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Shades of Gray
Subsolid Nodule Considerations and Management
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Subsolid nodules are common on chest CT imaging and may be either benign or malignant. Their varied features and broad differential diagnoses present management challenges. Although subsolid nodules often represent lung adenocarcinomas, other possibilities are common and influence management. Practice guidelines exist for subsolid nodule management for both incidentally and screening-detected nodules, incorporating patient and nodule characteristics. This review highlights the similarities and differences among these algorithms, with the intent of providing a resource for comparison and aid in choosing management options.

KEY WORDS: American College of Chest Physicians; British Thoracic Society; Fleischner Society; ground-glass; subsolid

Subsolid nodules (SSNs) include both pure ground-glass nodules (GGNs) and part-solid nodules (PSNs) and are increasingly detected on chest CT scans. In addition to the spectrum of primary adenocarcinoma of the lung, potential diagnoses include a number of alternate malignancies as well as benign lesions.

A range of imaging techniques and clinical concerns need to be considered when constructing differential diagnoses and establishing management guidelines. Of particular concern is the correlation among various morphologic CT appearances, including attenuation, shape, and internal complexity, in characterization and serial assessment for potential growth. In this regard, technical factors may profoundly influence nodule detection and encourage consistency in nodule assessment and reporting.

To date, multiple management algorithms have been developed to address these challenges, in both screening and nonscreening populations. These include those of the American College of Chest Physicians (CHEST), the British Thoracic Society (BTS), the Fleischner Society, the American College of Radiology (ACR), and the National Comprehensive Cancer Network (NCCN).

Despite considerable overlap, including prioritization of shared decision-making, no one algorithm, either for screen-detected or incidentally identified nodules, is universally accepted. The current review compares and

ABBREVIATIONS: ACR = American College of Radiology; BTS = British Thoracic Society; CHEST = American College of Chest Physicians; GGN = ground-glass nodule; IELCAP = International Early Lung Cancer Action Project; NCCN = National Comprehensive Cancer Network; PSN = part-solid nodule; SSN = subsolid nodule

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contrasts these algorithms, providing a resource for comparison that may aid in choosing management options.

Technical Aspects of Imaging and Reporting Subsolid Nodules

Current algorithms for lung nodules share essential CT acquisition and reporting considerations, regarding slice thickness, reconstruction algorithm, display windows, and value of multiplanar reformatted images (Table 1).4,6-13

Applying consistent CT parameters enables reliable comparison across serial examinations. Full inspiratory images are universally recommended for lung nodule evaluation,9,10 with use of the lowest possible radiation exposure.6,8,10 Contrast enhancement is unnecessary.4,9 The presence of contrast increases dose and measured volume, mass, and mean attenuation of SSNs.14

Contiguous thin-section images improve nodule detection and feature evaluation,6,7 with management algorithms recommending 1-mm slice thickness and evaluation on lung windows at thinnest collimation. Mediastinal soft tissue display windows may aid in determining the presence of solid components within an SSN.11,12

Sagittal and coronal image reconstruction aids SSN detection,6,7 which may be challenging in the setting of interstitial or smoking-related lung disease. Lung cancers in interstitial lung disease most often develop adjacent to or within regions of fibrosis,15 and review of non-axial reconstructions may exclude nodularity or identify convexities typical for scarring in regions of parenchymal abnormality, such as paravertebral or apical fibrosis (Fig 1).

Maximum and minimum intensity projection images may improve detection of solid nodules and SSNs, respectively.6,16 Volume rendering6,9 and computer-aided diagnosis9 are additional tools. Computer-aided diagnosis had a higher sensitivity for SSNs than visual detection (88.4% vs 34.2%) in 2,303 baseline screening examinations from the Multicenter Italian Lung Detection trial.17

Ultimately, nodule size is fundamental when deciding on a management approach. All nodule aspects are included in overall measurement, preferably on the high-frequency, sharp reconstruction algorithm, with reporting of size in the plane of maximal dimension.10

Approaching Management Algorithms: Patient Factors

Practice guidelines addressing SSN management include those for screening-detected nodules from the American College of Radiology.4-9 These algorithms specify applicable patient populations and incorporate patient and nodule-specific risk factors for lung cancer.
Risk of malignancy is a major consideration affecting nodule management guidelines and is often based on clinical judgment. The CHEST guidelines define high (> 65%), intermediate (5%-65%), and low (< 5%) malignancy risk categories incorporating clinical factors.
### TABLE 2  Management Algorithms for Subsolid Nodules

| Variable | Incidental SSNs | Screen-Detected SSNs |
|----------|----------------|----------------------|
| **Population for which guidelines applicable** | | |
| - Individuals with SSNs | Adults aged ≥ 18 y with SSNs | Age ≥ 35 y |
| - Adults aged ≥ 18 y with SSNs | Individuals with SSNs | No active malignancy |
| - Individuals with SSNs | - Individuals with SSNs | Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
| - Age ≥ 35 y | - No active malignancy | - Non-immunocompromised |
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| - Age ≥ 35 y | - No active malignancy | - Non-immunocompr
| Variable                      | Incidental SSNs | Screen-Detected SSNs |
|-------------------------------|-----------------|----------------------|
| **Follow-up imaging intervals** | Annual surveillance:  
- Stable GGN > 5 mm  
- Stable PSN ≤ 8 mm  
Surveillance at 1, 2, and 4 y from baseline in stable SSNs with low risk of malignancy (< 10%); malignancy risk assessed by Brock model and morphology (solid component size, pleural indentation, presence bubble lucencies), as well as factors such as smoking history and history of lung cancer | Annual:  
- Stable GGN > 5 mm, and discursion of active surveillance for GGN ≤ 5 mm  
- Stable PSN ≤ 8 mm  
Every 2 y:  
- Stable GGN  
- Consider for multiple persisting < 6 mm GGNs in high-risk patients  
Annual:  
- Stable PSN  
Annual surveillance:  
- Lung-RADS 1 or 2  
6-mo surveillance (Lung-RADS 3):  
New SSN  
3-mo surveillance (Lung-RADS 4A):  
- PSN with new/growing < 4 mm solid component | Annual:  
- New or Stable GGN  
- Stable PSN ≤ 5 mm  
- Stable PSN ≥ 6 mm with 6- to 7-mm solid component |
| **Size/density threshold for escalation** | Persistent GGN:  
- > 10 mm may proceed to nonsurgical biopsy and/or surgical resection  
- Increase in size or solid component may warrant further evaluation, including consideration for resection  
Persistent PSN:  
- Persistent stable SSN at 3-mo surveillance with higher risk of malignancy (> 10%) may proceed, based on patient preference, to CT surveillance, image-guided biopsy, or resection/nonsurgical treatment  
- Increase in size ≥ 2 mm in GGN:  
- Persistent PSN > 8 mm:  
- Further evaluation with nonsurgical biopsy or surgical resection; PET may be considered for staging prior to surgical intervention | Persistent PSN > 8 mm:  
- Further evaluation with nonsurgical biopsy or surgical resection; PET may be considered for staging prior to surgical intervention  
- Persistent GGN: Consider resection if growth or solid component develops  
- Persistent PSN: Solid components ≥ 6 mm highly suspicious for invasive pathology  
- Nodules with suspicious morphology (lobular, bubble lucencies), growing | PET/CT (when solid component ≥ 8 mm) and/or tissue sampling depending on malignancy risk and comorbidities:  
- Solid component ≥ 8 mm (Lung-RADS 4B) or  
- New/growing ≥ 4 mm solid component (Lung-RADS 4B)  
Chest CT with contrast and/or PET:  
- New/growing PSN with ≥ 4 mm solid component  
- Stable PSN with ≥ 8 mm solid component |
### TABLE 2 (Continued)

