Malignant Nodules Detected on Lung Cancer Screening CT: Yield of Short-Term Follow-Up CT in Showing Nodule Growth

Suzanne C. Byrne, MD[1], Mark M. Hammer, MD

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lung cancer, lung cancer screening, lung nodule, Lung-RADS

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BACKGROUND. Lung-RADS recommends 3-month follow-up for category 4A nodules and downgrading to category 2 of all category 3 or 4 nodules that are unchanged for 3 months or longer, indicating benign behavior. This guidance may be problematic considering the potential for slow-growing cancers in that lack of nodule growth, particularly at short follow-up intervals, may provide false reassurance.

OBJECTIVE. The purpose of this study was to evaluate the yield of short-term follow-up CT in showing growth among malignant nodules detected on lung cancer screening CT.

METHODS. This retrospective study included 76 patients (53 women, 23 men; median age, 68 years) with a positive lung cancer screening CT result (Lung-RADS category ≥ 3) between June 2015 and May 2021 with a subsequent lung cancer diagnosis and at least one follow-up CT examination at least 3 months before diagnostic or therapeutic intervention. Semiautomated software was used for linear and volumetric nodule measurements. Diameter was defined as the mean of short- and long-axis measurements. For solid nodules, growth was defined as an at least 1.5-mm increase in mean diameter or an at least 25% increase in volume; part-solid nodules, an at least 1.5-mm increase in solid-component mean diameter or an at least 25% increase in volume; and ground-glass nodules, an at least 3-mm increase in mean diameter or development of a new solid component within the nodule.

RESULTS. Median time to growth was 13 months by linear and 11 months by volumetric measurement. Frequency of growth at 3 months was 5% by linear and 7% by volumetric measurement. By linear measurement, median time to growth and frequency of growth at 3 months were 13 months and 7% (solid nodules), 18 months and 6% (part-solid nodules), not reached and 0% (ground-glass nodules), not reached and 0% (category 3 nodules), 13 months and 6% (category 4A nodules), 6 months and 11% (category 4B nodules), and 12 months and 10% (category 4X nodules).

CONCLUSION. Malignant nodules manifest growth slowly on follow-up CT, and 3-month follow-up CT has very low yield. Stability at 3-month follow-up should not instill high confidence in benignancy, and downgrading all such nodules to Lung-RADS category 2 may be problematic.

CLINICAL IMPACT. This study highlights the possibility of slow-growing malignancy and associated challenges in application of Lung-RADS to management of unchanged nodules on follow-up imaging.

Multicenter trials have shown that lung cancer screening (LCS) with low-dose CT reduces lung cancer mortality [1, 2]. For example, in the United States, the National Lung Screening Trial (NLST) showed a 20% relative reduction in lung cancer deaths among 55- to 74-year-old individuals with a smoking history of 30 pack-years or greater [2]. In addition, the Dutch-Belgian Randomized Lung Cancer Screening Trial (NELSON) showed a 26% reduction in lung cancer deaths at 10-year follow-up among men at high risk who underwent LCS CT [1]. The findings of these and other studies have led to national and international recommendations for use of low-dose CT in LCS programs [3, 4]. Given the increased use of CT for LCS, robust algorithms for appropriate triage of LCS-detected lung nodules are important for ensuring optimal patient management.

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[1]Both authors: Department of Radiology, Harvard Medical School, Brigham and Women's Hospital, 75 Francis St, Boston, MA 02115. Address correspondence to S. C. Byrne (scbyrne@bwh.harvard.edu, @scbyrne2).

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Various recommendations provide guidance for evaluation of nodules detected in LCS. These include the American College of Radiology Lung-RADS [5], which is based primarily on linear measurement of nodule size, and the algorithm used in the NELSON trial [6], which is based primarily on nodule volume and growth rate. For nodules that persist on follow-up CT examinations, both Lung-RADS and NELSON include growth criteria to determine the need for further follow-up. In these algorithms, nodules that are not growing or, in NELSON, are slowly growing do not warrant further dedicated follow-up. Specifically, in Lung-RADS version 1.1 (v1.1) the presence of stability for at least 3 months is a basis for downgrading nodules from category 3 or 4 to category 2 [5]. Category 2 nodules are considered to exhibit benign behavior or appearance and have very low likelihood of becoming a clinically active cancer (< 1% risk of malignancy according to Lung-RADS v1.1) [5]. Resumption of annual screening in 12 months is recommended for patients with category 2 nodules.

