Lung Cancer Screening: Where We've Been and Where We're Going

2014 Dialogue

March 20, 2014

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

Out of the Dark Ages

Into the Modern Era

Current Challenges:

1. How to communicate screening results into informed decision making

Current Challenges:
2. How to Safely and Efficiently Provide the Screening

Future Challenges:
3. How to Efficiently Integrate Advances

Current Challenges:

1. How to communicate screening results into informed decision making

Shared Decision Making
Potential Screenee Questions

- How do we answer the natural question by the person seeking seeking
- Doctor, when a lung cancer is found in a CT screening program, how likely is it to be cured?

- Many other questions as well
- Doctor, does the size of the cancer matter?
- Doctor, what about my age and smoking history?
- Doctor, what if they find something else?

CT Screening Studies: Enrollment

Name	Study years	Enroll-ment	Age	Pack-years	Years quit	Cancer Base-line	Rate Ann-ual	Cancer rate per round*
ELCAP	1993-1999	1,000	60+	10+	N/A	2.7%	0.6%	
NY-ELCAP	2001-2005	6,295	60+	10+	N/A	1.7%	0.4%	
I-ELCAP	1993-ongoing	62,931	40+	0+	N/A	1.1%	0.3%	
Nagano	1996-1998	5,483	40-75	0+	N/A			0.5%*
Mayo	1999-2003	1,520	50-75	20	< 10	2.0%	0.6%	
NLST	2002-2007	26,309	55-74	30	< 15			0.9%*
NELSON	2004-2010	7,557	50-75	15	< 10	0.9%	0.9%	
Cosmos	2004- 2010	5,200	50-85	20	<10	1.1%	0.8%	

*Cancers identified in all rounds/(enrollees x rounds of screening)

A broad spectrum of age, pack-years of smoking, and years quit

CT Screening Studies:
Stage I Cancers: 62% - 91%

Name	Study years	Enrollment	Cancers	c Stage I	c & p Stage I
ELCAP	1993–1999	1,000	34 + 2	29 (81%)	29 (81%)
NY–ELCAP	2001–2005	6,295	121 + 3	112 (90%)	105 (85%)
I–ELCAP	1993 – ongoing	62,931	874 + 11	721 (81%)	677 (77%)
Nagano*	1996–1998	5,483	61+ 2		41 (91%)
Mayo*	1999–2003	1,520	63 + 3		41 (63%)
NLST*	2002–2007	26,309	649 + 44		407 (59%)
NELSON	2004–2010	7,557	197+ 3		148 (71%)
Cosmos*	2004–2010	5,201	159 + 3		115 (71%)

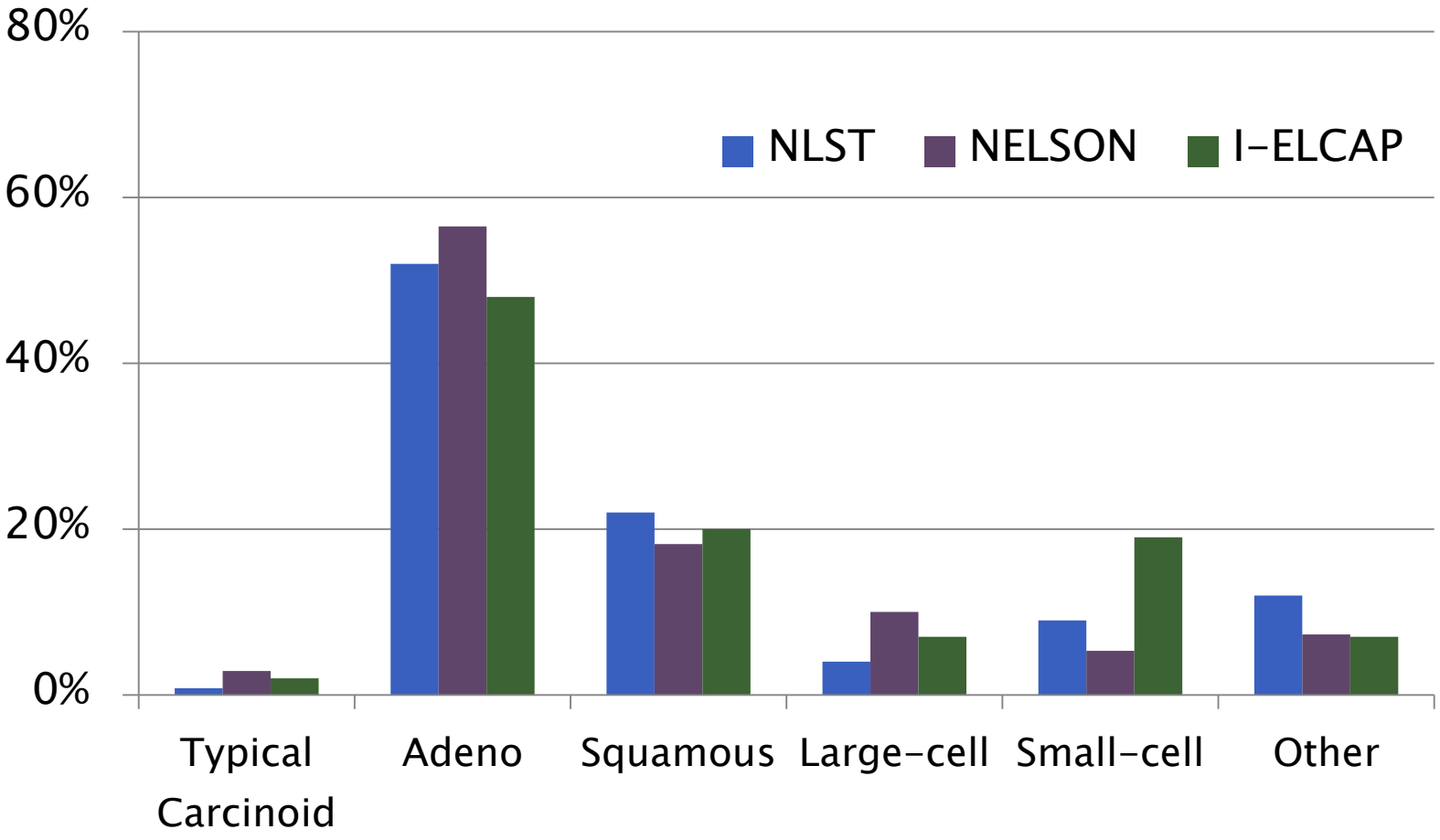
*6th AJCC

Clinical staging determines treatment and does not depend on # resections

Pathologic staging has changed from AJCC 6th to 7th edition (BAC now in–situ)

