Approach to Pulmonary Nodules

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Pulmonary Nodules

- Treatment and follow up of pulmonary nodules are often a clinical challenge.
- The primary goal of pulmonary nodule management is to determine if the nodule is malignant or benign.

Approach to Pulmonary Nodules

- Successful management is about relationships
- Your relationship with the patient
- Your relationship with your colleagues
- Your relationship with the guidelines and current recommendations

Approach to Pulmonary Nodules

- Definitions
- Etiology
- Lung Cancer
- Classification
- Characteristics
- Growth Rate
- Risk Factors
- Fleishner Society 2017
- ACR Lung RADS
- Approach
Pulmonary Nodule
(Definition)

- Well circumscribed round lesion measuring up to 3 cm in diameter surrounded by aerated lung.
- Pulmonary lesions > 3 cm are lung masses

Etiologies of Pulmonary Nodules

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious granuloma (80%)</td>
<td>Adenocarcinoma (50%)</td>
</tr>
<tr>
<td>Endemic Fungi</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Atypical mycobacterium</td>
<td>Small cell carcinoma</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Metastasis</td>
</tr>
<tr>
<td>Hamartoma</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>AV malformation</td>
<td>Carcinoid</td>
</tr>
<tr>
<td>Intrapulmonary lymph node</td>
<td></td>
</tr>
</tbody>
</table>

Lung Cancer

- Leading cause of cancer mortality in both men and women in the US
- 3rd most common cause of cancer
- 225,000 new diagnosis per year
- 160,000 deaths per year
Risk Factors for Lung Cancer

- Cigarette smoking
- Age
- COPD
- Pulmonary fibrosis
- Exposures
- Genetic predisposition

Classification

- Solid: More common

- Sub-solid:
  - Pure ground glass: nodule with higher density than surrounding tissue but does not obscure the underlying lung
  - Part solid: Nodule with at least part ground glass appearance

Classification

- Solid: Most common type of nodule
  - Blocks out the lung tissue under it

Classification (Sub-solid)

• Most sub-solid nodules are transient and represent infection or hemorrhage

• Persistent sub-solid nodules can represent primary lung cancer (adenocarcinoma)

Characterization of Nodules (Margins)

• Smooth: Less likely malignant

Characterization of Nodules (Margins)

• Spiculated: “sun burst”

• Not diagnostic but highly associated with malignancy


Characterization of Nodules (Margins)

• Lobulated: intermediate probability of malignancy

Courtesy of E. Jackson 2017
**Characterization of Nodules (Size)**

- Likelihood of malignancy correlates with nodule diameter.
- Nodule size is the dominant factor in management.
- 75% of nodules > 2.0 cm are malignant.
- 1% of nodules between 2-5 mm are malignant.

**Characterization of Nodules (Size)**

- Based on the average of long and short axis diameters.
- Measurements should be made with electronic calipers.
- Measurements should be rounded to the nearest whole millimeter.

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**Characterization of Nodules (Doubling Time)**

- Doubling time: Assessed based on the volume of the nodule.
- One doubling time: 26% increase in diameter.
- Solid malignant nodules: Average doubling time of 160-180 days & range 20-400 days.

**Characterization of Nodules (Doubling Time)**

- Sub-solid malignant nodules: Longer doubling times.
- Average 1346 days (3.6 years) to double in volume.
- Nodules should be followed at least 5 years before being considered benign.
Characterization of Nodules (Location)

- Nodules in the upper lobes are more likely to be malignant

Characterization (Benign) Calcification

- Diffuse
- Central
- Laminated
- Popcorn

Risk Assessment

Low Risk:
- Young age
- Non smoker
- Smaller nodule size
- Regular margins
- Location other than the upper lobe

Risk Assessment

High risk:
- Older age
- Smoking
- History of extra thoracic malignancy
- Larger size
- Irregular margins
- Upper lobe location

### Risk Assessment Models
- Most commonly used model (Mayo Clinic model)
- 3 clinical predictors
  - Smoking history
  - Age
  - Extra thoracic cancer
- 3 Imaging predictors
  - Nodule diameter
  - Spiculated margin
  - Upper lobe predominance

### Risk Assessment Signs and Symptoms
- Clubbing
- Hemoptysis
- Weight loss
- Night sweats
- New diffuse bone pain

### Nodule Management Guidelines
- Determine which nodules are benign and need no further evaluation
- Determine which nodules are suspicious for malignancy
  - Fleischner Society 2017:
  - ACR Lung RADS:

### Fleischner Society 2017
- Incidentally encountered lung nodules detected on Chest CT in adults who are 35 years or older.
- Should not be used for
  - Patients with known primary cancers who are at risk for metastases
  - Immune compromised patients
  - Patients younger than 35
  - Lung cancer screening
### Solid Nodules < 6mm
- Nodules < 6 mm (5mm) do not require routine follow up in most patients
- High risk patients: with suspicious nodules may warrant 12 month follow-up
  - Upper lobe location
  - Suspicious morphology