This guidance to downgrade stable nodules to category 2 can be problematic in the context of slow-growing cancers. Subsolid nodules, comprising part-solid nodules (PSNs) and pure ground-glass nodules (GGNs), are commonly encountered on LCS CT and may represent indolent malignancies [7]. Subsolid nodules that persist on follow-up CT are more likely to represent adenocarcinomas than to represent benign entities, such as focal fibrosis [8, 9], and some lung adenocarcinomas, such as those of mucinous histology, have very long doubling times. Carcinoid tumors (rare low-grade malignant neoplasms constituting approximately 1–2% of all lung cancers) may also exhibit slow growth [10]. The management of unchanged nodules by use of recommendations such as Lung-RADS is challenging, as lack of nodule growth, particularly when assessed at a short follow-up interval, may provide a false sense of security.

If cancerous nodules detected on LCS CT are highly unlikely to exhibit grow at 3-month follow-up chest CT, a screening interval of 3 months may be of limited utility. We conducted this study to evaluate the yield of short-term follow-up CT in showing growth among malignant nodules detected on LCS CT.

HIGHLIGHTS

Key Finding

- *Among LCS-detected nodules initially managed by follow-up CT and ultimately diagnosed as lung cancer, the median time to growth was 13 months by linear measurement and 11 months by volumetric measurement. The frequency of growth at 3 months was 5% by linear and 7% by volumetric measurement.*

Importance

- *As malignant nodules are slow to manifest growth, 3-month follow-up CT has limited yield, and 3-month stability should not be considered assurance of benignancy.*

Methods

Patients

This retrospective study was granted institutional review board approval. The requirement for written informed consent was waived. The study was performed in a health care network that includes two tertiary academic centers and two community hospitals. LCS programs had been established at all sites in the network since 2004. The network electronic health records were reviewed to identify all patients who underwent LCS CT from June 2015 to May 2021. The search results were reviewed to identify patients with a positive LCS CT result (i.e., Lung-RADS category 3 or higher) and a subsequent diagnosis of lung cancer who underwent at least one follow-up chest CT examination at least 3 months after the first positive LCS CT and before any invasive intervention for lung cancer diagnosis or treatment. Diagnoses of lung cancer were initially identified through review of billing records. Cases were then manually reviewed by a fellowship-trained thoracic radiologist (M.M.H., 6 years of posttraining experience) to confirm the diagnosis of lung cancer based on the billing records and to ensure that the dominant nodule reported on the first positive LCS CT corresponded to the site of primary lung cancer. Lung cancer diagnoses were either confirmed pathologically or determined empirically in multidisciplinary discussion resulting in a decision to treat the patient for lung cancer on the basis of nodule growth. A single dominant nodule per patient was analyzed. A total of 17 patients in the current study had been included in a prior study of Lung-RADS that focused on lung cancer risk in nodules detected at LCS [11].

Chest CT Examinations

The initial positive LCS CT examinations were interpreted clinically by 1 of 27 fellowship-trained thoracic radiologists (1–45 years of experience). They interpreted the examinations using the Lung-RADS version current at the time of interpretation. The Lung-RADS categories were extracted from the clinical reports of the first positive LCS CT examinations.

For each patient, images were reviewed from the first positive LCS CT examination (i.e., the first examination depicting the nodule); the first follow-up CT performed after at least a 3-month interval; and, if available, additional chest CT performed immediately before an invasive diagnostic or therapeutic intervention for lung cancer (hereafter, the additional later follow-up CT). The examinations were reviewed by a fellowship-trained thoracic radiologist (S.C.B., 6 years of posttraining experience), who recorded the density of the detected nodule (classified as solid nodule, PSN, or GGN) on the first positive examination and also measured the nodule on each CT examination using advanced visualization software (Syngo.VIA, Siemens Healthcare). The software allows semiautomated nodule segmentation, yielding long-axis diameter, short-axis diameter, and volume. For each nodule, the mean diameter was calculated as the mean of the long- and short-axis diameters. For PSNs, the mean diameter and volume were determined for both the entire nodule and the solid component. For GGNs, the investigator also assessed whether follow-up CT showed that a solid component had developed within the nodule. All CT examinations of an individual patient were evaluated concurrently. Data were entered by means of a research electronic data capture application (REDCap, version 11, REDCap Consortium) [12] and then analyzed with JMP Pro software (version 15, SAS Institute).

Determination of Nodule Growth

Nodule growth since the first positive CT examination was defined for solid nodules as an at least 1.5-mm increase in mean diameter or an at least 25% increase in volume; for PSNs, as an at

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least 1.5-mm increase in mean diameter of the solid component or an at least 25% increase in volume of the solid component; and for GGNs, as an at least 3-mm increase in mean diameter or development of a new solid component within the nodule [6]. For GGNs, development of a new solid component was deemed to represent growth by volumetric rather than by linear measurement.