SUGGESTION: GIVE BOTH CLINICAL AND PATHOLOGIC STAGING

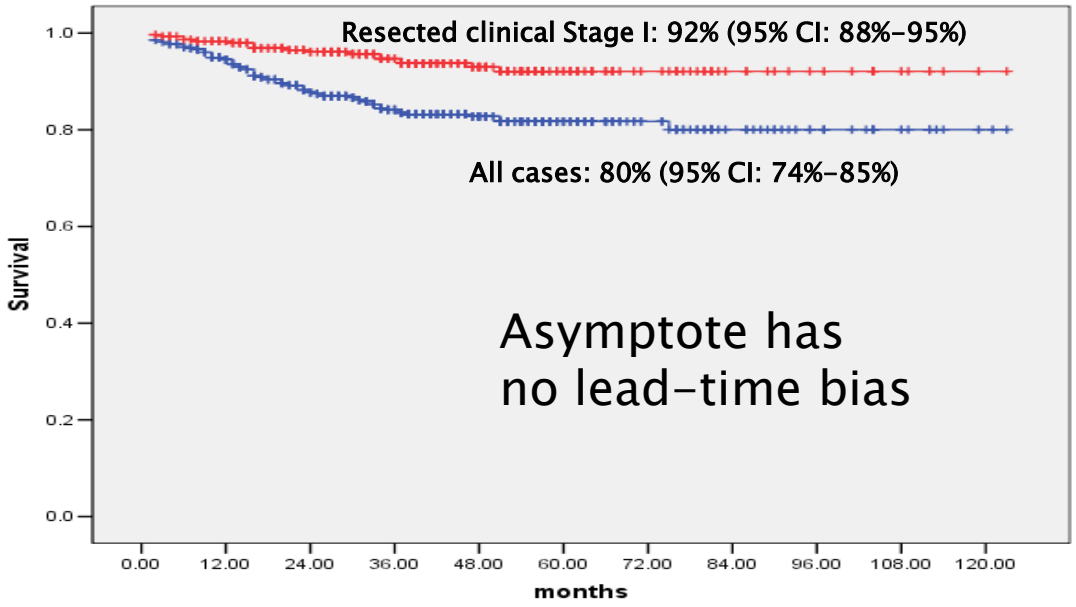
Distribution by Cell-type: NLST vs. NELSON vs. I-ELCAP



Cure rate: I-ELCAP

1. Overall cure rate: 80%

   The case fatality rate is the complement: 20%



2. Gain in curability or reduction in case fatality is:
   = (90% – 20%)/90% = 78%

3. As expected, higher than the SEER estimate of 71%

National Lung Screening Trial

- Trial was stopped as analysis showed a 20% reduction – Oct 2010
  - In the 6-year mortality rate of those in the CT arm as compared to those in the CXR arm
- Reported in N Engl J Med 2011

I-ELCAP and NLST Comparison

- Cure rate of 80% in I-ELCAP is compatible with a mortality reduction of 20% in the NLST

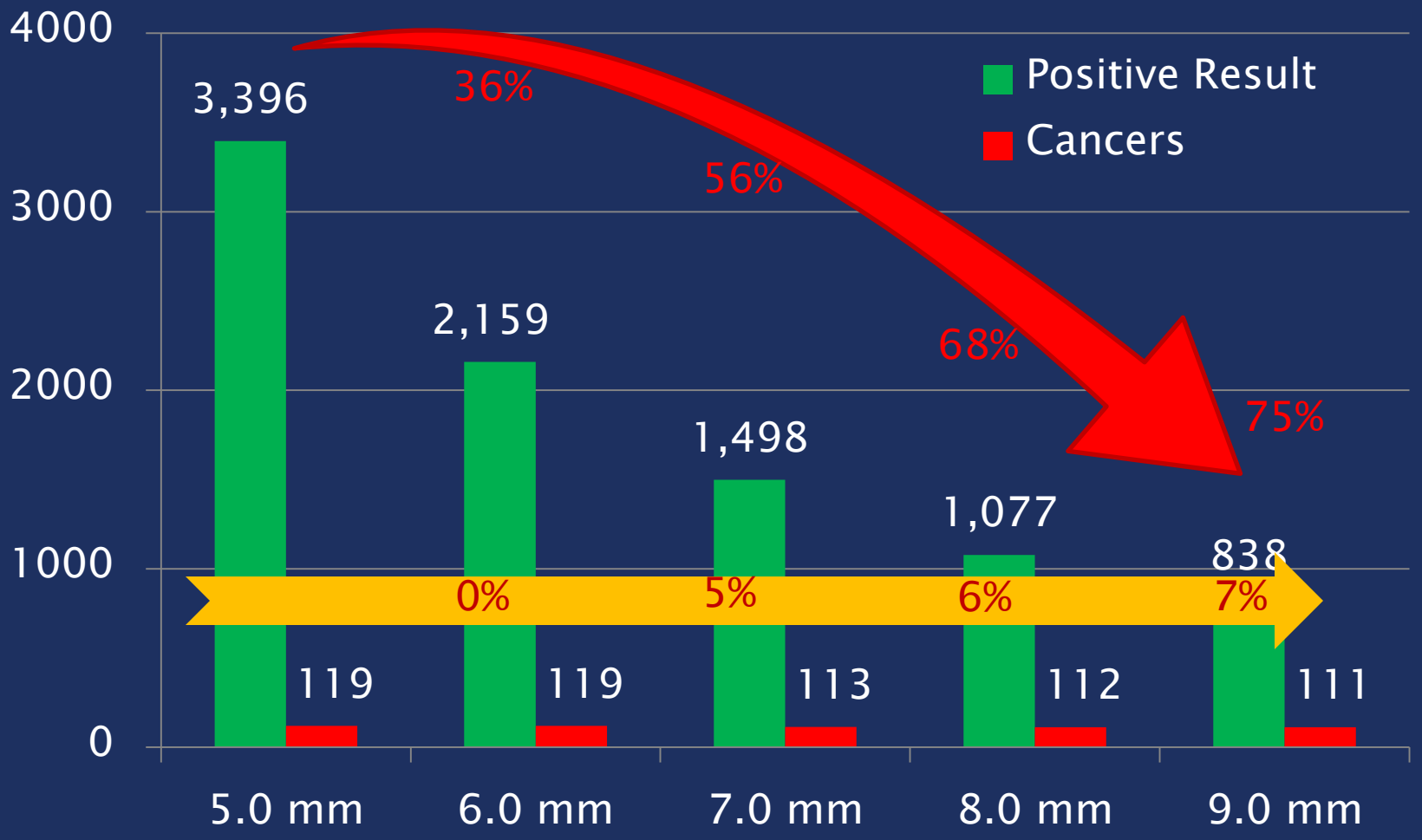
- Concern: If the benefit is wrongly stated as being too small, screening is not perceived as being worthwhile

Current Challenges:
2. How to Safely and Efficiently Provide the Screening

The Devil is in the Details

The Regimen of Screening

Baseline: frequency of positive result and dx of lung cancer among 21,136 recent participants



Henschke CI 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.

Regimen: Baseline

I-ELCAP RECOMMENDATIONS			
Baseline Round of Screening		Each Annual Repeat Round of Screening	
1. First Annual Repeat Screening, if			
Negative:	No NCN (noncalcified nodules)		
Semi-positive:	Largest part-solid or solid NCN < 6 mm in avg. diameter		
Semi-positive:	Nonsolid NCN of any size		
2. Follow-up CT scan in 3 months, if			
Positive:	**Largest part-solid or solid NCN 6-14 mm in avg. diameter***		
Suspicious:	Growth** at a malignant rate on 3 mos. f-up CT		
3. Immediate workup (PET, Bx, or 1 mo f-up CT), if			
Suspicious:	If largest part-solid or solid NCN ≥ 15 mm in avg. diameter		
Additional work-up in 10% of baseline participants (steps 2 and 3) during the first year; about 7% of participants in each year of annual repeat screenings (steps 2 and 3)			
* if NCN ≥ 10 mm and very suspicious in appearance, immediate PET scan is an option. Note that hamartomas and granulomas are typically of this size			
**The solid component of the NCN is measured, growth is at a malignant rate if the relative change in volume is more than:			
a) 65% for nodules 3-6 mm; b) 50% for nodules 6-7 mm; c) 40% for nodules 8-9 mm; d) 30% for nodules > 10 mm			
For detailed description, see I-ELCAP protocol (www.IELCAP.org), pages 7 and 8.			
Any screening participant diagnosed with lung cancer and treated for curative intent should continue with annual CT screening			

