

Description and Implementation of a Quality Control Program in an Imaging-Based Clinical Trial¹

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Rationale and Objectives. The American College of Radiology Imaging Network is participating in the National Lung Screening Trial, a large, multicenter, randomized controlled trial, comparing multidetector helical computed tomography (MDCT) versus chest radiography (CXR) in screening for lung cancer. Because the threshold for detection of disease is an inherent function of image quality, and consistent image quality is necessary to track changes in suspicious findings, our purpose was to develop an image quality control (QC) program across all clinical sites for both modalities.

Materials and Methods. The primary goals of the QC program include standardization of imaging protocols, certification of imaging equipment, and ongoing, periodic evaluation of the equipment calibration and image quality. Minimum standards for equipment and standardized cross-platform acquisition protocols are achieved via radiologist and physicist attestation forms and web-distributed technique charts, respectively. Imaging equipment performance standards are implemented through an initial machine certification process that includes equipment calibration. Ongoing assessment of equipment performance and calibration, as well as adherence to established imaging protocols, is accomplished via periodic submission of calibration records and phantom images. Participant-specific image acquisition parameters are entered into a web-based centralized database and variations from established protocols are automatically flagged for review. Participant radiation dose can be estimated from the image acquisition parameters applied to the imaging equipment calibration measurements. A radiologist visual review committee also evaluates participant images for diagnostic quality. Data are collected from 23 independent centers, representing 14 models of MDCT scanners from four manufacturers, and CXR systems that include film-screen, computed radiography, and direct digital radiography systems.

Results. Widespread imaging protocol variation in extant clinical practice—as well as variability in equipment technology, image acquisition parameters, manufacturer terminology, and user interface—have required careful standardization as a prerequisite to trial participation and ongoing image QC. Acceptable ranges for image acquisition parameters have been refined to accommodate continuously evolving equipment platforms and the scope of participant size and body habitus.

Conclusion. Standardization of imaging protocols is a critical component of image-based clinical trials, predicated on ongoing dialogue between sites and a centralized review committee.

Key Words. Lung cancer screening; standardizing CT protocols; quality control in imaging based clinical trials.

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Lung cancer is the leading cause of cancer death in both men and women in the United States (1). Lung cancer screening is of considerable interest, based on the premise that early detection may reduce lung cancer-specific mortality. Both chest radiography (CXR) and computed tomography (CT) have been proposed as screening tests, though to date, neither has been shown to reduce lung cancer mortality. In 2002, the National Cancer Institute (NCI) launched the National Lung Screening Trial (NLST), a randomized, controlled trial comparing low-dose helical CT with CXR to determine which screening test will better lower lung cancer deaths among individuals at high risk. The trial represents the union of two groups: a grant through the American College of Radiology Imaging Network (ACRIN), sponsored by the Cancer Imaging Program, Division of Cancer Treatment and Diagnosis, NCI (ACRIN-NLST); and a contract, the Lung Screening Study (LSS), managed by the Division of Cancer Prevention, NCI (LSS-NLST). Protocol requirements, primary and secondary endpoints, and critical data elements on case report forms have been harmonized across the NLST. After eligibility determination, participants are randomized to receive either low-dose helical CT or CXR annually for 3 years, with regular follow-up thereafter (through 2009) to determine medical outcomes. Trial-wide enrollment was completed at 33 primary sites (23 ACRIN-NLST sites; 10 LSS-NLST sites) in April 2004 and included 53,476 participants. This article describes the quality control processes governing the imaging equipment platforms, acquisition parameters, and image quality for the 23 ACRIN-NLST sites, which recruited 18,862 participants.

The sensitivity of an imaging modality to detect and track an abnormality is a function of both the characteristics and quality of the image. Because image characteristics vary dramatically as a function of acquisition protocol, it is important to define the imaging task (Fig 1). In lung cancer screening, the detection task is typically the observation of focal lung opacities, or nodules, of inherently high attenuation, within the low attenuation background of the lung parenchyma. The screening test is usually repeated at some time interval, for which reason cumulative radiation exposure is important to consider. In the case of lung cancer screening, the inherently high contrast between lung nodules and surrounding aerated lung tolerates low radiation doses, despite lower signal to noise characteristics in the image. However, because both the signal and noise of the image affect the detectability of lung nodules, the imaging protocol must strike a balance between the ability to detect nodules and adherence to a low radiation dose.

In lung cancer screening tests, concepts of “image quality” and “quality control” are vague, and imply that a single standard exists. Unlike mammography, in which federal regulatory bodies define and mandate standards of image quality, such standards have not been defined in lung screening, though general standards exist for CXR imaging through accrediting bodies such as the American College of Radiology (2). In light of this, any controlled trial comparing CT and CXR requires that rigorous image quality standards be defined and that effective image quality control programs be implemented. Furthermore, within the context of a multicenter trial, the standards and acquisition protocols adopted must account for the diversity in available equipment platforms and the introduction of future imaging platforms over time, without compromising the validity of the comparison between CT and CXR arms. Finally, the implementation of a QC program across multiple sites requires practical consideration of time, staff, and test equipment locally available at participating institutions.

