Lung-RADS: Pushing the Limits

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Introduction

For lung cancer screening (LCS) computed tomography (CT), the American College of Radiology (ACR) developed the Lung CT Screening Reporting and Data System (Lung-RADS) in 2014, which was modeled on the success of the Breast Imaging Reporting and Data System (BI-RADS). Lung-RADS is a tool that facilitates standardized reporting and management of abnormal findings at LCS CT (1,2). The primary goal of Lung-RADS is to minimize variation in the management of LCS CT–detected lung nodules so that LCS can be implemented effectively in radiology practices outside the purview of a clinical trial. Lung-RADS is also an important component of LCS CT quality assurance and registry reporting. Data collected from LCS programs help with practice audits and facilitate outcome monitoring and research on an institutional level and a national level. Further study of the effectiveness of LCS can lead to the optimization of screening criteria and to ideal management of screening-detected lung nodules and can guide the development of future versions of Lung-RADS.

In response to the recommendation of the U.S. Preventive Services Task Force and the coverage decision by the Centers for Medicare and Medicaid Services for lung cancer screening (LCS) computed tomography (CT), the American College of Radiology introduced the Lung CT Screening Reporting and Data System (Lung-RADS) in 2014 to standardize the reporting and management of screening-detected lung nodules. As with many first-edition guidelines, questions arise when such reporting systems are used in daily practice. In this article, a collection of 15 LCS-related scenarios are presented that address situations in which the Lung-RADS guidelines are unclear or situations that are not currently addressed in the Lung-RADS guidelines. For these 15 scenarios, the authors of this article provide the reader with recommendations that are based on their collective experiences, with the hope that future versions of Lung-RADS will provide additional guidance, particularly as more data from widespread LCS are collected and analyzed.

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

■ Describe LCS scenarios in which Lung-RADS guidance is unclear or scenarios that are not currently addressed in Lung-RADS.

■ Explain how volume doubling time can help guide management of a nodule that was depicted at imaging performed before baseline LCS CT.

■ Recognize that growth of a nodule can include an increase in diameter and an increase in density.

See www.rsna.org/education/search/RG.
For some radiologists and referring providers, confusion may arise as to when to use the Lung-RADS guidelines and when to use the Fleischner Society guidelines for the follow-up of lung nodules. Table 3 summarizes the main differences between these two sets of guidelines. Lung-RADS was developed specifically for use in LCS CT reporting. The recently published updated guidelines of the Fleischner Society for the management of incidentally detected lung nodules specifically state that the updated guidelines do not apply to LCS.

Referring providers and radiologists may be confused about whether to perform a diagnostic CT examination or a LCS CT examination when a clinical suspicion for lung cancer exists. One of the exclusion criteria for LCS CT (or any screening examination) is signs or symptoms that can be attributed to the disease for which screening is being performed. Thus, for patients in whom lung cancer is suspected, LCS CT should not be performed, and patients should instead undergo a diagnostic chest CT examination.

Volume doubling time may be used to predict solid pulmonary nodule behavior as benign or malignant. Generally, the observed volume doubling times of lung cancers range from 20 days to 360–400 days. For solid pulmonary nodules, volume doubling times of less than 20–30 days are usually associated with benign causes—commonly, inflammatory or infectious causes. Volume doubling times greater than 400–480 days are also usually associated with benign nodules, with only 3%–4% of non–small cell lung carcinomas reported to have volume doubling times of more than 400 days.

Persistent subsolid nodules are more likely to be malignant than other nodule types, and the risk of malignancy increases with the size of the solid component.

A decrease in nodule size is not always benign, particularly with an increase in attenuation, and continued surveillance may be appropriate.

### TEACHING POINTS

- For some radiologists and referring providers, confusion may arise as to when to use the Lung-RADS guidelines and when to use the Fleischner Society guidelines for the follow-up of lung nodules. Table 3 summarizes the main differences between these two sets of guidelines. Lung-RADS was developed specifically for use in LCS CT reporting. The recently published updated guidelines of the Fleischner Society for the management of incidentally detected lung nodules specifically state that the updated guidelines do not apply to LCS.

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- A decrease in nodule size is not always benign, particularly with an increase in attenuation, and continued surveillance may be appropriate.

As is often the case with the first iteration of a set of guidelines, questions and controversies arise once those guidelines are implemented in daily practice, affecting radiologists, referring providers, and patients. Uncertainties primarily arise from differing interpretations of the Lung-RADS document and from scenarios that are not currently addressed or are incompletely addressed in the Lung-RADS guidelines. In this article, 15 clinical vignettes are used to highlight a variety of ambiguous scenarios, and recommendations are provided for managing these situations that are based on our collective experiences.

### Fifteen Clinical Scenarios

**Scenario 1:** New Lung-RADS Category 3 (probably benign) solid lung nodule in a patient who is aging out of the screening program.

