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Canadian Association of Radiologists Journal 65 (2014) 121−134

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Thoracic and Cardiac Imaging / Imagerie cardiaque et imagerie thoracique

# The Lung Reporting and Data System (LU-RADS): A Proposal for Computed Tomography Screening☆

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**Abstract**

Despite the positive outcome of the recent randomized trial of computed tomography (CT) screening for lung cancer, substantial implementation challenges remain, including the clear reporting of relative risk and suggested workup of screen-detected nodules. Based on current literature, we propose a 6-level Lung-Reporting and Data System (LU-RADS) that classifies screening CTs by the nodule with the highest malignancy risk. As the LU-RADS level increases, the risk of malignancy increases. The LU-RADS level is linked directly to suggested follow-up pathways. Compared with current narrative reporting, this structure should improve communication with patients and clinicians, and provide a data collection framework to facilitate screening program evaluation and radiologist training. In overview, category 1 includes CTs with no nodules and returns the subject to routine screening. Category 2 scans harbor minimal risk, including <5 mm, perifissural, or long-term stable nodules that require no further workup before the next routine screening CT. Category 3 scans contain indeterminate nodules and require CT follow up with the interval dependent on nodule size (small [5-9 mm] or large [≥10 mm] and possibly transient). Category 4 scans are suspicious and are subdivided into 4A, low risk of malignancy; 4B, likely low-grade adenocarcinoma; and 4C, likely malignant. The 4B and 4C nodules have a high likelihood of neoplasm simply based on screening CT features, even if positron emission tomography, needle biopsy, and/or bronchoscopy are negative. Category 5 nodules demonstrate frankly malignant behavior on screening CT, and category 6 scans contain tissue-proven malignancies.

**Résumé**

En dépit des résultats positifs d'un récent essai clinique randomisé visant le dépistage du cancer du poumon par tomodensitométrie (TDM), l'instauration ou la diffusion des pratiques de dépistage continue de soulever des défis de taille, en ce qui concerne notamment la classification non équivoque du risque relatif et le bilan proposé pour évaluer les nodules décelés par dépistage. Après avoir analysé la documentation scientifique actuelle, nous avons formulé une proposition de système de données et de déclaration à six niveaux, appelée méthodologie LU-RADS (Lung-Reporting and Data System), qui permet de classifier les résultats des tomodensitométries de dépistage en fonction du nodule présentant le risque le plus élevé de cancer du poumon. Dans le cadre de la méthodologie LU-RADS, plus les résultats correspondent à un niveau élevé, plus le risque de malignité est élevé. Le niveau LU-RADS renvoie également directement à des recommandations concernant le cheminement de suivi. Ainsi, comparativement aux comptes rendus descriptifs actuels, cette méthodologie devrait améliorer la communication avec les patients et les cliniciens, et fournir un cadre de collecte de données qui facilitera l'évaluation du programme de dépistage et la formation des radiologistes. En résumé, dans le cadre de la méthodologie LU-RADS, la catégorie 1 correspond aux examens de tomodensitométrie qui ne révèlent aucun nodule et exigent simplement du patient qu'il poursuive le programme de dépistage périodique. Les résultats de catégorie 2 font état d'un risque minimal, notamment de nodules de moins de 5 mm, de nodules péri-scissuraux ou de nodules stables à long terme qui n'exigent aucune autre mesure avant la tenue de la prochaine tomodensitométrie de dépistage périodique. Les résultats de catégorie 3 révèlent des nodules de nature indéterminée. Une tomodensitométrie de suivi doit alors être réalisée, dans un intervalle qui varie selon la taille du nodule (selon qu'il s'agit d'un petit nodule de 5 à 9 mm ou d'un gros nodule de ≥ 10 mm et possiblement transitoire). Pour leur part, les résultats des examens tomodensitométriques de catégorie 4 présentent des caractéristiques



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0846-5371/$ - see front matter 
http://dx.doi.org/10.1016/j.carj.2014.03.004

suspectes et se subdivisent en trois catégories: 4A, faible risque de malignité; 4B, probabilité d'adénocarcinome de bas grade; et 4C, probabilité de malignité. Les nodules des catégories 4B et 4C sont associés à une forte probabilité de néoplasie simplement en raison des caractéristiques observées par tomodensitométrie de dépistage, et ce, même si une tomographie par émission de positons (TEP), une ponction-biopsie ou une bronchoscopie révèle des résultats négatifs. Enfin, les nodules de catégorie 5 révèlent une séméiologie maligne nettement observable par TDM de dépistage, alors que ceux de catégorie 6 contiennent des tissus dont la malignité a été prouvée.


*Key Words:* Nodule risk; Lung cancer screening; Lung nodules; Low-dose computed tomography; National lung screening trial; LU-RADS

The success of computed tomography (CT) screening for lung cancer in the research setting challenges policy makers to provide universal access for patients at high risk. Many organizations, including the U.S. Preventative Services Task Force, recommend CT screening for patients at high risk [1–4]. However, implementation of screening outside the research setting is problematic, and appropriate concerns have been raised not only in the radiology literature [5,6] but also in the wider medical field [2,7]. Most radiologists are aware that lung nodules are common, the vast majority of nodules are benign, and that not all worrisome lung nodules require the same workup. However, primary care physicians and the public in general may not understand these principles. Indeed, a common perception among patients is that lung nodules are equivalent to lung cancer [8]. Successful implementation of screening CT programs will focus on clear communication of nodule malignant risk by the interpreting radiologist, which will help to avoid inappropriate referrals, repeated CTs, and interventions.

In this article, we propose a classification scheme for lung nodules found on baseline and follow-up screening CTs. The purpose of this classification is to facilitate communication with clinicians, provide a framework for data collection and analysis (including outcomes and quality assurance), and train radiologists new to screening CT. This classification scheme incorporates and summarizes existing guidelines and expert-opinion protocols (such as those produced by the American Academy of Chest Physicians, the National Comprehensive Cancer Network, and the Fleischner Society) and builds upon the strengths of existing screening classification systems [9–11]. It is acknowledged that the precise divisions of lung nodule categories and their corresponding management may vary among lung cancer screening programs based on resource availability. Furthermore, the subcategories may be refined as further evidence emerges. However, it should be emphasized that the principal aim of this document is to establish subcategories of nodules that differ substantially based on management and the likelihood of malignancy, and to establish a nomenclature that can assist clinicians and patients.

The Lung Reporting and Data System (LU-RADS) is based on the successful and widely accepted breast imaging classification, the BI-RADS (Breast Imaging Reporting and Data System; American College of Radiology, Reston, VA) [12]. LU-RADS includes 6 categories based on CT appearance, with an emphasis on serial CT findings. Each category is associated with a risk of primary lung malignancy and specific recommendations for workup. This categorization of nodules allows referring physicians a more sophisticated approach to a "positive" screening CT by emphasizing that different types of nodules require a different workup. A summary of the LU-RADS system, including the nodule characteristics for each category and the reporting and follow-up recommendations, is provided in Table 1. Because patients may harbor many nodules, the final recommendation on the CT report is based on the nodule with the highest risk of malignancy and the appropriate associated management strategy.

LU-RADS categories and management recommendations are based on a review of screening CT research in high-risk patient populations. The possible role of LU-RADS for the reporting and workup of incidental nodules or for nodules found in patients who are not at high risk for thoracic malignancy cannot be addressed in this article due to a lack of research evidence.