In the ACRIN-NLST, the quality control program for both CT and CXR modalities encompassed five major objectives: 1) ensure that image acquisition parameters were appropriate for the detection task; 2) standardize the acquisition parameters across multiple equipment platforms and institutions while anticipating evolving technology; 3) strike a balance between image quality and ionizing radiation exposure; 4) continuously monitor consistency of image quality; and 5) implement a program that ensures protocol compliance. A five-member team of physicists with expertise in CT and CXR was charged with developing and overseeing a program to meet these objectives in the ACRIN-NLST.

DETERMINATION OF IMAGING ACQUISITION PARAMETERS

CT Acquisition Parameters and Standardization

The term “low-dose helical CT” is descriptive, yet imprecise; there is no standard definition of what constitutes low radiation exposure, and scan protocols vary depending on individual machine capabilities. CT protocols vary in the number of acquisition channels, channel width, detector configuration, acquired slice thickness, pitch, kVp, tube current rotation time, and reconstruction kernel. For example, scans for the Early Lung Cancer Action Project (ELCAP) were performed on a single slice scanner using 140 kVp, 40 milliamp-seconds (mAs) per rotation, pitch 2, and 10-mm slice thickness (3). In 2003, Swensen et al published results on lung cancer screening with low-dose

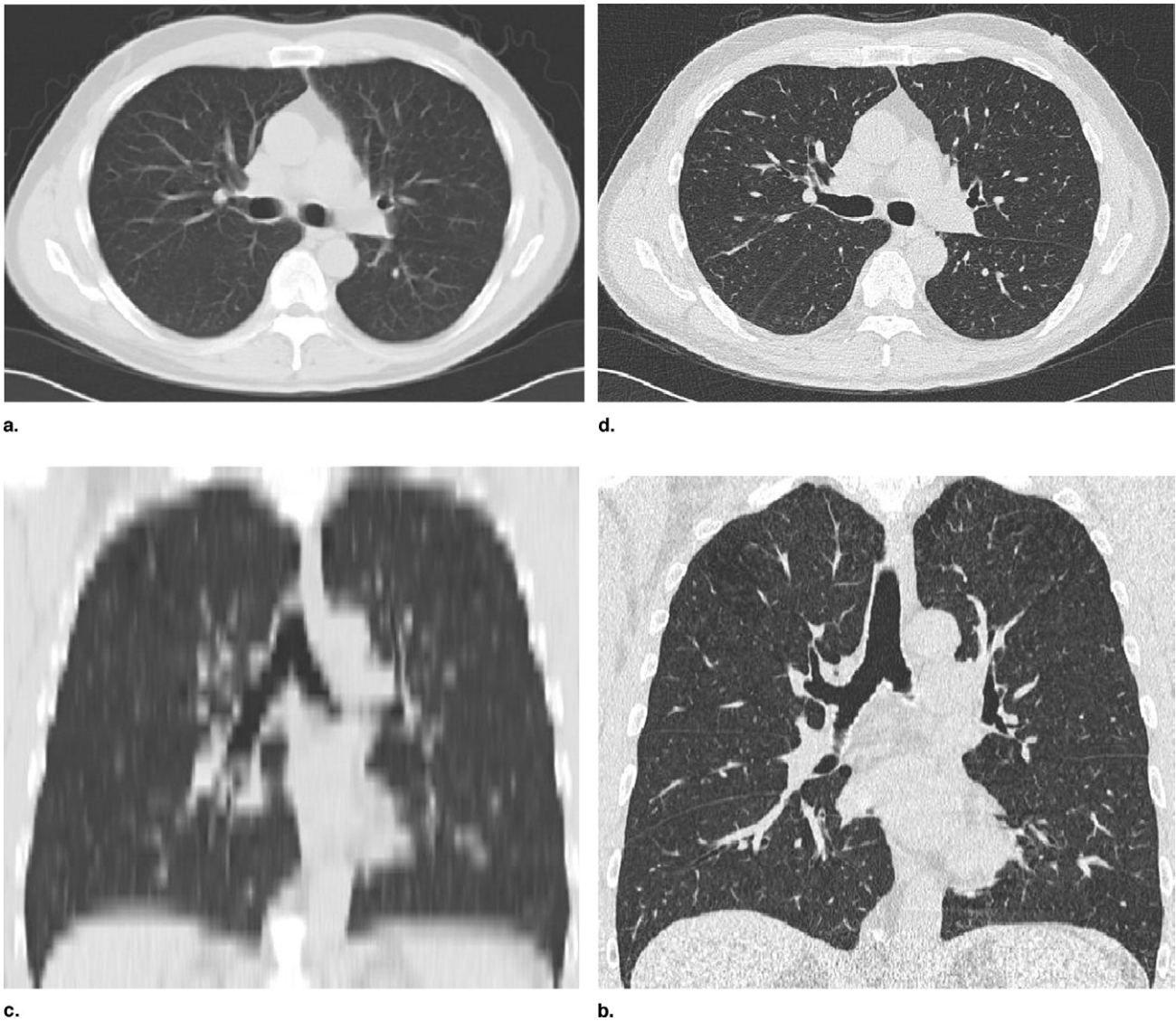


Figure 1. Impact of imaging protocol on computed tomography (CT) image quality. Axial and coronal reconstruction on left (**a,c**) performed with 10 mm slices and a smooth reconstruction kernel. Images on right (**b,d**) are with 1-mm slice and a sharp kernel.

