Chapter 3

CT Lung Cancer Screening

After completing this chapter, the learner should be able to:

- List the risks for developing lung cancer
- Discuss who should be screened for lung cancer
- Implement a low-dose CT lung cancer screening protocol
- Describe techniques for minimizing radiation dose
- Discuss what makes low-dose CT an effective screening tool
- Explain the risks of undergoing low-dose CT for lung cancer screening

INTRODUCTION

Unlike mammography for breast cancer screening or colonoscopy for colon cancer screening, early-stage lung cancer screening was not recommended until 2013. Low-dose CT (LDCT) lung screening exams are typically performed on patients who are at increased risk for lung cancer because of age, family history of lung cancer, or history of smoking. Early detection of lung cancer may increase the length of survival, and earlier stage cancers may even be cured.[1] The medical community estimates that lung cancer screening could prevent as many as 4,000-8,000 deaths a year.[2]

LUNG CANCER FACTS

In the United States, lung cancer claims more lives than the next three cancers combined: colorectal, breast, and prostate.[1] The American Cancer Society estimated that in 2015, 220,000 Americans were diagnosed with lung cancer and 150,000 lives were lost to lung cancer.

Lung cancer claims more lives than colorectal, breast, and prostate cancer combined.

Overall, lung cancer accounts for 27% of all cancer deaths and is the leading cause of cancer death in both men and women. Lung cancer primarily occurs in older patients, with an average age of 70 at the time of diagnosis. Less than 2% of new lung cancers are diagnosed in patients younger than 45.[1]

For both smokers and non-smokers:

- 1 in 13 men and 1 in 16 women will develop lung cancer
- Black men are about 20% more likely to develop lung cancer than white men
- Black women are about 10% less likely to develop lung cancer than white women
- Both black and white women have lower lung cancer rates than men

More than 50% of those who have lung cancer will die within one year of diagnosis.[3] Fortunately, the overall incidence of lung cancer is trending downward due to tobacco prevention and control measures.[4]

LUNG CANCER RISKS

The greatest risk factor for developing lung cancer is cigarette smoking; 90% of lung cancers in the United States are linked to smoking. Tobacco smoke contains more than 7,000 toxic chemicals, 70 of which are known to cause cancer in both people and animals.[5] Quitting smoking at any age lowers the risk of developing lung cancer, but the risk will always be higher for current or former smokers than for someone has who never smoked.

Exposure to **second-hand smoke**, caused by burning tobacco products, is also a risk; each year more than 7,000 lung cancer deaths are linked to exposure to second-hand smoke.[1]

Third-hand smoke is residual nicotine and other chemicals left on indoor surfaces by tobacco smoke.

Recent research has focused on **third-hand smoke**, which is residual nicotine and other chemicals left on indoor surfaces by tobacco smoke. It is believed that this residue reacts with common indoor pollutants to create a toxic cancer-causing mix that poses a potential threat to nonsmokers and especially to children. The Mayo Clinic reported that, "Studies show that third-hand smoke clings to hair, skin, clothes, furniture, drapes, walls, bedding, carpets, dust, vehicles, and other surfaces, even long after smoking has stopped."[6] Third-hand smoke cannot be easily removed since it builds up over time and cannot be eliminated by airing out the room, opening the window, using fans or air conditioners, or confining smoking to one area of the home.[6] The research on third-hand smoke is limited, and further studies are required to better define the impact of third-hand smoke on the health of individuals as well as on the public at large. [7]

The EPA estimates that radon is responsible for approximately 20,000 new cases of lung cancer annually.

Exposure to **radon** is the second leading cause of lung cancer. Radon is an odorless, naturally-occurring, radioactive gas produced by decaying uranium in the ground. Radon can become trapped in homes by moving up through the ground into cracks and holes in the foundation and sometimes reaching dangerously high levels. The U.S. Environmental Protection Agency (EPA) estimates that radon is responsible for approximately 20,000 new cases of lung cancer annually[8] (**Table 1**).