| Variable | Incidental SSNs | Screen-Detected SSNs |
|----------|-----------------|----------------------|
|          | ACPP, 20134     | British Thoracic Society, 20155 | Fleischner Society, 20177 | American College of Radiology, Lung-RADS, 20198 | National Comprehensive Cancer Network, 20209 |
| Surveillance end point for stable lesions | | | | |
| ● Increase in size or solid component may warrant further evaluation, including consideration for resection | consider resection/nonsurgical treatment, or surveillance | solid component, or solid component > 8 mm may proceed to PET, biopsy, or resection | Consider biopsy or surgical excision: | |
| ● > 8 mm should proceed to PET, nonsurgical biopsy, and/or resection | ● Growth or altered morphology including new/increased solid component at 3-mo surveillance: resection or nonsurgical treatment favored over observation | | ● GGN: Growing (>1.5 mm) ≥ 20 mm | |
| ● PET may be used when solid component > 8 mm | | | ● If high suspicion of lung cancer after PET: | ○ Stable PSN with ≥ 8 mm solid component | |
| | | | ○ New/growing PSN with ≥ 4 mm solid component | |

**Surveillance end point for stable lesions**
- At least 3 y
- Limited or no follow-up may be elected by patients with life-limiting comorbidities, or those who prefer avoiding treatment for potentially indolent lung cancers

- At least 3 y for nonsolid (pure ground-glass) nodules > 5 mm, and consider ongoing annual surveillance beyond 3 y
- Consider also annual surveillance for pure GGNs ≤ 5 mm depending on clinical judgment and patient preference
- Minimum 5 y

- Age
- Life-limiting comorbidity

- Until patient is no longer a candidate for definitive treatment

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**CHEST** = American College of Chest Physicians; GGN = pure ground-glass nodule; PSN = part-solid nodule; SSN = sub-solid nodule (GGN or PSN).

4Practice guidelines addressing SSN management include those for screening-detected nodules from the American College of Radiology.

5Malignancy risk assessed by Brock model and morphology (eg, solid component size, pleural indentation, presence bubble lucencies), as well as factors such as smoking history and history of lung cancer.

7Factors, including age, comorbidities, and treatment-associated risks, should be considered.

8Endorses use of Brock calculator.
of age, smoking history, and previous cancer, and nodule features including size, margin, upper lobe location, imaging behavior (PET and serial CT imaging), and nonsurgical histopathology results. The CHEST risk categories are incorporated in the Fleischner Society guidelines, which recommend risk assignment based on the CHEST low-risk category and grouping of the intermediate- and high-risk categories. The BTS and NCCN also consider both clinical risk factors and radiologic nodule features.

Qualitative risk prediction, based on clinician judgment, or quantitative, model-based risk prediction are encouraged by the CHEST guidelines. There are several models, or probability calculators, synthesizing clinical and imaging features, such as the Bayesian Inference Malignancy Calculator, Brock, Herder, Mayo Clinic, Thoracic Research Evaluation and Treatment, and Department of Veterans Affairs models.

Each of the models is derived from specific patient populations. Model performance is optimal when applied to populations similar to those from which the model was derived. For this reason, separate CHEST consensus guidelines for Asia were developed indicating that diagnostic risk calculators may not apply to Asian patients due to the higher rate of lung cancer in women, as well as the higher prevalence of TB and environmental exposures.

The CHEST recommends the Mayo Clinic probability model in the US population, developed and validated from a patient cohort with incidentally detected nodules on chest radiography. The Department of Veterans Affairs model is similarly based on incidentally detected nodules, albeit in the higher risk veteran population. Screening data inform the Brock model, synonymous with the PanCan or Vancouver models, in reference to the screening cohorts.

