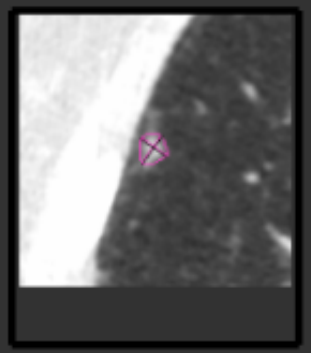


NOT FOR CLINICAL USE

AIRC Research Chest CT Explore
Lung Lesions

L1

Right Upper Lobe

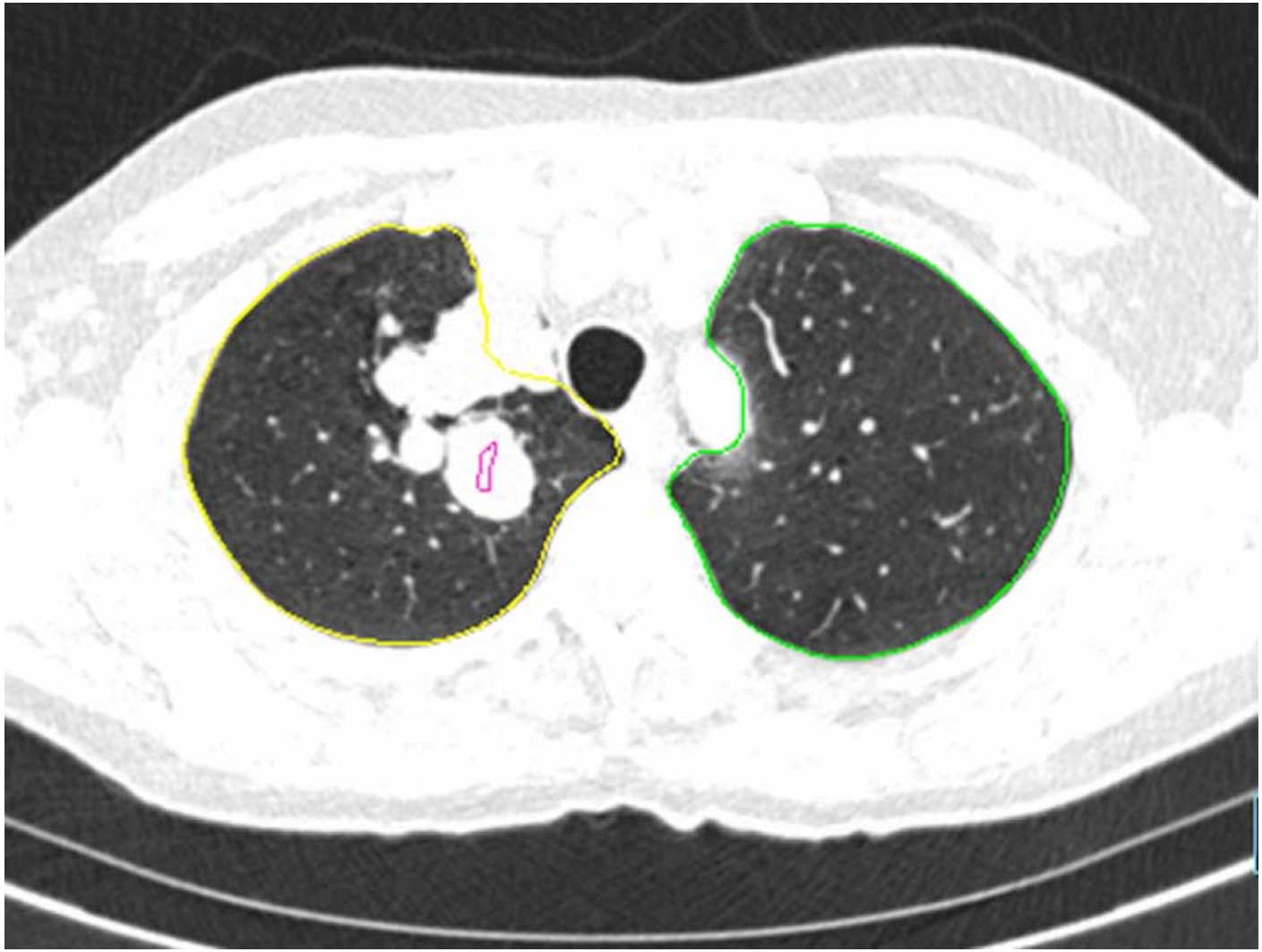


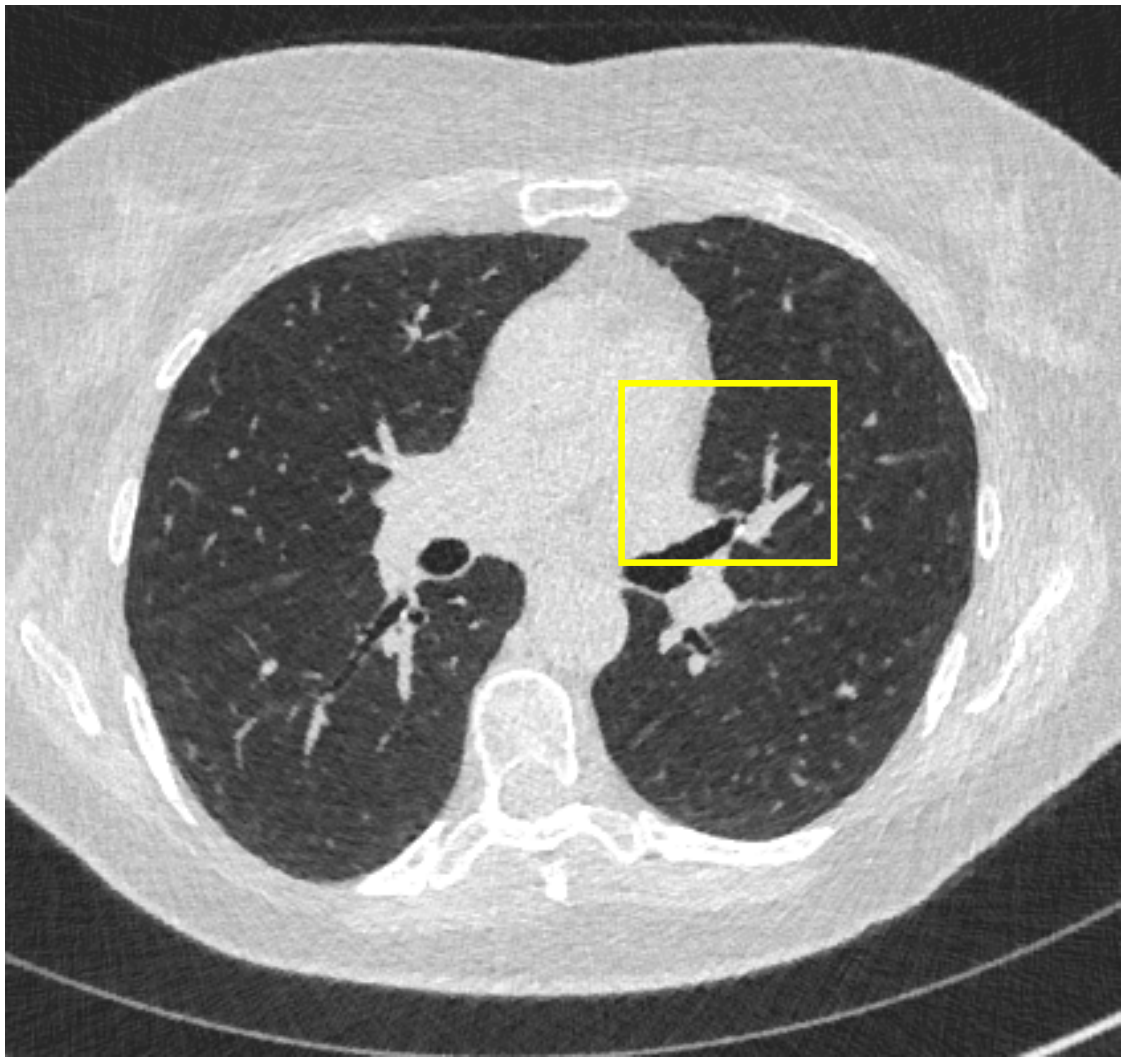
2022-11-11 Current

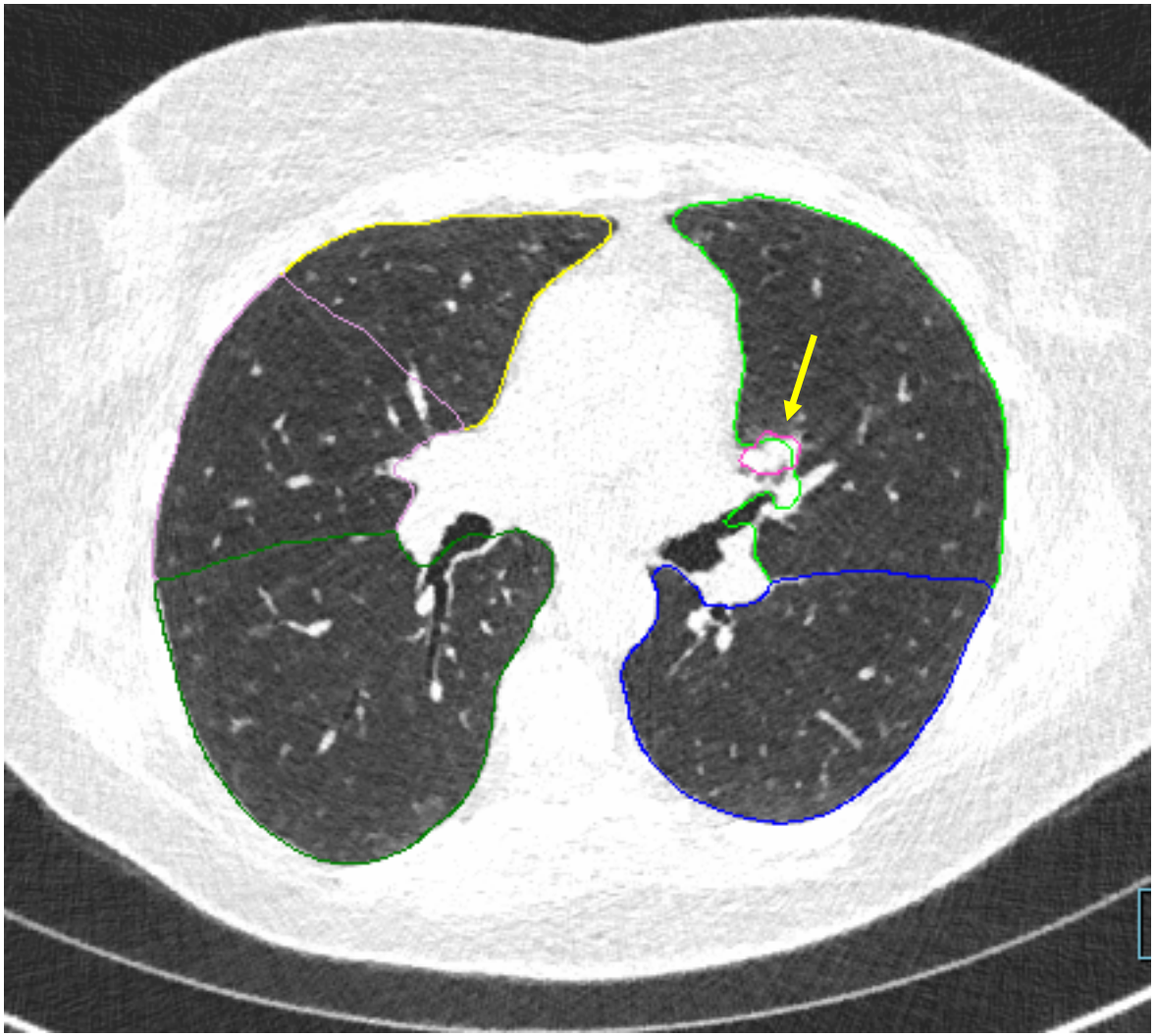
| | |
|---|---|
| Max. 2D Ø [mm] | 8.3 |
| Min 2D Ø [mm] | 7.4 |
| Mean 2D Ø [mm] | 7.8 |
| Max. 3D Ø [mm] | 8.3 |
| Volume [mm³] | 84.6 |
| Characteristics | Solid |
| Lung RADS | 3 |

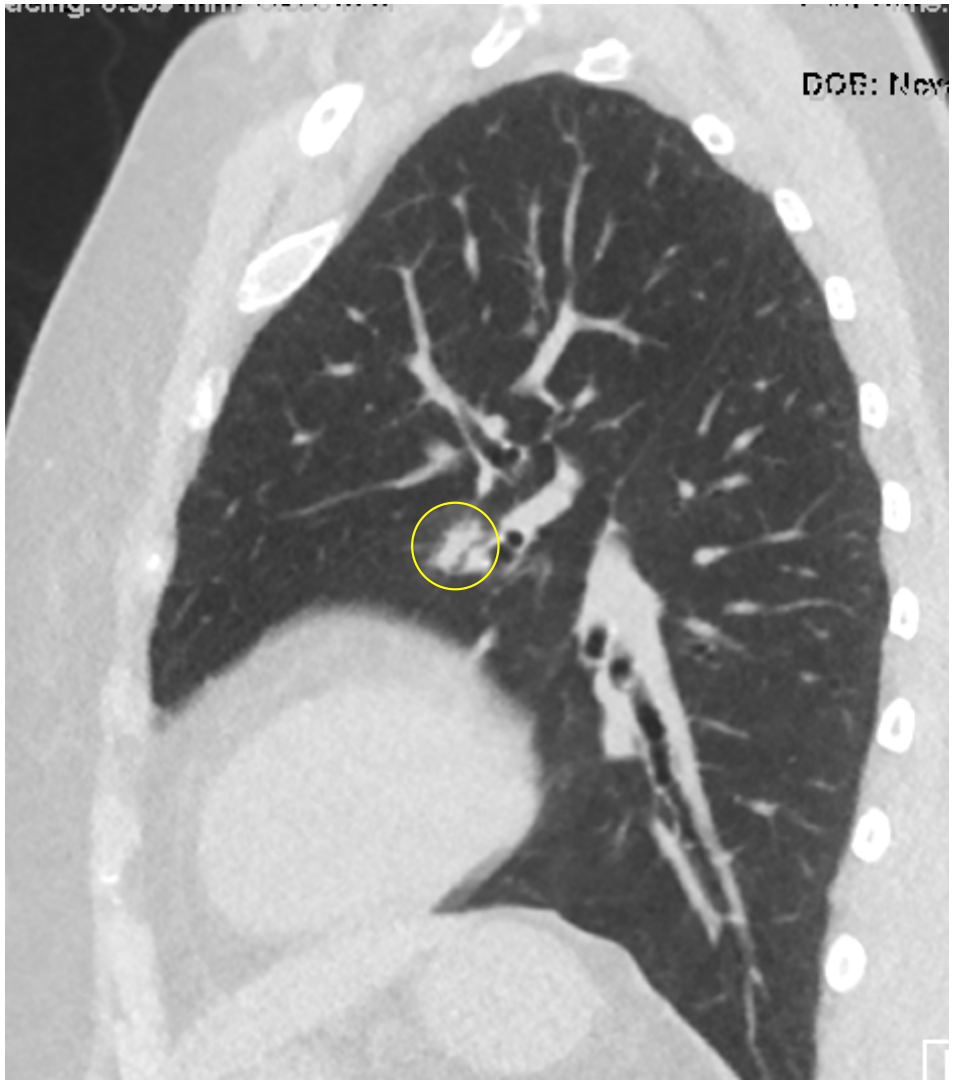
# Detection

- Second read
- Concurrent read
- Primary read and “rule out”



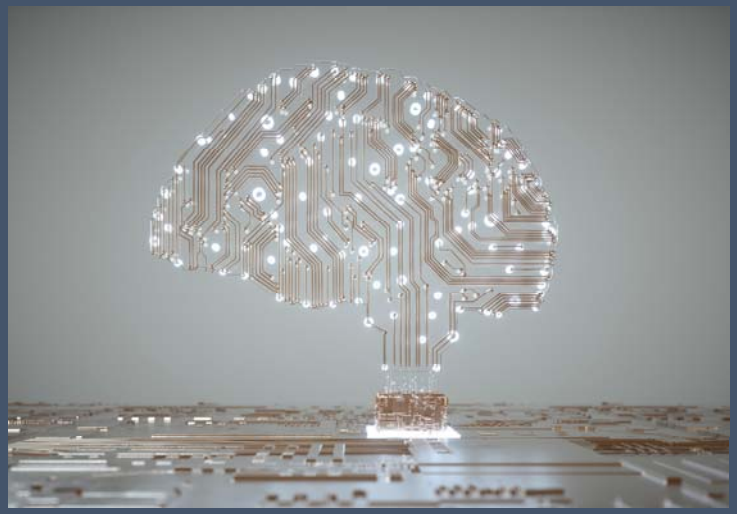





DOB: Nov

# The Need for Data

- Deep learning is one of the most exciting recent advancements in artificial intelligence (AI)
- AlexNet, one of the first deep learning algorithms, was trained on 1.2 million images
- One of the first deep learning system for detection of diabetic retinopathy was trained on over 128,000 retinal images graded by a panel of over 50 ophthalmologists



Krizhevsky A, Sutskever I, Hinton GE. "ImageNet classification with deep convolutional neural networks," Comm ACM, 60(60: 84-90, 2017.
Gulshan V, Peng L, Coram M, et al. "Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs," JAMA, 316(22):2402-2410, 2016.

