

Typical and Atypical Appearances of Lung Cancer

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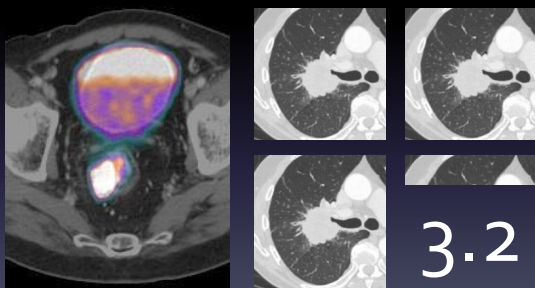
1

Lung Cancer is Important



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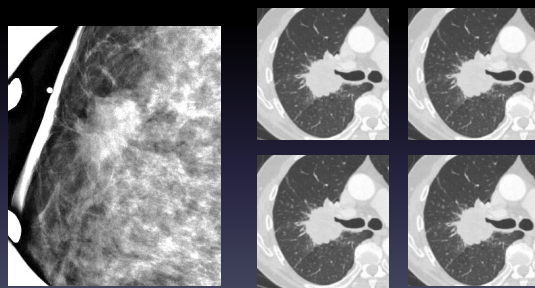
The Scourge of Cancer



American Cancer Society: <http://www.cancer.org/groups/content/@epidemiology/surveillance/documents/document/acspc-037113.pdf>

3

The Scourge of Cancer



American Cancer Society: <http://www.cancer.org/groups/content/@epidemiology/surveillance/documents/document/acspc-037113.pdf>

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The Scourge of Cancer

17.6

American Cancer Society: <http://www.cancer.org/jacs/groups/content/@epidemiology/surveillance/documents/document/acspc-037133.pdf>

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Lung Cancer is Important

A CT scan image showing a large, central lung mass, likely a tumor.

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Lung Cancer is Important

Adenocarcinoma Pre-invasive Lesions Neuroendocrine

Squamous Cell Carcinoma Mucinous

Carcinoid Salivary Gland Type Carcinomas

Large Cell Small Cell Carcinoma

NSCLC Lepidic Predominant Minimally invasive adenocarcinoma

Adenocarcinoma in situ

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Lung Cancer is Important

Squamous Cell Carcinoma

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Lung Cancer is Important

Squamous Cell Carcinoma

- 30% lung carcinomas
- Cigarette smoking associated
- Arises in bronchi
- Early disease course presentation
- Hilar metastases eventually, uncommon early mets
- Local invasion
- Atelectasis, consolidation, mucoid impaction, bronchiectasis common
- 30% present in lung periphery (30% of 30%?) (% of all peripheral nodules?)
- Central; necrosis/cavitation more common than other NSCLC

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Lung Cancer is Important

Squamous Cell Carcinoma	Adenocarcinoma, Subtypes	Carcinoid tumor
<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion
Adenocarcinoma	Small Cell Carcinoma	Salivary Gland Type Carcinomas
<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion
Pre-invasive Lesions	Large Cell Carcinoma	Dedifferentiated Tumors
<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion 	<ul style="list-style-type: none"> • 30% lung carcinomas • Cigarette smoking associated • Arises in bronchi • Early presentation • Hilar presentation, uncommon early mets • Local invasion

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What do I need to know?

1. Typical, "Slam Dunk," Appearance
 - Prediction based on appearance
 - Expected spread? next step?
 - Evaluate concordance
 - Good to know

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What do I need to know?

1. Typical, Slam Dunk, Appearance
2. Easy to remember/notable variants

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What do I need to know?

1. Typical, Slam Dunk, Appearance
2. Easy to remember/notable variants
3. Important tidbits
 - Issues with biopsies
 - Issues with staging
 - FDG PET

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The Message

- Typical and select atypical appearances are easy to remember and matter
- A few scattered, key facts will take you the rest of the way!

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Topics

Adenocarcinoma

Squamous cell

Small Cell

Large Cell

Carcinoid

Salivary Gland

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Topics

Adenocarcinoma

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Small Cell

Large Cell

Carcinoid

Salivary Gland

INCIDENCE ↓

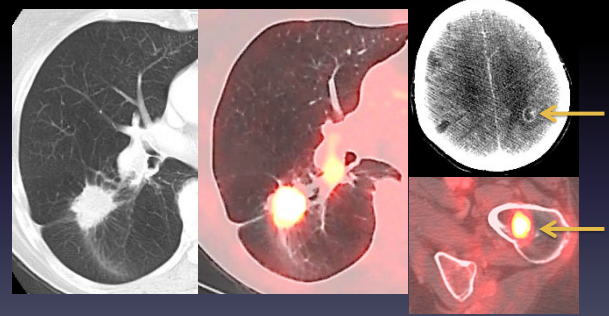
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Lung Cancer

- Classic, "Slam Dunk," Appearance, Description, and Examples
- Easy to remember & notable, variants, tidbits
- AT THE END: tie some appearances together

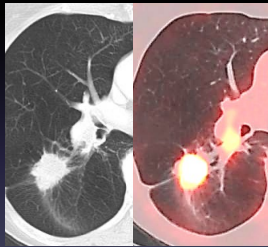
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Classic Adenocarcinoma



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Classic Adenocarcinoma



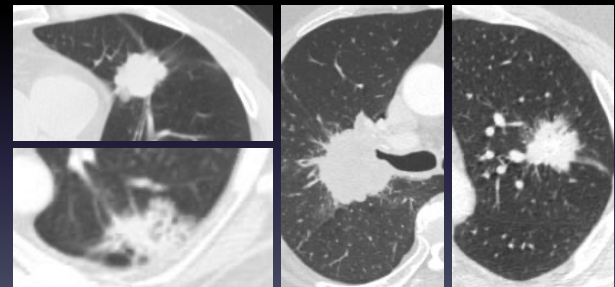
SLAM DUNK APPEARANCE:

- Peripheral, spiculated SPN
- Early oligo-metastases and invasion
- Demographic: Older smoker

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Classic Adenocarcinoma

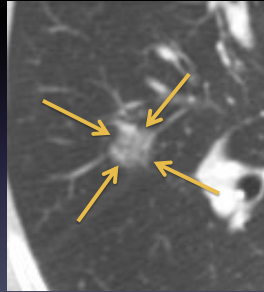
Other examples



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Adenocarcinoma, Pre-invasive

- Ground glass nodules
- “Adenocarcinoma Spectrum”
- Different talk!



Travis. J of Thorac Oncol. 2011. 6(2):244-86.