**Scenario 2:** Lung mass in a patient with vague symptoms.

**Scenario 3:** Solid suspicious (Lung-RADS category 4B) nodule with very slow growth rate.

**Scenario 4:** Ground-glass nodule that increases in density but remains stable in size.

**Scenario 5:** Ground-glass nodule with slow growth rate.

**Scenario 6:** How to measure and classify a part-solid nodule.

**Scenario 7:** Nodule that decreases in size but increases in attenuation.

**Scenario 8:** Nodule with characteristic features of an intrapulmonary lymph node.

**Scenario 9:** Airway (endotracheal or endobronchial) nodule.

**Scenario 10:** Incidental potentially important finding other than lung cancer detected at low-dose LCS CT.

**Scenario 11:** Reenrolling patients in the LCS CT program after a stable abnormality.

**Scenario 12:** Low-dose LCS CT of a patient with a recent respiratory infection.

**Scenario 13:** Categorization of a cavitary lung nodule or nodules.

**Scenario 14:** Low-dose LCS CT of a patient with a history of a treated lung malignancy.

**Scenario 15:** Low-dose LCS CT of a patient with a treated low-risk nonlung malignancy.

### Scenario 1: New Lung-RADS Category 3 (probably benign) Solid Lung Nodule in a Patient Who Is Aging out of the Screening Program

An 80-year-old man, who was about to turn 81 years old in 3 months, underwent a final annual LCS CT examination, and a new 5-mm solid nodule was detected. On the basis of Lung-RADS, this nodule would be classified as a Lung-RADS category 3 (probably benign) finding (Table 1) (2). How should this case be managed?

For patients with a new 5-mm solid nodule, Lung-RADS recommends a follow-up low-dose CT examination in 6 months. This patient will be 81 years old at that time and will no longer satisfy the eligibility criteria for LCS.

Many organizations advocate LCS, and they have differing recommendations for who should be screened (Table 2) (3–5). Currently, the two organizations that dictate reimbursement for LCS, the Centers for Medicare and Medicaid Services and the U.S. Preventive Services Task Force, propose 77 years and 80 years, respectively, as the upper age limit for LCS (3,4).

The patient in this scenario will no longer qualify for LCS because of his age. However, managing actionable findings in individuals who no longer qualify for nodule management under the purview of the LCS program requires guidance. Because this CT examination was performed as part of LCS, a Lung-RADS category 3 should be assigned, and a 6-month follow-up “diagnostic” low-dose CT examination should be recommended, because one can presume that
more, the Fleischner Society guidelines do not apply to new or enlarging lung nodules.

Although both sets of guidelines were developed for different scenarios and although none of the guidelines apply to patients aging out of LCS, for the patient in this vignette, we suggest continuing to follow up the nodule outside the screening program with use of the time frames suggested in Lung-RADS, because it is currently the only practice standard that addresses new or growing nodules, provided the patient is healthy enough to undergo treatment if the nodule proves to be actionable.

If the nodule is stable in this particular case, one could report that the stability of the nodule is suggestive of benign etiology or behavior (on the basis of the Lung-RADS description of category 2, because stable category 3 nodules fall back into category 2). However, it would be inappropriate to assign a Lung-RADS category or to recommend follow-up LCS CT, because the patient is no longer eligible for LCS. There is no correct answer for when to stop monitoring this nodule, because there are no guidelines, but it is certainly

<table>
<thead>
<tr>
<th>Table 1: Lung-RADS Categories 3, 4A, and 4B</th>
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<tr>
<td><strong>Category</strong></td>
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<tr>
<td>3: Probably benign</td>
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Note.—Adapted and reprinted under a CC BY 4.0 international license from the ACR (2). PET/CT = dual-modality imaging with positron emission tomography (PET) and CT.

*Depending on the probability of malignancy and comorbidities.
Table 3: Comparison between Lung-RADS Guidelines and Fleischner Society Guidelines for the Management of Pulmonary Nodules

<table>
<thead>
<tr>
<th>Lung-RADS Guidelines</th>
<th>Fleischner Society Guidelines</th>
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<tbody>
<tr>
<td>Single version published in 2014 (2) (addresses solid and subsolid nodules)</td>
<td>Updated version published in 2017 (6) (addresses solid and subsolid nodules)</td>
</tr>
<tr>
<td>Old versions published in 2005 for solid nodules (7) and in 2013 for subsolid nodules (8)</td>
<td>Does not address how to manage nodules that are new or growing</td>
</tr>
<tr>
<td>Developed for the management of nodules in the setting of LCS CT</td>
<td>Developed for the management of incidentally detected nodules</td>
</tr>
<tr>
<td>Includes management of nodules that are new or growing</td>
<td>Applies to patients older than 35 years of age, with no upper age limit</td>
</tr>
<tr>
<td>Applies to all patients undergoing LCS CT</td>
<td>Does not apply to immunosuppressed patients or those with a history of malignancy</td>
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</table>

Note.—Numbers in parentheses are reference citations.
controversial, given the patient’s age. Discussing this with the ordering provider and weighing the benefits and risks may help with this decision.

**Scenario 2: Lung Mass in a Patient with Vague Symptoms**

A 63-year-old woman had a 39-mm mass detected at baseline LCS CT (Fig 1). A retrospective review of the electronic medical record disclosed that the patient had complained of new neck pain. What signs and symptoms should preclude LCS CT and prompt diagnostic chest CT evaluation for lung cancer outside an LCS CT program?

