Lung Nodules and Malignancy: Radiologic Assessment

Julie Takasugi
Department of Radiology
VA Puget Sound Health Care System
University of Washington SOM

“Nodule/Mass on chest radiograph in smoker”

- Clinical Assessment
  - Clinical Risk of malignancy
  - Patient's suitability & preferences for surgical treatment
  - Suitability for nonsurgical treatment
  - Follow-up

- Radiologic Assessment
  - Radiographic probability of malignancy
  - Suitability for tissue sampling when appropriate
  - Staging
  - Suitability for non-surgical treatment when appropriate
  - Response to treatment and monitoring for recurrence
Case 1. Which calcified nodule cannot be considered benign?

A  B  C  D

To be considered benign, a calcified nodule must show the following characteristics:

1. Solid nodule
2. Smooth margination
3. Benign pattern of calcification

Target calcification  Central calcification
Popcorn calcification  Diffuse calcification
To be considered benign, a calcified nodule must show the following characteristics:

1. Solid nodule
2. Smooth margination
3. Benign pattern of calcification

<table>
<thead>
<tr>
<th>Target calcification</th>
<th>Central calcification</th>
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</thead>
<tbody>
<tr>
<td>Popcorn calcification</td>
<td>Diffuse calcification</td>
</tr>
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</table>

Fat in a nodule

- Hamartoma
- Unless patient has h/o
  - Liposarcoma
  - Renal cell ca

Courtesy of Jeffrey Kanne, MD
Dept. Radiology, University of Wisconsin
Fat in a nodule

- Hamartoma
- Unless patient has h/o
  - Liposarcoma
  - Renal cell ca

An irregularly margined nodule cannot be considered benign regardless of the type of calcification present. Eccentric calcification cannot be considered a benign type of calcification.
Examples of calcification not considered benign

Dystrophic
Psammomatous

Amorphous

Case 2. 59 yo M smoker with cough

Which radiographic feature makes this lesion worrisome for malignancy?

A. Lack of calcification
B. Location (right lower lobe)
C. Margins
D. Size
Lung Nodule/Mass: Definitions

**Solitary Pulmonary Nodule**
- Single, round, radiographic opacity (well- or poorly-defined) measuring up to 3 cm in diameter

**Dominant Pulmonary Nodule**
- Single, dominant/larger nodule accompanied by ≤ 10 smaller nodules
- (10 = arbitrary number)

**Mass**
- Rounded radiographic opacity measuring more than 3 cm in diameter

**More than 10 nodules**
- Management
  - Metastatic disease
  - Infection
  - Inflammation

ACCP: Chest 2013;143(5)(Suppl):e93S

Nodule vs Mass: Goal of Further Evaluation

**Nodule**
- Benign
  - No further evaluation
- Indeterminate
- Malignant

**Mass**
- Staging
- Treatment

**Risk Factors**
- Clinical
- Radiologic

Observe

Staging/Treatment

This calculator should be used for high risk population only, not for nonsmokers. [http://www.brocku.ca/lung-cancer-risk-calculator](http://www.brocku.ca/lung-cancer-risk-calculator)
### Nodule: The likelihood of malignancy

<table>
<thead>
<tr>
<th>Nodule</th>
<th>Radiologic</th>
<th>Clinical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Size</td>
<td>Smoking</td>
</tr>
<tr>
<td>Benign</td>
<td>Margins</td>
<td>Age/Gender</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Location</td>
<td>Exposures</td>
</tr>
<tr>
<td>?</td>
<td>Growth</td>
<td>Family history</td>
</tr>
<tr>
<td>Malignant</td>
<td>Attenuation</td>
<td>Other malignancies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lung disease</td>
</tr>
<tr>
<td>Staging</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treat if a candidate and patient desires therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palliation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Radiologic
- Margins
- Location
- Growth
- Attenuation
- Size

#### Clinical
- Smoking
- Age/Gender
- Exposures
- Family history
- Other malignancies
- Lung disease

#### Radiologic
- Spiculation
- Lobulated
- Smooth
- Upper lobe, R/L

- Solid – stability x 2 years
- Subsolid – stability x 3+ years
Case 3. Noncalcified nodules < 8mm in diameter found during lung cancer screening. Radiographically, which is the most likely to be malignant and which is least likely to be malignant?

