CT Lung Cancer Screening Part 1

Session Moderator:

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Marshfield, Wisconsin

Session Program:

Imaging Education

CT Lung Cancer Screening Part 1

- First Presentation:
  - CT Lung Cancer Screening and the Medical Physicist: Background, Findings and Participant Dosimetry Summary of the National Lung Screening Trial (NLST)
  - Presenter: Randell Kruger, PhD, Marshfield Clinic, Marshfield, WI
- Second Presentation:
  - CT Lung Cancer Screening and the Medical Physicist: A Dosimetry Summary of CT Participants in the National Lung Screening Trial (NLST)
  - Presenter: Choonsik Lee, PhD, National Cancer Institute, Bethesda, MD

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CT Lung Cancer Screening Part 1

- Learning Objectives
  - Review and summarize relevant NLST findings and conclusions
  - Understand the scope and scale of the NLST specific to participant dosimetry
  - Provide a comprehensive review of NLST participant dosimetry assessments
  - Summarize the results of an investigation providing individualized organ dose estimates for NLST participant cohorts

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CT Lung Cancer Screening and the Medical Physicist:

Background, Findings and Participant Dosimetry Summary of the National Lung Screening Trial (NLST)

Randell Kruger, PhD, Marshfield Clinic, Marshfield, WI

- Ministry Saint Joseph's Hospital is a 504-bed tertiary care teaching institution and the second largest hospital in the state

Introduction and Background

- Lung Cancer Statistics (American Cancer Society, ACS)[1]
  - Estimated 1.1 billion active smokers in the world
    - About half will die due to the health consequences of smoking
  - Excluding skin cancer, lung cancer is the second most common cancer for both men and women in the US
    - 13% of all new cancers
      - 2015 estimated: 221,200 new cases
    - 27% of all cancer deaths
      - 2015 estimated: 158,040 deaths
  - Costliest cancer to society (National Institute of Health)
    - Once diagnosed patients require multimodality therapy that is very expensive and complex
    - Direct costs $12 billion
    - Indirect costs $36 billion
  - Early-stage lung cancers develop asymptomatically
    - Only 8% of stage III and IV tumors were operatively managed in 2014

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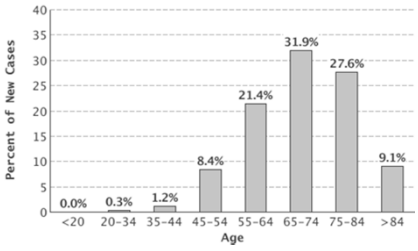
Introduction and Background

- Lung Cancer Risk (US Preventive Services Task Force, USPSTF)[3]
  - Smoking history single most important causative factor
    - 85% of new cases are current or former heavy smokers (30+pack-year)
    - Lifetime risk for a never smoker: 0.2-1.4%, heavy smoker: 18.5-24.4%
  - Age is a risk factor, average age at diagnosis is 70



[2]National Cancer Institute SEER 18 2005-2012, All Races, Both Sexes

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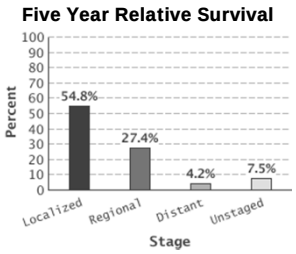
Introduction and Background

- Lung Cancer Lethality
  - 5-year survival rate of 17.4%
    - Compared to 99.7% for prostate and 90.3% for breast cancers
  - Poor prognosis, 90% with lung cancer die of the disease
    - 75% of patients present with advanced local or metastatic disease
    - Deaths greater than colon, breast, and prostate cancer combined



[2]National Cancer Institute SEER 18 2005-2011, All Races, Both Sexes

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Introduction and Background

- Lung Cancer Screening – Chronological Review
  - American College of Radiology (ACR)
    - Screening practice registry (2015)
    - Screening center designation (2014)
  - Center for Medicare & Medicaid Services (CMS)
    - Proposed yearly CT screening for selected patients (2014)
  - US Preventive Services Task Force (USPSTF)
    - Final approval for annual CT screening (2013)
  - National Lung Screening Trial (NLST)
    - Findings published 2011-2013, screening 8/02-9/07

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NLST Introduction

- NLST introduction
  - Randomized controlled trial funded by the National Cancer Institute, conducted by two organizations
    - Lung Screening Study (LSS)
    - American College of Radiology Imaging Network (ACRIN)
  - Recruited 53,439 asymptomatic participants that were randomly assigned to one of two study groups
  - Chest radiography (CXR)
    - 26,724 participants
    - 73,733 exams acquired
    - 92 chest imaging systems
  - Low Dose Computed Tomography (LDCT)
    - 26,715 participants
    - 75,133 exams acquired
    - 97 multidetector CT scanners