Statistical Analysis

Characteristics of patients and nodules were summarized with descriptive statistics. Lung nodule growth was summarized in terms of the percentage of nodules showing growth on the first follow-up CT examination and the median time to growth among nodules showing growth on the basis of either the initial follow-up CT or the additional later follow-up CT examination when available. These endpoints were computed among all nodules and among nodules stratified by density and Lung-RADS category on the first positive CT examination, They were also computed with linear and volumetric measurements. Corresponding Kaplan-Meier curves were generated to show the time to nodule growth with information from both the first follow-up CT examinations and the additional later follow-up CT examinations when available for both linear and volumetric assessment. These Kaplan-Meier curves were used to derive the percentage of nodules with growth 3 months and 6 months after the initial CT examination. Density and Lung-RADS category on the first follow-up examination were summarized for nodules exhibiting growth at 3 months by linear measurements. The Wald test was used to test for a significant difference between linear and volumetric measurements in terms of the percentage of nodules exhibiting growth on the first follow-up examination. A value of $p < .05$ was used as the threshold for statistical significance. Analysis was performed with JMP Pro software (version 16.2, SAS Institute).

Results

Demographic Characteristics

A total of 21,388 LCS CT examinations were performed in the health care network during the study period. Of these, 2910 had a positive result (i.e., Lung-RADS category 3 or higher). These examinations were performed in a total of 791 unique patients who had a billing diagnosis of lung cancer. Of these, 223 patients underwent at least one follow-up chest CT examination performed at least 3 months after the first positive LCS CT. Patients were then excluded for the following reasons: retrospective review revealed no actual diagnosis of lung cancer despite the billing diagnosis ($n = 79$), the primary lung cancer was not related to the dominant nodule detected on the first positive LCS CT ($n = 28$), treatment was initiated before the 3-month follow-up CT examination ($n = 38$), and the chest CT images were unavailable for review ($n = 2$). These exclusions resulted in a final study sample of 76 patients (53 [70%] women, 23 [30%] men; median age, 68 years; range, 55–

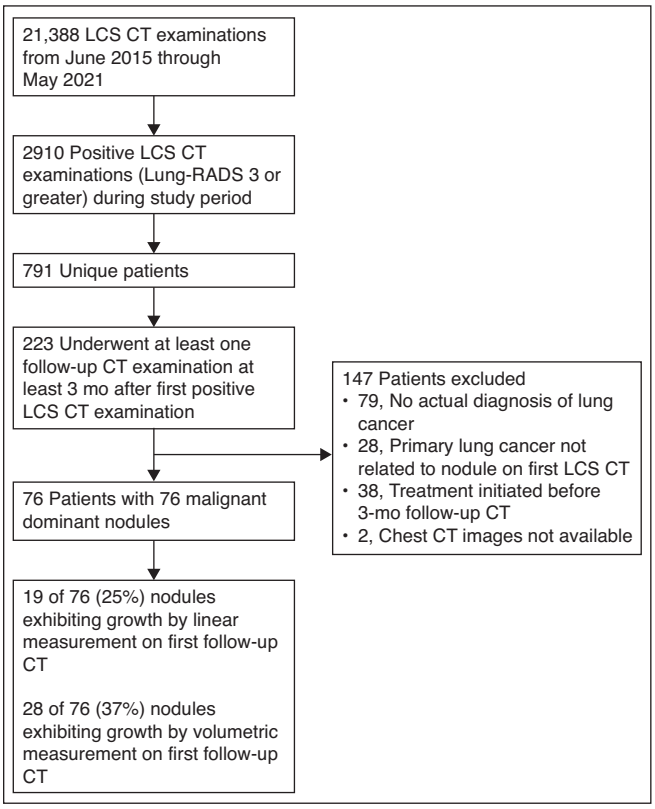

Fig. 1—Flowchart shows steps in patient selection. LCS = lung cancer screening.

TABLE 1: Demographic Characteristics of Study Sample ($n = 76$)

Characteristic	Value
Age (y)	
Median	68
Range	55–78
Sex	
Male	23 (30)
Female	53 (70)
Lung nodule size on first positive CT examination (mm)	
Median	10
Range	5–34
Lung-RADS category on first positive CT examination	
3	23 (30)
4A	34 (45)
4B	9 (12)
4X	10 (13)
Pathologic subtype of lung cancer	
Adenocarcinoma	53 (70)
Squamous cell carcinoma	11 (14)
Non–small cell lung cancer not otherwise specified	1 (1)
Carcinoid	1 (1)
No pathologic diagnosis (empirical treatment)	10 (13)

Note—Except for age and nodule size, data are numbers of patients with percentage in parentheses. Some percentages do not total 100 owing to rounding.