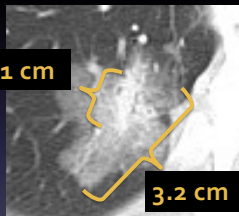
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The Neoplasm Formerly Known as BAC

- Can suggest pre-invasive neoplasm if
 - Ground glass and < 3 cm
 - No (or < 5mm) solid components
 - Completely different follow up, prognosis, etc.
- If > 3 cm, or >5 mm solid, this is invasive

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Adenocarcinoma, GGO Predominant

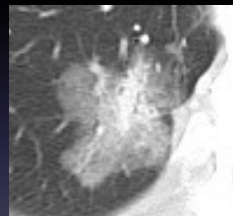


- Ground glass predominant nodule/mass
- Formerly – “mixed Adeno/BAC”.
- “Lepidic predominant (Invasive) Adenocarcinoma”
- Genetically different: EGFR exon 21 missense

Lee et al. Radiol 2013. 267(1):254-64.

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Adenocarcinoma, GGO Predominant



- Much better prognosis
- Fewer metastases
- Co-existent pre-invasive lesions

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Adenocarcinoma, GGO Predominant

> 3cm overall
> 5 mm solid

> 3cm overall
> 5 mm solid

> 5 mm solid

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Adenocarcinoma, GGO Predominant

Do we diagnosis these ultimately?

- Pathology final diagnosis
- Lepidic-predominant is 1 of 5 non-mucinous subtypes.

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Adenocarcinoma, GGO Predominant

Not good!

Solid

Micro-papillary

Papillary

Acinar

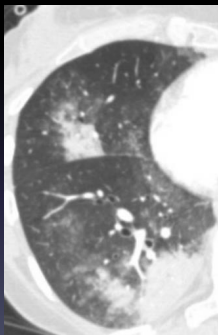
Lepidic Ground Glass

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Adenocarcinoma, Mucinous

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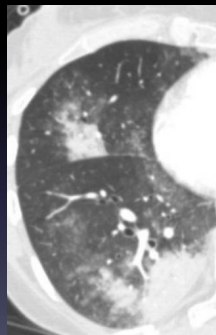
Adenocarcinoma, Mucinous



- Mucinous (Invasive) Adenocarcinoma
- Don't be confused: formerly "Mucinous BAC"

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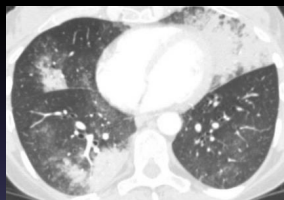
Adenocarcinoma, Mucinous



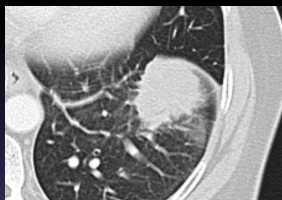
- Distinct appearance and unique genetics (KRAS mutation)
- Bad prognosis
- High FDG avidity

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Mucinous: Actually Two Types



"Penumonic"
"Consolidative"

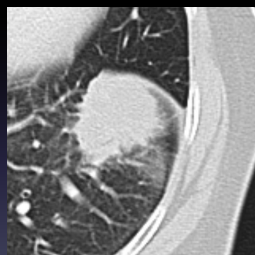


"Nodular"
"Solitary Pulm. Nodular"

Watanabe et al. Ann Thor Surg. 99(3):975-981.
Lee et al. J Thor Onc. 11(7):1064-1073.

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Nodular Mucinous Adeno



- Majority of mucinous adenos
- Can be AIS/MIA
- Lower FDG avidity
- Average level survival

Watanabe et al. Ann Thor Surg. 99(3):975-981.
Lee et al. J Thor Onc. 11(7):1064-1073.

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Adenocarcinoma, Variants

- Pre-invasive
- Lepidic-predominant
- Pneumonic Mucinous Variant
- Colloid Variant
- Fetal Variant
- Enteric Variant

} Common

} Important

} Rare....

} ...let's ignore!

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Adenocarcinoma, Variants

- Pre-invasive
- Lepidic-predominant
- Pneumonic mucinous variant

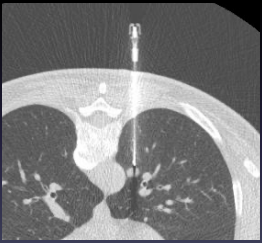
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Adenocarcinoma, Mutations

What do I need to know about "molecular testing"?!?!?

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Adenocarcinoma, Mutations



→ Does it look like an adenocarcinoma?

↓

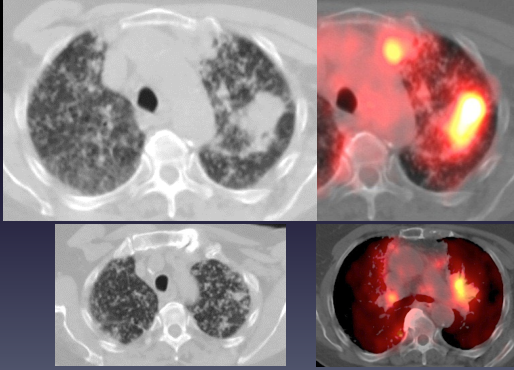
Test for "drugable" mutations

↓

Treat with drugs

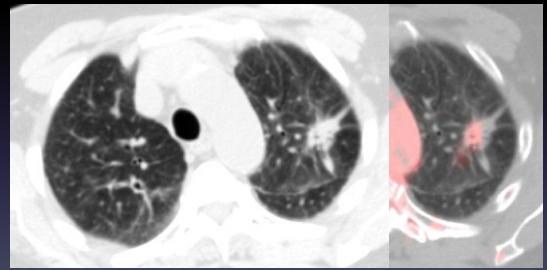
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Adenocarcinoma, Mutations



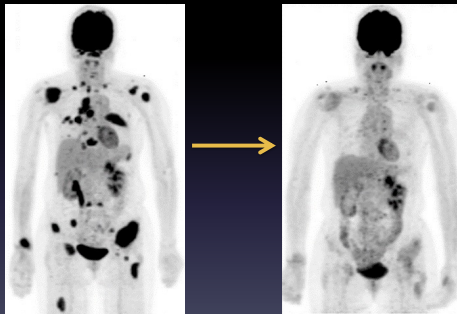
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Adenocarcinoma, Mutations



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Adenocarcinoma, Mutations



...and low toxicity!!!

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Adenocarcinoma, Mutations

EGFR	5 drugs	15%
ALK	5 drugs	5%
BRAF	1 drug	4%
		76%?

Halpenny D. JTI. 35(1): 26-36, 2020.

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Adenocarcinoma, Mutations

Issue #2:

Resistance

(which may lead to another biopsy)

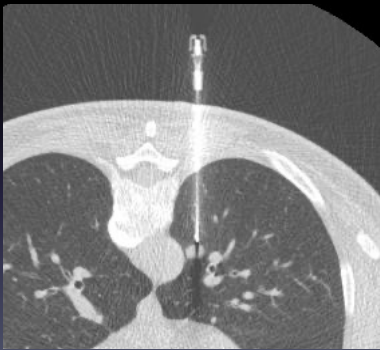
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Adenocarcinoma, Mutation

- Why do we want to know this?
 - Understand how patients will be treated
 - Relates to prognosis (EGFR – good; KRAS – bad)
 - Affects when we may have to re-biopsy
 - Affects our biopsy technique...