helical CT using a four detector row scanner, 120 kVp, 40 mAs, pitch 1.5, and 5-mm slice collimation (4). A confounding factor in standardization of image acquisition is the lack of current, consistent definitions for commonly used parameters that influence image quality and dose. For example, CT x-ray tube output exposure can be expressed as milliamp (mA), milliamp-seconds (mAs)/slice, or effective mAs (milliamp seconds/scan pitch). Scan pitch itself is inconsistently defined and may have to be derived from the variables of table incrementation per gantry rotation (I), number of active detector channels (N), and detector collimation (T), where $\text{pitch} = I/(N * T)$ (5).

Scan protocol factors influence the spatial, contrast, and noise characteristics of the image, partial volume averaging effects, and the ability to mitigate physiologic motion. Currently, no explicit standards exist that describe CT protocols and image reconstruction kernels appropriate to specific diagnostic tasks. Protocols used in clinical practice are generally the product of vendor suggestion, local radiologists' familiarity with the clinical literature or personal preferences on image appearance.

For the NLST, the interpretation task with CT was to detect, characterize, and follow focal lung nodules of 4-mm diameter or greater. The equipment and protocols

Modulation Transfer Functions

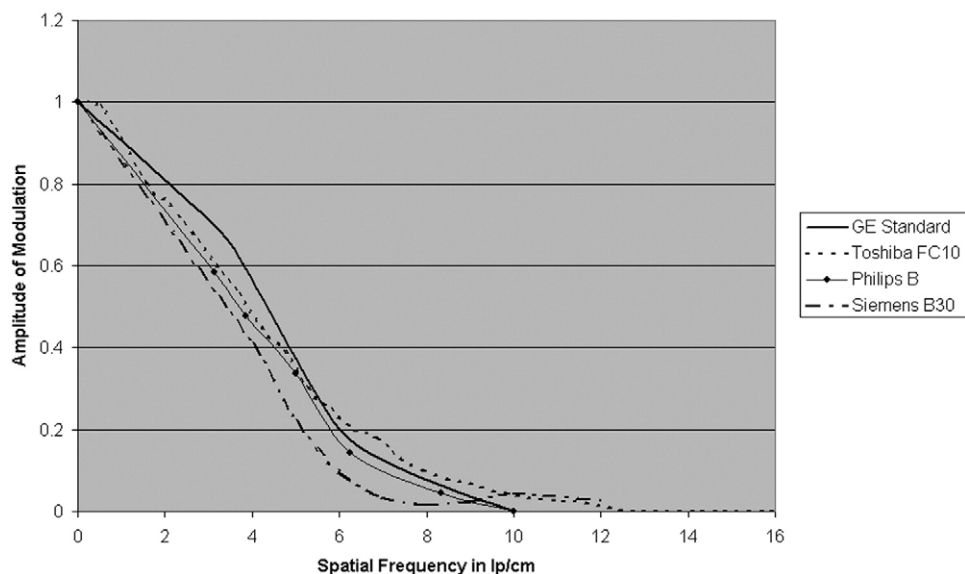


Figure 2. Modulation transfer function (MTF) curves comparison for computed tomography reconstruction filters used for National Lung Screening Trial imaging, by manufacturer.

