

# **VA PARTNERSHIP Increase ACCESS to LUNG SCREENING**



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**Clinical Co-PI:** Claudia Henschke, PhD, MD  
**Technical Co-PI:** Rick Avila, MS

# 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

# 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

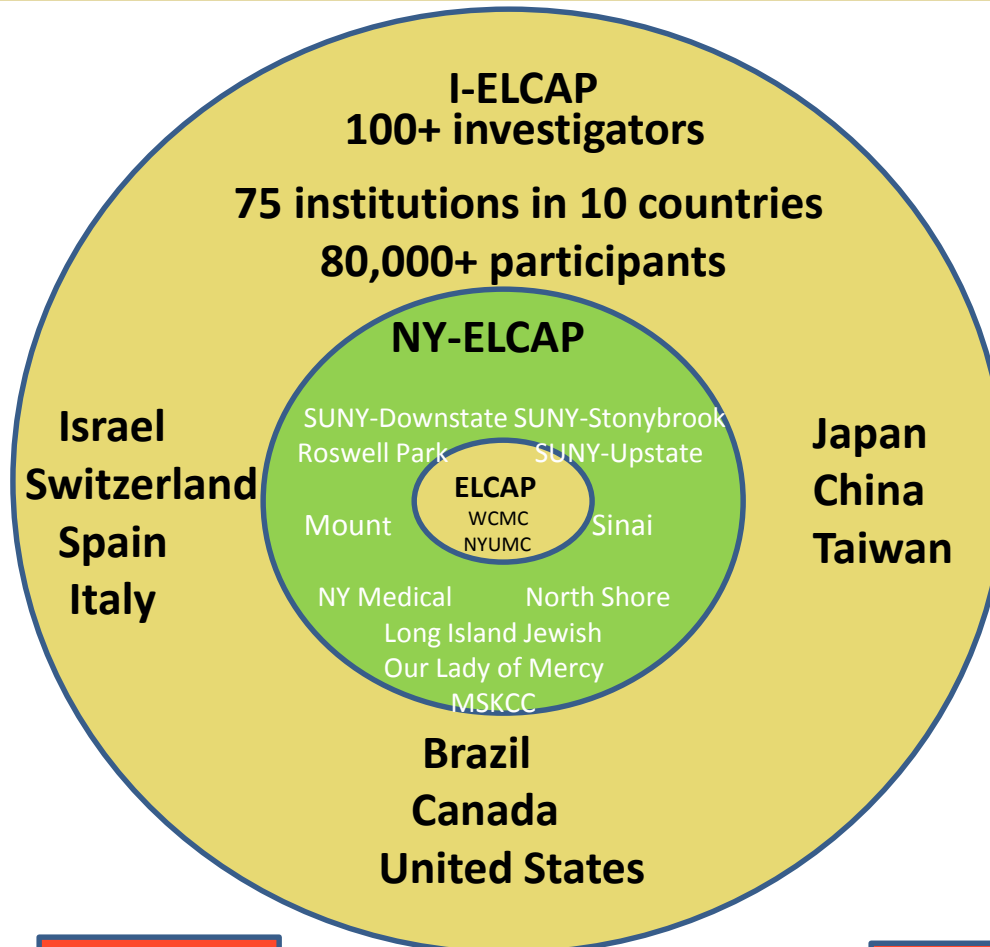
Study design

Screening protocol

Pathology protocol

Regimen of screening

Lung cancer size, stage, cure rate