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Adenocarcinoma, Mutations



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Adenocarcinoma, Gene Mutations


What do I need to know about "molecular testing"?!?!?

That's it.

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Adenocarcinoma, PET

- It's cancer
- It's hypermetabolic



- MaxSUVs typically moderate (4-12)
- Pre-invasive, lepidic-predominant, indolent, & treated tumors often lower or background level

Li et al. Lung Canc 2010, 68:394-7.
Bille et al. Eur J of Cardio-Thor Surg. 2013; 43: 574-79.

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Topics

~~Adenocarcinoma~~

Squamous cell

Small Cell

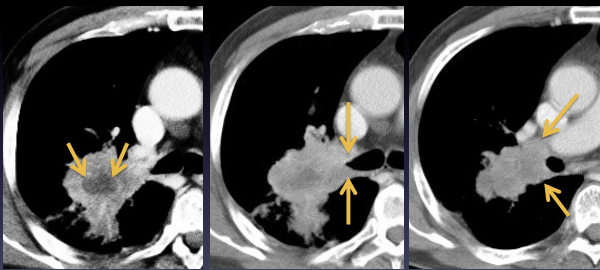
Large Cell

Carcinoid

Salivary Gland


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Classic Squamous Cell Carcinoma



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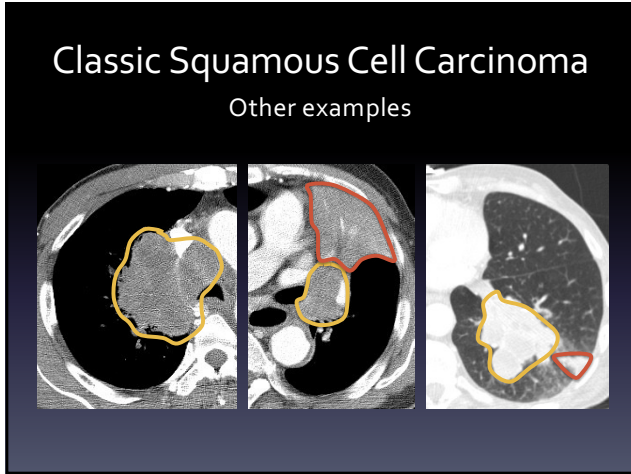
Classic Squamous Cell Carcinoma



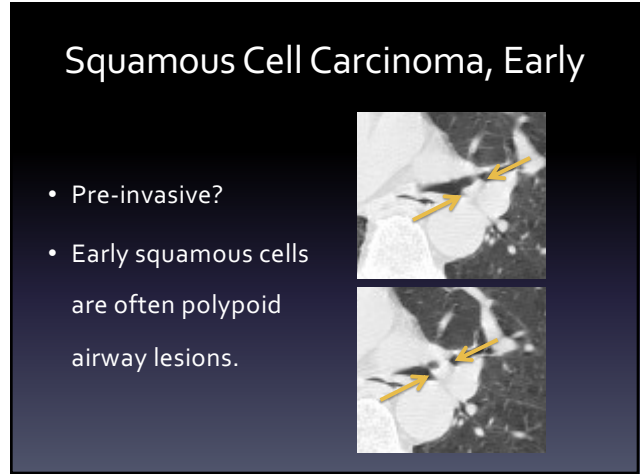
SLAM DUNK APPEARANCE:

- Central, invasive, cavitary tumor
- Symptoms/signs of obstruction
- Early metastases uncommon
- Demographic: Heavy smoker

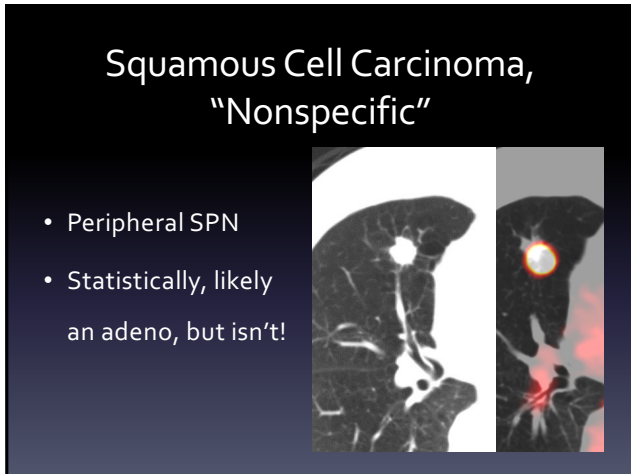
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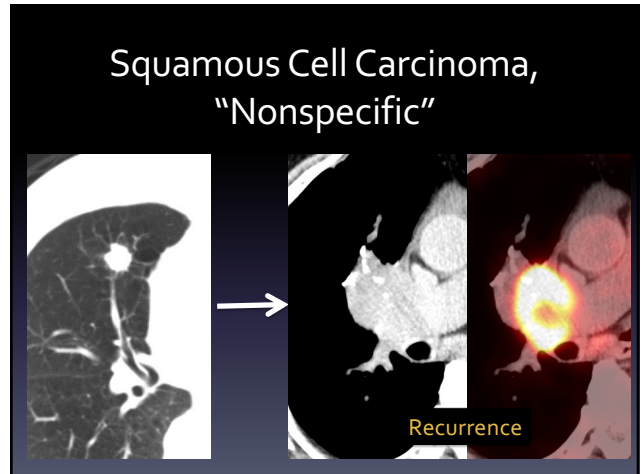
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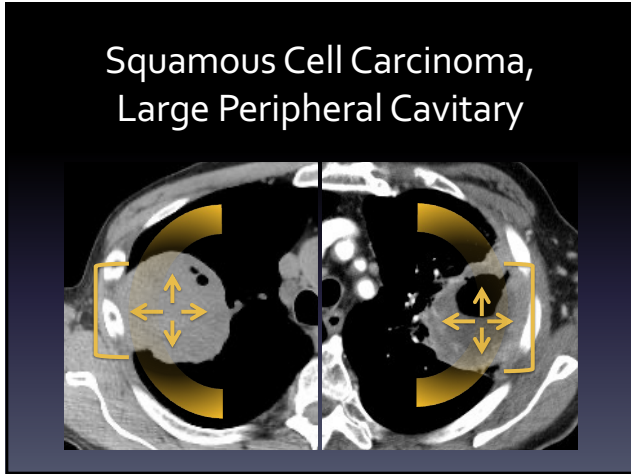
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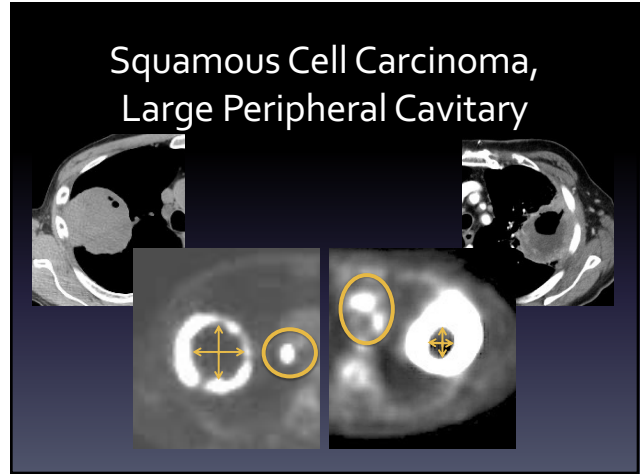
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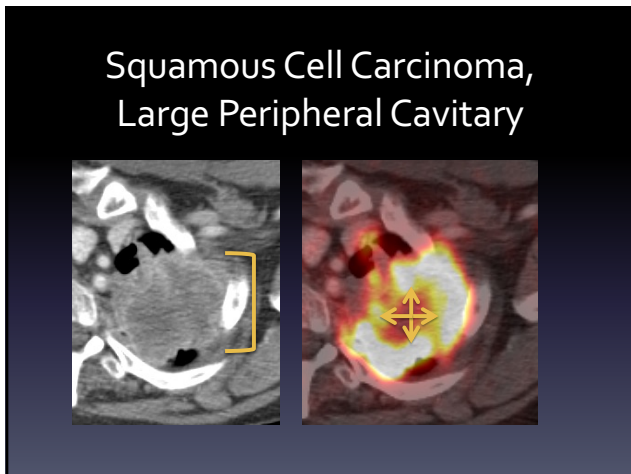
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Squamous Cell Carcinoma Variants

