

*May 2, 2011*

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Vice President  
Research*

 RUSH UNIVERSITY  
MEDICAL CENTER  
IT'S HOW MEDICINE  
SHOULD BE

## *Application of Quantitative CT Imaging to Early Lung Cancer Management: Accelerating Progress*



# Workshop Locations



Start Here. Start Now.

- **Workshop I-** Washington DC
- **Workshop II-** Annapolis, MD
- **Workshop III-** Bethesda, MD
- **Workshop IV-** Oak Brook, IL
- **Workshop V-** Oak Brook, IL
- **Workshop VI-** Bethesda, MD
- **Workshop VII-** Bethesda, MD
- **Workshop VIII-** Bethesda, MD

**Prevent Cancer Foundation vision in 2004 to accelerate drug development for early lung cancer**

[www.preventcancer.org](http://www.preventcancer.org)



*25 Years* of progress through prevention

SPECIAL THANKS TO THE  
**WORKSHOP SPONSOR**

Carolyn R. "Bo" Aldigé  
*Prevent Cancer Foundation*

**STEERING COMMITTEE**

Chair:

- James L. Mulshine  
*Rush University Medical School*

Members:

- |   |  |
|---|--|
| • Ricardo S. "Rick" Avila<br><i>Kitware, Inc.</i>                   | • Raul San Jose Estepar<br><i>Brigham and Women's Hospital</i> |
| • Thomas M. "Tom" Baer<br><i>Stanford Photonics Research Center</i> | • David F. Yankelevitz<br><i>Mount Sinai Medical Center</i>    |

## Special Note

***This pre-competitive Research Workshop  
is supported by unrestricted grants to  
Prevent Cancer Foundation: No products  
are being endorsed in this forum***

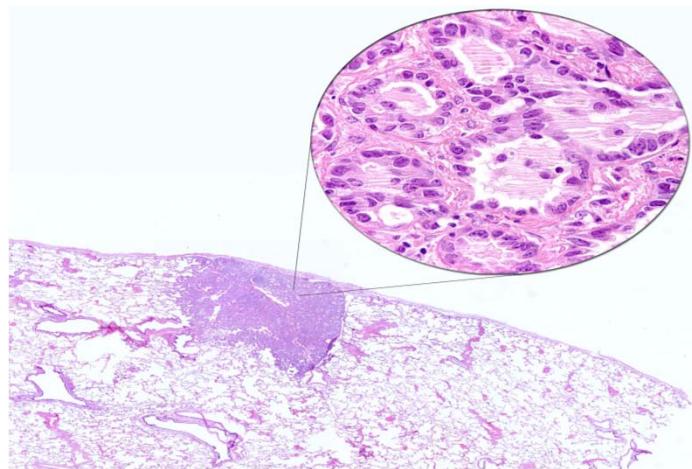
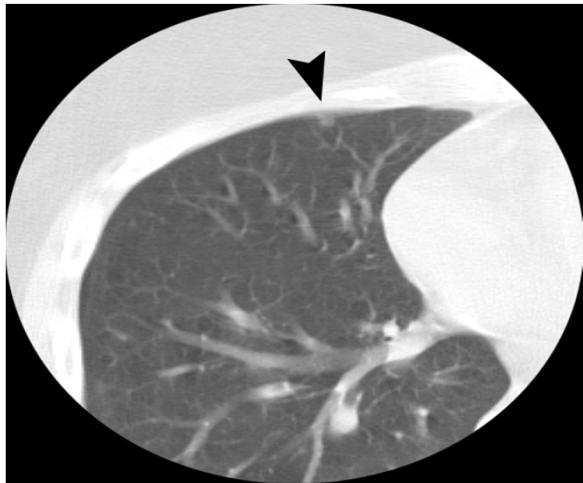
# Impetus for Workshop

- Four Reasons
  - Lung Cancer is a major public health challenge
  - CT of lung is a rapidly improving medical imaging modality
  - the information density conveyed in a high resolution medical image is rapidly exceeding the capacity of medical practitioners to absorb
  - Drug development of lung cancer suboptimal

- **Tobacco use causes more deaths each year than alcohol use, car crashes, suicide, AIDS, homicide, and illegal drug use combined\***
- **In addition, smoking accounts for \$167 billion annually in health care expenditures and productivity losses\***
- **Number of new cases will increase by 50% by 2030 (JCO.2008.20.8983)**