had to ensure that the whole chest could be imaged in a single, suspended, maximal breath-hold, and maintain an acceptably low radiation exposure. Multidetector scanners were mandated to satisfy these imaging requirements and to enable elective additional prospective reconstructions of the volumetric data beyond that mandated by the protocol. As a reference point for establishing visual image quality, published protocols from other screening studies and actual low-dose helical scans representing a range of technical parameters across scanner platforms were reviewed by a committee of ACRIN radiologists. Based on this review, consensus was established on ranges of technical parameters to guarantee acceptable to excellent image quality. With this visual reference standard, the physics committee established target acquisition guidelines, which included the use of MDCT scanners with four or more channels, gantry rotation times of ≤ 0.8 seconds, pitch (table movement per rotation/x-ray beam width) range from 1.25 to 2.0, nominal reconstruction thickness of ≤ 2.5 mm, contiguous reconstruction intervals, and x-ray beam energy of 120 kVp. The choice of reconstruction kernel was predicated on representing the attenuation of a focal opacity without exaggeration of its border attenuation to minimize the false impression of calcification in small subcentimeter micronodules. Relatively smooth reconstruction kernels were selected to avoid edge enhancement processes that have been shown to artificially

increase the Hounsfield units (HU) of lung lesions in single-slice conventional CT scanners (6). Standardization across platforms was accomplished by choosing the closest equivalent kernel from each scanner make and model, based on modulation transfer function analyses of test CT images reconstructed with different kernels from representative NLST scanners (Fig 2). These modulation transfer function curves were either obtained directly from the manufacturers or measured using standard methods (7).

The range of tube current had to balance acceptable levels of image noise and subjective assessments of image quality against patient dose. Whereas diagnostic chest CT scans generate computed tomography dose index volume ($CTDI_{vol}$) values in the vicinity of 16–20 mGy (8,9), tube current selections and gantry rotation times for NLST were designed to achieve a target $CTDI_{vol}$ dose range of 2–3 mGy based on review of representative datasets across multiple scanners. Note that reliable dose comparisons between CT scanning platforms and protocols require careful adherence to current CT dose definitions. For our standardization, $CTDI_{vol}$ is equal to $CTDI_w / \text{scan pitch}$, where $CTDI_w$ is $(2/3 CTDI_{100} \text{ periphery} + 1/3 CTDI_{100} \text{ center})$ for a 32-cm diameter Plexiglas body phantom, and scan pitch is table incrementation per gantry rotation over total collimation, $P = I/(N * T)$, as described previously.

Over the course of the trial, 14 scanner platforms from four manufacturers were incorporated into the NLST install base. Machine-specific NLST scan protocols have been developed for each, tailored to the individual design capabilities of scanner. To promote cross-platform consistency, a CT technique chart of the machine-specific protocols was created for web-based access (Table 1). This chart provides a comprehensive list of scanner variables for all CT scanner makes and models used in the NLST and is used by sites to program the NLST protocols into their scanners. In all, 18 individual technical parameters have been identified across scanners. Thus, for each scanner, individual protocol parameters are tailored to achieve images of comparable image quality while satisfying minimum standards of radiation exposure, scan acquisition time, and measured spatial, contrast, and noise quality. Where input variables vary among scanners, shaded regions of the chart indicate which variables are specified as user input options at the scanner operator console and which are calculated. X-ray tube current exposure values are presented as allowable ranges; the lower value for typical patients and the upper intended for scans of large patients. To address variations in clinical practice for the acquisition of scout topogram images, which can contribute significantly to total patient dose in a low-dose screening paradigm, the NLST protocol chart recommends they be obtained using a low-dose technique (precise technique not specified) with the x-ray tube parked at gantry bottom in the posteroanterior projection, and with the participant positioned supine to minimize breast dose (10). CT tube current modulation, a potential dose-saving feature found on some newer scanners, was not allowed to prevent the introduction of an additional variable whose effect on image quality could not be easily quantified or standardized.

CXR Acquisition Parameters and Standardization

Projectional X-Ray imaging is the longest standing diagnostic imaging modality and the de facto standard for chest imaging. Because of its widespread installation base, ubiquitous use, and the recent transition from analog to digital technologies, there is considerable variability in CXR image quality and consistency. In addition to subject-specific factors such as size and body habitus, a wide range of technical variables influence the spatial, contrast, and noise characteristics and relative radiation exposure of the projectional image. For the purposes of the NLST, the selection of acquisition devices had to encompass the

equipment variation across 23 sites without compromising image quality.

The minimum requirements for enrollment of CXR equipment and chest radiographic image acquisition in the NLST were adapted from published standards of the American College of Radiology (2) and consensus among the participating institutions. Acquisition devices can include screen-film, computed radiography (CR), or digital radiography (DR). The following general standards were adopted for CXR:

- An equivalent speed of 200 or greater for film-screen and for CR/DR systems calibration.
- Fixed geometry units with a source-to-image distance of 6–10 feet, depending on use of air gap.
- High kilovoltage technique of 100–150 kVp.
- Exposure time not exceeding 40 msec.
- Anti-scatter grids of 10:1 ratio or greater, and at least 103 lines/inch (40 lines/cm) for stationary or 80 lines/inch (32 lines/cm) reciprocating.
- Nominal focal spot size of 0.6–1.2 mm.
- Rotating anode x-ray tubes with a half value layer of 3 mm aluminum or greater at 100 kVp.
- Typical skin entrance dose not to exceed 0.30 mGy for screen film and DR systems, or 0.40 mGy for CR systems.