Risk assessment models can be applied at multiple points in nodule management. For example, the BTS guidelines suggest risk prediction at two separate junctures along the management algorithm, initially using the Brock calculator to determine if malignancy risk is > 10%. When malignancy risk is estimated to be < 10%, BTS guidelines advise CT surveillance over biopsy or resection for SSNs. For patients who undergo further evaluation with PET/CT imaging, the BTS guidelines suggest using the Herder risk assessment model, which incorporates fluorodeoxyglucose activity with Mayo-predicted probability, to guide subsequent management.

For screen-detected nodules, Lung-RADS categorizes findings and standardizes management, and recommends the Brock calculator for risk stratifying patients with category 4B or 4X (very suspicious) lesions. Brock model inputs include age, sex, family history, emphysema, nodule size, nodule spiculation, number of nodules, lobar location, and nodule attenuation (solid, partially solid, or nonsolid).

The Brock model is the only validated model incorporating nodule attenuation and thus SSNs. Of note, the Brock model is based on a screening population (50-75 years of age) with smoking history, which may affect its performance when applied to female nonsmokers, in whom a higher incidence of SSNs/indolent lung adenocarcinomas are reported. Studies have evaluated the efficacy of models when applied to differing populations and roles, and knowledge of their performance in these scenarios is important. A future role may exist for model-based patient selection for lung cancer screening.

Management of small nodules may also be aided by the application of models. Some clinical factors associated with higher lung cancer risk are not reflected in risk models. As noted in the NCCN guidelines, COPD and interstitial lung disease are risk factors for lung cancer but are not specifically included in the Brock model. The incidence of lung cancer in patients with interstitial lung disease and COPD is nearly threefold higher than in patients with COPD alone. In the National Lung Screening Trial cohort of > 25,000 participants, those with asymptomatic interstitial abnormalities (eg, baseline reticulonodular opacities, honeycombing, fibrosis, scarring) had a higher incidence of and mortality from lung cancer.

Family history is included in both the NCCN and Brock model risk assessments. In a pooled analysis from the International Lung Cancer Consortium, having a first-degree relative with lung cancer conferred 1.5 times increased risk, after adjustment for smoking and additional risk factors.

Young Patient Age

The risk for malignancy is low in younger patients. The incidence of all cancers in adolescents and young adults is only approximately 75.5 per 100,000, with lung cancer among neither the most common nor the most deadly cancers for patients aged < 40 years. However, certain clinical and radiologic features may render particular

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nodules more suspicious, warranting closer follow-up regardless of age. The Fleischner, BTS, and CHEST guidelines address incidentally detected nodules, with BTS guidelines applicable to adults aged $\geq 18$ years and Fleischner guidelines applicable to individuals aged $\geq 35$ years. In patients aged $< 35$ years presenting with SSNs, recommendations are therefore based on the clinical scenario.

**Patients With Prior or Extrathoracic Primary Malignancy**

Guidelines for incidentally detected nodules are not intended for patients with known primary neoplasms in whom metastatic disease would be a consideration. This rationale applies more for solid nodules; however, SSNs may uncommonly represent metastases, in which case their behavior and neoplastic potential depend on the type and grade of the primary malignancy.

Lymphomas, mucinous GI neoplasms, extrapulmonary adenocarcinomas, and tumors associated with hemorrhage creating ground-glass opacity may all present as SSNs. Ground-glass attenuation produced by metastases is infrequently due to the lepidic growth that characterizes most lung adenocarcinoma spectrum lesions. Metastatic lesions initially presenting as SSNs may exhibit aggressive rather than indolent behavior. Therefore, close follow-up is prudent in oncology patients with new SSNs.

**Reconciling Management Algorithms: Survelling Nodules**

Surveillance recommendations for SSNs are guided by the main cause for persistent SSNs: lesions on the spectrum of lung adenocarcinoma. Lung adenocarcinoma spectrum lesions are currently...
classified pathologically by using the International Association for the Study of Lung Cancer system, which has been integrated into the World Health Organization TNM staging (Fig 2, Table 3). This classification applies to small (≤3 cm) nonmucinous lung adenocarcinomas with ground-glass attenuation and lepidic growth patterns on pathology. The algorithms direct surveillance primarily based on nodule size and ground-glass or part-solid density.