*\*CDC. Annual smoking-attributable mortality, years of potential life lost, and productivity losses---US, 1997--2001. MMWR 2005;54:625--8.*

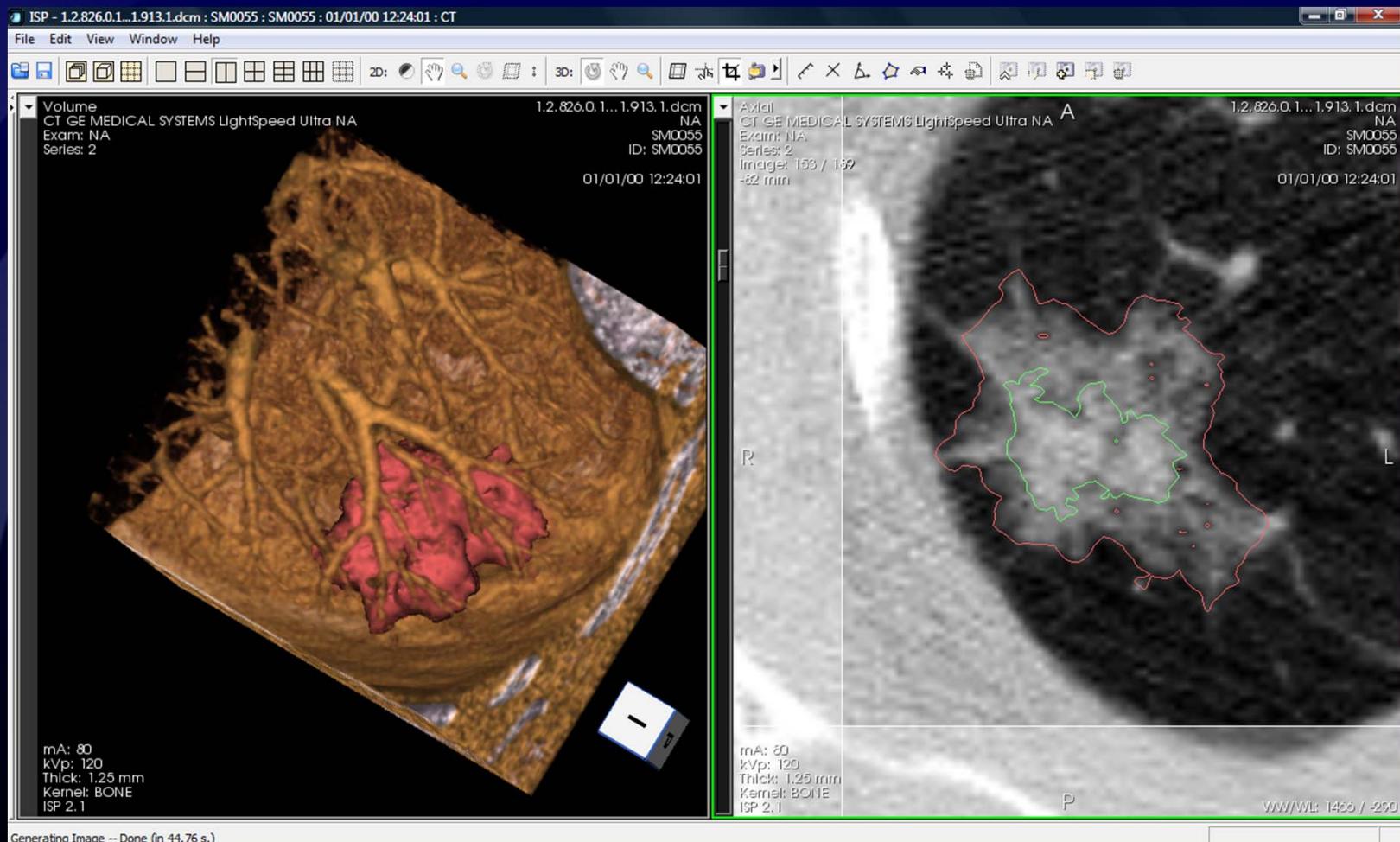
## Impact of CT on Lung Cancer Management



- CT resolution doubling every two yrs for > decade
- Improved microprocessor capabilities
- Image processing capabilities evolving rapidly
- NCI supporting image database research to facilitate tool development (LIDC & RIDER Databases)
- Finding smaller CAs drives changes in clinical care