Symptoms of lung cancer are vague and can overlap with other smoking-related comorbidities such as chronic obstructive pulmonary disease, cardiovascular disease, and head and neck cancers. Referring providers and radiologists may be confused about whether to perform a diagnostic CT examination or an LCS CT examination when a clinical suspicion for lung cancer exists. One of the exclusion criteria for LCS CT (or any screening examination) is signs or symptoms that can be attributed to the disease for which screening is being performed. Thus, for patients in whom lung cancer is suspected, LCS CT should not be performed, and patients should instead undergo a diagnostic chest CT examination. Signs and symptoms that should raise suspicion for lung cancer include chest pain, worsening cough, hemoptysis, and unintended weight loss.

Symptomatic patients with lung cancer are much more likely to have advanced-stage disease, and patients in whom limited-stage small cell lung carcinoma was diagnosed at an annual LCS CT examination were more likely to be asymptomatic (9).

**Scenario 3: Solid Suspicious (Lung-RADS Category 4B) Nodule with Very Slow Growth Rate**

At baseline LCS CT, a 74-year-old woman had a 19-mm solid nodule, which had measured 11 mm at an abdominal CT examination performed 12 years earlier (Fig 2). On the basis of Lung-RADS, this screening-detected nodule should be classified as category 4B (suspicious) because of the increase in size (Table 1) (2). However, considering the time interval of 12 years between the earlier CT image (comparison image) and the LCS CT image, how should this nodule be managed?

One situation not addressed in the current version of Lung-RADS is categorizing and managing a nodule that was present on examinations performed before the baseline LCS CT examination. One option would be to manage this nodule as a nodule depicted at a follow-up LCS CT examination, but the definition of growth (at least a 1.5-mm increase in diameter) complicates matters because of the 12-year interval between the two CT examinations in this patient. If we strictly apply the Lung-RADS definition of growth, this nodule should be classified as category 4B, with a probability of malignancy of more than 15% because of a diameter increase of 8 mm, a finding potentially leading to an invasive workup. On the other hand, one can argue that if the 8-mm increase in diameter was divided evenly over the 12-year time span, then the annual growth rate would not meet the 1.5-mm threshold. However, with only two data points, there is no way to determine the true growth curve.

Volume doubling time may be used to predict solid pulmonary nodule behavior as benign or malignant (Fig 3) (10,11). Generally, the
observed volume doubling times of lung cancers range from 20 days to 360–400 days. For solid pulmonary nodules, volume doubling times of less than 20–30 days are usually associated with benign causes—commonly, inflammatory or infectious causes. Volume doubling times greater than 400–480 days are also usually associated with benign nodules (10,11), with only 3%–4% of non–small cell lung carcinomas reported to have volume doubling times of more than 400 days (10,12). These volume doubling times do not apply to pure ground-glass nodules, which are discussed separately. The use of volume doubling time as a discriminator in the context of LCS has been proposed to reduce false-positive screening findings, unnecessary follow-up examinations, and additional workups (13). Currently available tools for radiologists include volume doubling time calculators and online lung cancer risk assessment tools such as the McWilliams lung cancer risk calculator (2,14,15).

Granulomatous inflammation and mesenchymal tumors fall into the types of solid lung nodules that have long volume doubling times. The presence of macroscopic fat, popcorn calcifications, or both in a solid nodule allows the confident diagnosis of a hamartoma, but these findings are often lacking in smaller hamartomas (16) (Fig 4). In the results of one retrospective study of biopsy-proven hamartomas detected at LCS CT, seven of nine hamartomas had volume doubling times greater than 550 days (range, 550–6000 days), one had a volume doubling time less than 450 days, and one had a decrease in volume at follow-up (16).

Another potential cause for a slowly growing solid nodule is a carcinoid tumor. These low-grade malignant neoplasms are rare, with an estimated frequency of 1.57 per 100,000 patients. In the results of one retrospective analysis of 28 pathologically proven carcinoid tumors, investigators showed that when the tumors were peripheral in location, 81% (13 of 16) were detected incidentally (17). CT features reported to help distinguish carcinoid tumors from benign lung nodules include lobulated margins, high attenuation on unenhanced CT images, avid contrast enhancement, and proximity to the airways. In the results of the same series, 13 (81%) of 16 peripheral carcinoids had direct airway involvement, defined as a component of the lesion located within or obstructing a visible airway (“tip of the iceberg” sign) (17). Indirect signs of airway involvement in peripheral carcinoids included peripheral hyperlucency (31%), peripheral bronchiectasis (25%), and peripheral opacity or atelectasis (19%), with 10 (63%) of 16 peripheral carcinoids having at least one indirect finding of airway involvement (17).
The calculated volume doubling time of the nodule in this vignette is 5.2 years. In this case, we are confident that this nodule is not an aggressive cancer, and we recommend assigning category 2 (benign or benign behaving) on the basis of the long volume doubling time and recommend continued LCS CT in 12 months. Although it may be argued that only two time points during a long time period do not guarantee that the nodule recently accelerated growth, we advocate for a conservative approach in a screening program. In this case, the nodule could also be assigned to category 4B on the basis of its size and growth; the recommendations can be based on footnote 9 in Lung-RADS, which states that the management of category 4B nodules should be based on the probability of malignancy on the basis of patient evaluation, preference, and the risk of malignancy. Therefore, a follow-up CT examination could be performed in 3 months, and if the nodule is stable, it could be assigned to category 2 and the patient returned to the LCS CT program. Future versions of Lung-RADS may incorporate volume doubling time as a measure to assess solid nodules, as is being suggested in Europe (13).

