VA PARTNERSHIP Incr**ease ACCESS to** LUNG SCREENING

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Sponsored by the Bristol-Myers Squibb Foundation and the VA Office of Rural Health

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

Initial VA Screening Program

- It was started as a pilot project at multiple VA centers
- The results were very varied
- Many problems due to insufficient infrastructure and management system
  - Wrong scanning protocol
  - Too many false positives

Kissinger et a. Implementation of lung cancer screening in the VHA. JAMA Intern Med 2017; 177: 399-406

VA-ELCAP Management System for VA-PALS

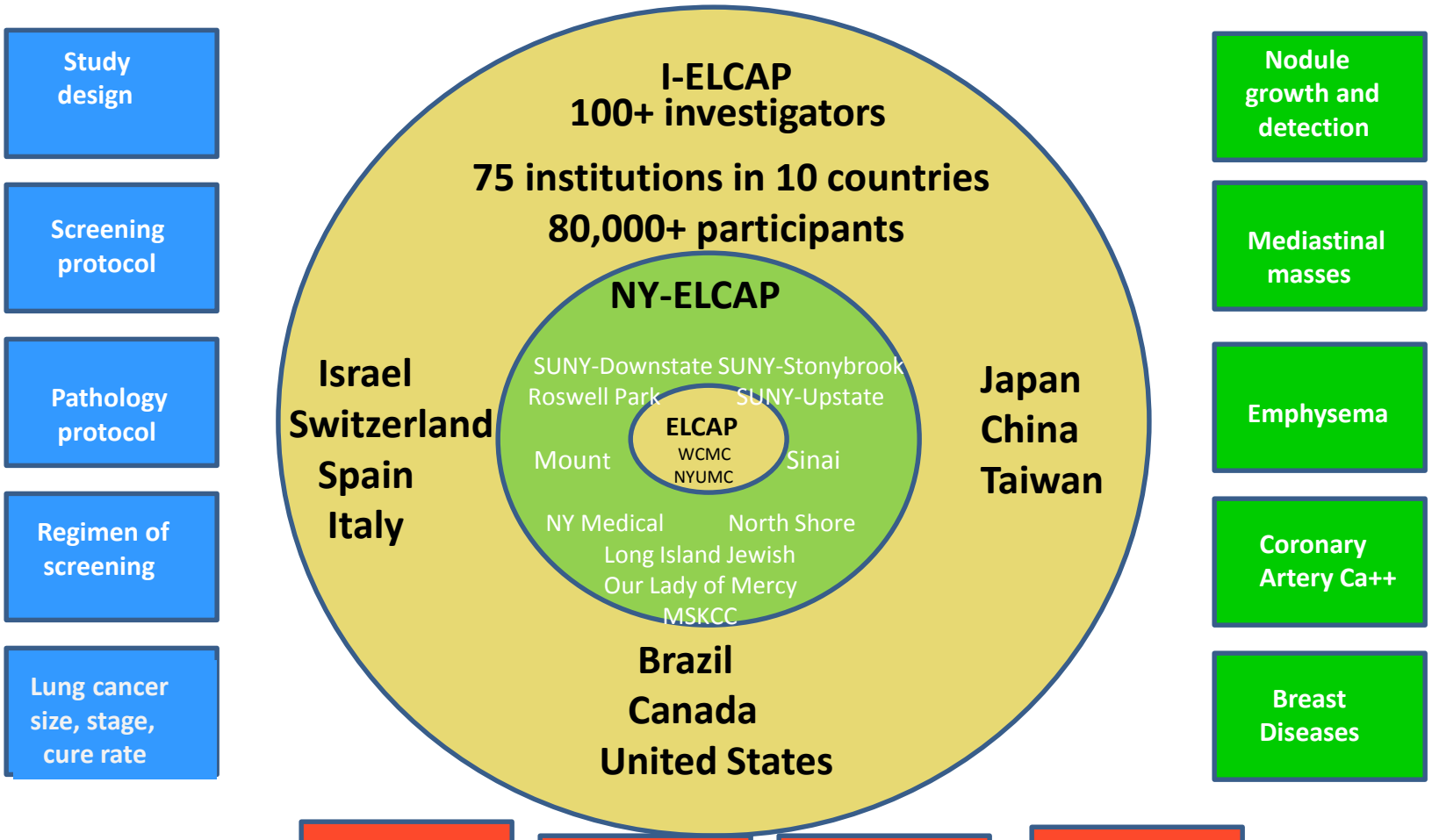
In process of being launched at the
Phoenix VA, followed by
St. Louis VA, and then 8 other VA centers

