Pulmonary Nodules:
Assessing Risk with CT and PET/CT

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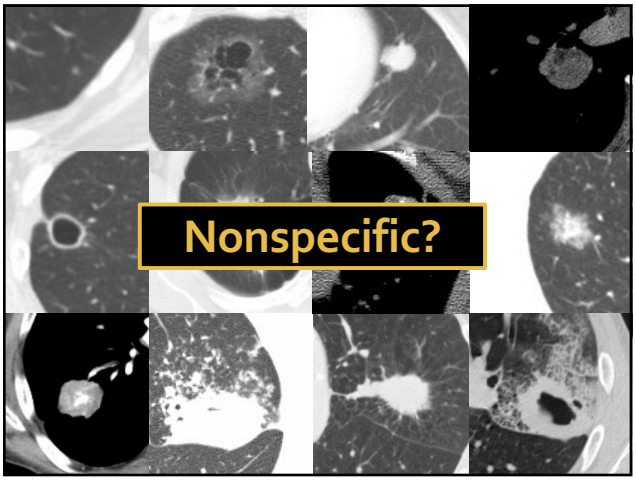

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How can you be helpful?

1. Look for definitively benign features.

Not definitely benign?

2. If small (<8 mm), recommend follow up.

Not small?

3. Assess risk of malignancy

Help guide management.

3

Topics

1. Definitively benign features
2. Small nodule follow up
3. Larger nodule risk assessment by CT and PET

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Definitively Benign Features

1. Benign Calcification
2. Fat
3. "Long Term" Stability
4. Small nodules in young people
5. Classic Perifissural nodules

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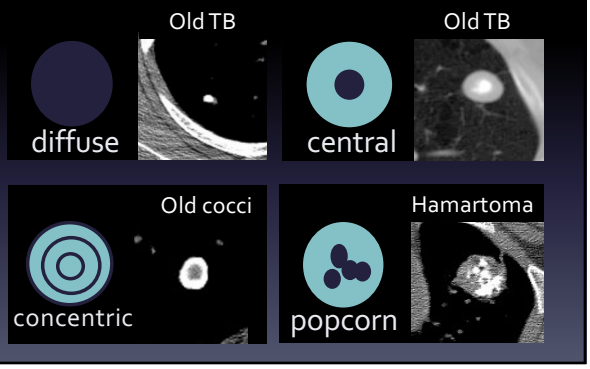
1. Benign Calcifications



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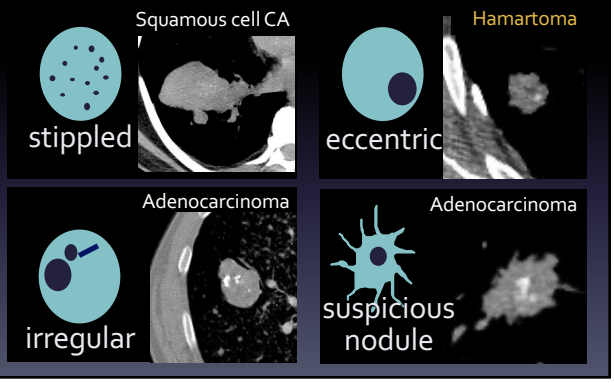
Indeterminate Calcifications



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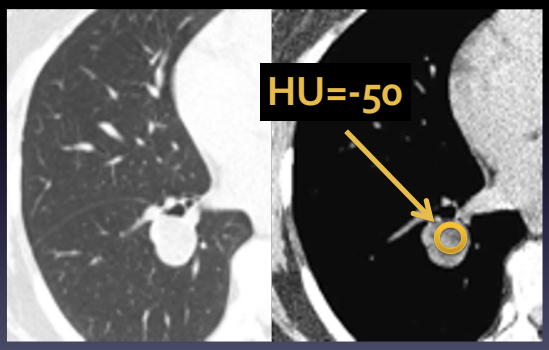
2. Fat



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3. "Long Term" Stability

- Solid Nodules: 2 years
- Ground Glass Nodules: 5 years? Forever?