### Solid Nodules 6-8 mm
- Low risk: Follow-up CT in 6-12 months depending on morphology and patient preference
- A 3rd CT at 12-18 months is optional

### Solid Nodules 6-8 mm
- High risk: Follow-up CT in 6-12 months depending on morphology and patient preference
- The 3rd CT should be obtained in 18-24 months
- The cancer risk is 0.5% - 2.0% for nodules in this size range

### Solid Nodules > 8mm
- Low and High risk: 3 month follow up combined with PET/CT and or tissue sampling
- Average risk of cancer in a 8 mm solitary nodule is 3.0%
Tissue Sampling

- CT guided biopsy
- EBUS TBNA
- Surgical Resection

Multiple Solid Nodules < 6 mm

- Low Risk patients: No routine follow up

Multiple Solid Nodules < 6 mm

- High Risk patients: Optional CT in 12 months based on morphology and patient preference

Multiple Solid Nodules 6-8 mm

- Low Risk patients: Follow up CT at 3-6 months
- Consider a 3rd CT at 18-24 months
Multiple Solid Nodules 6-8 mm

- High Risk patients: Follow up CT in 3-6 months
- 3rd CT at 18-24 months

Multiple Solid Nodules >8 mm

- Low and High Risk patients: Repeat CT in 3-6 months
- 3rd CT at 18-24 months

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<table>
<thead>
<tr>
<th>Size</th>
<th>Single</th>
<th>Multiple</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 6 mm (≤10mm³)</td>
<td>Low risk</td>
<td>High risk</td>
<td>No routine follow</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Optional CT at 12 months</td>
</tr>
<tr>
<td>6-8 mm (10-200mm³)</td>
<td>Low risk</td>
<td>High risk</td>
<td>CT at 6-12 mo; then consider CT at 18-24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>CT at 6-12 mo; then CT at 18-24</td>
</tr>
<tr>
<td>&gt; 8 mm (≥200mm³)</td>
<td>Low risk</td>
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<td></td>
<td>CT at 3-6 mo; then CT at 18-24</td>
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Solitary Sub-solid Nodule < 6 mm

- Low Risk: No routine follow up is recommended
- High Risk: follow up CT at 2 and 4 years

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http://www.radiologyassistant.nl/en/p5905aff4788ef/fleischner-2017-guideline-for-pulmonary-nodules.html by Onno Mets and Robin Smithuis the Academical Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands
<table>
<thead>
<tr>
<th>Solitary Sub-solid Nodule &gt; 6 mm</th>
<th>Solitary Sub-solid Nodule &gt; 6 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Follow up CT scan at 6-12 months</td>
<td>• Pure ground glass nodules that are 6 mm or larger may be followed safely for 5 years.</td>
</tr>
<tr>
<td>• 3rd CT in 2 years (year 3)</td>
<td>• Growth is seen in an average of 3-4 years or less</td>
</tr>
<tr>
<td>• 4th CT in 2 years (year 5)</td>
<td></td>
</tr>
<tr>
<td>• Total follow up is 5 years</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Solitary Part Solid Nodules &lt; 6 mm</th>
<th>Solitary Part Solid Nodules &gt; 6 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No routine follow up is recommended</td>
<td>• Solid component less than 6 mm in diameter</td>
</tr>
<tr>
<td></td>
<td>• Follow up CT is recommended at 3-6 months</td>
</tr>
<tr>
<td></td>
<td>• Follow up CT scans annually for a minimum of 5 years to assess the solid component</td>
</tr>
<tr>
<td>Solitary Part Solid Nodules &gt; 6 mm</td>
<td>Solitary Part Solid Nodules &gt; 6 mm</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>----------------------------------</td>
</tr>
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</table>
| • Solid component greater than 6 mm in diameter  
  • Follow up CT in 3-6 months | • The larger the solid component the greater the risk of  
  • Malignancy  
  • Invasiveness  
  • Metastasis |
| • Solid component greater than 8 mm or suspicious characteristics  
  • PET/CT  
  • Biopsy  
  • Resection | |

<table>
<thead>
<tr>
<th>Multiple Sub-solid Nodules &lt; 6 mm</th>
<th>Multiple Sub-solid Nodules &gt; 6 mm</th>
</tr>
</thead>
</table>
| • Follow up CT in 3-6 months  
  • Consider CT at 2 years  
  • Consider CT at 4 years | • Follow up CT at 3-6 months  
  • Subsequent management based on most suspicious nodule |
Sub-Solid Nodules