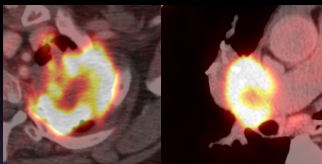
1. Earliest: polypoid airway lesion
2. Nonspecific: SPN
3. Large, peripheral, cavitory

Not genetically different, it seems.

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Squamous Cell Carcinoma, PET

- It's cancer
- It's hypermetabolic
- Moderate-high (MaxSUV ~6-16), overlaps some with adeno
- Small lesions will have a lower MaxSUV (of course!)



Li et al. Lung Canc 2010, 68:394-7.
Bille et al. Eur J of Cardio-Thor Surd. 2013, 43: 574-79.

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Squamous vs. Adeno

- Adenocarcinoma is now the most common
 - Associated with pollution: small particles (<2.5 um) in filtered cigarettes and environment
 - Less of a smoking association
 - Not a vastly different prognosis

Galvin. Radiology 2013, 268(1):9-11.
Turner. Am J Respir Crit Care Med 2011, 184(12):1374-81.
Lomnicki. Environ Sci Technol 2008, 42(13):4982-8.

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Topics

~~Adenocarcinoma~~

~~Squamous cell~~

Small Cell

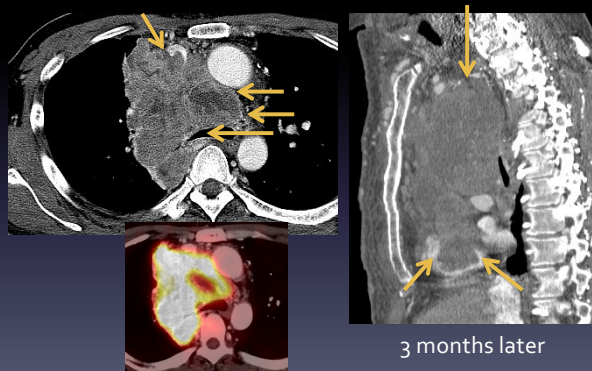
Large Cell

Carcinoid

Salivary Gland

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Classic Small Cell Carcinoma



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Classic Small Cell Carcinoma



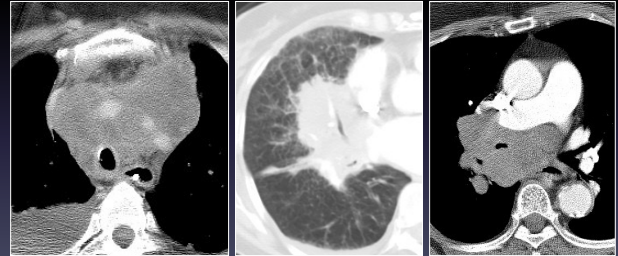
SLAM DUNK APPEARANCE:

- Massive, central, aggressive tumor w/ extensive lymph node involvement
- Distant mets common
- Classic demographic: smoker +/- paraneoplastic syndrome

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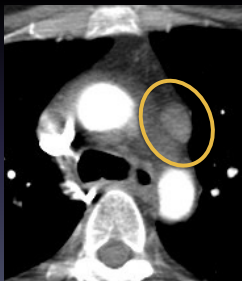
Classic Small Cell Carcinoma

Other examples



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Classic Small Cell Carcinoma, "Small Small Cell"



- Path proven solitary mediastinal node w/ small cell. No pulm nodule.
- Paraneoplastic syndrome.
- Very uncommon

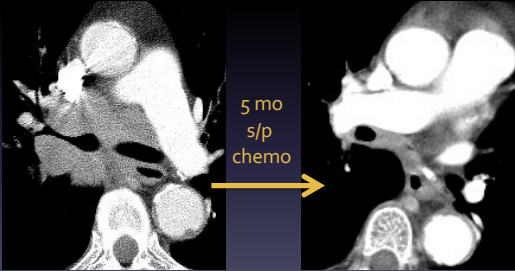
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Classic Small Cell Carcinoma, Prognosis and Treatment

- Horrible prognosis
- 90% are Stage IV at presentation
- Chemotherapy often. Local disease: chemoradiation. Rarely surgery.

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Classic Small Cell Carcinoma, Prognosis and Treatment



5 mo
s/p
chemo

Chemotherapy can work...for a while.

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Classic Small Cell Carcinoma, Staging

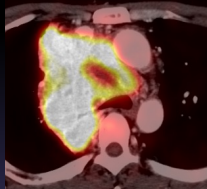
- Historically: Limited vs. extensive
 - Limited: single hemithorax, ipsilateral and contralateral LN (inc mediastinal, supraclav)
 - Note: "limited" still indicates radiation treatment
- 2018 8th edition staging should be used.
 - 55, 40, 5, 0% survival at 5 years.

Nair. RadioGraphics 2011. 31: 215-238.
UyBico SJ. RadioGraphics 2010. 30:1163-81.

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Small Cell Carcinoma, PET

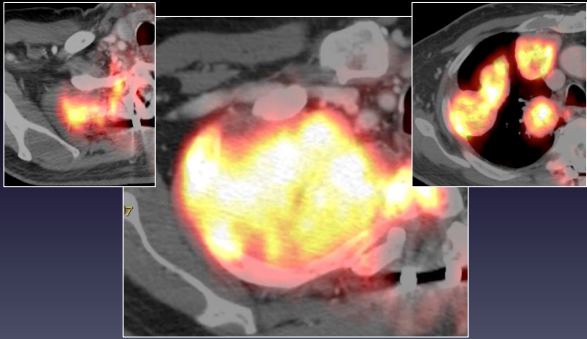
- It's **BIG TIME** cancer
- It's **BIG TIME** hypermetabolic
- PET useful in confirming/excluding limited disease for XRT (or VERY limited for surgery).



