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

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### 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

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**Pulmonary Nodule**

![Image of Pulmonary Nodule](image)

Courtesy of E. Jackson 2017
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>
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<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

<table>
<thead>
<tr>
<th>Pure Ground Glass</th>
<th>Part Solid</th>
</tr>
</thead>
</table>

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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the Academic Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands
### 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
## Solid Nodules

<table>
<thead>
<tr>
<th>Solid</th>
<th>Size</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>Low risk</td>
<td>No routine follow</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Optional CT at 12 months</td>
</tr>
<tr>
<td>Multiple</td>
<td>Low risk</td>
<td>No routine follow</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>Optional CT at 12 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>Low risk</td>
<td>CT at 6-12 mo, then consider CT at 18-24</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>CT at 6-12 mo, then CT at 18-24</td>
</tr>
<tr>
<td>Multiple</td>
<td>Low risk</td>
<td>CT at 3-6 mo, then consider CT at 18-24</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>CT at 3-6 mo, then CT at 18-24</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>All</td>
<td>Consider CT at 3 mo, PET/CT or Biopsy</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>Low risk</td>
<td>CT at 3-6 mo, then consider CT at 18-24</td>
</tr>
<tr>
<td></td>
<td>High risk</td>
<td>CT at 3-6 mo, then CT at 18-24</td>
</tr>
</tbody>
</table>

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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


Onno Mets and Robin Smithuis the Academical Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands
### Solitary Sub-solid Nodule > 6 mm

- Follow up CT scan at 6-12 months
- 3rd CT in 2 years (year 3)
- 4th CT in 2 years (year 5)
- Total follow up is 5 years

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### Solitary Sub-solid Nodule > 6 mm

- Pure ground glass nodules that are 6 mm or larger may be followed safely for 5 years.
- Growth is seen in an average of 3-4 years or less
**Solitary Part Solid Nodules < 6 mm**

- No routine follow up is recommended

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**Solitary Part Solid Nodules > 6 mm**

- Solid component less than 6 mm in diameter
- Follow up CT is recommended at 3-6 months
- Follow up CT scans annually for a minimum of 5 years to assess the solid component
## Solitary Part Solid Nodules > 6 mm

- Solid component greater than 6 mm in diameter
  - Follow up CT in 3-6 months

- Solid component greater than 8 mm or suspicious characteristics
  - PET/CT
  - Biopsy
  - Resection

## Solitary Part Solid Nodules > 6 mm

- The larger the solid component the greater the risk of
  - Malignancy
  - Invasiveness
  - Metastasis
<table>
<thead>
<tr>
<th>Multiple Sub-solid Nodules &lt; 6 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Follow up CT in 3-6 months</td>
</tr>
<tr>
<td>• Consider CT at 2 years</td>
</tr>
<tr>
<td>• Consider CT at 4 years</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multiple Sub-solid Nodules &gt; 6 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Follow up CT at 3-6 months</td>
</tr>
<tr>
<td>• Subsequent management based on most suspicious nodule</td>
</tr>
</tbody>
</table>
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>≥ 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>≥ 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>≥ 6 mm</td>
<td>CT at 3-6 months. Subsequent management based on most suspicious nodule</td>
</tr>
</tbody>
</table>

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

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

Lung Cancer: Screening
Release Date: December 2013

Recommendation Summary

Summary of Recommendation and Evidence

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
<th>Grade (What's This?)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults Aged 55-80, with a History of Smoking</td>
<td>The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.</td>
<td>B</td>
</tr>
</tbody>
</table>


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
  - < 6mm
  - New nodules < 4mm
- Part-solid nodules
  - < 6 mm on base line screening
- Ground glass nodules
  - < 20 mm
  - > 20 mm and unchanged

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**Lung RADS Category 2**

- 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
  - > 6mm < 8 mm
  - New nodule 4-6 mm

- Part-solid nodules
  - > 6mm with a solid component of < 6 mm
  - New < 6 mm total diameter

- Ground glass nodules
  - > 20 mm on baseline CT

Lung RADS Category 3

- 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

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**Lung RADS Category 4A**

- 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

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**Lung RADS Category 4B**

- 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

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