# Small Solitary Nodules

# Small Solitary Nodules

- Small

# Small Solitary Nodules

- Small
- Solitary

# Small Solitary Nodules

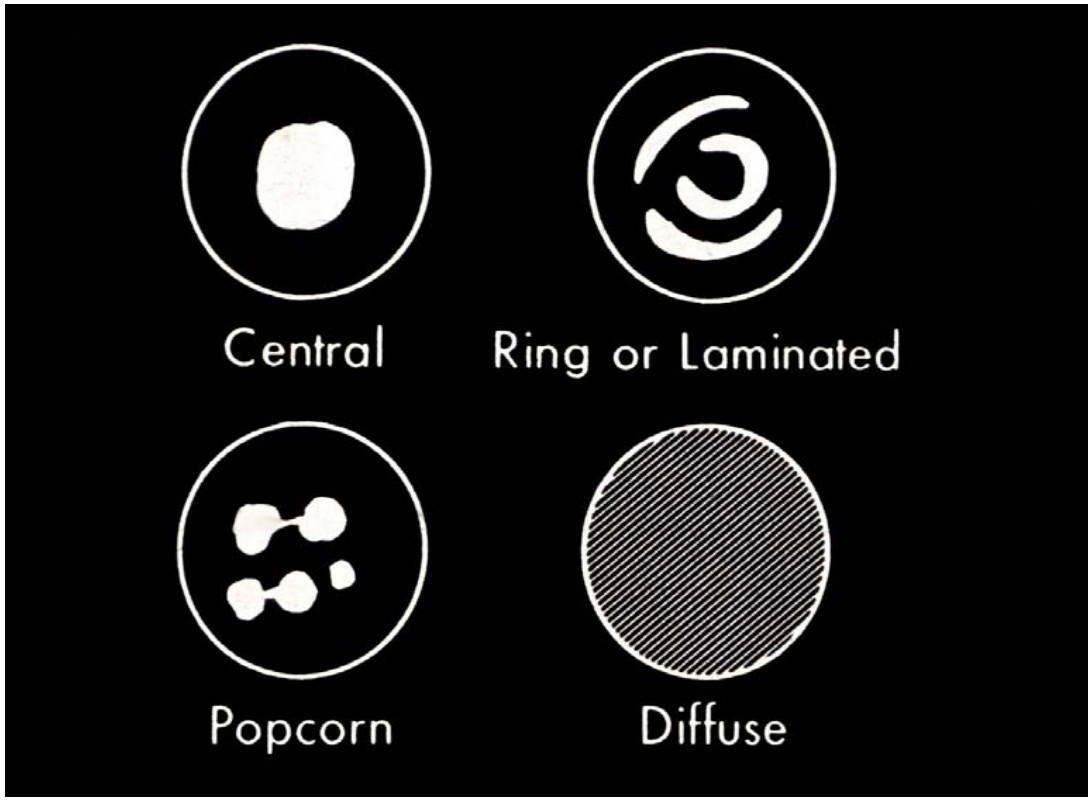
- Small
- Solitary
- Nodule

# Commonly accepted criteria

Benign patterns of calcification

Cancers grow at a malignant rate

# Patterns of Calcification



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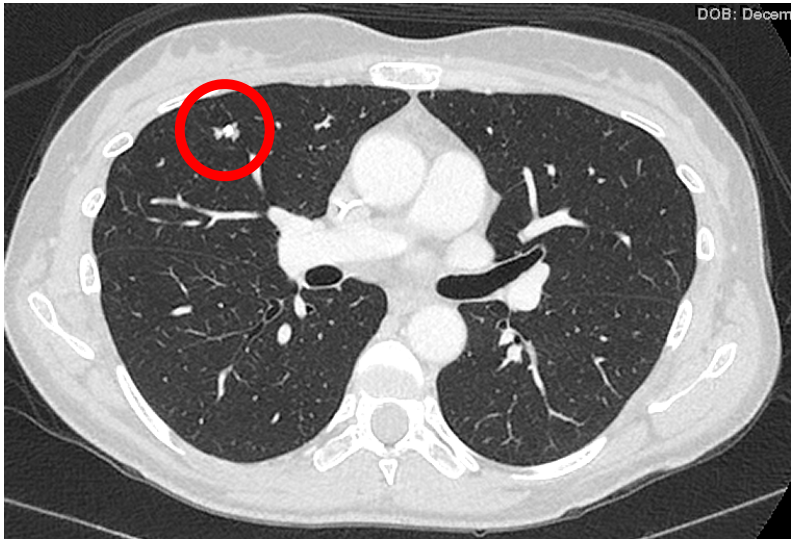

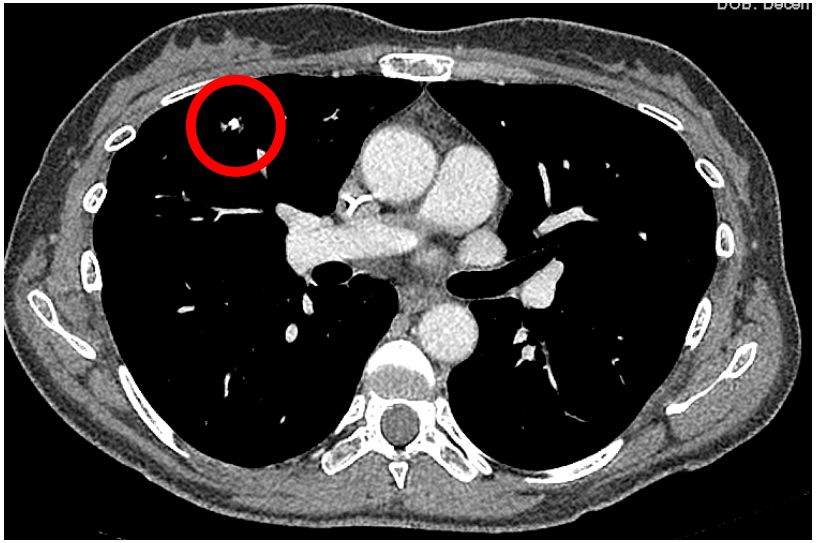

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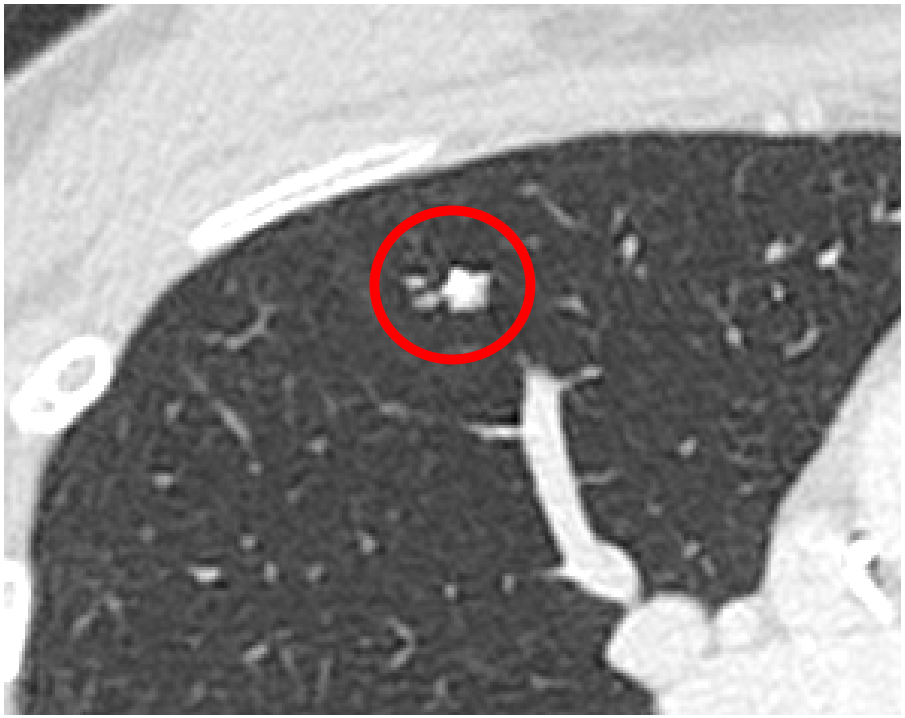

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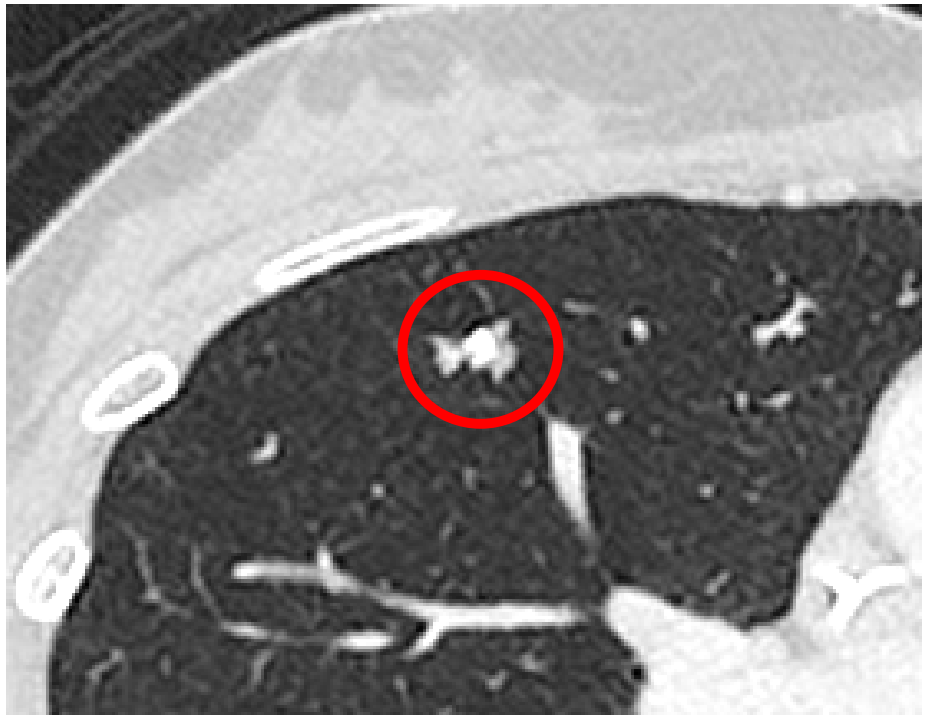

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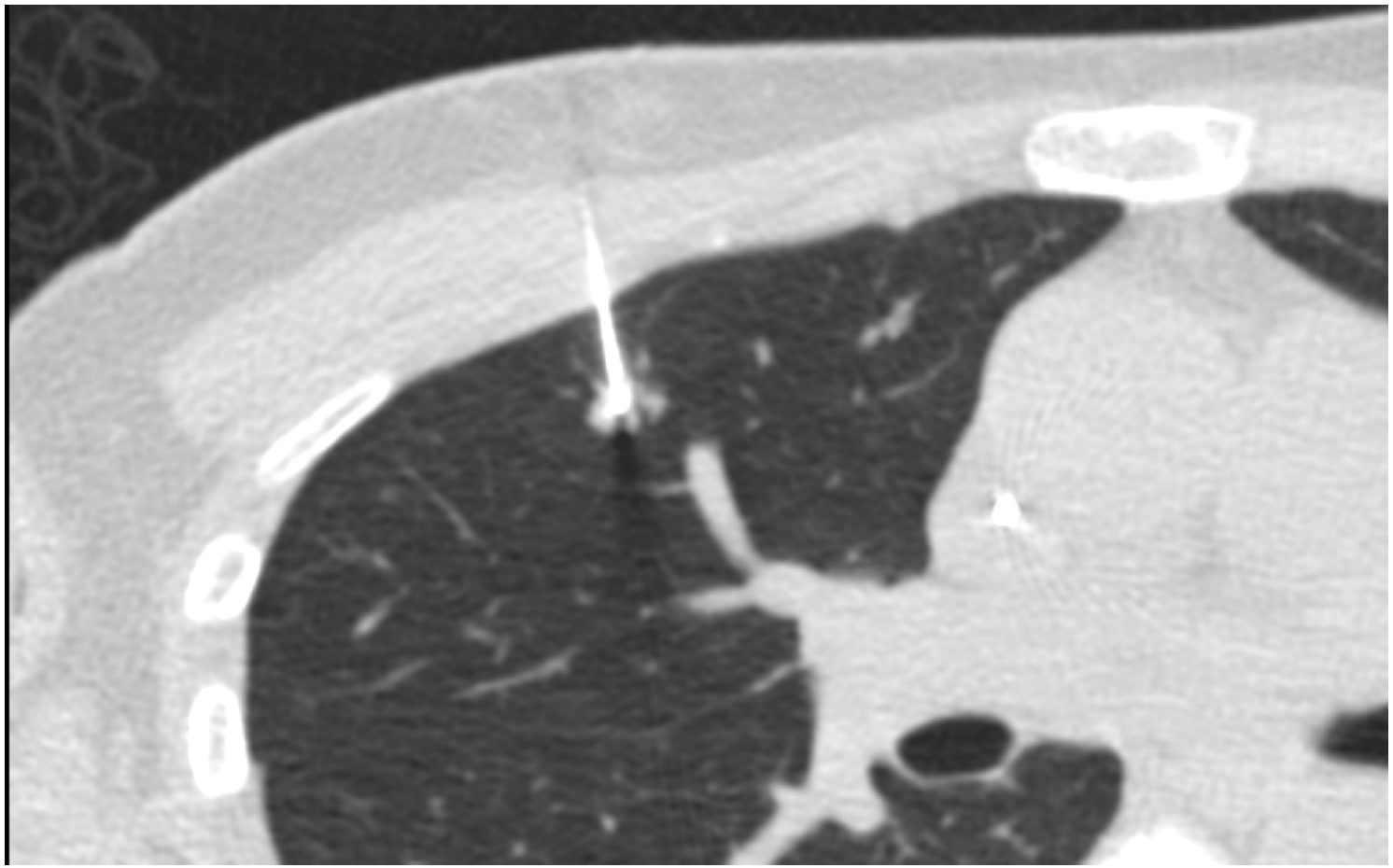
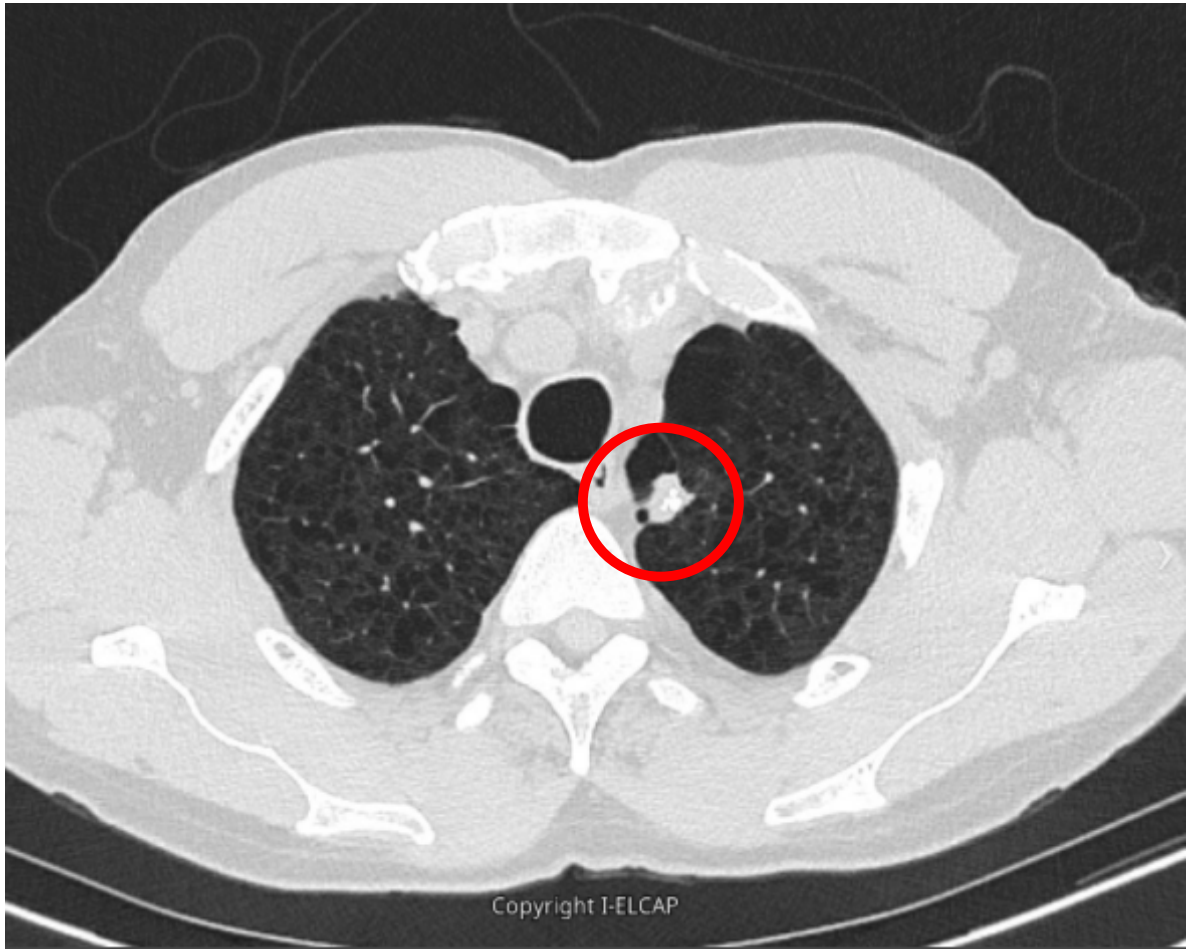
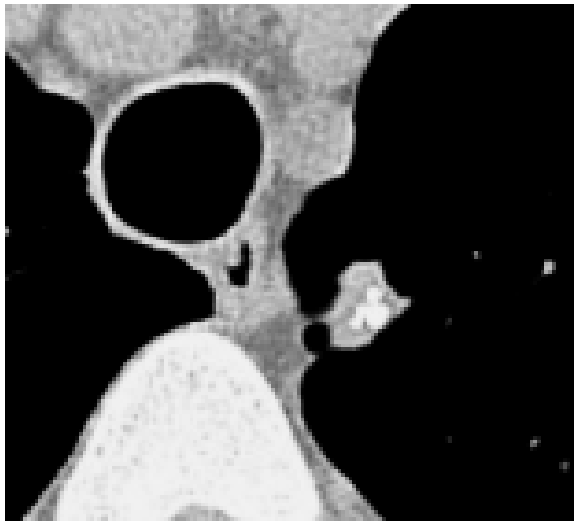
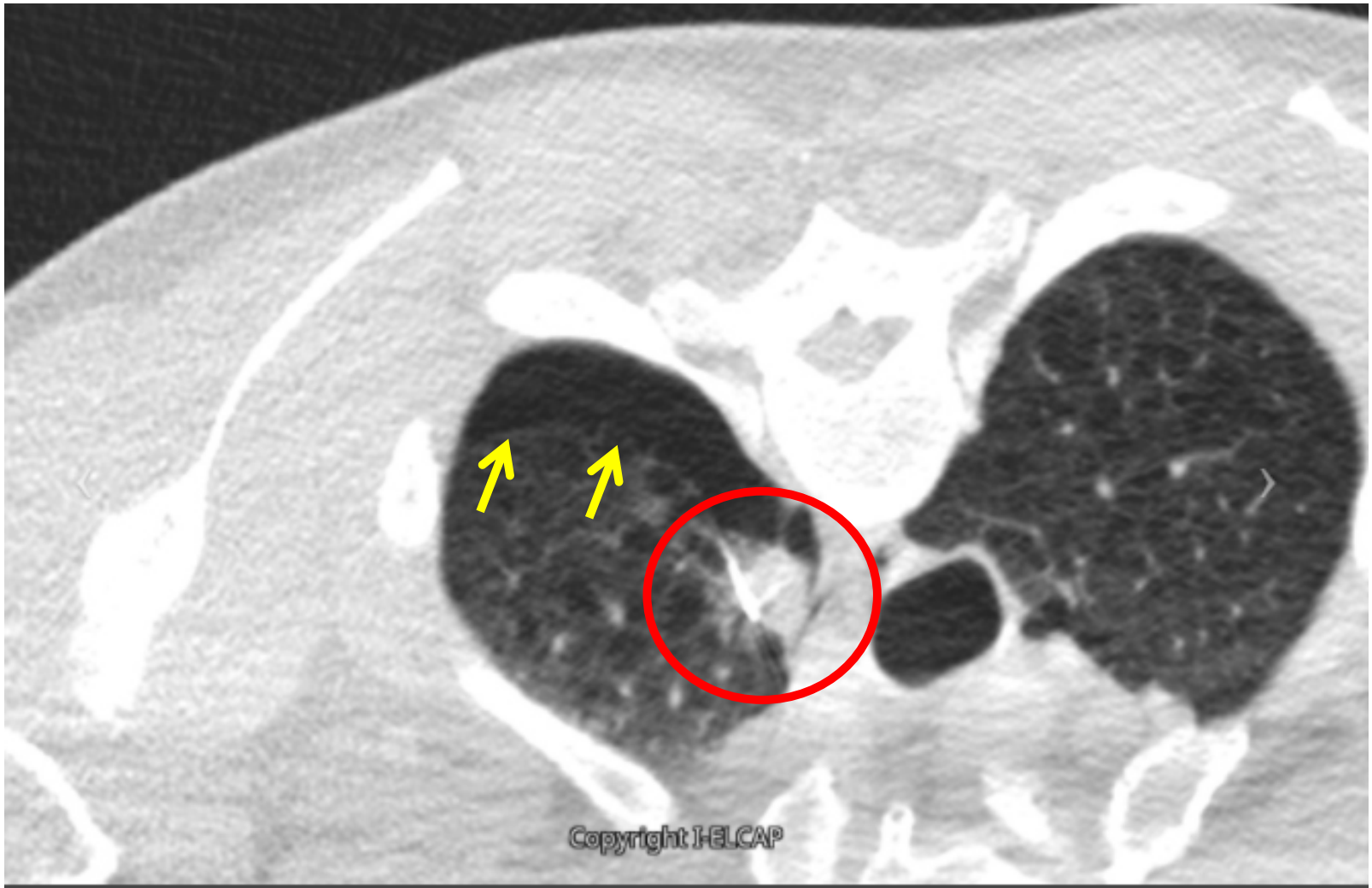


# Dense Central Calcification






Biopsy the left upper lobe nodule.