NLST EQUIPMENT QUALITY CONTROL

Quality control of NLST imaging equipment is coordinated between the ACRIN-NLST Physics Committee, ACRIN Image Management, and the 23 clinical sites. Equipment certifications, dates of submission, and the results of any required phantom testing are tracked through a web-based database accessible to both the ACRIN-NLST Physics Committee and ACRIN Image Management.

CT Equipment Quality Control

Ongoing quality control of CT equipment is a two-pronged effort: initial and annual equipment certifications for all scanners used in the NLST and bimonthly water phantom tests. For reasons of practicality, site testing relies on two readily available phantoms: a standard CTDI phantom, and the sites' scanner's manufacturer-supplied water phantoms. In addition to capturing individual scanner descriptions and capabilities,

Table 1
ACRIN/NLST CT Technique Comparison Chart: Scanner Specific Techniques Mandated by NLST Protocol

Parameter	GE QXi 4-slice/0.8 sec	GE LS Plus 4-slice/0.5 sec	GE Ultra 8-slice/0.5 sec	GE – LS 16 16-slice/0.5 sec	GE – VCT(64) 64-slice/0.5 sec
kV	120	120	120	120	120
Gantry Rotation Time	0.8 sec	0.5 sec	0.5 sec	0.5 sec	0.5 sec
mA (Regular patient-Large patient values)	50–100	80–160	80–160	80–160	50–100
mAs (Regular-Large) ¹	40–80	40–80	40–80	40–80	25–50
Scanner effective mAs ² (Reg-Lg)	26.7–53	26.7–53	29.6–59.2	29.1–58.2	27–53
Detector Collimation (mm)—T	2.5 mm	2.5 mm	1.25 mm	1.25 mm	0.625 mm
Number of active channels—N	4	4	8	16	64
Detector Configuration—N × T	4 × 2.5 mm	4 × 2.5 mm	8 × 1.25 mm	16 × 1.25 mm	64 × 0.625 mm
MODE (Thick/Speed)	2.5/HS/15	2.5/HS/15	1.25/HS/13.5	1.25/1.375/27.5	.625/.984/39.37
Table incrementation (mm/rotation)—I	15 mm	15 mm	13.5 mm	27.5 mm	39.37 mm
Pitch ([mm/rotation]/beam collimation)—I/NT	1.5	1.5	1.35	1.375	0.984
Table Speed (mm/second)	18.75 mm/sec	30 mm/sec	22.5 mm/sec	55 mm/sec	78.74 mm/sec
Scan Time (40 cm thorax)	22 sec	13 sec	18 sec	7.3 sec	5.1 sec
Nominal Reconstructed Slice Width	2.5 mm	2.5 mm	2.5 mm	2.5 mm	2.5 mm
Reconstruction Interval ³	2.0 mm	2.0 mm	2.0 mm	2.0 mm	2.0 mm
Reconstruction Algorithm ³	STD	STD	STD	STD	STD
# Images/Data set (40 cm thorax)	200	200	200	200	200
CTDI _{vol} Dose in mGy ⁴ (Regular-Large)	2.8–5.6 mGy	2.4–4.9 mGy	3.1–6.2 mGy	2.7–5.4 mGy	2.2–4.4 mGy

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

equipment certifications serve to monitor scanner image performance and verify that the correct scanning protocol is being administered to participants. Annual machine performance tests include:

- Measurements of CTDI_{vol} dose on a standard 32-cm body phantom.

- Water calibration: mean region of interest (ROI) values of 0 ± 4 HU.
- Image noise measurements: ROI standard deviation of 15–40 HU.
- Field uniformity measurements: regional ROI mean differences ≤ 7 HU.
- Assessment for artifacts.

Table 1
(Continued)

Parameter	Siemens Vol Zoom/Sensation 4 4-slice/0.5 sec 4 × 2.5	Siemens Vol Zoom/Sensation 4 4-slice/0.5 sec 4 × 1	Siemens Sensation 16 16 × .75	Siemens Sensation 64 64 × 0.6 (beam collimation 32 × 0.6)
kV	120	120	120	120
Gantry Rotation Time	0.5 sec	0.5 sec	0.5 sec	0.5 sec
mA (Regular patient-Large patient values)	75–150	80–160	75–150	50–100
mAs (Reg-Lg) ¹	37.5–75	40–80	37.5–75	25–50
Scanner effective mAs ² (Reg-Lg)	25–50	20–40	25–50	25–50
Detector Collimation (mm)—T	2.5 mm	1 mm	0.75 mm	0.6 mm
Number of active channels—N	4	4	16	32
Detector Configuration—N × T	4 × 2.5 mm	4 × 1 mm	16 × .75 mm	32 × 0.6 mm
Collimation (on operator console)	N/A	N/A	N/A	64 × 0.6 mm
Table incrementation (mm/rotation)—I	15 mm	8 mm	18 mm	19.2 mm
Pitch ([mm/rotation]/beam collimation)—I/NT	1.5	2	1.5	1.0
Table Speed (mm/second)	30 mm/sec	16 mm/sec	36 mm/sec	38.4 mm/sec
Scan Time (40 cm thorax)	13 sec	25 sec	11 sec	11 sec
Nominal Reconstructed Slice Width	3 mm	2 mm	2 mm	2 mm
Reconstruction Interval ³	2.0 mm	1.8 mm	1.8 mm	1.8 mm
Reconstruction Algorithm ³	B30	B30	B30	B30
# Images/Data set (40 cm thorax)	200	223	223>	223
CTDI _{vol} (Dose in mGy) ⁴	2.0–4.1 mGy	2.8–5.5 mGy	1.9–3.8 mGy	1.9–3.8 mGy

Shaded fields are user input fields on scanner console. Other values are either calculated or derived from inputs.

¹The lower exposure bound is a guideline; lower exposures are acceptable provided diagnostic image quality is preserved. The upper exposure is a fixed limit.

²For Siemens and Philips scanners, users input “effective mAs” or “mAs slice” at the scanner console; which is defined as (mA • time)/pitch. For others, this value is calculated for comparison only.

³This table shows the reconstruction parameters required by the ACRIN protocol; sites may create additional reconstructions with other intervals and algorithms.

⁴CTDI_{vol} represents dose measured in 32 cm acrylic (PMMA) phantom; it does not represent radiation dose to a patient. Individual sites may see variations up to ±20%.

Definitions:

T = Z axis collimation, or width of one data channel. In multi-detector CT scanners, several detector elements may be grouped together to form one data channel.

N = # data channels, or the actual number of data channels used during an acquisition.

I = Increment, or the table increment *per rotation* of the x-ray tube in a helical scan.

The measurements of CTDI_{vol} are required to be performed using the approved protocol from the NLST CT technique chart. NLST physics auditors verify that site reported CTDI_{vol} measurements do not exceed established values for participating scanner make and model when using machine specific low-dose protocols. In addition to the annual certification, the water phantom tests are required to be submitted bimonthly for each participating scanner. A detailed manual of operations explicitly describes the methods for conducting all tests. Similarly, dose calculation worksheets are provided to assure consistency and assist sites in calculating and reporting clinical dose estimates of dose length product and patient effective dose derived from measured CTDI_w values (11,12).

Further promoting accessibility and consistency, the equipment certification forms, manual of operations, dose worksheets, and bimonthly water phantom test forms are all web-accessible.

Annual and bimonthly scanner evaluations include forms completed by the site accompanied by soft copy images of the relevant CTDI and water phantom scans, both submitted to ACRIN. In this way, the reported values for water calibration, noise, and field uniformity can be confirmed by comparison with screen-saved images demonstrating the measurement ROIs. Further, adherence to scan protocol can be validated against the acquisition technical factors recorded in the Digital Imaging and Communications in Medicine (DICOM) header of the

image. All phantom images are transmitted to ACRIN, and subsequently to the Physics Committee for review and analysis using Preview TeleImaging Software (CRW Imaging, 2004). Quality control problems are followed up directly with the participant site by an assigned member of the Physics Committee.

CXR Equipment Quality Control

Whereas standardized phantoms exist for measuring CT scanner characteristics, no widely available standard phantom existed at trial initiation for CXR; as such, no practical method for quantifying CXR image quality was readily available. Performance of the CXR units focuses on verification of x-ray output calibration. Annual equipment certification forms capture information describing the x-ray generators and tubes, x-ray system geometry, and antiscatter grid characteristics. Required measurements of the x-ray system include half value layer and exposure output air kerma measurements as a function of tube kilovoltage over a clinically relevant range. These machine-specific measurements allow estimates of participant dose and are compatible with tests typically conducted for regulatory and accreditation purposes. Participating sites also describe the image receptor used. For screen film receptors, approximate system speed, manufacturer, and a description of the film processor quality control program are recorded. For CR or DR systems, sites document the manufacturer make and model, method of calibration, and range of relative exposure index clinically used. In addition, sites complete information on the type of image display for interpretation and the image archive used for CXR. As with CT, all CXR equipment certification requirements and instructions are described in a manual of operations, and the required forms and manual are posted to the website.

