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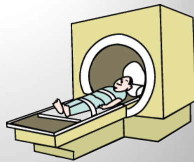

CT in Clinical Trials

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Professor, Imaging Physics Department

Disclosures

ACR – CT Accreditation Reviewer

Gammex – Research agreement

Background – around 2000

Rationale for lung cancer screening seemed obvious, but lack of mortality specific evidence

NIH funded National Lung Screening Trial (NLST) through:
- Lung Screening Study (LSS)
- American College of Radiology Imaging Network (ACRIN)
- ~$250 Million

Imaging study – very large (goal 50,000 subjects), complex

Heavy involvement with biostats & IT

National Lung Screening Trial (NLST)

53,456 participants, 55-74 years, w 30+ pack year smoking history
Baseline exam + 2 subsequent annual exams (3 total per subject)

ACRIN	LSS
n = 18,842 subjects	n = 34,614 subjects
CT vs CXR	CT vs CXR

Data eventually pooled, analyzed
Results showed real benefit for CT screening
20% reduction in lung cancer mortality in the CT arm
US Preventive Services Task Force statement
CT Lung Screening now performed in increasing numbers

US Preventive Services Task Force

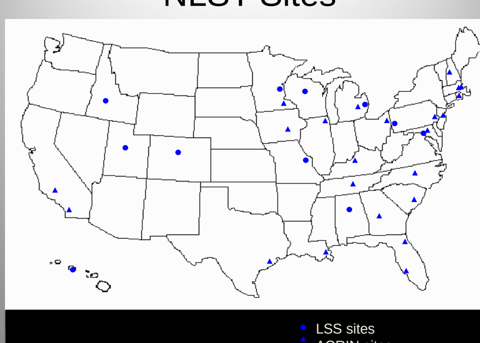
The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

December, 2013

U.S. Preventive Services TASK FORCE

NLST Sites



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Way back when, once upon a time, at the start….

Concept of NLST was very controversial
Anticipated lots of scrutiny no matter what the trial result
Wanted to be sure that the images would not be a target:
- quality
- consistency (opposite of variability)

Also – radiation dose was a BIG concern (Screening!)

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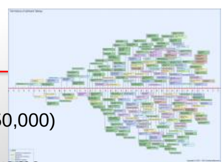
Timeline…



Launched September 2002
Recruitment halted April 2004 (target 50,000)
Follow up continued
~90% of all subjects completed all 3 exams

Physicists included in budget 2002 - 2010 (consultants)

Medical Physics NLST Publications -

2006 Academic Radiology (Cagnon) – QC program for NLST
2010 AJR (Cody) – CTDI of NLST scanners
2011 AJR (Larke) – Effective Dose of NSLT subjects
2017 AJR (Lee) – Organ dose estimates of NLST subjects

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CT Physicists…

ACRIN	LSS
Dianna Cody (Chair)	Fred Larke (Chair)
Christopher Cagnon	Randell Kruger
Phil Judy	Michael Flynn
Michael McNitt-Gray	Xizeng Wu

CT Physics Team

Needed to find a balance between:
- Excellent & consistent quality (QC)
- Reasonable for site personnel to execute
- Team approach – find that sweet spot

Divided up the monitoring duties

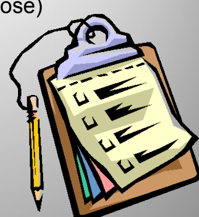
Regular t-cons to discuss data/issues

NLST overall goals/design

Multi-slice CT scanners ONLY – thin sections, fast
"Low-Dose" (~1/4 routine chest dose)
Effective mAs ~ 20-30 mAs
Lung masses ≥ 4mm
- Solid, part-solid, ground glass

Positive screens → follow-up
Blood, urine, sputum specimens
- 15 sites
- ~10,000 subjects
- + lung tumor pathology blocks

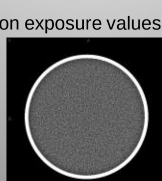
Primary endpoint: mortality



CT Physics Requirements

Phantom images submitted for review:
- Verify protocol parameters being applied
- Confirm acceptable IQ using that parameter set

Annual dosimetry measurements:
- Confirm radiation exposure values using parameter set



Physics ACRIN/NLST QC paper

Image Acquisition Parameters – 4 manufacturers, 14 scanner models (n = 96)
Initial 'certification' submission
Annual performance tests
- CTDIvol on 32cm phantom with NLST scan protocol
- Water phantom (0±4 HU) w/NLST scan protocol
- Image noise – std deviation in water phantom 15-40 HU w/NLST scan protocol
- Field Uniformity in water phantom w/NLST protocol ≤7 HU
- Artifact assessment (water phantom scanned w/NLST protocol)

Bimonthly water phantom image submission

Cagnon CH, et al. Description and implementation of a quality control program in an imaging-based clinical trial. Acad Radiol 13: 1431-1441, 2006.