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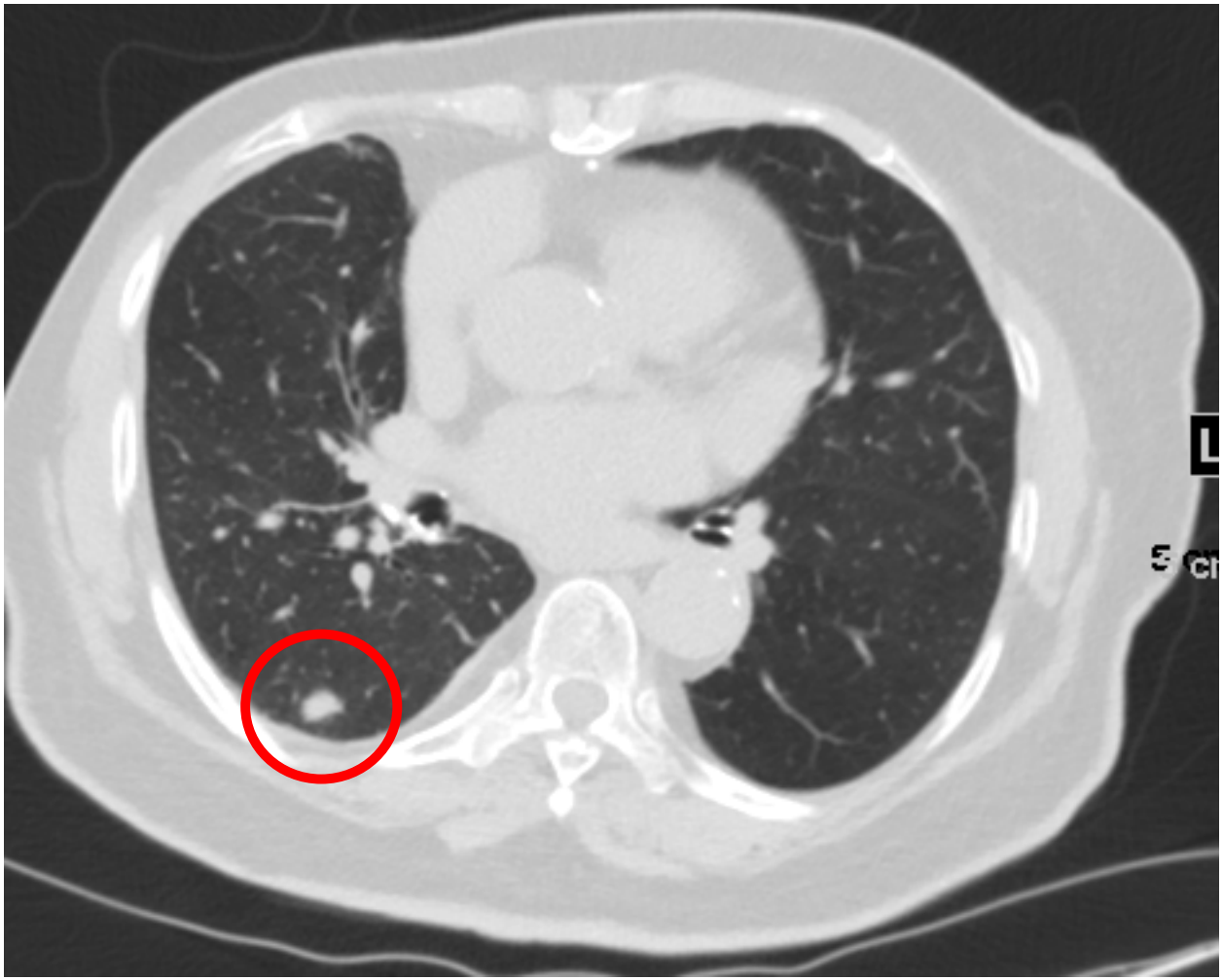

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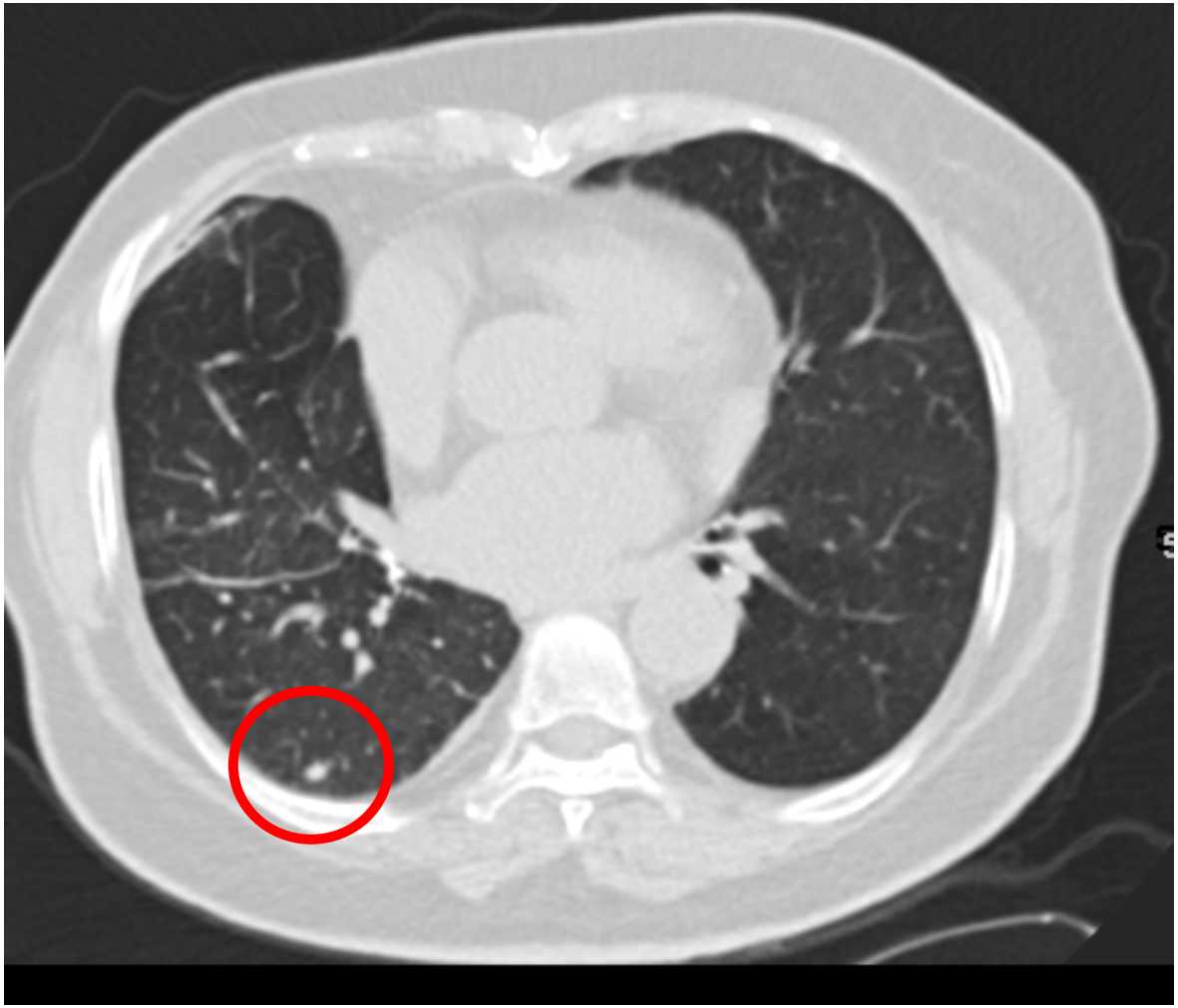

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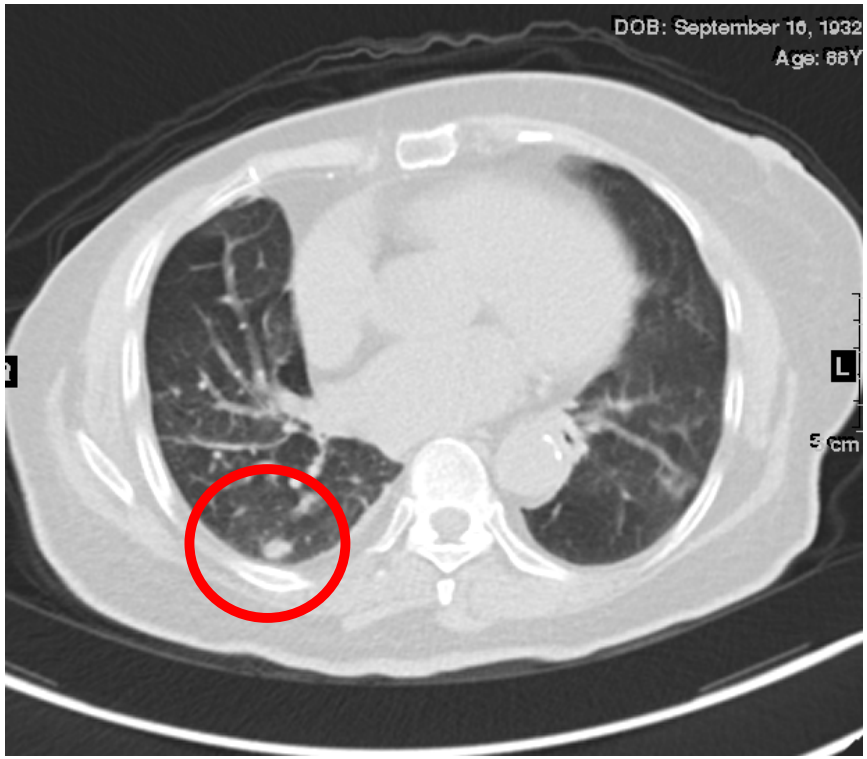


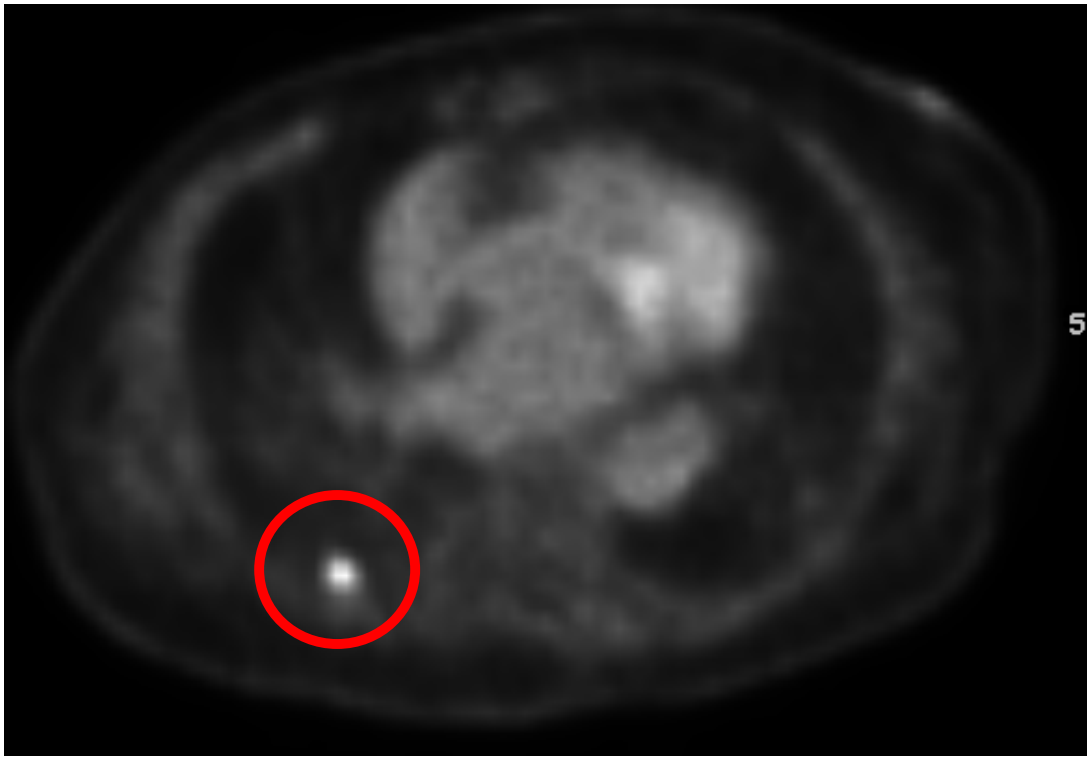

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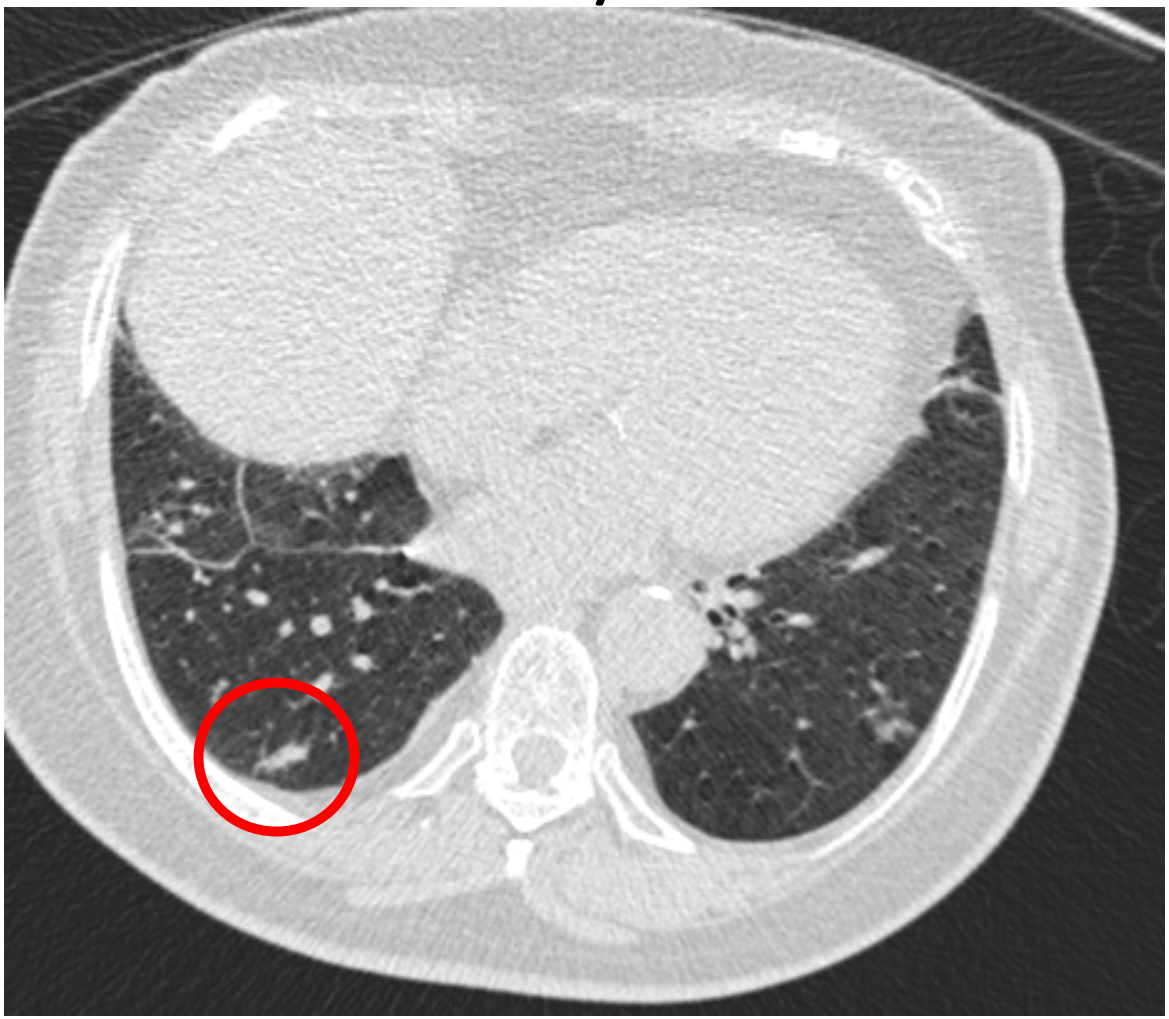
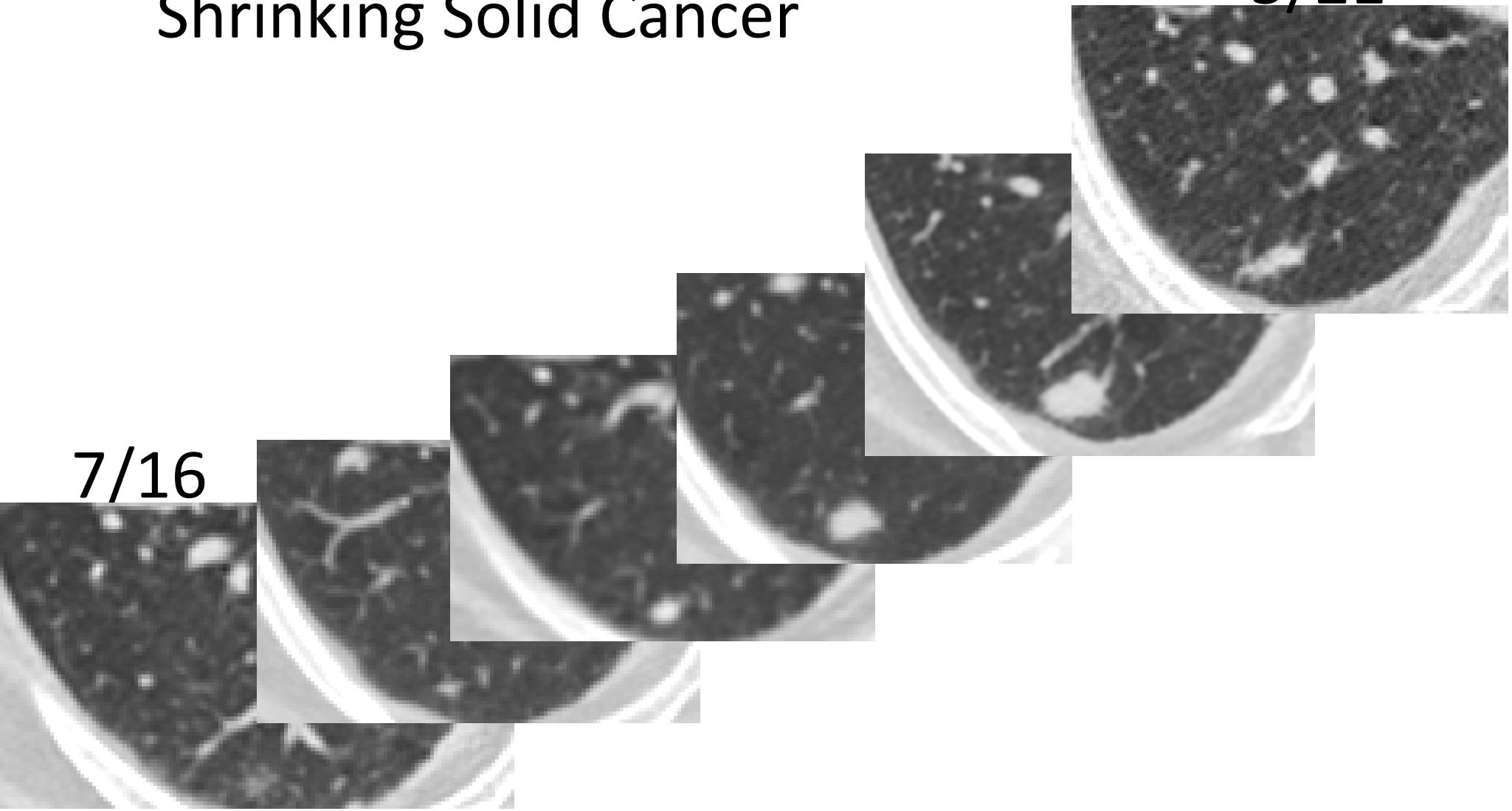