**Attenuation**

1. Pure ground glass  
2. Mixed solid/GGO  
3. Solid  
4. Solid, perifissural

A. 2 and 3  
B. 3 and 4  
C. 2 and 4  
D. 3 and 1

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**Pulmonary lymph nodes**

Subpleural  
*Shape:*  
- Triangular  
- Oval, round  
- Rectangular  
- Dumbbell  
*Connections:*  
- Interlobular septum  
- Pulmonary vein  
- Lower > Upper lungs  
Often associated with fissures
**Solid SPN**

Solid nodules – the most common type of nodule, 2nd least likely to be malignant.
Most benign lesions – granulomas, fungi, TB, inflammatory lung disease, etc, are solid.
Risk of malignancy in solid nodules 5-8 mm diameter: 2-6%

Most lung cancers and metastases are solid nodules.

**Pure ground glass or nonsolid nodules:**

**Causes:**
- Malignant: Minimally invasive adenocarcinoma
- Benign: Infection, blood, inflammation
- Premalignant: Atypical adenomatous hyperplasia, Adenocarcinoma in situ

**Recommendations:**
- < 5 mm do not necessarily need follow-up CT
- Between 5-10 mm, follow-up with CT 3 months, if unchanged, continue follow-up annually x 3+ yrs
- > 10 mm, persists for 3 months, presume cancer. (20-25% will still prove to be benign on resection). Consider surgery if enlarging or solid component develops
Part-solid SPN:

Likelihood of malignancy – highest in part-solid nodules.

40-50% of part-solid < 1.5 cm are malignant.

Greater risk of malignancy with increasing nodule size, especially if solid component represents > 50% of the nodule or is enlarging. Solid component often contains invasive adenoca, GGO = AAH or adenoca in situ.

Nodule Size (Lung Ca Screening, Pan-CAN)

McWilliams et al. NEJM 2013;369:910-9
Case 4A. Which radiographic characteristic helps most in differentiating benign from malignant cavitary disease

1. Air-fluid level
2. Wall thickness
3. Size
4. Internal debris

Cavity wall thickness

- Maximal wall thickness
  - < 4 mm, 19/20 (95%) benign
  - 5-15 mm, 16/22 (73%) benign
  - >16 mm, 16/19 (84%) malignant

Woodring et al. AJR 1980: 135:1269-71
Wall thickness alone should not be used to distinguish benign from malignant disease

**Lung Abscess**

**Squamous Cell Ca**

**Causes of cavitary processes**

**Thin wall**
- Metastatic disease
- Vasculitides: GPA
- Infections: Coci, PJP, Echinococcus, Papillomatosis, post-infectious lung cyst, TB
- Trauma: Pulmonary laceration
- Bland/septic embolism
- LCH
- LAM
- Congenital cysts
- Emphysema/Bulla

**Thick wall**
- Primary lung cancer
- Metastatic disease
- Lymphoma
- Vasculitides: GPA, RA
- Infections: Lung abscess, TB
- Bland/septic embolism
- LCH
- Sarcoidosis
- PMF/Conglomerate masses
- Trauma: Hematoma, laceration
4B. Which of the following primary tumors is most likely to cause cavitary metastases in the lung?

1. Melanoma
2. Cervical carcinoma
3. Renal cell carcinoma
4. Breast adenocarcinoma
5. Prostate adenocarcinoma

Cavitary Lung Metastases

- NSCCA Lung
- Cervical carcinoma
- Colon carcinoma
- Squamous cell ca of head and neck
- Sarcoma

- May have thin or thick walls
- Often coexist with solid nodules
- Often smoothly marginated
- Variable size in same individual
- Peripherally located
4C. Man with hemoptysis – Lucency is noted around the mass in the upper lobe. What is this sign?

1. Monad’s Sign
2. Air-crescent sign
3. Luftsichel sign
4. Walking Man sign

Case 5A. CT guided transthoracic needle biopsy requested for a suspicious lesion.

Which of the following is an absolute contraindication for biopsy?

1. Non-suppressible coughing
2. Uncorrectable coagulopathy
3. Uncooperative patient
4. Contralateral pneumonectomy
5. None of the above
Case 5B. The patient indicates that he feels “dizzy” during the procedure. His blood pressure and pulse are normal. Post biopsy images are shown below. What should you do?