Early Diagnosis and Treatment Research Foundation is providing the ELCAP Management System to the VA for this purpose

Largest CT Screening Cohort in the World

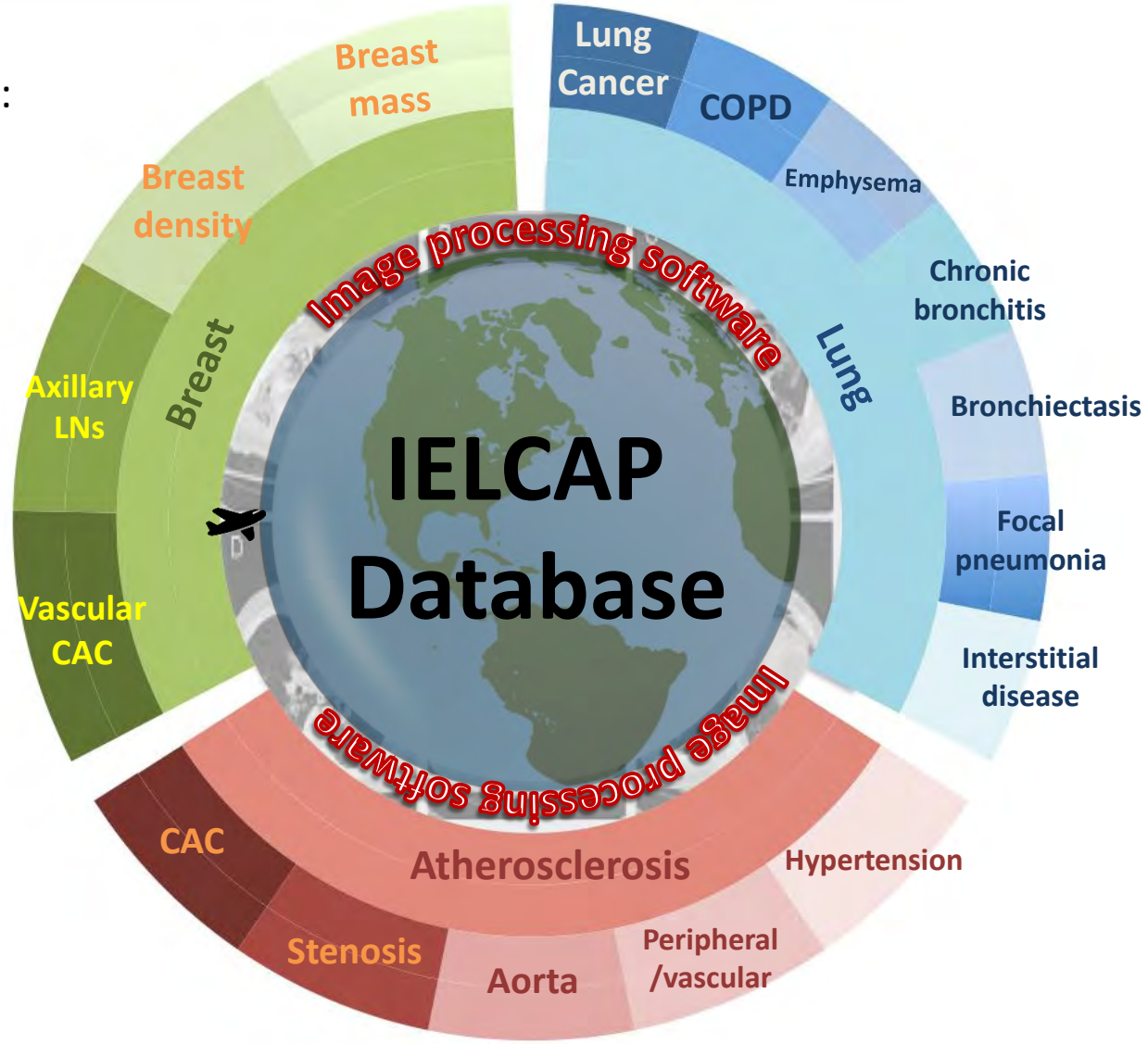
ELCAP to NY-ELCAP to International-ELCAP