*Mulshine JL, Sullivan D, NEJM, 352, 2005*

# Part Solid Lesion: How do you describe?



Data Courtesy of the Public Lung Database to Address Drug Response (Cornell)

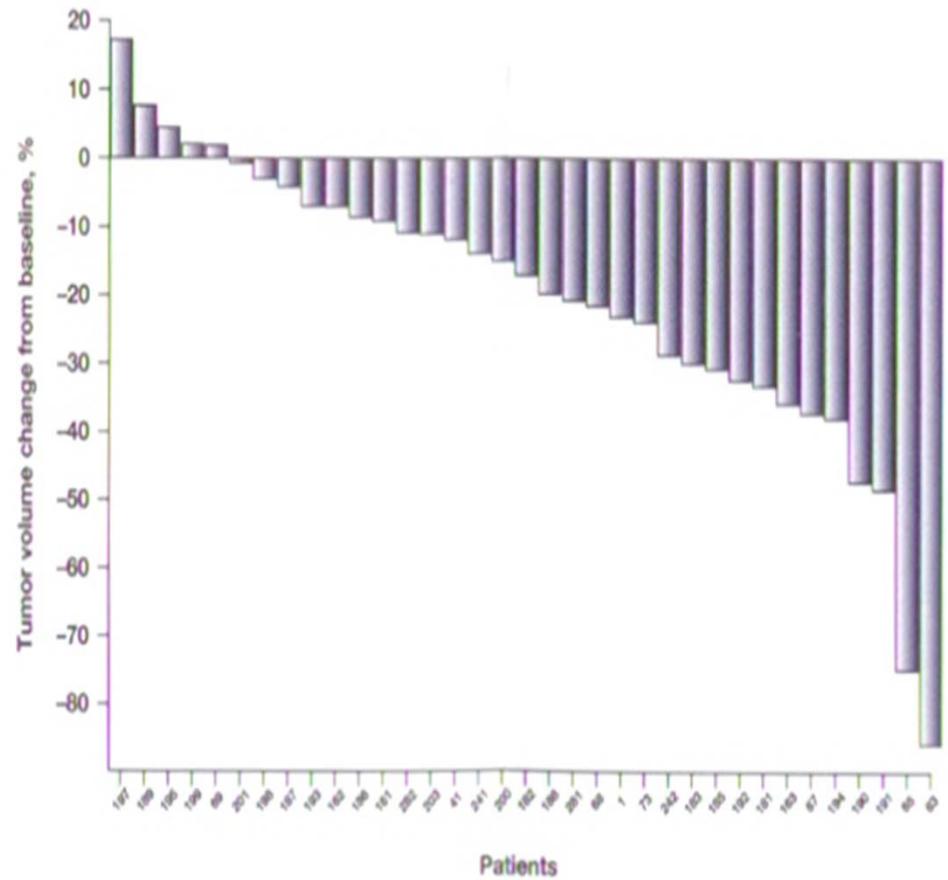


## Preop Treatment with Pazopanib

- New trial design evaluating drug effect in early lung CA
- Pazopanib, a GSK, dual kinase, VEGF inhibitor with activity in lung CA
- **Pazopanib will now be evaluated in RCT of adjuvant RX**

N Altorki, Proc ASCO, 2008

Figure 2.—Tumor volume response in all patients.



*Waterfall plot showing tumor volume growth quantitated from CT scans for all study patients*

## New Model for Lung CA Development

- Evaluate relevant target with good safety profile in Phase I trial
- Move to Neoadjuvant Window Trial
- Move to Adjuvant Trial
- Move to Chemoprevention Trial