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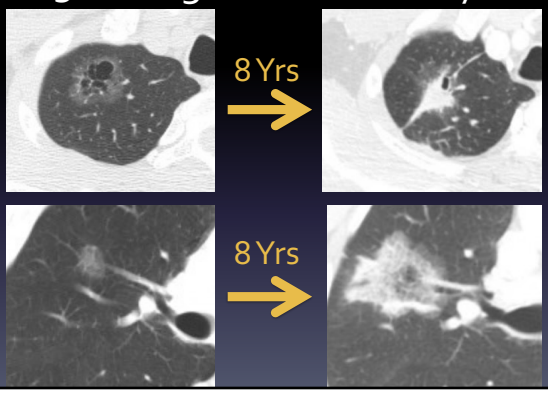
3. "Long Term" Stability



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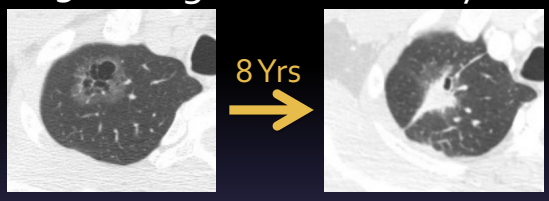
3. "Long Term" Stability



Lee et al:
> 5 mm SSN: 2% grew after 5 yrs of stability
Usually > 10 mm
No deaths in the cohort
Consider one f/u at 9 years?

Lee. Radiology. 295(2):448-

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4. Small Nodules in Young Patients

- "Small":

  <8mm or so, depending on appearance

- "Young"

  <35 years old, per Fleischner Society Guidelines

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5. Perifissural Nodules

Typical:

Fissure-attached

Homogenous, solid

Smooth margins

Oval, lentiform, triangular

McWilliams et al. NEJM. 2013; 369:910-9.
De Hoop *et al.* Radiology. 2012; 265: 611-6.
Ahn *et al.* Radiology. 2010; 254:949-56.

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5. Perifissural Nodules

~20-30% of nodules

Various sizes: 1-13 mm

Up to 15% can grow

3 studies: 0 cancers

Fleischner: f/u "not recommended"

Lung-Rads v2022: <1 cm = Cat 2

McWilliams et al. NEJM. 2013; 369:910-9.
De Hoop *et al.* Radiology. 2012; 265: 611-6.
Ahn *et al.* Radiology. 2010; 254:949-56.

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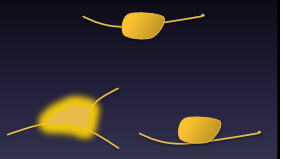
5. Perifissural Nodules

Non perifissural nodules must be followed per guidelines



McWilliams et al. NEJM. 2013; 369:910-9.
De Hoop *et al.* Radiology. 2012; 265: 611-6.
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Not Definitely Benign?

- If the nodule is < 8 mm, provide follow up recommendations.

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Fleischner Society Guidelines

Recommendations for Follow-up and Management of Nodules Smaller than 8 mm Detected Incidentally at Nonscreening CT

Nodule Size (mm)*	Low-Risk Patient†	High-Risk Patient‡
≤4	No follow-up needed§	Follow-up CT at 12 mo; if unchanged, no further follow-up‖
>4–6	Follow-up CT at 12 mo; if unchanged, no further follow-up‖	Initial follow-up CT at 6–12 mo then at 18–24 mo if no change‖
>6–8	Initial follow-up CT at 6–12 mo then at 18–24 mo if no change	Initial follow-up CT at 3–6 mo then at 9–12 and 24 mo if no change
>8	Follow-up CT at around 3, 9, and 24 mo, dynamic contrast-enhanced CT, PET, and/or biopsy	Same as for low-risk patient

Note.—Newly detected indeterminate nodule in persons 35 years of age or older.
* Average of length and width.
† Minimal or absent history of smoking and of other known risk factors.
‡ History of smoking or of other known risk factors.
§ The risk of malignancy in this category (<1%) is substantially less than that in a baseline CT scan of an asymptomatic smoker.
‖ Nonsolid (ground-glass) or partly solid nodules may require longer follow-up to exclude indolent adenocarcinoma.