Training and Attestation Forms: CT and CXR

To ensure that each site understands the ACRIN-NLST imaging equipment standards and technical parameters, individually signed attestation forms are required from each site's radiologist/principal investigator and physicist. The radiologist attestation form reviews all imaging protocols; the physicist attestations review the equipment specifications, as well as the type/frequency of equipment quality control measures required for each NLST imaging modality. These signed forms serve as documentation that each NLST site has reviewed and agrees to abide by equipment requirements and technical factors as described in the protocol. Finally, a quality control compact disc

(CD) was developed by NLST radiologists to demonstrate parameters of good image quality and examples of practices to avoid. This CD is reviewed at each site, for each modality, by all radiologists and lead technologists, who are then responsible for disseminating these protocol requirements to all technologists who will perform images as part of ACRIN-NLST. Documentation of this review is retained in the site regulatory binders with the signatures of the physicians and lead technologists.

IMAGE QUALITY CONTROL: PATIENT PARTICIPANT CT AND CXR IMAGES

In the ACRIN-NLST, all image data are stored electronically at ACRIN Headquarters Image Management Archive (Philadelphia, PA). The ACRIN-NLST image quality program is designed to ensure that all images in the trial conform to a minimum standard of quality and that there are redundant systems in place to identify image quality issues early on (eg, whether they relate to technical parameters or factors of positioning). Several mechanisms exist to optimize and track image quality. CT and CXR case report forms record image acquisition specifics for each patient (Table 2). This provides a first level of attention to the standard protocol by the technologist. The same case report form is later reviewed by the radiologist in the course of interpretation, permitting the entered fields to be checked. In the case of CT, a third level of parameter checking exists: CT data files are all in DICOM format, and header data are automatically reviewed at ACRIN headquarters for critical technical parameters of kVp, mA (or equivalent measure, depending on manufacturer), slice thickness, reconstruction interval, and reconstruction kernel. Patient scan deviations from the CT protocol specifications for the particular scanner are logged and can be communicated to the site.

Finally, based on an initial pilot study, a random sample of 20% of CT and 16% of CXR examinations are selected for standardized review by a core team of radiologists. The visual review is designed to detect deficiencies in image quality that cannot be characterized by review of technical parameters, including poor positioning, incomplete imaging of the lung fields, submaximal inspiratory breath-hold, excessive motion, incorrect field of view or collimation for participant size, image artifacts, incorrect annotation, incorrect technical parameter, or other problems that compromise the diagnostic quality of the examination. This visual review is used to track

Table 2
Patient Case Report Forms: Image Acquisition Factors Recorded for CT and CXR Specific to Each Randomized Patient

CT		CXR	
Number of Exam attempts	<i>In rare event of poor inspiration or scanner problem a scan may be repeated</i>	Number of exposures taken	<i>Total number of exposures including any repeats not submitted</i>
X-ray tube voltage	<i>Restricted to 120 kVp</i>	Number of images submitted	<i>Total number of images submitted for reading. Large patients might require two offset PA images</i>
Exposure/Tube current Milliamperes: (mA), milliamp-sec: (mAs) Effective mAs: (mAs/ pitch)	<i>Scanner platform dependent: Acceptable ranges as per NLST CT technique chart</i>	Image receptor type	<i>Screen-film, CR, DR</i>
FOV	<i>Display Field of View</i>	X-ray tube voltage	<i>Acceptable range: 100–150 kVp</i>
Reconstruction algorithm/filter	<i>Scanner specific recon. filters as per NLST CT technique chart</i>	Tube current: mA or tube current & exposure time product: mAs	<i>Either may be available dependent on X-ray generator. mA range restricted to 100–1000 mAs normally not to exceed 10</i>
Technologist		exposure time (msec)	<i>If available, normally not to exceed 40</i>
		Exposure value	<i>Relative exposure indication value if known (typically available on CR units)</i>
		CXR Unit I.D.	<i>To match NLST certified machine to randomized patient</i>
		Technologist	

trends and provide feedback to sites experiencing problems with image quality.

IMAGING EQUIPMENT INSTALLATION BASE

In all, 23 medical institutions from across the country are enrolled in the ACRIN-NLST trial. These sites represent 48 CT scanners encompassing 14 models from four manufacturers: GE (Waukesha, WI), Philips (Best, Netherlands), Siemens (Erlangen, Germany), and Toshiba (Tustin, CA). The number and type of scanners is not fixed, but varies over time as sites regularly replace or update equipment used for NLST. All are helical, MDCT scanners encompassing 4-, 8-, 16-, and 64-slice machines with gantry rotation times ranging from 0.33 to 0.8 seconds. Forty-five CXR units are enrolled in the trial, including those that use 200–400 equivalent speed film-screen combinations from Agfa (Ridgefield

Park, NJ), Fuji (Stamford, CT), and Kodak (Rochester, NY); CR units of various models from Agfa, Fuji, and Kodak; and DR units from GE, Philips, and Siemens, as well as one Philips Thoravision. Of note is the rapid progression in imaging technology that has occurred during the course of the trial. Over the first 3 years of the NLST, the CT equipment base has evolved from mainly 4- and 8-slice scanners to a current mix that is predominantly 16 slice, with several 64-slice machines. In a similar trend, 50% of the initial distribution of CXR imaging was performed with film screen; in the third quarter of year 2005, CXR imaging in the NLST is nearly exclusively CR and DR.