Time to Market??—Under 7years

# Measuring Progress

6 Workshops since 2004  
1 Interim COPD Meeting

QIBA  
FDA  
NIST

Interim  
Meetings

Annual  
Workshop

PCF/Cornell Database  
NCIA  
Give-A-Scan

Standards &  
FDA Approval

Large Open Image  
Databases

Accelerate  
Development of  
Therapy  
Assessment  
Methods

Algorithms &  
Reference  
Methods

Reproducibility  
& Comparison

Early Clinical Trials  
NIST BioChange  
Volcano

Quantitative CT Monograph

Oncology Workshop Reports  
ISP Oncology Special Issue

Publications

Open Source  
Lesion Sizing Toolkit





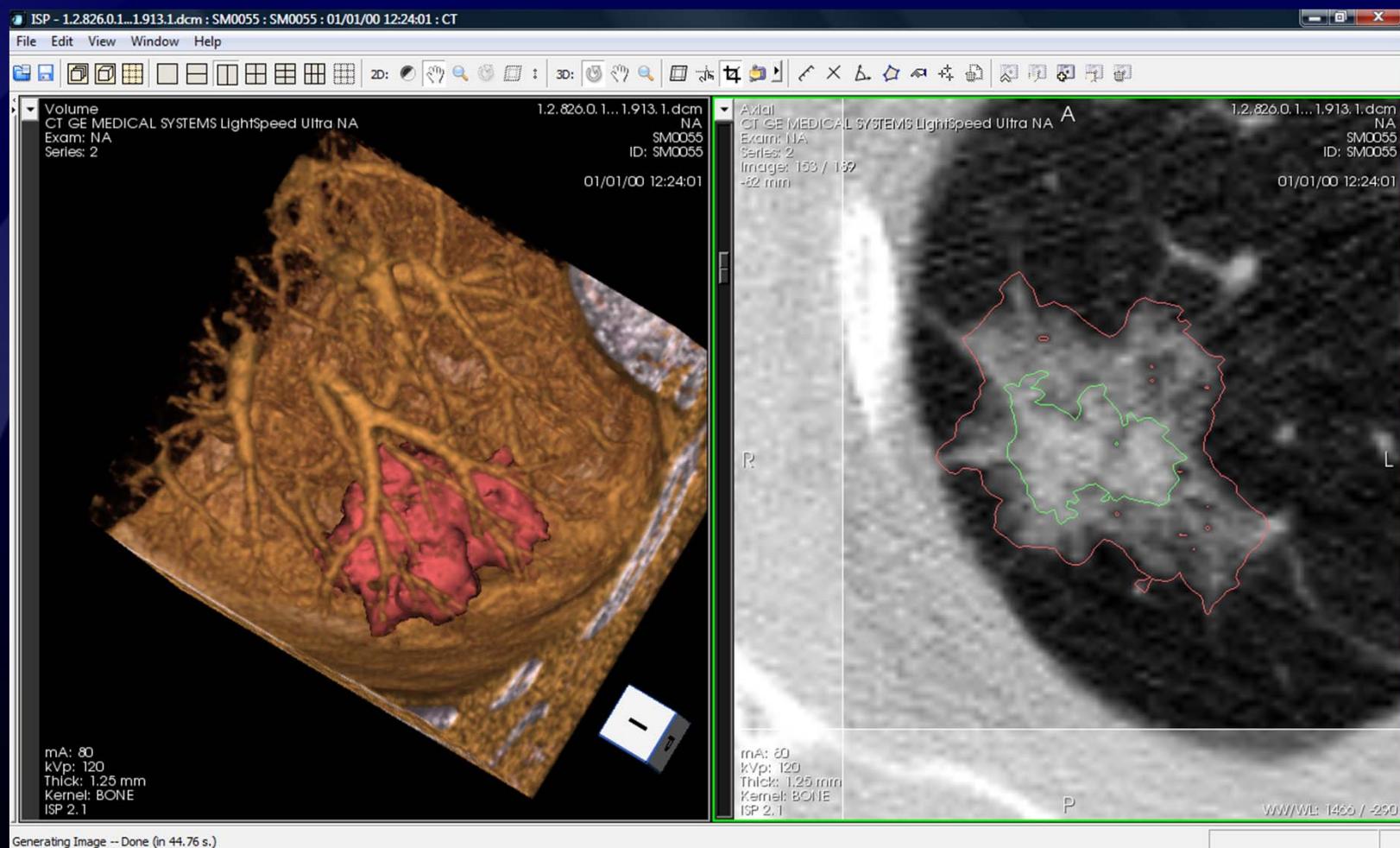
# Volumetric CT: A Potential Biomarker of Response

1 December 2008

*Andrew Buckler*

*Director, Cross-Modality Imaging Systems, Philips Healthcare  
Chair, Volumetric CT Team, Quantitative Imaging Biomarker Alliance*

# Value-added of 3-D Visualization



Data Courtesy of the Public Lung Database to Address Drug Response (Cornell)



# Uncomfortable Truth, 2011

- We have not defined the value proposition of quantitative CT in lung cancer.
  - What does it do best?
  - How does it change the status quo?
  - Who are the right champions?

# Implications of the NLST Result

- The NLST is a prospective randomized controlled trial
- Randomization: 1:1
- Number of subjects: 50,000
- Number of screening sites: 30 sites, including current PLCO sites (10), and ACRIN sites (20)
- Accrual now complete
- Duration: 3 screening rounds, with follow-up to 2009—extended to 2011

*Results of Interim Analysis of Primary Endpoint  
Reported on Oct. 20, 2010*

Arm	Person years (py)	Lung cancer deaths	Lung cancer mortality per 100,000 py	Reduction in lung cancer mortality (%)	Value of test statistic	Efficacy boundary
CT	144,097.6	354	245.7	20.3	-3.21	-2.02
CXR	143,363.5	442	308.3			

Deficit of lung cancer deaths in CT arm exceeds that expected by chance, even allowing for multiple looks at the data.

# NLST Executive Committee

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- Denise R. Aberle, MD
- Christine D. Berg, MD
- William C. Black, MD
- Timothy R. Church, PhD, MS
- Richard M. Fagerstrom, PhD
- Barbara Galen, MSN, CRNP, CNMT
- Ilana F. Gareen, PhD
- Constantine Gatsonis, PhD
- Jonathan Goldin, MD, PhD
- Barnett S. Kramer, MD, MPH
- David Lynch, MD
- Irene Mahon, RN, MPH
- Pamela M. Marcus, MS, PhD
- Dorothy Sullivan
- Carl J. Zylak, MD

National Cancer Institute:  
DCP, EDRG, Lung Screening Study  
DCTD, Cancer Imaging Program, Bethesda, MD  
American College of Radiology Imaging Network, Philadelphia, PA

