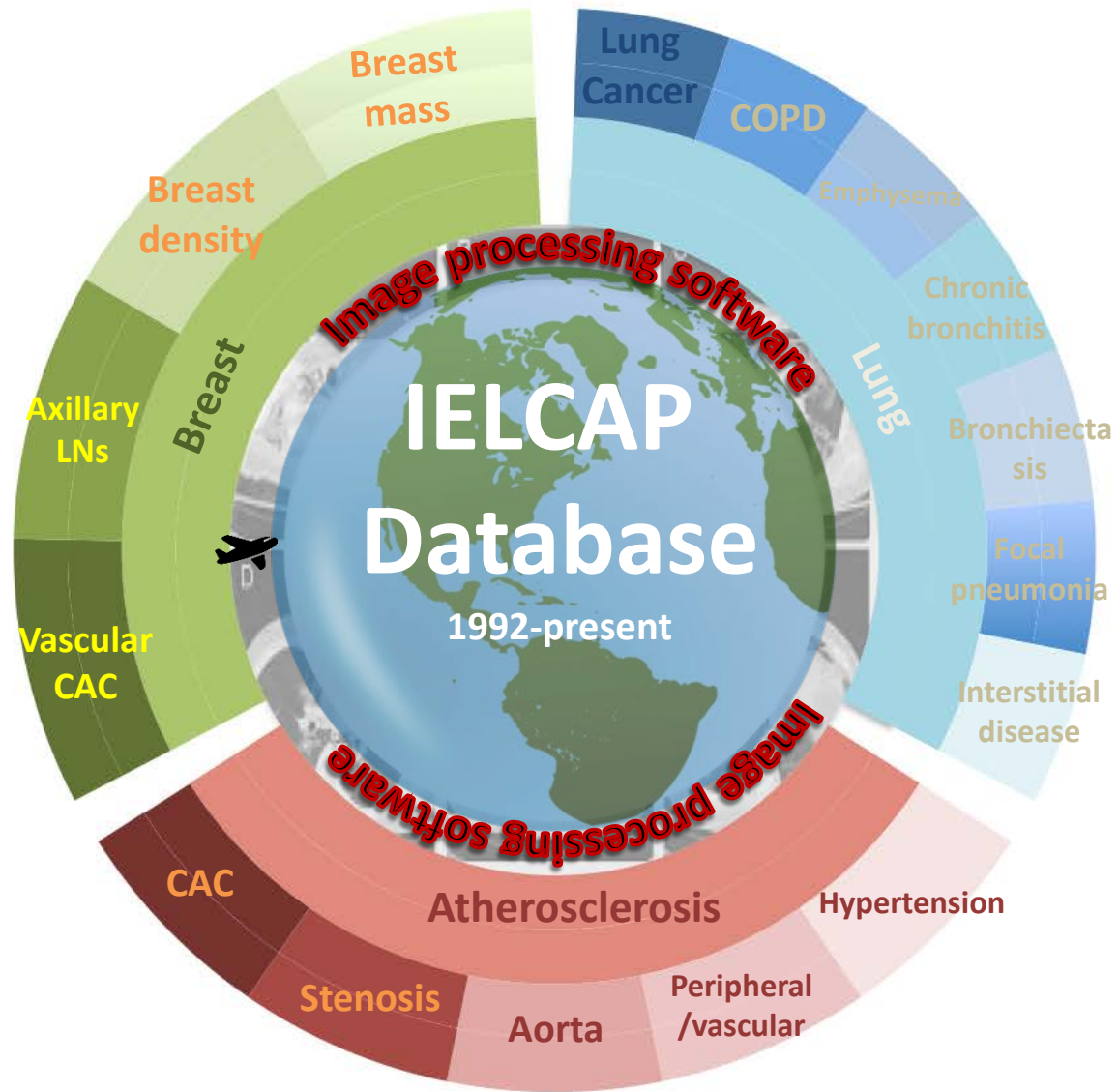


# THE BENEFITS OF “BIG DATA”

# Disclosures

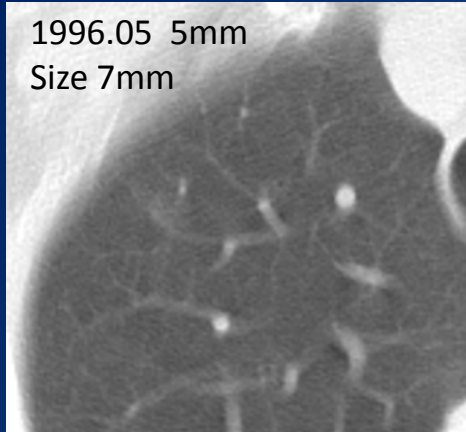
- I am a named inventor on a number of patents and patent applications relating to the evaluation of pulmonary nodules on CT scans of the chest which are owned by Cornell Research Foundation (CRF).
- As of April 2009, I signed away any financial benefit including royalties and any other proceeds related to the patents or patent applications owned by CRF.
- I am the President of the Early Diagnosis and Treatment Research Foundation



# Cohort of People

- Undergoing CT screening for lung cancer
- 1992-ongoing
- Long-term outcome
- Robust data on less frequent findings
- 75,000 + people enrolled
- Single slice imaging to the latest state of the art

1996.05 5mm  
Size 7mm



1996, 10mm non-solid nodule

1996-2012, non-solid nodule,  
slow growth

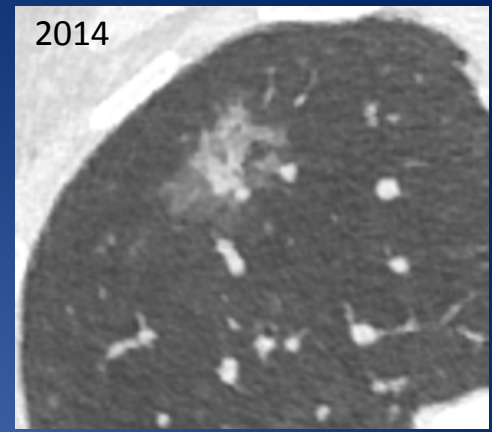
2013, suspicious to become  
part-solid nodule

2014, definitely to become  
part-solid nodule

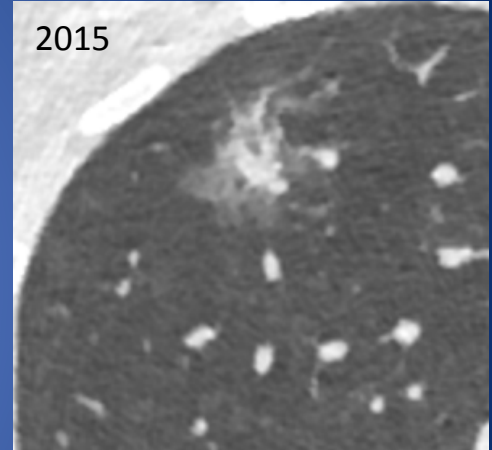
2015, increase in allover size  
and its solid component

Now she is 85 yo.