**Scenario 4: Ground-Glass Nodule That Increases in Density but Remains Stable in Size**

A 66-year-old woman had a ground-glass nodule with increasing attenuation but unchanged diameter (Fig 5). If confronted with this situation at LCS CT, what would be the appropriate Lung-RADS category and management of this nodule (Table 1) (2)?

Subsolid nodules include a spectrum of focal areas of increased lung attenuation. Subsolid nodules can be divided into (a) pure ground-glass nodules, which are defined as focal areas of increased lung attenuation through which normal structures are visible, and (b) part-solid nodules, which are defined as ground-glass nodules with solid components, the latter of which obscure underlying structures (8,18). Subsolid nodules have a
growth behavior that is different from that of solid nodules. A subsolid nodule can grow not only by increasing in diameter but also by increasing in attenuation, which can manifest as the development of a solid component or by enlargement of only the solid component without a change in the overall diameter, resulting in an overall increase in mass. These features of growth have been associated with an increased risk of malignancy. Persistent subsolid nodules are more likely to be malignant than other nodule types, and the risk of malignancy increases with the size of the solid component (6,10,11).

Currently, the only definition of growth in Lung-RADS is described in footnote 4, where growth is defined as an increase in diameter of at least 1.5 mm. Although Lung-RADS addresses new or growing solid components as a measure of growth of part-solid nodules, it does not address the growth of ground-glass nodules manifesting as a diffuse increase in attenuation. Future versions of Lung-RADS may clarify the concept of growth, but until then, radiologists should recognize other findings indicative of nodule growth and view them with appropriate suspicion. Mass, which combines the nodule density and volume, has been reported to be a more accurate assessment of nodule growth, when compared with diameter or volume measurements alone (19).

Nodules that diffusely increase in attenuation but not in size do not fall clearly into a category. Although there is not a clear solid component, the increase in attenuation is consistent with growth, which makes the nodule suspicious. Because the increase in attenuation is suggestive of a developing invasive component and a change in mass, it would be appropriate to assign category 4X to nodules with this behavior. Category 4X gives radiologists discretion to use their experience and judgment when a particular situation is not clearly described but the imaging findings are highly suspicious for lung cancer. In the description of category 4X, such features include spiculations, a ground-glass nodule that doubles in size in 1 year, and enlarged lymph nodes.

**Scenario 5: Ground-Glass Nodule with Slow Growth Rate**

When classifying a ground-glass nodule in Lung-RADS, all ground-glass nodules that either (a) measure less than 20 mm, or (b) measure 20 mm or greater and are stable or slowly growing fall into category 2. The term slowly growing is not precisely defined in Lung-RADS and, as such, is open to the radiologist’s interpretation. Until the term slowly growing is defined in a future version of Lung-RADS, the following several key points about ground-glass nodules should be considered, to make appropriate recommendations.

Subsolid nodules can result from infection, inflammation, a scar, hemorrhage, or a neoplasm (Figs 6, 7). The first step in assessing a ground-glass nodule is to determine whether it is transient or persistent; a nodule that is due to infection, inflammatory conditions, or hemorrhage will resolve. If a ground-glass nodule persists, it can still be benign (eg, organizing pneumonia or focal fibrosis) (11) (Fig 8). When malignant, lung nodules with ground-glass attenuation are nearly always adenocarcinomas (6,10). Features of pure ground-glass nodules considered to be risk factors for malignancy include a diameter of greater than 10 mm and the presence of cystic changes, which are also described as internal lucencies (6). As discussed in scenario 4, development of a solid component is also a feature suggestive of malignancy. Investigators have shown that ground-glass nodules smaller than 5 mm have a less than 1% risk of transforming into a malignant lesion (20). About 7% of ground-glass nodules 5–10 mm in diameter have features of invasive adenocarcinoma (Fig 9). Ground-glass nodules larger than 10 mm have a higher risk of being adenocarcinoma in situ or minimally invasive adenocarcinoma...
(Fig 10), although approximately 20%–25% of such ground-glass nodules are benign (11).

The volume doubling times of ground-glass nodules are quite variable but typically are longer than the volume doubling times of solid nodules and part-solid nodules. The volume doubling times of adenocarcinomas manifesting as pure ground-glass nodules have been reported to be longer than 400 days and up to 1436 days (11). Investigators have shown that the growth of most ground-glass nodules (including adenocarcinomas) is slow enough that annual surveillance is appropriate, thereby avoiding overdiagnosis and aggressive, potentially harmful intervention. Sawada et al (21) reported no adverse outcome related to a delay in therapy in patients who underwent resection of subsolid nodules only after growth was apparent at CT. Furthermore, the most recent Fleischner Society guidelines have been updated to reflect the indolent nature of these lesions (6). An increase in the maximum diameter of more than 1.72 mm is needed to identify true growth of a ground-glass nodule, according to one group of investigators (22). It is best practice to compare all nodules with the most remote examination available, to optimize sensitivity for the detection of change.