MacMahon. Radiology 2005; 237: 395.

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MacMahon. Radiology 2005; 237: 395.

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Fleischner Society Guidelines: 2017

MacMahon H, Naidich DP, Goo JM, Lee KS, Leung AN, Mayo JR, Mehta AC, Ohno Y, Powell CA, Prokop M, Rubin GD, Schaefer-Prokop CM, Travis WD, Van Schil PE, Bankier AA.
Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017.

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Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: 6–8 mm (100–250 mm³)	Size: >8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT, PET/CT, or tissue sampling at 3 months	Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT, PET/CT, or tissue sampling at 3 months	Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: ≥6 mm (≥100 mm³)	Comments
Single			
Ground-glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A–4C).
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.
* Dimensions are average of long and short axes, rounded to the nearest millimeter.
† Consider all relevant risk factors (see Risk Factors).

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Fleischner Society Guidelines: 2017

- Solid and Subsolid in one table
- More complex: hard to memorize
- There are "optional" CTs
- Considers risk, density, multiplicity
- Key number: 5 mm (<6 mm)

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Fleischner 2017: Key Questions

Partial Scans:

No

Nodule in the bases/apices:

Immediate chest CT for "large or very suspicious"

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Fleischner Society Guidelines: 2017

Large/Suspicious (generally >8 mm)

- –Close CT follow up
- –PET
- –Biopsy

MacMahon. Radiology 2005; 237: 395.

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Fleischner Society Guidelines: 2017

Large/Suspicious (generally >8 mm)

- –Close CT follow up → Conservative
- –PET → Costly
- –Biopsy → Invasive

Christensen. AJR 2006; 187: 1361.

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Not Definitely Benign and Not Small?

Assess risk of malignancy

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CT Features: Size

< 4mm 0%

4-7 mm 1%

8-20 mm 15%

>20 mm 81%

Swensen. Radiology 2005; 235: 259

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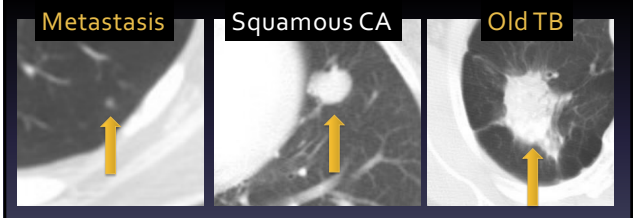
CT Features: Size



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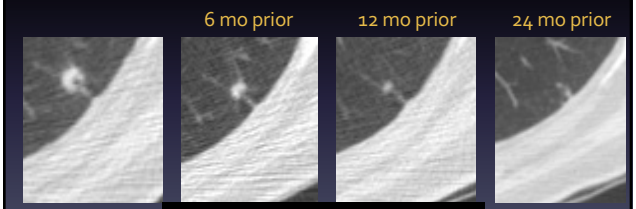
CT Features: Growth

Slow to moderate growth suggests malignancy



Adenocarcinoma

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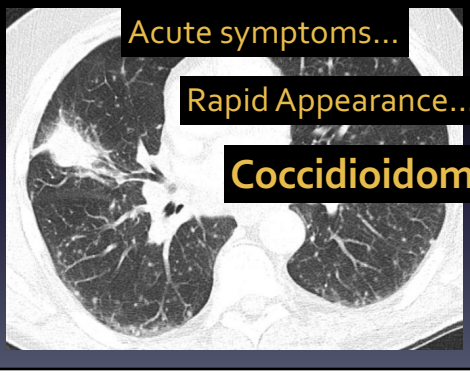
CT Features: Growth



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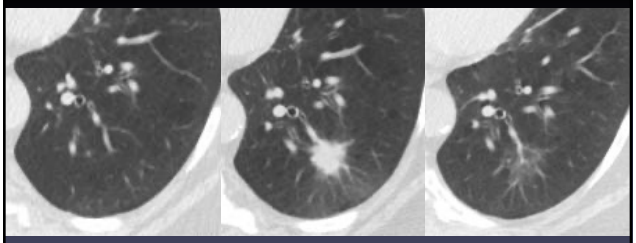
CT Features: Growth



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CT Features: Decrease in Size?