1. Place a chest tube
2. Position patient in left decubital position
3. Position patient in right decubital position
4. Leave patient flat, supine

Arterial Air Embolism

<table>
<thead>
<tr>
<th>Requirement for air embolism</th>
<th>How does it happen</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Direct communication between air source and vessel</td>
<td>1. Needle tip is located within a vein and the hub is open to air and patient breathes – inhalation creates negative venous pressure and air is pulled into vessel</td>
</tr>
<tr>
<td>2. Pressure gradient favors passage of air into the vessel rather than blood out of the vessel (negative venous pressure relative to atmospheric pressure)</td>
<td>2. Bronchovenous fistula caused by needle or needle tract</td>
</tr>
<tr>
<td></td>
<td>3. Biopsy of cavitory lesion, needle course through a vessel</td>
</tr>
</tbody>
</table>
### Air Embolism

<table>
<thead>
<tr>
<th>Pulmonary/Venous</th>
<th>Systemic/Arterial</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Air introduced into right heart and pulmonary circulation</td>
<td>• Air introduced into left heart and systemic circulation</td>
</tr>
<tr>
<td>• Small amounts of venous air usually causes no or minor symptoms</td>
<td>• Occasionally asymptomatic</td>
</tr>
<tr>
<td>• Large amounts of air may cause blockage of blood flow into pulmonary artery, decreased cardiac output</td>
<td>• May be catastrophic – stroke, MI, death</td>
</tr>
</tbody>
</table>

### Venous or Pulmonary Air Embolism

<table>
<thead>
<tr>
<th>Air introduced into right heart and pulmonary circulation</th>
<th>LLD/Trendelenburg may displace large bubbles in RVOFT – relieving air-block</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 100% supplemental oxygen</td>
<td>• If not successful, chest compressions should be performed to force air out of RVOFT and into smaller pulmonary vessels, improving forward flow</td>
</tr>
<tr>
<td>• Position in left lateral decub position, trendelenburg or combo</td>
<td>• Remove embolized air – aspirate from RV via central venous catheter (if present)</td>
</tr>
<tr>
<td>• RVOFT positioned inferior to RV causes air to migrate superiorly within RV, less likely to embolize</td>
<td></td>
</tr>
</tbody>
</table>
## Systemic or Arterial Air Embolism

<table>
<thead>
<tr>
<th>Air introduced into left heart and systemic circulation</th>
<th>High flow supplemental O₂ increases resorption rate of embolized air by reducing partial pressure of nitrogen in blood which produces gradient for diffusion of nitrogen from air bubbles back into blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position flat, supine. Arterial flow more forceful and air bubbles are propelled forward by arterial flow even in Trendelenburg. Trendelenburg can exacerbate cerebral edema caused by cerebral air embolism</td>
<td>If cardiopulmonary/neurologic deficits develop: hyperbaric oxygen therapy (HBO) ASAP – preferably within 6 hr, but up to 30 h. Benefits of HBO weighed against potential risk of transport to HBO facility</td>
</tr>
<tr>
<td>Supportive care: mechanical ventilation, vasopressors, volume resuscitation</td>
<td></td>
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</tbody>
</table>

## Clinical features of air embolism

<table>
<thead>
<tr>
<th>None</th>
<th>Dizziness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodynamic collapse</td>
<td>Tachypnea</td>
</tr>
<tr>
<td>Acute insufficiency of lungs, brain, spinal cord, heart</td>
<td>Tachycardia</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Hypotension</td>
</tr>
<tr>
<td>Substernal CP</td>
<td>Wheezing</td>
</tr>
<tr>
<td>Sense of impending doom</td>
<td>Crackles</td>
</tr>
<tr>
<td>Light-headedness</td>
<td>Respiratory failure</td>
</tr>
<tr>
<td></td>
<td>Altered mental status</td>
</tr>
<tr>
<td></td>
<td>Focal neurologic deficits</td>
</tr>
<tr>
<td></td>
<td>Seizure</td>
</tr>
</tbody>
</table>
Case 6. Which thoracic malignancy is least likely to cause this syndrome?

1. Hodgkins Disease
2. Non-Hodgkins Lymphoma
3. Squamous cell carcinoma
4. Small cell carcinoma
Superior vena cava syndrome

**Etiology:**
- Malignancy 60-85% cases
  - NSCLC – 50%
  - SCLC – 25%
  - NHL – 10%
- Nonmalignant
  - Thrombosis - indwelling vascular devices
  - Fibrosing mediastinitis
  - Radiation fibrosis

**Malignant SVC syndrome may be caused by**
- SVC extrinsic compression by tumor or lymph nodes
- Direct tumor invasion into vessel

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Superior vena cava syndrome

**Imaging**
- Chest Radiograph
- Chest CT or MRI

**Histologic Diagnosis**

**Treatment**
- Chemotherapy
- Radiation
- Stenting
- Medical support
Case 7. 60 yo M with recent onset of bilateral knee pain

Further evaluation should include which of the following:
1. MRI both knees
2. Nuclear medicine bone scanning
3. Chest radiograph
4. Joint aspiration
5. PET-CT scan

Case courtesy of Dr. H. Mann, Univ Utah

Case 7. Hypertrophic osteoarthropathy

- Abnormal proliferation of skin and osseous tissue at distal parts of extremities include clubbing, periostosis of tubular bones, synovial effusion
- Primary – not associated with other medical disorders
- Secondary – associated with lung cancer, pulmonary infections, CF, R to L cardiac shunts, Hodgkins, cirrhosis.