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NLST Demographics

- NLST participant demographics
  - Eligibility criteria
    - Smoking history: current or former heavy smokers with at least a 30 pack-years of cigarette smoking (former smokers within last 15 years)
      - 47% of participants had a >50 pack-year smoking history
    - Participants annually screened for three years
      - Compliance rate > 90% for all groups and screening interval
    - Age: 55 to 74
      - Males: 31,523 (59%)
      - Females: 21,916 (41%)
  - Multi-centered trial
    - 33 screening centers
    - Enrollment period: 8/02 - 4/04
    - Screening period: 8/02 - 9/07
    - Event reporting through 12/09
    - Findings published 2011-2013

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NLST Demographics

MN and WI provided 19.3 % of the NLST participants from three screening centers; Mayo Clinic, University of Minnesota, Marshfield Clinic Health System

Study group	Screening center	Location	Accrual, No. of participants
ACRIN	1. Beth Israel Deaconess Medical Center	Boston, MA	629
	2. Brigham and Women's Hospital	Boston, MA	540
	3. Brown University, Rhode Island Hospital	Providence, RI	827
	4. The Cancer Institute of New Jersey	New Brunswick, NJ	88
	5. Dartmouth-Hitchcock Medical Center	Lebanon, NH	575
	6. Emory University	Atlanta, GA	1231
	7. Jewish Hospital Rudd Heart and Lung Center	Louisville, KY	1971
	8. Johns Hopkins University	Baltimore, MD	1670
	9. Mayo Clinic, Jacksonville	Jacksonville, FL	288
	10. Mayo Clinic, Rochester	Rochester, MN	1183
	11. Medical University of South Carolina	Charlestown, SC	578
	12. Moffitt Cancer Center	Tampa, FL	787
	13. Northwestern University	Chicago, IL	426
	14. Ochsner Medical Center	New Orleans, LA	504
	15. St. Elizabeth Health Center	Youngstown, OH	1046
	16. University of California, Los Angeles	Los Angeles, CA	1687
	17. University of California, San Diego	San Diego, CA	155
	18. University of Iowa	Iowa City, IA	1154
	19. University of Michigan Medical Center	Ann Arbor, MI	857
	20. University of Pennsylvania	Philadelphia, PA	386
	21. University of Texas M.D. Anderson Cancer Center	Houston, TX	782
	22. Vanderbilt University	Nashville, TN	465
	23. Wake Forest University	Winston-Salem, NC	1113
	Total		18842
LSS	24. Georgetown University Medical Center	Washington, DC	1827
	25. Henry Ford Health System	Detroit, MI	3395
	26. Marshfield Clinic Research Foundation	Marshfield, WI	2520
	27. Pacific Health Research & Education Institute†	Honolulu, HI	2359
	28. University of Alabama at Birmingham	Birmingham, AL	5052
	29. University of Colorado Denver	Aurora, CO	3743
	30. University of Minnesota School of Public Health	Minneapolis, MN	6618
	31. University of Pittsburgh Medical Center	Pittsburgh, PA	2177
	32. University of Utah Health Sciences Center	Salt Lake City, UT	3159
	33. Washington University School of Medicine	St Louis, MO	3764
	Total		34614
Total			53456

* ACRIN = American College of Radiology Imaging Network; LSS = Lung Screening Study.

† Formerly known as Pacific Health Research Institute.

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NLST Objectives and Findings

- Objective
  - Determine whether lung cancer screening using low-dose multidetector helical CT reduces lung cancer-specific mortality relative to a single view chest radiograph in a high-risk cohort
- Findings
  - Reduction in mortality from lung cancer achieved based on low-dose CT screening
  - Demonstrated a 20% reduction in lung-cancer-specific mortality in high-risk patients

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NLST Objectives and Findings

- Compared to CXR, low-dose CT had a higher sensitivity and low specificity

Interval	Low-dose CT		Chest Radiography	
	Sensitivity	Specificity	Sensitivity	Specificity
T_0	93.8	73.4	73.5	91.3
T_1	94.4	72.6	59.6	94.1
T_2	93.0	83.9	63.9	95.3

- All-cause mortality was 6.7% lower in the low-dose CT group than the CXR group

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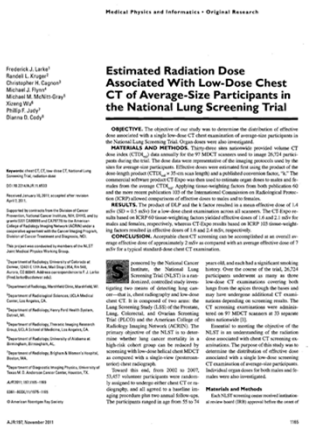
NLST CT Summary

- Results published in AJR[5] Nov 2011, NLST CT Working Group authors
  - Fred Larke, MS
  - Randell Kruger, Ph.D.
  - Chris Cagnon, Ph.D.
  - Michael Flynn, Ph.D.
  - Mike McNitt-Gray, Ph.D.
  - Xizeng Wu, Ph.D.
  - Philip Judy, Ph.D.
  - Dianna Cody, Ph.D.