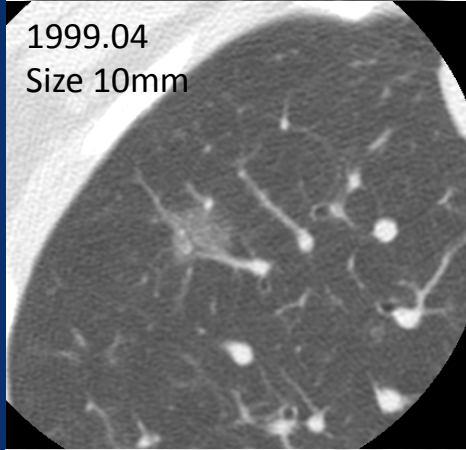
2014



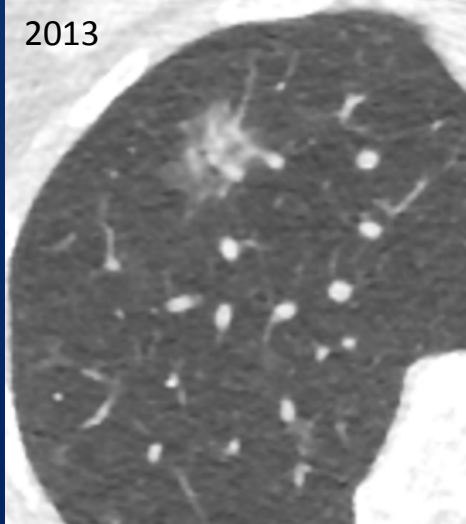
2015



1999.04  
Size 10mm



2013



What should we do next step?

# The regimen for screening

## Baseline round

- 1000 people screened
  - 20-30 cancers
  - 80% Stage I
- Type of nodules, most < 6mm
  - Solid: 250 people
  - Part-solid: 40 people
  - Nonsolid: 30 people
  - Some nodules resolve

## All annual repeat rounds

- 1000 people screened
  - ??? cancers
  - ??? Stage I
- Type of nodules
  - Solid: ?? people
  - Part-solid: ? people
  - Nonsolid: ? people
  - A higher % resolve than on baseline

What is the difference between the baseline and the subsequent annual rounds of screening?

# The regimen for screening

## Baseline round

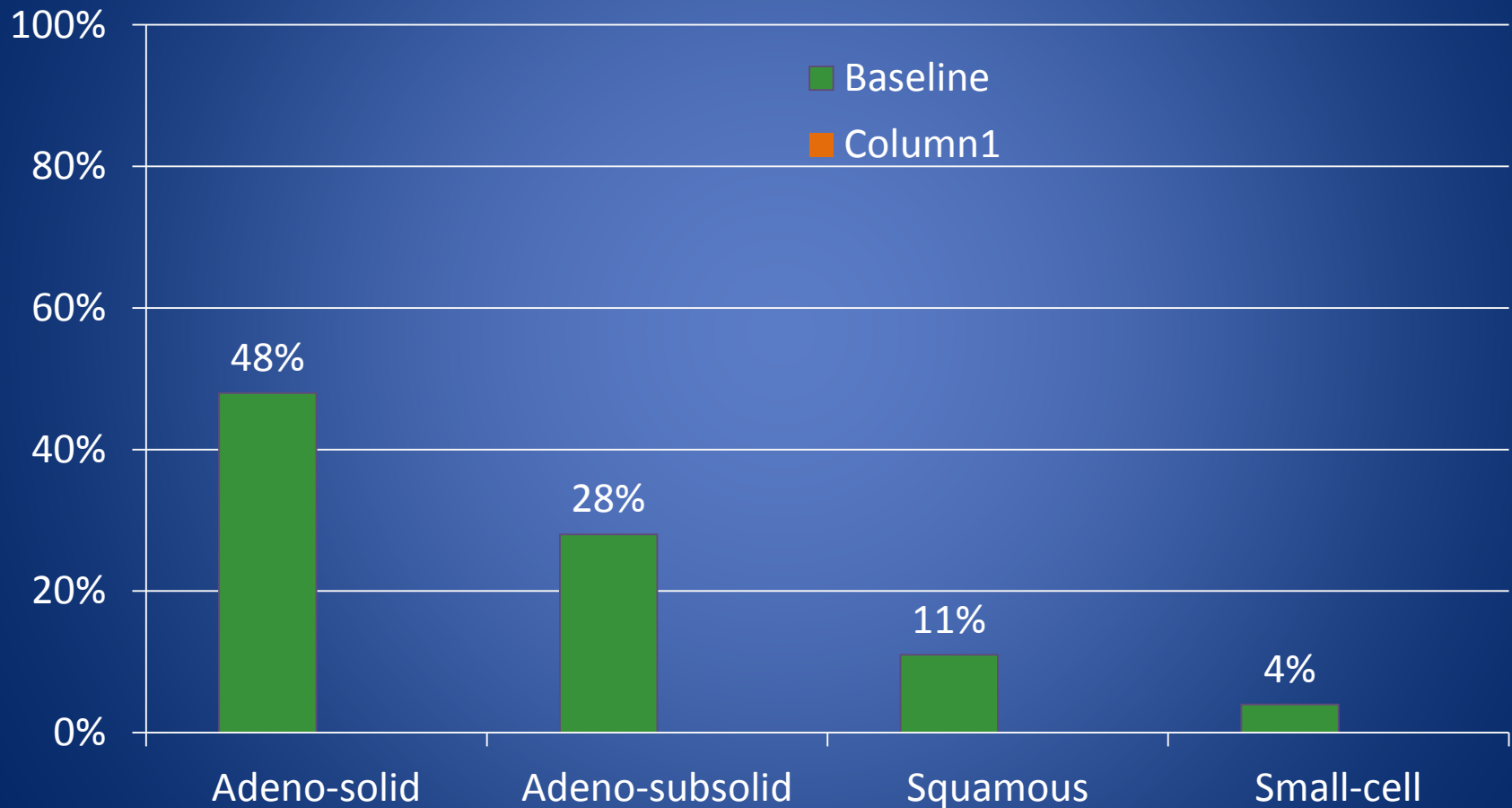
- 1000 people screened
  - 20-30 cancers
  - 80% Stage I
- Type of nodules, most < 6mm
  - Solid: 250 people
  - Part-solid: 40 people
  - Nonsolid: 30 people
  - Some nodules resolve