## LU-RADS 1

### Finding: No Nodule

### Management: Return to Regular Screening

This category applies to screening CTs in which no nodules are seen. Although the likelihood of lung malignancy in the next 2 years is very low, malignancy may arise in a nodule present but not detected, an interval nodule, or a malignancy not detectable by screening [13,14].

*Reporting and Management of LU-RADS 1 Nodules*

Patients and physicians need to be made aware of the limitations of screening CT and should be reminded that, even after a category 1 CT, the development of concerning symptoms (eg, unexplained hemoptysis) should prompt clinical evaluation. The report also should include a recommendation to return to regular screening and specific information regarding the timing of the next screening CT.

## LU-RADS 2

### Finding: Benign Nodule

### Management: Return to Regular Screening

This category includes nodules with an extremely high likelihood of benign etiology. For the current state of

Table 1
LU-RADS summary (for use in screen detected nodules in patients at high risk for lung cancer)

| | Examples | Comments |
|---|---|---|
| 1. No nodule | | Return to regular screening; risk of malignancy related to interval cancer, cancer not detectable by CT, and nodules present but not identified |
| 2. Benign nodule | Nodules $<$ 5 mm; perifissural opacities; benign calcification hamartoma<br>Core biopsy benign; solid stable for 2 y; subsolid stable for 5 y, round atelectasis | Safe to return to annual screening; risk of malignant diagnosis before next screen very low; no benefit for earlier follow up |
| 3. Indeterminate; requires serial LDCT | **Small:** 5-9−mm nonenlarging nodule with $<$2 y (solid) or $<$5 y stability (subsolid) | Follow up as per schedule (Fleischner or screening-specific guidelines; note, some suggest following up new nodules more closely than baseline nodules) |
| | **Large:** baseline or new nodule $\geq$ 10 mm with any possibility of transient inflammatory process, eg, new or baseline subsolid nodules $\geq$10 mm, or eg, inflammatory clinical or CT features (rapid development, multifocal, satellite nodules, air bronchogram, or ground-glass border) | Follow up in 6-12 wk to exclude transient inflammatory process; no improvement is worrisome (reclassify into category 4) |
| 4. Suspicious | **4A. Low risk of malignancy**; solid nodule ($\geq$10 mm) with benign features but CT not definitive for category 2; eg, well-defined roughly spherical nodule likely hamartoma or granuloma | Review all possibly relevant prior imaging; needs workup; at minimum, follow-up at 3 mo; refer; other possibilities: core biopsy, PET (negative PET is reassuring in this category; value of positive PET dependent on rate of granulomatous disease) |
| | **4B. Likely in situ or minimally invasive adenocarcinoma**; nonresolving subsolid opacity $\geq$ 10 mm (with solid component $\leq$ 5 mm) | Risk of preinvasive or minimally invasive disease high; refer; surgical biopsy and/or resection vs annual screen if stable; PET and biopsy are not routinely recommended (high false negatives) |
| | **4C. Likely malignant**<br>1. Worrisome persistence; nonresolving part solid nodule $\geq$ 10 mm (solid portion $>$ 5 mm)<br>2. Worrisome change; malignant growth rate in solid nodule or portion<br>3. Worrisome baseline; lobulated or spiculated entirely solid nodule $\geq$10 mm with no inflammatory CT or clinical features, no ground-glass border | Risk of malignancy very high in high-risk screening population<br>Refer<br>Benefit of PET is in staging not diagnosis<br>Negative PET, bronchoscopy, or biopsy is discordant and should prompt multidisciplinary review |
| 5. Malignant by CT | Invasion of chest wall or mediastinum. | As per 4C |
| 6. Tissue malignant | Eg, positive FNA, core, bronchoscopy, or surgical resection | False-positive results possible but very rare with FNA; assuming that the patient remains a treatment candidate and no regular CT for disease surveillance, continued screening is recommended |

CT = computed tomography; FNA = fine needle aspiration; LDCT = low dose CT; LU-RADS, Lung-Reporting and Data System; PET = positron emission tomography.

knowledge, this includes nodules with benign patterns of calcification (entirely calcified, a complete calcified ring, or central calcification); solid nodules ≥5 mm that demonstrate no or minimal growth over at least a 2-year period and subsolid nodules ≥5 mm that demonstrate no growth over at least a 5-year period [15]; perifissural opacities with benign features (ie, smooth well-defined subcentimetre solid nodules located along a fissure and with an oval, lentiform, or polygonal shape [Figure 1] [16,17]); fat-containing nodules that meet criteria for hamartoma (−40 to −120 HU in at least 8 voxels) [18,19]; round atelectasis (abuts pleural surface and is associated with volume loss, pleural abnormality, and bronchovascular swirling) [20]; and nodules with a specific benign diagnosis obtained by core biopsy. The category also includes nodules of any density that measure <5 mm (approximately 60 $mm^3$) [21–23]. The unifying principle for this diverse list of opacities is that there appears to be no benefit for workup before the next screening CT. Ground-glass nodules smaller than 5 mm are often transient and inflammatory. When persistent, these nodules are often foci of atypical adenomatous hyperplasia and do not require follow-up prior to the next screening CT [17].

Analysis of solid nodules <5 mm has shown a malignant rate of 0.0%-0.2% after 1 or 2 years of follow-up [21,24,25]. The long-term malignant rate of these tiny nodules is less well documented. In Milan, a 4-year study of 1035 smokers at high risk found that 3 of 238 nodules ≤5 mm on the baseline examination were eventually determined to be malignant [26]. Even if a <5-mm nodule is malignant, there appears to be no benefit in follow-up earlier than 1 year because growth is difficult to reliably detect in small nodules, and 1 year later the malignancies remain T1N0 [14,21,24,26,27]. Based on data from the National Lung Screening Trial, the Dutch-Belgian Randomized Lung Cancer Screening Trial (NELSON), the Mayo Clinic study and the British Columbia Cancer Agency study, the risk of a lung cancer diagnosis within 2 years of a category 1 or 2 examination is estimated at 0.2%-0.3% [22,25,28–30] and is largely influenced by the underlying risk of the patient for lung cancer.

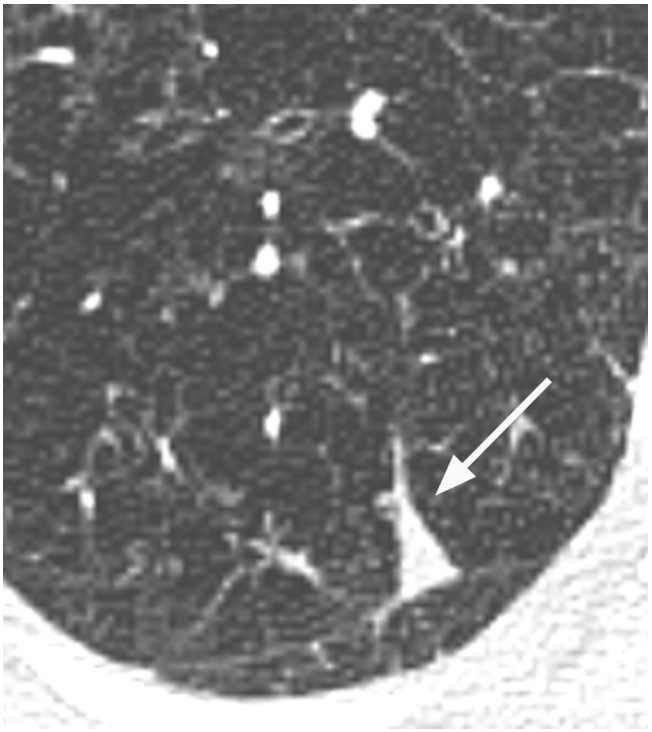

Figure 1. Perfissural opacity. Axial baseline computed tomography, demonstrating a 10 × 6-mm, solid, well-defined nodule (arrow) along the path of the right major fissure in a patient who was a high-risk smoker. This is characterized as Lung Reporting and Data System 2 (benign nodule).