- Untreated regressing nodules are usually benign
- Transient decreases in size can occur in lung cancer uncommonly
- A single follow up with slight size decrease still requires follow up

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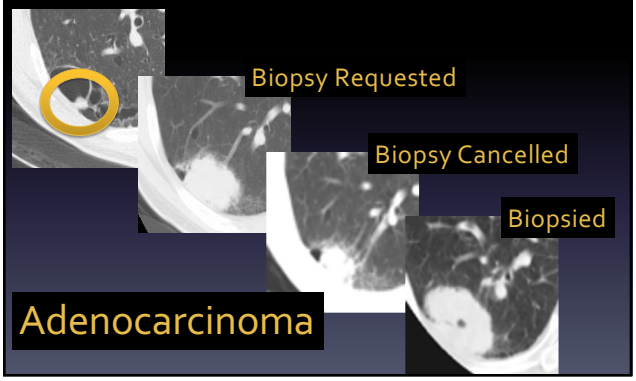
CT Features: Decrease in Size?



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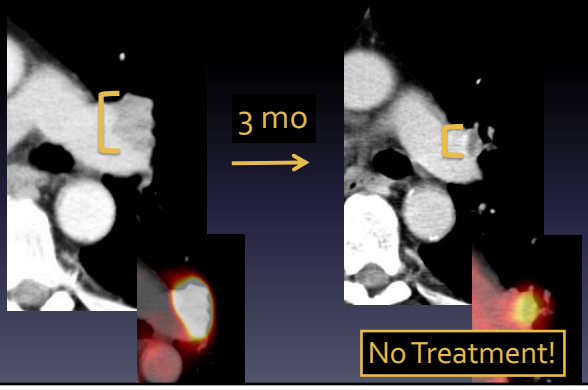
CT Features: Decrease in Size?



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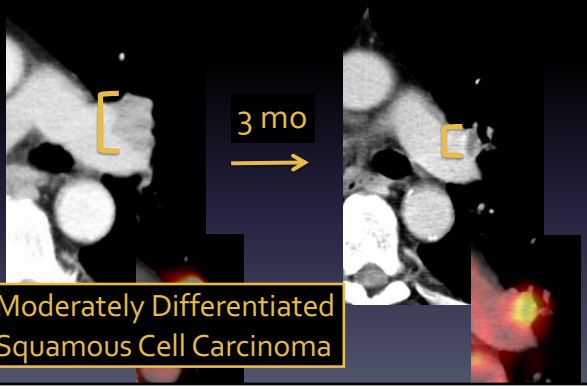
CT Features: Decrease in Size?



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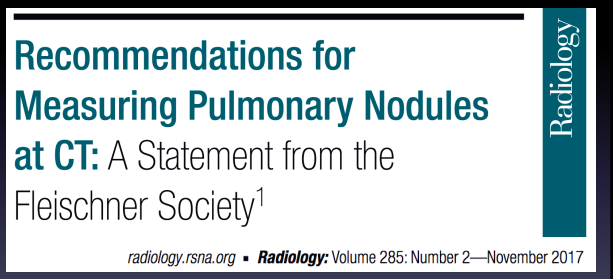
How to Measure a Nodule



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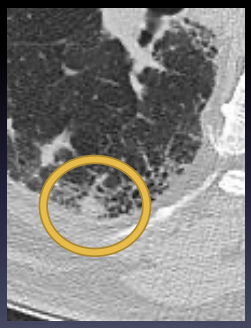
How to Measure a Nodule

- <1.5 mm slices
- Sharp filter
- Full inspiration
- Lung windows



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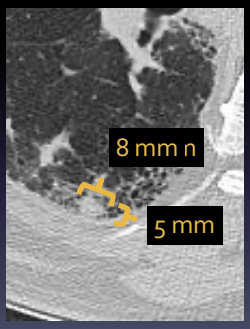
How to Measure a Nodule

- Long axis
- Same slice short axis
- Averaged 6.5 → 7 mm



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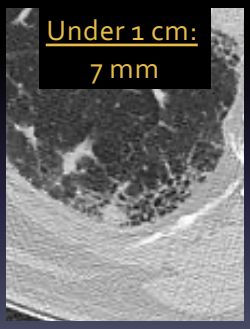
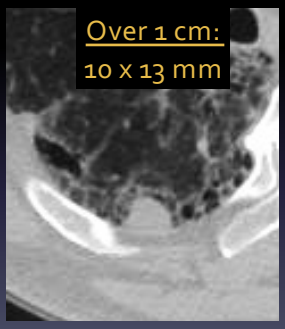
How to Measure a Nodule





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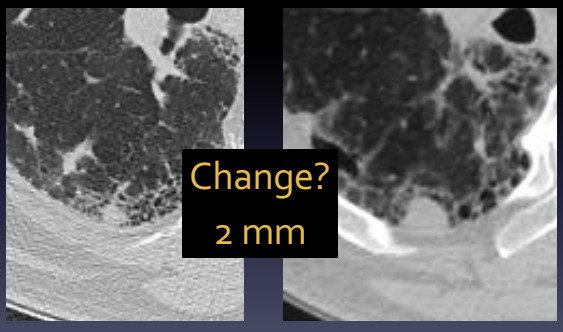
How to Measure a Nodule



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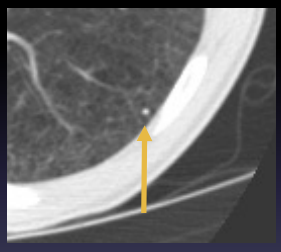
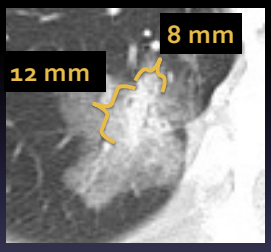
How to Measure a Nodule



"Micronodule"
<3 mm



Solid vs GGO:
Measure both

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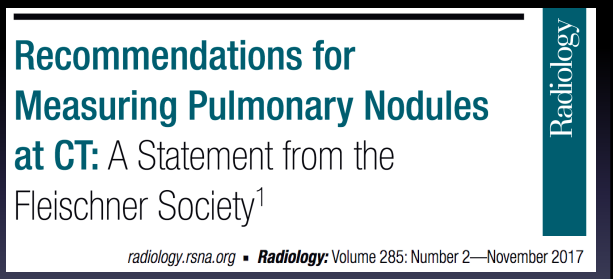
How to Measure a Nodule



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CT Features: Border

- 89% of nodules with spiculation are cancer
- Spiculation is caused by lymphatic/vascular invasion and fibrosis
- DDX for spiculated nodules: granulomatous disease

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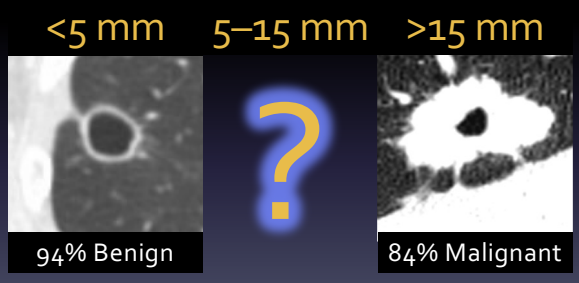
CT Features: Cavitation



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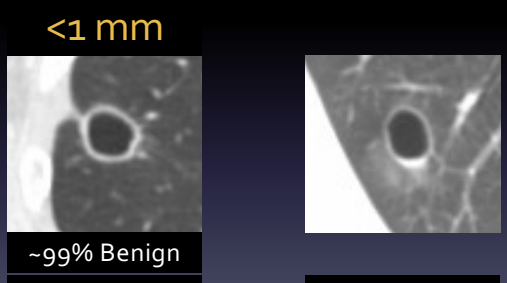
CT Features: Cavitation