**Determining Nodules Necessitating Follow-up: Size, Density, and Number**

For incidentally detected SSNs, size threshold necessitating follow-up is typically 5 mm. This reflects that nodules ≤ 5 mm correspond to atypical adenomatous hyperplasia. The CHEST consensus guidelines for Asia recommend considering surveillance for even smaller SSNs, recognizing the increased risk in this population. The Fleischner guidelines also suggest that CT follow-up at 2 and 4 years may be obtained in Asian populations for solitary nodules ≤ 5 mm, as these may represent preinvasive lesions.

PSNs are managed differently than nonsolid nodules due to their association with invasive lung adenocarcinoma. The Fleischner guidelines note a potential limitation in discerning small solid aspects of already-small nodules, thus generally considering all PSNs to be at least 6 mm in size, although follow-up is not precluded for smaller nodules if morphologically suspicious or the patient is high risk. A multiplicity of nodules, irrespective of size and/or pure ground-glass density, would be followed up in 3 to 6 months as per the Fleischner guidelines. Multiple SSNs, when persistent, most often represent synchronous or metachronous lung primaries rather than

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**TABLE 3**] IASLC Staging: Pathologic Criteria

| Atypical Adenomatous Hyperplasia | Adenocarcinoma in Situ | Minimally Invasive Adenocarcinoma | Invasive Adenocarcinoma |
|-----------------------------------|------------------------|-----------------------------------|------------------------|
| Total size ≤ 0.5 cm               | Size < 3 cm            | Size ≤ 3 cm                       | T1a: solid component, 0.6-1 cm |
| No invasive component             | Pure lepidic (ground-glass) | Predominantly lepidic            | T1b: solid component, 1.1-2 cm |
|                                  | No invasive component (acinar, papillary, micropapillary, solid, colloid, enteric, fetal, invasive mucinous) | Invasive component ≤ 5 mm in any one focus | T1c: solid component, 2.1-3 cm |

IASLC = International Association for the Study of Lung Cancer.

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**TABLE 4**] Differential Considerations for Subsolid Nodules

| Primary Lung Adenocarcinoma       | Non-Primary Lung Adenocarcinoma Etiologies                           |
|-----------------------------------|---------------------------------------------------------------------|
| Atypical adenomatous hyperplasia  | Transient infection (eg, aspergillosis, candidiasis)                |
| Adenocarcinoma in situ            | Transient inflammation                                              |
| Minimally invasive adenocarcinoma | Focal interstitial fibrosis                                          |
| Invasive adenocarcinoma           | Organizing pneumonia                                                |
| Mucinous adenocarcinoma           | Eosinophilic pneumonia                                              |
|                                   | Alveolar sarcoid                                                    |
|                                   | Drug reaction                                                       |
|                                   | Vasculitis (granulomatosis with polyangiitis)                       |
|                                   | Endometriosis                                                       |
|                                   | Mucosa associated lymphoid tissue (MALT) and lymphoproliferative disorders |
|                                   | Metastatic lesions (including melanoma; renal carcinoma; breast, GI, and pancreatic adenocarcinomas) |
intrapulmonary metastasis. This pattern most often occurs in female nonsmokers, in both North American and Asian groups.

Decisions regarding surveillance vs treatment for persisting SSNs require evaluating each nodule individually, such as in terms of overall and solid component size. The most suspicious nodule may not be the largest nodule.

Establishing Nodule Persistence

Persistence of a nodule has significant implications upon differential diagnosis (Table 4), including malignant (Figs 2 and 3) and benign (Fig 4) causes. Establishing persistence of a subsolid lesion is recommended by the CHEST, BTS, and Fleischner guidelines, because up to 70% of SSNs may be transient. The CHEST Consensus Asian Guidelines further suggest that empiric antimicrobial agents may be appropriate for PSNs > 8 mm in size.

