



## Evaluating Pulmonary Nodules

- Pulmonary nodules  $\leq 4$  mm have a low risk of being cancerous; nodules between 4-8 mm are of intermediate risk for cancer; follow up CT scans for both categories are recommended on different schedules
- Pulmonary nodules  $> 8$  mm and mixed solid/ground glass nodules are suspicious for cancer; percutaneous needle aspiration biopsy (PNAB), positron emission tomography (PET), or video assisted thoracic surgery (VATS) should be considered
- A detailed guideline algorithm for the management of pulmonary nodules found on chest x-ray or CT is presented

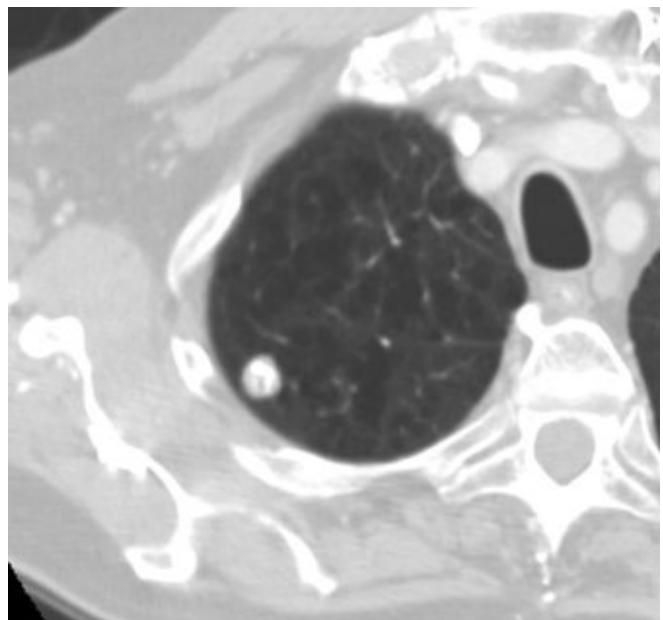
Increased utilization of chest CT examination has resulted in a dramatic escalation in the number of newly detected solitary pulmonary nodules, defined as round lesions  $< 3$  cm in diameter surrounded by lung parenchyma. Although the risk of finding cancer is 30-40% in radiographically discovered pulmonary nodules, thin section CT is 10-20 times as sensitive and can detect much smaller nodules. Size is an important predictor of the likelihood of malignancy and recent evidence indicates that pulmonary nodules  $\leq 4$  mm have an extremely small risk of cancer, especially in those with no history of cancer. In light of this new evidence, fewer short-term follow-up CT scans are necessary for most patients with small pulmonary nodules. Therefore, new recommendations have been developed for patient follow-up that varies according to the risk of cancer.

In some cases, benign nodules (granulomas, hamartomas) can be definitively diagnosed by CT examination because they have distinctive patterns of calcification and fat (which are not found in malignancies) (Figure 1). If the diagnosis is not definitively benign, follow up is dependent on the patient's risk factors for cancer and the size and imaging characteristics of the nodule.

The first step is to establish if the nodule is a new finding or, if not, whether it is stable or increasing in size. This requires comparing it to any available previous images (Figure 2). If there are no previous images and the nodule was detected on a chest radiograph, the next step is to evaluate it with CT.

### Nodules with Low to Intermediate Risk for Cancer

The likelihood of malignancy is  $< 1\%$  for nodules  $\leq 4$  mm and 6% for those between 4-8 mm. Nodules  $< 8$



**Figure 1.** A 12 mm pulmonary nodule in right upper lung with a calcification pattern indicating that this is a benign hamartoma or granuloma.

mm are too small to biopsy percutaneously or to evaluate with a PET scan. Therefore, the best option is to watch and wait, with follow up CT scans at intervals that depend on nodule size, patient age, history of malignancy, and likelihood of infection (Figure 2). Patients aged 18-35 yrs have a much smaller likelihood of malignancy than older adults ( $< 1\%$  of all lung cancers). Therefore, unless there is a history of malignancy, less rigorous follow-up CT is recommended than for older patients with nodules  $\leq 8$  mm.