Regimen: Annual Repeat

I-ELCAP RECOMMENDATIONS	
Baseline Round of Screening	Each Annual Repeat Round of Screening
	1. Next Round of Annual Repeat Screening, if
	Negative: No new or growing NCN
	Semi-positive: Largest new part-solid or solid NCN < 3 mm in avg. diameter
	Semi-positive: New nonsolid NCN of any size
	2. Follow-up CT scan in 6 months, if
	Positive: New or growing part-solid or solid NCN 3-6 mm in avg. diameter
	Suspicious: Growth** at a malignant rate on 6 mos. f-up CT
	3. Follow-up CT in 1 month, if
	Positive: New or growing part-solid or solid NCN ≥ 6 mm in avg. diameter
	Suspicious: If growth** at a malignant rate on 1 mo. f-up CT
Additional work-up in 10% of baseline participants (steps 2 and 3) during the first year; about 7% of participants in each year of annual repeat screenings (steps 2 and 3)	
* if NCN ≥ 10 mm and very suspicious in appearance, immediate PET scan is an option. Note that hamartomas and granulomas are typically of this size	
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The Regimen Determines the Frequency of Stage I at Dx and The Cure Rate

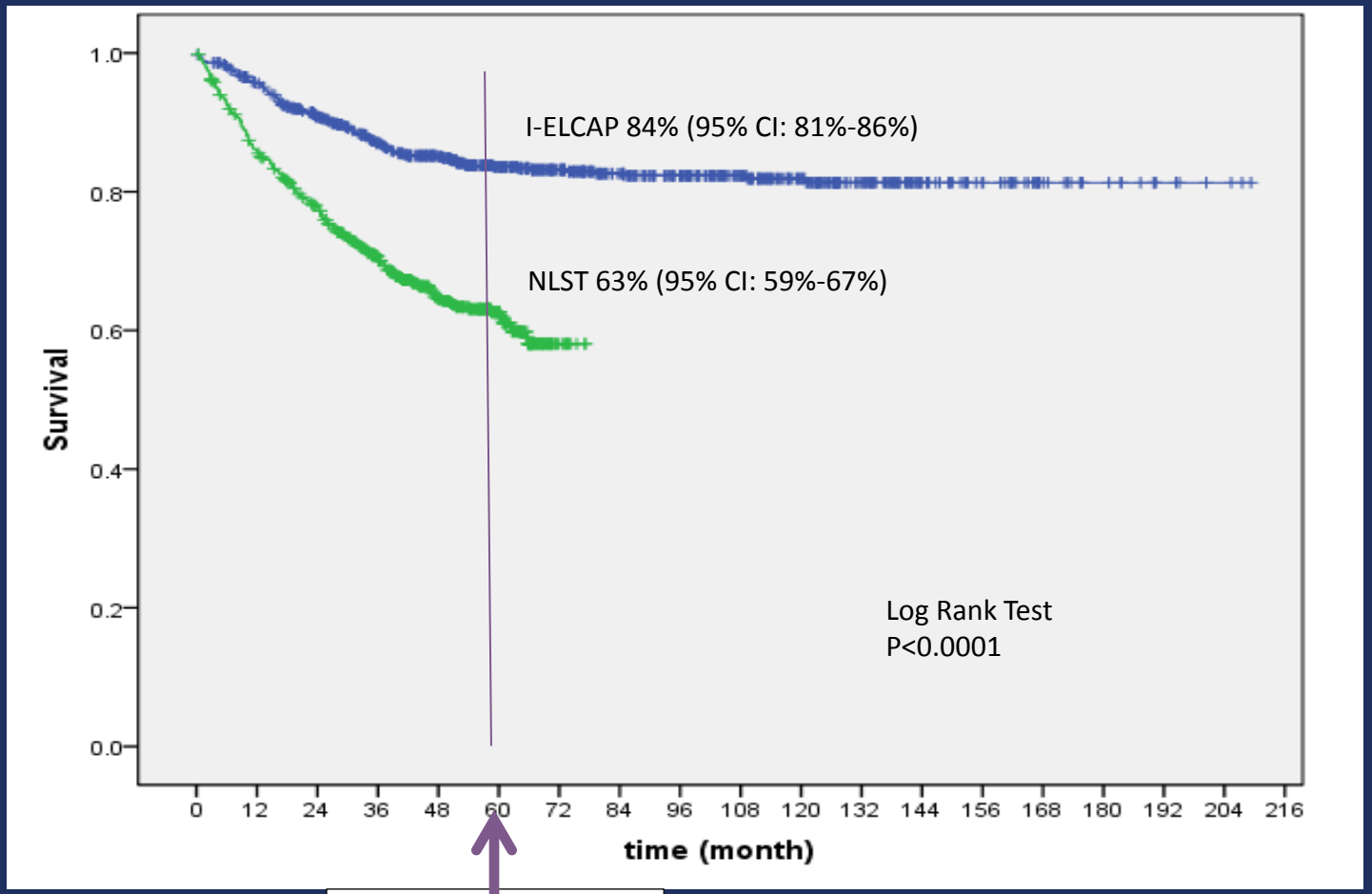
I-ELCAP	NLST
78%	**62%**
N = 788	N =649

Stage is pathologic if resected, otherwise clinical

Frequency of Stage I Determines Ultimate Cure Rate

Figure 1. Five-year Kaplan-Meier lung cancer specific survival rates for all screen-diagnosed cases in I-ELCAP (N = 788) and NLST (N = 649).

Five year KM survival rates



The authors thank the National Cancer Institute (NCI) for access to the NCI's data collected by the NLST. The statements contained herein are solely those of the authors and do not represent or imply concurrence or endorsement by NCI.

Other Diagnoses:

Emphysema

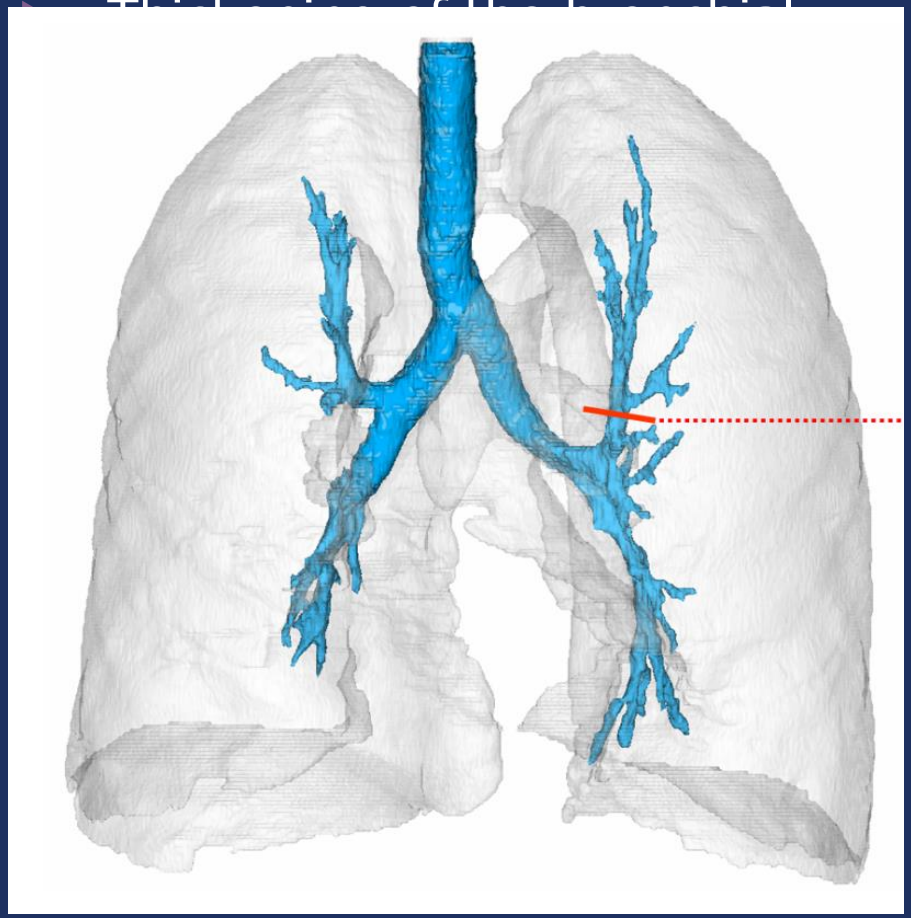
Usual Interstitial Pneumonitis

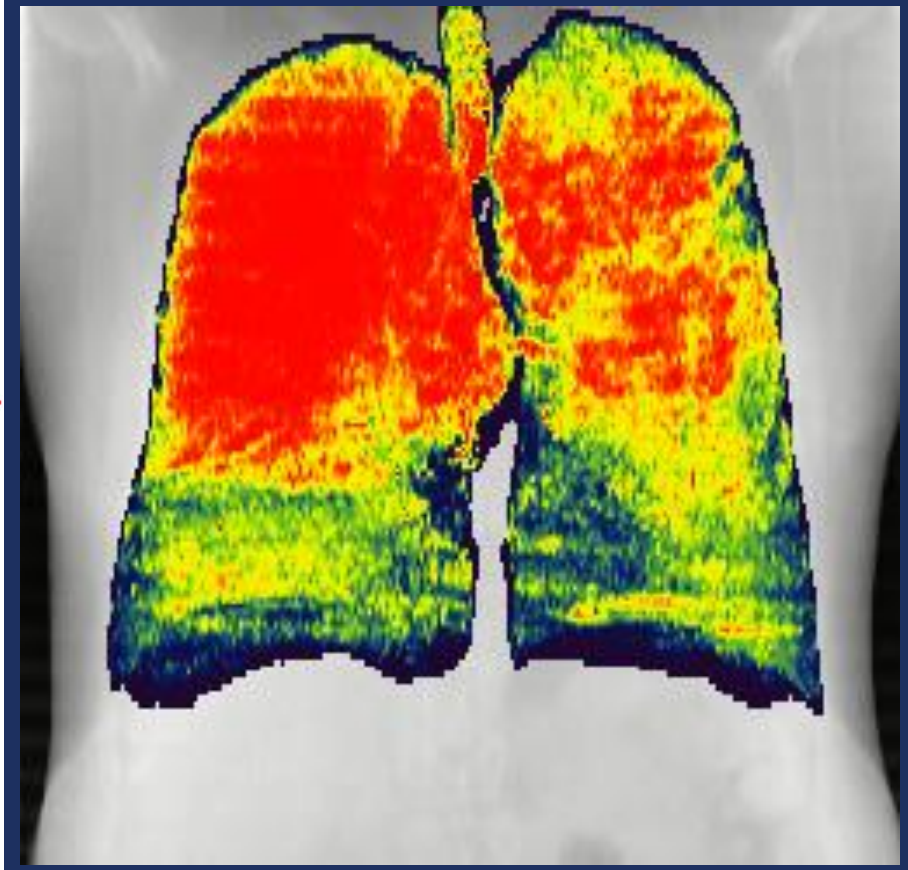
Cardiac Disease

Risk of Breast Cancer

Automated Analysis

Airway wall thickness and Emphysema on CT





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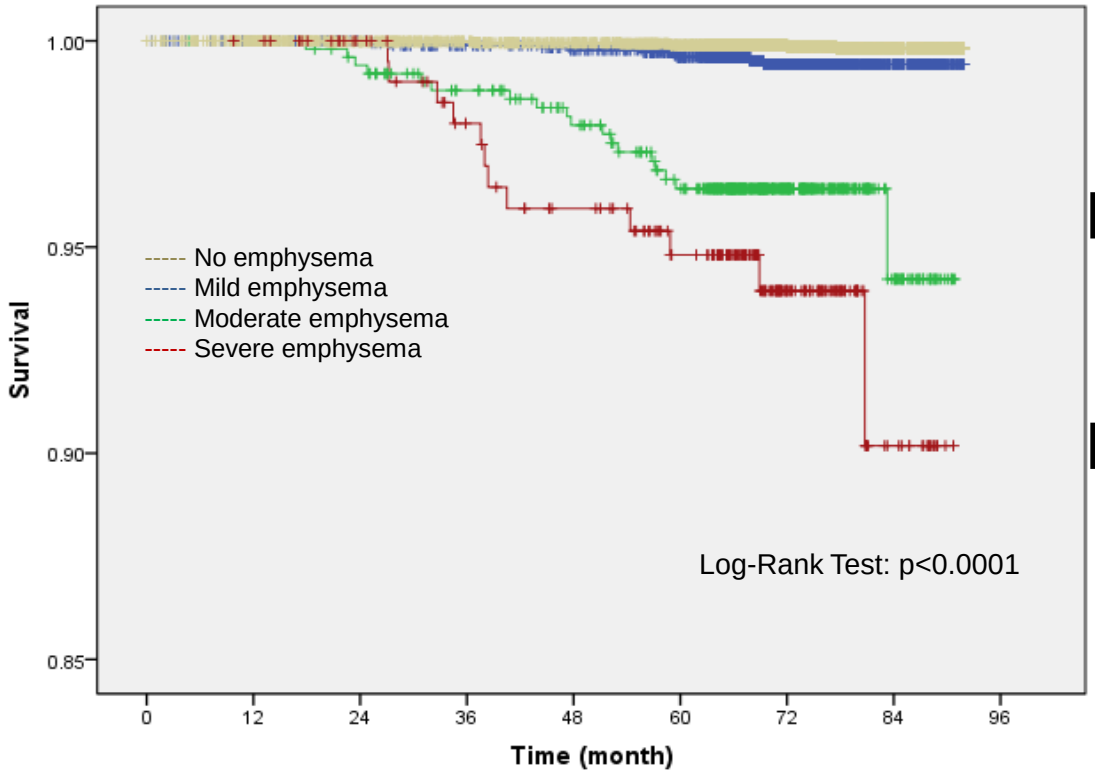
COPD-specific Survival Rates (n = 9,047)
adjusted by age, sex, smoking history and diabetes

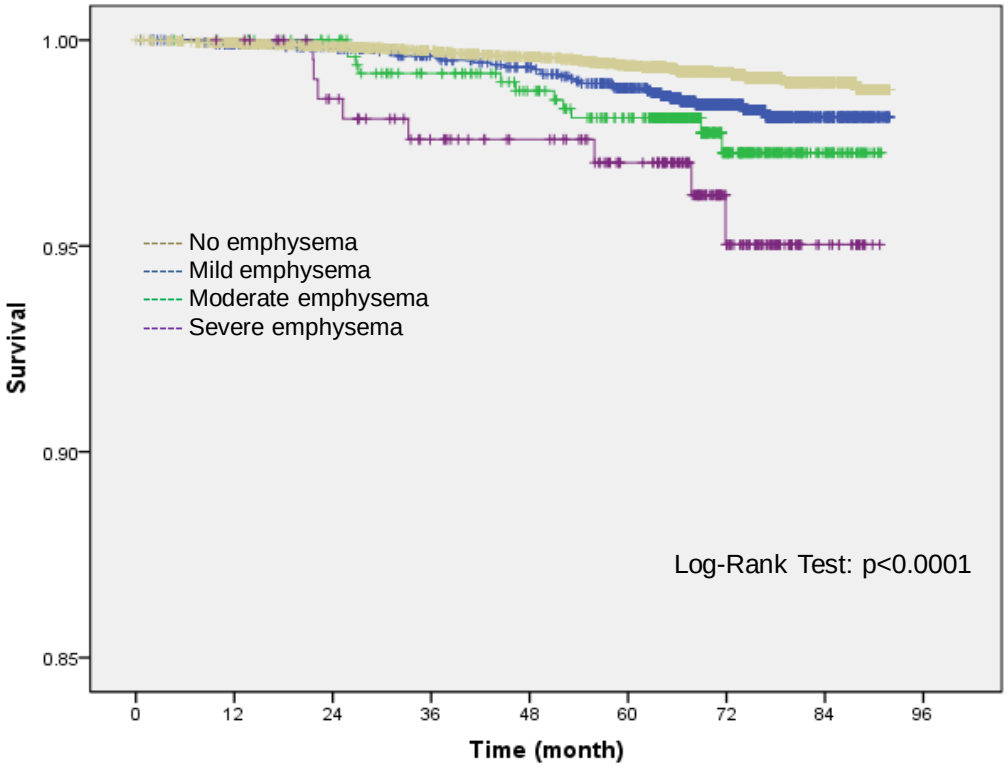


Moderate:
HR = 17.3 (9.5–52.3)