Individualized CT screening depends on indicators of risk
e.g., current smokers, former smokers, never smokers



OTHER CT FINDINGS

Further areas:
Liver
Adrenals
Thyroid



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QA Needed for Processes

- Scanner
- Scanning
- Protocol
- Readers
- Recommendations

Scanner

- Scanner type and model will be collected
- Protocol reviewed
- QIBA small nodule conformance

Scanning

- Dose monitoring
- Scan monitoring (overscanning)
- Scan quality

NELSON Conclusion

- Volume CT screening results in a low referral rate (2.3%) and a very substantial reduction in lung cancer screening mortality

- However, volumetric assessment is still in its infancy and needs further standardization

Volumetrics

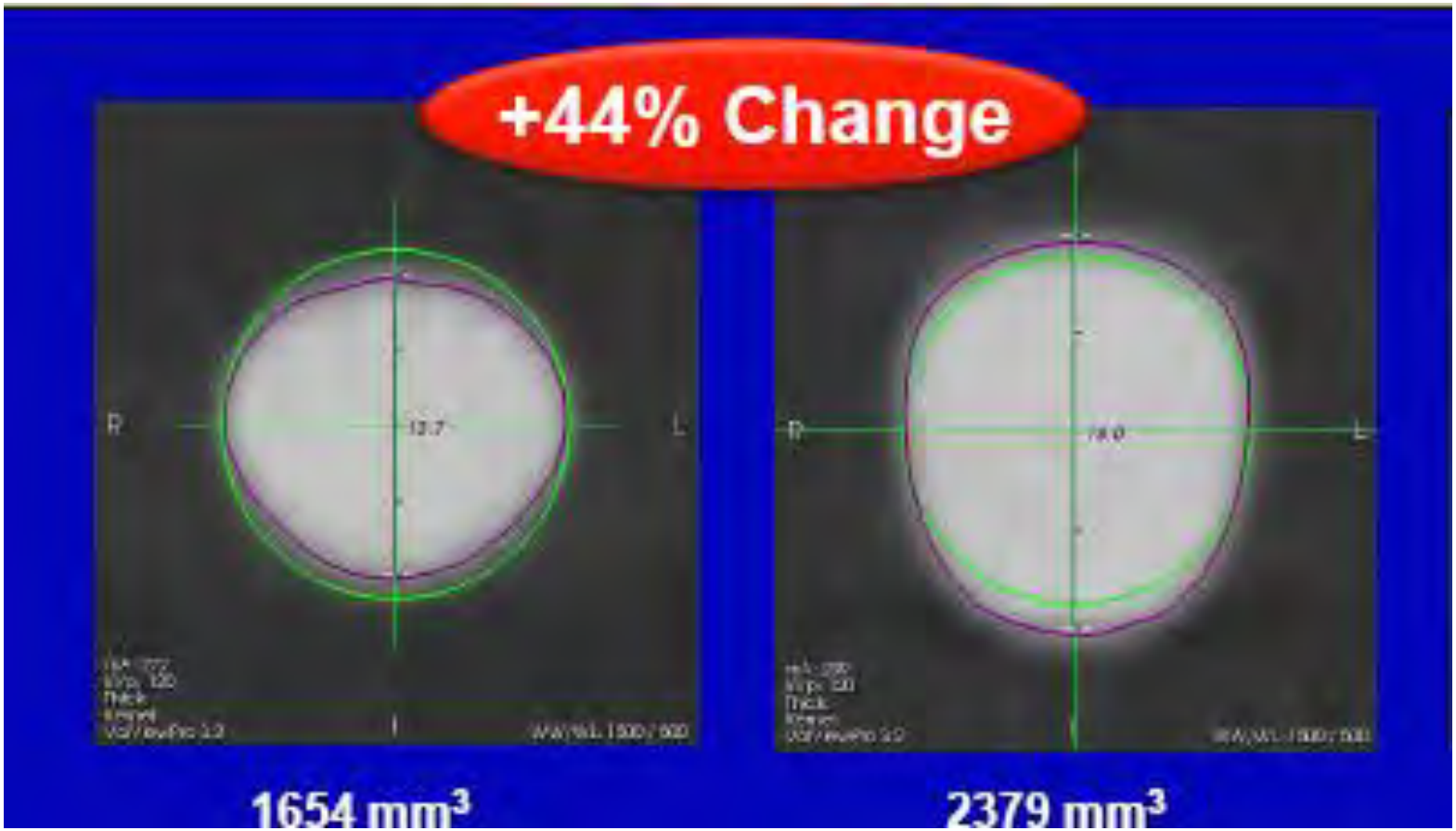
- We introduced it in 1999

- Yankelevitz DF, Gupta R, Zhao B, Henschke CI. Small Pulmonary Nodules: evaluation with repeat CT-preliminary experience. Radiology 1999; 212:561-6
- Zhao B Reeves A, Yankelevitz DF, Henschke CI. Three-dimensional multi-criterion automatic segmentation of pulmonary nodules of helical CT images. Optical Engineering 1999; 38:1340-7