# Shrinking Solid Cancer



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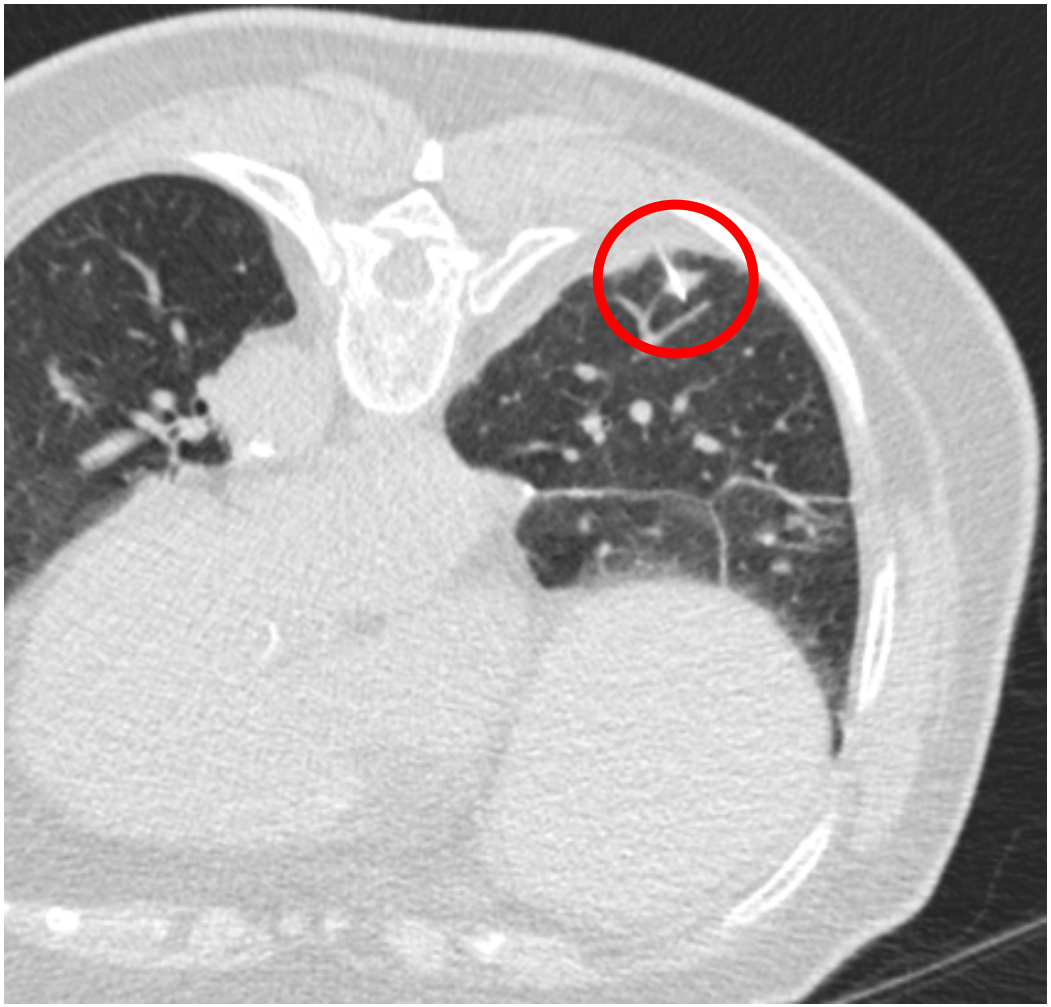


**Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults**

**A: Solid Nodules***

| Nodule Type | Size | | | Comments |
|---|---|---|---|---|
| | <6 mm (<100 mm³) | 6–8 mm (100–250 mm³) | >8 mm (>250 mm³) | |
| 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 | | Comments |
|---|---|---|---|
| | <6 mm (<100 mm³) | ≥6 mm (>100 mm³) | |
| 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). |

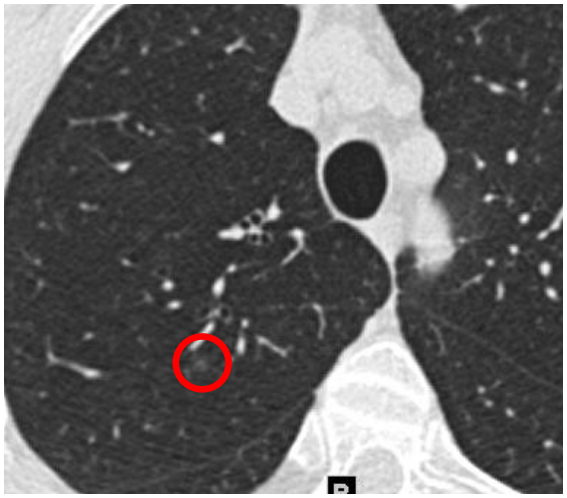
Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

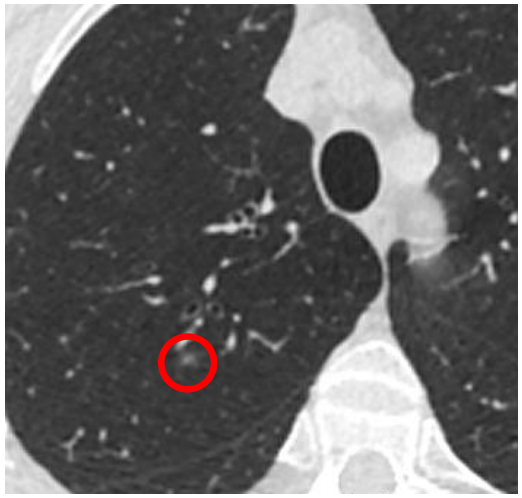
† Consider all relevant risk factors (see Risk Factors).

MacMahon H. Rad 2017

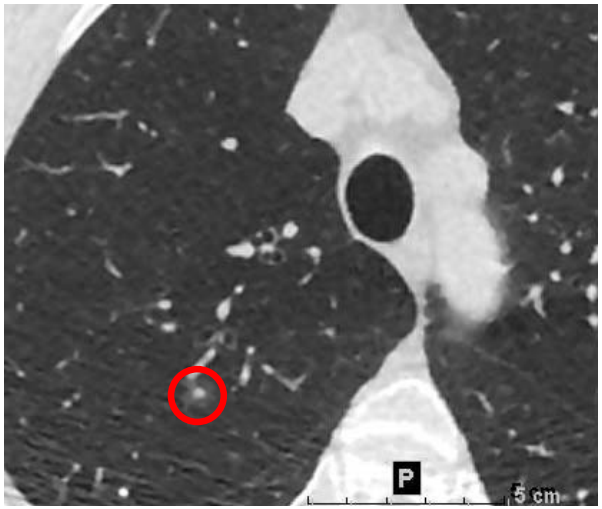
2009



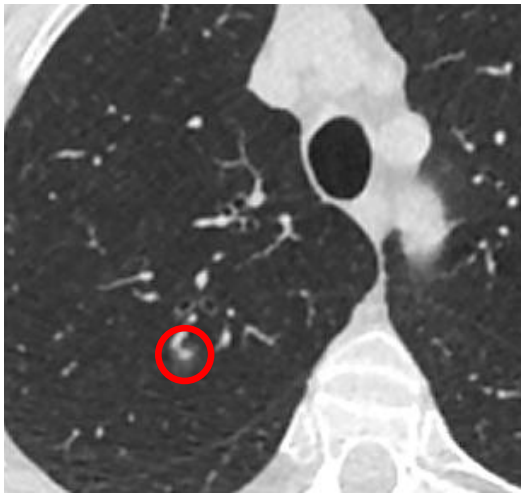
2010



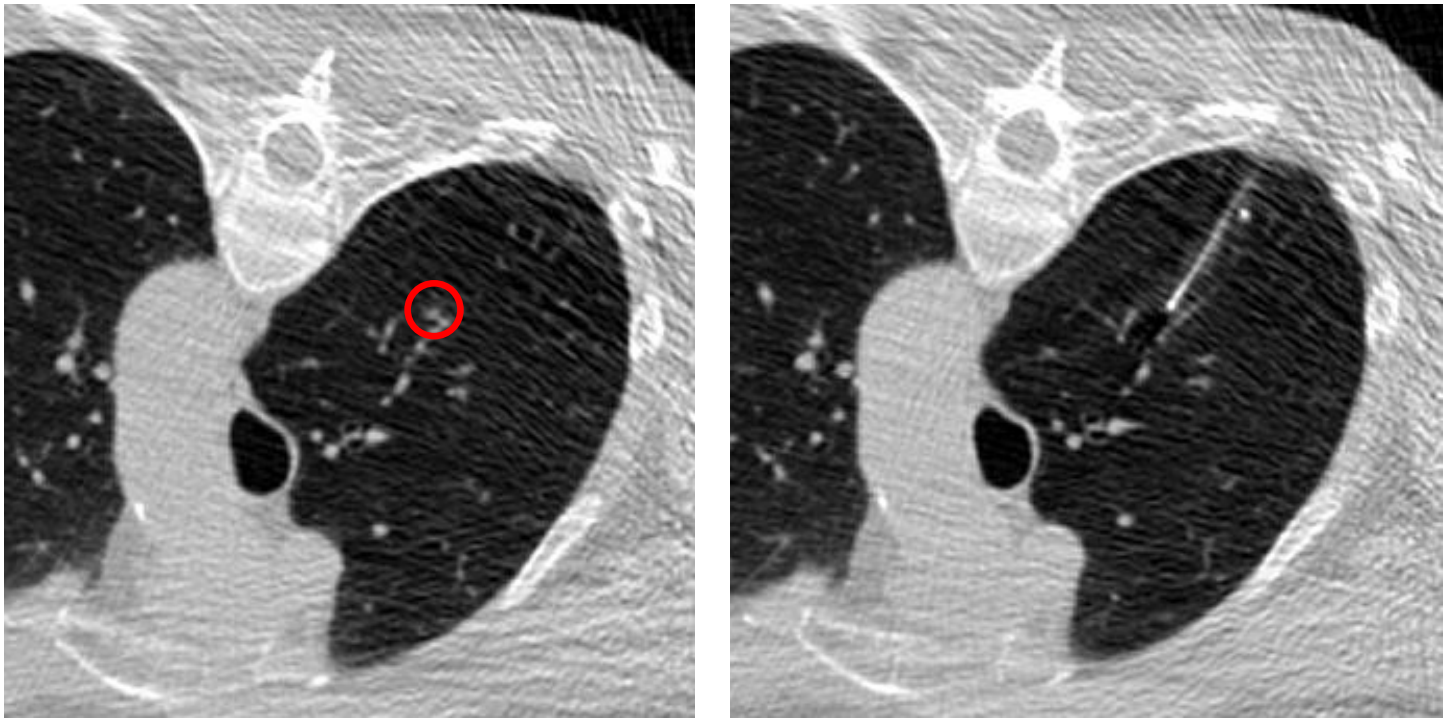
2012




2013



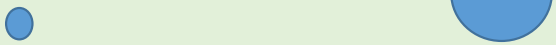
# New Reality of Screen Detected Lung Cancer



# Fundamental Approach

All management protocols for lung nodules, both incidental and in the context of lung cancer screening, are based on their size (volume, average diameter) and consistency (solid, part-solid, nonsolid).

## SOLID NON-CALCIFIED NODULES

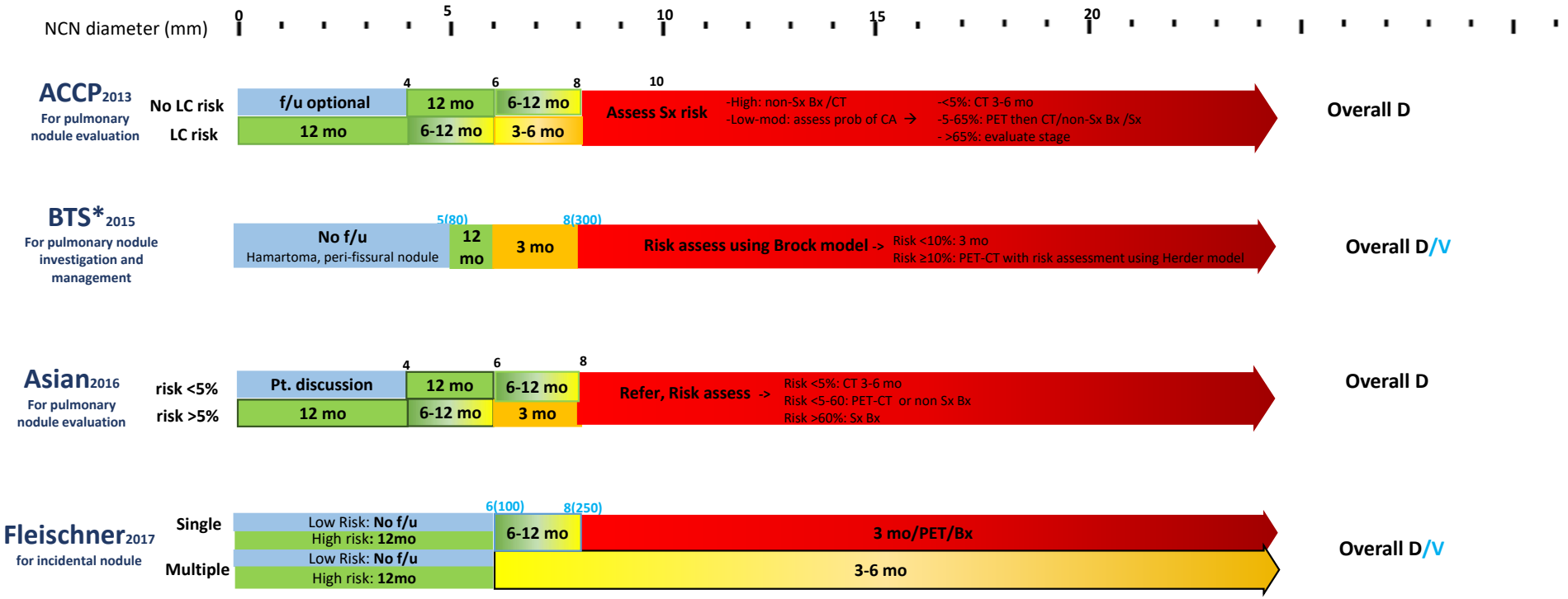


| | | | |
|---|---|---|---|
| **Size** | **Small** | **Intermediate** Typically 4-20 mm | **Large** |
| **Probability of malignancy** | **Low** | **?** | **High** |
| **Recommended Workup** | **Annual repeat** | **Follow-up CT to determine growth (at malignant rate) WHEN?** | **Immediate Intervention** |