Lung-RADS incorporates all of this information by simply classifying all stable or slowly growing ground-glass nodules in category 2 (benign appearance or behavior). Behavior is what would best describe these nodules. Only time will tell if these nodules are, or will ever become, clinically relevant cancers. In this era in which all screening tests are being scrutinized, radiologists must be clear and must educate referring providers that even though a ground-glass nodule may be malignant, it can be safely observed to avoid overdiagnosis. When faced with the controversial question of when to intervene in a patient with a slowly changing ground-glass nodule (Fig 11), clear communication with the referring provider can avoid misinterpreting slow interval growth as an impetus for aggressive intervention. Although this path may be more challenging because no formal definition of the term slowly growing exists, radiologists are encouraged to discuss the options of surveillance versus more aggressive evaluation, including the potential consequences of more aggressive workup of these indolent lesions, with the other members of the patient care team.
Two items to consider with respect to the definition of the term *slowly growing* in future versions of Lung-RADS are the concepts of mass (attenuation) change and change during longer time intervals (eg, 2–3 years). Some investigators advocate for adjusting screening intervals to risk-defined models (13), including increasing the screening interval to 2 years in selected patients with subsolid nodules at LCS CT (23). In the results of another study, investigators have shown no protective effect on mortality in patients undergoing annual screening compared with biennial screening (24). However, in the findings from a study derived from the Dutch-Belgian NELSON trial, investigators showed that a 2.5-year screening interval was associated with (a) higher interval cancer rates, compared with 1- and 2-year screening intervals, and (b) a higher proportion of patients with an advanced disease stage in the final screening round, compared with previous rounds (25). This area is controversial and will likely be studied heavily in the future as data from LCS continue to accumulate.

**Scenario 6: How to Measure and Classify a Part-Solid Nodule**

A 69-year-old man had a right upper lobe nodule at baseline LCS CT (Fig 12). Which Lung-RADS category should be assigned?

Evaluation of some lung nodules can be challenging for radiologists, especially part-solid nodules. Challenges include determining what is the solid component, if any, and how to measure the solid component. The inter- and intraobserver agreement in the classification of nodules as solid or subsolid is highly variable (26). The Fleischner Society guidelines recommend evaluating part-solid lung nodules by using lung window settings with a sharp filter to better assess the extent of the solid component (6). However, how does one measure a solid component when it is not discrete?

We asked thoracic radiology colleagues across the country how they would categorize the nodule in Figure 12, and responses included categories 3, 4A, 4B, and 4X. The disagreement was related to the measurement of the solid component. However, all radiologists agreed that this nodule was suspicious for lung adenocarcinoma. This example is another one in which the X modifier allows radiologists to use their clinical judgment to decide how to best manage a suspicious nodule. For this nodule, the most conservative approach would be to repeat imaging in 3 months to assess for change. If the nodule is stable, Lung-RADS category 2 would be assigned, and yearly screening would resume. However, given the high suspicion for primary lung adenocarcinoma, biopsy or resection could be considered. This patient ultimately underwent resection, and the results of histopathologic examination of the specimen from resection disclosed a primary lung adenocarcinoma with a mucinous component. Consider the use of the X modifier in complex subsolid nodules such as this one. Management options should be targeted to each patient.
Scenario 7: Nodule That Decreases in Size but Increases in Attenuation

Figure 13 is an example of a malignant nodule that decreased in size but increased in attenuation. Lung-RADS currently does not address nodules that decrease in size. Several investigators have documented that adenocarcinomas can transiently decrease in size, presumably related to the development of a fibrous component and associated collapse. However, this decrease in size is usually associated with an increase in attenuation (6,11,27). For these reasons, radiologists should recognize that cancer growth may not always be exponential and that the overall volume of a malignant nodule may decrease at some point. As mentioned in other scenarios, assessment of mass may play a role in the future as the LCS data are analyzed with more long-term studies.

A decrease in nodule size is not always benign, particularly with an increase in attenuation, and continued surveillance may be appropriate. The nodule in Figure 13 could be assigned either to category 4B (on the basis of a part-solid nodule with an enlarging solid component >4 mm) or to category 4X, given that the appearance is highly suspicious for malignancy, even though there is a slight decrease in size.

Scenario 8: Nodule with Characteristic Features of an Intrapulmonary Lymph Node

A 72-year-old man had a 4-mm perifissural nodule with characteristics of an intrapulmonary lymph node at baseline LCS CT (Fig 14). How should this nodule be classified?

The terms perifissural nodule and intrapulmonary lymph node are often used interchangeably. Many investigators have hypothesized that perifissural nodules are normal lymph nodes located in the lung parenchyma. These solid lung nodules are well circumscribed, smoothly margined, and in contact with or in proximity to a fissure or pleural surface (usually within 20 mm from the pleural surface). Intrapulmonary lymph nodes are usually triangular, oval, or polygonal; and they often have a thin septal attachment (Figs 15, 16). On multiplanar reformatted images, intrapulmonary lymph nodes are often nonspherical and flat or triangular. They are more commonly seen in the lower lungs.
below the level of the carina (28–30). The median diameter of intrapulmonary lymph nodes ranges from approximately 1 mm to 6 mm, but they can be larger (28,30,31).