Fisher et al. Annals of Oncol 2007. 18:338-345.
Sohn. Onkologie 2012. 35:432-8.
Xanthopoulos. J Thorac Oncol 2013. 8(7):899-905.

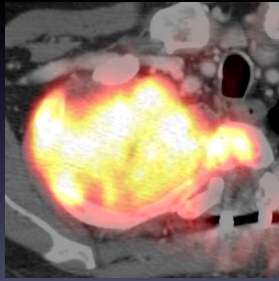
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Large Cell Carcinoma



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Classic Large Cell Carcinoma



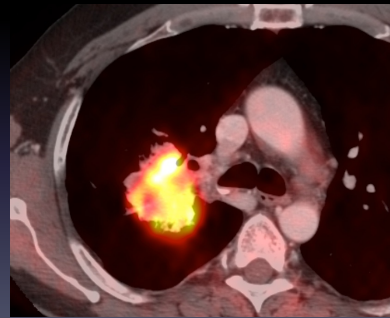
SLAM DUNK APPEARANCE:

- Large (>4 cm) peripheral mass in a smoker
- Metastasizes early, poor prognosis
- Aka "A bad tumor that's not an adeno, squam, or small cell."

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Classic Large Cell Carcinoma

Other example



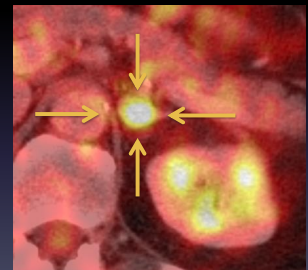
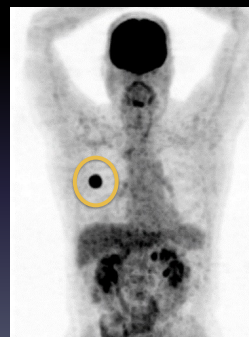
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Large Cell, Neuroendocrine

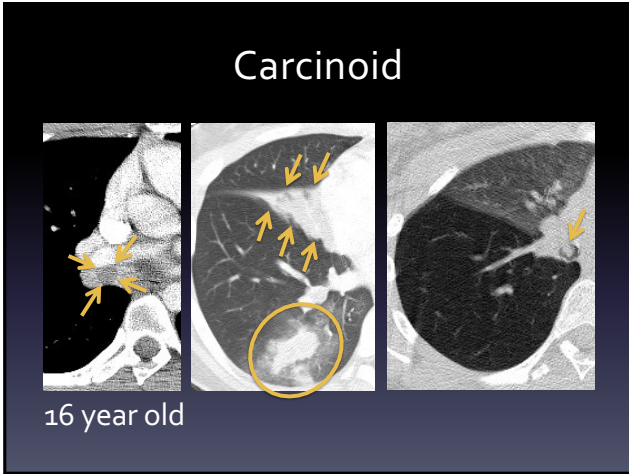
- Histologically diagnosed, but you may hear about it
- So is it more **Large Cell?**
- Or more **Neuroendocrine?**
- Don't get confused!

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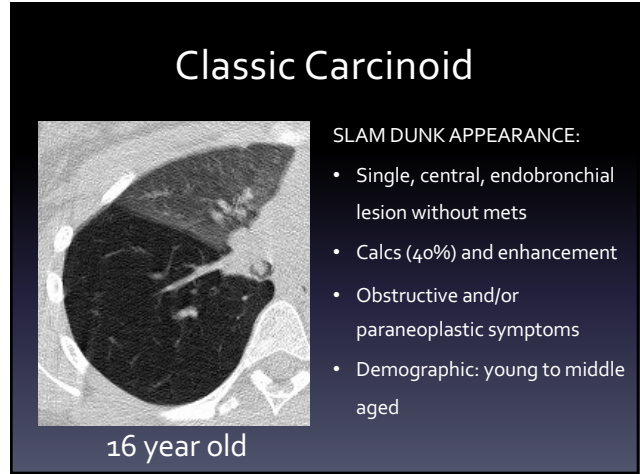
Large Cell, Neuroendocrine



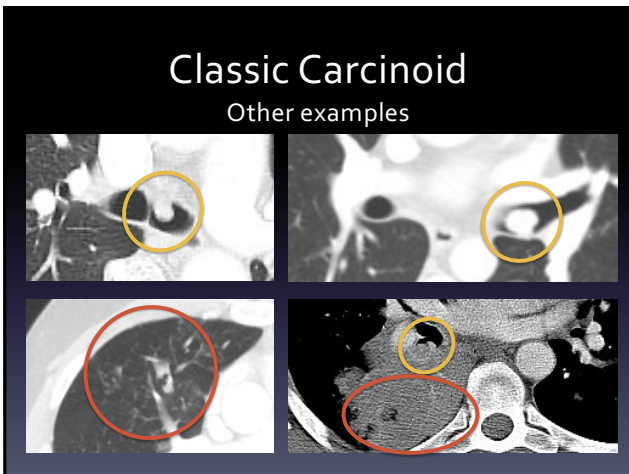
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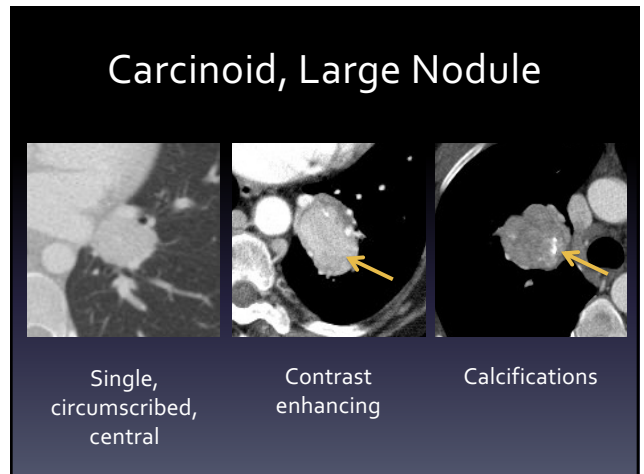
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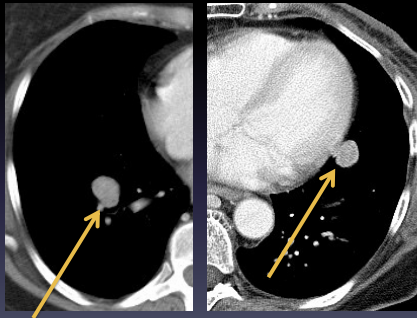


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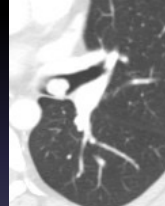
Carcinoid, "Non specific" Nodule



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Carcinoid, Aggressive

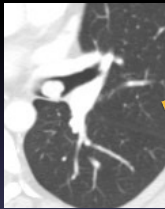
Carcinoid



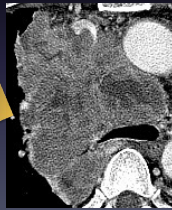
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Carcinoid, Aggressive