**Time interval varies by protocols (typically 3- or 6-mo)**

- **Measurement error**

# SOLID NODULE/ INCIDENTAL NODULE



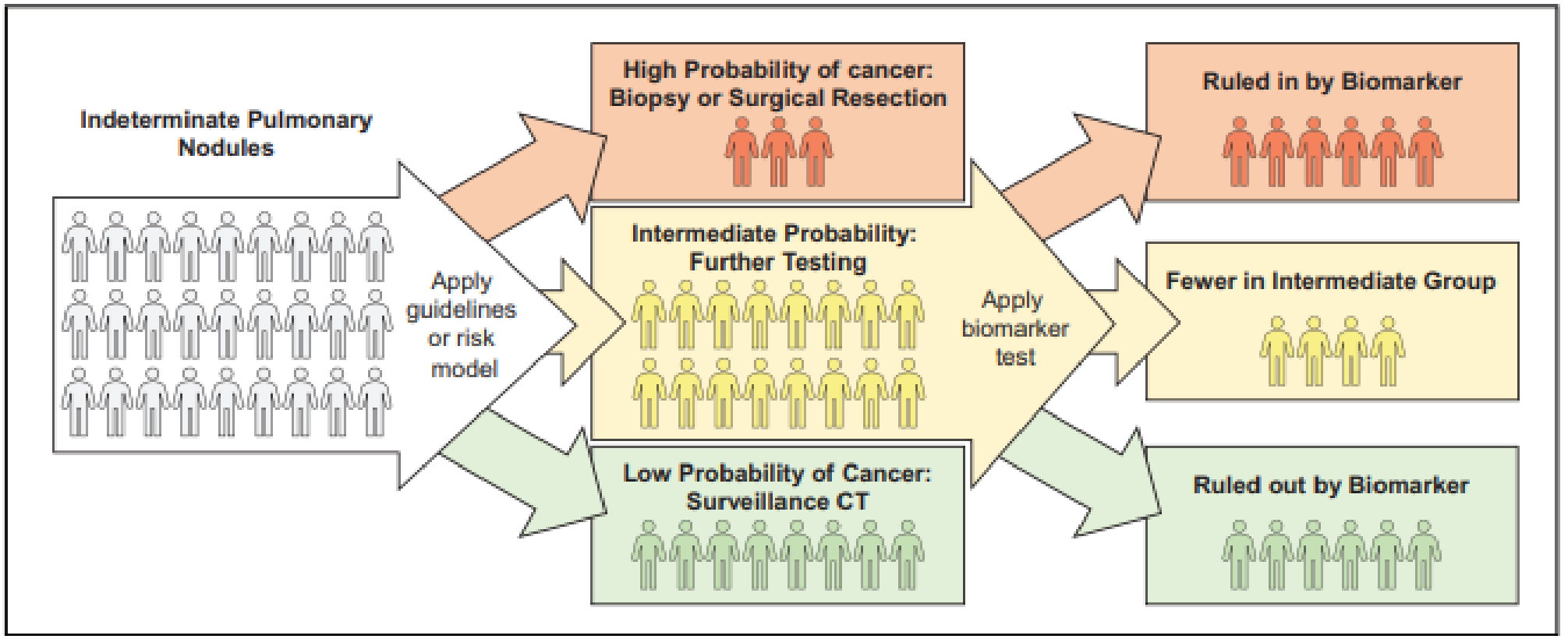

* BTS uses the same diagnostic approach for nodules detected incidentally as those detected through screening.

mo = month; wk = week; Bx = biopsy; Sx = surgical, PET = positron emission tomography; CE-CT = contrast CT; wu = work-up, f/u = follow up; MDT = multidisciplinary team

**Observations on growth rates of human tumors**
AJR Am J Roentgenol, 76 (1956), pp. 988-1000

“The definition of cancer, its diagnosis and its prognosis all depend upon descriptions of growth. To the layman a synonym for cancer is `growth'.”

Collins VP




Paez R. Curr Op Pul Med: 2021

## Lung-RADS® Version 1.1

Assessment Categories Release date: 2019

| Category Descriptor | Lung-RADS Score | Findings | Management | Risk of Malignancy | Est. Population Prevalence |
|---|---|---|---|---|---|
| Incomplete | 0 | Prior chest CT examination(s) being located for comparison<br>Part or all of lungs cannot be evaluated | Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed | n/a | 1% |
| Negative<br>No nodules and | 1 | No lung nodules<br>Nodule(s) with specific calcifications: complete, central, popcorn, concentric | | | |

| | | | | | |
|---|---|---|---|---|---|
| **Probably Benign**<br><br>Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer | **3** | **Solid nodule(s):**<br>≥ 6 to < 8 mm (≥ 113 to < 268 mm$^3$) at baseline **OR**<br>new 4 mm to < 6 mm (34 to < 113 mm$^3$)<br>**Part solid nodule(s)**<br>≥ 6 mm total diameter (≥ 113 mm$^3$) with solid component < 6 mm (< 113 mm$^3$) **OR**<br>new < 6 mm total diameter (< 113 mm$^3$)<br>**Non solid nodule(s)**<br>(GGN) ≥ 30 mm (≥ 14137 mm$^3$) on baseline CT or new | 6 month LDCT | **Risk of Malignancy**<br>1-2% | 5% |
| **Suspicious**<br><br>Findings for which additional diagnostic testing is recommended | **4A** | **Solid nodule(s):**<br>≥ 8 to < 15 mm (≥ 268 to < 1767 mm$^3$) at baseline **OR**<br>growing < 8 mm (< 268 mm$^3$) **OR**<br>new 6 to < 8 mm (113 to < 268 mm$^3$)<br>**Part solid nodule(s):**<br>≥ 6 mm (≥ 113 mm$^3$) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm$^3$) **OR**<br>with a new or growing < 4 mm (< 34 mm$^3$) solid component<br>**Endobronchial nodule** | 3 month LDCT; PET/CT may be used when there is a ≥ 8 mm (≥ 268 mm$^3$) solid component | 5-15% | 2% |

| | | | | | |
|---|---|---|---|---|---|
| | 4X | features or imaging findings that increases the suspicion of malignancy | *may be recommended to address potentially infectious or inflammatory conditions* | | |
| Other Clinically Significant or Potentially Clinically Significant Findings (non lung cancer) | S | **Modifier - may add on to category 0-4 coding** | As appropriate to the specific finding | n/a | 10% |

# Risk Assessment (Clinical and Imaging)

- Mayo Clinic
- Veterans Affairs
- Brock University

Age, smoking history, environmental and occupational exposure, COPD, fibrosis, family and personal history, sex

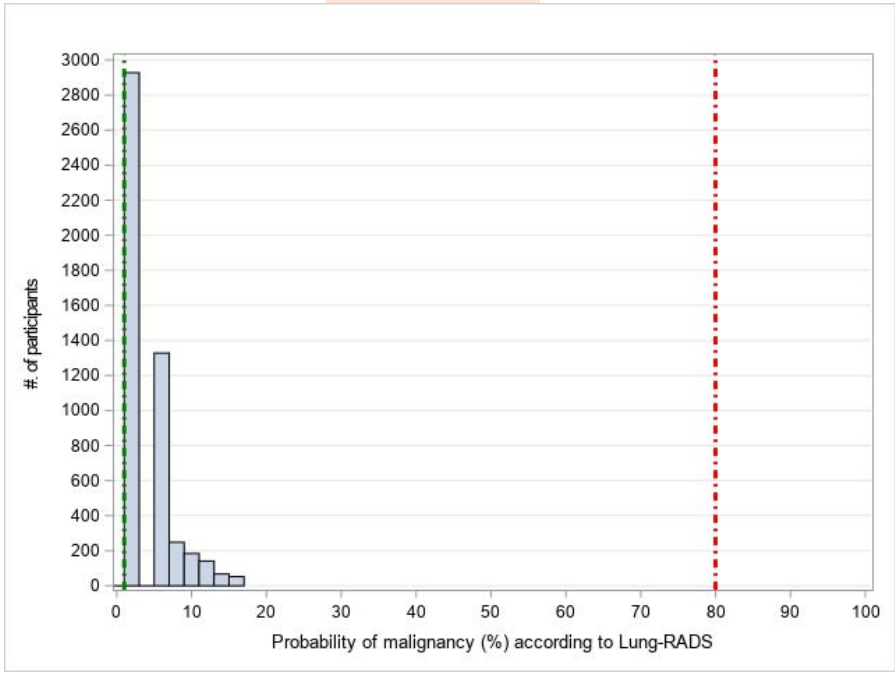
Rarely documented in reports

Maiga A. JAMA Surg: 2017

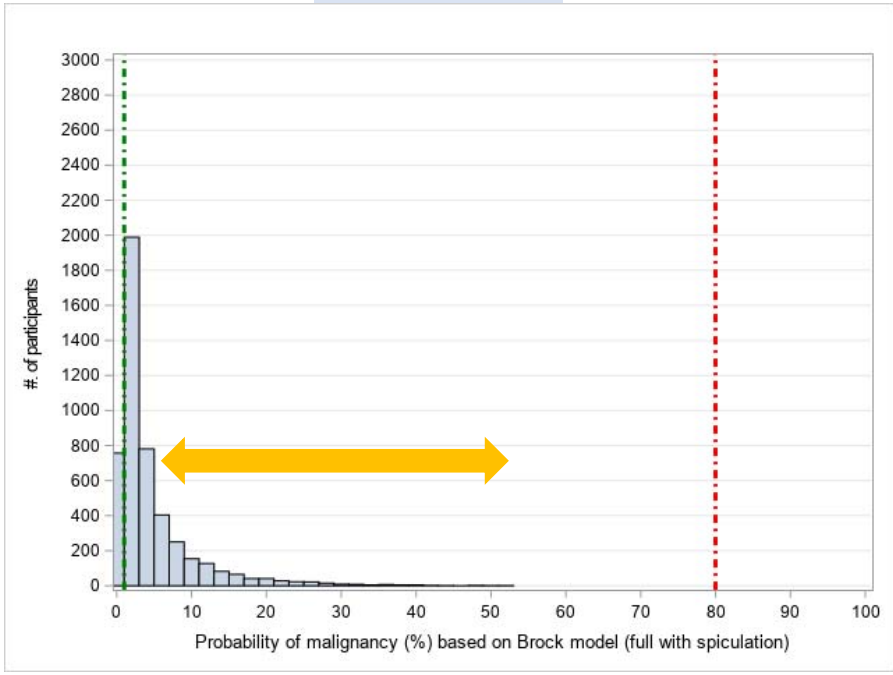
# 4948 I-ELCAP participants with 6-15mm solid NCNs

*Lung-RADS 3&4A category (Risk of malignancy: 1-15%)*

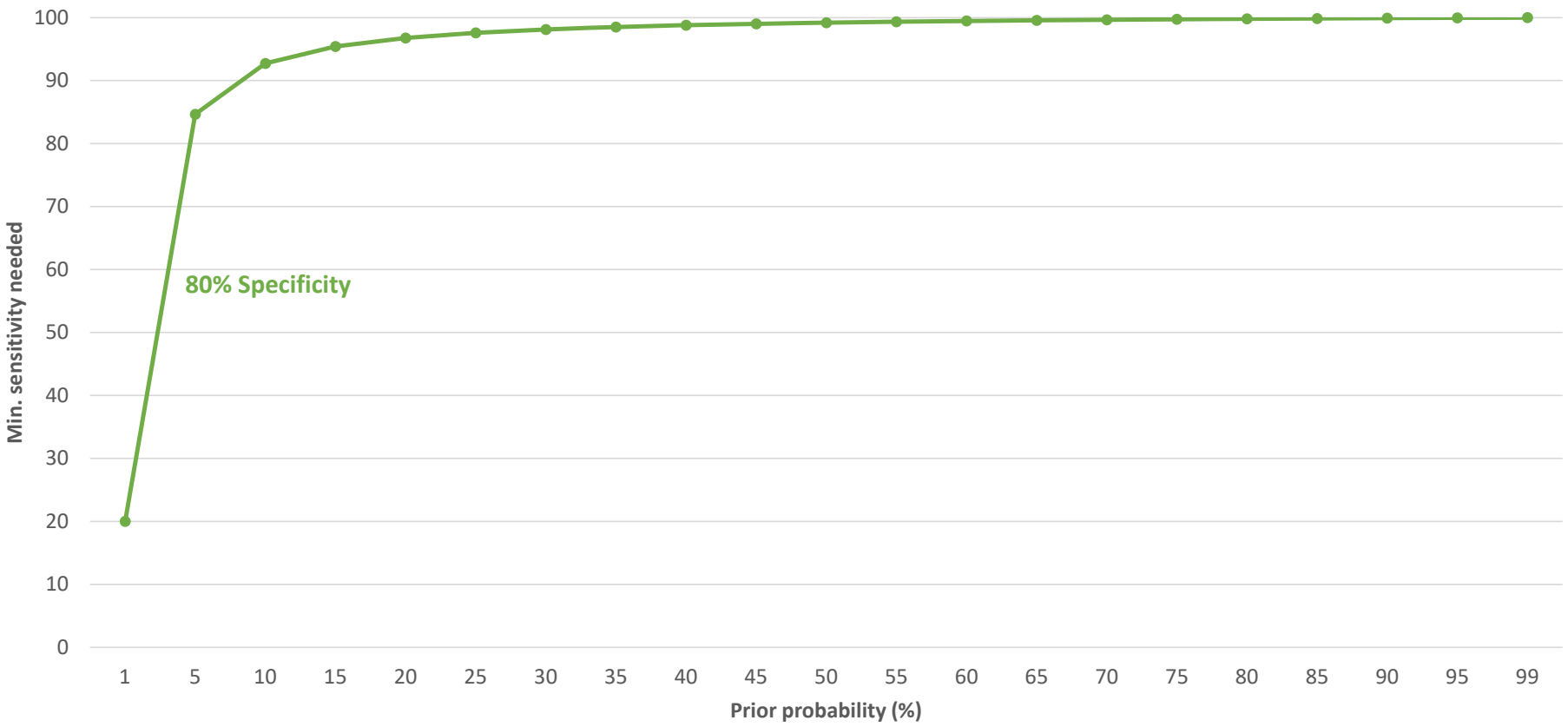
**Lung-RADS**



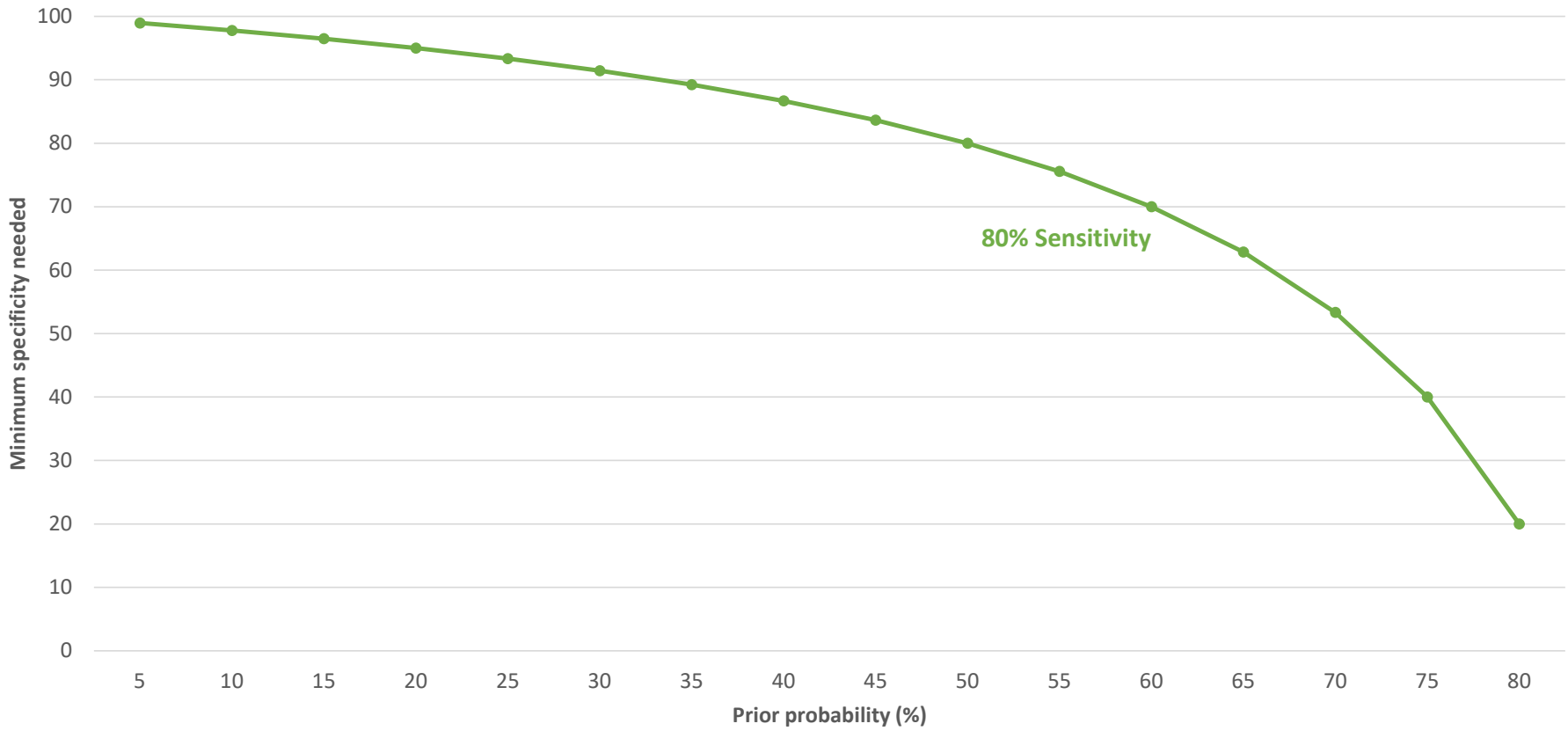

Brock model



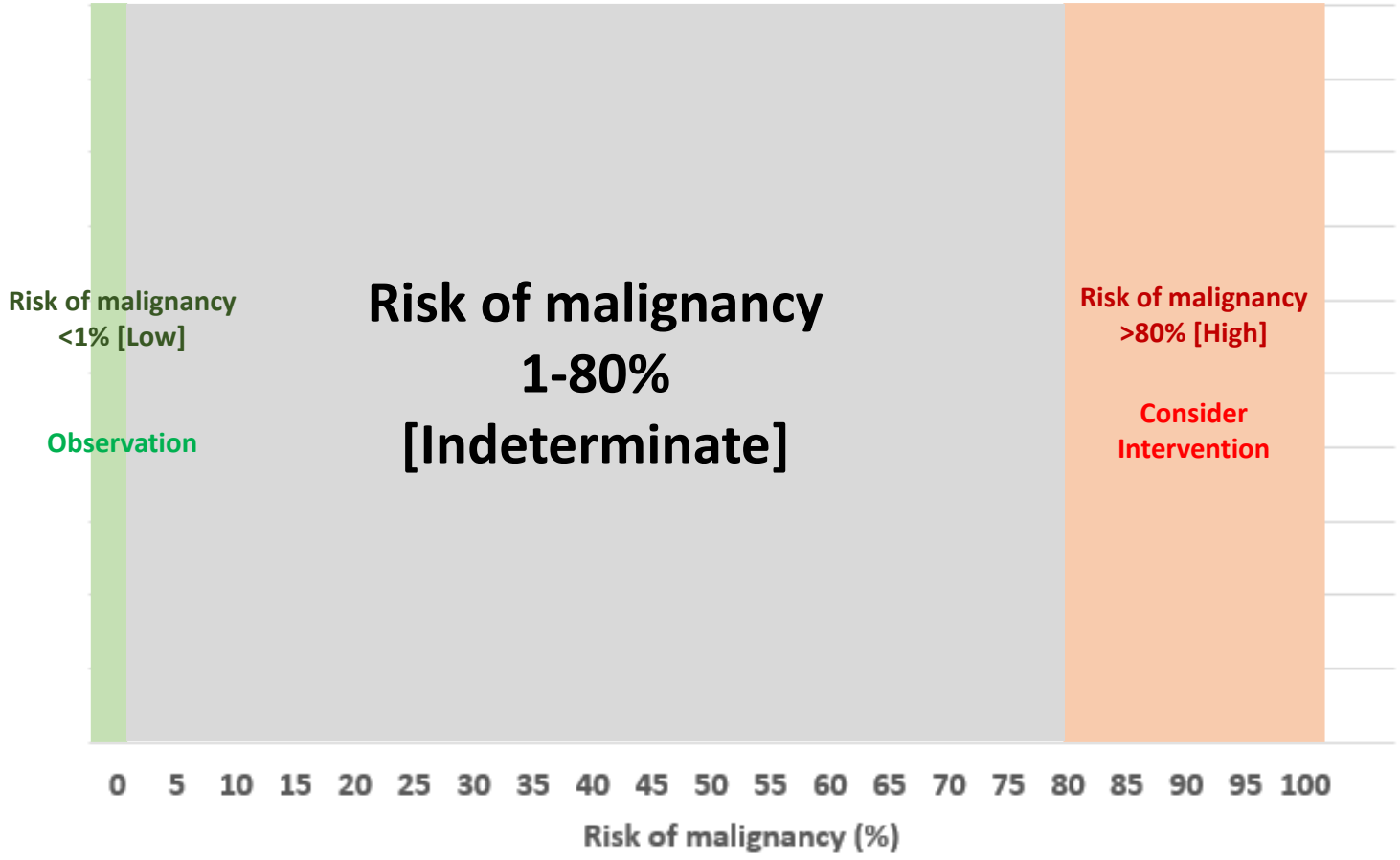
# LR- (rule out): Minimum sensitivity needed to decrease posterior probability to <1%