Case courtesy of Dr. H. Mann, Univ Utah
Case 8. 67 yo with 4 cm LUL mass and FDG-PET avid left supraclavicular node

Assuming that the node is metastatic, what nodal category would this be?

- 1. NX
- 2. N1
- 3. N2
- 4. N3
- 5. M1

Lymph Nodes

- N0 – No regional nodal metastases
- N1 – Metastases to ipsilateral peribronchial and or ipsilateral hilar and intrapulmonary nodes
- N2 – Metastases to ipsilateral mediastinal and/ subcarinal nodes
- N3 – Metastases in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular nodes
- Nx – Regional nodes not assessable

American Joint Committee on Cancer, 7th Edition
Lymph drainage pattern

Left upper lobe
- Drains to left upper hilar nodes
- Upper segmental lesions may drain directly to left upper mediastinal nodes (station 5, 6)

Lymphatic Drainage

Left lower lobe
- Drains to lower left hilar nodes
- May drain directly to subcarinal mediastinal nodes (7)
- May drain to inferior pulmonary ligament (9) or periesophageal (8) mediastinal nodes
Lymphatic Drainage

Right Upper Lobe

- Drains to upper hilar nodes
- May drain directly to upper right mediastinal nodes (4)

Lymphatic Drainage

Right Middle/Lower Lobe

- Drain to inferior hilar nodes
- May drain directly to subcarinal mediastinal nodes (7)
- RLL may drain directly to periesophageal (8) or inferior pulmonary ligament (9) mediastinal nodes
Lymphatic Drainage

The most common mediastinal nodal drainage pattern from right-sided lung cancers

Lymphatic Drainage

The most common mediastinal nodal drainage patterns from left-sided lung cancers
Case 9. 40 yo M with cough, weight-loss, fatigue

Which of the following diseases is most likely?

1. Invasive adenoca of the lung
2. Pulmonary lymphoma
3. Pulmonary amyloidosis
4. Metastatic colon carcinoma
Pulmonary nodule/masses with air-bronchograms

Differential Diagnosis
- Adenocarcinoma with lepidic growth pattern
- Primary pulmonary lymphoma
- Pulmonary amyloidosis
- Sarcoidosis
- Infection

Case 10A. Ex-navy submariner with cough - Given the chest radiograph on the left, which of the following radiologic procedures/exams should be recommended?

1. CT guided biopsy
2. CT chest without IV contrast
3. CT chest with IV contrast
4. PET-CT
5. Comparison with old chest radiograph
Case 10A. Ex-navy submariner with cough - Given the chest radiograph on the left, which of the following radiologic procedures/exams should be recommended?

1. CT guided biopsy
2. CT chest without IV contrast
3. CT chest with IV contrast
4. PET-CT
5. Comparison with old chest radiograph

Ex-navy submariner with cough. No comparison radiographs
Ex-navy submariner with cough. CT with IV.

MIP Images
Case 10B. Ex-navy submariner with cough. CT with IV. Which of the following are CT criteria for this entity’s diagnosis?

1. Pleural disease
2. Comet-tail sign
3. Ipsilateral volume loss
4. Homogenous enhancement

A. 1, 2, 3
B. 1, 3
C. 2, 4
D. All of the above

Round atelectasis – CT criteria

- Lung which is folded upon itself, mass abuts pleura
- Pleural disease must exist
- Ipsilateral volume loss
  - Change in position of fissures, diaphragm, mediastinum, hila
- Homogenous enhancement
  - During pulmonary venous phase
- Comet-tail sign
Case 11A. 63 yo M, smoker with hoarseness. Where is there tumor?

1. Left hilum only
2. Left hilum, AP window
3. Left hilum, bilateral upper mediastinum
4. Bilateral upper mediastinum

Bilateral upper mediastinal and left hilar node involvement
Case 11B. 63 yo M, smoker with hoarseness.

True or False:
The station 6 lymph nodes indicated by the red arrow are accessible for tissue sampling via cervical mediastinoscopy.