Source of Risk	% of Lung Cancer Patients
Active smoking	90%
Radon exposure	10%
Occupational exposure **Outdoor air pollution**	10-17%

Table 1. The risk for lung cancer can exceed 100% because of the interactions among different types of exposures.[3]

Other causes of lung cancer include:[9]

- workplace exposure to asbestos, arsenic, diesel exhaust, silica, chromium, uranium, and coke (used to manufacture iron)
- personal or family history of lung cancer
- radiation therapy to the chest
- diet (potentially)
- air pollution
- gene mutations

IMPORTANCE OF EARLY DETECTION OF LUNG CANCER

Early detection and diagnosis of lung cancer is vital for initiation of treatment. Unfortunately, symptoms of the disease usually do not develop until the cancer has reached an advanced stage. Lung cancers diagnosed in later stages have very poor five-year survival rates. The *type* of cancer also impacts five-year survival. For example, small cell lung cancer spreads at very early stages and therefore has a much poorer prognosis than does non-small cell lung cancer.[10] Regardless of the type of lung cancer, early detection is critical as the chance of survival decreases with time.

Lung cancer is often discovered serendipitously. Because lung cancer does not produce symptoms in its earlier stages, it is usually detected by chest X-ray or CT performed for another reason and noted in the radiology report as an incidental finding.[11]

Given the importance of early detection, the U.S. Preventative Services Task Force recommends yearly lung cancer screening with low-dose CT for patients who are at high risk for developing lung cancer.[12] The U.S. Preventative Services Task Force characterizes high risk for lung cancer as people who are between the ages 55 and 80 years old, have a history of heavy smoking, and are current smokers or smokers who have quit within the last 15 years. Heavy smoking is defined as having a smoking history of 30 **pack-years** or more, meaning smoking an average of one pack of 20 cigarettes a day for 30 years. 30 pack-years could also be reached by averaging two packs a day for 15 years.[12]

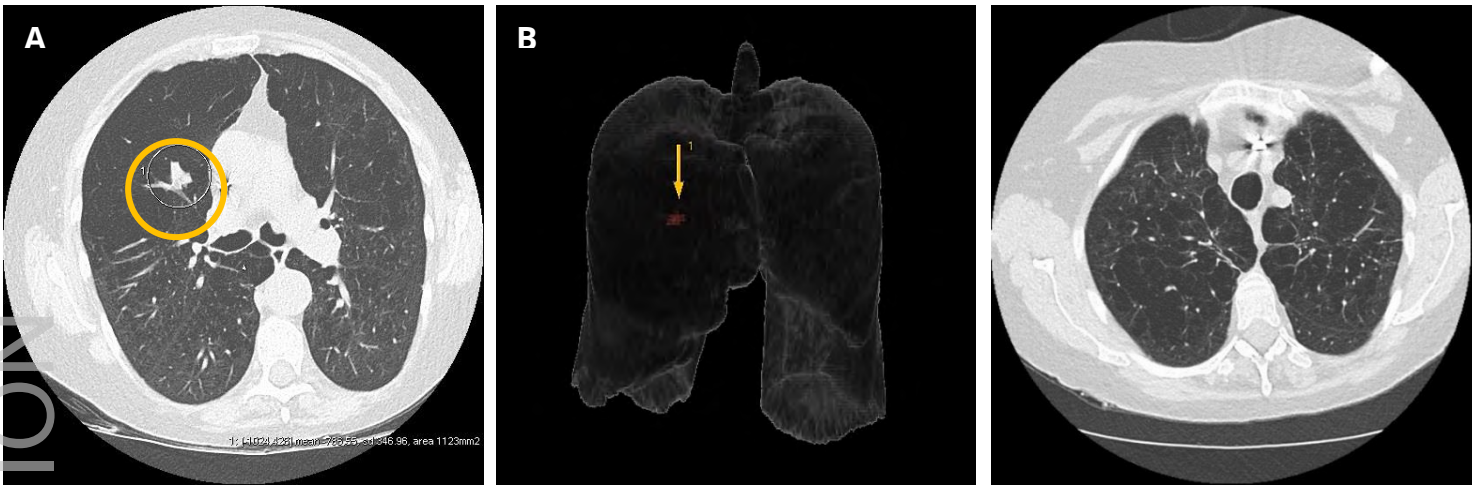

Figure 1. (*left, center*) Patient with right upper lobe nodule. (A) LDCT, (B) 3D LDCT. mSv =1.29.

Figure 2. *(right)* Axial LDCT of upper lobes showing emphysema. Note the areas of lucency, which represent trapping of air in the alveoli.

LOW-DOSE LUNG CT SCREENING PROTOCOL

CT lung screening exams are performed using mAs levels lower than for a standard CT chest exam and can be performed with or without the use of iodinated contrast. Because lung tumors are high-contrast structures compared to air-filled lungs, increased image noise has minimal impact on the ability of the radiologist to diagnose small tumors (**Figures 1-2**).

While pre-set scan protocols are available on CT scanners, it is the responsibility of the radiologist and CT technologist to develop a low-dose protocol that maintains diagnostic quality while minimizing radiation dose.

CMS Requirements

The Centers for Medicare and Medicaid Services (CMS) has established requirements for imaging facilities to receive reimbursement for low-dose lung screening CT.[13]

1. Perform LDCT with volumetric CT dose index (CTDIvol) of ≤3.0 **mGy** for an average-sized patient (5'7" and 155 lbs.) with appropriate decreases for smaller patients and appropriate increases for larger patients.
2. Utilize a standardized lung nodule identification, classification, and reporting system.
3. Make smoking cessation interventions available for current smokers.
4. Collect and submit data to a CMS-approved registry.

ACR Protocol for Low-dose Lung Imaging

The American College of Radiology (ACR) provides guidance for developing a lung screening CT scan protocol and recommends annual review and updates of lung screening protocols.[14] The scan protocol should specify:

1. Use of helical acquisition
2. Collimation, table increment, and pitch as appropriate
3. kVp and mAs appropriate to body habitus
4. Superior and inferior scan ranges of area of interest to be imaged
5. Reconstructed image thickness and interval
6. Reconstruction algorithm and level and window settings
7. Scan field of view and matrix size
8. Image reformatting

Protocols should be developed with the assistance of a medical radiation physicist and the manufacturer of the scanner. Scan techniques should produce diagnostic quality images using the lowest possible radiation dose. **Table 2** is an abbreviated version of the technical specifications for lung cancer screening recommended by the ACR.[15]

Parameter	Scanner Specification
Scanner type	Multidetector CT (minimum 4 detectors)
kVp	100-140 for a standard-sized patient (5'7", 155 lbs)
mAs	Set in combination with kVp to meet CTDIvol of ≤3.0 mGy for a standard-sized patient
Maximum tube rotation time	≤0.5 seconds
Pitch	0.7-1.5
Respiration	Single breath-hold acquisition
Scan acquisition time	≤15 seconds
Reconstructed image width	≤2.5mm
Reconstructed image spacing	≤ image width
Reconstruction algorithm	standard (mediastinum and lung)
CTDIvol	≤3.0 mGy for a standard-sized patient

Table 2. ACR protocol guidelines for ACR-designated lung cancer screening centers.[15]

The ACR offers an accreditation program for imaging facilities to become an ACR Designated Lung Cancer Screening Center. The ACR sets protocol guidelines that meet CMS requirements for reimbursement, as well as provides an excellent resource for protocol development.

Manual and automatic adjustments of volumetric CT dose index

According to the ACR cancer screening specifications, adjusting volumetric CT dose index to account for varying patient body habitus can be accomplished either manually or with automatic adjustments.

The scanner can be adjusted manually using low-dose lung screening protocols for small, medium, or large patients. Each protocol has a size-specific mAs and **kVp** setting. The standard-sized patient protocol must meet the ACR and CMS requirements for a CTDIvol of $\leq$ 3.0 mGy.[14, 15]

Automated techniques employ automatic exposure controls (AEC), including tube current modulation and automated kV selection tools that adjust for varying patient size.[14, 15]

Lung CT Screening Reporting and Data System

In 2014, the ACR released the Lung CT Screening Reporting and Data System (Lung-RADS™) (see **Table 3** at the end of this chapter). Lung-RADS is a quality assurance tool developed to standardize lung cancer screening CT reporting and recommendations, reduce confusion in lung screening CT interpretations, and to facilitate outcome monitoring. The consistent use of assigning Lung-RADS assessment categories assists clinicians in understanding the disposition of their patients based on LDCT as well as in auditing lung cancer screening CT practices and programs. Lung-RADS should be included in the radiologist's report to standardize reporting and management recommendations.[16, 17]

Iterative Reconstruction Reduces Radiation Dose

As with calcium scoring and CCTA, the use of iterative reconstruction during image acquisition for lung cancer screening can decrease radiation dose by 50% or more while maintaining acceptable image quality.

The use of iterative reconstruction can decrease radiation dose by 50% or more while maintaining acceptable image quality.

A 2015 publication by Kim et al reported the results of scanning patients using three different low-dose CT protocols, including two ultra-low dose protocols that employed iterative reconstruction. Despite the significantly lower radiation doses, the ultra-low dose scans using IR helped visualize pulmonary lesions just as well as the standard low-dose protocol. However, the quality of the images of patients with a body mass index (BMI) >25 was reduced, and emphysema was less likely to be diagnosed when using an ultra-low dose protocol with IR.[18]

EFFICACY OF LOW-DOSE LUNG CT AS A SCREENING TOOL

National Lung Screening Trial

The National Lung Screening Trial (NLST) compared low-dose lung CT to standard chest X-ray for the detection of lung cancer. From 2002 - 2004, the NLST enrolled 53,454 current or former heavy smokers ages 55 to 74 from 33 medical centers. The participants were required to have a minimum 30 pack-year smoking history and also have no signs, symptoms, or history of lung cancer. Patients were randomly assigned to undergo three annual screenings with either low-dose CT or single-view posterioanterior chest X-ray. Data collection on cases of lung cancer and deaths from cancer continued through the end of 2009.[19, 20]

Study findings revealed that the participants who received low-dose CT scans were 20% less likely to die from lung cancer than were those in the chest X-ray group. The rate of positive screening tests was 24.2% for low-dose CT and 6.9% for standard chest X-ray over all three screening rounds. This is equivalent to three fewer deaths per 1,000 people screened in the CT group over a period of about seven years of observation.[19, 20]

Liverpool Lung Project

In 2015, the Liverpool Lung Project (LLP) in the United Kingdom also published positive results for LDCT on the early detection of lung cancer. In the UK, 75% of lung cancers are detected at later stages, when treatment is often ineffective. The LLP study enrolled 4,000 high-risk patients. Half of the participants underwent LDCT and the other half had no screening at all. Some patients did undergo follow-up LDCT at 12 months depending on the results of their baseline CT scan.

The results of the LLP study revealed that 42 (2.1%) of the 1,994 participants who underwent LDCT were diagnosed with cancer; 34 of those confirmed cases were diagnosed from the baseline scan, and the additional eight from the 12-month follow-up scan. Importantly, 28 of the 42 confirmed cases were diagnosed at Stage 1 when treatment is most effective. A cost analysis showed that routine scanning of high-risk patients could be affordable in the UK. The study authors hope that the trial results will "contribute to the decision to run a national lung cancer screening program."[21]

American Lung Association

The American Lung Association (ALA) recommends low-dose CT for lung cancer screening. The ALA's endorsement of LDCT was impacted by studies showing it was the only lung cancer screening tool that actually reduces the risk of dying from lung cancer. The use of other common screening exams — sputum **cytology** and chest X-ray — have been shown *not* to decrease the chances of dying from lung cancer, and the standard chest X-ray is no longer recommended for lung cancer screening by the ALA.[22]

The American Lung Association's lung cancer screening questionnaire can be found at http://lungcancerscreeningsaveslives.org/[23]

Lung Cancer Screening May Prevent Unnecessary Surgeries

In 2015, Walker et al reported a low rate of unnecessary surgeries on patients who had undergone low-dose CT lung screening exams. The study followed 1,654 patients from 2012-2014 who underwent LDCT. The study findings revealed that surgical intervention for a benign finding was rare, with only 5 of the 1,654 participants undergoing surgery that ultimately was deemed unnecessary, for a rate of 0.3%. Four of those tumors were benign and the fifth was a breast metastasis to the lung. However, 20 participants did undergo surgery for lung cancer, 18 of which were found in the early stages. These results support low-dose CT as an effective screening tool for lung cancer, again in part because of its low rate of unnecessary surgeries.[24]

RADIATION DOSE FOR LOW-DOSE AND STANDARD-DOSE CHEST CT

We have learned that both CMS and ACR require low radiation doses for lung cancer screening CT with a CTDIvol of ≤ 3mGy for a standard-sized patient; use of iterative reconstruction can further lower effective radiation doses below 1 mSv.[13, 14] Participants from the National Lung Screening Trial received a mean **effective dose** of 1.4 mSv for the low-dose protocol compared to a standard-dose CT chest exam at 7.0 mSv.[25]

A standard-dose CT scan with an effective dose of 10.0 mSv "may be associated with an increase in the possibility of fatal cancer of about 1 chance in 2,000."[25] Since the natural incidence of fatal cancer for Americans is about 1 in 5, CT scans between 1.0 mSv and 10.0 mSv can increase the risk of cancer very minimally - in other words, the risk of radiation-induced cancer from exposure to 1.0 mSv is much smaller than the natural risk of cancer for any one person.[25] Since low-dose CT for lung cancer screening is recommended for a very large demographic, reducing radiation dose while maintaining diagnostic quality is vital for ensuring the lowest number of radiation-induced cancers (**Figure 3)**.

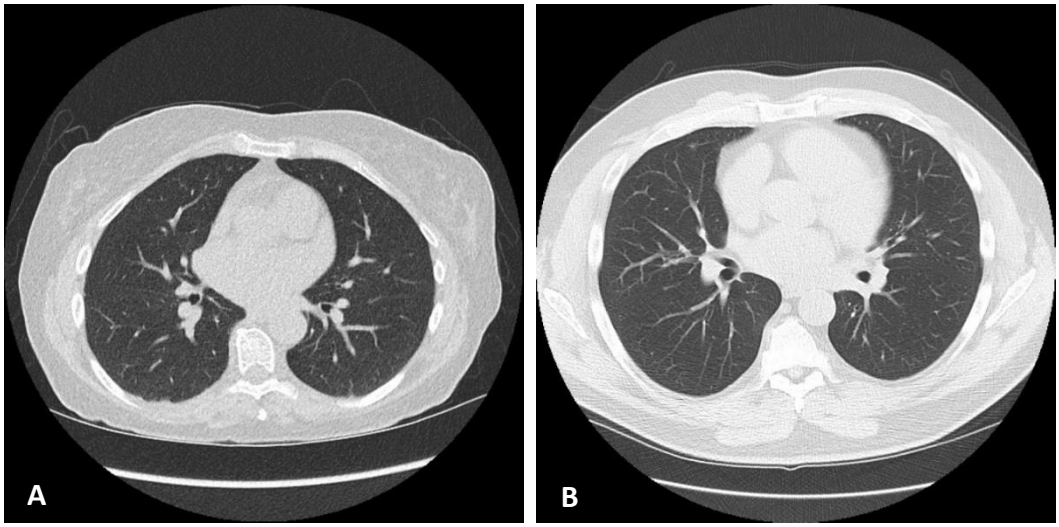

Figure 3. (A) LDCT with IR=0.5 mSv, (B) standard-dose CT with IR=4.0 mSv.

Risks of Screening

Lung cancer screening carries at least three risks:

- A lung cancer screening test can suggest that a person has lung cancer when no cancer is present, in other words, a false positive result. These erroneous findings can lead to unnecessary follow-up testing and surgeries that carry inherent risks.
- A lung cancer screening test could detect a cancer that may never have caused a problem. Overdiagnosis can lead to unnecessary treatment.
- Radiation from repeated CT exams can cause cancer in otherwise healthy people.

These risks underscore why lung cancer screening is recommended only for adults who have no symptoms but who are at increased risk for developing the disease because of their smoking history, family history of lung cancer, and age.[26]

SUMMARY

Low-dose CT for lung cancer screening has become a highly effective tool in the fight against lung cancer.

The American Lung Association endorses low-dose CT for lung cancer screening as it is the only screening exam that has been shown to decrease the number of deaths from the disease. The National Lung Screening Trial found that LDCT outperformed standard chest X-ray in lowering the number of lung cancer deaths. Because LDCT is effective in detecting lung cancers in its early stages, Medicare now provides coverage for many of its beneficiaries. Finally, the American College of Radiology provides guidance in protocol development to meet CMS requirements for reimbursement for ACR Designated Lung Cancer Screening Centers.

Lung-RADS™ Version 1.0 Assessment Categories

Category	Category Descriptor	Category	Findings	Management	Probability of Malignancy	Estimated Population Prevalence
Incomplete	-	0	prior chest CT examination(s) being located for comparison part or all of lungs cannot be evaluated	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed	n/a	1%
Negative	No nodules and definitely benign nodules	1	no lung nodules nodule(s) with specific calcifications: complete, central, popcorn, concentric rings, and fat containing nodules	Continue annual screening with LDCT in 12 months	<1%	90%
Benign Appearance or Behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	solid nodule(s): <6mm new <4mm part solid nodule(s): <6mm total diameter on baseline screening non solid nodule(s) (GGN): <20mm OR ≥20mm and unchanged or slowly growing category 3 or 4 nodules unchanged for ≥3 months			
Probably Benign	Probably benign finding(s)-short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	solid nodule(s): ≥6mm to <8mm at baseline OR new 4mm to <6mm part solid nodule(s): ≥6mm total diameter with solid component <6mm OR new <6mm total diameter non solid nodule(s) (GGN) ≥20mm on baseline CT or new	6 month LDCT	1-2%	5%
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	solid nodule(s): ≥8mm to <15mm at baseline OR growing <8mm OR new 6mm to <8mm part solid nodule(s): ≥6mm with solid component ≥6mm to <8mm OR a new or growing <4mm solid component endobronchial nodule	3 month LDCT; PET/CT may be used when there is a ≥8mm solid component	5-15%	2%
		4B	solid nodule(s): ≥15mm OR new or growing and ≥8mm part solid nodule(s): a solid component ≥8mm OR a new or growing ≥4mm solid component	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the probability of malignancy and comorbidities. PET/CT may be used when there is a ≥8mm solid component.	>15%	2%
		4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy			
Other	Clinically significant or potentially clinically significant findings (non lung cancer)	S	modifier – may add on to category 0-4 finding	As appropriate to the specific finding	n/a	10%
Prior Lung Cancer	Modifier for patients with a prior diagnosis of lung cancer who return for screening	C	modifier – may add on to category 0-4 finding	-	-	-

IMPORTANT NOTES FOR USE:

1. Negative screen: does not mean that an individual does not have lung cancer
2. Size: nodules should be measured on lung windows and reported as the average diameter rounded to the nearest whole number; for round nodules, only a single diameter measurement is necessary
3. Size Thresholds: apply to nodules at first detection and that grow and reach a higher size category
4. Growth: an increase in size of > 1.5mm
5. Exam Category: each exam should be coded 0-4 based on the nodule(s) with the highest degree of suspicion
6. Exam Modifiers: S and C modifiers may be added to the 0-4 category
7. Lung Cancer Diagnosis: Once a patient is diagnosed with lung cancer, further management (including additional imaging such as PET/CT) may be performed for purposes of lung cancer staging; this is no longer screening
8. Practice audit definitions: a negative screen is defined as categories 1 and 2; a positive screen is defined as categories 3 and 4
9. Category 4B Management: this is predicated on the probability of malignancy based on patient evaluation, patient preference and risk of malignancy; radiologists are encouraged to use the McWilliams et al assessment tool when making recommendations
10. Category 4X: nodules with additional imaging findings that increase the suspicion of lung cancer, such as spiculation, GGN that doubles in size in 1 year, enlarged lymph nodes, etc.
11. Nodules with features of an intrapulmonary lymph node should be managed by mean diameter and the 0-4 numerical category classification
12. Category 3 and 4A nodules that are unchanged on interval CT should be coded as category 2, and individuals returned to screening in 12 months
13. LDCT: low dose chest CT

Table 3. Lung-RADS™ Version 1.0 Assessment Categories. Released April 28, 2014. Available at: http://www.acr.org/~/media/ACR/Documents/PDF/QualitySafety/Resources/LungRADS/AssessmentCategories.pdf

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