Typical Carcinoid



Small cell

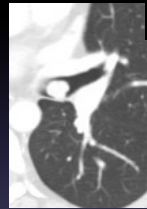


Secretory Granules
Paraneoplastic syndromes
Neuroectodermal origins

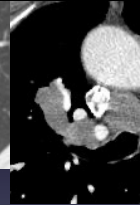
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Carcinoid, Aggressive

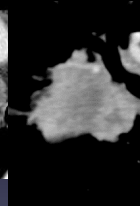
Typical Carcinoid



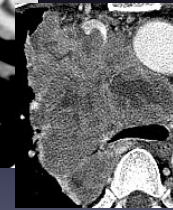
Atypical Carcinoid



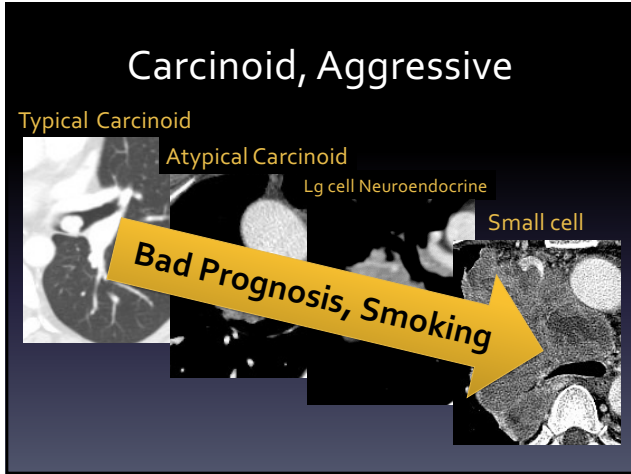
Lg cell Neuroendocrine



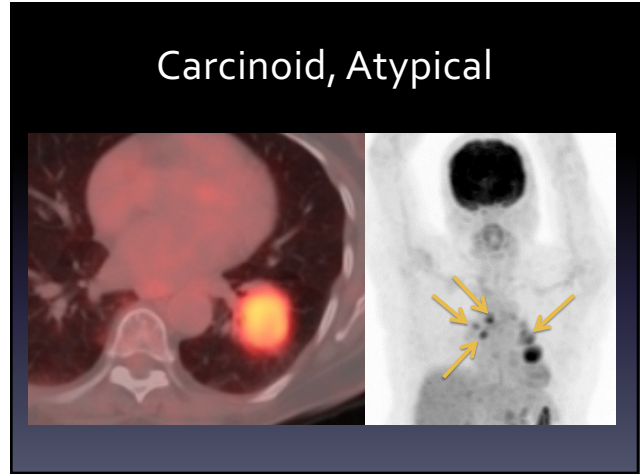
Small cell



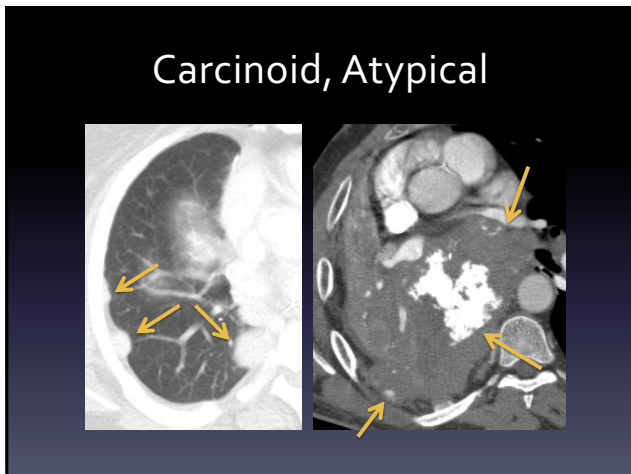
80



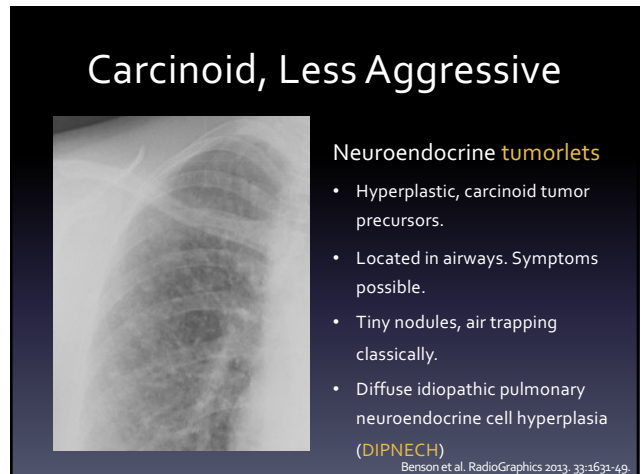
81



82

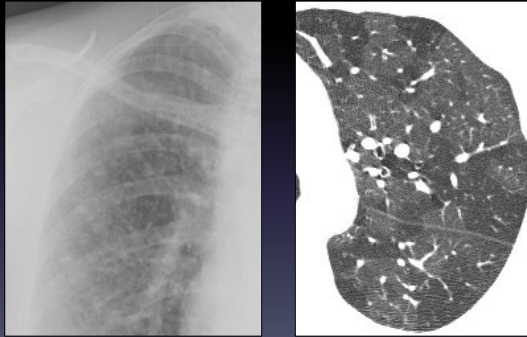


83



84

Carcinoid, Less Aggressive



85

Carcinoid Variants

- Larger nodule (circumscribed, CE, calcs)
- Nonspecific nodule
- Atypical carcinoid
- Tumorlets

86

Carcinoid, Staging

- Historically: not staged like other NSCLCs
- 2018 8th edition staging should be used.
 - Carcinoid: 93, 85, 75, 57% survival at 5 years
 - Small cell: 55, 40, 5, 0% survival at 5 years.

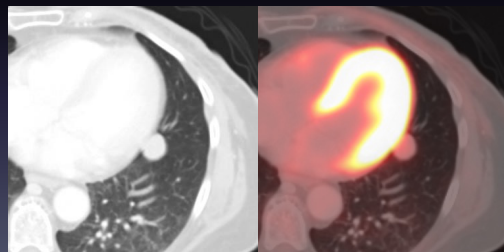
Nair. RadioGraphics 2011. 31: 215-238.
UyBico SJ. RadioGraphics 2010. 30:1163-81.