For participants of the International Early Lung Cancer Action Project (IELCAP), nearly 20% of PSNs and 26% of nonsolid nodules identified on baseline decreased in size or resolved. Comparably, in 622 PSNs and GGNs from the National Lung Screening Trial cohort, 28% resolved on follow-up imaging. In addition, in 264 SSNs from the Dutch Belgian Lung Cancer Screening trial (NELSON) cohort, 63% resolved on follow-up. SSNs identified on follow-up rounds compared with baseline are more likely to resolve: in IELCAP, 66% of new nonsolid nodules and 70% of new PSNs decreased in size or resolved. Given the likely transience for new SSNs on subsequent screening examinations, Lung-RADS version 1.1 suggests that new large nodules may be surveilled at a short 1-month interval rather than proceeding to further evaluation. Similarly, the NCCN algorithm for a newly detected SSNs on follow-up first asks whether there is suspected infection/inflammation and, if so, recommends low-dose CT imaging in 1 to 3 months.

New SSNs on follow-up examinations in patients without malignancy are favored to be transient given the indolent nature of SSNs, with reported volume doubling times of 457 to 568 days for PSNs and 469 to 813 days for GGNs. Similar to IELCAP findings, data from the NELSON trial showed that 67% of newly detected SSNs (on 1-, 3-, and 5.5-year incidence screening rounds) resolved, and new SSNs after baseline occurred in < 1% of participants. Although three of 16 nonresolving newly detected SSNs were malignant in NELSON (adenocarcinoma in situ in two nodules, and stage 1A invasive adenocarcinoma in one nodule), favorable staging of these lesions despite protracted referral after 1 year did not support the need for more aggressive management.

Transient nodules are also common in patients with extrapulmonary malignancies; in a retrospective study of 78 patients with extrapulmonary malignancies, new SSNs were commonly transient (36 of 78 nodules). Younger age, male sex, and peripheral eosinophilia are associated with resolving subsolid opacities. Nodule features such as detection on a follow-up examination, multiplicity, ill-defined margins, nonspiculated margins, and large solid component are
more often associated with SSN transience, as are polygonal shape (as opposed to round), mixed density (rather than pure ground-glass), and larger size. In contrast, pleural retraction and “bubble” lucencies are more common in persisting SSNs.

**Confirming Nodule “Growth”**

Overall nodule size and solid component size are associated with pathologic staging as well as outcomes for lung adenocarcinoma spectrum lesions. Establishing nodule growth is based on change in size ≥ 2 mm as per the Fleischner and BTS guidelines and > 1.5 mm as per the Lung-RADS version 1.1 of the ACR, as smaller changes are within measurement error. Volumetric growth is an additional parameter included in both the BTS and Lung-RADS algorithms and may facilitate earlier lung cancer diagnosis. The NELSON trial classified screen-detected nodules into growth and subsequent management categories based on volume doubling time; in SSNs, volumetric segmentation was applied to the solid portion and diameter for the overall nodule. This method recognizes the challenges in defining SSNs that can contribute to inaccurate segmentations.

Nodule progression may also manifest as new or increasing solid component, or uniform increase in attenuation. Nodule mass, incorporating both attenuation and volume, is associated with less intraobserver and interobserver variability compared with either diameter or volume alone, and an earlier indicator of nodule growth for SSNs. A change in this

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**Figure 4 – A-E, Non-neoplastic etiologies for subsolid nodules.**

A. Organizing pneumonia: 45-year-old man with cutaneous T-cell lymphoma and multiple subsolid and solid nodules, including the imaged right middle lobe nodule with coursing air bronchogram. Wedge resections of multiple nodules, including the right middle lobe nodule, demonstrated organizing pneumonia.