Nodule growth and detection

Mediastinal masses

Emphysema

Coronary Artery Ca++

Breast Diseases

Conferences @ 6 months

Computer analytics

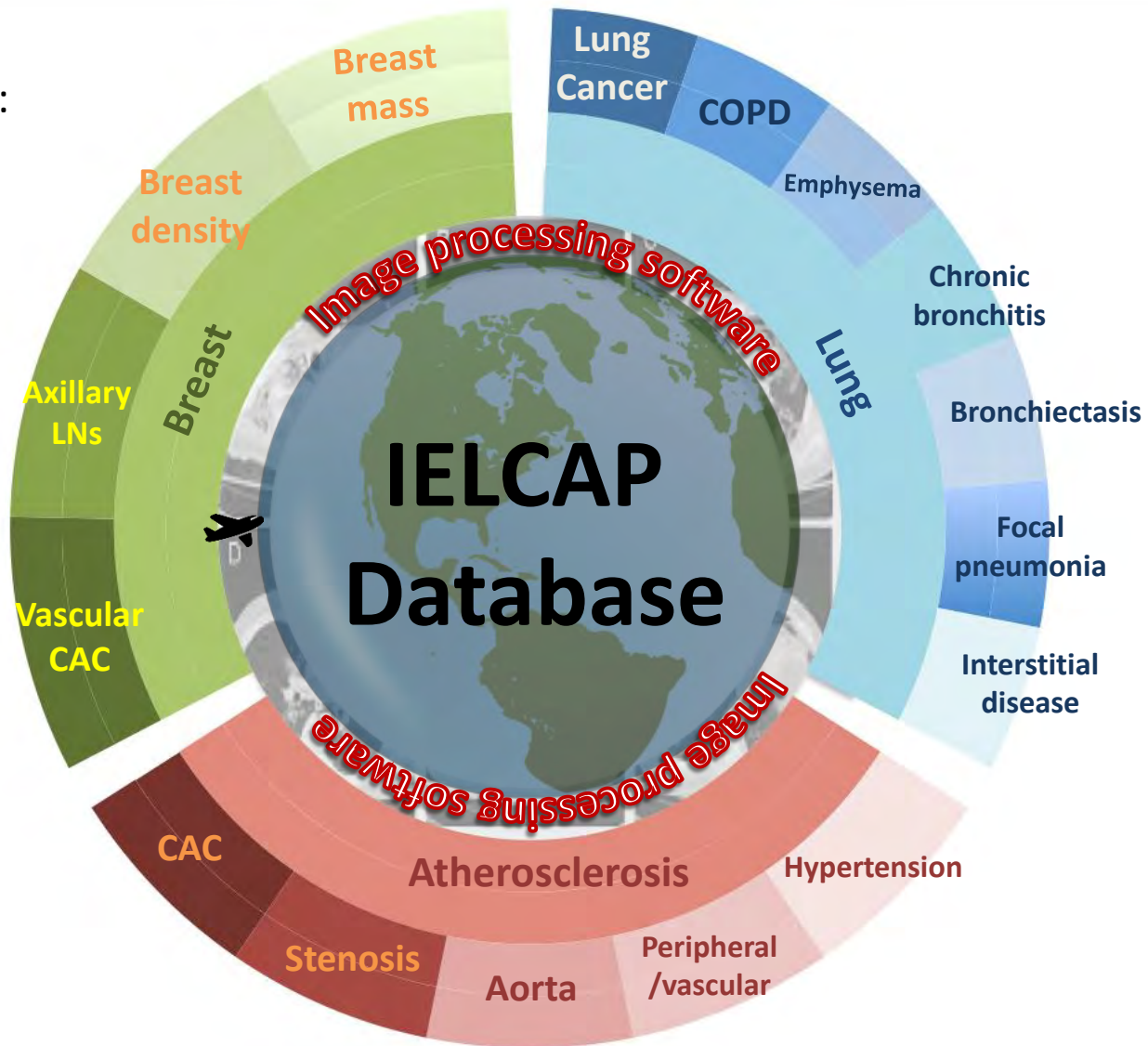
Continuous Quality Improvement

Publications 200+

# 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

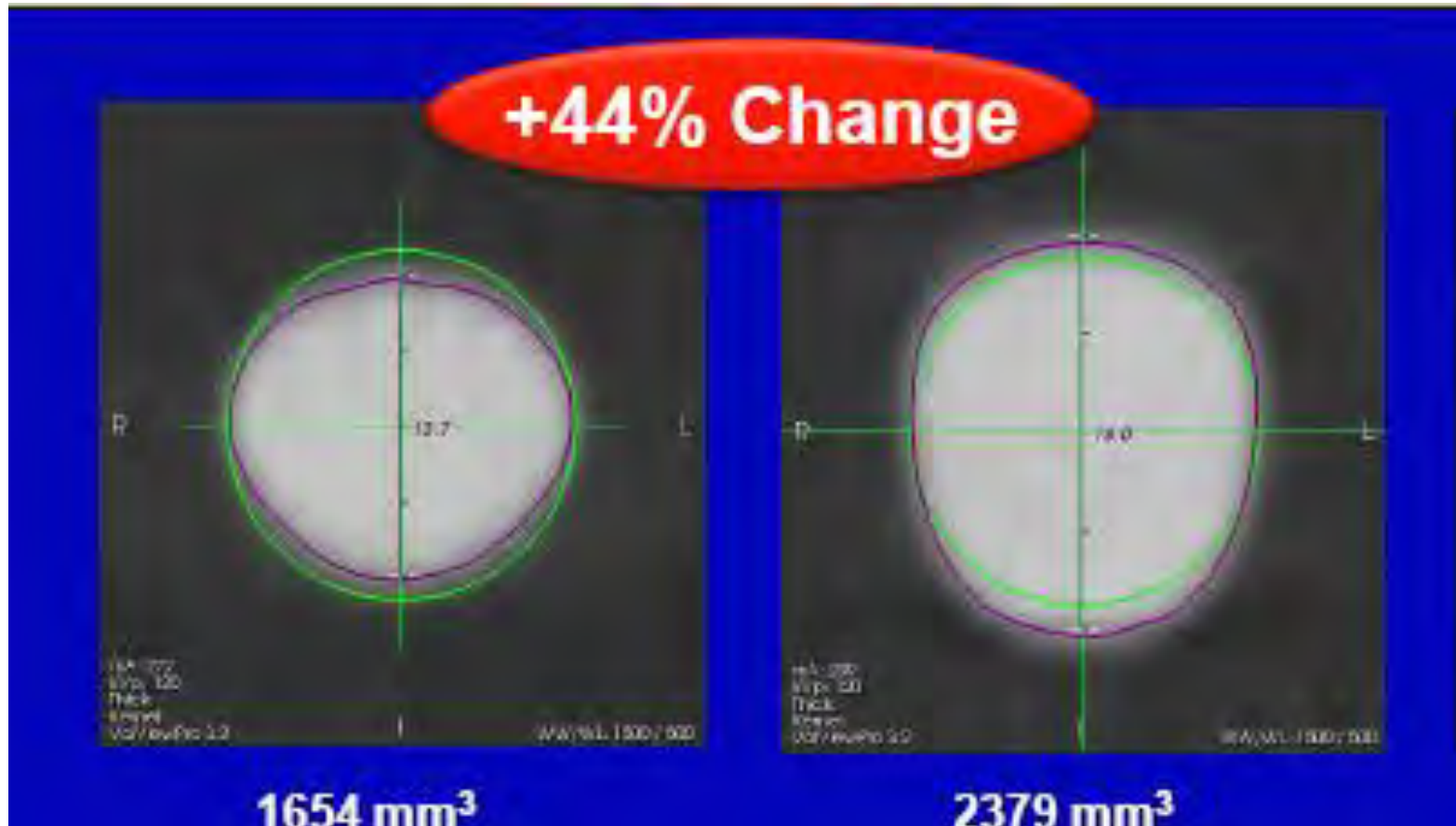
- Volume CT screening results in a low referral rate (2.3%) and a very substantial reduction in lung cancer screening mortality