TABLE 2: Summary of Analyses of Nodule Growth

Characteristic	No. With Growth on First Follow-Up CT[a]		Median Time to Growth (mo)[a]		No. With Growth at 3 Mo[b]		No. With Growth at 6 Mo[b]	
	Linear	Volumetric	Linear	Volumetric	Linear	Volumetric	Linear	Volumetric
No. of nodules	19/76 (25)	28/76 (37)	13	11	4 (5)	5 (7)	15 (23)	22 (33)
Density								
Solid	15/43 (35)	18/43 (42)	13	9	3 (7)	4 (9)	11 (30)	12 (33)
Part-solid	2/18 (11)	9/18 (50)	18	6	1 (6)	1 (6)	2 (12)	9 (53)
Ground-glass	2/15 (13)	1/15 (7)	Not reached	Not reached	0 (0)	0 (0)	2 (14)	1 (8)
Lung-RADS category								
3	6/23 (26)	6/23 (26)	Not reached	15	0 (0)	0 (0)	3 (13)	3 (13)
4A	6/34 (18)	11/34 (32)	13	11	2 (6)	3 (9)	5 (19)	9 (34)
4B	5/9 (56)	7/9 (78)	6	5	1 (11)	1 (11)	5 (62)	6 (67)
4X	2/10 (20)	4/10 (40)	12	Not reached	1 (10)	1 (10)	2 (20)	4 (47)

[a]Values are numbers of nodules with percentage in parentheses.
[b]Values are numbers of nodules with percentage in parentheses, as derived by Kaplan-Meier analysis.

78 years) with a total of 76 malignant dominant nodules. Figure 1 summarizes the flow of patient selection, and Table 1 summarizes baseline patient and nodule characteristics. The lung cancer diagnosis was confirmed pathologically in 66 (87%) patients and established empirically in 10 (13%) patients. Among the pathologic diagnoses, 53 (70%) were adenocarcinoma, 11 (14%) were squamous cell carcinoma, one (1%) was non–small cell lung cancer not otherwise specified, and one (1%) was carcinoid.

Findings on First Positive Lung Cancer Screening CT Examinations

On the first positive LCS CT examination, the Lung-RADS assessments were category 3 in 23 (30%) patients, category 4A in 34 (45%), category 4B in nine (12%), and category 4X in 10 (13%). Nodule density was solid in 43 (57%), PSN in 18 (24%), and GGN in 15 (20%). The median nodule diameter was 10 mm (range, 5–34 mm). The median diameter of solid nodules was 8.5 mm (range, 5.0–33.5 mm), of PSNs was 10.8 mm (range, 6.5–20.5 mm), and of GGNs was 12.5 mm (range, 6.5–24 mm). The median diameter of the solid component of PSNs was 4.5 mm (range, 2.5–11 mm).

Lung Nodule Growth

The median interval between the first positive LCS CT examination and the next immediate follow-up chest CT examination was 6 months (range, 3–11 months). An additional later follow-up chest CT examination was available for 41 (54%) patients. The median follow-up interval when the additional later follow-up examinations were included was 8.5 months (range, 3–36 months).

All nodules—Findings regarding nodule growth are summarized in Table 2. Growth on the first follow-up CT examination was observed by linear measurement in 19 (25%) nodules and by volumetric measurement in 28 (37%) nodules ($p < .001$). The median time to growth was 13 months according to linear measurements (Fig. 2) and 11 months according to volumetric measurements. According to the Kaplan-Meier analysis, at 3 months, 5% of nodules exhibited growth by linear measurement and 7% by volumetric measurement, and at 6 months, 23% exhibited growth by linear measurements and 33% by volumetric measurement. Figures 3 and 4 show malignant nodules that did not exhibit growth at 3-month follow-up.

Nodules stratified by density—On the first follow-up CT examination, 15 of 43 (35%) solid nodules, 2 of 18 (11%) PSNs, and 2 of 15 (13%) GGNs exhibited growth by linear measurement. The median time to growth, as determined by linear measurement, was 13 months for solid nodules, 18 months for PSNs, and not reached for GGNs (Fig. 5). According to the Kaplan-Meier analysis, 7% of solid nodules, 6% of PSNs, and 0% of GGN exhibited growth at 3 months by linear measurement. At 6 months, the corresponding values were 30%, 12%, and 14%. Table 2 shows results based on volumetric measurements.

Nodules stratified by Lung-RADS category—On the first follow-up CT examination, 6 of 23 (26%) category 3 nodules, 6 of 34 (18%) category 4A nodules, five of nine (56%) category 4B nodules, and 2 of 10 (20%) category 4X nodules by linear measurement were observed. The median time to growth, as determined by linear measurement, was not reached for category 3 nodules, was 13 months

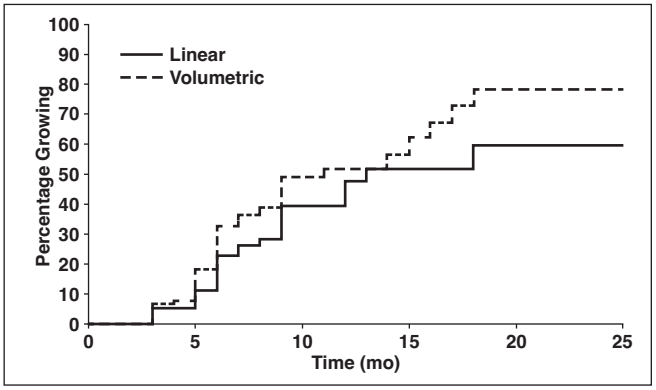

Fig. 2—Graph of Kaplan-Meier curves shows nodule growth over time based on linear and volumetric nodule measurements.

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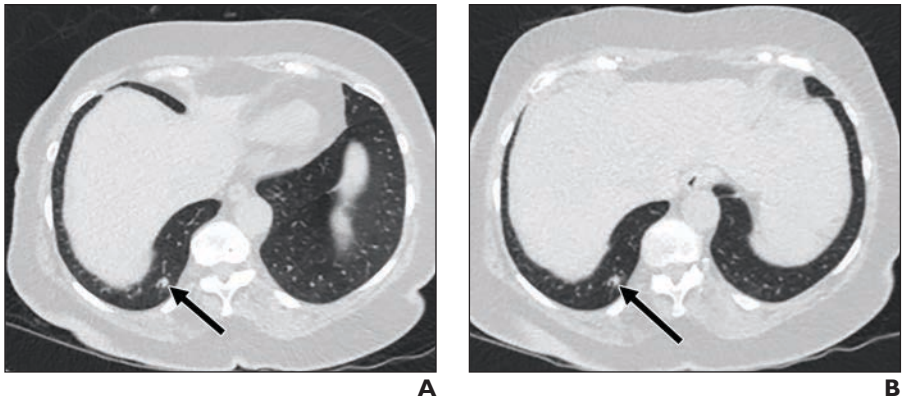

Fig. 3—72-year-old woman undergoing lung cancer screening (LCS).
A, Axial LCS CT image shows 9 × 5 mm (197 mm³) solid nodule (*arrow*) in right lower lobe. Nodule was assigned Lung-RADS category 4X.
B, Follow-up axial LCS CT image obtained 3 months after **A** shows size of nodule (*arrow*) is 10 × 5 mm (224 mm³), indicating absence of growth. Patient underwent right lower lobe wedge resection; pathologic diagnosis was primary lung adenocarcinoma.

for category 4A nodules, was 6 months for category 4B nodules, and was 12 months for category 4X nodules (Fig. 6). Based on the Kaplan-Meier analysis, the proportion of nodules that had grown at 3 months by linear measurements was 0% for category 3 nodules, 6% for category 4A nodules, 11% for category 4B nodules, and 10% for category 4X nodules. The proportion of nodules that had grown at 6 months by linear measurements was 13% for category 3 nodules, 19% for category 4A nodules, 62% for category 4B nodules, and 20% for category 4X nodules. Table 2 shows corresponding results for volumetric measurements.

Malignant nodules with growth at 3 months—Four nodules exhibited growth at 3 months by linear measurement. Three of these were solid. Of these three nodules, two were initially reported as category 4X with a recommendation for PET/CT and referral for specialist consultation. In these two cases, 3-month follow-up chest CT showed growth of 3 mm and 5 mm. The other solid nodule was initially reported as category 4A with a recommendation for specialist consultation and 3-month follow-up CT and exhibited growth of 3 mm on the follow-up CT. The fourth nodule was a PSN that was initially reported as category 4B with a recommendation for specialist consultation. The 3-month follow-up CT showed 3 mm of growth overall and 2.5 mm of the solid component. Figure 7 shows a malignant nodule with growth at 3-month follow-up.

Discussion

In this study performed in a large health care network with an established LCS program, we evaluated the frequency of growth of LCS-detected nodules on follow-up CT examinations performed at least 3 months after the LCS CT that were eventually diagnosed as cancer. Growth was slow to occur overall; the median time to growth was 13 months by linear measurement and 11 months by volumetric measurement. In addition, the finding of growth on an initial 3-month follow-up CT was uncommon (5% by linear measurement, 7% by volumetric measurement). On the first follow-up CT, including that performed more than 3 months after the initial LCS CT, 25% of nodules exhibited growth by linear measurement and 37% by volume measurement. The long intervals needed for growth to manifest and the absence of growth at 3 months in most instances were observed across nodule densities and initial Lung-RADS category assignments. Although volumetric measurements resulted in observation of somewhat higher frequencies of growth, only a small fraction of nodules exhibited growth at 3 months, even by volumetric measurements.

The overall slow growth of malignant nodules in our sample highlights the challenges that indolent lung cancers present for radiologists, pulmonologists, and thoracic surgeons. Lung-RADS v1.1 indicates that nodules assigned category 3 or 4 that are stable for at least 3 months should be reclassified as category 2, which corresponds with a benign appearance and a less than 1% risk of malignancy. According to our analysis, however, most malignant nodules for which follow-up imaging is performed appear to be stable for at least 3 months. Such short-term stability should not afford a high level of assurance that the nodule is benign even though it meets criteria for being downgraded to Lung-RADS category 2. Accordingly, when making the category 2 reassignment at follow-up imaging, radiologists may wish to highlight the possibility that the nodule represents an indolent malignancy, to ensure that the patient is not lost to further follow-up.

Lung-RADS v1.1 recommends 6-month follow-up CT for category 3 nodules and 3-month follow-up CT for category 4A nodules. Follow-up imaging is not recommended for category 4B and 4X nodules; such nodules should be further evaluated with diagnostic chest CT, PET/CT, or tissue sampling. For category 4B and 4X nodules that are considered potentially infectious or inflammato-

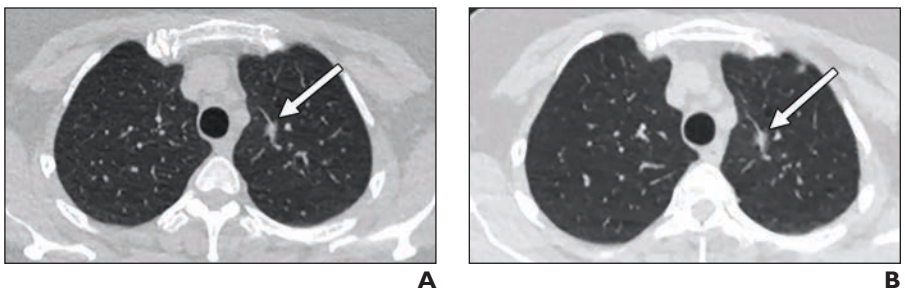

Fig. 4—58-year-old woman undergoing lung cancer screening (LCS).
A, Axial LCS CT image shows 13 × 8 mm (585 mm³) part-solid nodule (*arrow*) in left upper lobe with solid component measuring 8 × 3 mm (55 mm³). Nodule was assigned Lung-RADS category 4X.
B, Follow-up axial LCS CT image obtained 3 months after **A** shows size of nodule (*arrow*) is 12 × 7 mm (498 mm³) with solid component measuring 8 × 3 mm (48 mm³), indicating absence of growth. Patient underwent left upper lobectomy; pathologic diagnosis was primary lung adenocarcinoma.

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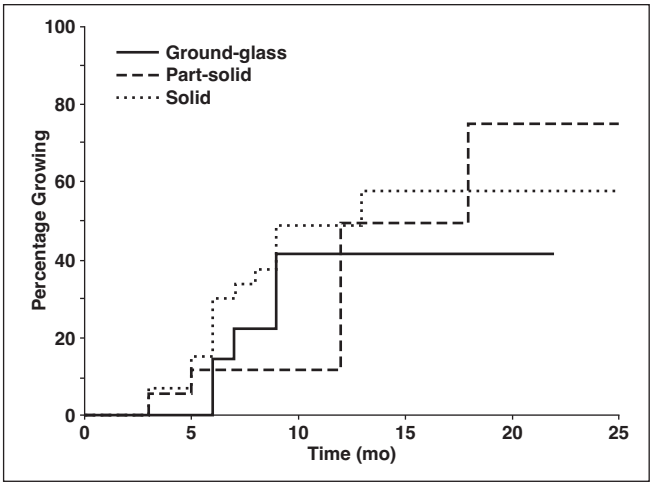

Fig. 5—Graph of Kaplan-Meier curves shows nodule growth over time based on linear measurements stratified by nodule density.

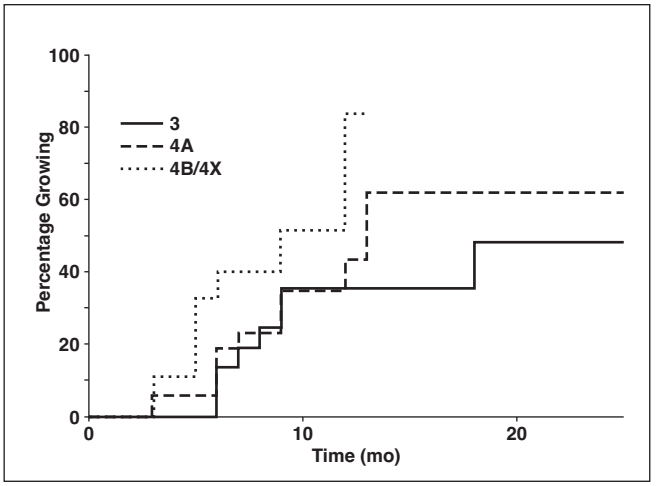

Fig. 6—Graph of Kaplan-Meier curves shows nodule growth over time based on linear measurements stratified by Lung-RADS category.

ry (e.g., newly developed on annual repeat LCS CT), initial 1-month follow-up CT may be performed before the diagnostic evaluation is pursued. Although category 4A and 4B nodules have defined criteria related to nodule size, category 4X encompasses category 3 or 4 nodules with additional features or imaging findings that increase the suspicion of malignancy, allowing radiologist discretion in terms of identifying such additional worrisome findings. Given the low yield of 3-month follow-up CT as is currently recommended for category 4A nodules, we advise that radiologists maintain a low threshold to initially assign category 4X rather than 4A to facilitate earlier lung cancer diagnoses. If category 4X is assigned, 1-month follow-up CT could be performed to assess whether the nodule is transient; if the nodule persists, further diagnostic workup could be performed. If the nodule is initially assigned category 4A (i.e., it does not have any features to justify a category 4X assignment and does not meet category 4B criteria), then a follow-up interval longer than 3 months may allow more time for a potentially indolent cancer to manifest growth and to avoid false assurance based on likely 3-month stability.

Although not following current Lung-RADS recommendations, radiologists could also consider upgrading a persistent nodule not exhibiting growth to Lung-RADS category 4X rather than downgrading the nodule to category 2. Such an approach could be adopted if the nodule is deemed suspicious on the basis of the radiologist's expertise and judgment, even though it does not exhibit growth. For example, the radiologist may consider upgrading the nodule to category 4X if it exhibits a minimal increase in size that does not meet Lung-RADS v1.1 criteria for growth [13, 14]. The use of category 4X in such situations can allow clearer communication with referring providers in comparison with downgrading the nodule to category 2 accompanied by additional language in the report expressing ongoing concern.

There were limitations to this study, including its retrospective design and small sample size. In addition, this study included patients from only a single health care network, potentially limiting generalizability. Another limitation was that we did not evaluate nodules on which immediate biopsy or resection was performed without first follow-up CT. These nodules have been larger and more suspicious, and thus we anticipate that they would have been more likely to have grown by 3 months. However, these nodules are also likely to have been initially classified as Lung-RADS category 4B or 4X and therefore would have warranted immediate diagnostic procedures (e.g., PET/CT, biopsy, or surgical resection) if managed in accordance with Lung-RADS v1.1 recommendations. We also did not evaluate findings on short-term follow-up CT in benign nodules, which would be highly unlikely to grow if not resolving. Furthermore, although we included all malignant category 3 and 4 nodules meeting the study inclusion criteria, Lung-RADS v1.1

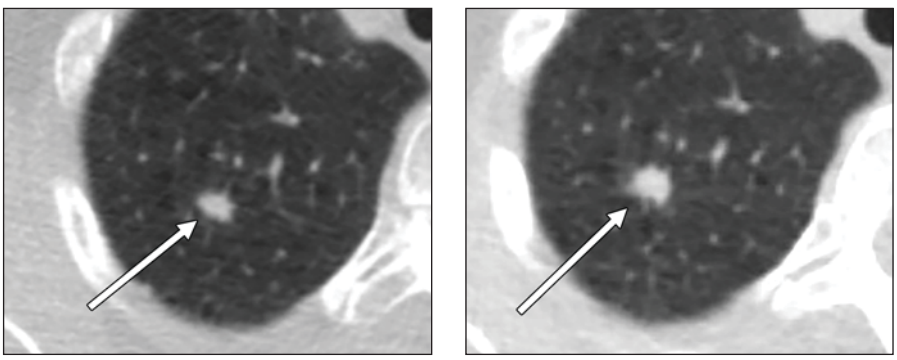

Fig. 7—67-year-old woman undergoing lung cancer screening (LCS).
A, Axial LCS CT image shows 10 × 7 mm (338 mm^3) solid nodule (*arrow*) in right upper lobe. Nodule was assigned Lung-RADS category 4X.
B, Follow-up axial LCS CT image obtained 3 months after **A** shows size of nodule (*arrow*) is 12 × 11 mm (392 mm^3), indicating nodule growth by both linear and volumetric measurements. Patient underwent right upper lobectomy; pathologic diagnosis was squamous cell adenocarcinoma.

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recommends 3-month follow-up CT only for category 4A nodules. Nonetheless, we believe our findings are relevant to all category 3 and 4 nodules because Lung-RADS indicates downgrading of all such nodules to category 2 if unchanged for at least 3 months. Another limitation is that although all nodules in the study sample were malignant, we did not stratify findings in terms of other histologic characteristics of the cancers. Finally, our study did not show benefit in terms of patient outcomes through earlier detection and thereby earlier surgical resection of indolent neoplasms (whether lung cancer or carcinoid).

In conclusion, for malignant nodules managed by follow-up LCS CT, the median time to growth was 13 months by linear measurement and 11 months by volumetric measurement. At initial 3-month follow-up, only 5% of malignant nodules exhibited growth by linear measurements and 7% by volumetric measurement. These findings highlight some concerns with Lung-RADS v1.1. The yield of initial 3-month follow-up CT, as recommended for category 4A nodules, is very low, given the time needed for growth to manifest. Moreover, 3-month stability should not provide high confidence that a category 3 or 4 nodule is benign, despite the Lung-RADS recommendation to downgrade such nodules to category 2. It remains imperative to recognize that 3-month stability does not signify benignancy and that reclassification of all such nodules as Lung-RADS category 2 may be problematic.

We suggested the following possible solutions: that radiologists consider using both volumetric and linear measurements to maximize growth detection; that when radiologists downgrade nodules to category 2 on the basis of 3-month stability, they include in the report additional language that expresses ongoing concern; that radiologists maintain a low threshold for assigning nodules an initial category of 4X rather than 4A to facilitate earlier diagnostic workup and cancer detection (potentially first performing 1-month follow-up CT to assess whether the nodule is transient); that a follow-up interval longer than 3 months be considered for category 4A nodules given the limited utility and potential false assurance associated with a 3-month follow-up examination; and that radiologists consider upgrading nodules to category 4X rather than downgrading to category 2 if the follow-up examination shows minimal increase in size not meeting criteria for growth. The Lung-RADS Committee could consider these possibilities in future versions of Lung-RADS.

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Editorial Comment: Stability of Screen-Detected Lung Cancers on Serial CT Examinations

Maximizing the effectiveness of lung cancer screening is a balance between judiciously detecting clinically significant lung cancers and avoiding unnecessary procedures. The American College of Radiology Lung-RADS provides management recommendations based on nodule-specific features and is continuously evolving as understanding of the nature of lung cancer evolves. CT is highly sensitive in lung nodule detection; however, most lung nodules are benign [1]. Lung cancer is the leading cause of cancer-specific mortality in the United States, however, and early detection is thus imperative to the success of screening.

In this study, Byrne and Hammer investigate growth patterns of screen-detected lung cancers on follow-up CT. The authors' estimates show that growth is observed in only 5% of cancers on 3-month follow-up CT and 23% of cancers on 6-month follow-up CT. The authors' conclusion is that lack of growth on short-term follow-up CT should not be taken as a surrogate for benignancy.

The slow growth of lung neoplasms presenting as subsolid nodules is well established. Persistent subsolid nodules have a high likelihood of representing neoplasms, but these neoplasms often exhibit indolent behavior. Delays in diagnosis and treatment of subsolid nodules seem to have a limited impact on prognosis [2].

Cancers presenting as solid nodules are more controversial, and early diagnosis may be more important than for cancers presenting as subsolid nodules. The current version of Lung-RADS downgrades stable category 3 and 4 lesions to category 2 lesions. The authors suggest that closer surveillance might be warranted. The authors also suggest more liberal use of category 4X, particularly for nodules suspected of growing that do not meet the at least 1.5-mm threshold described in Lung-RADS. One unanswered question is whether continued CT surveillance, rather than more aggressive early intervention, has a negative impact on rates of regional and distant spread.

Brett M. Elicker, MD
University of California, San Francisco
San Francisco, CA
brett.elicker@ucsf.edu

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