## All annual repeat rounds

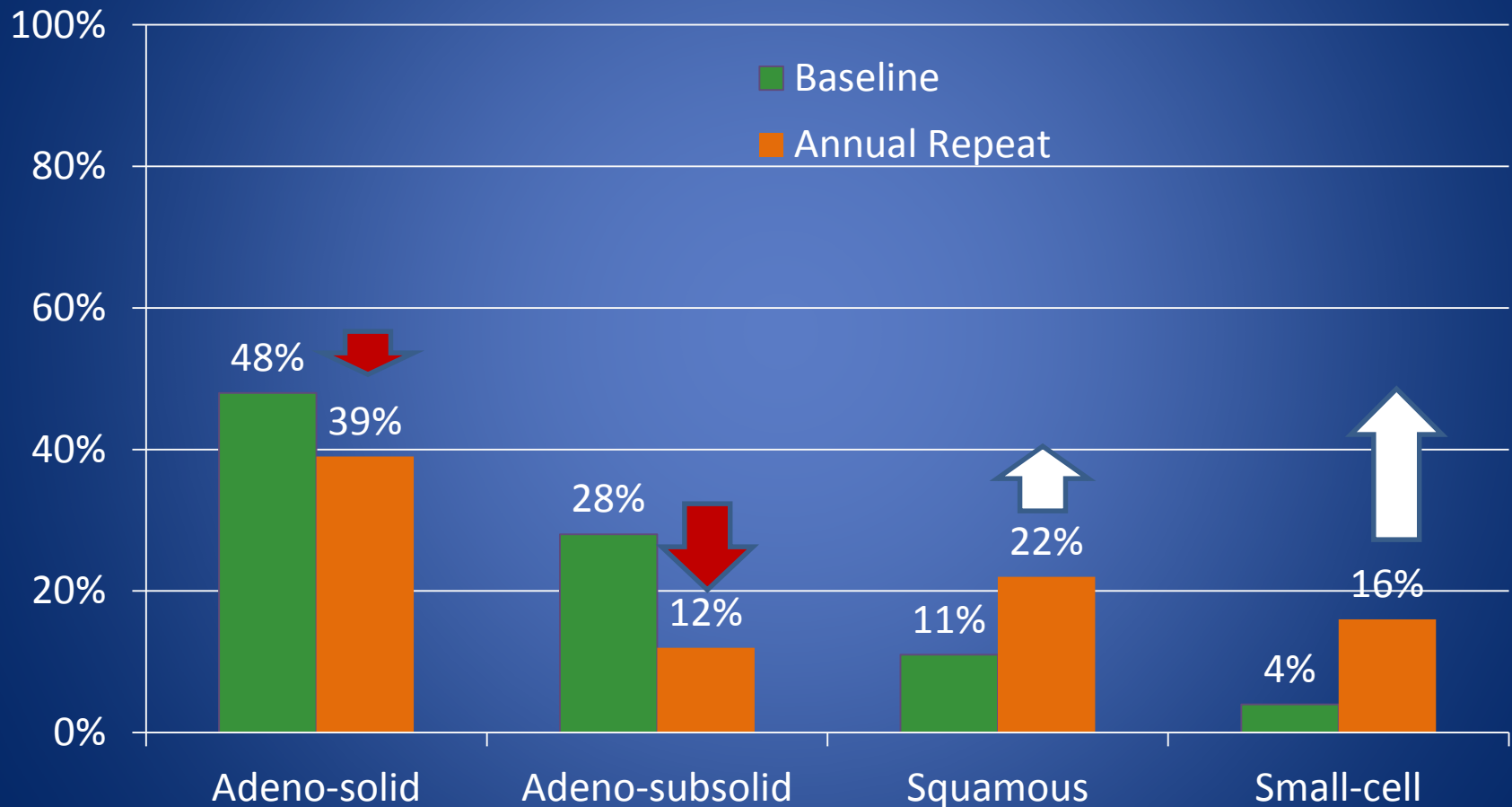
- 1000 people screened
  - 5-9 cancers
  - 80% Stage I
- Type of nodules
  - Solid: 30 people
  - Part-solid: 2 people
  - Nonsolid: 2 people
  - A higher % resolve than on baseline



# Baseline vs. Annual Repeat: Distribution by cell type



# Baseline vs. Annual Repeat: Distribution by cell type



Tumor aggressiveness is indicated by the change from baseline to annual repeat

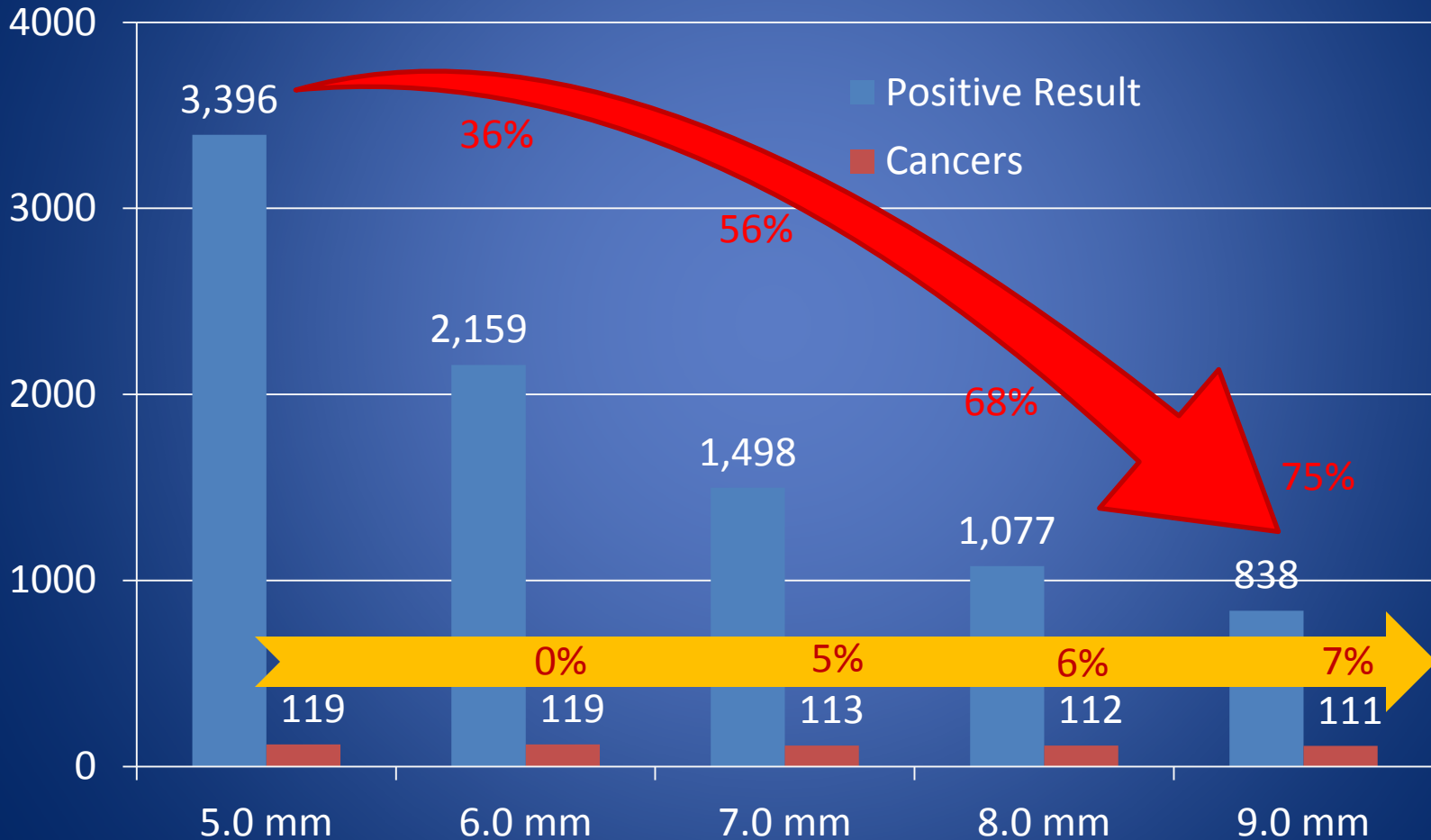
# Threshold for Workup of Nodules

- Developed in I-ELCAP
  - focused on imaging since 2006
  - slice thickness of 1.25 mm or less
- Validated in the NLST
  - images collected 2002-2006
  - slice thickness 2.5-3.0 mm

