

Follow-up and Management of Indeterminate Lung Nodules Detected Incidentally on Nonscreening CT

Purpose

To increase awareness of the medical evidence for follow-up testing, improve communication between rendering and ordering physicians, reduce unnecessary patient radiation exposure, improve the cost effectiveness of lung nodule evaluation, and increase primary care physician comfort with managing this evaluation while maintaining a high level of sensitivity in early diagnosis of the few lung cancers that are found among this cohort of patients.

Overview

Small pulmonary nodules are common incidental findings on chest and abdominal CT scans. Lung cancer screening CT trials have demonstrated that up to 51% of smokers, over 50 years of age, will have one or more such nodules, the vast majority of which are benign. The risk of malignancy as a cause of any such nodule in these high risk populations is best correlated with nodule size such that the likelihood of malignancy is 0.2% for nodules <3 mm, 0.9% for nodules 4-7 mm and 18% for 8-20 mm nodules. The original Fleischner Guidelines were not based on nodule type, only size and risk. (1) However, more recently, it has been demonstrated that solid and subsolid nodules behave differently and require different follow-up protocols. (2) As reported by Henschke et al in a study of 233 instances of positive findings at baseline low-dose CT screening examinations, among 44 (19%) resected subsolid lesions, malignancy was diagnosed in 15 (34%). The malignancy rate for solid nodules was 7% ($P < .001$). Importantly, the malignancy rate for part-solid ground glass nodules (GGNs) was 63%, compared with 18% for pure GGNs. Even after adjusting for size, the malignancy rate for part-solid GGNs again proved significantly higher than that for either solid or pure GGNs ($P = .03$). Similar to solid lesions, large pure GGNs are more likely to be invasive. (2)

Past recommendations, based largely on pre-CT era follow-up of lung nodules seen on chest radiograph (CXR), called for a large number of follow-up studies to be performed resulting in additional radiation exposure, and have not clearly demonstrated improvements in long term health outcomes nor to be cost-effective. (1) Although widely recognized, the Fleischner Guidelines have not been universally implemented and recent studies have sited good awareness but inconsistent conformance to the guidelines. (3) Consequently, an advisory committee was formed in 2011 by the Quality Collaborative to develop Community-wide guidelines and was reconvened in 2014 to address new science in the management of subsolid nodules. The advisory committee included members from the physician community, area hospitals and health plans. The physician representation included internists, pulmonologists, and diagnostic and thoracic radiologists. Additional input from the community was instrumental in the review and development process of these guidelines.

As a result, the Monroe County Medical Society through its Quality Collaborative has chosen to adopt the updated Fleischner Society Guideline recommendations for follow up and management of incidentally found lung nodules. (2) These guidelines are based on a greatly improved understanding of the natural history of solid and subsolid (Pure Ground Glass and Part-Solid) lung nodules gleaned from CT based lung cancer screening trials performed over the last decade. This data suggests that solid nodule follow up intervals and duration can be individualized based on patient risk factors for lung cancer, nodule size and nodule characteristics. The follow up intervals for subsolid nodules is based solely on nodule size with longer time intervals for a longer duration.

The two recommendations below were developed to help physicians implement the Community Guidelines through a standardized process. Pay close attention to the two entirely separate sections, one addressing the management of solid and the other subsolid nodules. Please note that these recommendations include those specific for the radiologist such as CT technique, nodule characterization and impression reporting as well as topics more germane to the clinician such as interval follow up recommendations, lung cancer risk stratification, and cautionary notes.

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Recommendations

Technique

The CT scans should use techniques designed to reduce radiation dose while maintaining adequate image quality As Low As Reasonably Achievable (ALARA). The use of dose modulation software and post processing algorithms may result in a further reduction in dose and are encouraged where available.

For consistency, it is recommended the patient be scanned lung apices to bases and images be reconstructed at 2 mm every 1 mm for solid nodules and at 1 mm every 1 mm for subsolid nodules.

Follow-up exams should be done without IV contrast.

Template Guidelines

In the findings section of the report, define:

Nodule Characteristics:

The characteristics of the nodule and the summary and recommendations are critical aspects of the report. The size of the nodule is the most important characteristic, although other characteristics such as spiculation can provide additional useful information.

- Size: average of length and width, largest nodule
- Composition: solid, ground-glass, mixed, calcified, fatty, enhancement, cavitory
- Borders: sharp, lobulated, spiculated, indistinct
- Calcification: none, benign pattern, indeterminate
- Location: lung, lobe
- Image location: series and image number

If a new nodule is found at a later time, follow up should be based on the characteristics of the new nodule along with the patient's risk factors and particular circumstances.