87

Carcinoid, PET

Indolent cancer

Low or background metabolism



88

Carcinoid, PET

Indolent cancer
Low or background metabolism

89

Carcinoid, Other Nuc Med

Order of sensitivity?
1. CT/MR
2. Octreotide/
New PET Agents
3. FDG PET

Jadvar. J Nucl Med 1997; 38:1382-1383

90

Carcinoid, Treatment

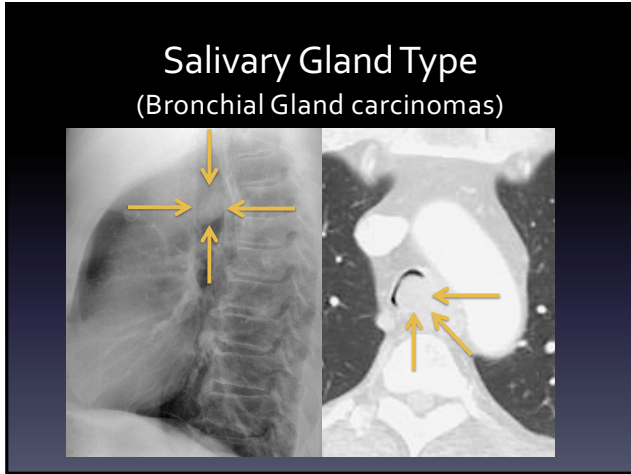
- Indolent, but can locally invade

91

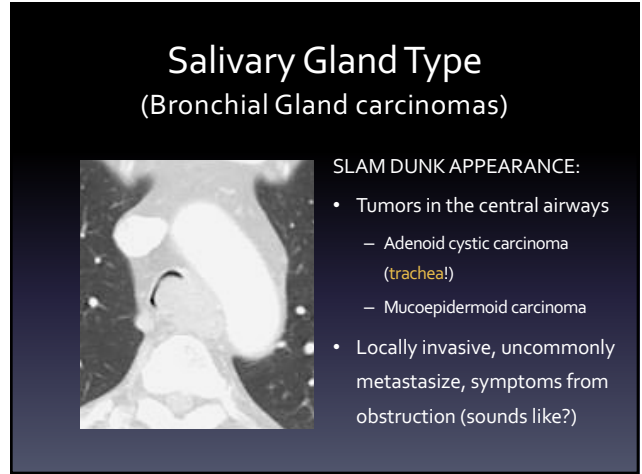
Topics

- ~~Adenocarcinoma~~
- ~~Squamous cell~~
- ~~Small Cell~~
- ~~Large Cell~~
- ~~Carcinoid~~
- Salivary Gland

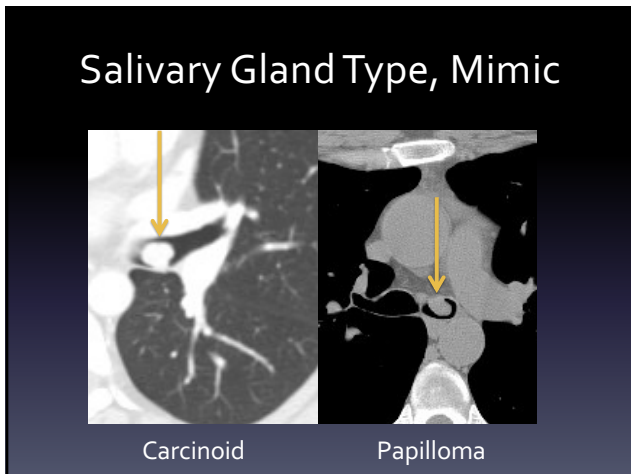
92



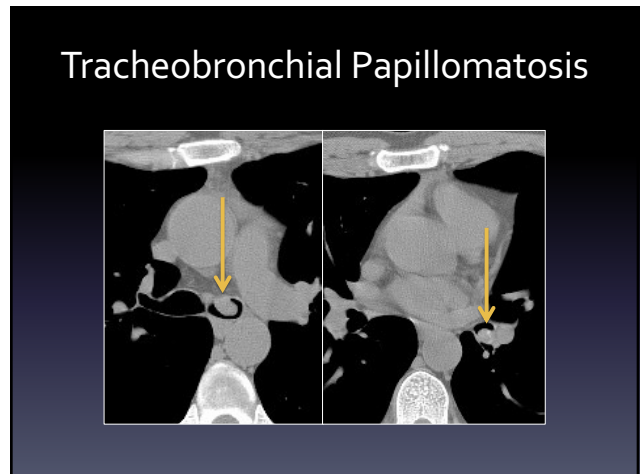
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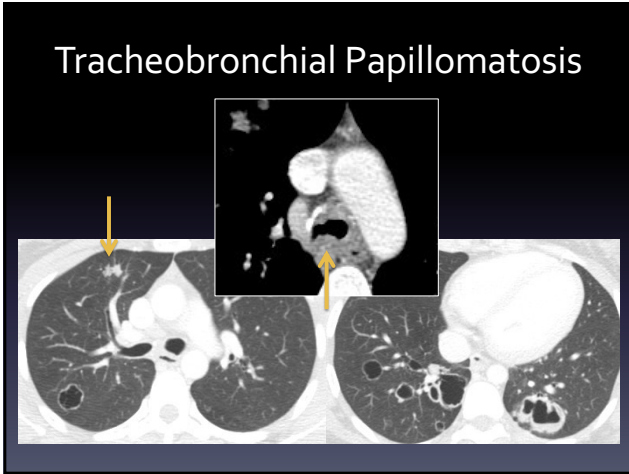
94



