Lung-RADS Version 1.1: Challenges and a Look Ahead, From the *AJR* Special Series on Radiology Reporting and Data Systems

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Cardiothoracic Imaging · Special Series Review

Keywords

lung cancer, lung cancer screening, Lung-RADS

Submitted: Sep 16, 2020
Revision requested: Oct 9, 2020
Revision received: Nov 12, 2020
Accepted: Jan 1, 2021
First published online: Jan 20, 2021

This article is available for credit.

The authors declare that they have no disclosures relevant to the subject matter of this article.

In 2014, the American College of Radiology (ACR) created Lung-RADS 1.0. The system was updated to Lung-RADS 1.1 in 2019, and further updates are anticipated as additional data become available. Lung-RADS provides a common lexicon and standardized nodule follow-up management paradigm for use when reporting lung cancer screening (LCS) low-dose CT (LDCT) chest examinations and serves as a quality assurance and outcome monitoring tool. The use of Lung-RADS is intended to improve LCS performance and lead to better patient outcomes. To date, the ACR's Lung Cancer Screening Registry is the only LCS registry approved by the Centers for Medicare & Medicaid Services and requires the use of Lung-RADS categories for reimbursement. Numerous challenges have emerged regarding the use of Lung-RADS in clinical practice, including the timing of return to LCS after planned follow-up diagnostic evaluation; potential substitution of interval diagnostic CT for future LDCT; role of volumetric analysis in assessing nodule size; assessment of nodule growth; assessment of cavitary, subpleural, and category 4X nodules; and variability in reporting of the S modifier. This article highlights the major updates between versions 1.0 and 1.1 of Lung-RADS, describes the system's ongoing challenges, and summarizes current evidence and recommendations.

Despite a steady decline in lung cancer mortality rates over the past few decades, lung cancer remains the leading cause of cancer death in the United States. The continued large proportion of patients with a late-stage lung cancer diagnosis accounts for the overall low 5-year survival rate of 19% [1]. The National Lung Screening Trial (NLST) published in 2011 showed a 20% decrease in lung cancer mortality among high-risk older current and former smokers undergoing lung cancer screening (LCS) with low-dose CT (LDCT) of the chest compared with chest radiography [2]. Also, fewer advanced-stage lung cancers were diagnosed on subsequent screening rounds in the LDCT group. These findings show the potential of LCS to identify earlier-stage curable disease. A subsequent large randomized trial, the Dutch-Belgian Randomized Lung Cancer Screening trial (NELSON), confirmed the mortality benefit of LCS with LDCT in high-risk groups [3]. Smaller randomized trials, not powered for a mortality benefit, showed a similar, although not statistically significant, result [2, 4, 5]. The NLST also showed the cost-effectiveness of LCS in 2014 [6]. In an effort to standardize the reporting and management of nodules found on LCS, the American College of Radiology (ACR) created Lung-RADS in 2014, updated to Lung-RADS 1.1 in 2019. This article summarizes current evidence and recommendations regarding Lung-RADS and discusses challenges associated with the use of Lung-RADS in clinical practice.

Lung-RADS: Definition and Relation to Lung Cancer Screening Reimbursement

Modeled after BI-RADS, Lung-RADS provides radiologists with a common lexicon and standardized nodule follow-up management paradigm for reporting LCS LDCT results. Lung-RADS categories are assigned on the basis of nodule size, growth, and morphology. With the exception of category 0 indicating an incomplete examination, the progressively higher numbered categories indicate an increasing risk of malignancy. Management

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doi.org/10.2214/AJR.20.24807

AJR 2021; 216:1411–1422

ISSN-L 0361–803X/21/2166–1411

American Journal of Roentgenology 2021.216:1411-1422.

recommendations are associated with each of the specified categories. Lung-RADS categories 1 (negative) and 2 (benign) constitute a negative LCS LDCT, whereas categories 3 (probably benign), 4A (probably suspicious), and 4B or 4X (suspicious) constitute a positive LCS LDCT. A modifier S may be appended to any of the Lung-RADS categories when an incidental finding is deemed clinically significant by the reporting radiologist.

Lung-RADS also serves as a quality assurance and outcome monitoring tool. Several professional societies have published eligibility criteria [7–10]. High-risk groups defined by the U.S. Preventive Services Task Force (USPSTF) and Centers for Medicare & Medicaid Services (CMS) are eligible for LDCT reimbursement by insurers without a copay [11]. The 2015 CMS coverage decision also requires facilities to submit data to a CMS-approved registry to be reimbursed for services. To date, the ACR's Lung Cancer Screening Registry is the only CMS-approved LCS registry [12]. Because the Lung Cancer Screening Registry requires Lung-RADS categories for reporting the results of LCS LDCT, the use of Lung-RADS is linked to reimbursement and has contributed to the system's rapid uptake.

Lung-RADS 1.1: Updates to Lung-RADS 1.0

In 2019, the ACR published Lung-RADS version 1.1 using evidence accumulated over the previous few years [13]. The Lung-RADS Committee, composed of eight leading experts in the field, identified areas for clarification and improvement according to a review of the available literature leading to the published updates. Differences between the initial and updated Lung-RADS versions are shown in Table 1. Increasing the size threshold of nonsolid nodules from 20 to 30 mm was according to evidence of such nodules' longer volume doubling time (VDT) and a generally more indolent course compared with solid and part-solid nodules [14–19]. Perifissural nodules measuring less than 10 mm in mean diameter that met the criteria for intrapulmonary lymph nodes as defined in the NELSON trial were reclassified as category 2 nodules (previously category 3 or 4A) [20–25] (Fig. 1). Together these changes are expected to reduce the false-positive screen rate given these nodules' low malignancy rates and the overall lower cancer diagnosis rate of Lung-RADS category 3 nodules. A new recommendation for 4B nodules was also added, allowing a short-interval follow-up LDCT to account for new or rapidly enlarging nodules that are likely infectious or inflammatory. The reported low rates of interval cancers support this recommendation, given that interim development of large neoplasms is believed to be unlikely [26]. The method for measuring and calculating mean nodule diameter was also clarified, with a recommendation to report mean nodule diameter to one decimal point [27]. In addition, as discussed subsequently, volumetric measurements were incorporated. Finally, the C modifier, previously assigned to lung cancer survivors who return to screening, was removed to avoid confusion between LCS and lung cancer surveillance for patients who have been disease-free for 5 or more years.