Image Acquisition Parameters - Example

Parameter	Philips MX8000 4-slice/0.5 sec 4 × 2.5	Philips MX8000 4-slice/0.5 sec 4 × 1	Philips MX8000 16 slice/0.5 sec 16 × .75	Toshiba Aquilion 4-slice/0.5 sec	Toshiba Aquilion 16-slice/0.5 sec
kV	120	120	120	120	120
Gantry Rotation Time	0.5 sec	0.5 sec	0.5 sec	0.5 sec	0.5 sec
mA (Regular patient-Large patient values)	75–150	80–160	75–150	80–160	80–160
mAs (Regular-Large)[1]	37.5–75	40–80	37.5–75	40–80	40–80
Scanner effective mAs[2] or mAs/slice[2] (Reg-Lg)	25–50	20–40	25–50	26.7–53.3	26.7–53.3
Detector Collimation (mm)—T	2.5 mm	1 mm	.75 mm	2 mm	2 mm
Number of active channels—N	4	4	16	4	16
Detector Configuration—N × T	4 × 2.5 mm	4 × 1 mm	16 × 0.75 mm	4 × 2 mm	16 × 2 mm
MODE (Thick/Speed)	N/A	N/A	N/A	N/A	N/A
Table incrementation (mm/rotation)—I	15 mm	8 mm	18 mm	12 mm	48 mm
Pitch ([mm/rotation]/beam collimation)—I/NT	1.5	2	1.5	1.5	1.5
Table Speed (mm/second)	30 mm/sec	16 mm/sec	36 mm/sec	24 mm/sec	96 mm/sec
Scan Time (40 cm thorax)	13 sec	25 sec	11 sec	17 sec	4.2 sec
Nominal Reconstructed Slice Width	3.2 mm	2 mm	2 mm	2 mm	2 mm
Reconstruction Interval[3]	2.0 mm	1.8 mm	1.8 mm	1.8 mm	1.8 mm
Reconstruction Algorithm[3]	B or C	B or C	B or C	FC 10	FC 10
# Images/Data set (40 cm thorax)	200	223	223	223	223
$CTDI_{vol}$ Dose in mGy[4] (Regular–Large)	2.0–4.1 mGy	2.8–5.5 mGy	1.9–3.8 mGy	3.0–6.0 mGy	2.7–5.4 mGy

AAPM CT Protocol website (+ TCM)

Radiation dose papers (3)

1. Cody DD, et al. Normalized CT Dose Index of the CT scanners used in the NLST. AJR 194: 1539-1546, 2010.

2. Larke FJ, et al. Estimated radiation dose associated with low-dose chest CT of average-size participants in the NLST. AJR 197: 1165 – 1169, 2011.

3. Lee C, et al. Body size-specific organ and effective doses of Chest CT screening examinations of the NLST. AJR 208: 1082 – 1088, 2017.

What we did well

Acquisition parameter sets by CT model
- Guide for study personnel at sites
- Very specific
- Helped provide image quality consistency

Looked for water QC images
- Not useful for intended purpose (water CT#)
- Very useful for checking connectivity of individual sites to archive system

What I wish we had done better:

Implement new technology somehow
- Tube Current Modulation!

Use of DICOM monitoring real-time to confirm protocol was being followed

Current challenge - New CT options

- Tube Current Modulation (versions, parameters)
- Iterative Reconstruction (many versions, parameters)
- Organ dose modulation
- CAD (lung)
- Dose Notification values
- Dual Energy? (LOTS of parameters/post processing options)
- Post processing options:
  - Metal artifact reduction
  - Multi-planar reformats
  - Maximum intensity projection images
- Report templates (structured reports)?
- Hanging protocol standards?

Ongoing QC?...

Consider if an accreditation program or other standard may suffice for following established processes?

(Don't reinvent the wheel…)

May have been sufficient for:
- Equipment certification
- Annual performance submission

General CT Pointers in Clinical Trials:

- Budget <u>must</u> include Medical Physics assistance!
  - Ballpark: $10-15K per year per physicist (need team)
- May need help well after image acquisition has ended
  - Last payment for 2010, acquisitions stopped 2006
- Nail down acquisition and reconstruction parameters on a <u>per scanner model</u> basis
- Include a method for confirming image transfer is ok
- Have a plan for implementing new technology as it becomes released during the trial (it WILL happen)