Intrapulmonary lymph nodes are extremely common and have been detected more frequently with increased routine use of thin-section CT. For example, up to one-third of lung nodules identified at LCS CT in one series were classified as perifissural (28). In the results of several LCS studies, investigators have shown that no lung nodules with features of intrapulmonary lymph nodes ultimately proved to be a lung cancer (6,28,32).

Lung-RADS addresses intrapulmonary lymph nodes in footnote 11, recommending that they should be managed as any other solid nodule on the basis of the mean diameter. Because most intrapulmonary lymph nodes fall into Lung-RADS category 2 (benign or benign behavior), management is to continue annual LCS as long as the patient meets the eligibility criteria. However, some radiologists do not routinely report or recommend follow-up of nodules with the classic features of intrapulmonary lymph nodes, conflicting with the Lung-RADS requirement to report and manage nodules on the basis of size. We believe that if there are multireader studies showing adequate agreement for the recognition of intrapulmonary lymph nodes, future versions of Lung-RADS may allow management of intrapulmonary lymph nodes as category 1 (definitely benign nodules), potentially reducing unnecessary follow-up and patient anxiety.

**Scenario 9: Airway (Endotracheal or Endobronchial) Nodule**

A 74-year-old man had a new endobronchial filling defect at LCS CT (Fig 17). What Lung-RADS category should be assigned, and how should this case be managed?

Cigarette smoke promotes mucin synthesis and mucous gland metaplasia and causes stasis of mucus with a variety of mechanisms (33). On CT images, these abnormalities may be apparent as bronchial wall thickening and mucus plugging, the latter of which can mimic endobronchial nodules. Lung-RADS suggests classifying endobronchial nodules as category 4A lesions, with recommendations including a follow-up low-dose CT examination.

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**Figure 13.** Invasive lung adenocarcinoma in a 68-year-old man. (a) Initial LCS CT: Axial unenhanced chest CT image (lung window settings) of the right lung shows a part-solid nodule (arrow) in the inferior right middle lobe. (b) Follow-up axial CT image obtained 3 months later than a shows slight contraction of the nodule, although the solid component (arrow) has enlarged.

**Figure 14.** Normal intrapulmonary lymph node in a 72-year-old man at LCS CT. Axial (a) and sagittal (b) unenhanced reformatted chest CT images (lung window settings) through the left lung show a triangular left lower lobe nodule (arrow) abutting the oblique fissure.

**Figure 15.** Normal intrapulmonary lymph node in a 75-year-old man. Axial contrast-enhanced chest CT image (lung window settings) of the right upper lobe shows a thin band of tissue (arrow) connecting the nodule to the pleural surface.
tion in 3 months, or PET/CT if the nodule has a solid component measuring 8 mm or greater. If these guidelines are strictly followed, patients could end up being scanned every 3 months, because mucus plugs are common in smokers and former smokers, and new foci of plugging may be found at each subsequent CT examination.

To avoid unnecessary CT examinations, knowledge of the appearances of airway secretions and mucus plugs is important. Features of secretions in large airways (Fig 18) include a thin and long linear configuration, a dependent or layering location, water attenuation, air bubbles within the filling defect, preservation of the adjacent cartilaginous rings, a complex shape, and attenuation of less than 21.7 HU, all of which have a high positive predictive value for secretions. In contrast, features highly predictive for neoplasm are a round or lobulated shape, attenuation of 21.7 HU or more, and internal fat or calcification (34). Unfortunately, retained or adherent secretions can have a variable composition and may not always demonstrate a classic appearance.

Several methods can help identify airway secretions with greater confidence. A repeat CT examination of the area of interest with use of a reduced dose technique after vigorous coughing is one option, because coughing might help clear secretions mimicking endobronchial lesions (35). Although this method has proved to be helpful to us in selected cases such as the one in this scenario, to our knowledge, no published studies exist that evaluate the utility of coughing for clearing secretions before scanning a patient. We suggest considering this option in patients with questionable endobronchial lesions if this option can avoid a more aggressive workup such as a PET/CT examination. Maximum intensity projections, which should be part of any LCS CT protocol, or two-dimensional reformatted images can improve confidence that an apparent endobronchial nodule is mucus by showing a rectangular configuration within an airway that parallels the adjacent pulmonary artery. As with all patients, mucus plugs should also prompt one to evaluate the affected airways to exclude a central obstructing process.

If the lesion remains indeterminate, an endobronchial nodule should be managed as a category 4A lesion according to Lung-RADS. In the findings from one study of approximately 53,000 patients who underwent LCS CT, investigators showed that of the 186 subjects who underwent follow-up evaluation (CT, bronchoscopy, or both) for endobronchial nodules, only seven had persistent endobronchial nodules, none of which were malignant (36). Unless there are features suggestive of a solid tumor such as invasion of the airway wall, expansion of the airway, or postobstructive atelectasis or infection, we favor a follow-up low-dose CT examination in 3 months over the performance of PET/CT or bronchoscopy.
Scenario 10: Incidental Potentially Important Finding Other than Lung Cancer Detected at Low-Dose LCS CT