<table>
<thead>
<tr>
<th>Subsolid</th>
<th>Size</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groundglass</td>
<td>&lt; 6 mm</td>
<td>No FU indicated</td>
</tr>
<tr>
<td></td>
<td>&gt; 6 mm</td>
<td>CT at 6-12 months to confirm persistence, then CT at 3 and 5 years</td>
</tr>
<tr>
<td>Part-solid</td>
<td>&lt; 6 mm</td>
<td>No FU indicated</td>
</tr>
<tr>
<td></td>
<td>&gt; 6 mm</td>
<td>CT at 3-6 months to confirm persistence, then annual CT for 5 years</td>
</tr>
<tr>
<td>Multiple</td>
<td>&lt; 6 mm</td>
<td>CT at 3-6 months. If stable CT at 2 and 4 years</td>
</tr>
<tr>
<td></td>
<td>&gt; 6 mm</td>
<td>CT at 3-6 months. Subsequent management based on most suspicious nodule</td>
</tr>
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Lung Cancer Screening

- In February of 2015 The Centers for Medicare & Medicaid Services (CMS) added lung cancer screening with low dose computed tomography (LDCT), as an additional preventive service benefit under the Medicare program.

Lung Cancer Screening Population

- Age 55-80*
- Current and former smokers within the last 15 years
- At least 30 pack years of smoking
- No signs or symptoms of lung cancer
- Medically fit for surgery


Lung RADS

- Lung imaging Reporting And Data System
- Classification system to aid low dose CT screening examinations
- Standardizes follow up and management decisions
- Similar to Fleisher criteria but designed for high risk population

Lung RADS Category 1

- Negative screen ( < 1% chance of malignancy)
- No nodules
- Lung nodules with specific findings favoring benign nodules
  - Complete calcification
  - Central calcification
  - Popcorn calcification
  - Laminated calcification

Characterization (Benign) Calcification

- Diffuse
- Central
- Laminated
- Popcorn


Lung RADS Category 1

- Repeat LDCT in 12 months in accordance with lung cancer screening guidelines
### Lung RADS Category 2

- **Benign appearance (< 1% chance of malignancy)**
- **Solid nodules**
  - < 6 mm
  - New nodules < 4 mm
- **Part-solid nodules**
  - < 6 mm on base line screening
- **Ground glass nodules**
  - < 20 mm
  - > 20 mm and unchanged

### Repeat LDCT in 12 months in accordance with lung cancer screening guidelines

### Lung RADS Category 3

- **Probably Benign 1-2% chance of malignancy**
- **Solid nodules**
  - > 6 mm < 8 mm
  - New nodule 4-6 mm
- **Part-solid nodules**
  - > 6 mm with a solid component of < 6 mm
  - New < 6 mm total diameter
- **Ground glass nodules**
  - > 20 mm on baseline CT

### 6 month follow up with low-dose CT
### Lung RADS Category 4A

- Suspicious 5-15% chance of malignancy

- Solid nodules
  - > 8 mm to < 15 mm baseline
  - New nodule >6 mm but <8 mm

- Part-solid nodules
  - > 6 mm total diameter solid component >6mm < 8 mm
  - New or growing < 4mm solid component

- 3 month follow up with low-dose CT
- PET/CT may be considered based on nodule characteristics and size

### Lung RADS Category 4B

- Suspicious > 15% chance of malignancy

- Solid nodule
  - > 15 mm
  - New or growing nodule >8mm

- Part-solid nodules
  - Solid component > 8 mm
  - New or growing > 4mm solid component

- Chest CT with or without contrast, as appropriate.
- PET/CT and/or tissue sampling should be considered.
Lung RADS Category 4X

- Suspicious > 15% chance of malignancy
- Category 3-4 nodules with additional features that increase suspicion of malignancy
  - Spiculation
  - Ground glass nodules that double in size in 1 year
  - Enlarged regional lymph nodes

Lung RADS Category 4X

- Chest CT with or without contrast, as appropriate.
- PET/CT and/or tissue sampling should be considered.

CT with or without Contrast

- CT with contrast: Indicated for patients with suspected hilar, mediastinal or pleural abnormalities.

PET

- Solid Nodules: PET has sensitivity and specificity of approximately 90% for detecting malignant nodules with a diameter of 10 mm or larger
- Sub-Solid Nodules: Sensitivity of 90% specificity of 71%
PET

False Negatives:
• Nodules less than 10 mm
• Well differentiated Cancers
• Carcinoid

False Positives:
• Infectious/Inflammatory granulomas

Approach

• 1. Compare old images if available
• 2. Risk stratify your patient and the nodule
• 3. Learn your patients preferences
• 4. Apply appropriate guidelines

References

5. http://www.scr.org/Quality-Safety/Lung-Cancer-Screening-Center
6. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017
9. Pulmonary Nodules Onno Mets and Robin Smithuis the Academical Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands