HHS Public Access

Author manuscript

AJR Am J Roentgenol. Author manuscript; available in PMC 2024 February 01.

Published in final edited form as:

AJR Am J Roentgenol. 2022 November ; 219(5): 735–741. doi:10.2214/AJR.22.27869.

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**[1]

[1]Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115

Abstract

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

Objective: To evaluate the yield of short-term follow-up CT in demonstrating growth among malignant nodules detected on lung cancer screening (LCS) CT.

Methods: This retrospective study included 76 patients (53 female, 23 male; median age, 68 years) with a positive LCS CT (Lung-RADS category ≥3) between June 2015 and May 2021, with a subsequent lung cancer diagnosis and at least one ≥3-month follow-up CT before diagnostic or therapeutic intervention. Semiautomated software was used for linear and volumetric nodule measurements; diameter was defined as mean of short- and long-axis measurements. Growth was defined for solid nodules as increase in mean diameter by ≥1.5 mm or volume by ≥25%; part-solid nodules as increase in solid-component mean diameter by ≥1.5 mm or volume by ≥25%; and ground-glass nodules as increase in mean diameter by ≥3 mm or new solid component.

Results: Median time to growth was 13 months by linear and 11 months by volumetric measurements. Frequency of growth at 3 months was 5% and 7% by linear and volumetric measurements, respectively. By linear measurements, median time to growth and frequency of growth at 3 months was 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: Growth is slow to manifest by malignant nodules managed by follow-up CT, and a 3-month follow-up CT has very low yield. Stability at 3-month follow-up should not provide high confidence in benignity, and downgrading all such nodules to category 2 may be problematic.

Clinical Impact: This study highlights challenges in application of Lung-RADS for management of unchanged nodules on follow-up imaging given possible slow-growing malignancy.

Correspondence: SCB, Department of Radiology, 75 Francis Street, Boston, MA 02115, scbyrne@bwh.harvard.edu, 617-732-6285.

Keywords

lung cancer screening; lung cancer; lung nodule; Lung-RADS

Introduction

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

Various recommendations provide guidance for evaluation of nodules detected by LCS. These include American College of Radiology Lung-RADS [5]. which is based primarily on linear measurement of nodule size, as well as the algorithm used in the Dutch 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 use growth criteria to determine the need for further follow-up. In these algorithms, nodules that are not growing or, for NELSON that are slowly growing, do not warrant further dedicated follow-up. Specifically, Lung-RADS version 1.1 (v1.1) uses the presence of stability for at least 3 months a basis to downgrade nodules from category 3 or category 4 to category 2 [5]. Category 2 nodules are in turn considered to have benign behavior or appearance, with a very low likelihood of becoming a clinically active cancer (<1% risk of malignancy per Lung-RADS v1.1) [5]; resumption of annual screening in 12 months is recommended for such patients.

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 (PSN) and pure ground glass nodules (GGN), are commonly encountered on LCS CT and may represent indolent malignancies [7]. Indeed, subsolid nodules that persist on follow-up CT are more likely to represent adenocarcinomas than benign entities such as focal fibrosis [8][9], and some lung adenocarcinomas (such as those of mucinous histology) have very long doubling times. Slow growth may also be observed by carcinoid tumors (rare low-grade malignant neoplasms representing approximately 1-2% of all lung cancers) [10]. The management of unhanged nodules using 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 grow on a 3-month follow-up chest CT, then a screening interval of 3 months may be of limited utility. We therefore

conducted this study to evaluate the yield of short-term follow-up CT in demonstrating growth among malignant nodules detected on LCS CT.

Methods

Patients

This retrospective study was granted institutional review board approval. The requirement for written informed consent was waived. The study was performed at a healthcare network that includes two tertiary academic centers and two community hospitals; LCS programs had been established at all sites within the network since 2004. The network's 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 that was performed 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 (MH, with 6 years of postraining 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 by multidisciplinary discussion resulting in a decision to treat the patient for lung cancer based on nodule growth. A single dominant nodule was analyzed per patient. A total of 17 patients in the present study were included in a prior study of Lung-RADS that focused on lung cancer risk in nodules detected on LCS [11].

Chest CT Examinations

The initial positive LCS CT examinations were interpreted clinically by one of 27 fellowship-trained thoracic radiologists with 1 to 45 years of experience; examinations were interpreted with Lung-RADS, using the current version as of the time of interpretation. The Lung-RADS categories were extracted from the clinical reports of the first positive LCS CT examinations.

For each patient, the images were reviewed for the first positive LCS CT (i.e., the first examination detecting the nodule); the first follow-up CT performed after at least a 3-month interval; and, if available, an additional chest CT representing the immediate prior chest CT 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 (SB, with 6 years of postraining experience), who recorded the detected nodule's density (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, Erlangen, Germany). The software allows for semiautomated nodule segmentation, yielding the nodule's 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 PSN, the mean diameter and volume were

determined for both the entire nodule and the solid component. For GGN, the investigator also assessed whether a solid component developed within the nodule on follow-up CT. All CT examinations in an individual patient were evaluated concurrently. Data were entered into REDCap [12] and then imported into JMP Pro (version 15, SAS Institute, Cary, NC) for analysis.

Determination of Nodule Growth

Nodule growth since the first positive CT was defined for solid nodules as an increase in mean diameter by at least 1.5 mm or an increase in volume by at least 25%; for PSN as an increase in mean diameter of the solid component by at least 1.5 mm or an increase in volume of the solid component by at least 25%; and for GGN as an increase in mean diameter by at least 3 mm or development of a new solid component within the nodule [6]. For GGN, development of a new solid component was deemed to represent growth by volumetric rather than by linear measurements.

Statistical Analysis

Characteristics of patients and nodules were summarized using 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 based on either the initial follow-up CT or the additional later follow-up CT when available. These endpoints were computed among all nodules and among nodules stratified by density and Lung-RADS category on the first positive CT, as well as computed using linear and volumetric measurements. Corresponding Kaplan-Meier curves were generated, demonstrating the time to nodule growth using information from both the first follow-up CT examinations and the additional later follow-up CT examinations when available, using both linear and volumetric assessment. These Kaplan-Meier curves were used to derive the percentage of nodules with growth at 3 months and at 6 months. Density and Lung-RADS category on the first follow-up examination were summarized for nodules showing 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 demonstrating growth on the first follow-up examination. A p value $<.05$ was used as a threshold for statistical significance. Analysis was performed using JMP Pro v 16.2 (SAS Institute, Cary, NC).

Results

Demographic Characteristics

A total of 21,388 LCS CT examinations were performed at the healthcare 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 that was 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 by the first positive LCS CT (n=28), treatment was initiated

before the 3-month follow-up CT (n=38), and the chest CT images were unavailable for review (n=2). These exclusions resulted in a final study sample of 76 patients, 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 median age was 68 years (range, 55-78 years). Of the 76 patients, 53 (70%) were female, and 23 (30%) were male. The lung cancer diagnosis was confirmed pathologically in 66 (87%) patients and established empirically in 10 (13%) patients. Of those with a pathologic diagnosis, 53 (70%) were adenocarcinoma, 11 (14%) were squamous cell carcinoma, 1 (1%) was non-small cell lung cancer, not otherwise specified, and 1 (1%) was carcinoid.

Findings on First Positive Lung Cancer Screening CT Examinations

On the first positive LCS CT examination, the Lung-RADS category was category 3 in 23 (30%), category 4A in 34 (45%), category 4B in 9 (12%), and category 4X in 10 (13%) patients. On the first positive LCS CT, the nodule density was solid in 43 (57%), PSN in 18 (24%), and GGN in 15 (20%). On the first positive LCS CT, the median nodule diameter was 10 mm (range, 5-34 mm). The median diameter for solid nodules was 8.5 mm (range, 5.0-33.5 mm), for PSN was 10.8 mm (range, 6.5-20.5 mm); and for GGN was 12.5 mm (range, 6.5-24 mm). For PSN, the median diameter of the solid component was 4.5 mm (range, 2.5-11 mm).

Lung Nodule Growth

The median interval between the first positive LCS CT and the immediate next follow-up chest CT was 6 months (range, 3-11 months). An additional later follow-up chest CT was available in X (X%) patients. The median follow-up interval when including the additional later follow-up examinations 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 was observed by linear measurements in 19 (25%) nodules and by volumetric measurements in 28 (37%) nodules ($p<.001$). The median time to growth was 13 months based on linear measurements (Fig. 2), and 11 months based on volumetric measurements. Based on the Kaplan-Meier analysis, the percentage of nodules that grew at 3 months was 5% by linear measurements and 7% by volumetric measurements, and the percentage of nodules that grew at 6 months was 23% by linear measurements and 33% by volumetric measurements. Figure 3 and Figure 4 show malignant nodules that did not exhibit growth at 3-month follow-up.

Nodules stratified by density——Growth on the first follow-up CT by linear measurements was observed for 15/43 (35%) solid nodules, 2/18 (11%) PSN, and 2/15 (13%) GGN. The median time to growth, as determined by linear measurements, was 13 months for solid nodules, 18 months for PSN, and not reached for GGN (Fig. 5). Based on the Kaplan-Meier analysis, the percentage of nodules that grew at 3 months by linear measurements was 7% for solid nodules, 6% for PSN, and 0% for GGN. The percentage of nodules that grew at 6 months by linear measurements was 30% for solid nodules, 12% for PSN, and 14% for GGN. Table 2 provides corresponding results using volumetric measurements.

Nodules stratified by Lung-RADS category——Growth on the first follow-up CT by linear measurements was observed for 6/23 (26%) category 3 nodules, 6/23 (18%) category 4A nodules, 5/9 (56%) category 4B nodules, and 2/10 (20%) category 4X nodules. The median time to growth, as determined by linear measurements, was not reached for category 3 nodules, 13 months for category 4A nodules, 6 months for category 4B nodules, and 12 months for category 4X nodules (Fig. 6). Based on the Kaplan-Meier analysis, the percentage of nodules that grew 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 percentage of nodules that grew 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 provides corresponding results using volumetric measurements.

Malignant nodules with growth at 3 months——Four nodules demonstrated growth at 3 months by linear measurements. Three of these were solid nodules. Of these three nodules, two were initially reported as category 4X with a recommendation for PET/CT and referral for specialist consultation, and showed growth of 3 mm and 5 mm on the 3-month follow-up CT; and one was initially reported as category 4A with a recommendation for specialist consultation and 3-month follow-up CT and showed growth of 3 mm on the follow-up CT. The remaining nodule was a PSN that was initially reported as category 4B, with a recommendation for specialist consultation; the 3-month follow-up CT showed growth by 3 mm overall and by 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 at a large healthcare network with an established LCS program, we evaluated the frequency of growth on follow-up CT examinations performed after at least 3 months among LCS-detected nodules that were eventually diagnosed as cancer. Growth was overall slow to occur, with a median time to growth of 13 months by linear measurement and 11 months by volumetric measurement. In addition, growth on an initial 3-month follow-up CT was uncommon (5% by linear measurements and 7% by volumetric measurements). The percentage of nodules showing growth on the first follow-up CT, including those performed later than 3 months, was 25% by linear measurements and 37% by volume measurements. The long intervals needed for growth to manifest, as well as the absence of growth at 3 months in most instances, were observed across nodule densities and initial Lung-RADS category assignments. While volumetric measurements resulted in observation of somewhat higher frequencies of growth, only a small fraction of nodules showed 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 ≥3 months should be reclassified as category 2, which corresponds with a benign appearance and a risk of malignancy of less than 1%. However, based on our analysis, most malignant nodules that initially undergo follow-up imaging will show at least 3 months of stability.

Thus, such short-term stability should not provide a high level of assurance in the nodule's benignity despite meeting criteria for downgrading to Lung-RADS category 2. Accordingly, when providing the category 2 reassignment at the time of 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 a 6-month follow-up CT for category 3 nodules and a 3-month follow-up CT for category 4A nodules. Follow-up imaging is not recommended for category 4B and 4X nodules; rather, such nodules should be further evaluated by diagnostic chest CT, PET/CT, or tissue sampling. For category 4B and 4X nodules that are considered potentially infectious or inflammatory (e.g., newly developed on an annual repeat LCS CT), an initial 1-month follow-up CT may be obtained before pursuing the diagnostic evaluation. While category 4A and 4B nodules have defined criteria relating to nodule size, category 4X encompasses "category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy," allowing radiologist discretion in terms of identifying such additional worrisome findings. Given the low yield of a 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, so as to facilitate earlier lung cancer diagnoses. If assigning category 4X, a 1-month follow-up CT could be obtained to assess whether the nodule is transient; if the nodule persists, further diagnostic workup could be performed at that time. If the nodule is initially assigned category 4A (i.e., it does not show any features to justify a category 4X assignment and does not meet category 4B criteria), then a longer follow-up interval than 3 months may provide more time for growth to manifest by a potentially indolent cancer while avoiding false assurance by the likely 3-month stability.

Although not following current Lung-RADS recommendations, radiologists could also consider upgrading a persistent nodule not showing growth to Lung-RADS category 4X, rather than downgrading the nodule to category 2. Such an approach could be adopted if deeming the nodule to be suspicious based on the radiologist's expertise and judgment, despite not showing growth. For example, the radiologist may consider upgrading the nodule to category 4X if the nodule shows 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 are limitations to this study, including its retrospective design and small sample size. In addition, this study only included patients from a single healthcare network, potentially limiting generalizability. Another limitation is that we did not evaluate nodules that underwent immediate biopsy or resection without first undergoing a follow-up CT. These are anticipated to have been larger and more suspicious nodules and thus 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, while we included all malignant category 3 and 4 nodules meeting study inclusion criteria, Lung-RADS v1.1 recommends a 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 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 does not demonstrate 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 that underwent follow-up LCT CT examinations, 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% and 7% of malignant nodules showed growth by linear and volumetric measurements, respectively. These findings highlight a couple of concerns with Lung-RADS v1.1. First, the yield of an 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 benignity, and that reclassification of all such nodules as Lung-RADS category 2 may be problematic. We have suggested a wide range of possible solutions, including that radiologists consider using both volumetric and linear measurements to maximize growth detection; that when radiologists downgrade nodules to category 2 based on 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 obtaining a 1-month follow-up CT to assess whether the nodule is transient); that a follow-up interval longer than 3 months by 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.

Acknowledgments

MMH reports funding from NIH 1R01CA260889-01

References

[1]. de Koning HJ et al. , “Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial,” N. Engl. J. Med, vol. 382, no. 6, pp. 503–513, Feb. 2020, doi: 10.1056/NEJMoa1911793. [PubMed: 31995683]

[2]. National Lung Screening Trial Research Team et al. , “Reduced lung-cancer mortality with low-dose computed tomographic screening,” N. Engl. J. Med, vol. 365, no. 5, pp. 395–409, Aug. 2011, doi: 10.1056/NEJMoa1102873. [PubMed: 21714641]

[3]. Wood DE et al. , “Lung Cancer Screening, Version 3.2018, NCCN Clinical Practice Guidelines in Oncology,” J. Natl. Compr. Cancer Netw. JNCCN, vol. 16, no. 4, pp. 412–441, Apr. 2018, doi: 10.6004/jnccn.2018.0020. [PubMed: 29632061]

[4]. Kauczor H-U et al. , “ESR/ERS white paper on lung cancer screening,” Eur. Radiol, vol. 25, no. 9, pp. 2519–2531, Sep. 2015, doi: 10.1007/s00330-015-3697-0. [PubMed: 25929939]

[5]. “Lung Rads | American College of Radiology.” https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/Lung-Rads. (accessed Feb. 08, 2022).

[6]. Xu DM et al. , “Nodule management protocol of the NELSON randomised lung cancer screening trial,” Lung Cancer Amst. Neth, vol. 54, no. 2, pp. 177–184, Nov. 2006, doi: 10.1016/j.lungcan.2006.08.006.

[7]. McWilliams A. et al. , “Probability of cancer in pulmonary nodules detected on first screening CT,” N. Engl. J. Med, vol. 369, no. 10, pp. 910–919, Sep. 2013, doi: 10.1056/NEJMoa1214726. [PubMed: 24004118]

[8]. Henschke CI et al. , “Lung cancers diagnosed at annual CT screening: volume doubling times,” Radiology, vol. 263, no. 2, pp. 578–583, May 2012, doi: 10.1148/radiol.12102489. [PubMed: 22454506]

[9]. MacMahon H. et al. , “Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017,” Radiology, vol. 284, no. 1, pp. 228–243, Jul. 2017, doi: 10.1148/radiol.2017161659. [PubMed: 28240562]

[10]. “Key Statistics for Lung Carcinoid Tumor.” https://www.cancer.org/cancer/lung-carcinoid-tumor/about/key-statistics.html (accessed Feb. 17, 2022).

[11]. Hammer MM and Byrne SC, “Cancer Risk in Nodules Detected at Follow-up Lung Cancer Screening CT,” Am. J. Roentgenol, 2021.

[12]. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, and Conde JG, “Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support,” J. Biomed. Inform, vol. 42, no. 2, pp. 377–381, Apr. 2009, doi: 10.1016/j.jbi.2008.08.010. [PubMed: 18929686]

[13]. Byrne SC and Hammer MM, “Use of Diagnostic CT and Patient Retention in a Lung Cancer Screening Program,” J. Am. Coll. Radiol. JACR, vol. 19, no. 1 Pt A, pp. 47–52, Jan. 2022, doi: 10.1016/j.jacr.2021.09.027. [PubMed: 34752759]

[14]. Mendoza DP et al. , “Lung-RADS Category 3 and 4 Nodules on Lung Cancer Screening in Clinical Practice,” Am. J. Roentgenol, Jan. 2022, doi: 10.2214/AJR.21.27180.

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 measurements and 11 months by volumetric measurement; the frequency of growth at 3 months was 5% and 7% by linear and volumetric measurements, respectively.

Importance:

As malignant nodules are slow to manifest growth, a 3-month follow-up CT has limited yield, and 3-month stability should not provide assurance of benignity.

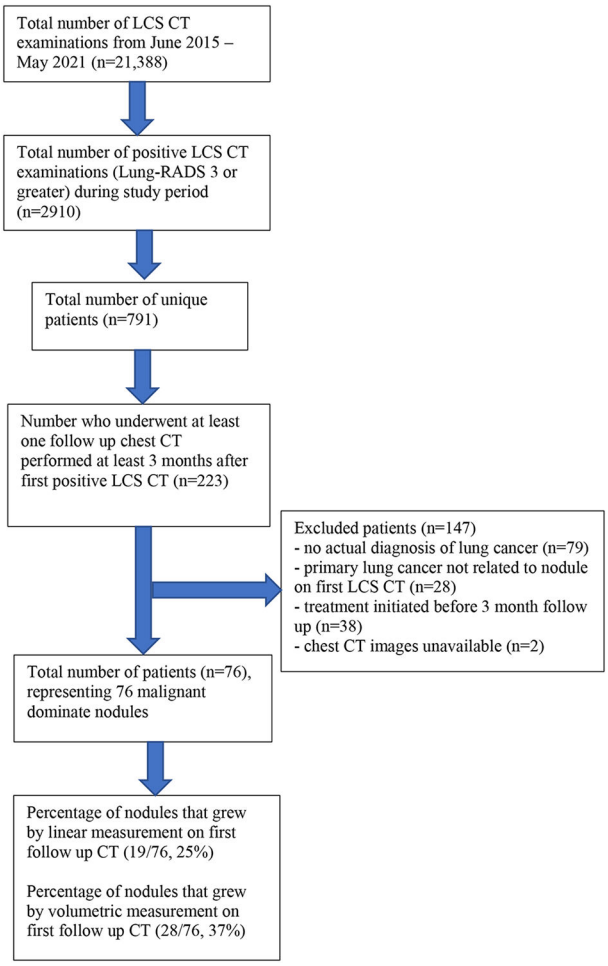

Figure 1.
Flow of patient selection. LCS = lung cancer screening.

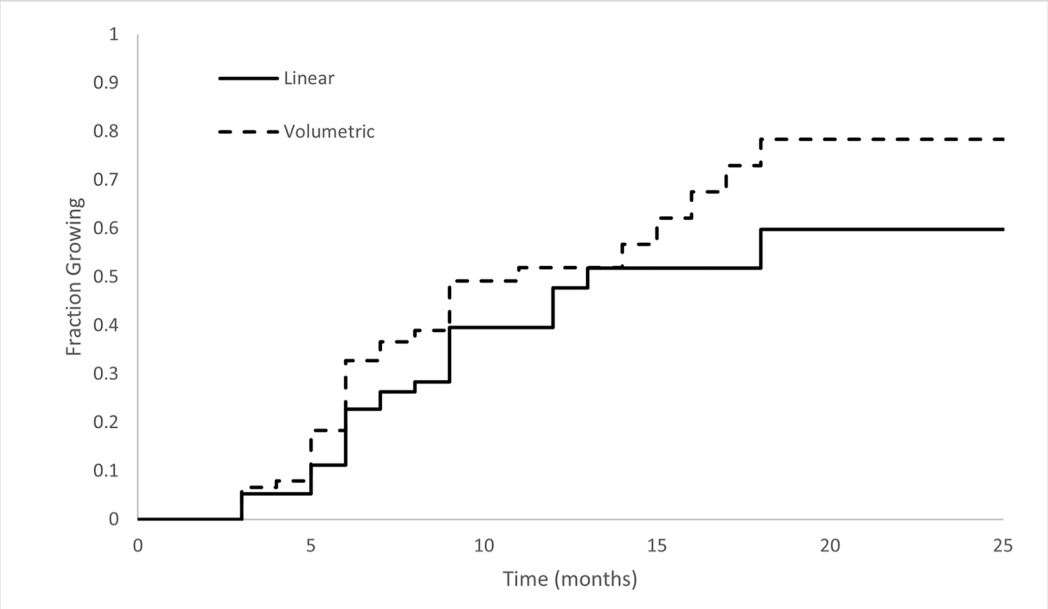

Figure 2.
Kaplan-Meier curves demonstrating nodule growth by time based on linear and volumetric nodule measurements.

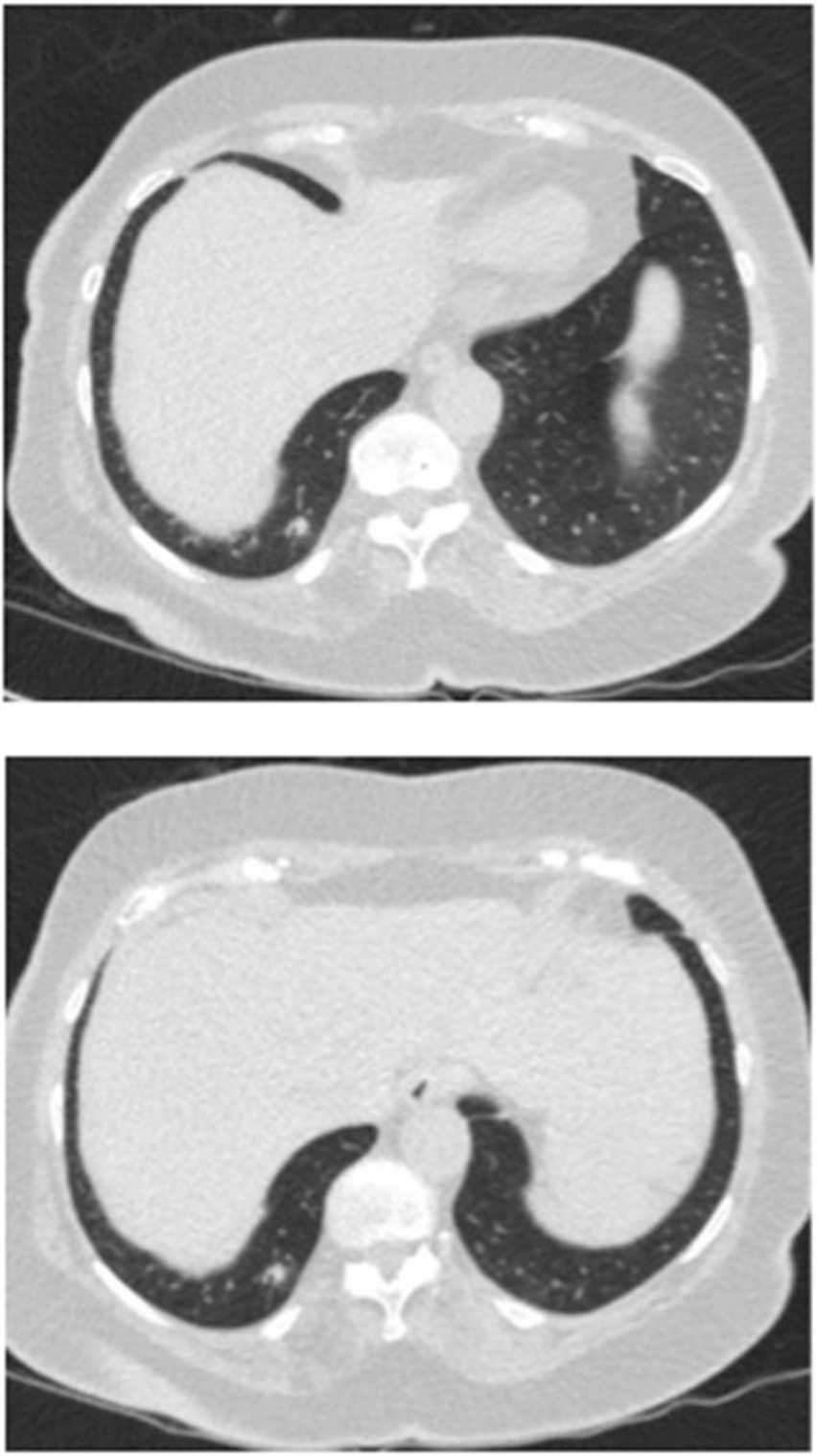

Figure 3.

72-year-old woman undergoing lung cancer screening (LCS). (A) Axial image from LCS CT shows 9 x 5 mm (197 mm^3) solid nodule in the right lower lobe (arrow). Nodule was

assigned Lung-RADS category X. (B) Axial image from follow-up LCT CT performed 3 months later shows nodule size of 10 x 5 mm (224 mm^3) (arrow), indicating absence of growth. The patient underwent right lower lobe wedge resection, yielding pathological diagnosis of primary lung adenocarcinoma.

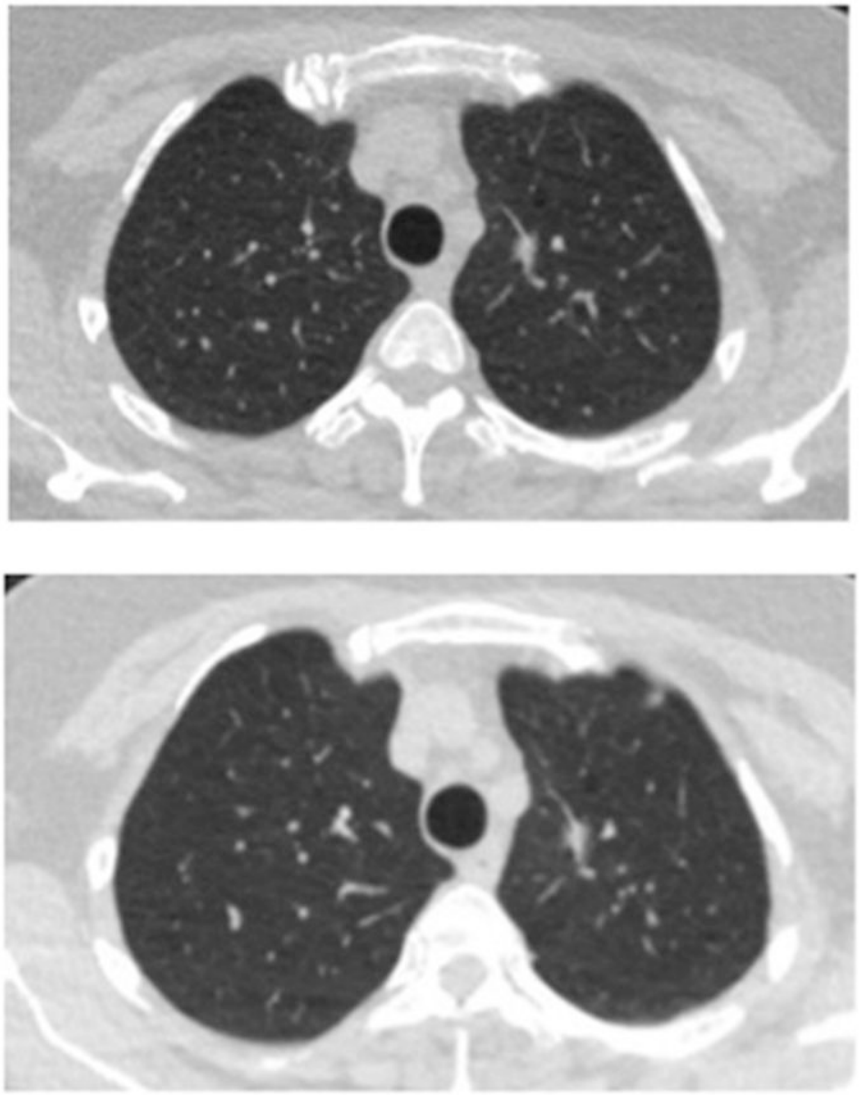

Figure 4.

58-year-old woman undergoing lung cancer screening (LCS). (A) Axial image from LCS CT shows 13 x 8 mm (585 mm^3) part-solid nodule in the left upper lobe (arrow), with solid component measuring 8 x 3 mm (55 mm^3) (arrow). Nodule was assigned Lung-RADS category X. (B) Axial image from follow-up LCT CT performed 3 months later shows nodule size of 12 x 7 mm (498 mm^3), with solid component measuring 8 x 3 mm (48 mm^3) (arrow), indicating absence of growth. The patient underwent left upper lobectomy, yielding pathological diagnosis of primary lung adenocarcinoma.

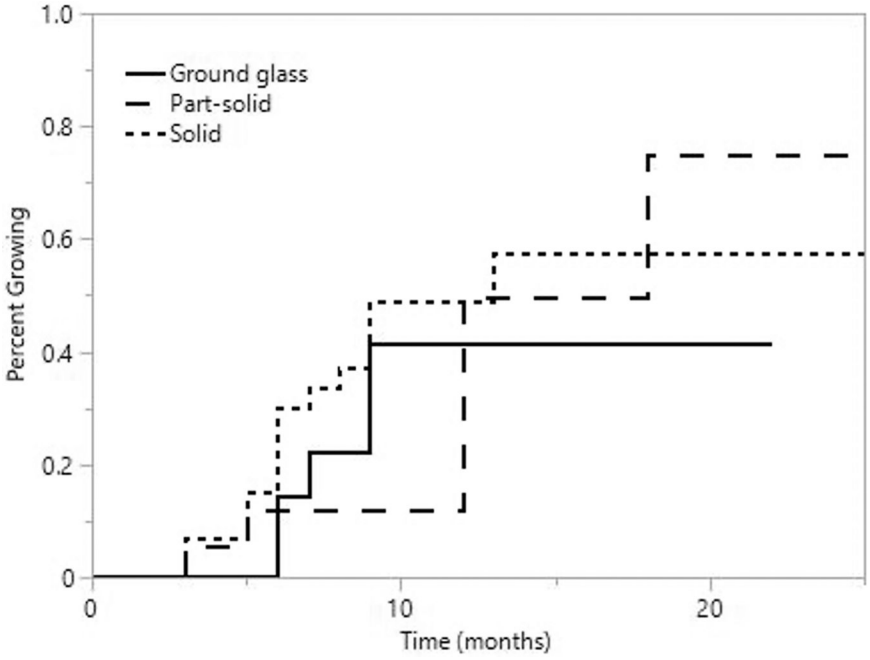

Figure 5.
Kaplan-Meier curves demonstrating nodule growth by time based on linear measurements, stratified by nodule density.

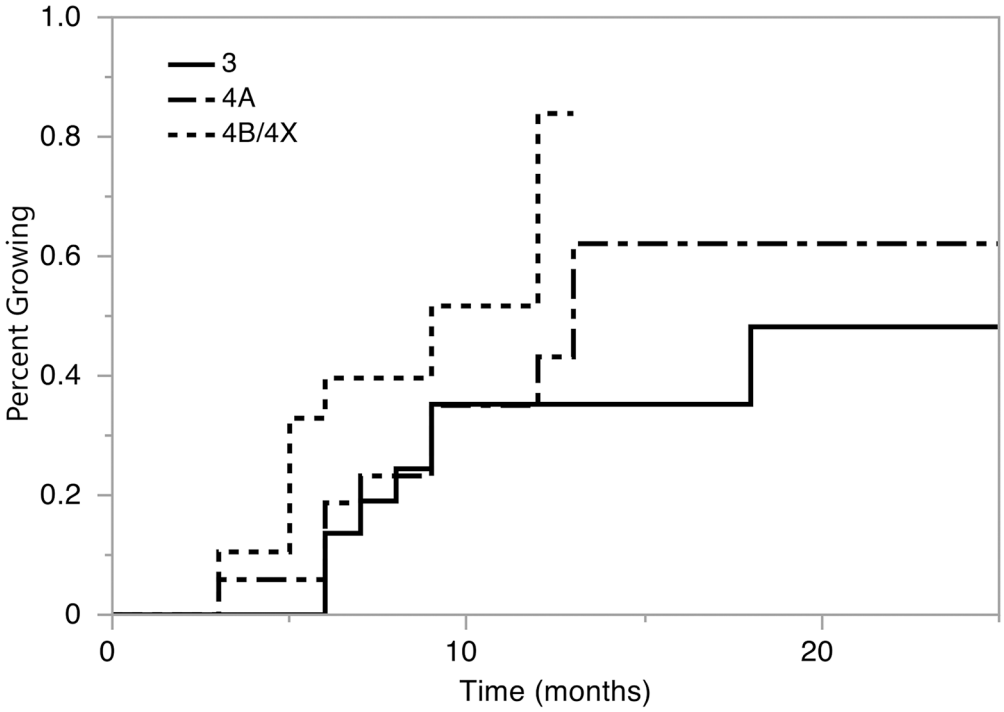

Figure 6.
Kaplan-Meier curves demonstrating nodule growth by time based on linear measurements, stratified by Lung-RADS category.