Case 11C. 63 yo M, smoker with hoarseness. Biopsy shows small cell lung cancer – PET CT done to stage

True or False:
There is no difference between small cell and non-small cell lung cancer staging in present-day clinical setting.
Clinical staging of small cell lung cancer

**Limited Disease**
- Tumor confined to the ipsilateral hemithorax and regional nodes able to be included in a single tolerable radiotherapy port

**Extensive Disease**
- Tumor beyond the boundaries of limited disease including distant metastases, malignant pericardial or pleural effusions, contralateral supraclav/hilar nodal involvement

Fleischner Recommendations for small, solid nodules incidentally detected at nonscreening CT

<table>
<thead>
<tr>
<th>Nodule size*</th>
<th>Low Risk Patient</th>
<th>High Risk Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 4mm</td>
<td>No f/u needed</td>
<td>F/u @ 12m, if unchanged no additional f/u</td>
</tr>
<tr>
<td>&gt;4-6mm</td>
<td>F/u 12m, if no change no further f/u</td>
<td>F/u 6-12m, then 18-24m if no change</td>
</tr>
<tr>
<td>&gt;6-8mm</td>
<td>F/u at 6-12m, then 18-24m if no change</td>
<td>F/u @ 3-6m, then 9-12m and 24m if no change</td>
</tr>
<tr>
<td>&gt;8mm</td>
<td>F/u 3, 9, 24m, dynamic CECT, PET &amp;/or Bx</td>
<td>Same as for low risk pt</td>
</tr>
</tbody>
</table>

* = average width & length
* Not applicable to pt c known malignancy, young patients, pt c sx
Fleischner recommendations for management of subsolid pulmonary nodules detected at CT

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Management Recommendations</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solitary pure GGO &lt;5 mm</td>
<td>No CT follow-up advised</td>
<td>Obtain contiguous 1-mm-thick sections to confirm if nodule is truly a pure GGO.</td>
</tr>
<tr>
<td>Solitary pure GGO ≥5 mm</td>
<td>Obtain follow-up CT at 6 months to confirm persistence or annual surveillance CT for a minimum of 3 years</td>
<td></td>
</tr>
<tr>
<td>Solitary part-solid nodule</td>
<td>Initial follow-up CT at 3 months to confirm persistence. If persistent and solid component ≤5 mm, then yearly surveillance CT for a minimum of 3 years. If persistent and solid component &gt;5 mm, then yearly surveillance CT for a minimum of 3 years. If persistent and solid component &gt;5 mm, then biopsy or surgical resection.</td>
<td>Consider PET/CT for part-solid nodules &gt;10 mm.</td>
</tr>
<tr>
<td>Multiple nodules</td>
<td>Varying low-dose CT, follow-up CT at 2 and 4 years.</td>
<td>Consider other causes for multiple nodules.</td>
</tr>
<tr>
<td>Pure GGO ≥5 mm without a dominant lesion</td>
<td>Obtain follow-up CT at 2 and 4 years.</td>
<td></td>
</tr>
<tr>
<td>Dominant nodule component/partsolid or solid component</td>
<td>Initial follow-up CT at 3 months to confirm persistence. If persistent, biopsy or surgical resection is recommended, especially for lesions with &gt;5 mm solid component.</td>
<td></td>
</tr>
</tbody>
</table>

Note: These guidelines assume metastatic evaluation, optimal with contiguous thin sections. They are not intended for patients with small (<5 mm), well-circumscribed, well-enhancing lesions. For lesions ≤2 cm, the guidelines assume that the management strategy is tailored to the individual patient, taking into account factors such as lesion size, growth rate, and presence of other medical conditions.

Nonsmall Cell Lung Cancer Staging

Primary Tumor (T)

- T1a: Tumor is <2 cm and does not invade the visceral pleura or mediastinum
- T1b: Tumor is >2 cm but ≤3 cm and does not invade the visceral pleura or mediastinum
- T2a: Tumor is ≤5 cm, adjacent to the visceral pleura but not invading it
- T2b: Tumor is >5 cm, adjacent to the visceral pleura but not invading it

Distant Metastasis (M)

- M0: No distant metastasis
- M1: Distant metastasis

Notes:

1. The above criteria are intended as a guide and should be applied in conjunction with clinical and radiological assessment.
2. The T and N categories are based on the presence or absence of tumor and lymph node involvement, respectively.
3. The M category is determined by the presence or absence of distant metastases.
4. The staging classification is based on the TNM system and is intended to provide a standardized method for the classification of lung cancer.
Growth Rates

• (Hasegawa et al. Br J Rad 2000;73:1252) 3y mass screening analysis of small lung cancers
  • Mean Volume Doubling Time (VDT) in smokers
    • GGO, 813d
    • Part solid, 457d
    • Solid, 149d
  • Mean Volume Doubling time in nonsmokers is even longer than in smokers

• 5mm nodule c 60d VDT reaches diameter of 20 mm in 12 m
• 5mm nodule c 240d VDT reaches 7.1 mm diameter in same period