*Reporting and Management of LU-RADS 2 Nodules*

Patients and referring physicians should be made aware that, even though a nodule is present, the likelihood of a lung cancer diagnosis in the next 2 years is extremely low. In fact, the risk of malignancy for a screening participant at high risk is now much lower than immediately before the CT. The CT report should state that referral or any other workup is not indicated. Greater care must be taken, however, if a screening program includes patients with prior malignancy. For a screening participant at risk for pulmonary metastases (such as survivors of invasive breast cancer), an earlier follow-up may be necessary for tiny solid nodules. The limitations of screening, as discussed for category 1, should be made clear. The report also should include a recommendation to return to regular screening and specific information regarding the timing of the next screening CT.

## LU-RADS 3

### Finding: Indeterminate Nodule

### Management: Follow-up Low-Dose CT

Category 3 nodules require follow-up CT before risk can be determined. A more advanced workup should be delayed until the behavior of the nodule on serial CT can be assessed. This category can be divided into new or nonenlarging small nodules (5-9 mm, approximately 60-500 $mm^3$) (S) and large nodules (≥10 mm or ≥500 $mm^3$) with any possibility of a transient inflammatory process (L). In both situations, the follow-up CT can be performed with the dose-reducing strategies of screening CT. Some screening centres may decide to limit radiation by confining the repeat CT to the area of interest.

*LU-RADS 3S. Small Nodules That Require Follow-up*

This includes nodules 5-9 mm that have not yet demonstrated 2 years of stability (for solid nodules) or 5 years of stability (for subsolid nodules). Several follow-up schedules have been published, including the Fleischner guidelines for solid nodules [31] and subsolid nodules [32]. Some screening-specific schedules, including those used by the International Early Lung Cancer Action Program (I-ELCAP) and NELSON, follow up new nodules on repeated annual scans more closely than those nodules seen on the baseline

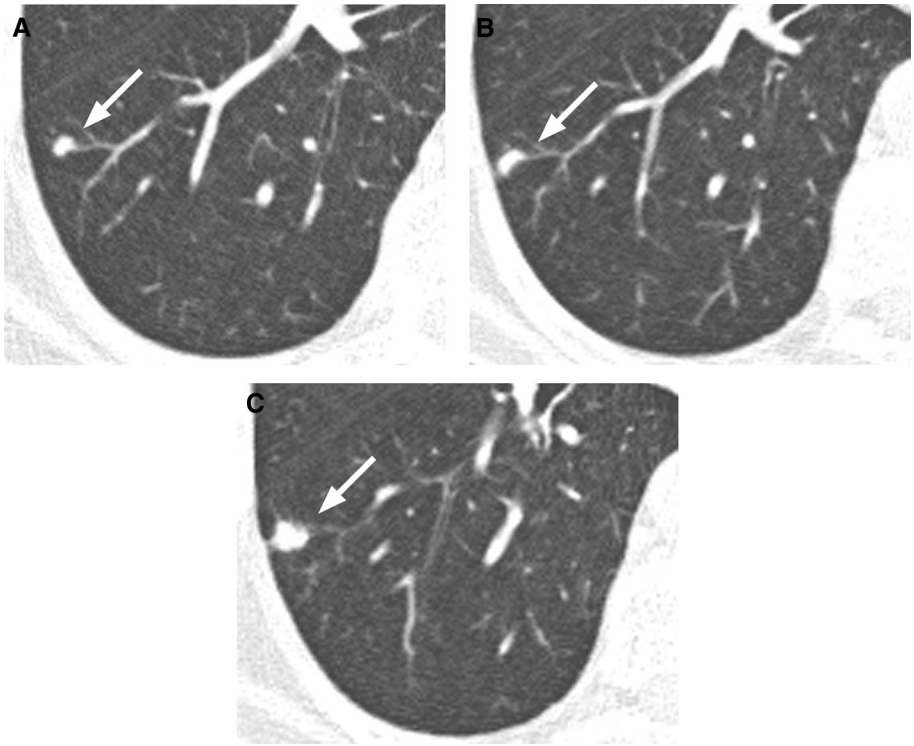


Figure 2. Progressively enlarging solid nodule. (A) Baseline screening computed tomography (CT), demonstrating a solid, 6 × 5-mm nodule in the right lower lobe (arrow). This is a Lung Reporting and Data System (LU-RADS) 3S nodule (indeterminate, requires serial CT). No enlargement was demonstrated on follow-up screening-type CT 3 months later (not shown), and the nodule remains category 3. (B) Follow-up CT 12 months after baseline, showing enlargement to 9 × 6-mm and the nodule (arrow) becomes LU-RADS 4C (likely malignant). The team was reluctant to proceed with surgery for a subcentimetre nodule, and a continued follow-up low-dose CT was performed. (C) The last CT before resection, 26 months after baseline examination, demonstrating further enlargement to 10 × 9 mm (arrow). Resected specimen revealed stage IA adenocarcinoma.

examination because interval malignancies are more aggressive and grow more quickly than prevalent malignancies [11,33]. LU-RADS is not designed to replace these follow-up schedules but to work with them. It is understood that different screening programs may adopt different follow-up schedules. Nodules remain in this category until they demonstrate sufficient stability to be reclassified into the LU-RADS 2 category or until they demonstrate worrisome change. If a solid nodule enlarges or a ground-glass nodule increases in density or grows to at least 10 mm, then the nodule becomes worrisome and should be reclassified as LU-RADS 4B or 4C (Figure 2).

Rates of malignancy for these small nodules are an area of growing research. A recently published risk model allows physicians to assign nodule risk by using patient demographics (including age) and nodule characteristics (including size and density) [34]. Data from the British Columbia Cancer Agency places the malignant rate at 1% for nodules in the 4-10 mm size [25]. The National Lung Screening Trial found a 2.4% risk of lung cancer in nodules between 7 and 10 mm but only a 0.3% risk in nodules between 4 and 6 mm [30]. Regardless of baseline size, once growth is identified, the risk increases substantially. By emphasizing the importance of serial CT for evaluation of LU-RADS 3S type nodules, the NELSON screening trial was able to reduce the percentage of positive screening scans to 2.6% relative to the 24.2% rate in the National Lung Screening Trial [23,29].

Based on analysis of screen-detected nodules, a volume-doubling time of less than 400 days in a solid nodule is generally considered consistent with a malignant growth rate [35]. Ground-glass neoplasms grow more slowly. Malignant nodules can grow irregularly with 1 part of the nodule remaining stable and other parts enlarging (Figure 3). In comparison with the most-remote CT images available, visual assessment of the proximity to adjacent structures and either multiplanar imaging or volumetric analysis may allow more confident identification of subtle growth. Because malignancies may occasionally regress in size transiently, a mild decrease in size on a single CT may not allow confident diagnosis of a benign etiology, and further follow-up as clinically indicated is recommended [36].