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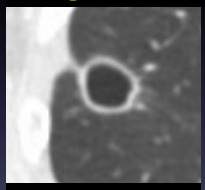
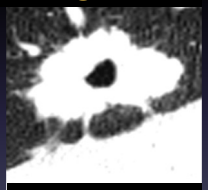
CT Features: Cavitation

<5 mm | 5–15 mm | >15 mm



94% Benign

?



84% Malignant

But: Honda JCAT 2007 showed no difference at all!

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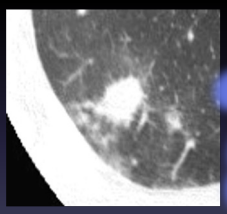
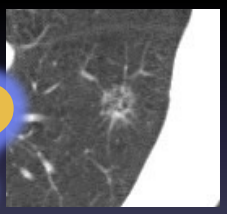
CT Features: Density



?



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CT Features: Density

Nodule density	% neoplastic
Solid	11
Mixed	48
GGO	59

Li. Radiology 2004; 233: 793

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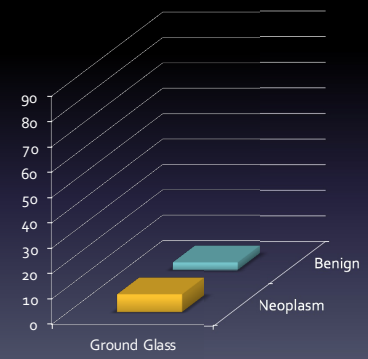
CT Features: Density



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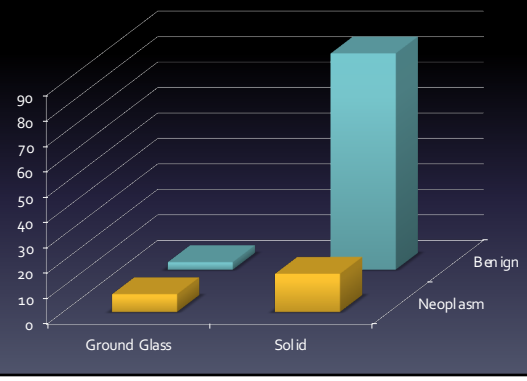
CT Features: Density



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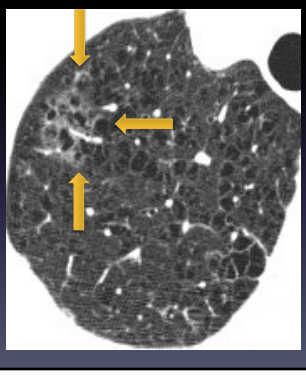
CT Features: Density



- If not a transient infection, the risk of neoplasm is high
- If neoplasm, likely an indolent one
- Bottom line: cannot Ignore

Kim. Radiology 2007; 245: 267

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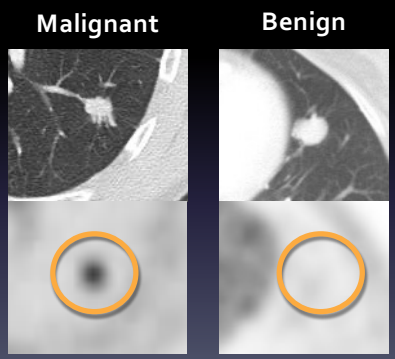
PET for Nodules: Basic Principle



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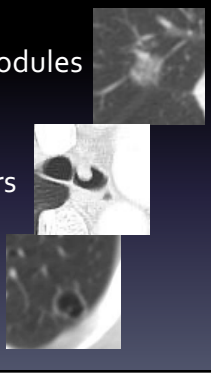
PET for Nodules: False Negatives?

- Ground glass nodules
- Indolent cancers
- Cystic nodules



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PET for Nodules: False Positives?