B. Fungal infection: 26-year-old woman with multiple predominantly solid nodules with ground-glass halo and recent history of cave-diving. Percutaneous core biopsy specimen revealed non-necrotizing granulomatous inflammation with Grocott methenamine silver-positive structures suggestive of fungal organisms.

C. Focal fibrosis: 46-year-old woman with history of smoking and mildly fluorodeoxyglucose-avid left upper lobe part solid nodule, with linear pleural extension. Percutaneous core biopsy revealed fibroelastic scar.

D. Drug reaction: 59-year-old man on immunotherapy for renal carcinoma, with the emergence of multiple bilateral ground-glass nodules coinciding with an increase in dosage of immunotherapy.

E. Alveolar sarcoid: 63-year-old man with World Trade Center Ground Zero exposure and left upper lobe subsolid lesions. The dominant mass appears to be a confluence of perilymphatic micronodules, compatible with pathologically proven alveolar sarcoid post-left upper lobectomy.
measure would reflect an increase in nodule size and/or density. Nodule mass assessment is recommended in the BTS guidelines, although it requires volumetric segmentation, and it may be more broadly recommended in the future. Accurate assessment of growth on CT imaging may be more difficult because of nodule attenuation, shape, location, and scan interval. Lesions adjacent the mediastinum or lung base may be affected by cardiac or inspiratory motion, and greater inspiratory effort inversely affects volume of solid nodules. Growth is more evident when comparing examinations separated by longer intervals, highlighting the need for comparison vs baseline studies in addition to the immediately prior imaging, which is especially useful for lesions with indolent behavior (Fig 5). Growth-rate precision also increases with a greater time interval between scans.

Contracting nodules are an uncommonly encountered pitfall, as nodules may at times decrease in size at points in their growth curve. Progressing nodules may contract in one or both dimensions with increasing soft tissue, related to fibrotic alveolar collapse, or increasing invasive components. Spurious contraction may be due to inflammatory components of cancers, which can be misinterpreted in the absence of continued follow-up imaging or investigation (Fig 6).

**Stable Large Pure GGNs**

Larger size in pure GGNs is associated with higher probability of invasive adenocarcinoma. Liu et al found that 35.4% (56 of 158) of pure GGNs represented invasive adenocarcinomas, significant for tumor volume $\geq 1,125$ mm$^3$. Lim et al reported that 39% of persistent pure GGNs $> 16$ mm were invasive adenocarcinomas. Nevertheless, the malignancy potential of stable or slowly growing nonsolid nodules $\geq 30$ mm is classified as Lung-RADS category 2, which implies a risk of malignancy estimate of $< 1\%$.

Recent risk-based stratification models suggest that the probability of malignancy for SSNs currently assigned to Lung-RADS categories 2 and 3 may be higher (3% and 13%, respectively) vs current risk predictions of $< 1\%$ and 1% to 2%. Future iterations may consider additional size-based risk stratifications, given that Lung-RADS category 2 GGNs that are $> 10$ mm in size have greater malignancy risk than subcentimeter GGNs. Current CHEST guidelines recommend that biopsy or resection may be considered for pure GGNs $> 10$ mm, and the BTS guidelines recommend the same approach even for stable persistent GGNs in which malignancy risk is $> 10\%$. The BTS guidelines also suggest that resection and nonsurgical treatment may be considered for GGNs increasing in size by $\geq 2$ mm. Lung-RADS has no recommendation for tissue sampling for pure GGNs, although category 4x may suggest tissue sampling for GGNs $\geq 30$ mm. These lesions may have indolent behavior, and it is unclear if aggressive management translates into improved outcomes.