# Threshold in Baseline Round

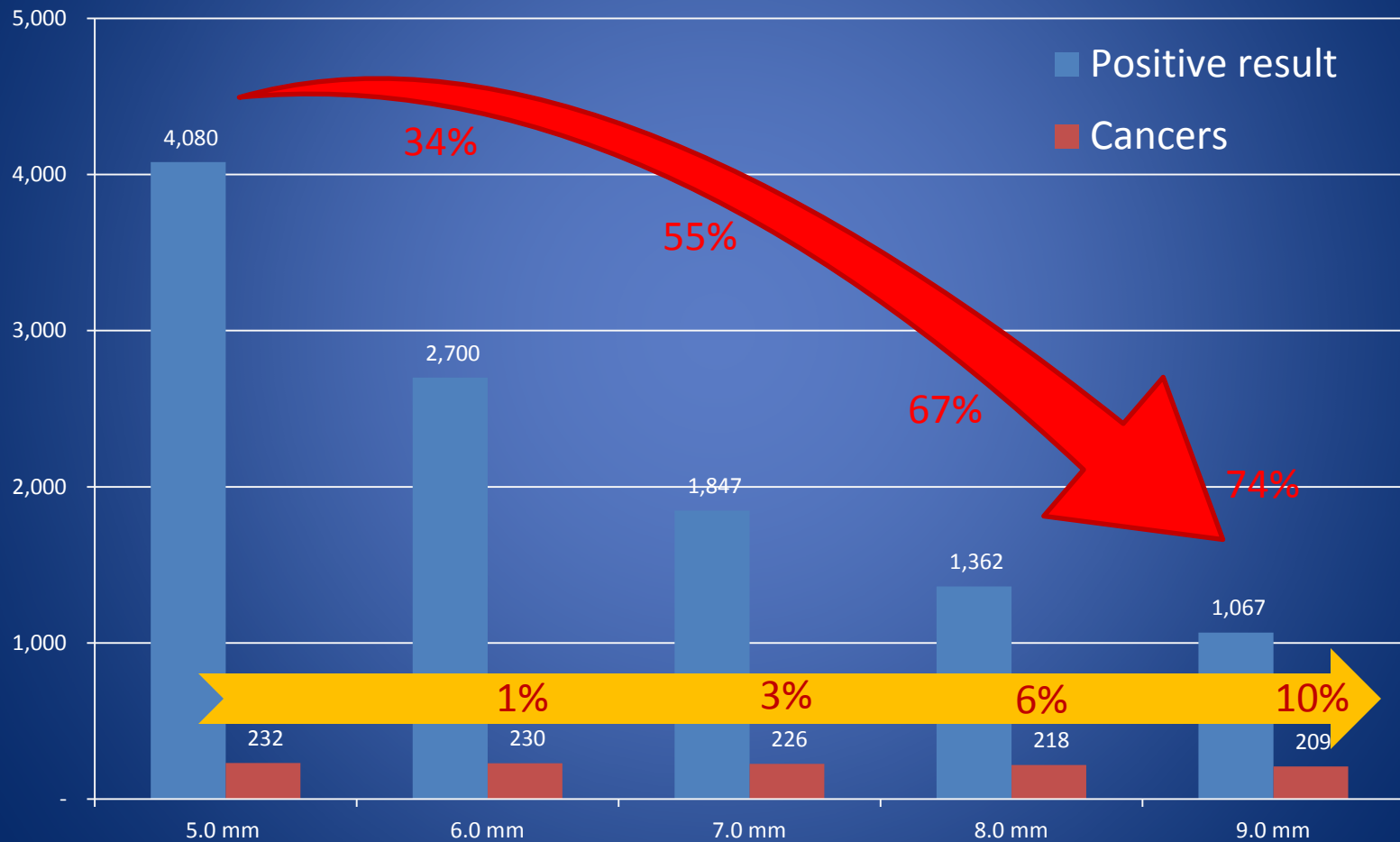
- NLST – use 4 mm in greatest length
- I-ELCAP
  - 1992-2000 no threshold; but thick section
  - 2000-2013 used 5.0 mm threshold
  - 2014-present 6.0 mm

# I-ELCAP Results



Henschke CI, Yip R, Yankelevitz DF et al. Definition of a positive test result in computed tomography screening for lung cancer: a cohort study. *Ann Intern Med.* 2013;158(4):246-52.