Figures 19 and 20 show incidental findings detected at LCS CT at our institutions. Which incidental findings require an S modifier? Incidental findings detected at diagnostic imaging studies are common (37) and are one of the criticisms of the use of low-dose CT for LCS. In the results of the National Lung Screening Trial (NLST), the rate of incidental findings needing additional evaluation was 10.2% at baseline and 7.5% overall (5). In a more recent retrospective study, investigators analyzed the data of 17,309 participants of the NLST (38). Of these participants, 58.7% of the patients had extrapulmonary findings (described as an abnormality beyond the lungs, pleura, chest wall, and hilar and mediastinal lymph nodes), and 19.6% had at least one finding that was considered potentially clinically important. Of those patients in which the location of the abnormality was available (70%), these abnormalities were located in the following organs and systems: cardiovascular system (8.5%), renal system (2.4%), hepatobiliary system (2.1%), adrenal glands (1.2%), and thyroid (0.6%). The prevalence of extrapulmonary malignancy was low at 0.39%, including malignancies of the kidney (0.26%), thyroid (0.08%), and liver (0.05%) (38).

The joint ACR–Society of Thoracic Radiology practice parameter for the performance and reporting of LCS CT states that the entire examination should be reviewed for other potentially important findings and the results reported in accordance with the practice parameter (39). Lung-RADS provides radiologists with the S modifier for “clinically significant or potentially clinically significant findings other than lung cancer” detected at LCS CT. However, the term *clinically significant or potentially clinically significant* is not defined, leaving the decision to the interpreting radiologist and potentially introducing local or regional variation in the reporting and management. Furthermore, although guidelines exist outside Lung-RADS for further management of some findings, no consensus exists for others. Finally, Lung-RADS does not address reporting or management of any incidental findings.

We encourage radiologists to adopt published management guidelines such as the ACR white papers on management of incidental findings at CT. Relevant to LCS, the ACR has guidelines for the management of incidentally detected thyroid...
nodules and abdominal abnormalities, including those in the gallbladder and biliary tract, arteries and veins, spleen, and lymph nodes (40–44). When no published guideline is available, local practice patterns should be aligned to ensure consistent practice within a screening program. Published literature with regard to each topic can be used to develop local-regional standards until these issues are addressed.

For example, in the results of a retrospective study of 9263 baseline screening examinations from the Early Lung Cancer Action Project (ELCAP) study, incidentally detected mediastinal masses were documented in 71 subjects (0.77%), and only one subject (0.01%) developed a mediastinal mass at a subsequent screening CT (45). Thymic masses were the most common, followed by thyroid lesions. Of the 41 thymic masses that were detected, only five were larger than 3 cm, of which one was a cyst, three were noninvasive thymomas, and one was a thymic carcinoma (45). Eighteen of the nonresected mediastinal masses were unchanged at follow-up imaging, five were larger, and two were smaller. No adverse outcomes were associated with 1-year surveillance of this population. All 16 thyroid masses were associated with goiter (45). Of the remaining 14 mediastinal masses, two were esophageal cancers, six were esophageal diverticula, two were lipomas, and four were purely cystic lesions and presumably benign (bronchogenic cyst, lymphangioma, pericardial cyst). Henschke et al (45) concluded that in a screening population, incidentally detected mediastinal masses could be managed conservatively, including thymic masses smaller than 3 cm in diameter.

Adopting local or established guidelines can minimize variation in reporting and avoid confusion and nonadherence to recommendations. We also encourage having the S modifier as a separate line in the impression and not leaving potentially important findings limited to the body of the report, with the description of the abnormality and clear management suggestions outlined in the impression to avoid potentially important findings being overlooked (46,47).

Table 4 (40–45,48,49) summarizes common incidental findings at chest CT and proposes management options. The S modifier should be reserved for findings that may lead to a health benefit if a behavior is modified or those that will lead to an adverse outcome if not further evaluated or treated. We do not encourage the use of the S modifier for the same findings at subsequent examinations if the findings have been addressed.

### Scenario 11: Reenrolling Patients in the LCS CT Program after a Stable Abnormality

A 76-year-old man had a 7-mm indeterminate solid nodule at a baseline LCS CT examination (Fig 21). Because no comparison images existed,
the CT finding was classified as Lung-RADS category 3, and follow-up was recommended in 6 months. Because the nodule did not change at the follow-up examination, the patient was returned to annual screening. Should the next screening examination be scheduled at 12 months from the original baseline LCS CT examination or at 12 months from the most recent LCS CT examination?

Footnote 12 in Lung-RADS states, “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.” The time point from which the 12 months is counted is less clear. The ACR recommends that the 12 months should be counted from the day of the LCS CT examination that prompted the follow-up examination, meaning that the patient should undergo the next round of screening 12 months after the baseline LCS CT examination in this case. Many radiologists, including some of the authors, believe that a change in less than a year is unlikely, so the 12 months should be counted from the most current LCS CT examination, or 18 months after the baseline LCS CT examination in this case. No data exist to support either position. Future Lung-RADS iterations will likely clarify this recommendation.

**Scenario 12: Low-Dose LCS CT of a Patient with a Recent Respiratory Infection**

A 67-year-old man underwent baseline LCS CT shortly after an acute respiratory illness, which was not reported to the primary care provider or the CT technologist, and residual consolidation was present at CT (Fig 22). How should the LCS CT examination be categorized?

As part of the shared decision-making process, patients should be asked about signs and symptoms of a recent respiratory tract infection. In general, patients with a recent respiratory tract infection should delay LCS for approximately 3 months to ensure that any residual lung inflammation has resolved.