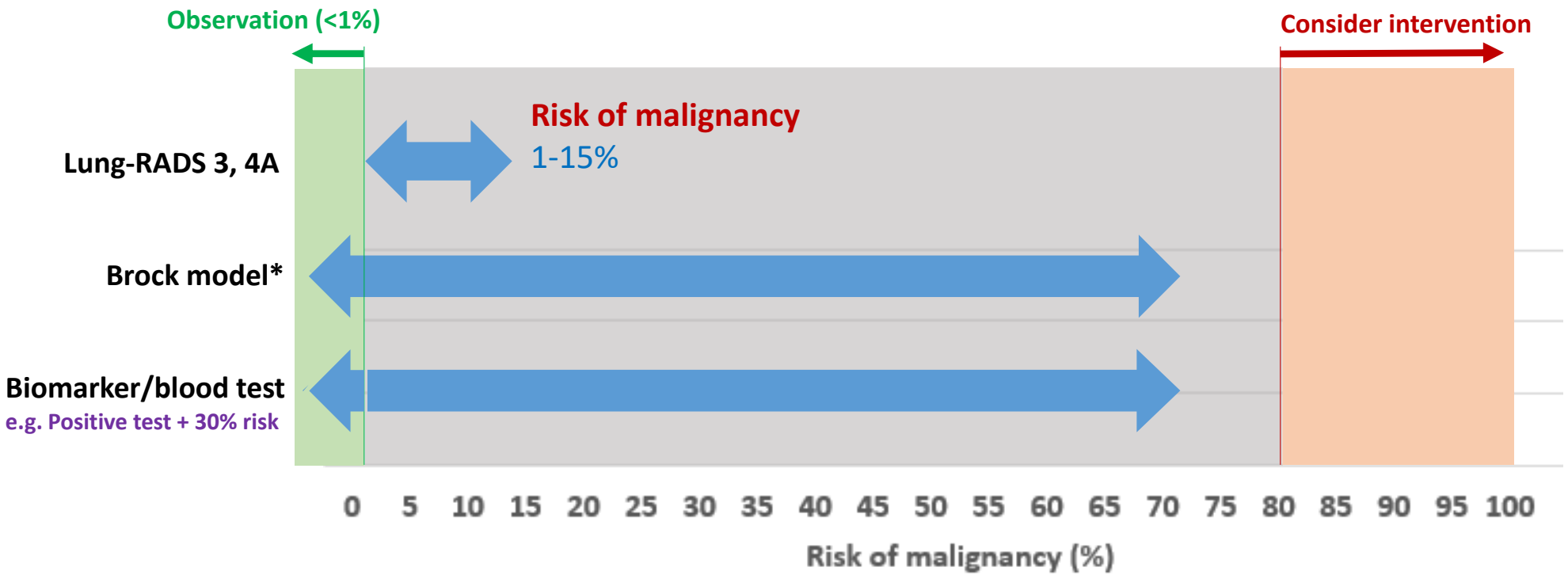
# LR+ (rule in): Minimum specificity needed to increase posterior probability to ≥80%



Assuming the threshold for intervention to be at 80% risk of malignancy and the threshold for surveillance to be 1% risk of malignancy



# Indeterminate nodule
# 6-15 mm part-solid or solid NCNs (Lung-RADS 3 & 4A)




*Using the full model with spiculation: the probability of lung cancer in a 77-yo female with family history of lung cancer, emphysema and a solitary 14.9mm spiculated part-solid nodule in the upper lobe is 72.9%.

median
The Imaging Phenomics Company®

**Press release – For immediate release**
**September 06, 2021 – 05:45 pm CEST**

# Median Technologies announces outstanding performance for its iBiopsy® Lung Cancer Screening CADx[1] to accurately characterize malignant vs benign lung nodules based on a large-scale patient cohort

- Results show cutting-edge performance of 95.2% sensitivity and 95.7% specificity for lung nodule characterization that could significantly impact lung cancer screening programs adoption.
- The large-scale study is based on a cohort of 1,696 patients with a total of 15,608 lung nodules.
- Further results on a fully automated end-to-end lung cancer screening CADe/CADx including nodule detection and characterization are expected in Q4, 2021.

**The performance of iBiopsy® CADx for the characterization of lung nodules shows an AUC of 0.991 and an outstanding sensitivity of 95.2% for a specificity of 95.7%**

**Study Population: the National Lung Screening Trial cases (NLST)**

# NEWS & EVENTS

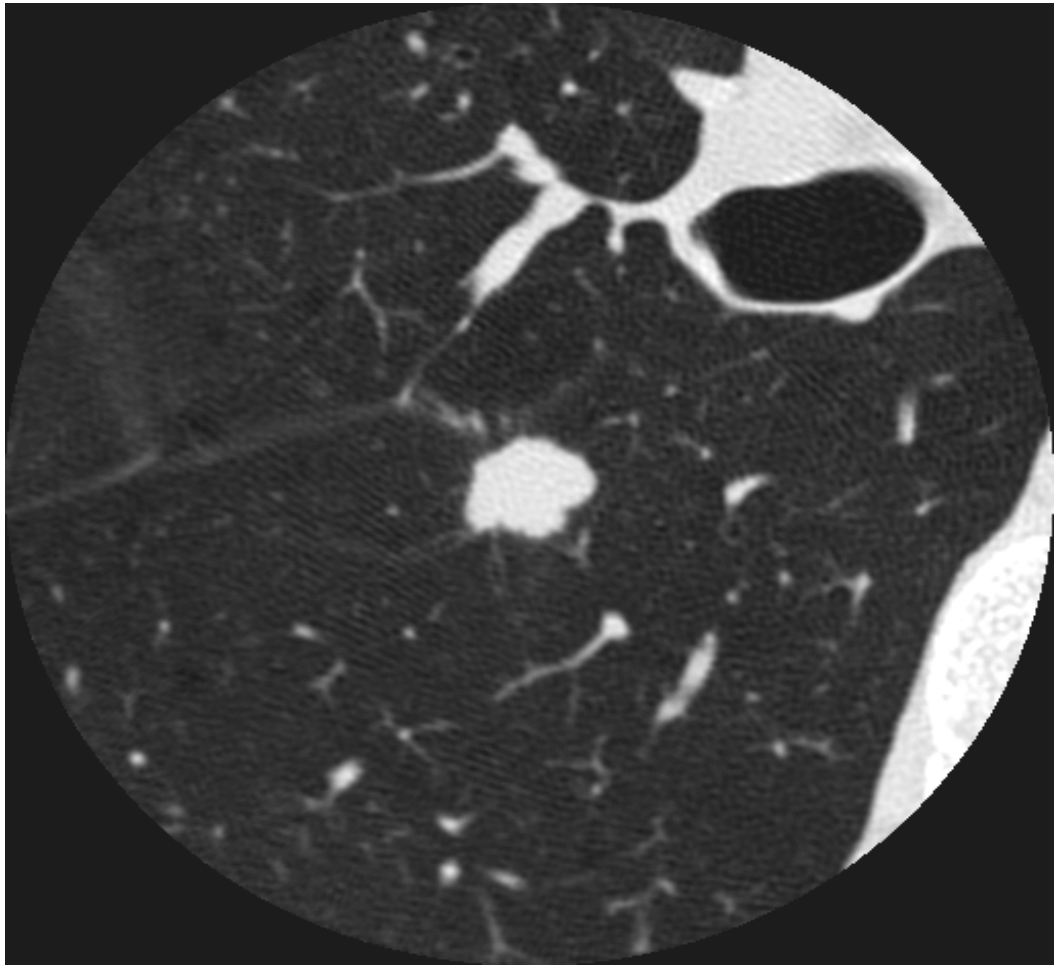
## US PRESS RELEASE: Optellum Receives FDA Clearance for the World's First AI-Powered Clinical Decision Support Software for Early Lung Cancer Diagnosis

Rhiannon Lassiter - March 23, 2021 - Clinical / News and PR

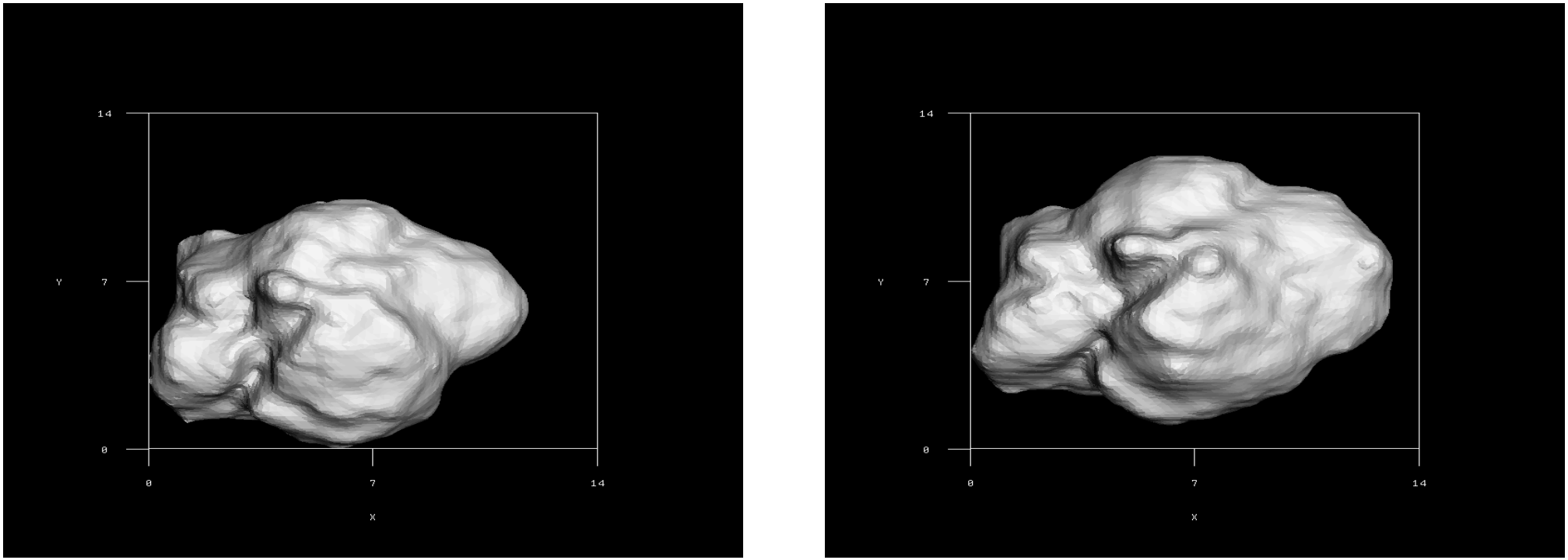
*Virtual Nodule Clinic empowers clinicians to make optimal clinical decisions in early-stage lung cancer diagnosis and is now commercially available in the United States.*

**Oxford, United Kingdom – March 23, 2021** – Optellum, a lung health company aiming to redefine early diagnosis and treatment of lung disease, today announced it received FDA 510(k) clearance for its Virtual Nodule Clinic. This revolutionary product is an AI-powered clinical decision support software for pulmonologists and radiologists managing patients with small lesions in the lungs called nodules that could represent early-stage lung cancer. This is the first such application of AI decision support for early lung cancer diagnosis cleared by the FDA.

# 10 mm Malignant Nodule

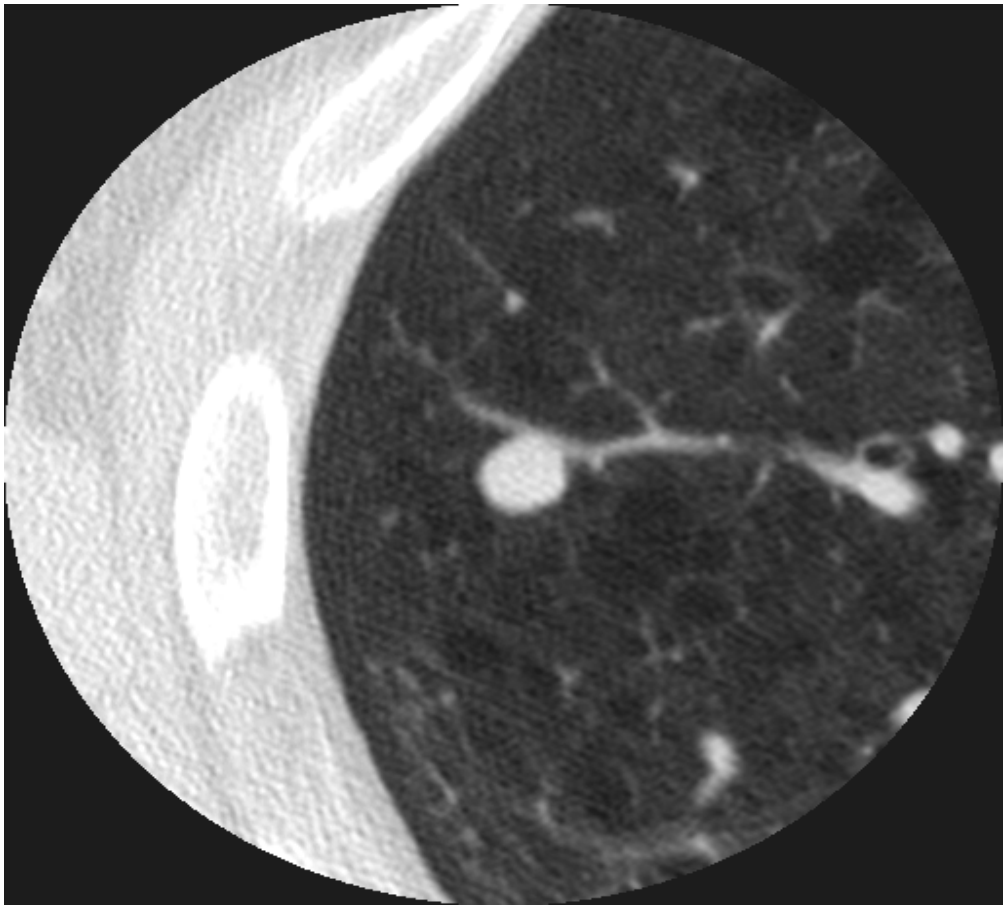


# Volumetric Growth Rate Analysis

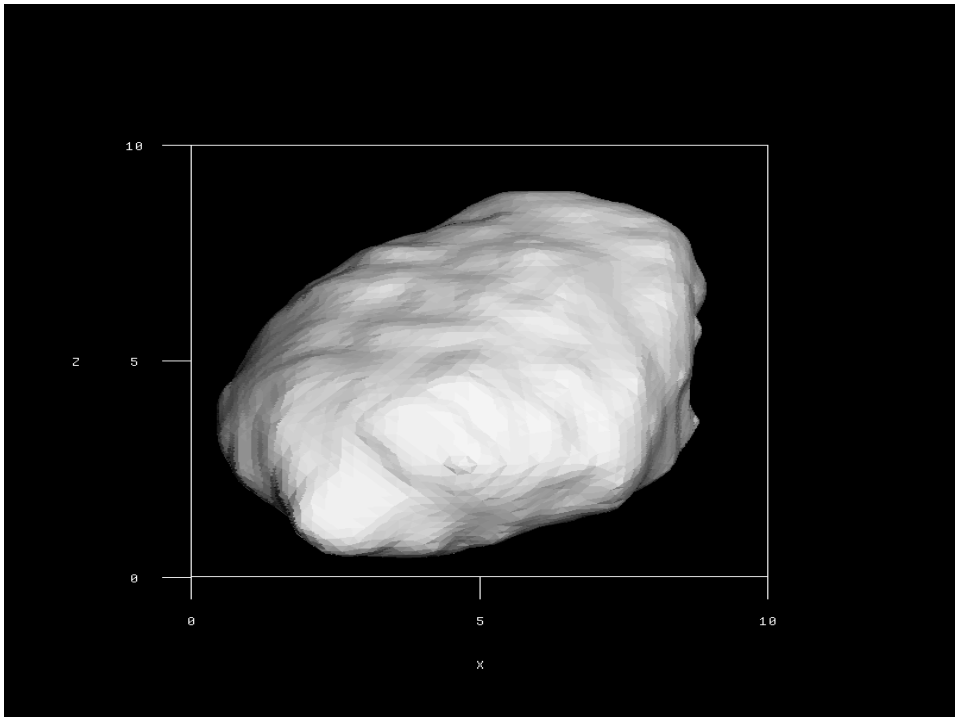


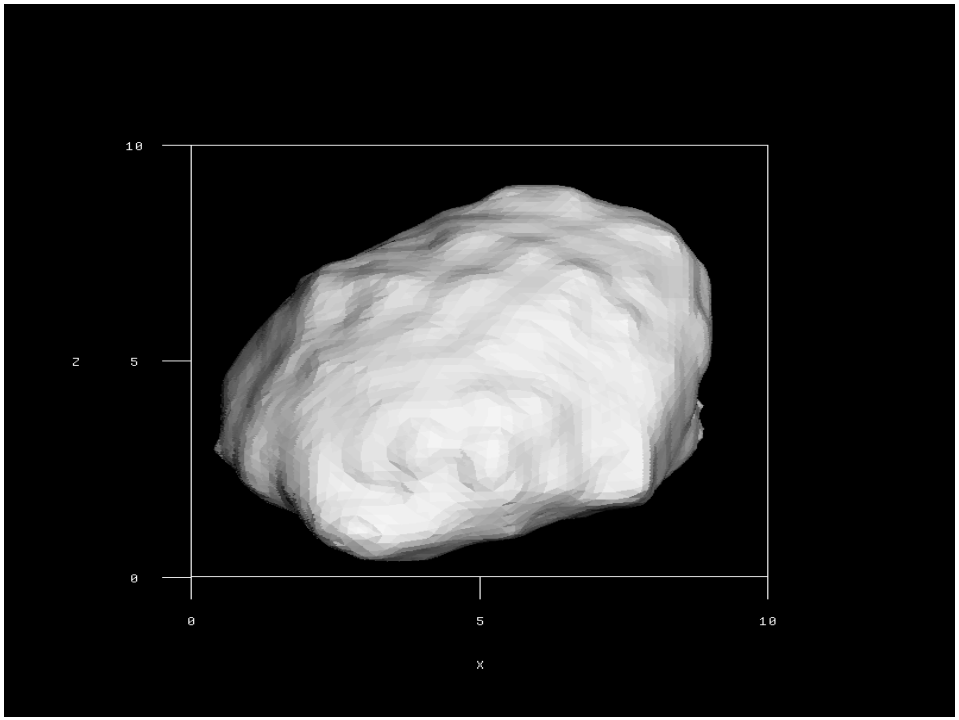

- 10 mm malignant pulmonary nodule at baseline and 32 days later
- MVGI = 22.0% -- Squamous Cell Carcinoma