**Reaching Management Determinations: Escalation and End Points**

The purpose of follow-up is to guide decision-making in the patient’s best interest. This includes an emphasis on shared decision-making.
Surveillance End Points and Delayed Progression

The choice between surveillance and action is influenced by an increase in nodule size, new or increasing solid component, and pace of growth as indicated by surveillance intervals. Biopsy, resection, or nonsurgical treatment can also be pursued for subsolid lesions in the setting of >10% malignancy risk per the BTS guidelines. The appropriate length of imaging surveillance for nonscreening patients with stable SSNs is an unanswered question. SSNs may exhibit lengthy volume doubling times, consistent with their often-indolent behavior. For example, in a retrospective cohort of 97 patients with SSNs, median volume doubling times ranged from 759 to 1,832 days, with more rapid volume doubling time for those nodules with solid components >5 mm. In this cohort, the upper limits of median volume doubling time for ground-glass lesions reached over 12 years.

For stable SSNs, CHEST recommends a minimum follow-up duration of 3 years, BTS 4 years, and Fleischner 5 years. The CHEST Clinical Practice Consensus Guidelines for Asia encourage consideration of ongoing surveillance beyond 3 years. A reasonable end point for surveillance of stable SSNs in nonscreening populations includes patient counseling, such as whether diagnosis and treatment would be pursued for progressing nodules. ACR and NCCN screening guidelines similarly suggest cessation of follow-up if patients are no longer candidates for...
definitive treatment, have life-limiting comorbidities, or would defer eventual treatment.

**PET/CT Imaging**

PET/CT imaging is not recommended to characterize GGNs or other SSNs with small solid components. Fluorodeoxyglucose avidity is nonspecific, and both false-positive and false-negative findings may occur (Fig 7). Infectious/inflammatory processes may result in false-positive outcomes for subsolid opacities. False-negative findings in SSNs may be due to lower metabolism of indolent lesions, lesions or solid components below the threshold for PET-CT spatial resolution, mucinous lesions, or location misregistration. PET is also of limited utility for preoperative staging of T1 SSNs.

**Tissue Sampling and Treatment Options**

The rate of benign diagnoses for SSNs following biopsy ranges from 6% to 39% and may be affected by
differing indications, referral patterns, and patient preferences, including desire for diagnostic certitude and level of risk tolerance. Benign diagnoses included fibrosis, organizing pneumonia, or presumed infection/inflammation. Biopsy of subsolid lesions has been associated with lower diagnostic accuracy compared with solid lesions, which may be due to lower cellularity. However, others have shown comparable diagnostic accuracy for malignancy comparing SSNs and solid nodules and up to 97% diagnostic accuracy in a series of 67 patients with ground-glass lesions sampled by using percutaneous core needle biopsy.

For primary invasive lung cancers in which definitive local therapy is possible, the NCCN and BTS guidelines favor parenchymal-sparing surgical resection. Radiotherapy and ablative therapies are additional local treatment options. For GGNs, localization may be necessary prior to surgical resection. Options for localization include CT-guided wire or marker placement; percutaneous injection of dye, radiotracer, or other material (Fig 8); or navigational bronchoscopic localization.

Radiation and other ablative therapies are most often pursued in nonsurgical candidates and increasingly as a lung-sparing treatment option in surgical candidates. This approach is especially relevant for patients presenting with multiple synchronous primary lesions. Simulation modeling has suggested superior outcomes with stereotactic body radiation therapy compared with lobectomy or nontherapy for SSNs. However, trials comparing these treatments to establish noninferiority of ablative options have failed to accrue participants. The gold standard remains surgical resection for patients who are surgical candidates.

Conclusions
Although there are overlapping and distinct aspects to the various algorithms for incidentally and screen-detected SSNs, all algorithms highlight shared decision-
making and patient counseling to reach practical management approaches. The side-by-side presentation of these guidelines may help prioritize the management options, with the understanding that ongoing research will refine recommendations. Lesion, patient, and even local epidemiologic factors are considerations needed to arrive at balanced management decisions. Future guidelines, such as those from CHEST, BTS, and the Fleischner Society, will continue to evolve in step with knowledge of SSN behavior and management.

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