# Kaplan-Meier Curves for Lung Cancer Case Survival (Lung Cancer Cause of Death)

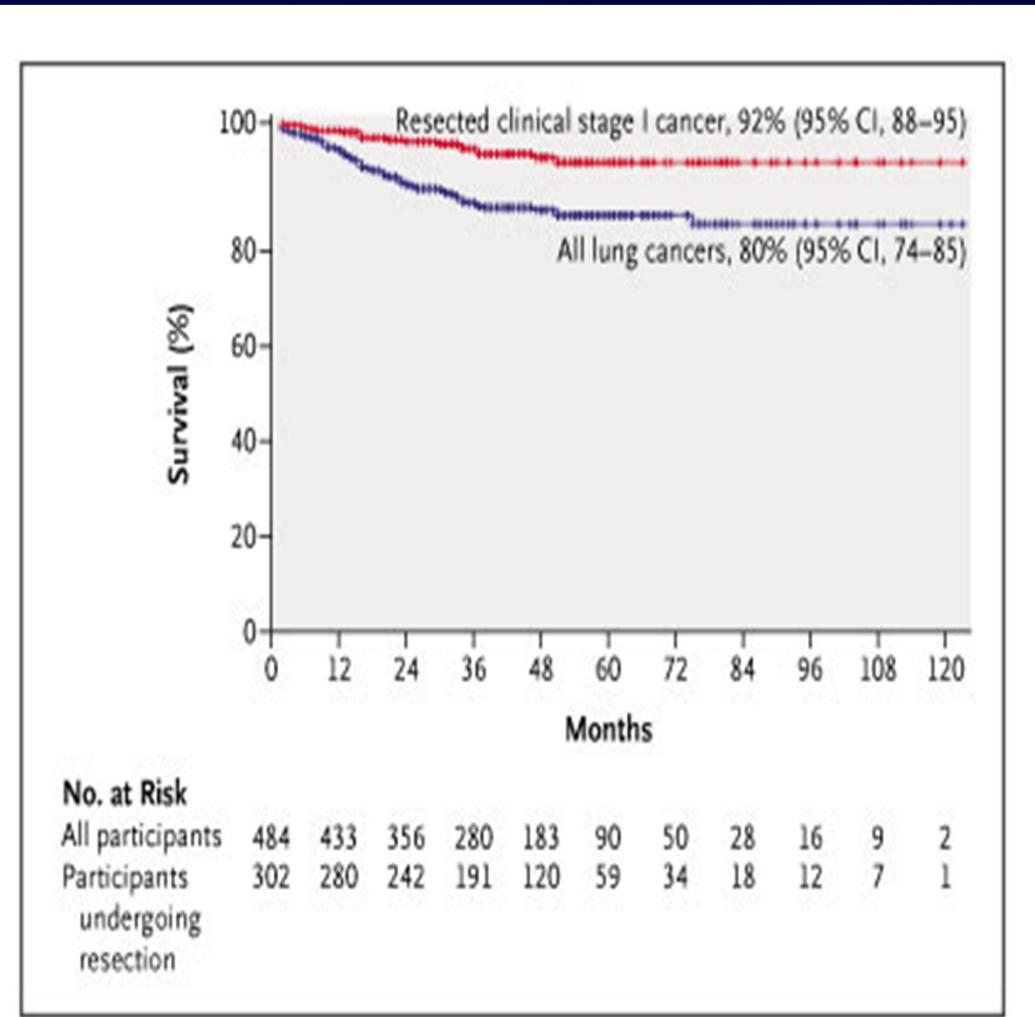
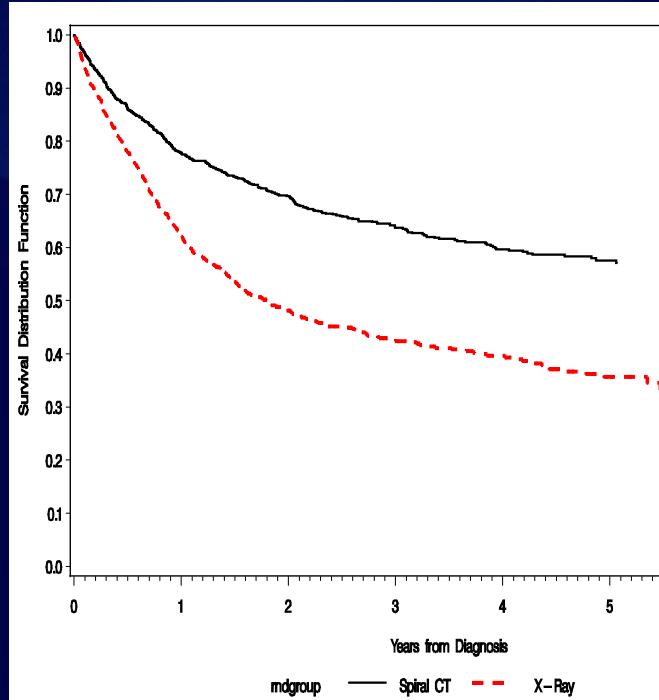


Table 11.5.3d

## *Progress with Lung CA Screening*

- **NELSON published diagnostic work up efficiency in NEJM and found a sensitivity of 95%, specificity of 99% and found no operative mortality with well tolerated clinical management**
- **I-ELCAP and NELSON use a growth criteria to separate clinically significant from non-malignant behaving nodules and both involve the use of image processing**
- **RSNA (QIBA) is defining QC/QS criteria**

## Needs for “Learning Healthcare System”

- **Adaptation to the pace of change**
- Stronger synchronicity of effort
- Culture of shared responsibility
- **New clinical research paradigm**
- Clinical decision support systems
- **Universal EHR**
- Tools for database linkage, mining and use
- **Notion of clinical data as a public good**
- Incentives aligned for practice-based evidence
- Public engagement
- Trusted scientific broker
- Leadership

*Institute of Medicine White Paper-The Learning Healthcare System, 2007*

# Integrating Detection & Monitoring

- QIBA has defined many sources of imaging variance for quantitative applications
- Quality control, standardization, etc may be conserved across both imaging uses
- Phantom use could be standardized across these two applications and COPD
- **Need to “refresh” on the strategic importance of large image archives**
- CT screening provides N> 125,000/3 sites the largest collection of serial images with clinical follow-up

## Workshop VIII Outcome Measures

- Review the status for both computational imaging and targeted drug development
- Define pre-competitive strategies to integrate computational imaging and drug development for lung cancer or COPD
- Develop software tools to allow accurate serial measurement of lung nodules
- Create an effective infrastructure to support developing strategic image/data archives to accelerate progress
- Discuss strategies with the advocacy community to communicate on the benefit of quantitative imaging

# Addressing False-Positive Image Challenge

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