# 8 mm Stable Nodule



# Volumetric Growth Rate Analysis




- 8 mm stable pulmonary nodule at baseline and 181 days later
- MVGI = 0.57%

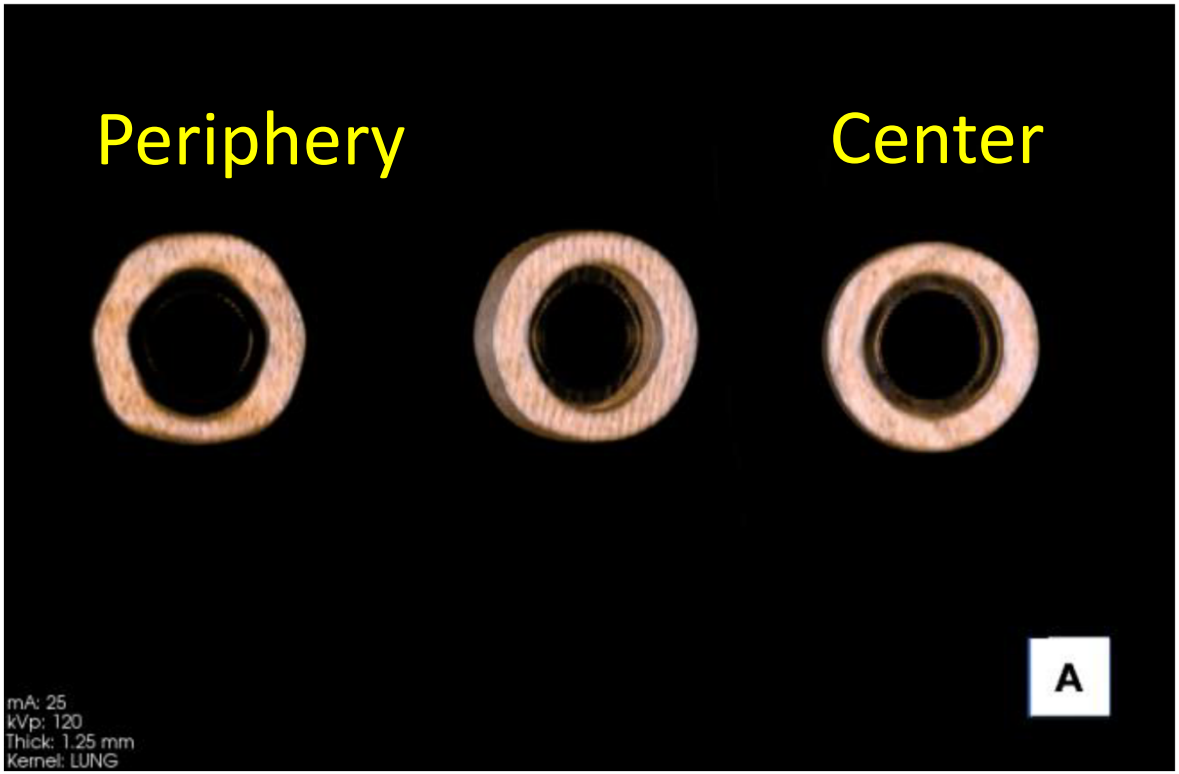
“In the arena of cancer research the initial impact was approximately that of a presentation on fire-making with two sticks, offered at a convention of nuclear physicists. The simplicity of the hypothesis does assault the accepted infinite complexity of etiology, biochemistry and cyto-kinetics of cancer. But until nuclear physicists solve our energy problem, there is some practical application for the warmth of a small fire kindled with two sticks.”

Collins VP. 1978

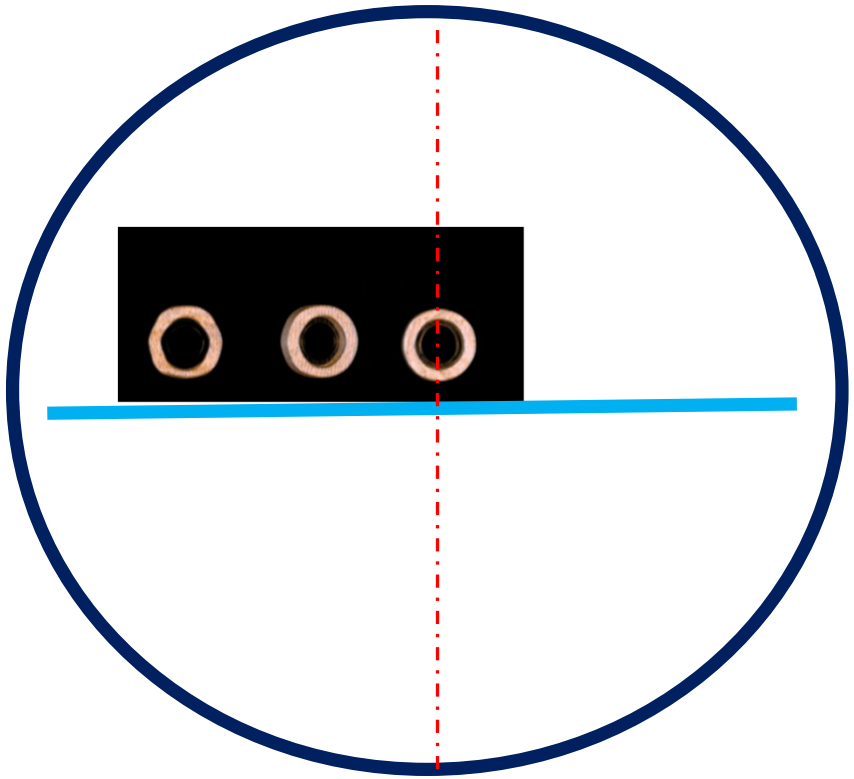
# Pay No Attention to the Man Behind the Curtain

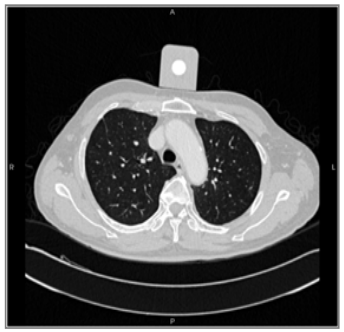

# CT Scan Scotch Tape Phantom (Calibration)

Magnified View



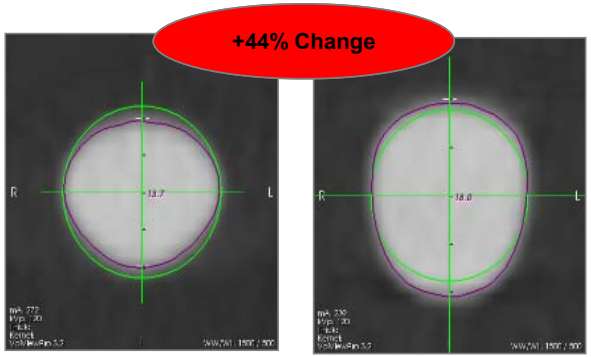

Phantom in CT Scanner





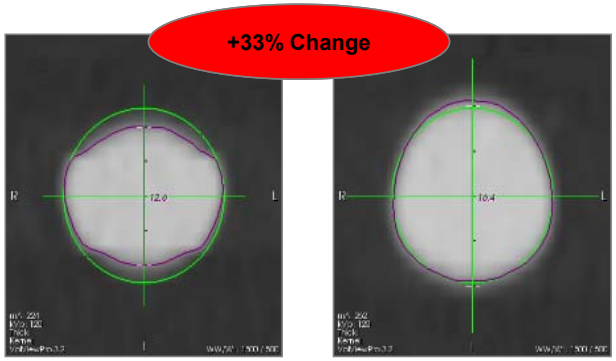
[Henschke, … Avila, J Med Imaging 2016]

**Model A**
**Site 1**




1654 mm$^3$ 2379 mm$^3$

**Model A**
**Site 2**

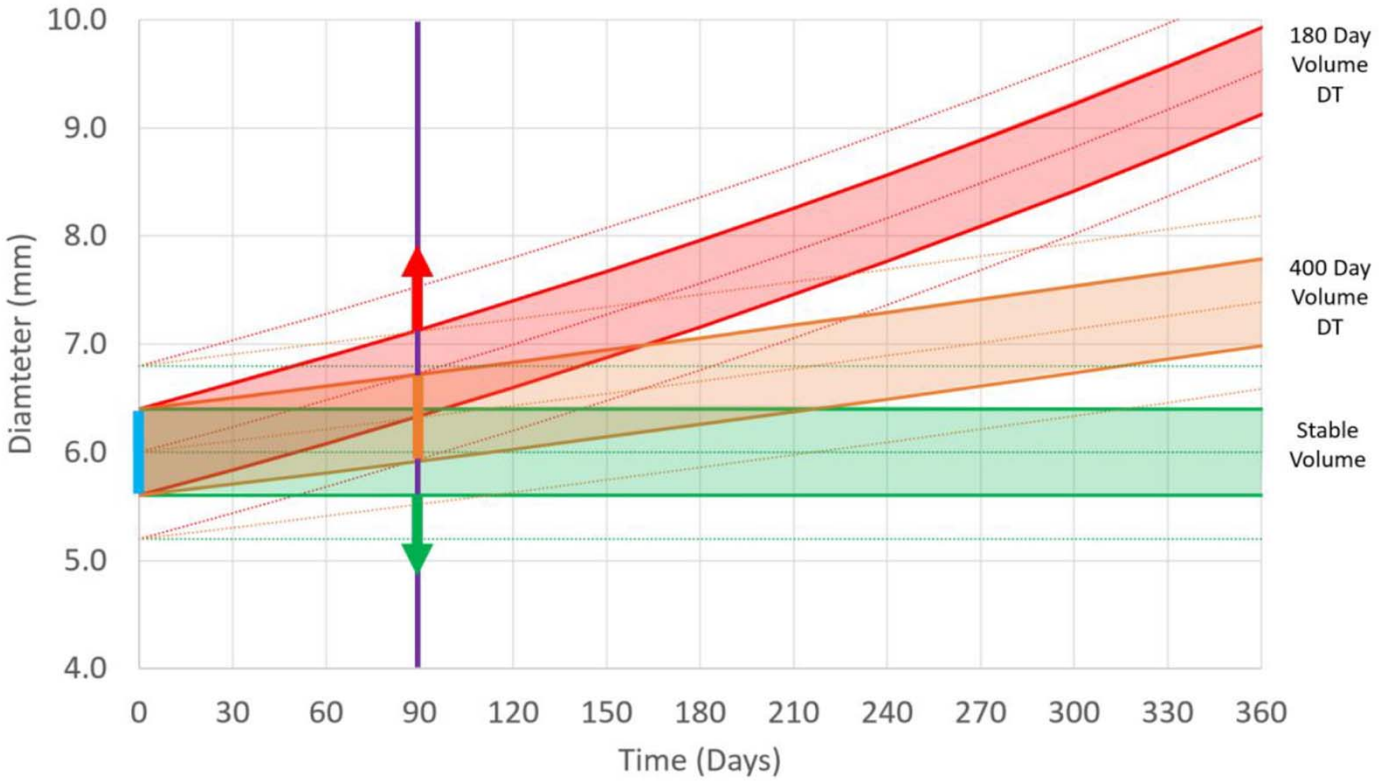



1601 mm$^3$ 2127 mm$^3$

Henschke CI. JMI: 2016

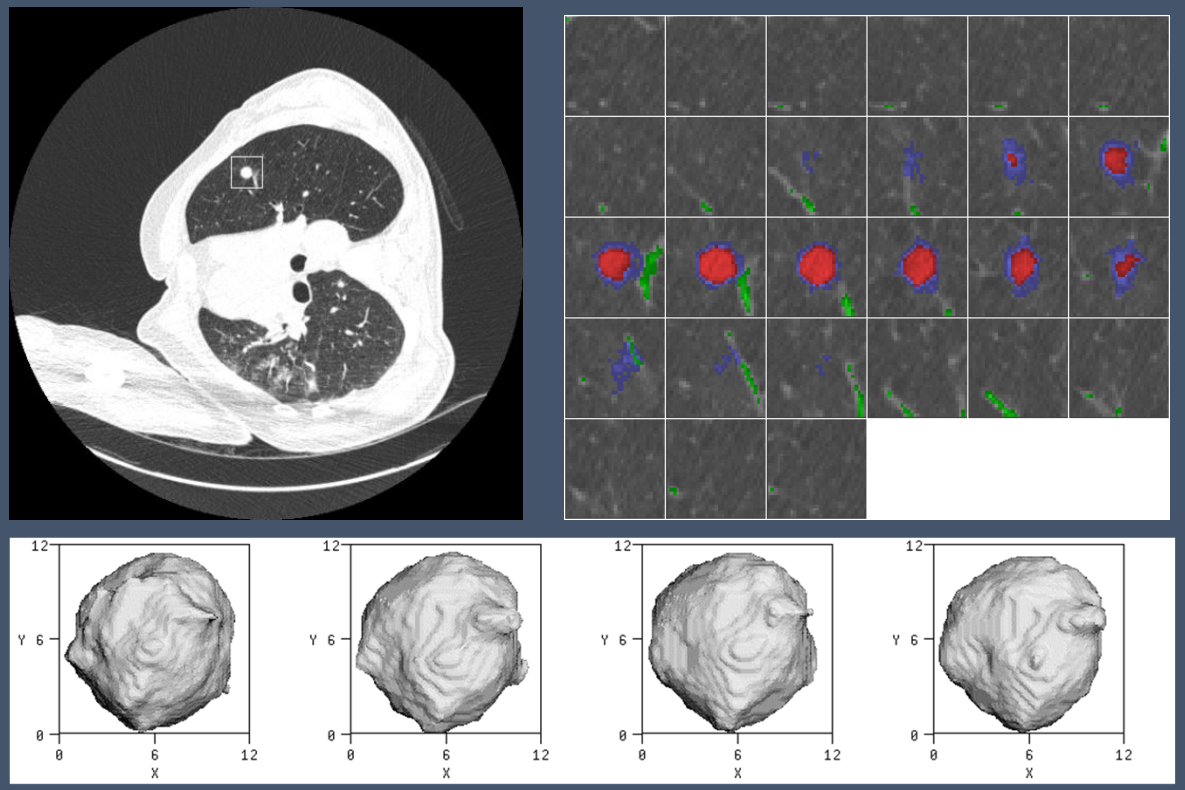
# Nodule Diameter Growth

What can we say if we use great CT imaging of a ~6mm nodule at baseline and again after 90 days?