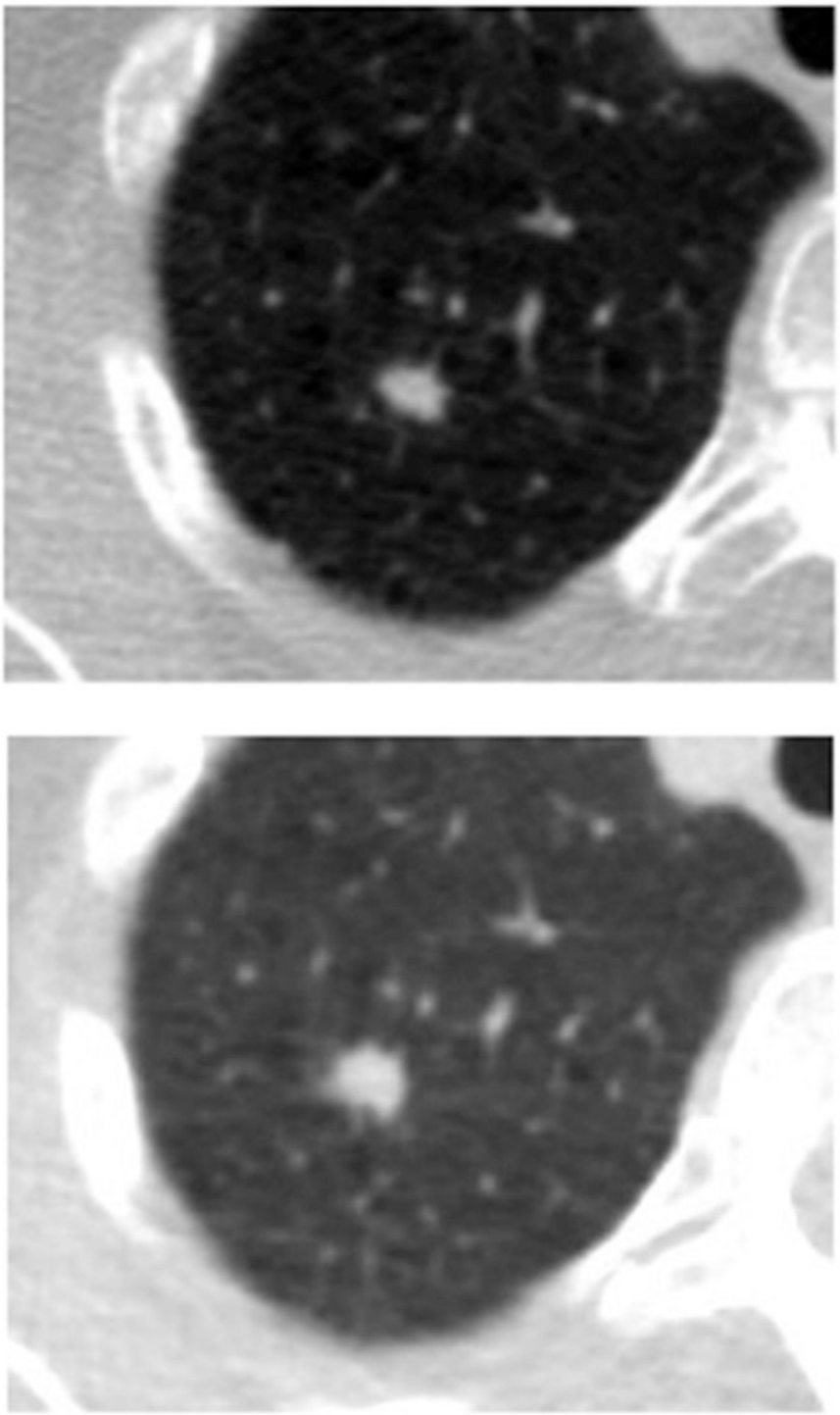

Figure 7.

67-year-old woman undergoing lung cancer screening (LCS). (A) Axial image from LCS CT shows 10 x 7 mm (338 mm^3) solid nodule in the right upper lobe (arrow). Nodule was assigned Lung-RADS category X. (B) Axial image from follow-up LCT CT performed 3 months later shows nodule size of 12 x11 mm (392 mm^3) (arrow), indicating nodule growth

by both linear and volumetric measurements. The patient underwent right upper lobectomy, yielding pathological diagnosis of squamous cell adenocarcinoma.

Table 1.

Demographic characteristics of study sample

Characteristic	Value (n=76)
Age (y)	
Median	68
Range	55-78
Sex	
Male	23 (30)
Female	53 (70)
Lung nodule size on first positive CT (mm)	
Median	10
Range	5-34
Lung-RADS category on first positive CT	
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)
Other NSCLC	1 (1)
Carcinoid	1 (1)
No pathologic diagnosis (empiric treatment)	10 (13)

Unless otherwise indicated, data represent number of patients, with percentage in parentheses.

NSCLC = non-small cell lung cancer

Table 2.

Summary of analyses of nodule growth

	Growth on First Follow-up CT[a]		Median Time to Growth (Months)[a]		Growth at 3 Months[b]		Growth at 6 Months[b]	
Nodules	**Linear**	**Volumetric**	**Linear**	**Volumetric**	**Linear**	**Volumetric**	**Linear**	**Volumetric**
All	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]Expressed as numerator and denominator, with percentage in parentheses.

[b]Expressed as number with percentage in parentheses, as derived by Kaplan-Meier analysis.