- Kostis WJ, Reeves AP, Yankelevitz DF, Henschke CI. Three-dimensional segmentation of solitary pulmonary nodules from helical CT scans. Proceedings of Computer Assisted Radiology in Surgery (CARS '99). (Eds: HU Lempke, MW Vannier, K Inamura, AG Farman). Elsevier Science 1999:203-7
- Yankelevitz DF, Reeves AP, Kostis WJ, Zhao B, Henschke CI. Small pulmonary nodules: volumetrically determined growth rates based on CT evaluation. Radiology. 2000; 217:251-6
- Kostis WJ, Yankelevitz DF, Reeves AP, Fluture SC, Henschke CI. Small pulmonary nodules: reproducibility of three-dimensional volumetric measurement and estimation of time to follow-up CT. Radiology 2004; 231:446-52.

- Showed results and images to NLST and NELSON starting in 1999

- NELSON started to use it in its trial

Measurement Uncertainty
Within seconds, 44% change: 172 VDT



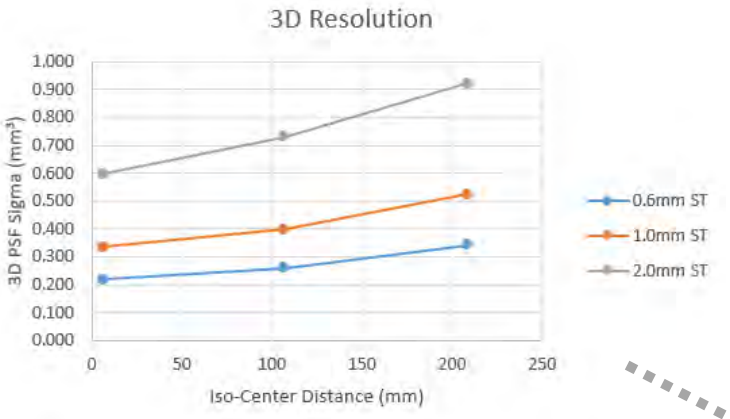
Henschke CI, Yankelevitz DF, Yip R, Archer V, Zahlmann G, Krishnan K, Helba B, Avila R. Tumor volume measurement error using computed tomography imaging in a phase II clinical trial in lung cancer. J Med Imag 2016; 3:035505