### *Reporting and Management of LU-RADS 3S Nodules*

Patients and referring physicians should be made aware that serial CT is the best way to evaluate these small non-enlarging nodules. Many follow-up schedules are available, including those released by the Fleischner Society [31,32]. The timing and frequency of follow-up is primarily influenced by size, with larger nodules in this group requiring shorter-interval follow-up CTs. The optimal timing interval

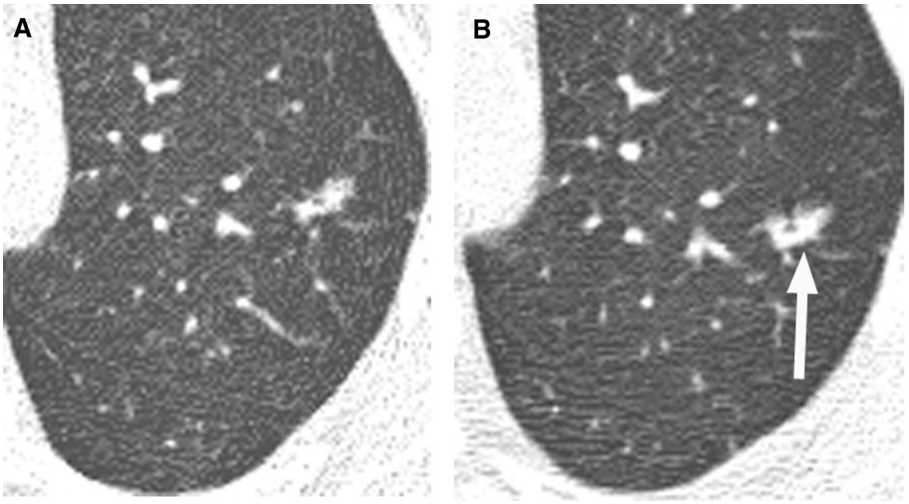


Figure 3. Subtle growth in adenocarcinoma. (A) A 11 × 5-mm (mean, 8 mm) solid nodule is seen on screening baseline computed tomography (CT) and is characterized as Lung Reporting and Data System (LU-RADS) 3S (indeterminate; requires serial CT). (B) Follow-up screening type CT was performed at 3 months (not shown) and showed no enlargement. CT at 9 months, showing no change in the maximum dimension. Careful inspection demonstrated subtle growth posteriorly (arrow), and the nodule is now classified as LU-RADS 4C (likely malignant). Pathology demonstrated invasive adenocarcinoma with lepidic features.

for follow-up CTs remains to be determined through ongoing research on existing lung cancer screening cohorts. For some nodules, the follow-up interval will coincide with the screening interval. Due to the low likelihood of malignancy, the risk of harm, and the difficulty with obtaining diagnostic results, additional workup of these small nodules is not recommended. Reports should note the low risk of malignancy and include a specific recommendation regarding the timing of the next CT.

*LU-RADS 3L. Large Nodules That Require Follow-up*

This includes all new or baseline nodules that measure at least 10 mm (approximately 500 $mm^3$) for which there are any CT or clinical features that suggest any possibility of a transient inflammatory process. Radiologists should strongly consider using this category for a new large solid nodule not seen, even in retrospect, on the last screening examination and for any new or baseline large subsolid nodule. The purpose of this category is to help ensure that transient inflammatory processes are not misidentified as malignant. Many guidelines suggest that biopsy, positron emission tomography (PET), or resection be considered for nodules that measure at least 10 mm [1,31]. However, for new or baseline nodules in which an inflammatory etiology is possible, short-interval screening-type CT often demonstrates resolution (Figures 4, 5). A large (≥10 mm) nodule that suddenly appears between annual screening CTs must have a short volume-doubling time (<30 days) and, therefore, is more likely to be a transient nodule than an equivalent-size nodule

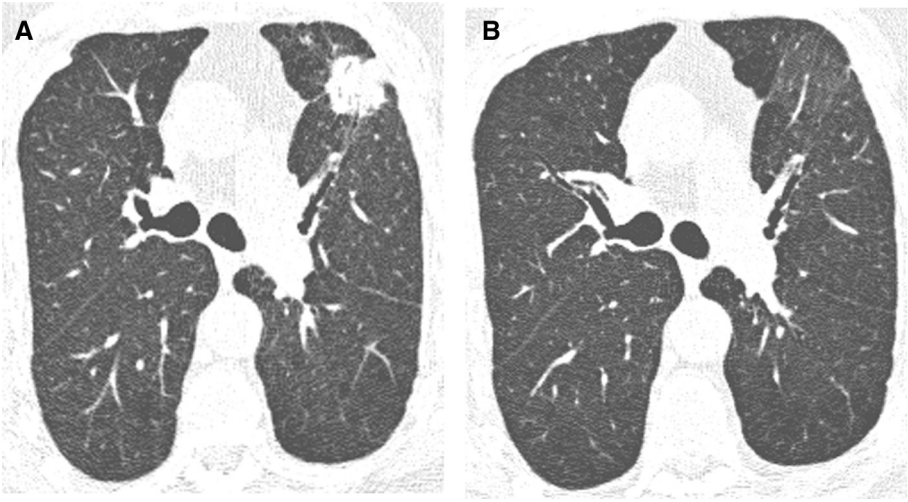


Figure 4. Transient solid nodule. Baseline screening computed tomography (CT) of a patient who was high risk and asymptomatic, demonstrating a 27 × 28-mm solid nodule in the left upper lobe. The nodule contains air bronchograms and should be classified as Lung Reporting and Data System (LU-RADS) 3L (indeterminate; requires follow-up CT). (B) Follow-up CT 8 weeks later, demonstrating near-complete resolution (LU-RADS 1).

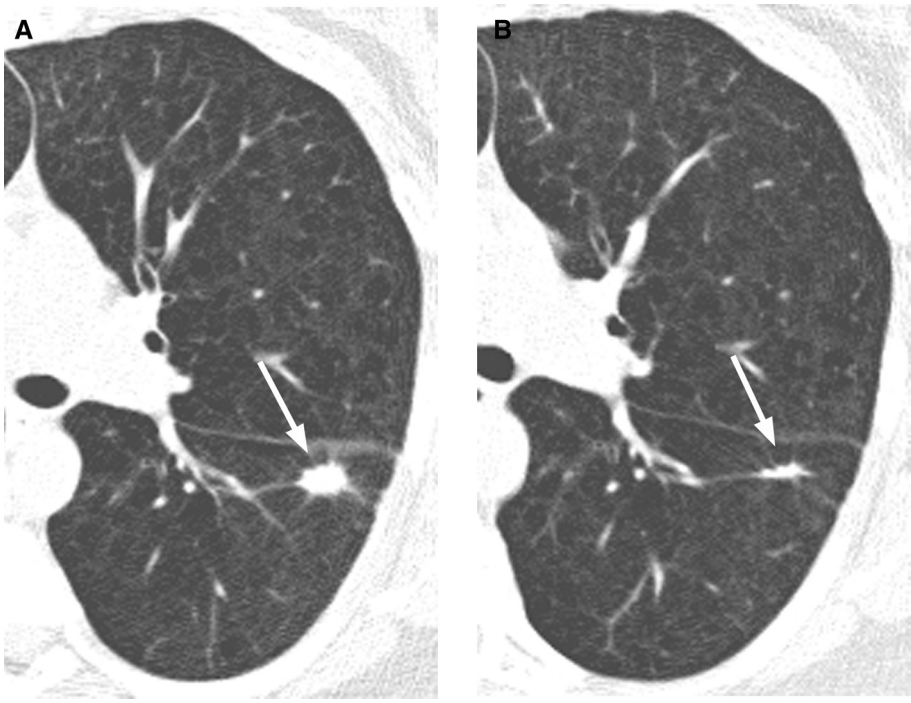


Figure 5. Transient spiculated nodule in a patient with a recent history of pneumonia. (A) Baseline computed tomography (CT) in a patient who was asymptomatic, demonstrating a solid spiculated 15 × 10-mm nodule in the left lower lobe (arrow). The patient was found to have had consolidation in the left lower lobe on a chest radiograph obtained for cough and fever 3 months before the baseline CT, and, therefore, the nodule was classified as Lung Reporting and Data System (LU-RADS) 3L (indeterminate; requires serial CT). (B) Follow-up 6 weeks later, demonstrating marked size decrease (arrow). Classification is now LU-RADS 2.

