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**

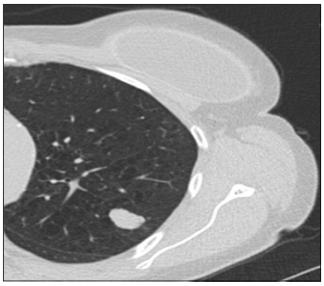
Approach to Pulmonary Nodules

- **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**

Pulmonary Nodule



Courtesy of E. Jackson 2017

Etiologies of Pulmonary Nodules

Benign	Malignant

• Infectious granuloma (80%)
  • Endemic Fungi
  • Atypical mycobacterium
  • Tuberculosis
	• Adenocarcinoma (50%)

• Hamartoma	• Squamous cell carcinoma
• AV malformation	• Small cell carcinoma
• Intrapulmonary lymph node	• Metastasis
	• Lymphoma
	• Carcinoid

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

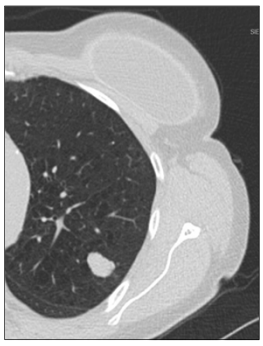
- Solid: More common
- Sub-solid:

  Pure ground glass: nodule with higher density than surrounding tissue but <u>does not</u> obscure the underlying lung

  Part solid: Nodule with at least part ground glass appearance

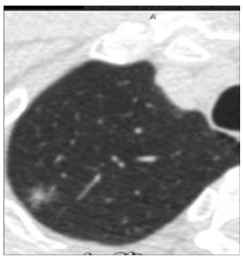
Classification

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



Classification

Pure Ground Glass



Part Solid

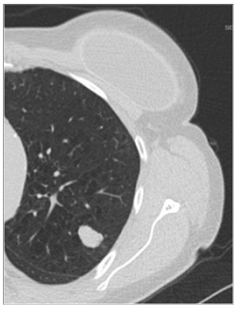
1. http://www.radiologyassistant.nl/en/p460f9fcd50637/solitary-pulmonary-nodule-benign-versus-malignant.html
2. http://www.radiologyassistant.nl/en/p5905aff4788ef/fleischner-2017-guideline-for-pulmonary-nodules.html

Classification (Sub-solid)

- Most sub-solid nodules are transient and represent infection or hemorrhage
- Persistent sub-solid nodules can represent primary lung cancer (adenocarcinoma)

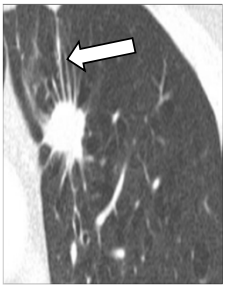
Characterization of Nodules (Margins)

- Smooth: Less likely malignant



Characterization of Nodules (Margins)

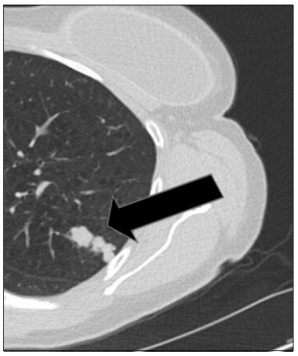
- Spiculated: "sun burst"
- Not diagnostic but highly associated with malignancy



http://www.radiologyassistant.nl/en/p460f9fcd50637/solitary-pulmonary-nodule-benign-versus-malignant.html

Characterization of Nodules (Margins)

- Lobulated: intermediate probability of malignancy



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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

http://www.radiologyassistant.nl/en/p5905af4788ef/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

Characterization of Nodules (Doubling Time)

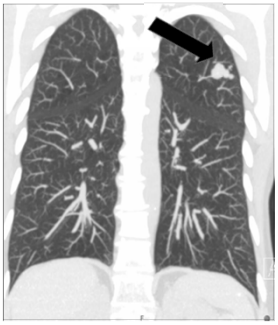
- Doubling time: Assessed based on the volume of the nodule.
- One doubling time: 26% increase in diameter
- Solid malignant nodules: Average doubling time of 160-180 days & range 20-400 days

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

http://www.radiologyassistant.nl/en/p460f9fcd50637/solitary-pulmonary-nodule-benign-versus-malignant.html

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 predicators
  - Smoking history
  - Age
  - Extra thoracic cancer
- 3 Imaging predicators
  - 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

Solid	Size	Follow up		
	< 6 mm (<100mm³)	Single	Low risk High risk	No routine follow Optional CT at 12 months
		Multiple	Low risk High risk	No routine follow Optional CT at 12 months
	6-8 mm (100-250mm³)	Single	Low risk High risk	CT at 6-12 mo, then consider CT at 18-24 CT at 6-12 mo, then CT at 18-24
		Multiple	Low risk High risk	CT at 3-6 mo, then consider CT at 18-24 CT at 3-6 mo, then CT at 18-24
	> 8 mm (> 250mm³)	Single	All	Consider CT at 3 mo, PET/CT or Biopsy
		Multiple	Low risk High risk	CT at 3-6 mo, then consider CT at 18-24 CT at 3-6 mo, then CT at 18-24

http://www.radiologyassistant.nl/en/p5905aff4788ef/fleischner-2017-guideline-for-pulmonary-nodules.htmby Onno Mets and Robin Smithuis the Academical Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands

Solitary Sub-solid Nodule < 6 mm

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

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

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

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

Multiple Sub-solid Nodules < 6 mm

- Follow up CT in 3-6 months
- Consider CT at 2 years
- Consider CT at 4 years

Multiple Sub-solid Nodules > 6 mm

- Follow up CT at 3-6 months
- Subsequent management based on most suspicious nodule

Sub-Solid Nodules

Subsolid	Size	Follow up
 Groundglass	< 6 mm	No FU indicated
	≥ 6 mm	CT at 6-12 months to confirm persistence, then CT at 3 and 5 years
 Part-solid	< 6 mm	No FU indicated
	≥ 6 mm	CT at 3-6 months to confirm persistence, then annual CT for 5 years
 Multiple	< 6 mm	CT at 3-6 months. If stable CT at 2 and 4 years
	≥ 6 mm	CT at 3-6 months. Subsequent management based on most suspicious nodule

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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.**

https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274

Lung Cancer Screening

Lung Cancer: Screening

Release Date: December 2013

Recommendation Summary

Summary of Recommendation and Evidence

Population	Recommendation	Grade (What's This?)
Adults Aged 55-80, with a History of Smoking	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.	B

Source: Final Update Summary: Lung Cancer: Screening. U.S. Preventive Services Task Force. July 2015.
https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening

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

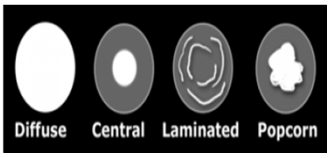
- Lung imaging Reporting And Data System
- Classification system to aid low dose CT screening examinations
- Standardizes follow up and management decisions
- Similar to Fleisher criteria but designed for high risk population

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



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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**

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**

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**

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

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2. Ost D, Fein AM, Feinsilver SH. Clinical practice. The solitary pulmonary nodule. N Engl J Med. 2003;348(25):2535-2542.
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9. Pulmonary Nodules Onno Mets and Robin Smithuis the Academical Medical Centre, Amsterdam and the Alrijne Hospital, Leiderdorp, the Netherlands