Findings suggestive of infection or other inflammatory processes are not addressed in Lung-RADS. Because a recent chest radiograph was available in this case and because the area of consolidation was deemed smaller at the LCS CT examination, this case was assigned to category 3 (probably benign), and a 6-month follow-up CT examination was recommended. The reasoning for this decision was that the area of consolidation persisted but was smaller.

Unnecessary follow-up imaging related to acute lung infection can be avoided with targeted questioning about any recent acute respiratory illness at the time of LCS CT scheduling, as well as by the technologist before the LCS CT examination is performed. Patients with clinical or radiologic findings of a recent acute respiratory tract infection should defer LCS CT.

**Scenario 13: Categorization of a Cavitary Lung Nodule or Nodules**

A 73-year-old man had a cavitary nodule in the left upper lobe at baseline LCS CT (Fig 23). How are cavitary nodules classified in Lung-RADS?

Lung-RADS does not address categorization and management of cavitary lung nodules. Many conditions can manifest as solitary or multiple cavitary nodules, including lung cancer, metas-
tasis, infection, granulomatosis with polyangiitis, and pulmonary Langerhans cell histiocytosis. Diffuse lung adenocarcinoma can manifest as multiple lung nodules, which can be cavitary.

Discussion of the differential diagnosis of cavitary nodules is beyond the scope of this review, but it is important to remember that encountering patients with cavitary metastasis, vasculitis, or pulmonary Langerhans cell histiocytosis in the setting of LCS would be unlikely. Because current or recent infectious symptoms are a contraindication for LCS, encountering infection manifesting as cavitary nodules would also be unusual, although it is worth remembering that some patients with infections such as nontuberculous mycobacterial infection or endemic fungal infection can be asymptomatic, with single or multiple cavitary pulmonary nodules (50).

Up to 22% of non–small cell lung carcinomas demonstrate cavitation (51). In order of frequency, the most common histologic types that show cavitation are squamous cell carcinoma, adenocarcinoma, and large cell carcinoma (52). Usually the cavity wall is thicker than 4 mm; and the thicker the wall, the higher the likelihood of malignancy. Irregular inner surfaces and mural nodules are more commonly associated with malignant lesions. Because of the overlap between malignant cavities and benign cavities, further evaluation is usually needed to establish an accurate diagnosis (Fig 24) (53,54).

We suggest classifying and managing a solitary cavitary lung nodule at LCS CT as if it were a solid nodule and appending the X modifier when the suspicion for malignancy is high or the S modifier if infection is suspected so that the appropriate workup can ensue. If multiple cavitary nodules are present, the S modifier would be the correct designation unless diffuse lung adenocarcinoma is suspected, in which case the X modifier should be appended. If the S modifier is used, management and follow-up of these nodules should be performed outside of the screening program, either with chest radiography or diagnostic CT.

**Scenario 14: Low-Dose LCS CT of a Patient with a History of a Treated Lung Malignancy**

A 67-year-old woman with a 35–pack-year history of smoking had undergone lobectomy for stage IA lung adenocarcinoma 7 years earlier. She was considered to be free of disease after 5 years of surveillance and currently wishes to undergo LCS. Is this patient eligible?

The peak incidence of recurrent lung cancer after definitive therapy is 2–3 years after treatment, and the annual risk of developing a new lung cancer is 3% (55). The American Association for Thoracic Surgery advocates annual screening for patients cured of lung cancer after 4 years of posttherapeutic surveillance as long as they are able and willing to undergo curative resection (55). The U.S. Preventive Services Task Force and the Centers for Medicare and Medicaid Services do not address screening patients with previously treated and presumptively cured lung cancer. However, Lung-RADS provides the C modifier for these patients, should they undergo LCS CT. Given the
current requirements for adherence to eligibility criteria, patients with previously treated lung cancers must still meet the standard LCS eligibility criteria. In this case, we would recommend that the patient enroll in the LCS program.

Scenario 15: Low-Dose LCS CT of a Patient with a Treated Low-Risk Nonlung Malignancy

Should a 62-year-old woman who was treated for stage I breast cancer 18 months ago who is eligible for LCS undergo LCS CT?

Current recommendations do not address patients who have been treated for nonlung malignancies, including those with a low risk of recurrence, such as early-stage breast cancer, localized prostate cancer, or low-grade lymphoma. The ACR suggests inquiring about previously diagnosed and treated malignancies as part of the shared decision-making process. We believe that LCS should be offered to eligible patients with a treated low-risk malignancy, given the reported mortality benefits of LCS. One proposed threshold to determine whether an eligible patient should undergo LCS CT is if the patient is more likely than not to be alive in the next 5 years.

Conclusion

Lung-RADS was modeled after the ACR’s successful BI-RADS, with the intention to standardize reporting and management of screening-detected lung nodules and to reduce the risks of overdiagnosis or unnecessary intervention in screened patients. Because Lung-RADS is in its first iteration at the time of this writing, management in several scenarios remains unclear. We expect that future versions of Lung-RADS will take into consideration these scenarios and provide guidance to radiologists. In the meantime, we offer our recommendations on the basis of the current literature and our collective experience.

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References