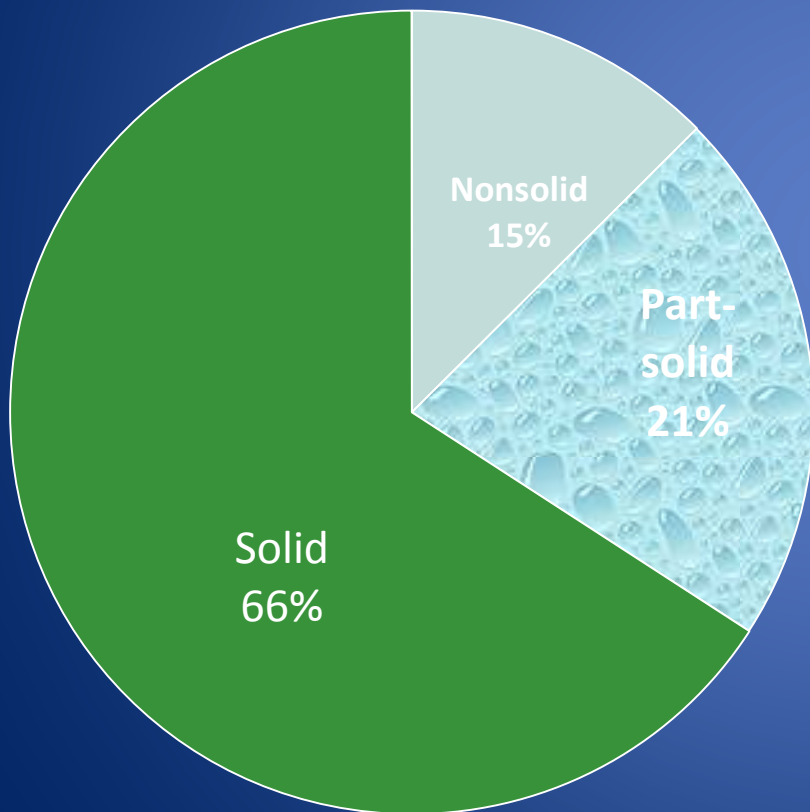
# NLST Positive results



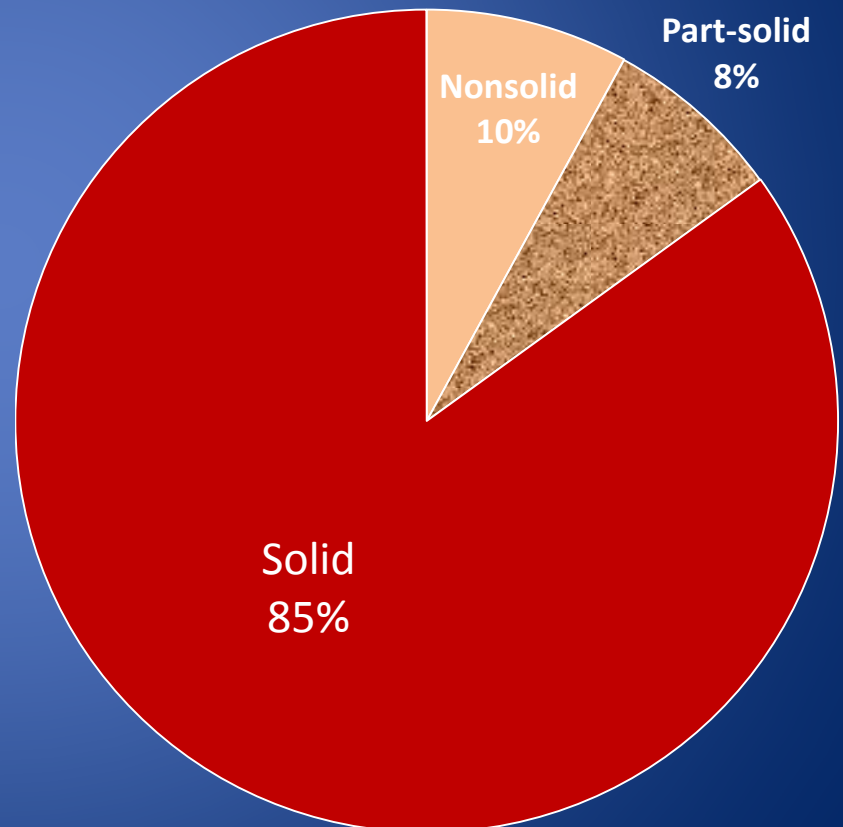
Yip R, Henschke CI, Yankelevitz DF, Smith JP. CT Screening for Lung Cancer: Alternative Definitions of Positive Test Result Based on the National Lung Screening Trial and International Early Lung Cancer Action Program Databases. Radiology. 2014 Jun 19:132950.

# Cancers manifesting in nonsolid, part-solid, and solid nodules: demonstration of length bias

**Baseline**



**Annual Repeat**



Increasing percentage of cancers in solid nodules on annual repeat screening. Thus, cancers in solid nodules are more aggressive than those in part-solid and nonsolid nodules

# The Approach

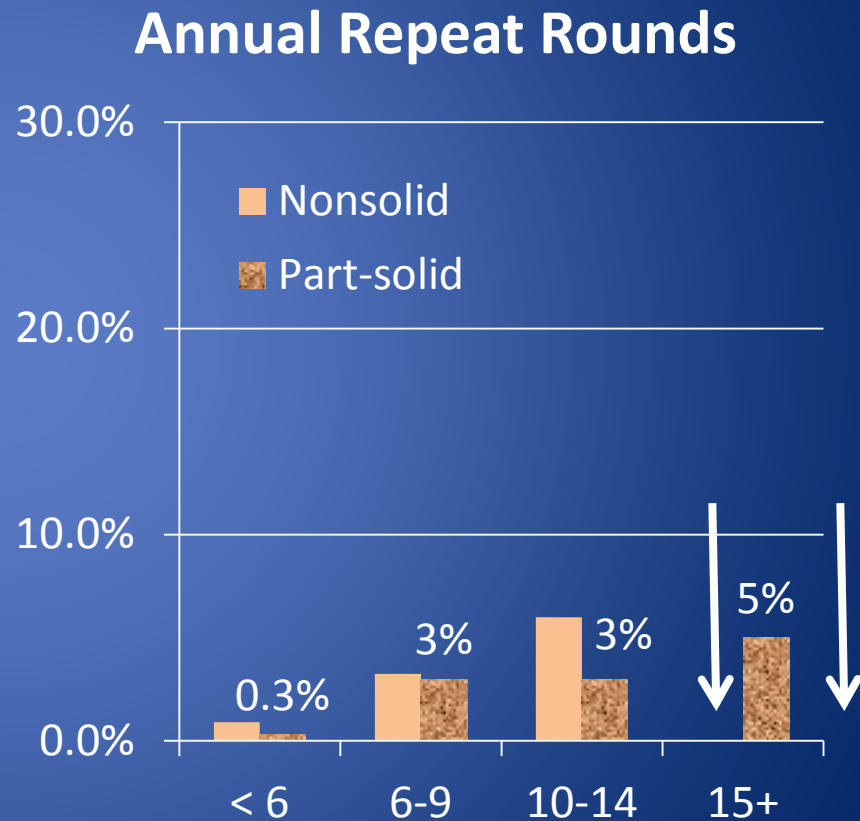
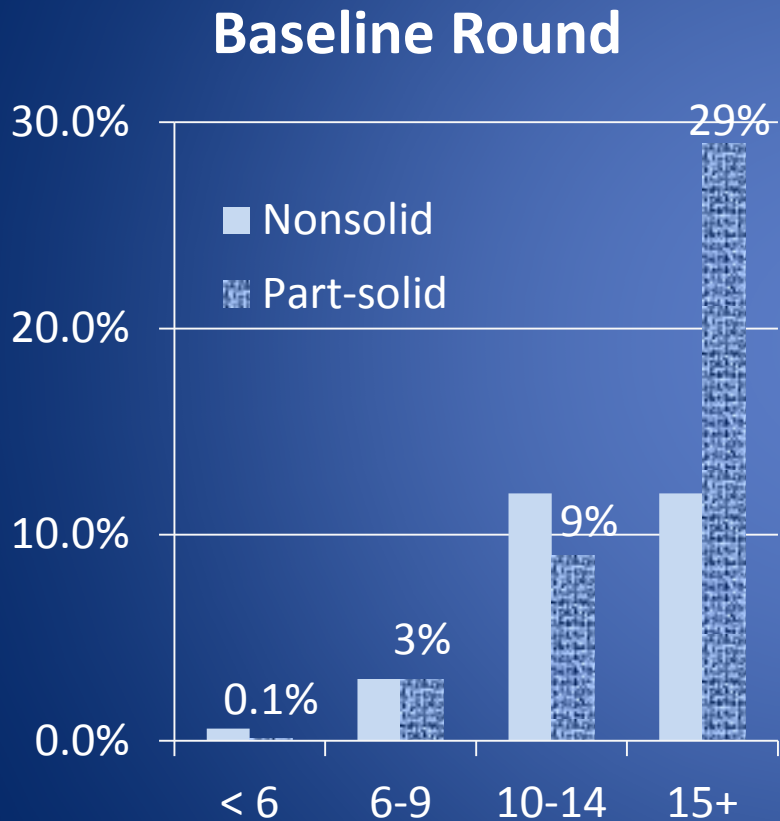
- Large databases with long-term followup
  - I-ELCAP database – has latest approaches
    - Follow-up since 1992
  - NLST database- stopped in 2006
    - Follow-up for 5-7 years
- Meta-analyses of the world literature