- Mostly infections, particularly granulomatous
- Inflammatory processes
- Lots of overlap with cancer SUVs

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PET for Nodules

- Threshold for positive?
  - Qualitative
    - Above Lung
    - Above Mediastinum
    - Above Liver
  - Quantitative
    - Max SUV = 2.5

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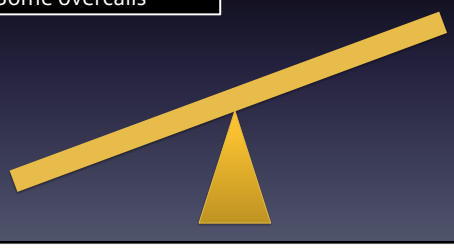
So which side do we want to be on?

Low threshold:
-Few missed cancers
-Some overcalls



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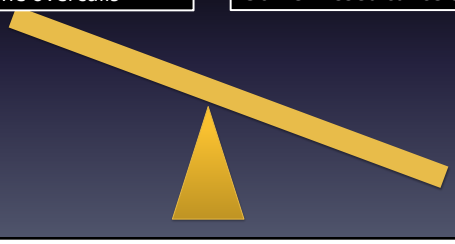
So which side do we want to be on?

Low threshold:
-Few missed cancers
-Some overcalls

High threshold:
-Confirms cancer well
-Some missed cancers



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So which side do we want to be on?

Low threshold:
-Few missed cancers
-Some overcalls

High threshold:
-Confirms cancer well
-Some missed cancers

What is needed?
- We don't need to "confirm cancer". That's what biopsies are for!
- We need a sensitive test, so if we don't find activity, it's reassuring, and we can avoid biopsy.

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PET for Nodules: A Low Threshold is Desired

	Sensitivity	Specificity
• HIGH threshold:	91%	91%
• LOW threshold:	97%	85%

1. Gould. JAMA 2001; 138: 724.
2. Fischer. Lancet Onc 2011; 2:659.
3. Lowe. J Clinical Oncology 1998; 16: 1075
4. Christensen. AJR 2006; 187: 1361.
5. Kim. JNM. 2007; 48: 214.

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PET for Nodules: High Sensitivity

- Lowest threshold
- Anything detectable (i.e. above background lung)

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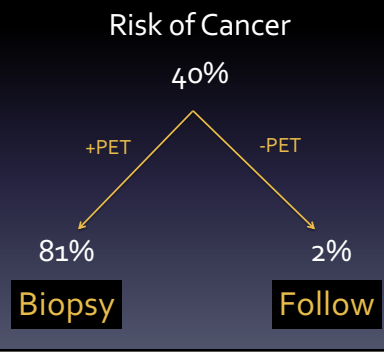
PET for Nodules: How good it is?



LR+ 6.4, LR-:0.04

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PET for Nodules: Conclusions

- Is covered by CMS (< 4 cm) and supported by "moderate" evidence:
- But, probably not cost effective beyond CT for many cases.
- Helps with high surgical risk patients and troubleshooting.

Fletcher. JNM 2008; 49:480.
Gould. Annals of Int Med 2003; 138: 724.
Barnett. Chest 2010; 137: 53.

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PET for Pulmonary Metastases

- Same principles
- Extra factor: expected tumor characteristics to alter your threshold
  - More Indolent: Carcinoid/treated met.
  - More Aggressive: Melanoma

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Nodule Size and PET: How Low Can You Go?

http://brilliantbash.wordpress.com/2010/09/12/sample-brilliant-bash-blueprint-tiki-party/

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Nodule Size and PET: How Low Can You Go?

- Classically: "1 cm"
- Better Answer: It Depends
  - Aggressive tumors in the apex: 7 mm?

  vs.

  - Non-aggressive tumors at the diaphragm: 15 mm?

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Topics Covered

1. Definitively benign features
2. Small Nodule Follow Up
3. Larger Nodule Risk Assessment

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THANK YOU!

Pulmonary Nodules:
Assessing Risk with CT and PET/CT

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