HIGHLIGHTS

- *Evidence supports the role of lung cancer screening (LCS) in achieving earlier lung cancer diagnosis and reduced lung cancer mortality.*
- *Created by the ACR, Lung-RADS provides a common lexicon, a management paradigm, and a quality assurance tool for LCS low-dose CT chest examinations.*
- *Future Lung-RADS updates should apply growing evidence from LCS experience to address ongoing challenges associated with the system's use in clinical practice.*

Ongoing Challenges

Challenges associated with the application of Lung-RADS in clinical practice have sparked discussions and raised questions that could potentially be addressed in future Lung-RADS iterations. This section discusses some of these challenges and perspectives.

Returning to Screening After Follow-Up: Should We Use Baseline Screening or Planned Follow-Up CT as Low-Dose CT Anniversary Date?

Lung-RADS 1.1 recommends that category 3 and 4A nodules be downgraded to category 2 if stable on follow-up diagnostic

TABLE 1: Comparison of the Initial 1.0 and Updated 1.1 Versions of Lung-RADS

Feature	Lung-RADS 1.0	Lung-RADS 1.1
Threshold for nonsolid nodule		
Category 2	< 20 mm or ≥ 20 mm and unchanged or slowly growing	< 30 mm or ≥ 30 mm and unchanged or slowly growing
Category 3	≥ 20 mm on baseline CT or new	≥ 30 mm on baseline CT or new
Size (mm) of perifissural nodules		
< 10 (< 524 mm^3)	Category classification dependent on size	Category 2 if typical features of an intrapulmonary lymph node
≥ 10 (≥ 524 mm^3)	Category classification dependent on size	Category classification dependent on size
Nodule size measurement	Mean diameter rounded to the nearest whole number	Mean diameter reported to one decimal point
Volumetric measurements	Not reported	Added next to the reported mean diameter
New large category 4B nodules	Similar management to other 4B nodules	Added 1-month follow-up low-dose CT
Modifier C	Specified in lung cancer survivors returning for screening	Removed

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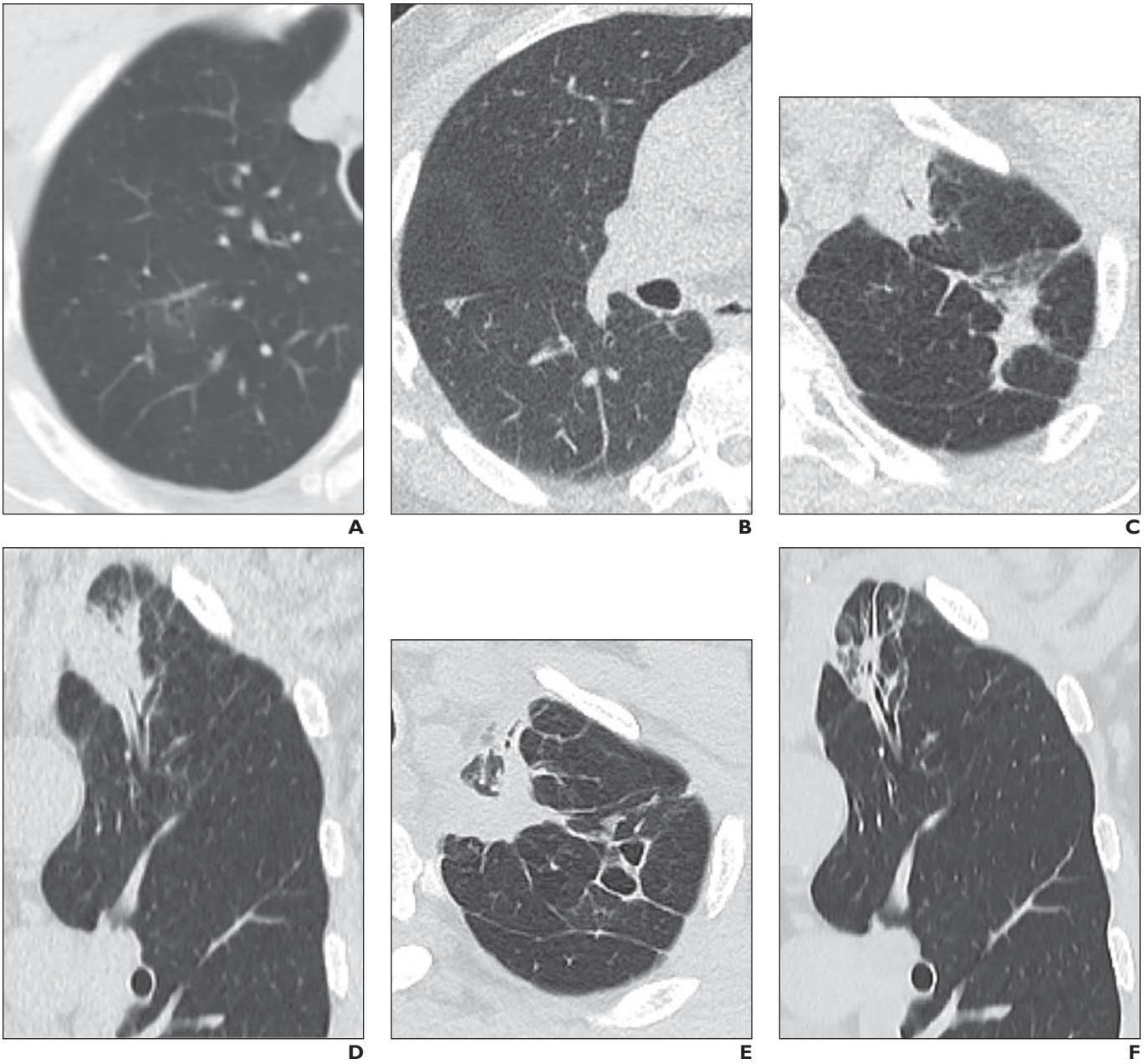

Fig. 1—Patients illustrating major updates from Lung-RADS 1.0 to Lung-RADS 1.1.
A, 55-year-old man with 16-pack-year smoking history presented for lung cancer screening (LCS) despite not meeting current eligibility criteria. Coned-down axial image from baseline low-dose CT (LDCT) of chest shows 20-mm right upper lobe nonsolid nodule consistent with category 2 nodule per Lung-RADS 1.1. Per Lung-RADS 1.0, this would have been classified as category 3 nodule requiring follow-up LDCT at 6 months.
B, 57-year-old man with 40-pack-year smoking history found to have right lower lobe nodule on baseline LDCT. Coned-down axial image from LDCT shows 6-mm perifissural triangular right lower lobe nodule with smooth margins. Per Lung-RADS 1.1, category 2 was assigned to nodule, and return for LCS in 12 months was recommended. This would have been classified as category 3 nodule per Lung-RADS 1.0, resulting in follow-up LDCT in 6 months.
C–F, 68-year-old man with 35-pack-year smoking history presented with new findings on yearly LDCT. Coned-down axial (**C**) and coronal (**D**) images show sizeable consolidation in left upper lobe. Findings were entirely new from prior baseline LDCT (not shown). Because infection was thought to be likely, category 4B was assigned with recommendation to return to LDCT in 1 month, representing new option in Lung-RADS 1.1. Lung-RADS 1.0 did not account for this possibility and would have resulted in recommendation to obtain chest CT, PET/CT, or tissue sampling. Coned down axial (**E**) and coronal (**F**) images from follow-up LDCT at 1 month show interval partial clearing of left upper lobe consolidation and development of pneumatocele.