# SUBSOLID NODULES nonsolid and part-solid

I-ELCAP

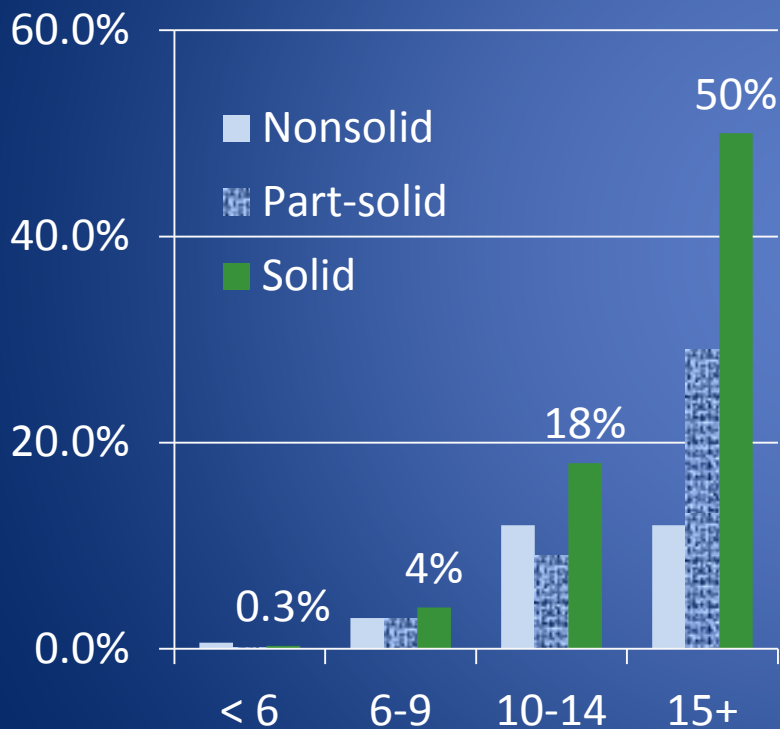
# Prevalence of Lung Cancer: Nonsolid and Part-solid Nodules



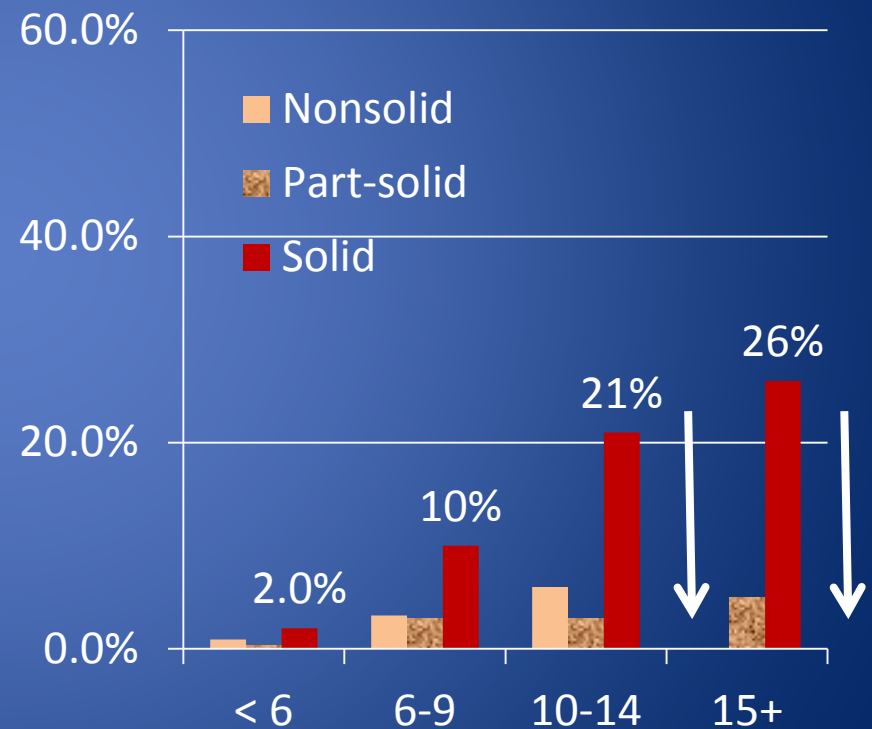
**Annual Repeat Rounds:**  
No cancer in nonsolid nodules 15+ or in part-solid nodules 31+

# Prevalence of Lung Cancer: Nonsolid, Part-solid, and Solid Nodules

## Baseline Round



## Annual Repeat Rounds



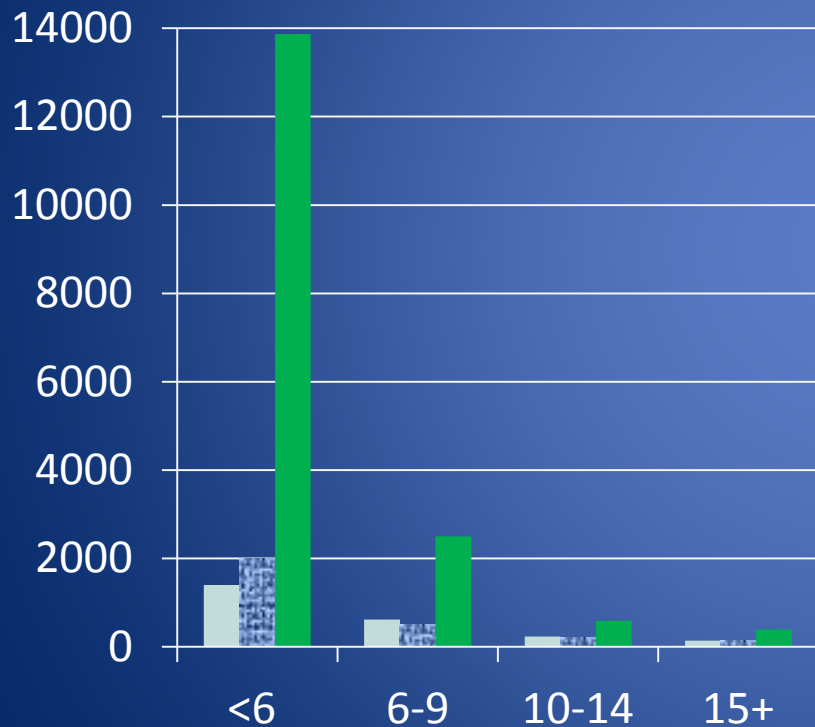
Annual Repeat Rounds:

No cancer in nonsolid nodules 15+ or in part-solid nodules 31+

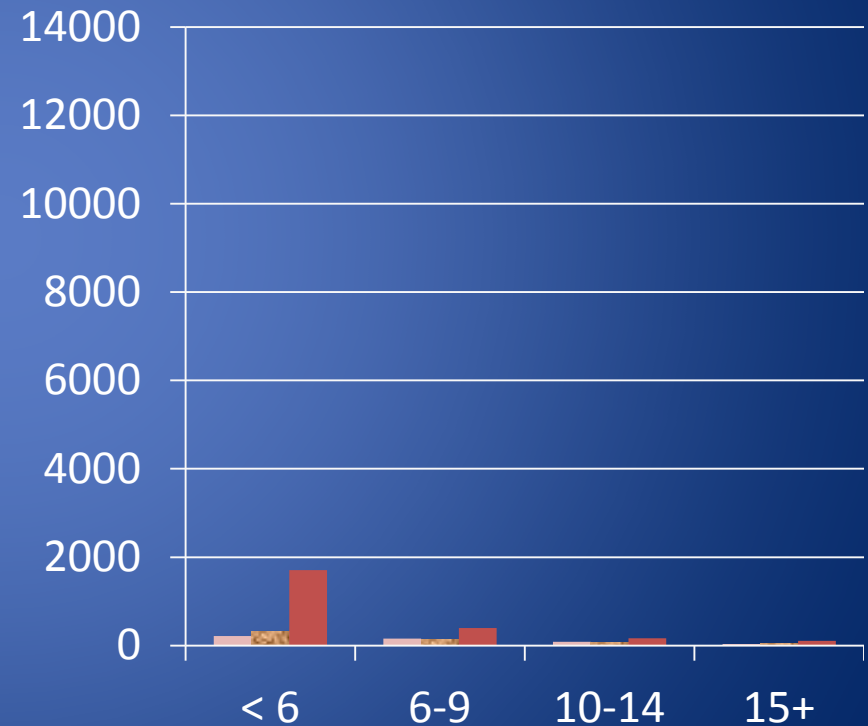
# Frequency and Resolution on Follow-up CT

# Nonsolid, Part-solid, and Solid Nodules: Frequency

**Baseline round**  
**N = 57,496**



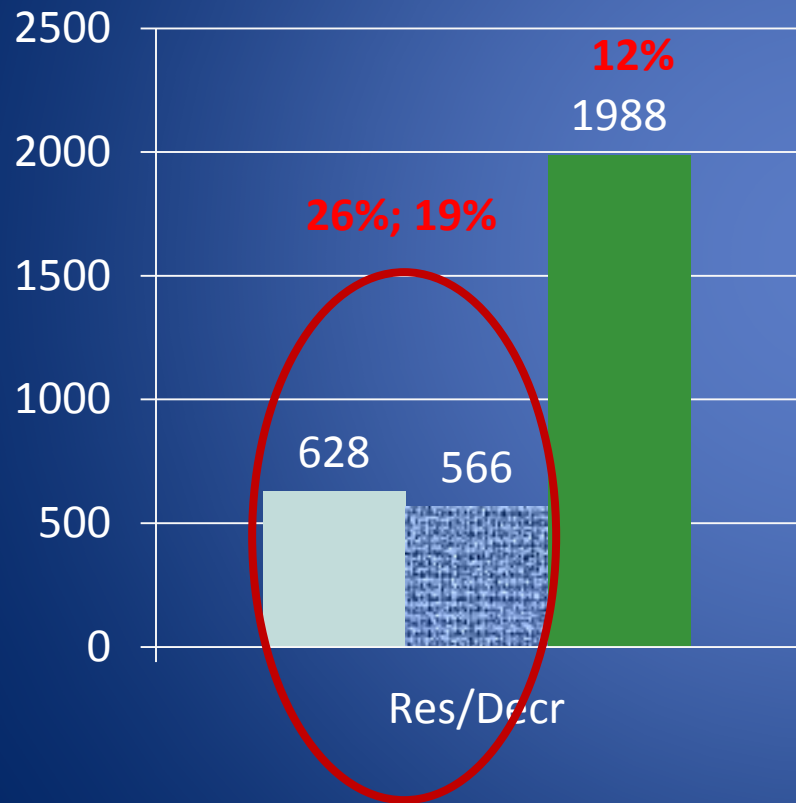
**Annual Repeat Rounds**  
**N = 64,677**



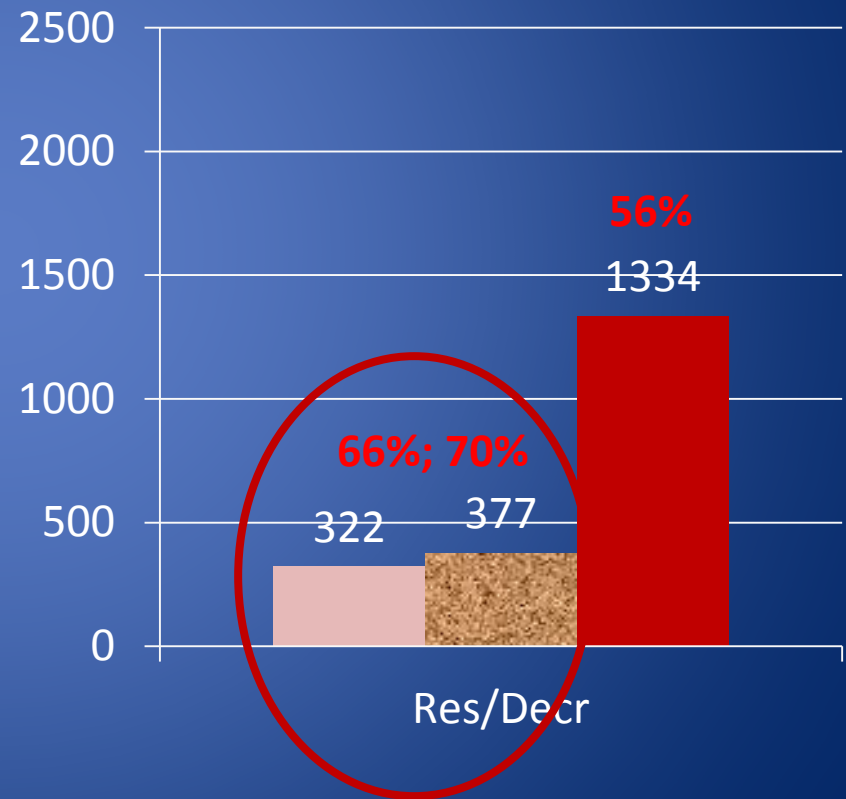
Much higher frequency of solid nodules on baseline, particularly for those < 10 mm in diameter (7 times higher)

# Nonsolid, Part-solid, and Solid Nodules: Follow-up

Baseline round  
N = 57,496



Annual Repeat Rounds  
N = 64,677



Like, nonsolid nodules, a higher proportion of part-solid nodules resolved or decreased in annual repeat: 70% vs. 19%

# I-ELCAP Subsolid Nodule Summary

- No lymph node metastases when solid component < 10 mm in diameter
- Solid component may be due to inflammation, mucus, scar, granuloma, etc.
- Follow-up important
  - High rate of resolution on annual CT scans
  - Growth assessment is helpful in distinguishing between lung cancer and non-malignant processes

# NONSOLID NODULES

## NLST Dataset

Yip R, Li K, Xu DM, et al. Radiology 2016. In press



# Conclusion on NSNs in NLST

- Unlikely that cases with lung cancer as COD occurred in solitary or dominant NSN as long as annual follow-up was done to assess change
- Lung cancers manifesting as NSN have an indolent course and can be managed with annual follow-up