## Nodules Suspicious for Malignancy

Approximately 50% of incidentally detected nodules >8 mm are malignant. Malignancy should be suspected in a patient with a prior history of cancer or in any case in which a nodule is increasing in size, has spiculated margins or mixed solid/ground glass attenuation. Patients of any age with a history of cancer should have close follow up intervals because metastases demonstrate more rapid growth (Figure 2). Diagnostic intervention should be considered for nodules >8 mm. Percutaneous needle aspiration biopsy (PNAB) will provide a definitive diagnosis with an accuracy of about 90% for malignant lesions and 60-80% for specific benign lesions. In cases in which the lesion is close to a central bronchus, bronchoscopy with transbronchial biopsy can be considered.

FDG-PET scans are useful in identifying metabolically active nodules that may require diagnostic biopsy,

information that is particularly helpful in patients with significant co-morbidities.

Relative contraindications for biopsy include mechanical ventilation, severe emphysema, prior pneumonectomy, anti-coagulant therapy, or pulmonary arterial hypertension. In addition, it is technically difficult to obtain definitive results with PNAB on pulmonary lesions close to the diaphragm. If it is not possible to perform PNAB, the choices are to surgically remove the nodule using video assisted thoracoscopic surgery (VATS), or perform follow-up CT scan (Figure 2).

Follow up is not necessary once a nodule has been demonstrated to be stable for 24 months, with the exception of nodules that have ground glass features on CT (Figure 3). Longer follow up is warranted because these features can be indicative of indolent cancers that can be stable or very slowly growing over several years.

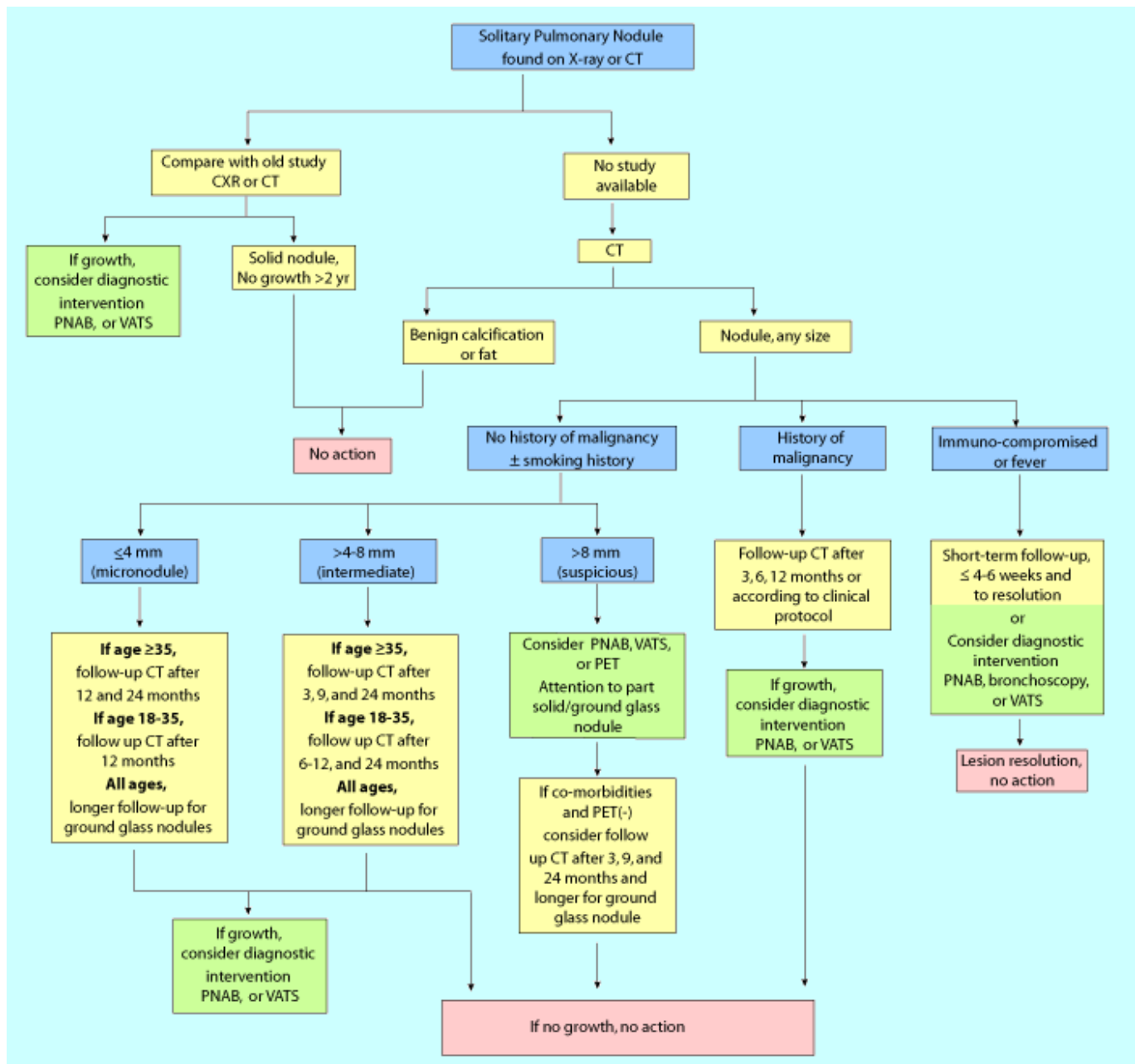
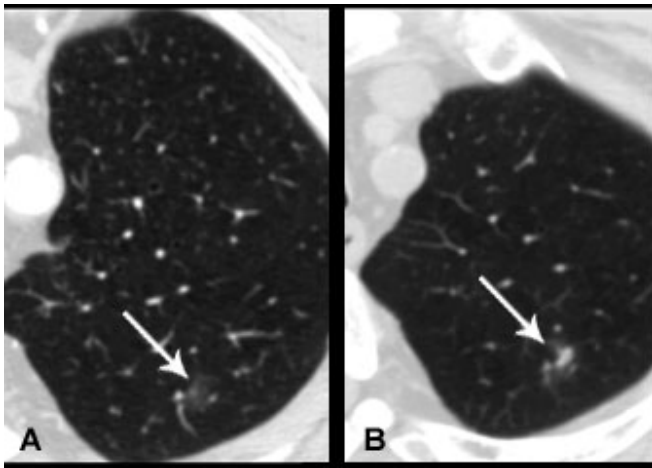