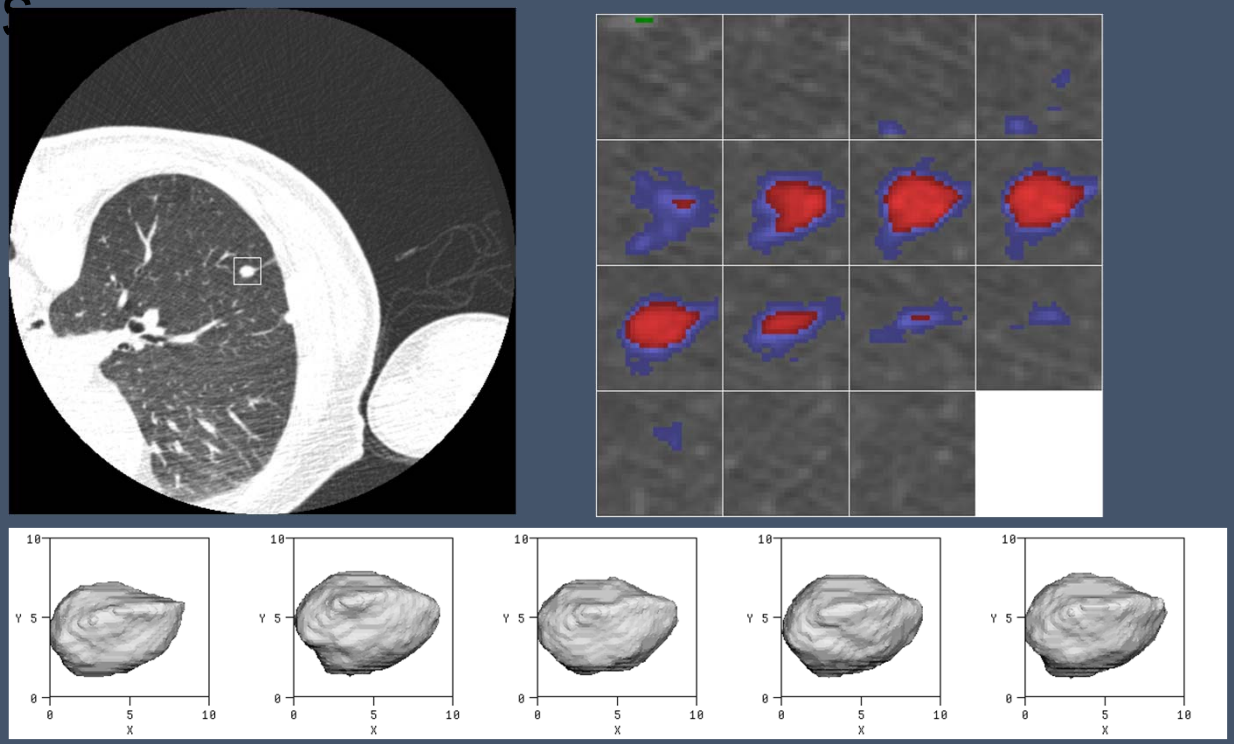
# Examples

A nodule was scanned 4x during an FNA biopsy – only minutes between each scan. Same scanner, 1.0 mm slice thickness, same protocol



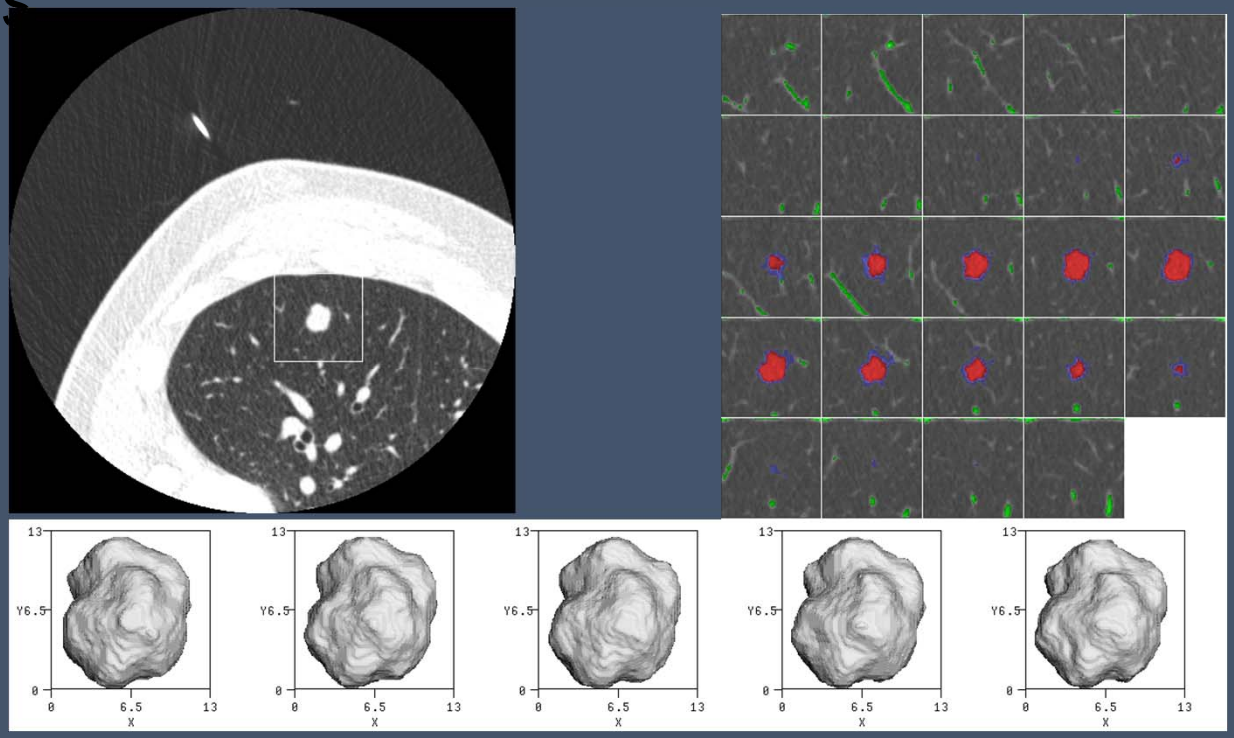

The average volume of this nodule was 476.5 $mm^3$ with an approximate diameter of 9.7 mm. The volume ranged from 412.7 to 586.6 $mm^3$, a relative difference of **36.6**%

# Examples



The average volume of this nodule was 139.8 $mm^3$ with an approximate diameter of 6.4 mm. The volume ranged from 113.0 to 154.6 $mm^3$, a relative difference of **30.0%**

# Examples




The average volume of this nodule was 590.6 $mm^3$ with an approximate diameter of 10.4 mm. The volume ranged from 586.5 to 599.0 $mm^3$, a relative difference of **2.1%**

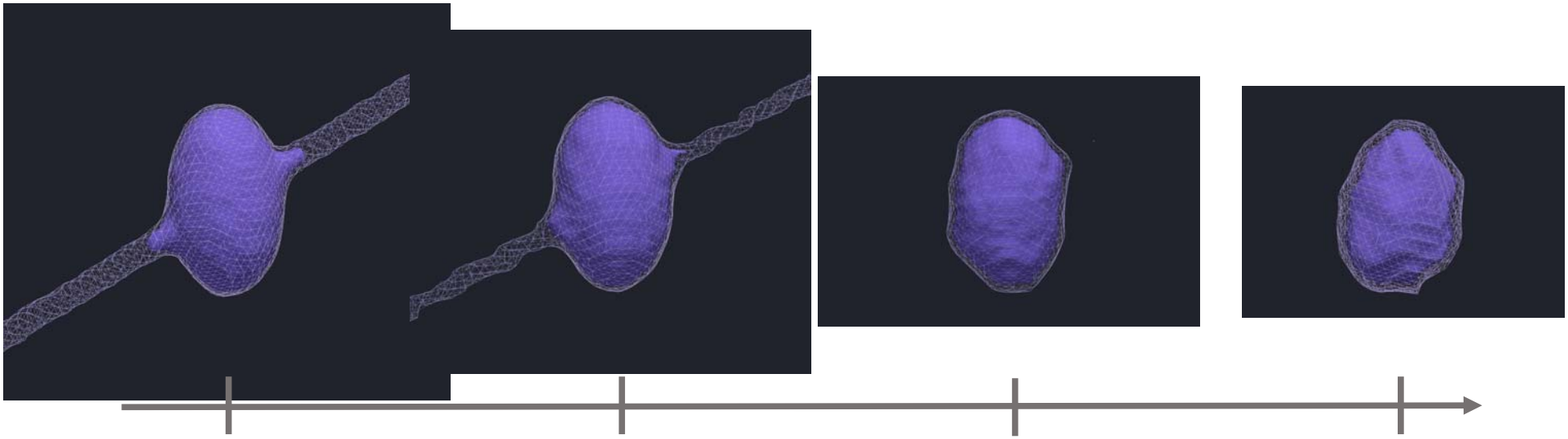
# Volumetrics: Current Reality

Even in the best-case scenario, using the same measurement algorithm, scanner, and scanning protocol, considerable measurement uncertainty exists in nodule volume measurement for nodules less than 20 mm.

Uncertainty is influenced by complex interactions of multiple factors including nodule size, complexity, location, type of scanner and scan parameters, and type of measuring software

# CT Image Quality Matters

Future Scanner | Best Global | Avg SLN Passing | Max SLN Limit



Based on International Phantom Data From Over 100 CT Scanners + Modeling and Simulation

# Impact of Delays in Treatment

- Recent meta-analysis found it could not be quantified due to heterogeneity and methodologic flaws
- National Cancer Database reported a 3.2% increase in mortality per week of delay
- Greater impact for early stage than late stage cancers
- Similar trends in National Cohort study from Taiwan

Zuniga PVS. Chest 2021

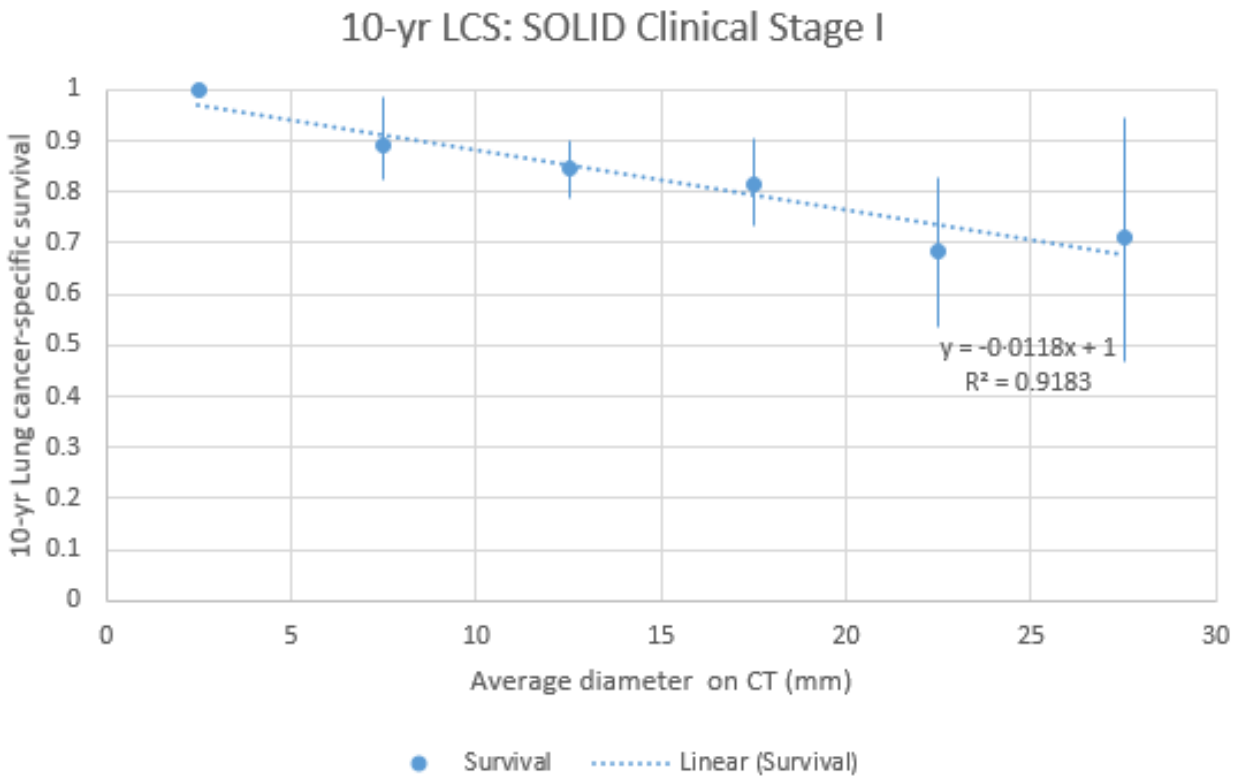
Khorana AA. Plos one 2019

Tsai C-H. BMJ open 2020

# Change in Prognosis Over Time

- Estimated the change in tumor size that would occur
  - over 3 months, 6 months, and also at 1 year (typical time delays)
  - volume doubling time (VDTs) of 60 days (fast), 120 days (moderate), and 240 days(slow).
- Examined the impact of delaying the diagnostic workup based on change in size (using simple exponential growth model)

Estimated 10-year lung cancer cure rates by average tumor diameter for the baseline solid non-small-cell lung cancers in the I-ELCAP database



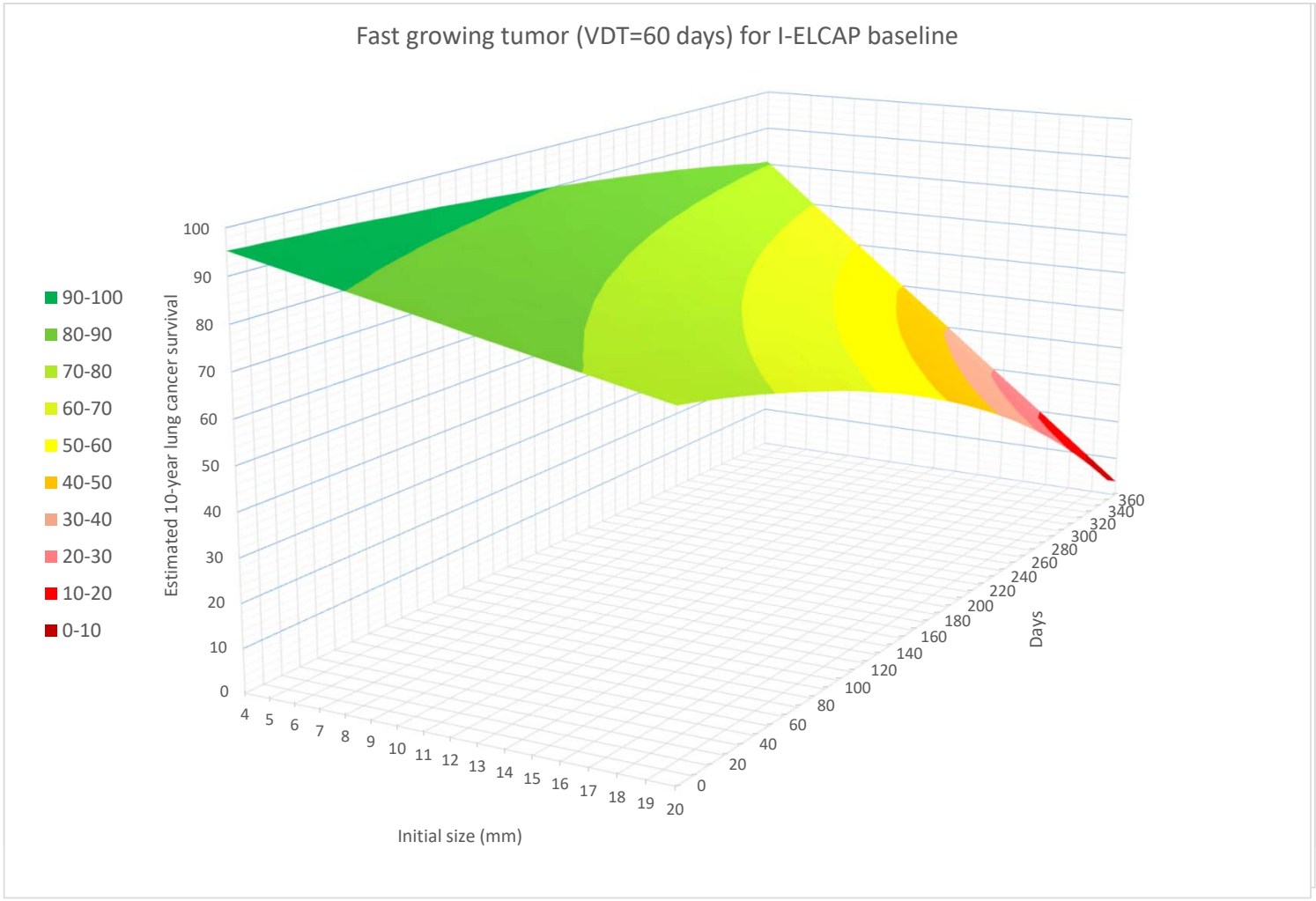
# Change in average tumor diameter for fast (F:VDT=60 days), moderate (M:VDT=120 days), slow (S: VDT=240 days) according to the initial average tumor diameter (mm)

| Initial size (mm)/ growth rate | Time between initial and follow-up CT | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 90 days later | | | 180 days later | | | 365 days later | | |
| | S | M | F | S | M | F | S | M | F |
| **4·0** | 4·4 | 4·8 | 5·7 | 4·8 | 5·7 | 8·0 | 5·7 | 8·1 | 16·3 |
| **5·0** | 5·5 | 5·9 | 7·1 | 5·9 | 7·1 | 10·0 | 7·1 | 10·1 | 20·4 |
| **6·0** | 6·5 | 7·1 | 8·5 | 7·1 | 8·5 | 12·0 | 8·5 | 12·1 | 24·5 |
| **7·0** | 7·6 | 8·3 | 9·9 | 8·3 | 9·9 | 14·0 | 9·9 | 14·1 | 28·5 |
| **8·0** | 8·7 | 9·5 | 11·3 | 9·5 | 11·3 | 16·0 | 11·4 | 16·2 | 32·6 |
| **9·0** | 9·8 | 10·7 | 12·7 | 10·7 | 12·7 | 18·0 | 12·8 | 18·2 | 36·7 |
| **10·0** | 10·9 | 11·9 | 14·1 | 11·9 | 14·1 | 20·0 | 14·2 | 20·2 | 40·8 |
| **11·0** | 12·0 | 13·1 | 15·6 | 13·1 | 15·6 | 22·0 | 15·6 | 22·2 | 44·9 |
| **12·0** | 13·1 | 14·3 | 17·0 | 14·3 | 17·0 | 24·0 | 17·1 | 24·2 | 48·9 |
| **13·0** | 14·2 | 15·5 | 18·4 | 15·5 | 18·4 | 26·0 | 18·5 | 26·3 | 53·0 |
| **14·0** | 15·3 | 16·6 | 19·8 | 16·6 | 19·8 | 28·0 | 19·9 | 28·3 | 57·1 |
| **15·0** | 16·4 | 17·8 | 21·2 | 17·8 | 21·2 | 30·0 | 21·3 | 30·3 | 61·2 |
| **16·0** | 17·4 | 19·0 | 22·6 | 19·0 | 22·6 | 32·0 | 22·7 | 32·3 | 65·2 |
| **17·0** | 18·5 | 20·2 | 24·0 | 20·2 | 24·0 | 34·0 | 24·2 | 34·3 | 69·3 |
| **18·0** | 19·6 | 21·4 | 25·5 | 21·4 | 25·5 | 36·0 | 25·6 | 36·3 | 73·4 |
| **19·0** | 20·7 | 22·6 | 26·9 | 22·6 | 26·9 | 38·0 | 27·0 | 38·4 | 77·5 |
| **20·0** | 21·8 | 23·8 | 28·3 | 23·8 | 28·3 | 40·0 | 28·4 | 40·4 | 81·6 |

**For a given VDT and time of the follow-up CT scan, the ability to measure true change will be easier for the larger nodules.**

**For a small slow or moderate growing LC, change would not be identified at 3 or 6 months.**

**However, change would be readily identified for a nodule with a moderate growth rate after 1 year**


Fast growing tumor (VDT=60 days) for I-ELCAP baseline
90-100
80-90
70-80
60-70
50-60
40-50
30-40
20-30
10-20
0-10
Estimated 10-year lung cancer survival
100
90
80
70
60
50
40
30
20
10
0
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
Initial size (mm)
0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360
Days

# Biomarker Impact

- Benefit of any biomarker test needs to balance the added benefit of earlier diagnosis (compared to waiting to assess for growth) against the potential increase in FP and FN diagnoses.
- Impact of time delay is greater for large nodules, although the impact of measurement error is less
- The ability to predict whether a nodule represents a fast or slow growing cancers should become a priority in protocol development.

# Conclusions

- Number of incidental nodules detected will continue to increase
- Management protocols are continuing to evolve, in large part driven by information derived from AI
- The major focus in management is moving from intermediate probability to either high or low probability and understanding the tradeoffs for each approach

# Thank You