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Estimated Radiation Dose Associated With Low-Dose Chest CT of Average-Size Participants in the National Lung Screening Trial

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NLST CT Summary

- Summary of 97 CT systems utilized

Manufacturer	Model	# Scanners
General Electric Healthcare	LightSpeed Plus 4	7
	LightSpeed Discovery 4	1
	LightSpeed Qxi 4	13
	LightSpeed Ultra 8	7
	LightSpeed 16	25
	VCT 64	1
Philips Healthcare	MX8000 (4)	7
	MX8000 (16)	2
	Brilliance 64	1
Siemens Healthcare	Sensation 4 (Volume Zoom)	12
	Sensation 16	12
	Emotion 16	1
	Sensation 64	2
Toshiba	Aquilion 4	3
	Aquilion 16	3

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NLST CT Summary

- CT participant screening parameters

NLST Specification	Typical Site Values
Multi detector CT – minimum 4 channels	4 or 16
kVp – 120 to 140	120
Pitch – 1.25 to 2.00	1.5
Effective mAs (mAs / pitch) – 20 to 60	20 - 40
Total Scan Time (35 cm) – max 25 sec	10 - 20 sec

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NLST CT Summary

- CT participant screening parameters

NLST Specification	Typical Site Values
Multi detector CT – minimum 4 channels	4 or 16
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Effective mAs (mAs / pitch) – 20 to 60	20 - 40
Total Scan Time (35 cm) – max 25 sec	10 - 20 sec

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NLST CT Summary

- ACR[4] lung cancer screening specifications

Scan Parameter	Parameter Specification
CT scanner type	multidetector, detector rows $\geq$ 4
kV	100 - 140
Pitch (IEC Definition)	0.7 – 1.5
Current adjustment	manual or automatic (patient size)
CTDIvol	$CTDIvol_{(standard\ size\ patient)} \leq 3$ mGy

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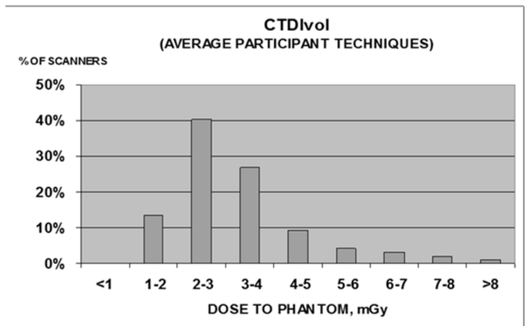
NLST CT Summary

- Measured CTDIvol for CTs used in NLST



Average $CTDI_{vol}$ = 3.3 mGy (Std Dev = 1.5 mGy)
Published in AJR[5], November 2011

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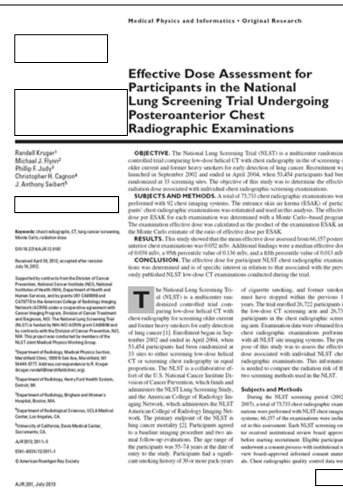
NLST CXR Participant Dosimetry: Introduction

- Chest radiography participant dose study published
  - AJR[6], July 2013
- Study Objective
  - Determine effective dose associated with individual NLST chest x-ray examinations


Medical Physics and Informatics • Original Research

Effective Dose Assessment for Participants in the National Lung Screening Trial Undergoing Posteroanterior Chest Radiographic Examinations

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NLST CXR Participant Dosimetry: Methods and Materials

- CXR Quality Control (QC)
  - 92 CXR acquisition systems at 33 sites
    - Included film-screen, CR and DR devices
    - Certification requirements were adapted from published ACR standards and consensus among the participating facilities
  - Initial and annual QC activities
    - Focused on verification of output calibration
    - Machine-specific measurements (annually)
      - HVL and radiation output (mR/mAs)