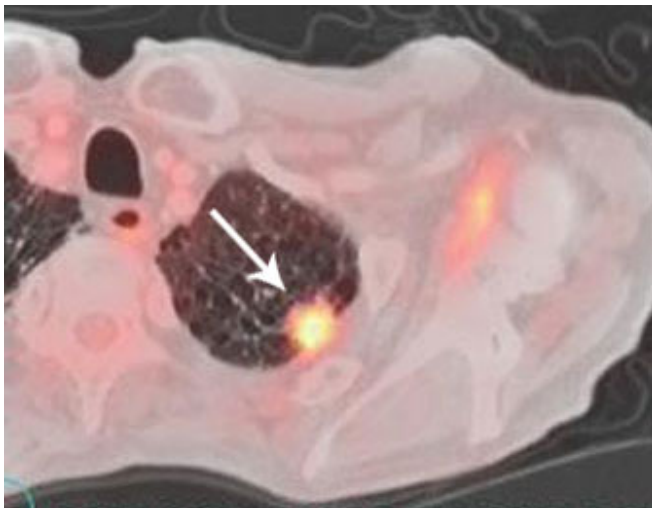
Figure 2. MGH Guideline Algorithm for Evaluating Pulmonary Nodules.



**Figure 3.** (A) CT image showing ground-glass nodule in right upper lobe of the lung. (B) Follow-up scan of the same patient 20 months later reveals progression to a mixed ground-glass/solid tumor. VATS confirmed that the lesion was malignant (adenocarcinoma).

### Nodules Suspicious for Inflammatory Processes

In patients who are immunocompromised or febrile, the possibility of an infection should be considered. For these patients, short-term follow-up CT is recommended in  $\leq 4-6$  weeks and then to resolution. Alternatively, diagnostic intervention with PNAB, bronchoscopy, or VATS can be considered as clinically indicated (Figure 2).