seen on a baseline screening CT [37,38]. Data from screening research suggest that short-interval follow-up of new large nodules seen on annual screens can avoid biopsy or other workup [14,38]. This strategy for large nodules has also been evaluated on baseline scans in the Canadian arm of I-ELCAP. In this study, 95% of patients with a positive baseline scan had short-interval follow-up CT, and 26% demonstrated resolution or decrease in nodule size [39], which confirmed the transient inflammatory nature of these indeterminate large nodules.

This concept is particularly important for subsolid nodules and nodules with an indistinct border. From 44%-70% of screen-detected subsolid nodules resolve [37,40]. The Fleischner Society guidelines for subsolid nodules highlights this fact and recommends that all new or baseline subsolid nodules have a short-interval follow-up, even when they measure ≥10 mm [32]. If these nodules demonstrate no improvement on subsequent examinations, the likelihood of malignancy is much higher (see LU-RADS 4B).

The decision to place a large nodule (≥10 mm or 500 $mm^3$) into LU-RADS category 3 may be difficult. The likelihood that a nodule is transient is increased if it is new, has indistinct or ground-glass margins, is at least partially of ground-glass density, is one of many new nodules, is clustered, is associated with other CT features of inflammation (eg, multifocal or tree-in-bud opacities), or if there is a history of respiratory infection in the past 3 months (Figure 5) [37,38,40]. A recent history of respiratory symptoms, hospital admission, emergency department visit, infectious symptomatology, and chest pain should be reviewed and made available to the reporting radiologist. Screening centres cannot rely on accurate requisitions and must obtain clinical information directly from the patient.

*Reporting and Management of LU-RADS 3L Nodules*

A 6-12−week follow-up interval has been suggested based on the assumption that 6-12 weeks will be sufficient to allow most inflammatory processes time to at least partially resolve but not so long as to substantially increase the risk that a lung malignancy will significantly progress in stage. A PET can be misleading and should be specifically avoided in this category until follow-up CT has been preformed. An active inflammatory process, even if asymptomatic, may show high levels of fluorodeoxyglucose (FDG) avidity. For a subsolid nodule, a high level of FDG avidity is more often demonstrated in benign inflammatory processes than in malignant ones [41]. Consider that a large new nodule has a higher likelihood of a false-positive PET result (due to the possibility of active inflammatory disease) than the same size nodule that has grown over the past year.

With the advent of high-quality thin-section CT and the continuous improvements in dose reduction, the value of serial screening-type low-dose CT as a diagnostic tool, rather than merely a screening tool, has received some attention [42-44]. Although serial CT cannot replace other workup

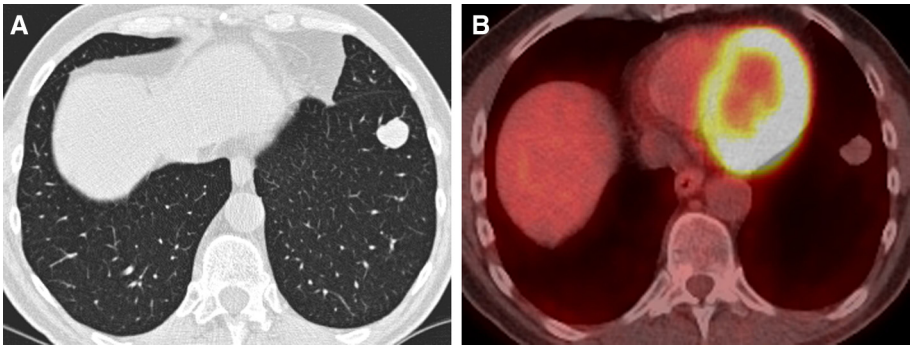


Figure 6. Lung Reporting and Data System (LU-RADS) 4A nodule (suspicious, low risk of malignancy). (A) Unenhanced computed tomography (CT), demonstrating a 17-mm, well-defined, roughly spherical, solid nodule with minimal lobulation. The nodule was thought to represent a hamartoma but macroscopic fat could not be confirmed by CT. The lesion was categorized as LU-RADS 4A (suspicious; low risk of malignancy). (B) Fluorodeoxyglucose positron emission tomography (PET), demonstrating no uptake. The negative predictive value of the PET for a low-risk solid nodule in a patient who is high risk is very good. In conjunction with the surgeon, the patient chose not to have the nodule resected. After 2 years of stability, it is reclassified as LU-RADS 2 (benign nodule). This figure is available in colour online at http://carjonline.org/.

strategies, it can be a less-invasive, less-expensive, and lower-radiation approach to the diagnostic evaluation of screen-detected nodules. If short-interval follow-up fails to demonstrate any resolution, then the large nodule becomes worrisome and can be reclassified into category 4. If the opacity decreases in size but does not resolve, then the radiologist may choose to follow up the lesion again before returning to the regular screening interval.

## LU-RADS 4

### Finding: Suspicious Nodule

### Management: Depends on Subcategory

See 4A, 4B, and 4C.

## LU-RADS 4A

### Finding: Suspicious; Low Risk of Malignancy

### Management: Workup

This category includes large solid nodules (10-25 mm), with benign but not definitive CT features, such as a well-defined roughly spherical nodule without microlobulations (Figure 6). Examples include a hamartoma without macroscopic fat or a noncalcified granuloma. In this category, every effort possible should be made to obtain prior imaging because this may establish a reassuring chronic nature. Depending on the location of the nodule, prior plain films or cross-sectional imaging not only of the chest but also of the abdomen, neck, or shoulder, for example, may reveal the nodule. Nodules in this category may grow; a volume-doubling time of more than 400 days for a solid nodule is generally regarded as consistent with benign disease [35]. It should also be noted that metastatic disease (especially solitary deposits) can demonstrate a similar appearance on a single CT; screening centres should be aware of any prior diagnoses of malignancy.

*Reporting and Management of LU-RADS 4A Nodules*

These nodules can pose a diagnostic challenge to the radiologist. Although PET may be of limited diagnostic use for other nodule categories, the negative predictive value of PET (ie, the likelihood that a negative result is correctly negative) is high for solid nodules in this category because the pretest probability of malignancy based on the CT features is low (Figure 6) [19]. The positive predictive value of PET will depend on the local rate of granulomatous disease, a common cause of false-positive examinations [44,45]. Even if workup is reassuring and suggests a benign etiology, continued serial CT is recommended. Once minimal or no growth is confirmed at the 2-year follow-up, these large nodules can be reclassified as LU-RADS 2. Tissue diagnosis is another option in this category, and a core biopsy is preferred because it has a higher likelihood of providing a specific benign etiology compared with fine needle aspiration [46]. Core biopsy with a specific benign etiology can allow the nodule to be classified as benign (LU-RADS 2).

Patients with category 4A nodules often require referral (pulmonologist or thoracic surgeon, depending on local practices). Many of these nodules will not require surgery, but the decision process should allow input from the patient after a complete discussion of the risks and benefits. In addition, a more thorough clinical assessment may reveal a benign etiology. The rate of malignancy in this category will be dependent on the local rate of granulomatous disease and the results of the workup.

## LU-RADS 4B

### Finding: Suspicious; Likely In Situ or Minimally Invasive Adenocarcinoma

### Management: Surgical Biopsy or Follow-up; Depending on the Patient

Nodules in this category measure $\geq$10 mm (>500 mm$^3$), are persistent (fail to resolve or improve on follow-up CT),

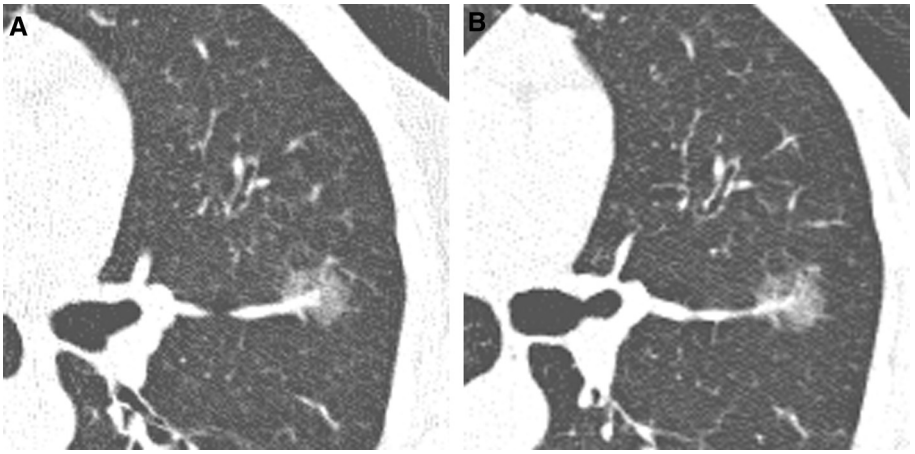


Figure 7. Persistent ground-glass opacity. (A) A 17-mm pure ground-glass opacity on baseline computed tomography (CT) is categorized as Lung Reporting and Data System 3L (indeterminate; requires serial CT). (B) Three months later, the CT shows no change, and the nodule becomes category 4B (likely low-grade adenocarcinoma). This 68-year-old woman underwent microcoil-guided resection. Pathology demonstrated stage IA adenocarcinoma in situ.

and are either entirely of ground-glass density or of ground-glass density with a solid portion that measures not more than 5 mm. Although these nodules have a neoplastic rate of 75%-80% [47−49], they often represent foci of preinvasive or minimally invasive disease; persistent pure ground-glass nodules have a high likelihood of adenocarcinoma in situ (Figure 7) and part-solid nodules with a solid component that measures $\leq$5 mm have a high likelihood of minimally invasive adenocarcinoma [50]. When resected, the 5-year survival rate for these neoplasms is near 100% [48,51,52]. The natural history of these lesions is less well understood, but certainly the slow growth rate suggests a much less aggressive behavior than other forms of lung cancer [53]. When multiple persistent ground-glass nodules are present, these likely represent multiple primary lesions rather than metastatic disease [54]. Two years of stability does not confirm benign etiology in this category [55−57]. Ground-glass neoplasms grow slowly, often with a doubling time of $>$600 days (Figure 8) [58,59]. A comparison should be made to the most recent prior CT and the most remote CT available.

*Reporting and Management of LU-RADS 4B Nodules*

Workup of these lesions, due to their lack of aggressive nature, may appear counterintuitive to those not familiar with screening. Neoplastic lesions in this category are unlikely to demonstrate high levels of FDG avidity [60−62]. PET is not indicated for staging purposes in this category because sub-solid nodules with a solid portion that measures not more than 5 mm are highly unlikely to demonstrate metastases

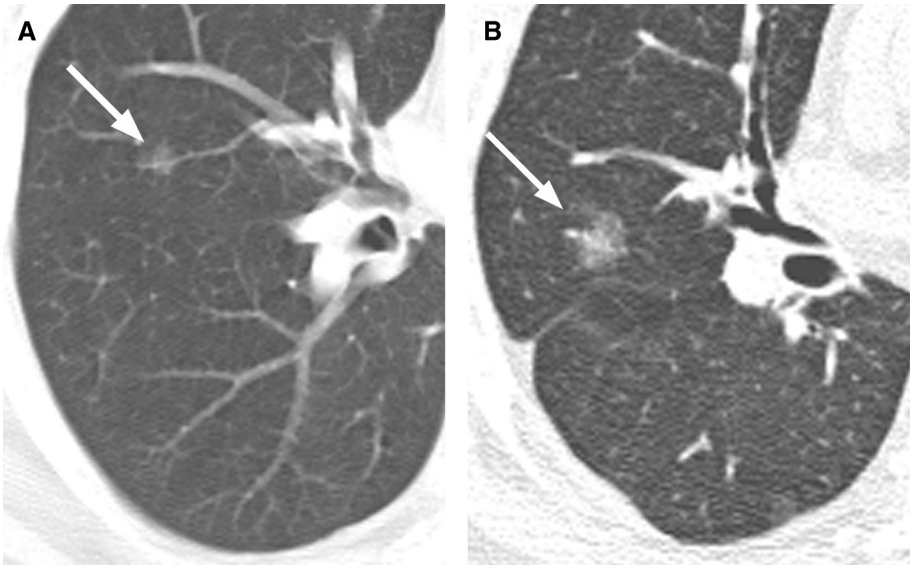


Figure 8. Enlarging ground-glass opacity. (A) Baseline computed tomography (CT), demonstrating an 8-mm ground-glass opacity (arrow) categorized as Lung Reporting and Data System (LU-RADS) 3S (indeterminate; requires serial CT). (B) CT obtained 5 years later, showing enlargement (arrow) to 14 mm (LU-RADS 4B, likely low-grade adenocarcinoma). Segmentectomy demonstrated adenocarcinoma in situ.

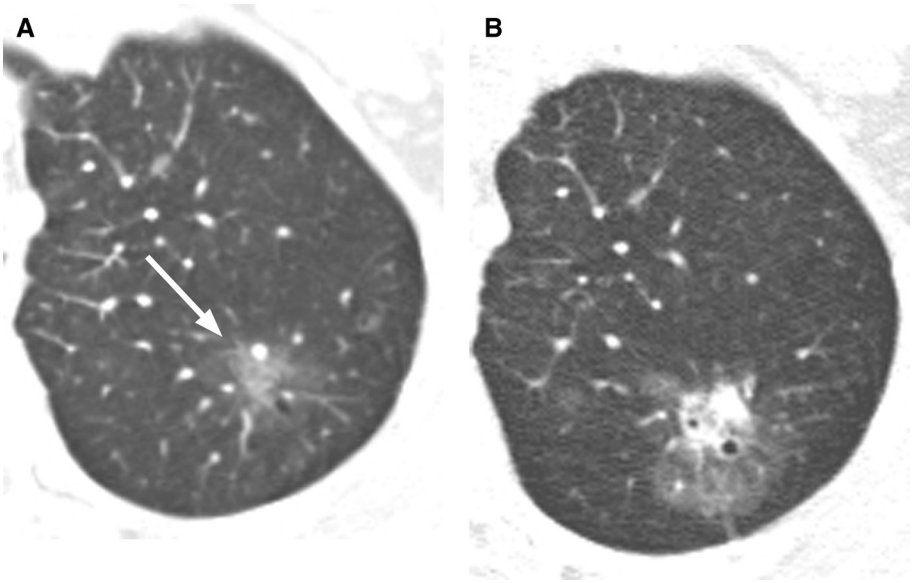


Figure 9. Subsolid nodule, demonstrating worrisome change. (A) An annual computed tomography (CT), demonstrating a persistent 14-mm pure ground-glass opacity (arrow). This is a Lung Reporting and Data System (LU-RADS) 4B nodule (likely low-grade adenocarcinoma). The patient was not referred to surgery and did not return for recommended follow-up. (B) CT 3 years later, showing the nodule has enlarged to 34 mm and contains a 12 mm solid portion. The nodule is now classified as LU-RADS 4C (likely malignant).

[49,50]. Many experts argue that there is no role for percutaneous sampling of subsolid nodules with a solid portion that measures ≤5 mm [63] because the yield is low [64]. The Fleischner Society guidelines recommend percutaneous core biopsy in subsolid nodules only to assist nonsurgical treatment [32].

Routine resection of category 4B nodules has been criticized for contributing to lead time bias and overdiagnosis of indolent cancer in screening trials [65]. Although these neoplasms grow slowly, they can progress to invasive adenocarcinoma (Figure 9) [66,67]. Regardless of the controversy regarding management of category 4B nodules, detection of these nodules should prompt referral to thoracic surgeon or pulmonologist/respirologist. Ideally, treatment and management decisions will be made as a team and in conjunction with the patient. Wedge resection may be an option for ground-glass nodules that measure >10 mm, especially when enlarging. Microcoil localization may assist resection because these nodules are often difficult to identify intraoperatively [68]. Patients who are not to receive initial resection should have yearly follow-up with a screening-type CT to monitor for an increase in overall size and in size of the solid component. Nodules with a growing solid component are more likely to be aggressive and should be reclassified into category 4C [69–71].

## LU-RADS 4C

### Finding: Suspicious; Likely Malignant

### Management: Confirm, Stage, and Treat

Category 4C nodules have CT or serial CT features that are very worrisome for invasive malignancy. These nodules are sufficiently worrisome that negative FNA, negative bronchoscopy, negative dynamic enhanced CT, and/or negative PET are discordant, and results should be treated with caution. This concept will be recognizable to those familiar with the BI-RADS category 4C. Worrisome CT features include (1) worrisome persistence: a lack of any improvement after short-interval follow-up of a large (≥10 mm) part-solid nodule with a solid portion of at least 5 mm; (2) worrisome growth: malignant growth rate of a solid nodule or solid portion of a nodule (Figures 2, 3, 9); or (3) worrisome baseline: a baseline well defined (ie, no ground-glass border) lobulated or spiculated solid nodule that measures at least 10 mm (500 $mm^3$) with no CT features or clinical possibility of inflammatory disease (Figure 10). Nodules in this category do not have benign CT features (ie, are not category 2 or 4A). Category 4C nodules in screening patients at high risk are almost always malignant. In areas endemic for granulomatous disease or fungal infection, the rate of malignancy in this category will be lower [44,45].

### *Reporting and Management of LU-RADS 4C Nodules*

Category 4C nodules should prompt urgent referral and definitive workup. However, negative PET-CT, negative FNA, and negative bronchoscopy may represent false-negative findings in this category, and any discordant results should prompt discussion. The primary benefit of PET for these screen-detected high-risk nodules in patients at high risk is in staging, not diagnosis [72,73]. Another possible benefit of PET in this category is in the evaluation of the patient with multiple part-solid nodules thought to represent multiple primary malignancies. PET can assist surgical decisions by identifying the more aggressive of the lesions [60].

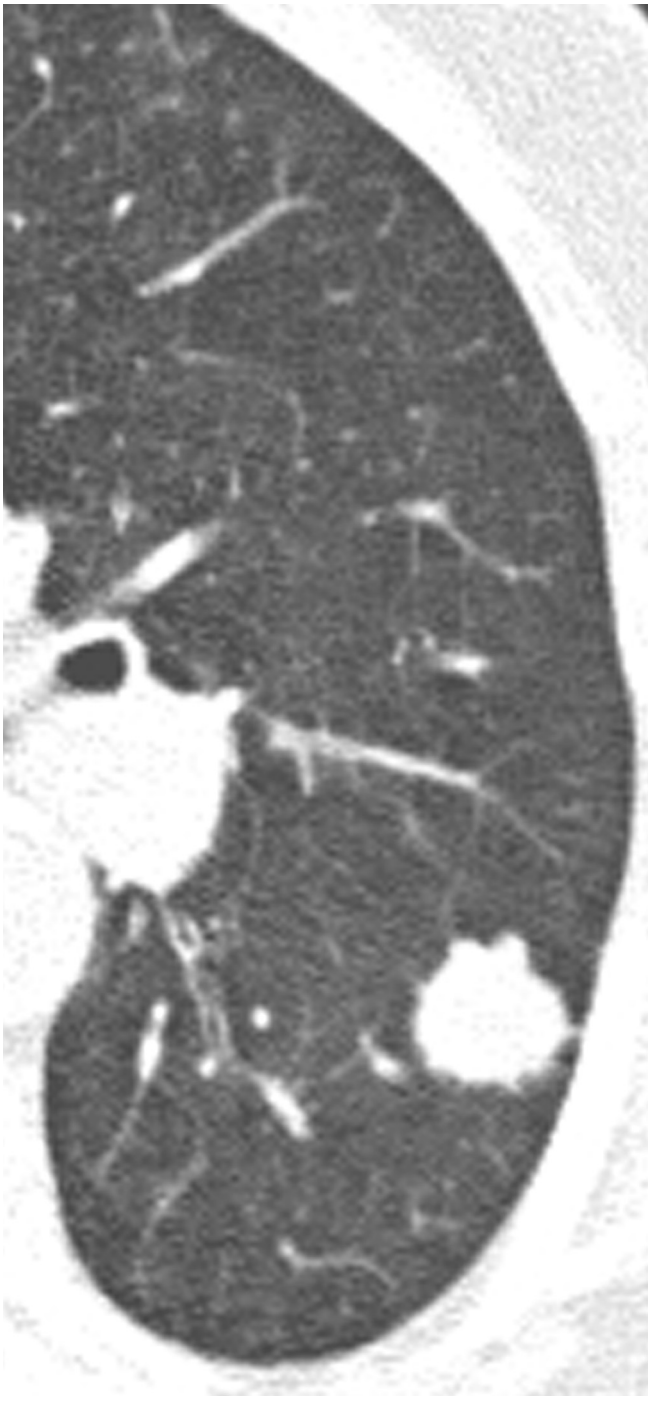

Figure 10. Worrisome baseline. Baseline computed tomography in a patient at high risk and asymptomatic, demonstrating an entirely solid, lobulated, 20-mm nodule with no ground-glass component or border. The nodule was classified as Lung Reporting and Data System 4C (likely malignant). Tissue diagnosis was positive for non−small-cell lung carcinoma.