Problem

- **Precise Quantitative CT Measurements Are Often Needed**
  - CT Lung Nodule Follow-Up, Cardiac Calcification Scoring
- **CT Scanners/Software Do NOT have The Tools To Support This**
  - Fundamental CT Scanner Performance Varies Widely – Even Within A Single Image
  - Multiple Scanners Are Often Used At A Clinical Site With Different Properties
  - Setting Up a High Quality Imaging Protocol Is Error Prone Due to Large Numbers of Scan Parameters and Continuously Changing Technology
- **Clinical Sites Are Now Able To Use a New Low-Cost Phantom and Online Phantom Analysis Tools To Consistently Achieve The Needed CT Image Quality For Specific Clinical Tasks**

CT Image Quality Issues

3D Resolution



Noise

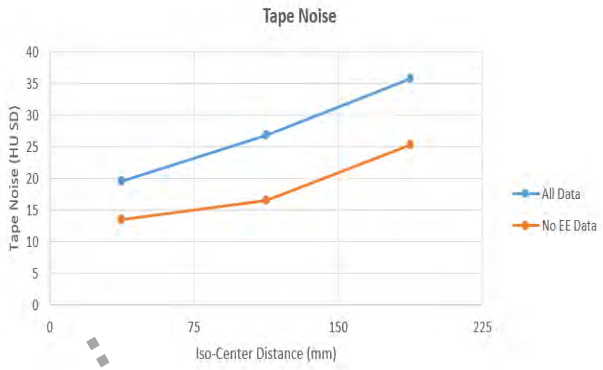
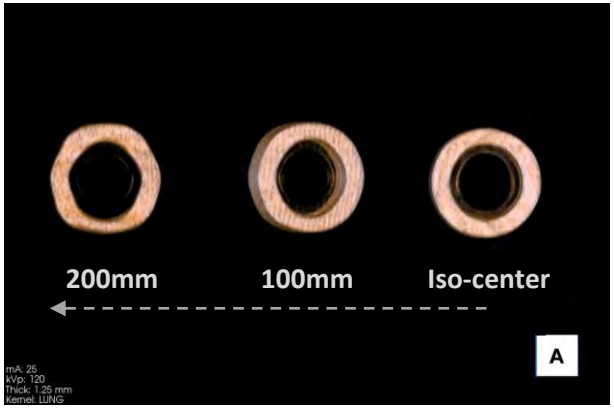
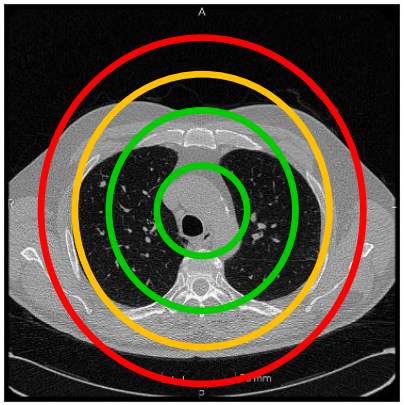