If incidental nodules are noted on a CT abdomen for which further evaluation is deemed appropriate, a dedicated diagnostic CT scan of the chest would be in order. However, this should be based on patient age and indication for abdominal CT.

These guidelines will not apply to every clinical situation. There may be specific cases where these general guidelines should not be followed. Whenever a provider makes a medical judgment that the guidelines should not be followed in the case of a specific patient this should be noted as an exception and the rationale for that judgment should be documented in the patient's medical record.

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The appropriate recommendation based on the nodule to be followed should be incorporated in every report. If risk factors are unknown; report both follow-up options. Below are the Fleischner Society Guidelines adopted by the MCMS for newly detected indeterminate nodule(s) in persons 35 years of age or older. The recommended follow up is based on the size of the largest indeterminate nodule and, for solid nodules, whether or not the patient is considered at low or high risk. In the occasion there are solid and subsolid nodules, both guidelines should be followed and combined when possible. Please note that in individual circumstances exceptions may be made in a clinician's assessment of a single case.

Fleischner Society Guidelines for Solid Nodules*

| Nodule Size | Follow-up for Low Risk Patient | Follow-up for High-Risk Patient |
|-------------|--|--|
| ≤ 4 mm | No follow-up needed | Follow-up CT at 12 mo; if unchanged, no further follow-up |
| > 4 - ≤6 mm | Follow-up CT at 12 mo; if unchanged, no further follow-up needed | Initial follow-up CT at 6-12 mo then at 18-24 mo if no change; then no further testing necessary |
| > 6 - ≤8 mm | Follow-up CT at 6-12 mo then at 18-24 mo if no change; then no further testing necessary | Initial follow-up CT at 3-6 mo then at 9-12 mo and 24 mo if no change; then no further testing necessary |
| > 8 mm | Follow-up CT at 3, 9, 24 mo, dynamic contrast enhanced CT, PET and/or biopsy | Same as for low risk patients |

Notes: diameter = average of length and width.

High risk is defined as one or more of the following:

- >20 pack year smoking history or equivalent second hand exposure
- Family history of lung cancer
- Occupational Exposure (asbestos, beryllium, silica, uranium, radon)
- Chronic Interstitial/Fibrotic Lung Disease

Low risk is defined as:

- Minimal or absent history of smoking or other known risk factors

Cautionary Notes:

- Caution is advised in the setting of fever/immunocompromised state which may require early pulmonary evaluation or follow up CT based on clinical concern for pulmonary infection.
- These guidelines may not apply for individuals with known or suspected malignant disease.

Fleischner Society Guidelines for Subsolid Nodules**

Subsolid Nodules include pure Ground Glass Nodules (GGN) and Part-Solid Nodules

| Nodule Size | Nodule Type | Recommended Follow-up |
|-------------|---------------------|---|
| ≤ 5 mm | Solitary GGN | No CT follow-up required. (a) |
| | Multiple GGN's | Follow-up CT at 2 and 4 yrs. (b) |
| | Solitary Part-Solid | Follow-up CT at 3 mo to determine persistence; if persistent and unchanged, yearly CT for a minimum of 3 yrs. (c) |
| | Multiple Part-Solid | Follow-up in 3 mo; if persistent, biopsy or surgical resection is recommended especially if the solid component becomes > 5 mm. (d) |
| > 5 mm | Solitary GGN | Follow-up CT in 3 mo; if persistent and unchanged, yearly CT for a minimum of 3 years. (e) |
| | Multiple GGN | Same as solitary GGN |
| | Solitary Part-Solid | Follow-up CT in 3 mo; if persistent and solid component < 5 mm, yearly CT for a minimum of 3 yrs; if solid component ≥ 5 mm, biopsy or surgical resection is recommended. (f) |
| | Multiple Part-Solid | Follow-up CT in 3 mo; if persistent, biopsy or surgical resection is recommended especially if solid component is ≥ 5mm. (d,f) |

Notes:

1. There are no data at present to suggest that traditional risk factors for lung cancer, such as smoking history or family history, are applicable to subsolid nodules. Therefore work-up of subsolid nodules is not stratified by cancer risk factors at this time.
2. Subsolid nodules, especially pure GGN's, exhibit an indolent growth pattern if persistent with doubling times of 3-5 yrs. Therefore follow-up of subsolid nodules is performed less frequently but for a longer duration than solid nodules.