DISCUSSION

We have developed a comprehensive QC program for the ACRIN-NLST that certifies all personnel and imaging equipment, standardizes imaging protocols, and limits

radiation exposure for both the CT and CXR screening examinations. The program is overseen by a dedicated Physics Committee, with all certifications and dates of data entry logged by a central database, into which ACRIN Image Management and the physicists can read and write. The QC program establishes an initial certification for all CT and CXR equipment platforms, followed by annual recertifications. Additionally, bimonthly water phantom tests are required for the CT arm. This QC program has been implemented in the context of a large, randomized, controlled trial across 23 institutions currently encompassing 48 CT scanners and 45 CXR machines.

Our experience with this program reinforces the central importance of having a physics core for imaging-based clinical trials to help define image quality standards as a critical foundation for standardizing protocols across technologies. Current state-of-the-art CT and CXR imaging modalities offer a wide and continually evolving range of technology options. As capabilities and complexity evolve, the physicist's role becomes increasingly important in developing imaging protocols tailored to specific imaging tasks and standardizing equivalent protocols across diverse platforms within a modality. It is appropriate to note that advances in technology do not necessarily alter or ease the imaging task. For instance, a primary advantage of a 16-slice CT scanner over a 4-slice CT is to allow complete lung scans of even the most breathing challenged patient in a single breath-hold. Acquiring slices thinner than 2 mm with faster rotation speeds may not prove an advantage for a detection task targeted at 4 mm nodules, and the clinical significance of detecting smaller nodules remains to be proven.

In a large clinical trial, the physics core also plays an invaluable role in validating trial results by assuring imaging protocols are appropriate for desired diagnostic image quality and radiation dose, established standards are achieved, and there is protocol compliance. Despite extensive reference tables and operation manuals for patient and phantom imaging, approximately half of all sites have required corrective intervention at one time or another. Problems encountered include incomplete or incorrect data submission, protocol adherence issues, problems with CT water calibration and exposure output measurements, and various data recording/form completion issues. In many cases, problems are related to local site communication issues involving the roles and responsibilities of the local NLST research assistant and coordinator, the modality technologist, the site physicist, and site principal investigator. Generally, problems can be quickly resolved

via prompt dialogue between physics committee members and site physicists and personnel. An effective QC program is able to quickly identify and correct such problems and protocol variations. Additionally, the program assists in auditing data, assuring they are valid, consistent, and within established norms. This is essential in a clinical trial in which the image data are the primary intervention, as with screening trials, but also where imaging plays a defining role in outcomes assessment.

It is interesting to note that a major mechanism used in the study for ensuring protocol compliance is reviewing parameters in the DICOM header. However, several technical parameters important in determining protocol compliance are not available in the header. For example, the detector configuration and pitch values are not available, though a recent supplement to the CT module has been created (13) but not yet implemented by manufacturers, which defines IEC pitch as well as several other useful parameters (eg, total beam collimation) for the DICOM header.

Among the lessons we have learned is the importance of web-based centralized data entry to facilitate and coordinate data collection for a large-scale, geographically diverse trial. Emphases on careful design of the data forms, database, and a web-accessible interface are crucial to maximizing efficiency and minimizing data errors. Design criteria include: thorough description of data fields, specification of acceptable data range limits, and prospective data entry verification as a means to identify—early on—quality control issues and inadvertent, easily corrected errors. Finally, a well-designed data entry system must be easily accessible by participants and auditors, and built to be easily collated and analyzed.

A successful QC program must also be enforceable across participating clinical sites. It is important to incorporate a mechanism to assure certification of imaging equipment before subject imaging. The flux in equipment platforms has demonstrated that means must also exist to address new machines that come on line and others that are phased out during the trial period. Similarly, mechanisms must exist to anticipate and efficiently incorporate new technologies and accommodate requisite modifications in acquisition protocols. Last, ongoing cooperation requires local site champions: physicists and study research assistants who are thoroughly invested in the trial; this might best be accomplished through direct financial incentives and salary support at the local level.

Finally, development and implementation of an effective image quality control program is vital to the success-

ful design of an imaging-based clinical trial. A physicist with expertise in the desired imaging modality makes an invaluable contribution by helping refine the imaging task and establishing effective, appropriate, and practical imaging equipment standards and protocols necessary to achieve it.

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