Marked:
HR = 43.7 (13.9–86.1)

Zulueta et al. Chest 2012; 141: 1216–23

Lung Cancer Survival Rates (n = 9,047)
adjusted by age, sex, smoking history and diabetes

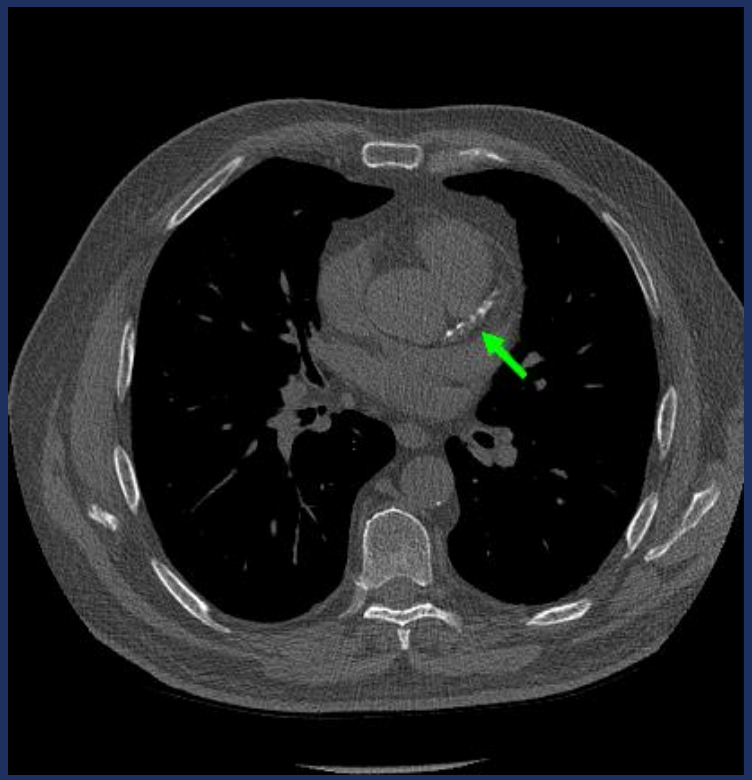


Marked:
HR = 3.2 (1.5 – 6.7)

Zulueta et al. Chest 2012; 141: 1216-23

Cardiac Disease on low-dose CT

- Ungated, low-dose CT

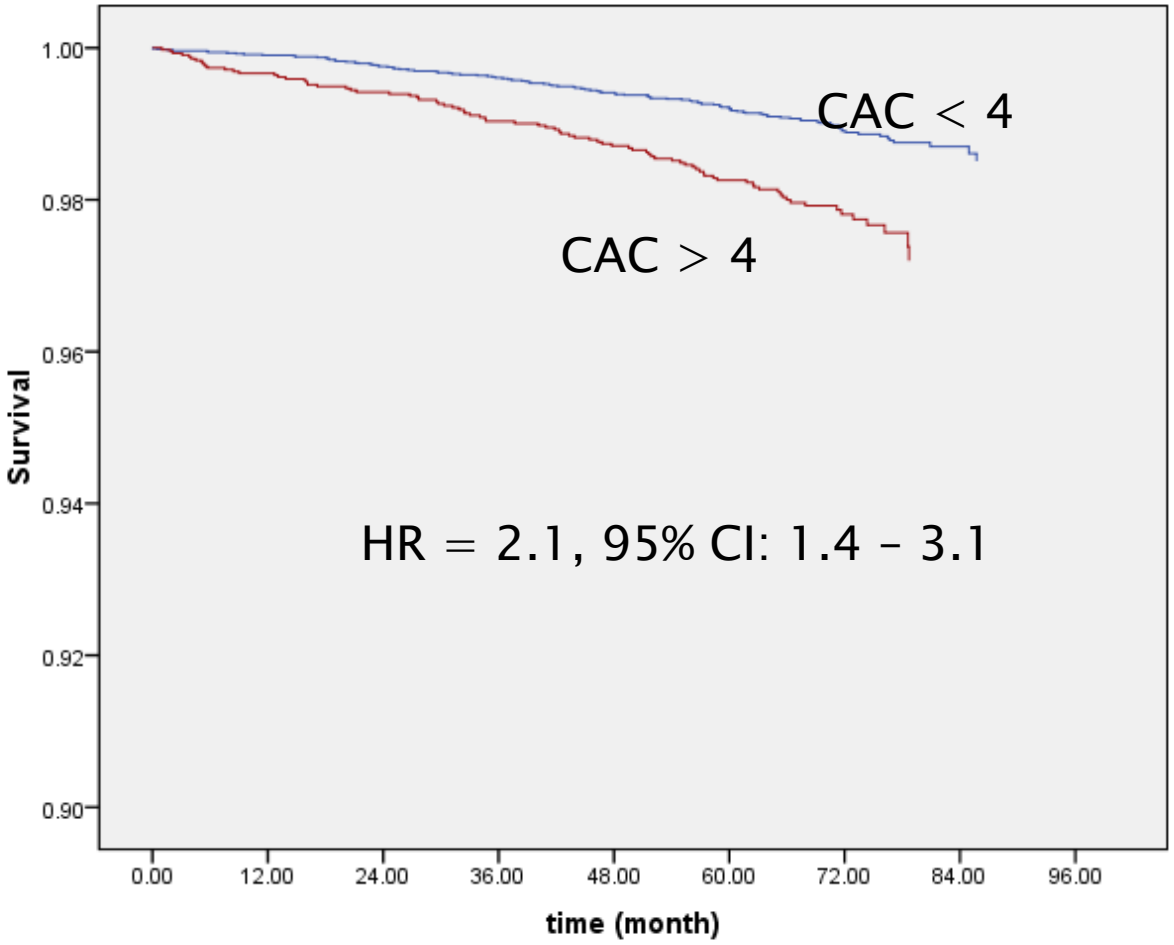


CAC Score

- Main, LAD, circumflex, right coronary arteries
- Extent of calcification in each artery: none (0), mild (1), moderate (2), marked (3)
- CAC score: 0 -12, for any given person

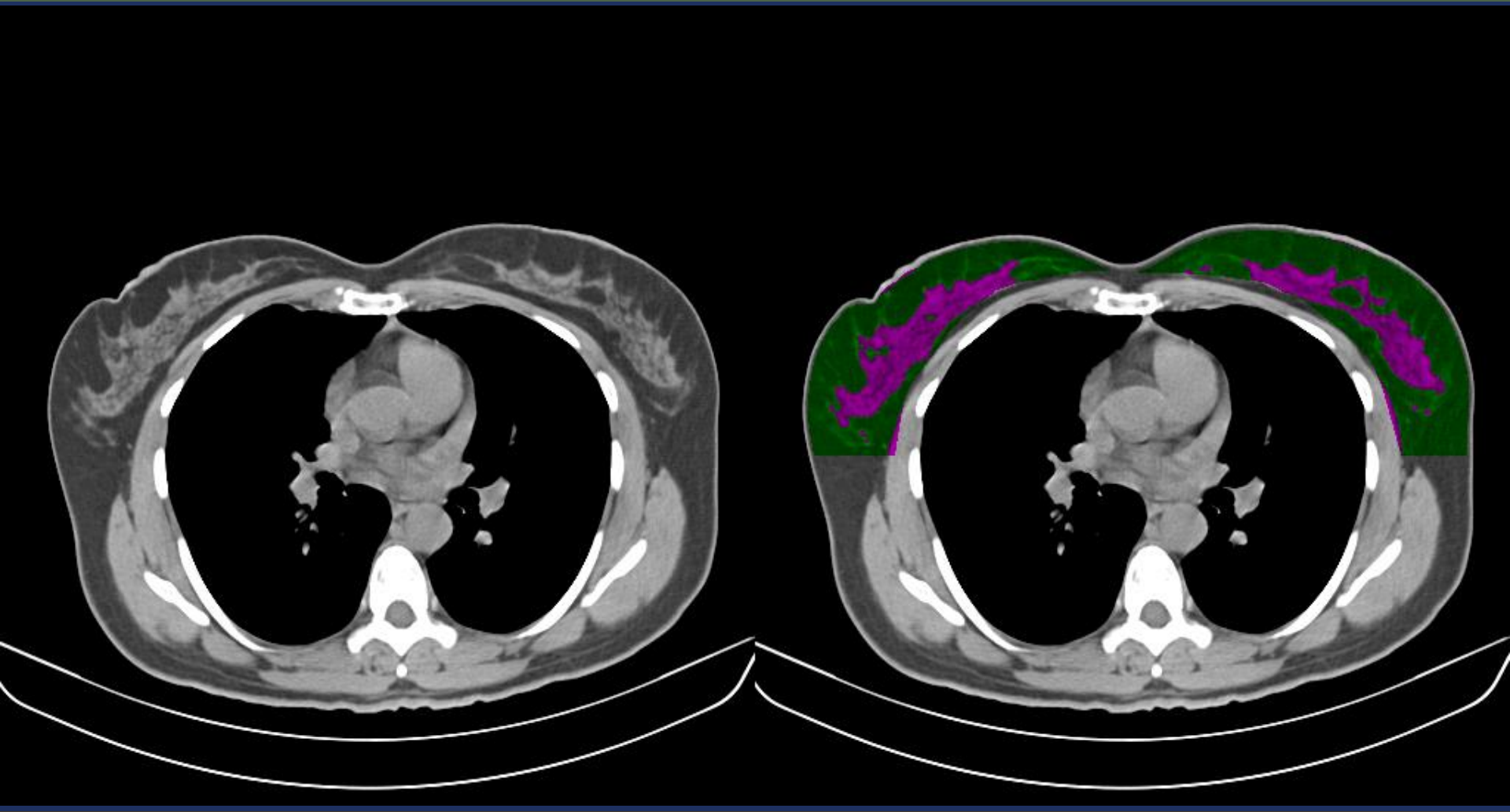
Shemesh et al. Clinical Imaging 2006; 239: 181–5
Shemesh et al. Radiology 2010; 257: 541– 8

Survival rates by CAC score (n = 8,872)
adjusted by age, sex, smoking history and diabetes



Shemesh et al. Radiology 2010; 257: 541–548

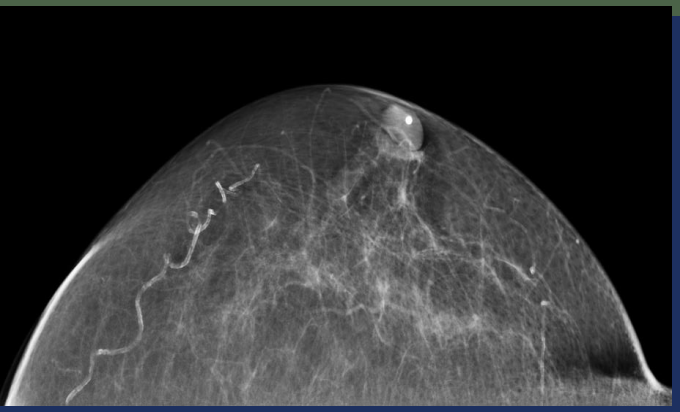
Breast Density:
Increased Density is an indicator of breast ca

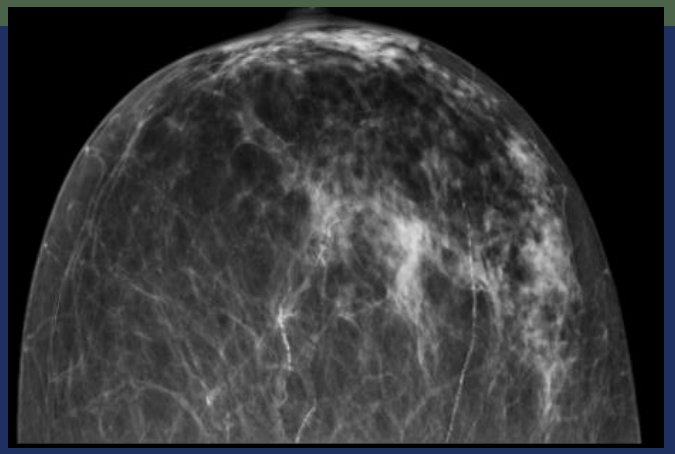


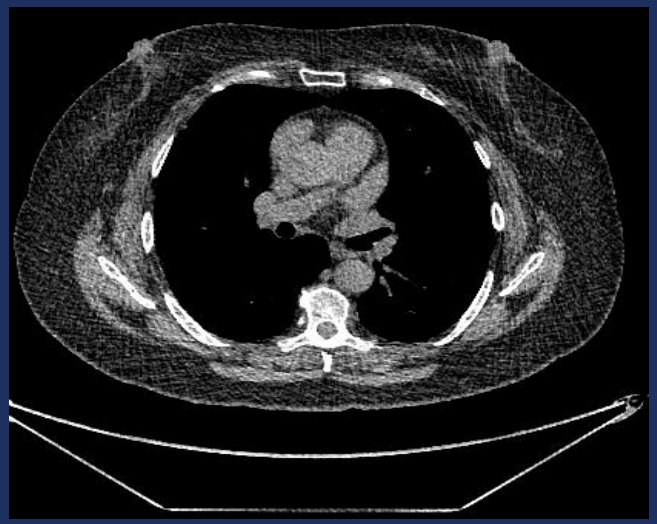
Salvatore et al. Radiology, In press 2014