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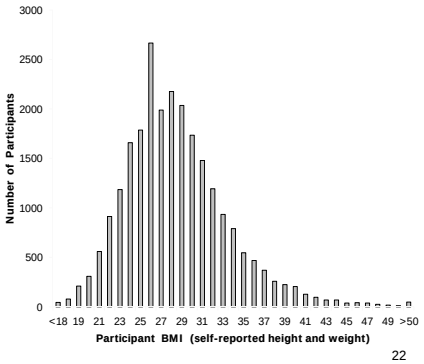
NLST CXR Participant Dosimetry: Methods and Materials

- NLST CXR protocol specified the collection of a participant's acquisition parameters
  - Imaging parameters
    - Tube potential,
    - Current and mAs
    - Exposure time
    - Detector system
  - Participant factors
    - Height and weight
    - Average BMI = 28



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NLST CXR Participant Dosimetry: Methods and Materials

- Monte-Carlo program
  - PCXMC, developed by the Finnish Radiation and Nuclear Safety Authority, Helsinki, Finland
    - PC based special purpose code for diagnostic radiology only dose calculations
    - Hermaphrodite mathematical phantom
- Effective dose assessment methodology
  - Product of exam entrance skin air kerma (ESAK) and the ratio [effective dose per ESAK]
    - Exam ESAK is the product of mAs and average x-ray tube output, measured annually by medical physicist

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NLST CXR Participant Dosimetry: Results and Conclusions

- 73,733 CXR examinations performed
- A CXR effective dose assessment was determined based on 66,157 exams
  - Data from 31 sites utilizing 90 CXR systems
  - Data from 26,732 CXR participants utilized
  - Mean Effective Dose (ED): 0.052 mSv
- Variations in tube potential and filtration had a minor influence on assessed ED
  - ED changed <20% at the max/min boundaries

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NLST CXR Participant Dosimetry: Results and Conclusions

- Comparison to other published studies[6]

Study or Location	Mean Effective Dose (mSv)	Reference	View	Effective Dose Variation
Dutch National Institute of Public Health (2004)	0.016	11	Posteroanterior	Coefficient of variation, 38%
National Radiological Protection Board, United Kingdom (1996)	0.017	12	Posteroanterior	Percentile (5th and 95th), 0.008–0.037 mSv
Nationwide Evaluation of X-ray Trends, chest radiography, United States (1984–2001)	0.026	21	Posteroanterior	SD, 0.001 mSv
National Lung Screening Trial, chest radiography, United States (2002–2007)	0.052		Posteroanterior	Percentile (5th and 95th), 0.013–0.136 mSv
UNSCEAR, Japan (2000)	0.057	13	Not reported	Variation range, 0.01–0.4 mSv
Switzerland (2002)	0.057	14	Posteroanterior	Relative error, 15%
Taiwan (2008)	0.06	15	Posteroanterior	Variability not reported
UNSCEAR, Netherlands (2000)	0.06	13	Not reported	Variation range, 0.01–0.4 mSv
UNSCEAR, Finland (2000)	0.10	13	Not reported	Variation range, 0.01–0.4 mSv
UNSCEAR, Norway (2000)	0.13	13	Not reported	Variation range, 0.01–0.4 mSv
UNSCEAR, Sweden (2000)	0.15	13	Not reported	Variation range, 0.01–0.4 mSv
UNSCEAR, Germany (2000)	0.30	13	Not reported	Variation range, 0.01–0.4 mSv

Note—UNSCEAR = United Nations Scientific Committee on the Effects of Atomic Radiation.

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Questions?

- Cited and significant references:
  - 1. American Cancer Society: http://www.cancer.org/cancer/
  - 2. National Cancer Institute: http://www.seer.cancer.gov/
  - 3. US Preventive Services Task Force: http://www.annals.org/
  - 4. American College of Radiology: http://www.acr.org/
  - 5. FJ Larke, et al. Estimated Radiation Dose Associated With Low Dose Chest CT of Average-Size Participants in the National Lung Screening Trial. American Journal of Roentgenology (AJR) 197:1165-1169 (2011).
  - 6. RL Kruger, et al. Effective Dose Assessment for Participants in the National Lung Screening Trial Undergoing Posteroanterior Chest Radiographic Examinations. American Journal of Roentgenology (AJR) 201:142-146 (2013).
  - 7. National Lung Screening Trial Research Team. Reduced Lung-Cancer Mortality with Low-dose Computed Tomographic Screening. New England Journal of Medicine 365:395-409 (2011).
  - 8. National Lung Screening Trial Research Team. Results of Initial Low-Dose Computed Tomographic Screening for Lung Cancer. New England Journal of Medicine 368:1980-91 (2013).

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