Conventional bronchoscopy is of limited use in evaluation of peripheral screen detected nodules [28].

If percutaneous biopsy is to be performed for a part-solid lesion, then the solid portion should be targeted. The solid portion in a malignant part-solid nodule often represents areas of invasive adenocarcinoma in an otherwise in situ neoplasm [54,57]. Prognosis is better predicted by the percentage of the nodule that is solid and by the size and growth of the solid portion rather than the size and growth of the nodule as a whole [69−71]. Therefore, for part-solid nodules, reports should include size and growth information both for the nodule as a whole and the solid component. A comparison should be made both to the most recent prior CT and to the most remote CT available.

## LU-RADS 5

### Finding: Malignant by CT

### Management: Confirm, Stage, and Treat

Category 5 lesions demonstrate frankly malignant behavior by CT. Examples include lesions that are invading the chest wall or the mediastinum. The risk of malignancy is very high for this category. Rarely, aggressive infectious processes or inflammatory infiltrative processes (such as actinomycosis or fibrosing mediastinitis) can result in a similar CT appearance. However, in the high-risk screening population, category 5 lesions will overwhelmingly represent malignancy.

*Reporting and Management of LU-RADS 5 Nodules*

Prompt referral or discussion with thoracic surgery or pulmonologist/respirologist is recommended so that resectability and options for tissue diagnosis can be assessed as soon as possible. If PET is obtained for any reason, then negative results should be considered discordant with the CT findings, and the case should be discussed. For unresectable tumours, tissue diagnosis is often necessary before radiation treatment or chemotherapy. Negative tissue sampling or negative bronchoscopy would be considered discordant and should be discussed.

## LU-RADS 6

### Finding: Tissue-Proven Lung Malignancy

### Management: Stage and Treat

Category 6 lesions show positive results on bronchoscopy, percutaneous tissue sampling, or surgical resection. Although patients with category 6 nodules would no longer be considered screening participants, the category is included to help facilitate data analysis. Many of these patients will have follow-up imaging, and a portion will not undergo surgical resection. In addition, because these patients have an elevated risk of a second primary bronchogenic cancer [74], they should remain in the screening program if they remain candidates for treatment and if they are not already receiving regular follow-up CT. Continued screening after resection is especially beneficial for patients who have had definitive treatment of early stage disease, particularly in situ or minimally invasive adenocarcinoma.

*Reporting and Management of LU-RADS 6 Nodules*

These patients require definitive staging and treatment.

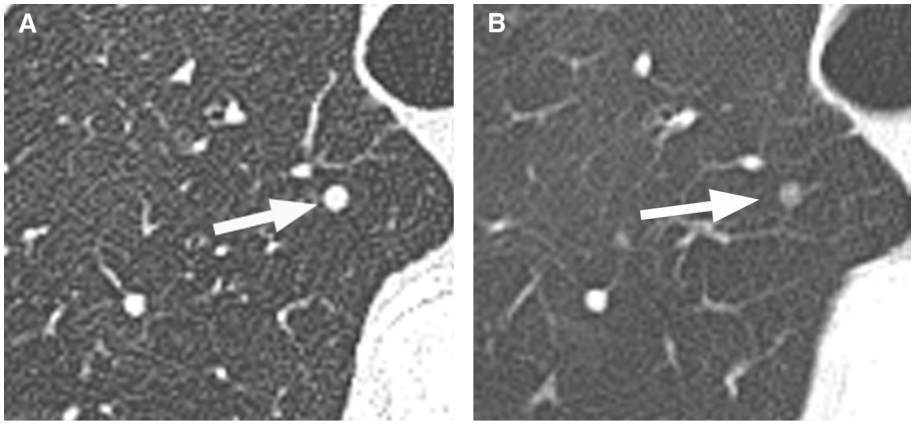


Figure 11. Effect of volume averaging on perceived nodule density. (A) Unenhanced computed tomography, with 1-mm slice thickness reconstructed axial images, demonstrating a 4-mm solid nodule (arrow). (B) When the same source data are reconstructed at 5-mm slice thickness, the nodule appears as ground glass (arrow).

## Technical Notes

Nodule size is measured on high spatial frequency images (lung and/or bone algorithm) and is defined as the mean of the longest diameter and its perpendicular diameter on a single transverse CT image. Diameter differences <2 mm have been shown to be unreliable and do not allow confident identification of nodule growth or regression [75]. Whereas volumetric analysis can have some practical limitations, it has been shown to be more accurate and reproducible than 2-dimensional measurements [76] and provides superior data for calculation of nodule doubling time [23]. With the 512 × 512 viewing matrix of current CT scanners and a full-body field of view (eg, 30 cm), the resultant pixel size (0.68 mm) is too large to allow accurate submillimetre measurement. Stability cannot be assessed unless all prior CTs, most importantly, the earliest CT, are reviewed. It should be noted that compared with noncontrast examinations, stable nodules on intravenous contrast-enhanced images may appear to have grown compared with previous noncontrast enhanced images [77].

A 1- or 2-mm–section thickness reconstruction is essential to minimize volume-averaging effects. Thin section improves the evaluation of nodule growth, nodule density, and changes in nodule density (Figure 11). Thin-section collimation (1-2 mm) intermediate spatial frequency images (standard and/or mediastinal algorithm) provide improved measurement of the solid component of nodules and allows identification of focal fat and calcification that may be missed on thick sections. Due to image noise effects, CT density measurements of fat and calcification should be obtained by using intermediate spatial frequency images. Changes in scanner kVp and the beam-hardening effects of shields (breast and thyroid) may lead to inaccuracies in density measurements anywhere in the field of view [78,79].

It also must be emphasized that, given the prebooked nature of screening CTs, clinical information on the requisition may be out of date. Clinical information obtained from the patient at the time of the CT regarding any recent respiratory, infectious, or inflammatory symptoms; history of malignancy; history of radiation to the lung; and prior lung imaging may be highly useful. Finally, every point of contact with the patient should be used to assist or support smoking cessation.

## Conclusion

Given the frequency of pulmonary nodules in the high lung-cancer risk CT screening population, there is substantial risk of incomplete communication and consequent nodule overinvestigation. The aim of LU-RADS is to provide a more standardized and informative CT report by classifying nodules into 1 of 6 categories, with associated management strategies. The evolution of high-quality thin-section CT imaging allows the LU-RADS classification to highlight the important diagnostic role of nodule change on serial low-dose screening CTs. Thus, the information obtained by using biopsy, PET, bronchoscopy, and intravenous contrast-enhanced CT adds to rather than supersedes that available from the screening CT data set. Improved classification of screen-detected nodules by using LU-RADS should reduce the costs and risk of unnecessary workup and improve the cost-effectiveness of proposed lung cancer screening programs.

## Acknowledgements

Many radiologists, thoracic surgeons, and pulmonologists reviewed this manuscript and provided invaluable suggestions. We especially thank Dr Anand Devaraj, Department of Radiology, St George's Hospital, London, United Kingdom. We thank Stacey Pyke, Diana Sonnichsen, Louise MacDonald and Melissa Butler for their assistance in preparing this manuscript.

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