CT and that patients be advised to return for screening at 12 months. Extensive debate has explored whether the 12-month interval should be according to the date of the planned interval follow-up CT related to their 3 or 4A status (i.e., 18 and 15 months, respectively, after the initial screening LDCT) rather than the initial annual screen [28, 29]. Advocates of the former approach suggest a higher likelihood of compliance with a set anniversary date, which aligns with health screening appointments often set around a birthday [30, 31]. Additionally, an annual LCS evaluation is accepted by the USPSTF and CMS for reimbursement,

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theoretically allowing patients to return at the 12-month mark after the abnormality was first identified at baseline [32]. The potential for greater growth rates of some lung cancers could also justify a shorter time to follow-up (e.g., 6–9 months instead of 12 months) [33]. Advocates of setting the annual repeat date from interval planned follow-up CT raise concern for additional unwarranted radiation and costs, citing the reluctance of certain commercial insurers to authorize the screening CT sooner than 12 months after the follow-up interval diagnostic CT. These advocates also question the clinical benefit of shorter follow-up intervals for stable nodules on the basis of the long VDT of many lung cancers [34]. The transient character of a proportion of indeterminate and suspicious nodules further strengthens the case for greater spacing between evaluations [35, 36]. The downgrading of many Lung-RADS category 3 nodules to negative screen category 2 with Lung-RADS 1.1 mitigates against this argument given that some of these nodules may ultimately prove malignant. A consensus regarding the optimal strategy has not been reached.

Interval Diagnostic Chest CT: Can It Substitute for a Future Low-Dose CT?

In one of its attestation forms, the ACR states that individuals "having undergone chest CT within 12 months should be excluded" from initial screening [37]. However, little evidence exists to guide referring physicians and radiologists when an interval diagnostic chest CT for a different indication (e.g., to rule out pulmonary embolism) is obtained in a patient actively enrolled in LCS. Whether and when a diagnostic chest CT may substitute for a future LCS LDCT is unclear. Considerations for such a substitution include the interval time between the diagnostic chest CT and LDCT, symptoms at the time of diagnostic chest CT, findings on diagnostic chest CT that may prevent full lung assessment for small lung nodules, diagnostic chest CT technique, and concerns about implications for registry reporting of diagnostic chest CT and radiation dose. For example, an aorta protocol CT obtained after a dilated aorta is performed in the same time interval when screening is due technically may meet the specifications for slice thickness, reconstruction interval, and coverage of an LDCT, but at a higher radiation exposure; performing an additional LDCT adds unnecessary dose exposure. The diagnostic chest CT will need to meet specific technical requirements according to ACR recommendations for the study to be considered an LCS CT. These include a slice thickness of 2.5 mm or smaller, at least 4 detector rows, and complete anatomic coverage of the thorax with a display FOV of 1 cm beyond the ribs. Standardized reporting that includes a Lung-RADS classification would be required.

Nodule Size: Can Volumetric Analysis Help?

Lung-RADS emphasizes nodule size and growth primarily according to 2D measurements. The 2D measurements are more accurate than single diameter measurements in RECIST for guiding cancer treatment decisions; each setting has a different degree of variance that may be tolerable for decision-making [34, 38–40]. Several studies have highlighted the limitations of 2D measurements, showing significant intraobserver and interobserver variability [41–43]. Scan acquisition at different degrees of inspiration also affects axial nodule measurements [44]. These intrinsic measurement errors may result in overestimation or underestimation of nodule size and size change (Fig. 2). Determination of nodule growth or lack of growth using caliper measurements may be erroneous, resulting in imprecise Lung-RADS categorization. Investigators have shown increased reproducibility with automated or semiautomated volumetric analysis, including measurement of solid components of part-solid nodules [45–47]. However, an increase in complexity and irregularity of nodule margins results in greater variability of 3D measurements and VDT [48, 49]. Measurements among different software programs also show substantial variability, making comparison difficult when the same software is not used consistently [47]. The first large LCS study to rely on volumetric measurements of nodules was the NELSON trial [3]. Lung-RADS 1.1 included volumetric measurements next to the mean diameter measurements both to accommodate practices that already were using volumetric measurement and to provide a path toward future standardization of volume measurements. However, the implementation of volumetric analysis in routine clinical practice has lagged. Further validation of quantification tools, time commitment by radiologists for monitoring of software output, seamless integration of not only fixed but dynamic interactive outputs into the radiologists' workflow at the PACS, and reimbursement for the use of computer-aided detection systems are critical to the incorporation of volumetric nodule analysis in clinical practice.

Nodule Growth: Should We Modify Our Approach?

Lung-RADS defines growth as a 1.5-mm increase in size. The Lung-RADS definition of growth applies to both total nodule size and the solid component of a part-solid nodule. A slightly higher threshold for growth of 2 mm is recommended by the

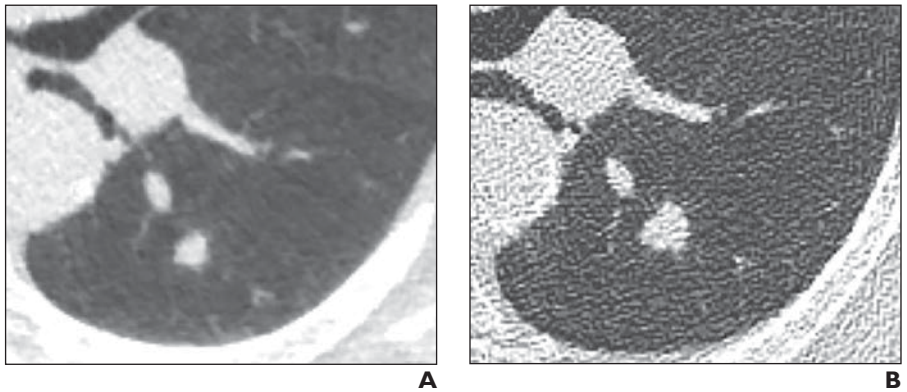

Fig. 2—69-year-old woman with 32-pack-year smoking history with non–small cell lung cancer. **A** and **B,** Coned-down axial images from baseline (**A**) and follow-up (**B**) low-dose CT of chest show interval increase in size and spiculation of left lower lobe solid nodule. Axial measurements reveal 40% increase in diameter (growth of 3.4 mm from 8.6 to 12.0 mm). Volumetric analysis (not shown) revealed approximately 400% increase in volume (from 0.34 to 1.31 cm^3), highlighting potential for increased sensitivity of volumetric imaging. Growth shown using either axial or volumetric measurements in this case results in Lung-RADS category 4B.

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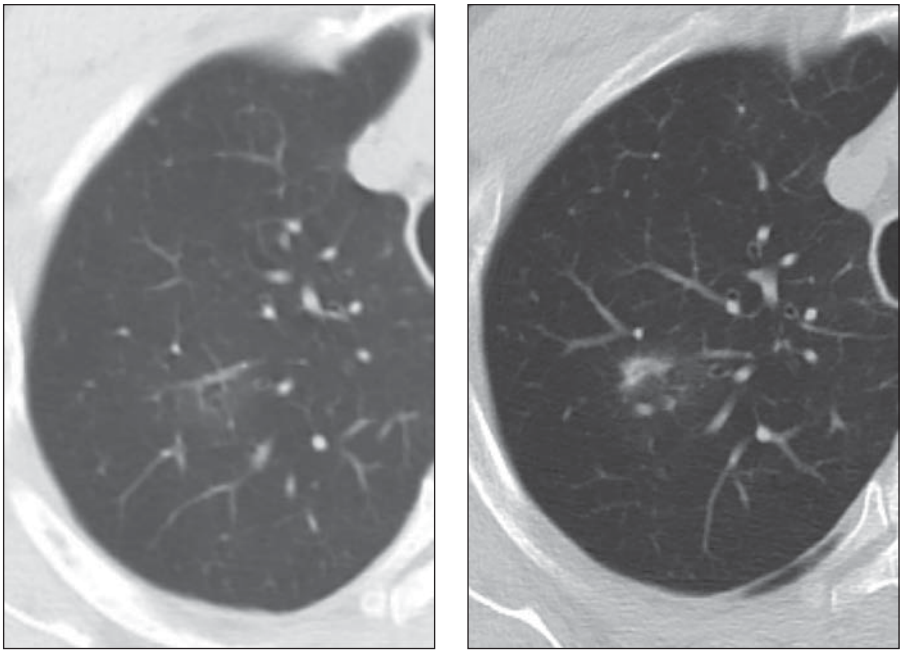

Fig. 3—55-year-old man with 16-pack-year smoking history and chronic obstructive pulmonary disease (same patient as Fig. 1A) presenting for lung cancer screening despite not meeting current eligibility criteria. Baseline low-dose chest CT (LDCT) showed nonsolid nodule (see Fig. 1A).
A and **B,** Coned-down axial images from follow-up LDCT show development of new solid (**B**) component within previously nonsolid nodule (**A**, obtained 9 months earlier than **B**), highly concerning for development of invasive component within preexisting adenomatous lesion. Lung-RADS category 4B was assigned according to current recommendations. Baseline axial image (see Fig. 1A) showed internal vacuoles within nodule, likely representing focally distorted airways, which is imaging feature associated with malignancy. Transbronchial biopsy showed atypical epithelial cells.

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Fleischner Society and the British Thoracic Society nodule guidelines [23, 50]. These recommendations are supported by a study that showed interobserver variability of up to 1.73 mm in measurement of nodules measuring 3–18 mm. The authors concluded that a confident statement of growth may only be made when the change in nodule size exceeds 1.73 mm [41]. In the NELSON trial, growth was defined as a 25% or greater increase in volume, which better captures changes in small nodules compared with an absolute change in mean diameter of 1.5 mm [3]. The Lung-RADS definition of growth does not address situations in which the interval between two evaluations exceeds 12 months [29]. In such situations, observing a strict definition of growth instead of a growth rate may give an inaccurate conclusion, the latter being more easily implemented using volumetric measurements that also calculate VDT. The threshold for slow growth that results in a category 2 classification for a nonsolid nodule is not defined in Lung-RADS; instead, these are managed according to a size threshold of 3 cm separating categories 2 and 3.

Assessment of VDT in determining growth allows a better determination of nodule behavior. Malignant nodules have a VDT ranging between 20 and 400 days, whereas benign conditions generally have shorter or longer doubling times [3, 51]. Nonsolid nodules, however, may require different VDT cutoffs. Lee [15] found a mean VDT of 1041 days in a persistent nonsolid nodule, and Obayashi et al. [14] found a longer VDT in adenocarcinomas associated with ground-glass opacity than in other cancer subtypes. Furthermore, growth rates of malignant nodules may vary over time [52]. In one small pilot study of lung cancer growth curves, four of 18 lung cancers (22%) decreased in volume over time; however, the nodules were small, and measurements were performed by visual assessment to the nearest millimeter by one reader [53]. The known error that occurs with measurement using this method may account for the observed decrease.

Although growth rates are important, arguably greater emphasis should be placed on other nodule characteristics, especially in the case of nonsolid nodules and part-solid nodules, guided by increasing understanding of the progression of adenomatous lesions. Studies have shown a succession of changes on imaging associated with some malignant nonsolid nodules, including development and growth of a solid component [16]. The solid part of the nodule is thought to reflect the invasive component of the lesion [54] (Fig. 3). Additionally, intralesional fibrosis and alveolar collapse associated with some malignant nonsolid nodules may result in increased attenuation and decreased size [55]. Nodule mass, consisting of the product of the nodule volume and CT attenuation, is also of interest in the assessment of these nodules. Mass measurement is less variable than volume measurement [16]. Changes in mass are associated with an acceleration of volume change [56]. The percentage change in the nodule mass exceeded the percentage change in the nodule dimensions, allowing increased sensitivity and earlier detection of change [16]. In Lung-RADS, for part-solid nodules, both the solid and nonsolid components are measured and used to determine reporting category and management.

Cavitary Nodules: How Should They Be Managed Using Lung-RADS?

Although cavitary nodules are associated with many disease processes, lung cancer is a primary consideration in a patient without symptoms undergoing LCS. Patients with other causes of cavitary lung nodules such as vasculitides, smoking-related lung disease, necrotizing infection, and metastatic disease are often symptomatic [29]. Cavitation, more common in lung cancer than lung metastasis, occurs in 12–22% of lung cancers, most commonly squamous cell carcinoma [57, 58] (Fig. 4). In the LCS setting, cavitary lung cancer may be less common than in incidental or symptom-detected lung cancer. In a series of 128 lung nodules, seven (5.5%) that were recommended for biopsy on LCS were cavitary [59]. The current Lung-RADS version does not specifically address the categorization and management of cavitary or cystic lung

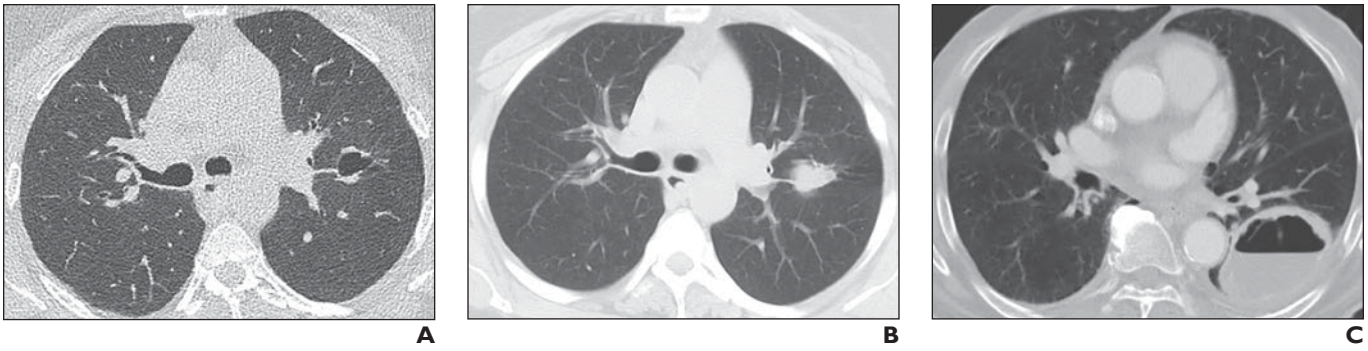

Fig. 4—Two patients with cavitary lung lesions.
A and **B,** 56-year-old woman with no symptoms with 54-pack-year smoking history presented for baseline lung cancer screening (LCS). Axial image (**A**) from baseline low-dose CT (LDCT) of chest shows thin-walled cavitary left upper lobe nodule with irregularly thickened walls. Chest CT (**B**) obtained 11 years before LCS enrollment shows solid nodule of similar size and margins at same location. Mild hyperlucency is suggested in adjacent peripheral lung. Cavitary nodule was thought to represent benign process associated with postinfectious or postinflammatory focal bronchiectasis, and Lung-RADS category 2 was assigned. Findings remained stable on subsequent chest CT obtained for suspicion of pulmonary embolism 15 months after LDCT in **A**.
C, 78-year-old man with 25-pack-year smoking history who had not been previously enrolled in LCS presented with fatigue. Under expanded eligibility criteria for LCS in U.S. Preventive Services Task Force draft recommendations, this patient would qualify for LCS. Axial CT shows thick-walled cavitary mass in left lower lobe with air-fluid level found to represent superinfected cavitary squamous cell carcinoma of lung. Thorough review of prior imaging and clinical history is essential in optimizing approach to cavitary lung nodules on LCS.

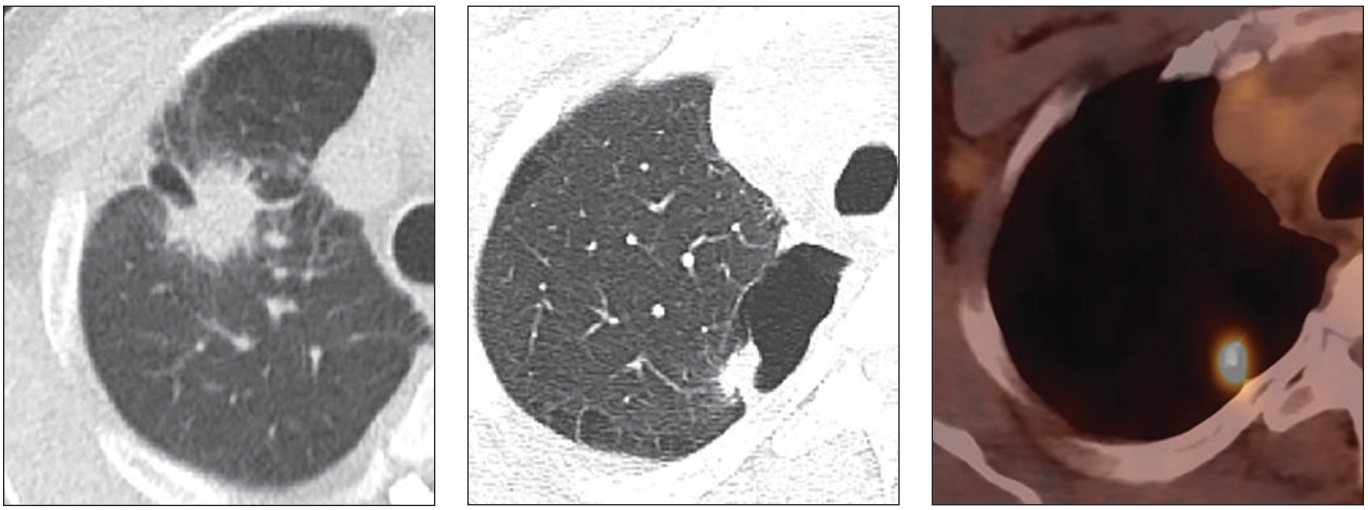

Fig. 5—Two patients with spiculated nodules associated with adjacent cystic spaces.
A, Coned-down axial image of follow-up low-dose chest CT (LDCT) of 73-year-old man with 88-pack-year smoking history shows new right upper lobe spiculated nodule with focal pleural retraction and paracicatricial emphysema. Imaging features associated with nodule are concerning for malignancy and could justify classification as Lung-RADS category 4X. Transbronchial biopsy of right upper lobe nodule revealed primary lung adenocarcinoma.
B and **C,** Coned-down axial image (**B**) from LDCT of 71-year-old man with 20-pack-year smoking history and chronic obstructive pulmonary disease shows irregular nodular thickening along margin of emphysematous space, which is change from patient's baseline LDCT (not shown). Fused PET/CT (**C**) shows avid metabolic uptake associated with nodule. Metabolically active mediastinal adenopathy was also present (not shown). Transbronchial biopsy of multiple lymph nodes revealed metastatic lung adenocarcinoma. Radiologists should closely evaluate new wall thickening of emphysematous space and paracicatricial emphysema associated with nodule on lung cancer screening because these findings may be associated with malignancy.

nodules. Whether cavitary nodules should follow the classification of solid nodules according to mean nodule size or wall-thickness measurement remains a point of discussion given conflicting studies attempting to discriminate benign from malignant nodules according to wall-thickness measurements [60–62]. Increased wall thickness may indicate a higher likelihood of malignancy and squamous cell carcinoma subtype and a poorer prognosis in adenocarcinoma subtypes [63, 64]. However, although wall-thickness thresholds have been reported, significant overlap exists between benign and malignant causes [61, 62]. Instances of cystic or cavitary lung cancer that progressed from thin-walled cystic lesions have been described but are a relatively uncommon manifestation of lung cancer [65, 66]. New or irregular thickening of an emphysematous space and an enlarging emphysematous space adjacent to a nodule should be regarded with suspicion [65] (Fig. 5). Authors of a recent review suggest classifying cavitary nodules as solid nodules according to overall nodule size, concurrent with the default application of Lung-RADS [29]. However, whether to include the cavitary component in the total nodule measurement remains a subject of discussion. Studies have

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investigated other possible indicators of malignancy in cavitary nodules, including the presence of nondependent or enhancing mural nodules, irregular inner margins, lack of adjacent centrilobular nodules, and absence of surrounding chronic fibrotic changes [62, 67]. When cavitary nodules with such features are encountered, radiologists may appropriately use Lung-RADS category 4X if they have an increased suspicion for malignancy and believe more aggressive clinical management is needed than would occur with Lung-RADS categories 3 or 4A.

Subpleural Nodules: Are They Comparable to Perifissural Nodules?

Perifissural solid nodules measuring 6–10 mm in mean diameter satisfy the appearance of intrapulmonary lymph nodes. Under a modification in Lung-RADS 1.1, these are now classified as category 2 nodules (previously category 3 or 4A). These nodules are consistently benign, even when growth rates approach those of malignant nodules [21, 68]. Subpleural nodules measuring 6–10 mm, which unlike perifissural nodules are not reclassified as benign in Lung-RADS 1.1, often have similar morphology, raising the question of whether they should be managed like perifissural nodules. However, less data support this change than the larger evidence base reported for perifissural nodules, including the sizeable dataset reported by the NELSON trial [24].

Earlier reports showed that 18% of subpleural nodules represented intrapulmonary lymph nodes. In patients who underwent thoracotomy, nearly all intrapulmonary lymph nodes were within 20 mm of the pleura and below the carina in the middle lobe or lower lobes [69, 70]. Other histologic correlates to subpleural nodules include pleural plaques, focal scars, and, less frequently, premalignant or malignant lesions [68, 71]. A septal attachment consisting of a linear density connecting the nodule to the adjacent pleura has also been suggested to be a reliable finding of an intrapulmonary lymph node, although neoplasms may also show vascular pleural attachments [20, 72, 73]. Investigators stated that a combination of these features in nodules smaller than 10 mm should consistently predict a benign cause [71, 72]. In a study of 72 nodules that were 1 cm or smaller, Takashima et al. [71] found 100% PPV and specificity for benignancy in nodules with at least two of the following three features: solid subtype, polygonal shape, and subpleural location. Consideration of both morphology and location for downgrading of pleura-based nonperifissural nodules to Lung-RADS category 2 may be possible if larger studies corroborate these results. Despite the comparability of subpleural and perifissural nodules, the current evidence has yet to reach the threshold for down-classifying subpleural nodules using Lung-RADS, and their categorization remains the same as for other nonperifissural solid nodules.

Category 4X: Should Additional Features Be Specified?

Certain imaging features may heighten the suspicion of malignancy even in smaller lesions. Lung-RADS 1.1 recommends classifying nodules that would typically be assigned category 3 or 4A that have features of malignancy disproportionate to these categories as category 4X, which carries the more acute management strategy of the highest Lung-RADS 4B category. A category 2 nonsolid nodule may also be upgraded to a category 4X if the mean diameter doubles in size on annual LCS LDCT. In Lung-RADS 1.1 footnote 10, spiculation, lymphadenopathy, and the doubling of a nonsolid nodule on annual follow-up are deemed markers concerning for malignancy [12]. This footnote ends with "etc.," implying the existence of other noteworthy features, although these are not detailed. Further Lung-RADS updates should enumerate these additional findings. Pleural tags and pleural retraction associated with a nodule have been known to occur more frequently in malignancy, but may also be associated with many benign causes. Similarly, focal architectural distortion of surrounding structures should be regarded with suspicion (Fig. 6). Pleural tags represent fibrotic bands radiating from the nodule and are described as histologic correlates of spiculation [74]. Pleural retraction is associated with an increased risk of visceral pleural invasion, particularly in the case of part-solid nodules [75]. With the increasing identification of peripheral adenomatous lesions, such features may be helpful. Another finding suggestive of malignancy is that of intralesional lucency, or pseudocavitation. The small vacuoles may represent cystic changes within neoplastic glands or patent small airways [23, 74] (Fig. 3). In the case of nonsolid nodules, the vessel-to-nodule relationship has been investigated and four groups have been described. Groups 1 and 2 are those in which the vessels course close to and through the nodule, respectively, without morphologic change and are thought to reflect a benign cause. Groups 3 and 4 include those in which vessels display morphologic changes and convergence or proliferation, respectively, and are thought to reflect malignant behavior and tumor-associated angiogenesis [76–79]. Such complex features, especially if combined, should lead to a higher index of suspicion and a more tailored use of the 4X classification (Fig. 7).

The S Modifier: How Can Variability in Reporting Be Minimized?

Lung-RADS recommends appending the S modifier when "clinically significant or potentially clinically significant" findings are noted that are not specifically related to pulmonary nodules. The frequency of such findings varies among studies, which is partly because of different definitions of clinical significance. In the Danish Lung Cancer Screening Trial, 7% of screened patients had a potentially significant finding on LDCT in contrast to 19.6% of screened patients in the NLST [80, 81]; however, in the setting of a research trial in which many patients imaged had no clinical medical records at the screening facility, the onus on reporting findings as significant may be higher than in practices in which medical records and comparison examinations may be present. In another study, 0.5% of screening volunteers had an extrapulmonary malignancy diagnosed because of a screening finding, representing 6.9% of all potentially significant incidental findings [82]. The determination of the relevance of incidental findings as significant or nonsignificant is left to the discretion of the radiologist, which may lead to bias and lack of consistency in reporting. The ACR Lung Cancer Screening Registry collects information on S findings, specifically calling out aortic aneurysms; coronary arterial calcification (moderate or severe); pulmonary fibrosis; mass lesions in the imaged neck, thorax, and upper abdomen that could represent malignancy; and other interstitial lung disease, with an additional nondirected category for other findings.

Radiologists should refer to the ACR white paper on managing incidental findings on thoracic CT for guidance to achieve

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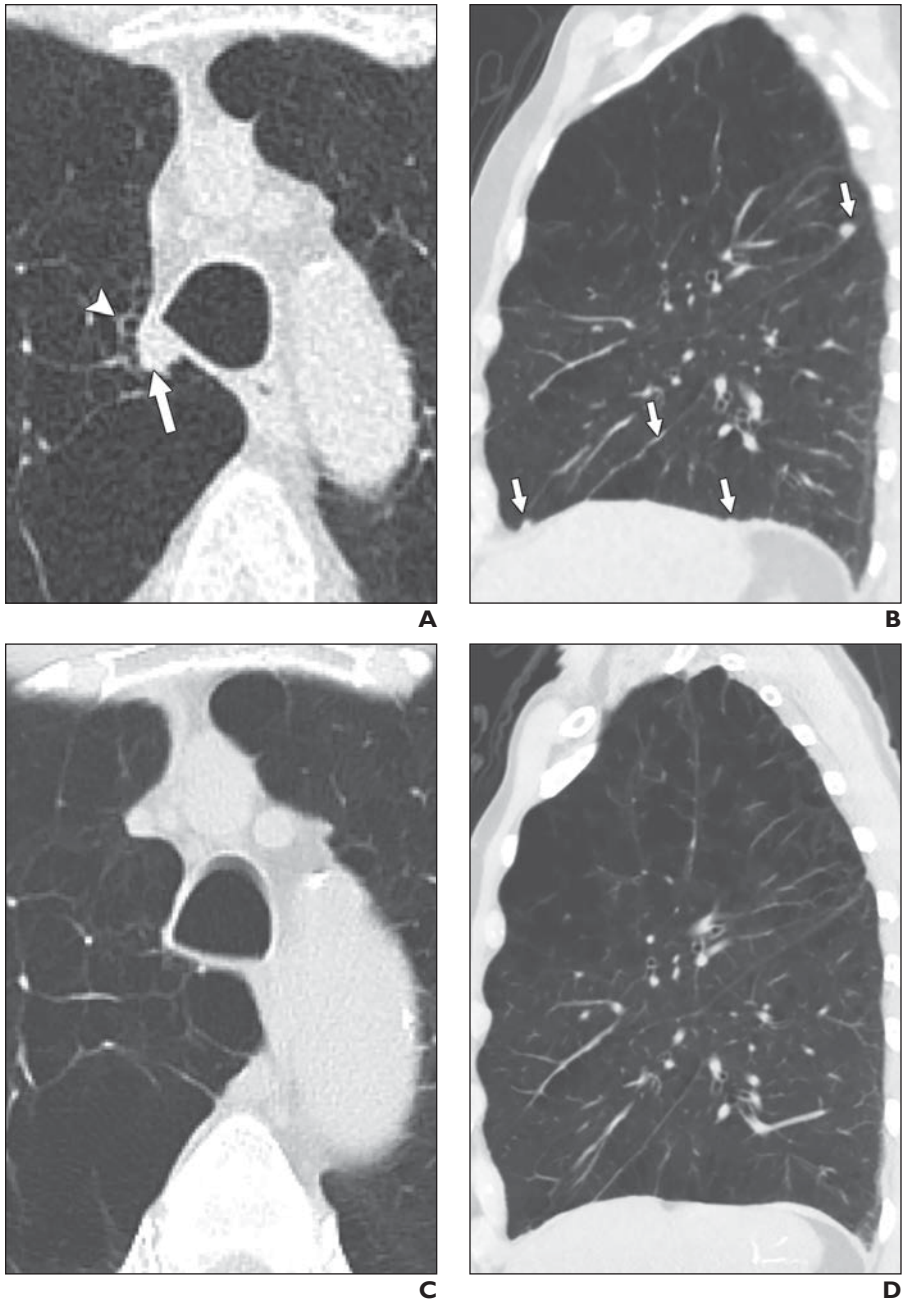

Fig. 6—70-year-old man with 40-pack-year smoking history who presented for lung cancer screening after being lost to follow-up for 2 years. **A–D,** Images from follow-up low-dose CT (LDCT) of chest (**A** and **B**) are contrasted to baseline evaluation (**C** and **D**). Coned-down axial image (**A**) shows new nodular thickening (*arrow*, **A**) in right upper paratracheal region and retraction of surrounding emphysematous spaces (*arrowhead*, **A**) compared with baseline (**C**). As with fissural retraction, this observation should lead to heightened level of suspicion, and classification as Lung-RADS 4X should be considered. Sagittal image (**B**) further increases suspicion, showing ipsilateral multifocal perifissural and pleural nodularity (*arrows*, **B**), new since baseline (**D**). Lung-RADS category 4X was assigned to follow-up LDCT because of spiculated appearance of nodule. Transbronchial biopsy of right upper lobe nodule revealed primary lung adenocarcinoma.

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consistent management of incidental thoracic findings [83]. In the setting of LCS, some authors question the value of adding the S modifier to common or expected imaging findings of smoking-related lung injury such as emphysema [29]. It would be reasonable to recommend adding the S modifier when management would be altered or when findings are new from prior imaging or are unknown according to information available in the electronic health record.

Additional Challenges in Clinical Practice

The issue of compliance to abnormal LCS CT recommendations remains of utmost importance. Only a small proportion (as low as 14.4% in one study [80]) of eligible individuals in the United States currently undergo LCS, with state-to-state variability [84]. For example, the state with the highest screening rate is Florida with 18.1% of eligible patients undergoing screening; the state with the lowest screening rate is Nevada at 6.5%. Conversely, individuals who do not currently meet accepted eligibility criteria are sometimes referred for LDCT [85]. Obstacles to proper LCS include lack of patient and provider awareness, skepticism regarding LCS benefits, socioeconomic status, suboptimal access to care in some rural areas, and both societal- and self-stigmatization [86, 87]. Efforts geared toward improved adherence should be implemented with these shortcomings in mind.