Image Quality Variability

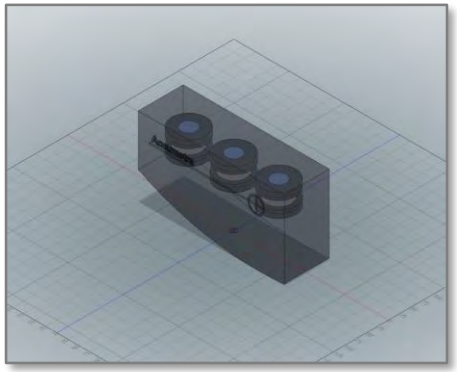
3D Spatial Warping





CT Image Quality Control

- **Using Low-Cost Phantoms and Cloud-based Services Will Help Clinical Sites and Studies To:**
  - Understand the quality of their CT imaging studies in terms of expected clinical task performance and fundamental image quality properties.
  - Optimize CT scanner acquisition protocol performance based on best protocols identified throughout the world for a specific scanner.
  - Monitor CT scanner and protocol performance and obtain alerts when protocol performance falters.
  - Make CT scanner image acquisition from different CT scanner models and manufacturers more consistent.



RSNA/QIBA now provides a conformance certification mark demonstrating the quality of a site's CT scanning and measurement of solid lung nodules.

Solution: RSNA QIBA CT Small Lung Nodule Profile

+ Conformance Phantom & Online Software

Quantitative Imaging Biomarkers Alliance

RSNA

2

3

4 **QIBA Profile:**

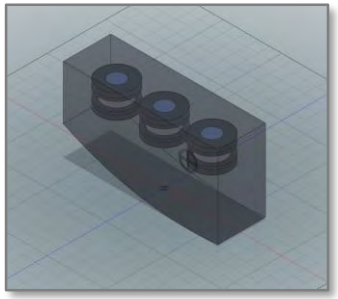
5 **Lung Nodule Volume Assessment and Monitoring in**

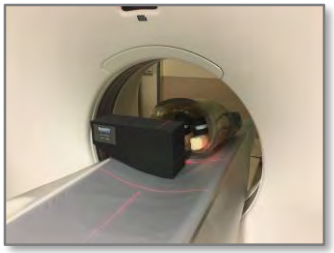
6 **Low Dose CT Screening**

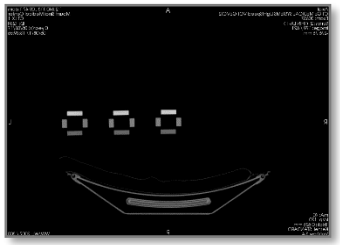
7

8 Stage: Publicly Reviewed (draft)

RSNA/QIBA Conformance Certification Pilot Project
Using Cloud-Based Computing Services







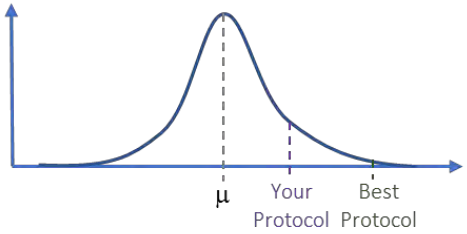
http://quality.rsna.org

Email

Upload

Optimize

Check Each Time Scanner or Protocol Changes and Once Per Year



Guidance

Webpages & FAQs

International CT Image Quality Monitoring

60 CTLX1 Phantoms Sent Out As Of 10/1/2018

Data Received & Analyzed From:

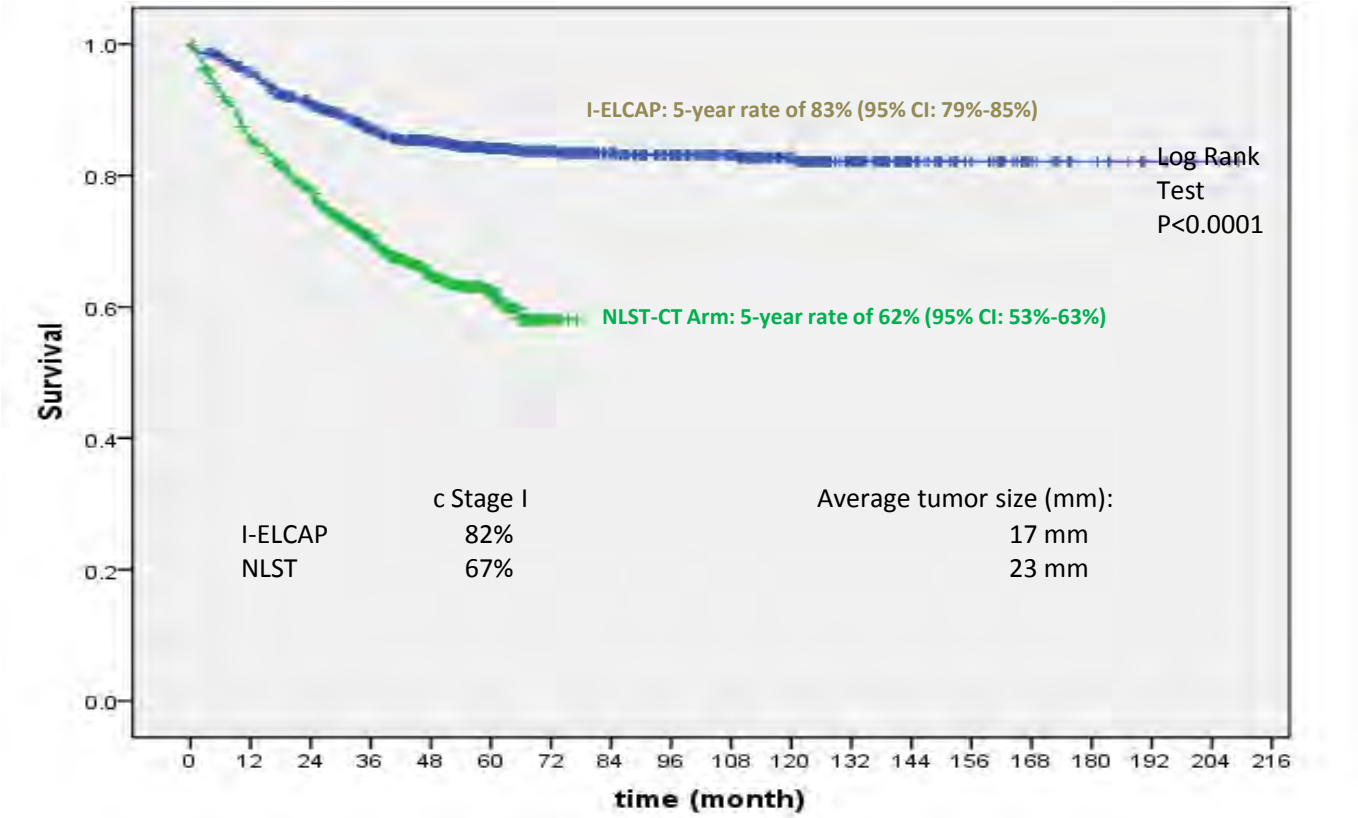
- ~30 Sites
- ~50 Unique CT Scanners
- > 200 CT Scans
- 4 Manufacturers
- Siemens, GE, Philips, Toshiba
- > 20 Different Scanner Models

The Screening Regimen:
Critical to Maximizing the Benefit Minimizing Harms

The Devil is in the Details

I-ELCAP and NLST Survival Rates

The benefit of having a regimen of screening with continuous updates together with a web-based electronic structured management system is shown by the results below



International Early Lung Cancer Action Program Investigators. The Impact of the Regimen of Screening on Lung Cancer Cure: A comparison of I-ELCAP and NLST. Inter J of Cancer Prevention 2015; 24: 201-8

Importance of Regimen:

Reduces unnecessary tests and particularly invasive procedures

Protocol

- I-ELCAP
- Lung-RADS
- European

I-ELCAP, ACR-LungRADS,European baseline protocols

a. Immediate workup PET, biopsy, follow-up CT	I-ELCAP	ACR-Scenario 1	ACR-Scenario 2	European
Solid NCN, largest	≥ 15.0 mm	≥ 8 mm	≥ 15 mm	≥ 10 mm
Part-solid NCN, largest	solid component ≥ 15.0 mm	solid component ≥ 8 mm	solid component ≥ 15 mm	NONE
b. 3-month LDCT				
Solid NCN, largest	≥6.0 mm but <15.0 mm	-	≥8 mm but < 15 mm	≥5 mm but <10 mm
Part-solid NCN, largest	solid component of NCN ≥6.0 mm but <15.0 mm	entire size of NCN ≥6 mm with solid component ≥6 mm but <8mm	entire size of NCN ≥6 mm with solid component ≥6mm but <8mm	entire size of NCN ≥5mm
Nonsolid NCN, largest*				≥5mm
c. 6-month LDCT				
Solid NCN, largest	NONE	≥6mm to <8mm	≥6mm to <8mm	NONE
Part-solid NCN, largest	NONE	entire size of NCN ≥6 mm with solid component <6 mm	entire size of NCN ≥6 mm with solid component <6 mm	NONE
Nonsolid NCN, largest**		≥20mm	≥20mm	

Henschke CI, Yip R, Ma T, Aguayo SM, Zulueta J, Yankelevitz DF for I-ELCAP Investigators. CT Screening for Lung Cancer:Comparison of three baseline protocols. In press. European Radiology. 2018

I-ELCAP, ACR-LungRADS, European

- All protocols recommend
  - 1) immediate workup, %
  - 2) delayed workup, %
  - 3) annual repeat screening %
- All use different thresholds for recommendations
  - 6.0mm for I-ELCAP, 6mm for LungRADS, 5mm European
- ACR-LungRADS recommends PET scans for NCNs, 8 mm or larger, although 3 month follow-up CT is an alternative, therefore 2 scenarios:
  - Scenario 1: immediate PET scan
  - Scenario 2: 3 month LDCT

I-ELCAP, ACR-LungRADS, European

For each protocol option, we calculated:

Percentage of participants recommended for workup

ER = # workups/# dx cancers

I-ELCAP, ACR-LungRADS, European

Overall protocol summary:

Total number of participants recommended for workup before first annual repeat and

ER = # participants/# LC diagnosis

Comparison of Protocols

ER = number of people requiring dx tests for each diagnosis of lung cancer

Workup	I-ELCAP		ACR-S1		ACR-S2		European	
	%	ER	%	ER	%	ER	%	ER
Immediate								
Workup/L ca								
3-month								
Workup/L ca								
6-month								
Workup/L ca								
OVERALL ER	**13.9**		18.3		18.3		31.9	

Henschke CI, Yip R, Ma T, Aguayo SM, Zulueta J, Yankelevitz DF for I-ELCAP Investigators. CT Screening for Lung Cancer:Comparison of three baseline protocols. In press European Radiology. 2018

Comparison of Baseline Protocols: Estimated % requiring biopsies and # participated biopsies/LC dx

Workup	I-ELCAP		ACR-S1		ACR-S2		European	
	%	ER	%	ER	%	ER	%	ER
Immediate								
Workup/L ca								
3-month								
Workup/L ca								
6-month								
Workup/L ca								
Biopsies	1.6%	2.2	6.0%	8.1	2.3%	3.2	3.3%	4.4

Henschke CI, Yip R, Ma T, Aguayo SM, Zulueta J, Yankelevitz DF for I-ELCAP Investigators. CT Screening for Lung Cancer:Comparison of three baseline protocols. In press European Radiology. 2018

First Round of Screening

- The first screening round is not a single test, but a two-step process
  - Starts with low-dose CT scan
  - If first low-dose CT is negative or the largest noncalcified nodule (NCN) is < 6.0 mm, come back for the first annual round of screening next year
  - in 10% of screenings, come back in 3 months to assess change on another low-dose CT

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Conclusion

- Differences among modern protocols lead to major changes in efficiencies.
- Accumulated knowledge and data should lead to continual updating of protocols
- Mechanisms should be place to enhance such updating

OTHER CT FINDINGS

Further areas:
Liver
Adrenals
Thyroid