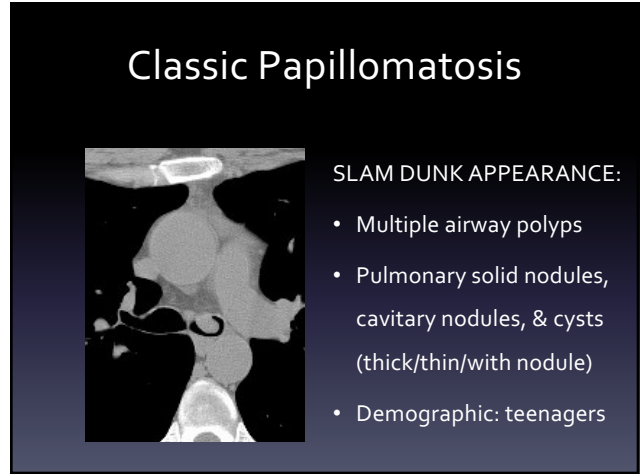
95



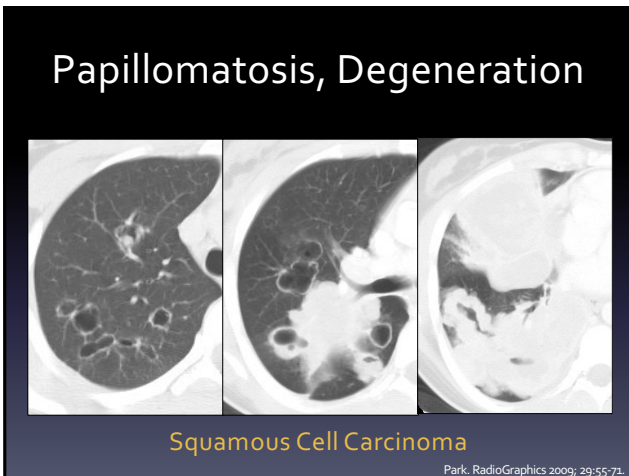
96



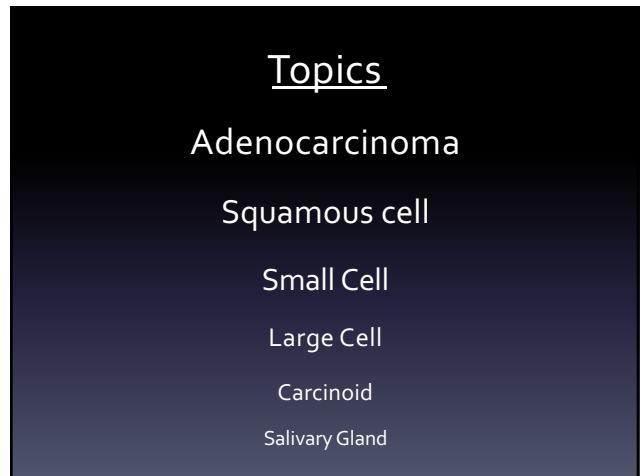
97



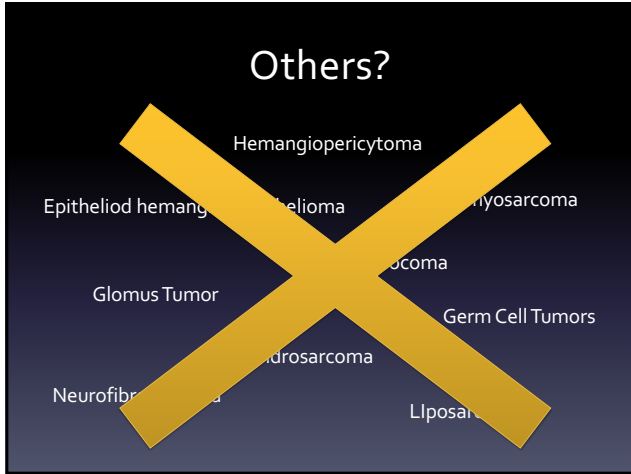
98



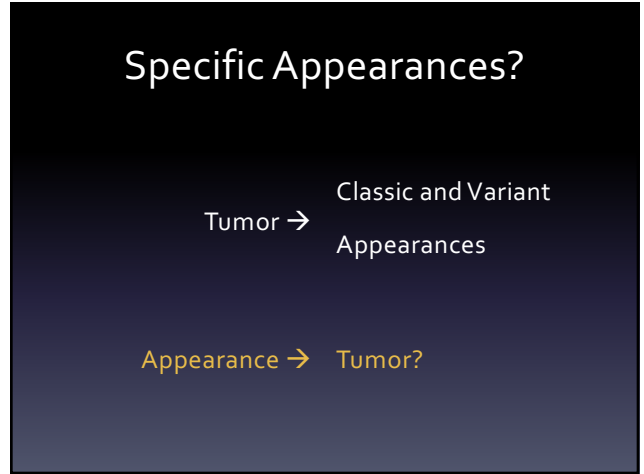
99



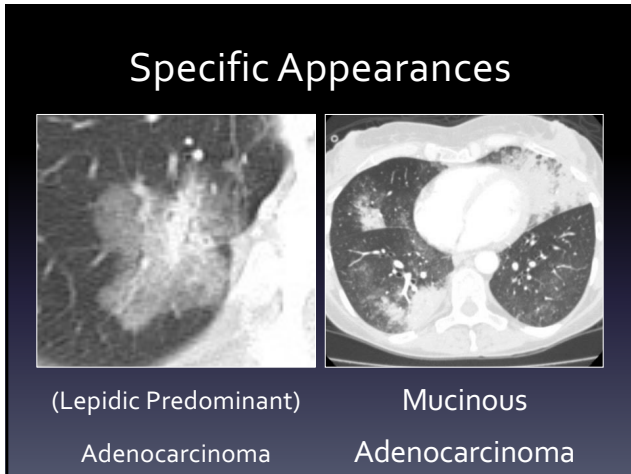
100



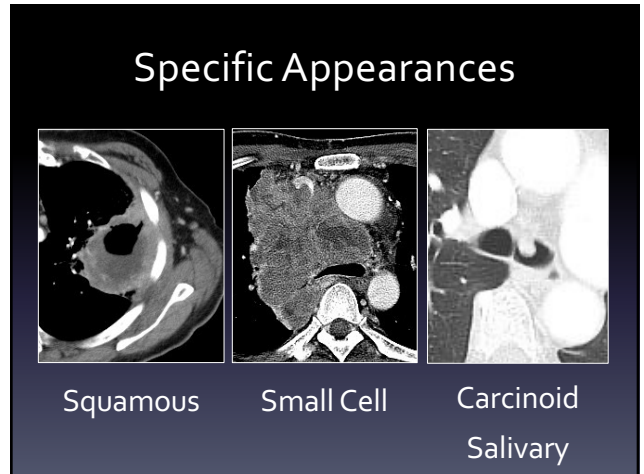
101



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103




104

Nonspecific appearances



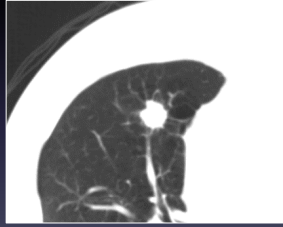
Solitary Pulmonary
Nodule



Medium Sized Mass

105

Nonspecific appearances



- Is this cancer?
- Can we biopsy it?
- Can we help stage it?

- Don't be too specific (and wrong!)

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The Message

- Typical and select atypical appearances are easy to remember and matter
- A few scattered, key facts will take you the rest of the way!

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Thank you!

Typical and Atypical Appearances of Lung Cancer

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Question 1

Which of the following types of lung cancer is most similar to pulmonary adenocarcinoma in terms of prognosis, biological behavior, and activity on FDG PET?

- Carcinoid
- Small Cell carcinoma
- Squamous cell carcinoma
- Salivary Gland Tumors

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Li, et al. *Lung Cancer*. 68(3):394, 2010.

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Question 2

A mixed-density, 4 cm pulmonary mass containing extensive ground glass and multiple small solid components is determined to be a non-small cell lung cancer. Which is likely to be the final pathologic diagnosis?

- A. Bronchioloalveolar carcinoma (BAC)
- B. Mixed adenocarcinoma/Bronchioloalveolar carcinoma (BAC)
- C. Mucinous adenocarcinoma
- D. Lepidic-predominant adenocarcinoma

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Lee, et al. Radiol. 267(1):254, 2013.

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Question 3

Small cell carcinoma should be staged similar to non-small cell lung carcinomas (IASLC 7th ed). Nonetheless, the older staging system (extensive vs. limited disease) has what advantage?

- A. More clearly indicates the proper treatment
- B. More accurately predicts prognosis
- C. More closely associates with the pathologic subtype
- D. More closely associates with activity seen on FDG PET

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Question 3

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UyBico SJ, et al. RadioGraphics. 30:1163, 2010.

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THANKYOU!

Typical and Atypical Appearances of
Lung Cancer

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