- However, volumetric assessment is still in its infancy and needs further standardization

# 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



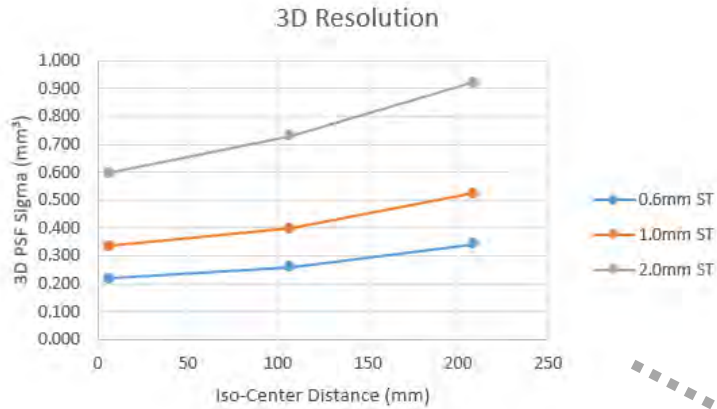
Henschke CI, Yankelevitz DF, Yip R, Archer V, Zahlmann G, Krishnan K, Helba B, Avila R. Tumor volume measurement error using computed tomography imaging in a phase II clinical trial in lung cancer. J Med Imag 2016; 3:035505

# Problem

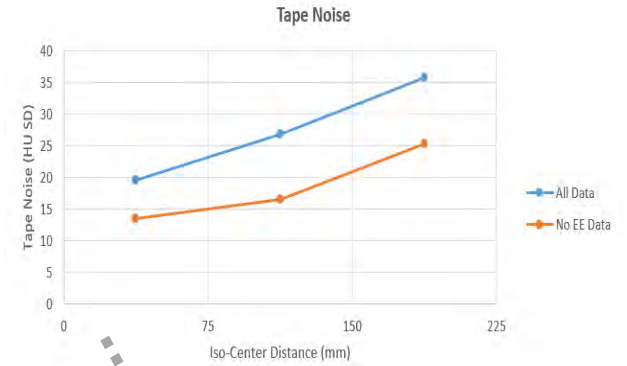
- **Precise Quantitative CT Measurements Are Often Needed**
  - CT Lung Nodule Follow-Up, Cardiac Calcification Scoring
- **CT Scanners/Software Do NOT have The Tools To Support This**
  - Fundamental CT Scanner Performance Varies Widely – Even Within A Single Image
  - Multiple Scanners Are Often Used 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**

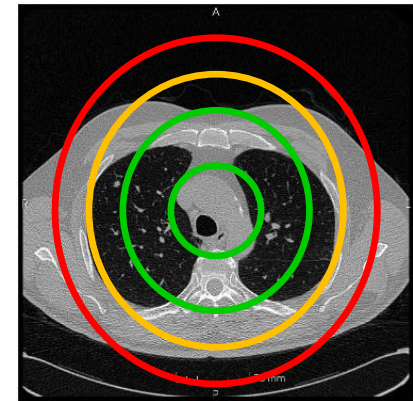
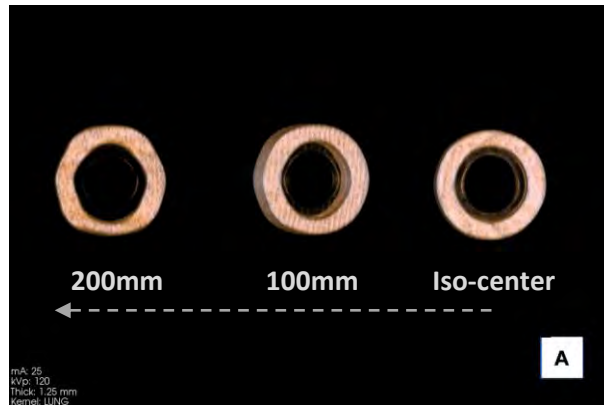


**Noise**



**Image Quality Variability**

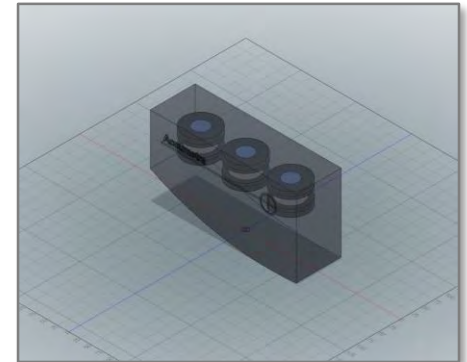
**3D  
Spatial  
Warping**



# 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



QIBA Profile: Lung Nodule Assessment in CT Screening Profile - 2017

Quantitative  
Imaging  
Biomarkers  
Alliance

The RSNA logo is positioned to the right of the text. Below the text is a grid of colored dots in various colors (blue, purple, green, red, pink) arranged in a pattern.

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3

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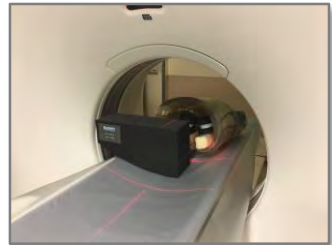
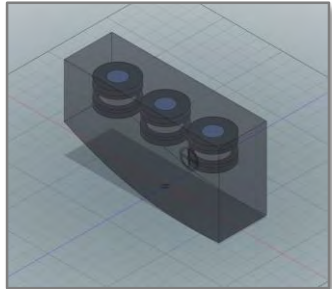
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**QIBA Profile:  
Lung Nodule Volume Assessment and Monitoring in  
Low Dose CT Screening**

Stage: Publicly Reviewed (draft)

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



<http://quality.rsna.org>

Email

Upload

**Accumetra**  
www.accumetra.com

**QIBA CT Small Lung Nodule (SLN) Profile**  
Automated CT Image Quality Conference Report  
Assessment Performed Using The Accumetra CT SLN Platform  
And ACCA Prototype Image Quality Assessment Software Platform (v0.7)  
December 10, 2017

**Scanner and Protocol Settings**

Manufacturer:	GE MEDICAL SYSTEMS	Tube kVp:	120.00
Scanner Model:	RevCT	Tube mA:	18.00
Scanner Station:	257005	Beam Treatment:	0.80
Study Date:		Shot Strategy:	0.80
Room Name:	STANDARD	Plan:	0.80

Scanning Area: 330.0 x 330.0 x 150.0 mm  
Volume Size: 512 x 512 x 128 voxels  
Shot Description: ISCTROPIC2  
Serial Instance UID: 1.2.840.113618.2.416.11280311896286284365507913430249  
Serial Instance UID: 1.2.840.113618.2.416.11280311896286284365507913430249  
Display Name: Small Lung Nodule (SLN) Profile

**Conformance Assessment Status**

The required number of CT SLN phantom modules was found (2).  
The DICOM file address is within acceptable limits for this analysis (≤ 1.25M).  
The DICOM slice spacing is within acceptable limits for this analysis (≤ 0.5mm).  
The DICOM CT scan pitch is within acceptable limits for this analysis (≤ 1.2).

All QIBA CT SLN Profile assessment conformance checks have passed for this CT scanner and image acquisition protocol.

**Measured Image Quality Characteristics**

The QIBA CT Small Lung Nodule Profile requires that CT image quality performance is verified for six fundamental image quality characteristics through the required CT image sets. The required CT scanner and image acquisition protocols to be used for Small Lung Nodule volume measurement. The performance of each of these characteristics is plotted from separate set of images to determine if they are within the required performance thresholds for QIBA Small Lung Nodule Profile image quality performance specifications. Additional information on these image quality characteristics including guidelines on improving performance is available at Accumetra's QIBA Conformance Certification Pilot Project Page.

(1) Edge Enhancement

Robust edge enhancement can significantly modify the HU values of objects in CT images and cause problems with quantitative measurement algorithms. We quantitatively tested your levels of edge enhancement at three distances from the center and found the values to be within QIBA CT SLN Profile specifications.

(2) 3D Resolution

Three-dimensional resolution greatly influences volumetric measurement performance of small objects in CT images. We quantitatively tested your 3D resolution at three distances from the center and found the values to be within QIBA CT SLN Profile specifications.

(3) Spatial Sharpening

Spatial sharpening can cause significant issues when performing quantitative measurements. We quantitatively tested your levels of spatial sharpening at three distances from the center and found the values to be within QIBA CT SLN Profile specifications.

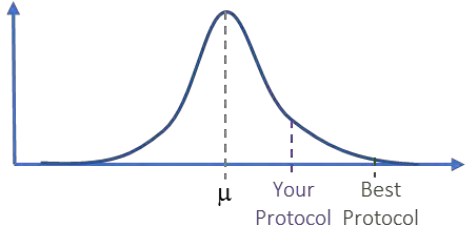
(4) 3D Resolution Aspect Ratio

Quantitative measurement algorithms work best when uniform resolution along all three CT imaging dimensions. We quantitatively tested the Z-axis aspect ratio of your imaging system at three distances from the center and found the values to be within QIBA CT SLN Profile specifications.

(5) HU Bias

Unintended HU bias is likely to be observed when performing quantitative measurements of objects in CT images. We quantitatively tested your levels of HU bias for six test objects measured at three distances from the center and found the values to be within QIBA CT SLN Profile specifications.

Check Each  
Time Scanner  
or Protocol  
Changes and  
Once Per Year



Guidance  
Webpages &  
FAQs

Optimize

# 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

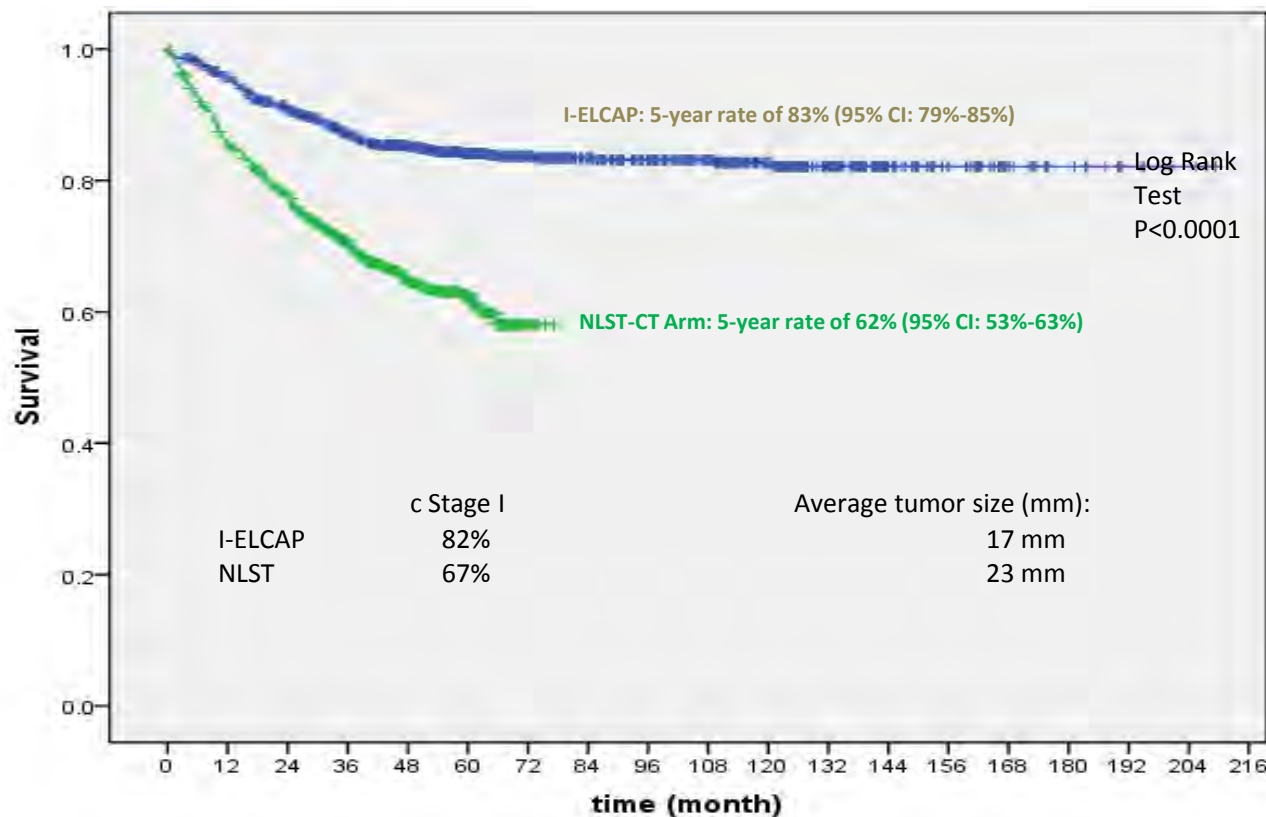
# The Screening Regimen: *Critical to Maximizing the Benefit* *Minimizing Harms*

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>b. 3-month LDCT</b>				
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
<b>c. 6-month LDCT</b>				
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

$ER = \# \text{ workups} / \# \text{ dx cancers}$

# I-ELCAP, ACR-LungRADS, European

Overall protocol summary:

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

$ER = \# \text{ participants} / \# \text{ LC diagnosis}$

# 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								
<b>OVERALL ER</b>		<b>13.9</b>		<b>18.3</b>		<b>18.3</b>		<b>31.9</b>

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