# NONSOLID NODULES

## Meta-analysis

Yip R, Wolf A, Tam K, et al. Lung Cancer 2016. In press

# Meta-analysis of NSNs

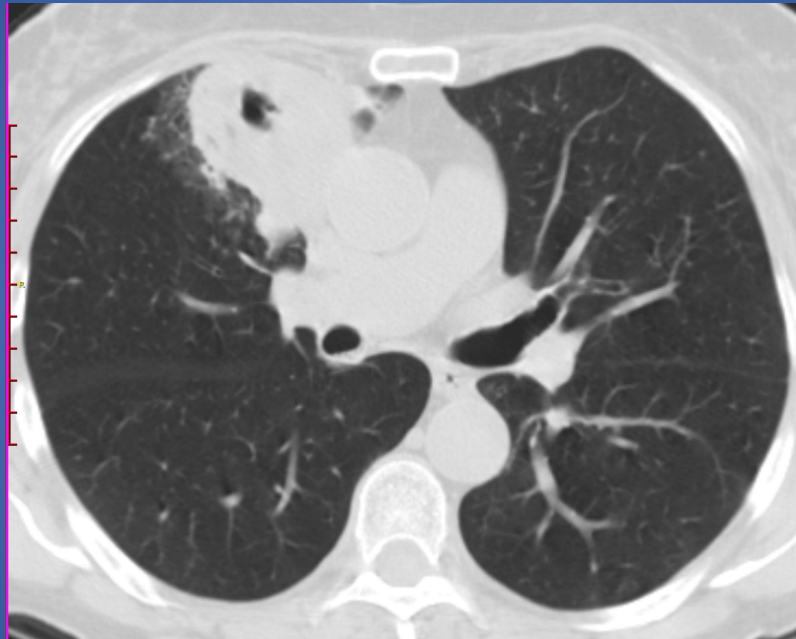
- Comprehensive review and re-analysis of literature on outcome of lung cancer manifesting as NSN
- 24 articles from 5 countries
- 704 people diagnosed with lung cancer manifesting as NSN
- All Stage I adenocarcinoma
- 5-year lung cancer-specific survival: 100%

# PART-SOLID NODULES

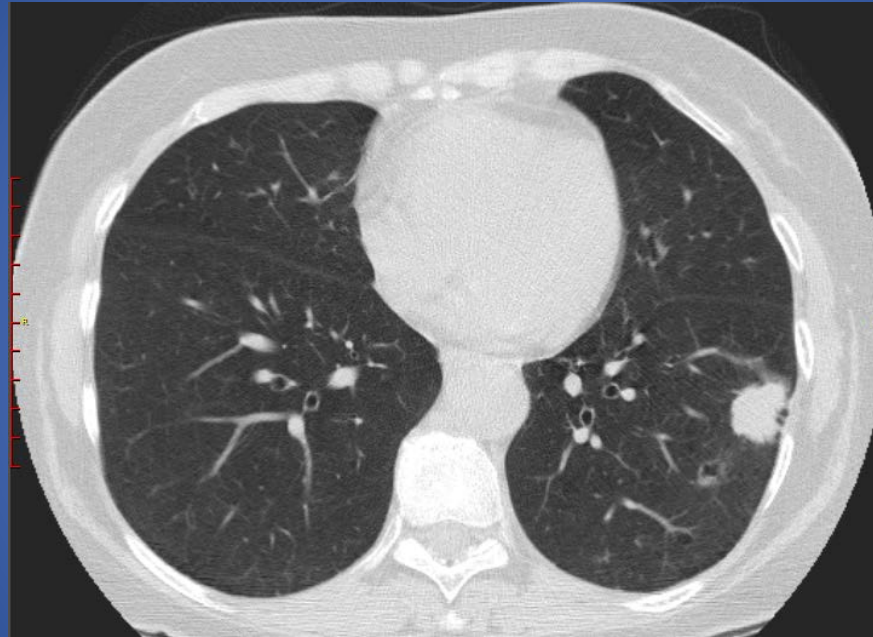
## NLST Dataset

Yip R, Xu DM, Li K, et al. Submitted

# Mixed Nodule in NLST



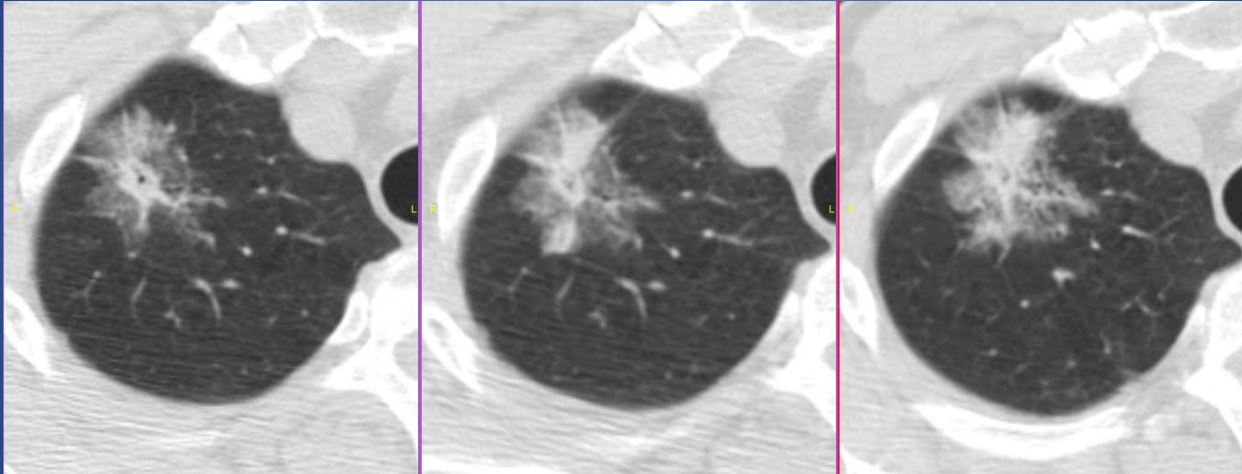
# Mixed Nodule in NLST



# Mixed Nodule in NLST



# Mixed Nodule in NLST





# Mixed Nodule in NLST

## Thick section CT



# NLST: Part-solid Nodules

- 20 cases with part-solid nodule
- 1 death

# Single Death in a Part-solid Nodule in NLST



Multi-lobar part-solid nodules, some of them > 30 mm in length at baseline  
This person underwent baseline and 2 annual repeat rounds of screening prior to diagnosis and died some 72 months (6 years) after randomization

Yip R, Xu DM, Li K, et al. Submitted

# Importance of the Definition of Part-solid Nodules

# Definition of Part-solid Nodules

- CT slice thickness of 1.25 mm or less
- If there is only one scan and the diameter of the solid component is more than 80% of the diameter of the nodule, consider it to be solid and workup accordingly.

# A New Cohort Study

Initiative on Early Lung Cancer  
Research on Treatment  
IELCART

# Stage I Lung Cancer

1. How much lung tissue should be resected?
  1. Lobectomy vs. limited resection
2. How many mediastinal lymph nodes need to be resected
  1. Full resection vs. sampling vs. targeted vs. none
3. Which cases can be followed by “watchful waiting?”
4. Quality of life issues



# IELCART

- Goal to enroll 3,000 patients in the next 3 years to address these questions
- Why?
- CALGB trial: started in 2005 with goal to enroll 1,100 patients, but in 2016 have not reached the reduced goal.
- Difficult to enroll in an RCT for early stage lung cancer