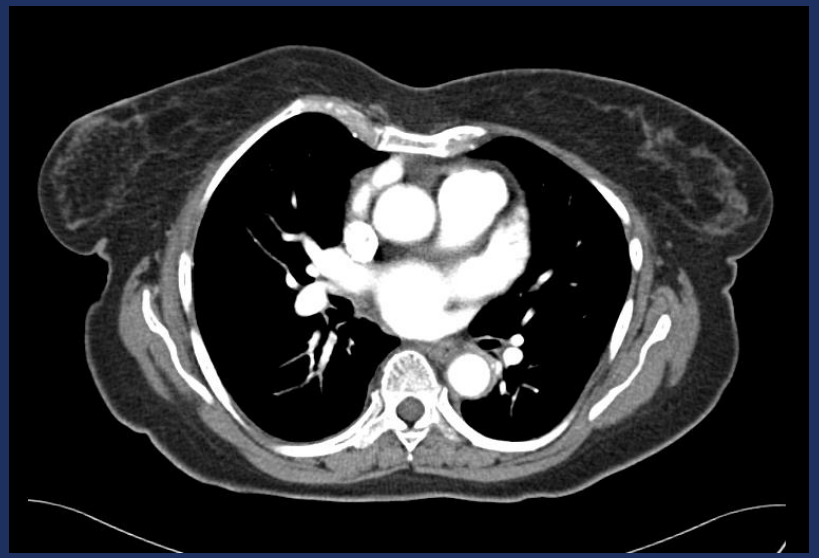
I-ELCAP

Bi-Rads: Grades: 1 and 2





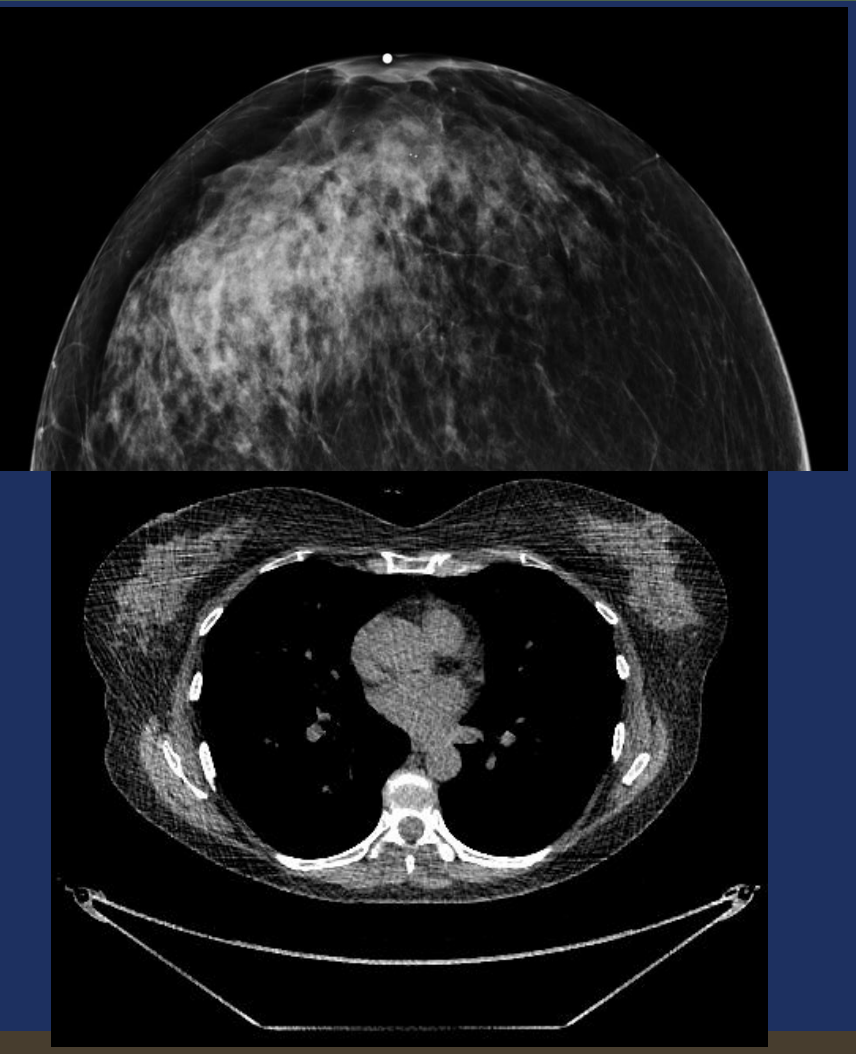




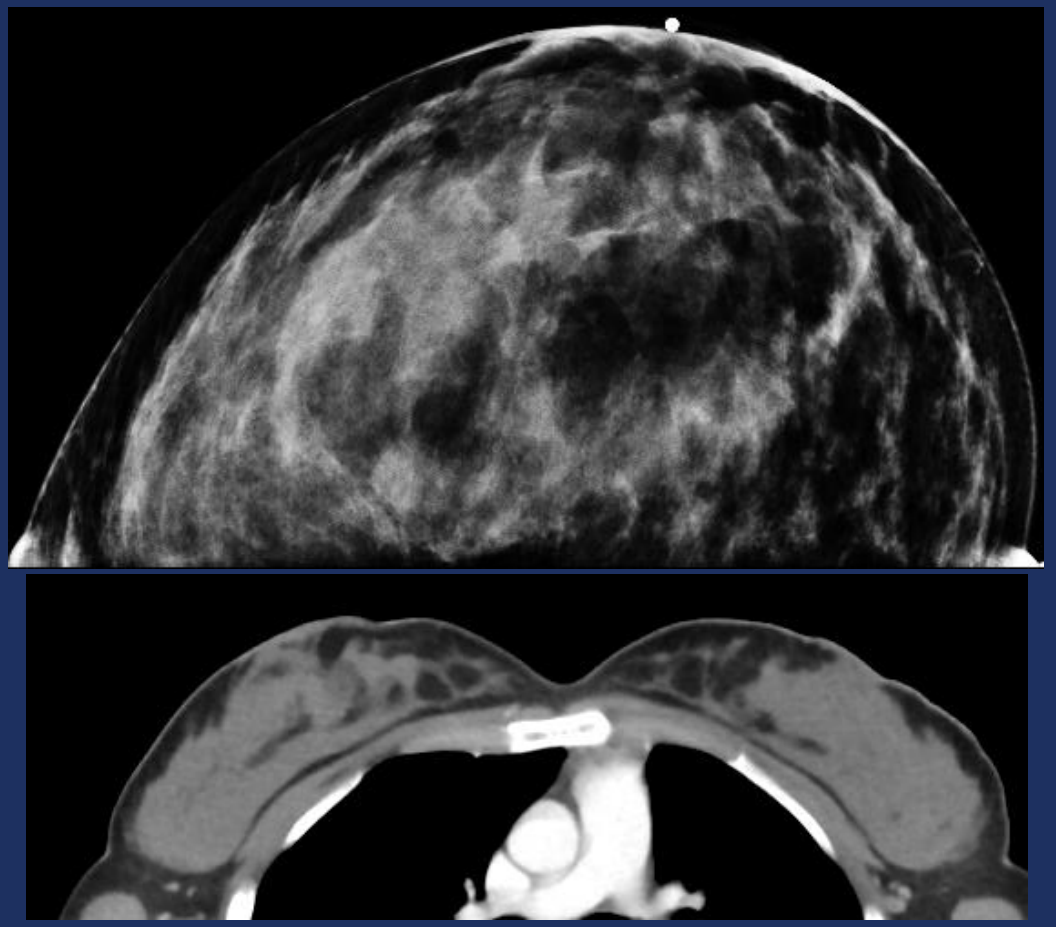
Grade 1

Grade 2

Bi-Rads: Grades: 3 and 4

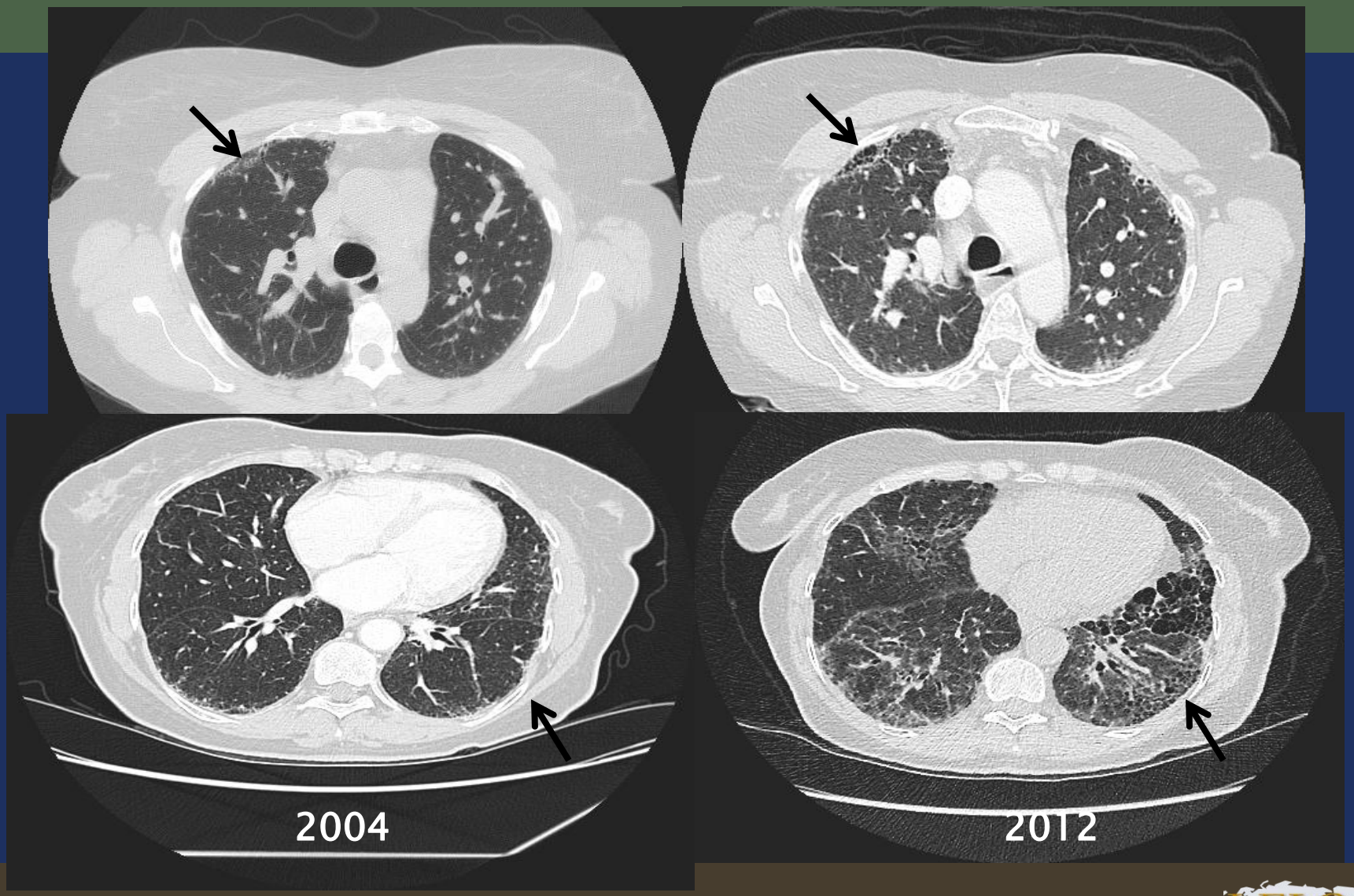


Grade 3



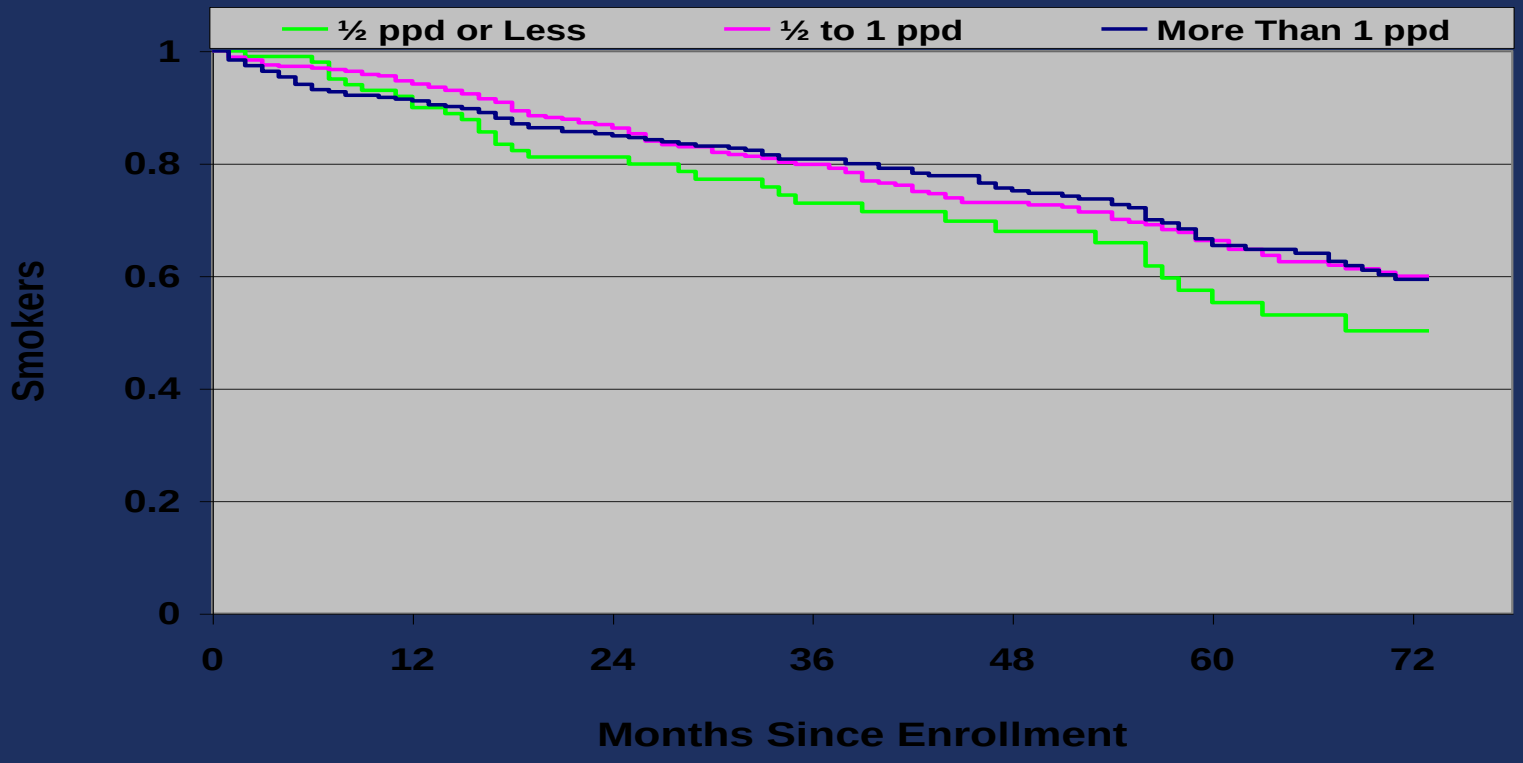
Grade 4

Usual Interstitial Pneumonitis



Salvatore M et al. RSNA Scientific Abstract 2012

Smoking Cessation Efforts are Important



Ostroff et al. Preventive Med 2001; 33:613–21
Anderson et al. Cancer Epidemiol Biomarkers Prev 2009; 18:3476–83

Future Challenges:
3. How to Efficiently Integrate Advances

Registry for Excellence in Lung Screening

- Capture data from screening on an ongoing basis
- Continually analyze and update the process of screening

A Most Exciting Advance in Health Care

Needs to be Implemented Responsibly