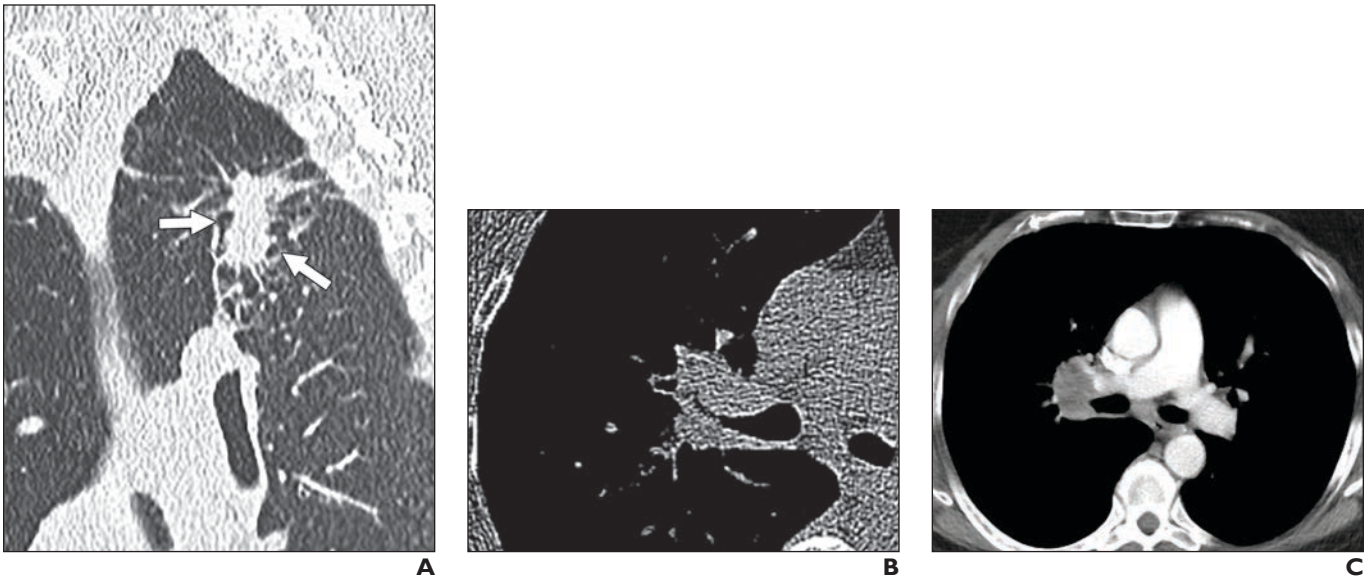

Fig. 7—55-year-old woman with 60-pack-year smoking history found to have right upper lobe nodule on lung cancer screening (LCS).
A, Coned-down sagittal image from low-dose CT (LDCT) of chest shows right upper lobe nodule (*arrows*) associated with paracicatrial emphysema and linear pleural attachments.
B, Coned-down axial image from LDCT shows ipsilateral right hilar adenopathy. Findings heightened suspicion for neoplasm, and Lung-RADS category 4X was assigned to nodule. Pathology revealed lung adenocarcinoma. Both right upper lobe nodule and right hilar adenopathy were metabolically active on subsequent PET/CT obtained 13 days after initial LDCT (not shown).
C, Axial image from follow-up enhanced chest CT 2 months after LCS shows persistence of right hilar adenopathy.

Ongoing Work, Advances, and Future Directions

Since the early and extensive work on computer-aided detection in the 1980s, computer-aided detection systems for the identification of pulmonary nodules on CT have been increasingly integrated into the clinical setting [88]. Recent years have seen tremendous advances in potential artificial intelligence applications in medical imaging. With the growing use of artificial intelligence and machine learning, increasingly complex algorithms may assist radiologists in the evaluation of pulmonary nodules and the generation of reports in concordance with Lung-RADS criteria. The supervised and progressive integration of algorithms into the workflow are likely to help significantly improve LCS performance metrics, from identifying patients in the electronic health record who would benefit from screening, to calculating lung cancer risk before and after integration of the CT findings, to minimizing reporting variation [89–91]. Recent reports have explored the advantage of combining patient characteristics with Lung-RADS to predict the risk of malignancy [92, 93]. For example, a model validated in patients from NLST and the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial used basic demographics and radiographic findings to select individuals with a long-term risk of lung cancer [90]. The model showed better discrimination than did CMS eligibility criteria for incident lung cancer in validation datasets [90]. Investigators developed models assessing the potential malignant behavior of nodules according to comparative volumetric analysis on LCS LDCT, which could prove useful for future iterations of Lung-RADS [94]. The ACR Assist initiative also aims to integrate artificial intelligence applications into the radiology workflow to provide streamlined clinical decision support tools as well as increased efficiency and homogenization of Lung-RADS reporting [91]. Although some currently available algorithms have yet to be tested in the clinical setting, preliminary reports on data from LCS trials are promising.

Only about one-quarter of patients with lung cancer meet the initial restrictive NLST screening criteria [95]. New draft recommendations of the USPSTF support the broadening of LCS eligibility, including the initiation of LCS at age 50 and reducing the minimum pack-years requirement to 20 [96]. Although great emphasis is currently placed on smoking history in most LCS guidelines, because of the lack of randomized trial data in nonsmokers, a growing in-

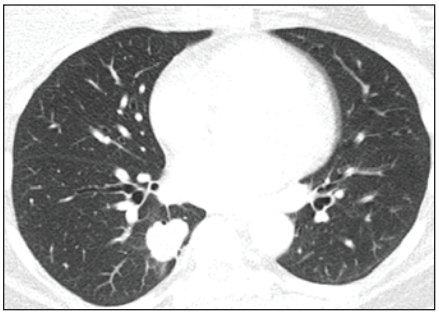

Fig. 8—51-year-old woman who had never smoked with right lower lobe nodule despite not meeting eligibility criteria for lung cancer screening (LCS). Axial image from diagnostic chest CT shows large right lower lobe subpleural solid nodule with mild surrounding ground-glass opacity. Pathology revealed poorly differentiated endothelial growth factor–positive adenocarcinoma. Changes in epidemiology of lung cancer with rising incidence of adenomatous lesions in younger nonsmokers will likely result in broader future LCS efforts and broader future use of Lung-RADS.

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cidence of non–small cell lung cancer in never-smokers continues to raise important questions regarding LCS in this population [97] (Fig. 8). Expansion of indications for LCS will necessarily lead to the application of Lung-RADS to a wider population.

The USPSTF screening guideline recommended annual screening for eligible individuals who are 55–80 years old [7]. According to this guideline, a negative Lung-RADS screen currently assumes an annual follow-up. However, the optimal screening interval to maximize detection rates and minimize cost and harm continues to be investigated. Moreover, the heterogeneity of risk within the target LCS population raises questions about the potential benefit of individualizing screening protocols. Some investigators have suggested that a negative initial LDCT may imply a lower lung cancer diagnosis risk up to 2 years [98]. Others, including the Early Lung Cancer Action Program investigators, have suggested that the annual new lung cancer diagnosis rate remains the same year after year from annual screening [99]. A tailored screening strategy made according to individual risk stratification, including prescreening risk and prior LDCT results, may be feasible on an individual basis but challenging to implement on a broad scale. Decisions to modify or personalize interval screening strategies in the future would need to be reflected in future Lung-RADS iterations.

Conclusion

LCS has the potential to make a substantial impact on lung cancer survival and achieve earlier diagnosis of disease and decreased mortality. Lung-RADS standardizes the reporting and management of findings on LDCT for LCS. Growing experience and evidence will help address many of the existing challenges in use of Lung-RADS in future iterations. Similar to other reporting and data systems such as BI-RADS, Lung-RADS will continue to be updated as new information becomes available, with the intent to ultimately improve LCS performance and lead to better patient care and outcomes.

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