Nodule Specific Remarks/Rationale:

- a. The low likelihood of malignancy of this lesion does not justify the monetary expense or excess radiation exposure associated with CT follow-up.
- b. The natural history of multiple small GGN's is unknown. Therefore a conservative follow-up strategy is recommended while alternative diagnoses such as respiratory bronchiolitis are considered.
- c. While the presence of a solid component to a subsolid nodule has been shown to increase the likelihood of an invasive carcinoma, solid components measuring < 5 mm more often represent carcinoma-in-situ or minimally invasive carcinoma and are best managed conservatively.
- d. Multiple part-solid nodules with a solid component that changes from < 5mm to ≥ 5mm have been found to represent multiple synchronous primary lung cancers. Furthermore, aggressive lung sparing resection of these lesions has been shown to be clinically beneficial for all histologies except mucinous adenocarcinoma. (4)
- e. Most of these lesions have been shown to be either benign (20%) or represent foci of atypical adenomatous hyperplasia, carcinoma-in-situ, or minimally invasive carcinoma. It has also been shown that delaying surgical resection until there is evidence of interval growth produced no adverse effect on patient outcome. (5)
- f. As in "d" above, the presence of a part-solid component increases the likelihood of invasive carcinoma which is especially true if the solid component exceeds 5 mm prompting a variable work-up strategy based on the size of the solid component.

*Adapted from the Fleischner Society Statement on CT of Small Pulmonary Nodules (Radiology 2005; 237:395-400). Available from: <http://radiology.rsna.org/content/237/2/395.full.pdf+html> **Adapted from the Fleischner Society Statement on Recommendations for the Management of Subsolid Pulmonary Nodules Detected at CT (Radiology; 266(1): 304-317). Available from: <http://pubs.rsna.org/doi/pdf/10.1148/radiol.12120628>

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Perspective on the Natural History of Subsolid Nodules

1182 patients deemed high risk for lung cancer have been followed with serial CT scans at NYU for 10 years. Of these, 239 patients were found to have 442 subsolid nodules. 116 (26.2%) are documented to have resolved on at least 2 follow-up scans, most within 3 months. 241 (54.5%) have remained stable while 40 (9.1%) decreased in size and 42 (9.5%) increased in size. (6)

Resources for Physicians

In support of the collaborative, Excellus BlueCross BlueShield examined a subset of Chest CT scan reports for calendar year 2010 in Monroe County. It is important to note that this was a qualitative analysis of the documentation in order to clarify the need for 1) standardization of reports, 2) to facilitate communication between the ordering and rendering physicians, and 3) to optimize evidence based care. Reports were examined for all the following variables including the size and characteristics of the nodule, a statement regarding risk factor status (e.g. known risk factors, or risk factor status unknown), and recommendations for or against follow-up CT testing. Based on the methodology published in the AJR in 2011, (7) 78% of the reports included documentation of all of the above relevant variables.

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References

1. MacMahon, H, Austin, JHM, Gamsu, G et al. Guidelines for Management of Small Pulmonary Nodules Detected on CT Scans: A Statement from the Fleischner Society. *Radiology* 2005; 237:395-400.
2. Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the Management of Subsolid Pulmonary Nodules Detected at CT: A Statement from the Fleischner Society. *Radiology* 2013;255(1):304-317.
3. Eisenberg, RL, Bankier, AA et al. Compliance with Fleischner Society Guidelines for Management of Small Lung Nodules: A Survey of 834 Radiologists. *Radiology* April 2010; 255: 218-224
4. Battafarano RJ, Meyers BF, Guthrie TJ, Cooper JD, Patterson GA. Surgical resection of multifocal non-small cell lung cancer is associated with prolonged survival. *Ann Thorac Surg* 2002;74(4):988-993.
5. Sawada S, Komori E, Nogami N, Segawa Y, Shinkai T, Yamashita M. Evaluation of lesions corresponding to ground-glass opacities that were resected after computed tomography follow-up examination. *Lung Cancer* 2009;65(2):176-179.
6. Greenberg AK, Lu F, Goldberg JD, Eylers E, Tsay J-C, et al. CT Scan Screening for Lung Cancer: Risk Factors for Nodules and Malignancy in a High-Risk Urban Cohort. *PLoS ONE* 2012;7(7): e39403.doi:10.1371/journal.pone.0039403.
7. Feely, MA, Hartman TE. Inappropriate Application of Nodule Management Guidelines in Radiologist Reports Before and After Revision of Exclusion Criteria. *AJR* 2011; 196: 1115-1119