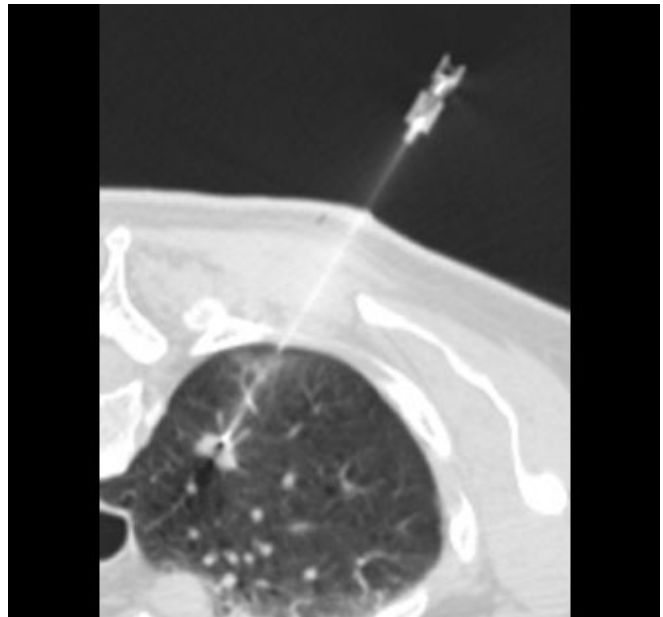


**Figure 5.** PET/CT scan showing high metabolic activity in pulmonary nodule, indicative of cancer or inflammation.

### Modalities for Evaluation of Nodules

Once a nodule has been classified as suspicious by CT evaluation, it can be further evaluated with PNAB, FDG-PET, or VATS. Table 1 compares the advantages and disadvantages of these modalities.

Histological examination of the cells obtained by PNAB (Figure 4) can frequently differentiate between malignant and infectious lesions, such as TB and fungal infections. In addition, the type of malignancy can be



**Figure 4.** Percutaneous needle aspiration biopsy (PNAB) of suspicious pulmonary nodule.

identified, which can help in determining which patients are candidates for surgery or chemotherapy. PNAB is associated with some minor complications. As many as 20% will have a small pneumothorax and 1-2% will have a pneumothorax large enough to require a chest tube. In addition, some patients will experience minor hemoptysis.

FDG-PET shows excellent sensitivity and specificity in detecting malignant nodules  $> 8$  mm (Figure 5). In addition, PET is more accurate in detecting lymph node metastases in the thorax and provides the added advantage of whole-body staging for lung cancer. Up to 11% of patients with lung cancer have occult extrathoracic metastases detected on PET that conventional staging missed. However, limitations in resolution preclude effective characterization of nodules  $< 8$  mm. In addition, certain tumors i.e. carcinoid, bronchioloalveolar cell carcinoma, and well differentiated adenocarcinoma demonstrate relatively low metabolic activity and are, therefore, not consistently detected with FDG-PET. (However, most of these tumors have features on CT that are suspicious for malignancy that would warrant further diagnostic evaluation.) Inflammatory diseases may also appear positive on FDG-PET scans, resulting in false positive findings for cancer. On occasion a nodule due to mycobacterial or fungal disease, sarcoidosis or organizing pneumonia will mimic a neoplastic pulmonary nodule.

**Table 1. Comparison of modalities for evaluating pulmonary nodules**

Modality*	Advantages	Disadvantages
<b>PNAB</b>	Histological diagnosis	Low diagnostic yield for nodules < 8 mm Minor pneumothorax, 20% Significant pneumothorax, requiring chest tube, 1-2% Minor hemoptysis, 2-5%
<b>FDG-PET</b>	Whole body image detects extra-pulmonary tumors  Can stage known lung cancer	Lower sensitivity for lesions < 8 mm False positives from inflammation False negatives from tumors with low metabolic rate
<b>VATS</b>	Definitive histological diagnosis	General anesthesia Hospitalization, 1-3 days (longer in cases of prolonged air leak in 2-15%) Arrhythmia, 3-4% Bleeding, 4%

\*PNAB = percutaneous needle aspiration biopsy, FEG-PET = 18-fluorodeoxyglucose positron emission tomography, VATS = video assisted thoroscopic surgery

### Patient Preparation and Procedures

For details about preparation for PET, see the Radiology Rounds article on [PET/CT](#), May 2004. [Pre-procedure preparation](#) information for PNAB can be found on the Thoracic Radiology web site.

### Scheduling

Both PET and CT examinations can be scheduled online through Radiology Order Entry ([[mghroe]]) or by calling 617-724-XRAY (617-724-9729). A consultation for PNAB of the lung can be requested by calling 617-724-4254 or by faxing a [Thoracic Biopsy Approval form](#) available on the MGH Radiology Department website. A consultation for VATS may be obtained from the Multidisciplinary Thoracic Oncology Clinic, 617-724-4000.

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### Further Information

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