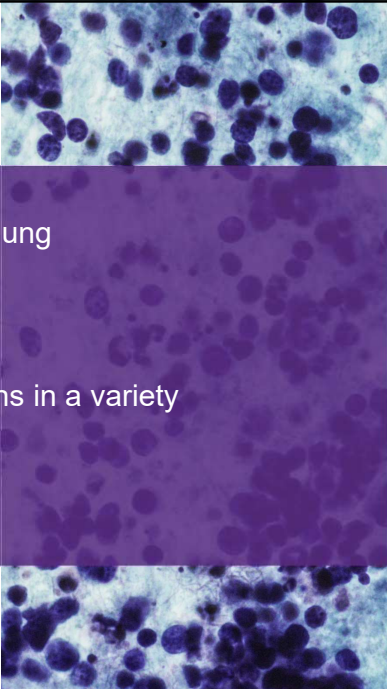


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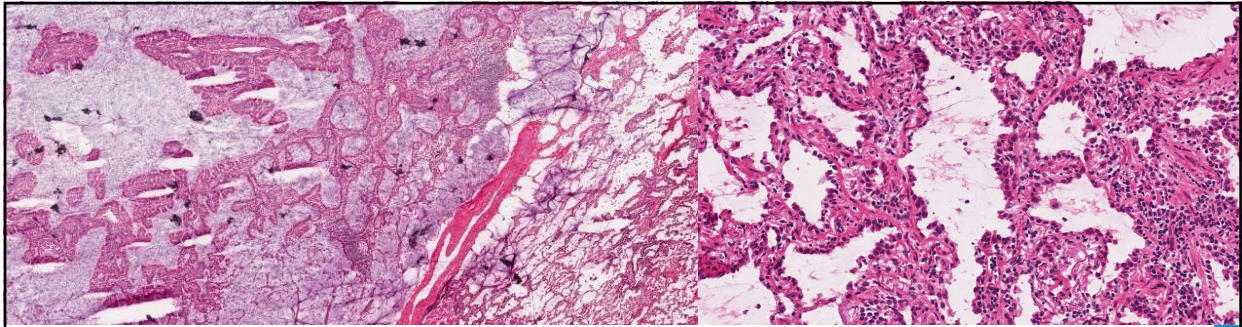
## Objectives

- Identify the features that help to distinguish between lung adenocarcinoma and its mimics at frozen section.
- Recognize pitfalls of thoracic frozen sections.
- Utilize practical skills to handle thoracic frozen sections in a variety of settings.

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The right side of the slide is decorated with three microscopic images of lung tissue sections, showing cellular morphology in shades of purple and blue.

2



## **THORACIC FROZENS: HOW TO STAY OUT OF TROUBLE**

**SANJAY MUKHOPADHYAY, MD**  
**DEPARTMENT OF PATHOLOGY**  
**CLEVELAND CLINIC**  
**@smlungpathguy**

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## **THORACIC FROZEN SECTIONS**

- **Most are easy, error rates are low**
- **What do we see at Cleveland Clinic?**
  - **Margins on lobectomies and wedges**
  - **Wedge resection of nodule: is it malignant or not?**
  - **Thymic and pleural biopsies (no good indication!)**
  - **Other miscellaneous rare things**

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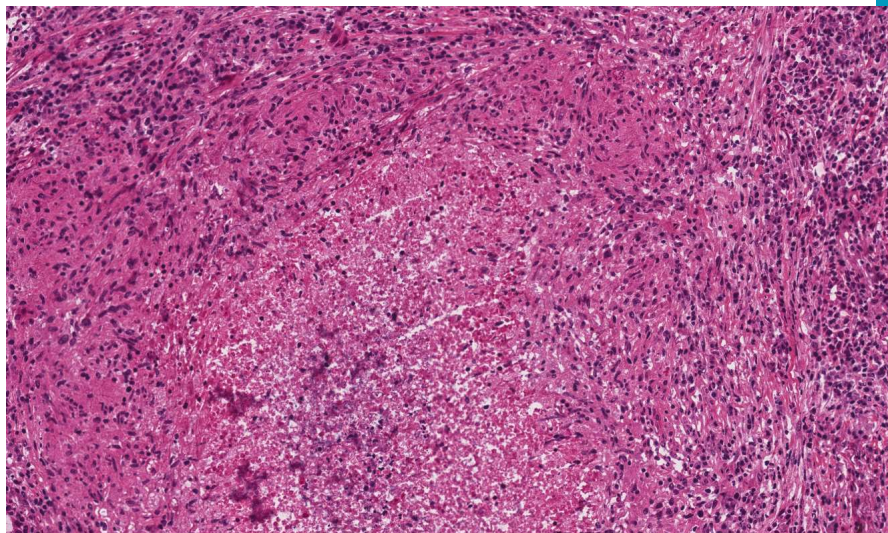


## Bronchial margin



5

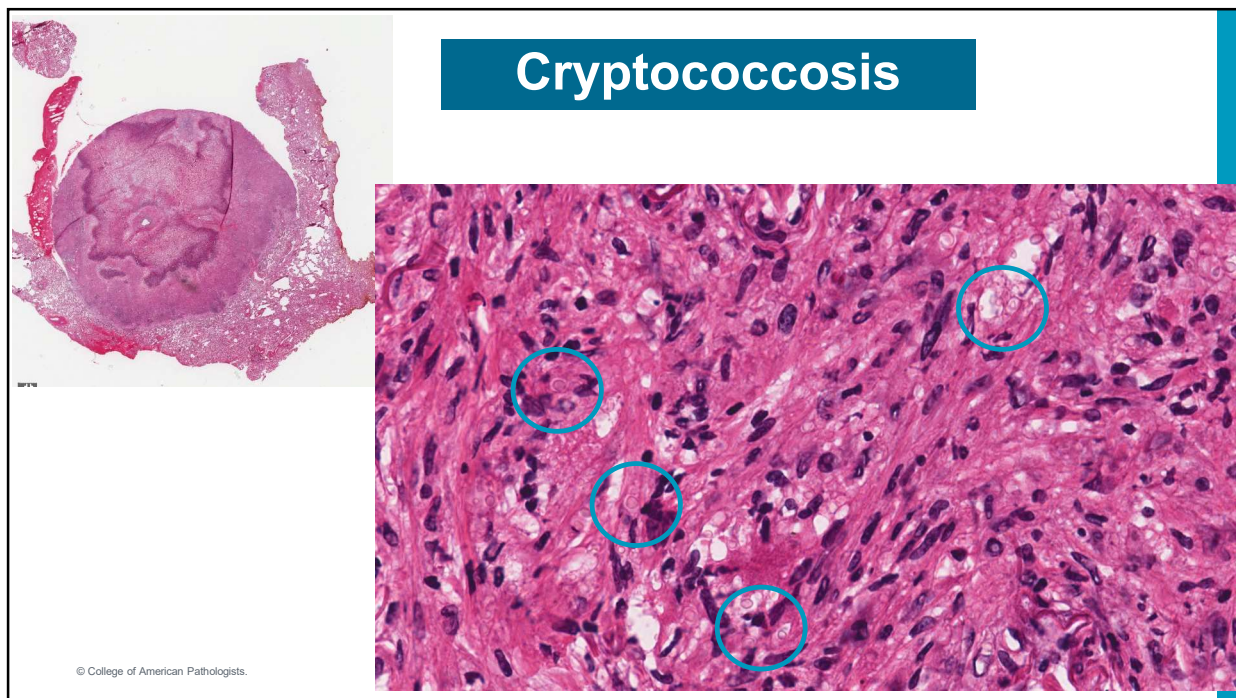
## Necrotizing granuloma



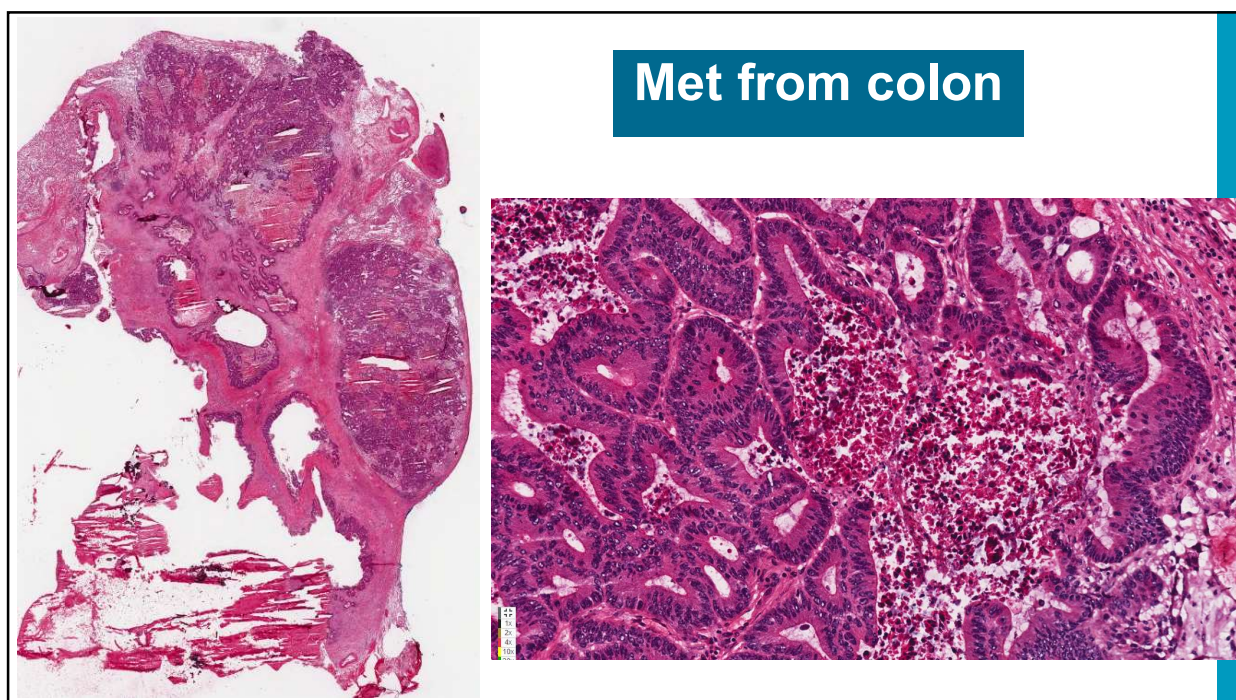
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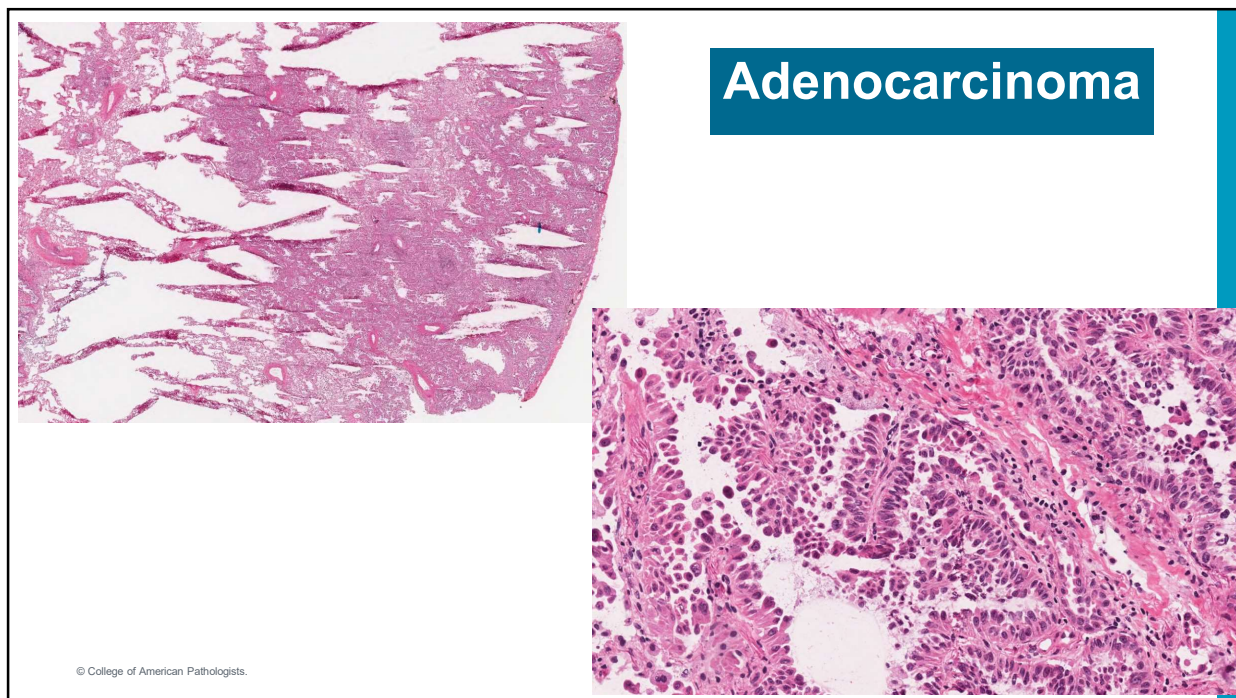


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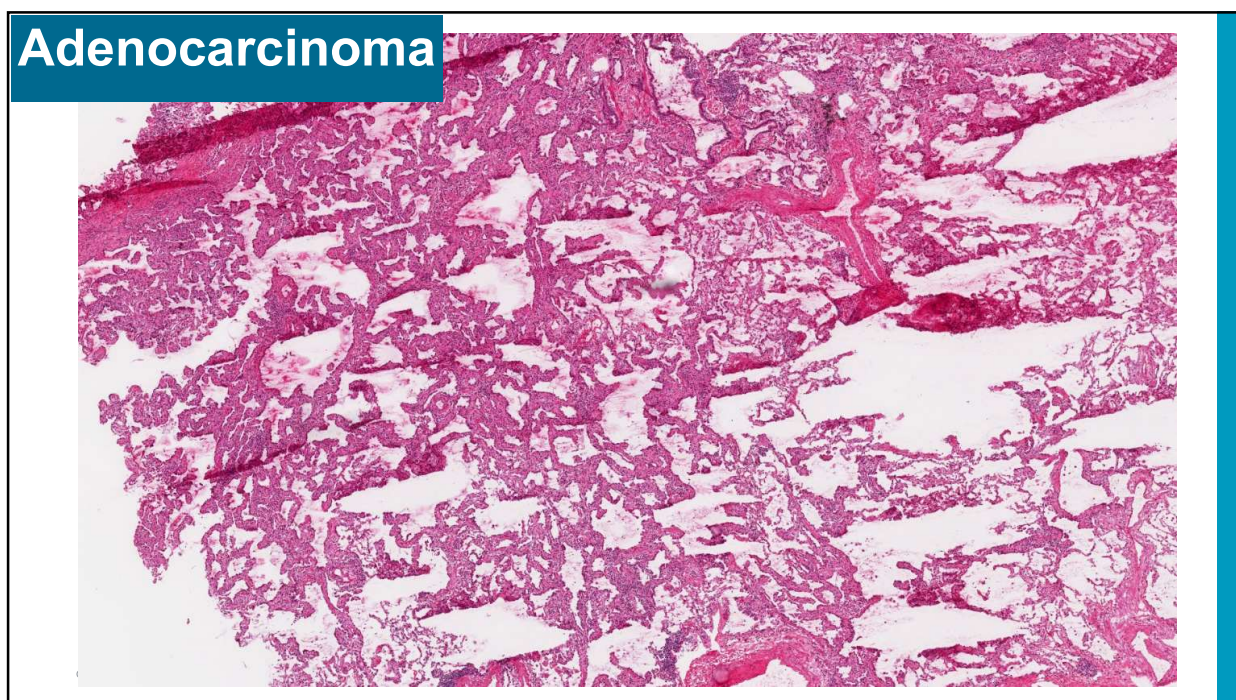


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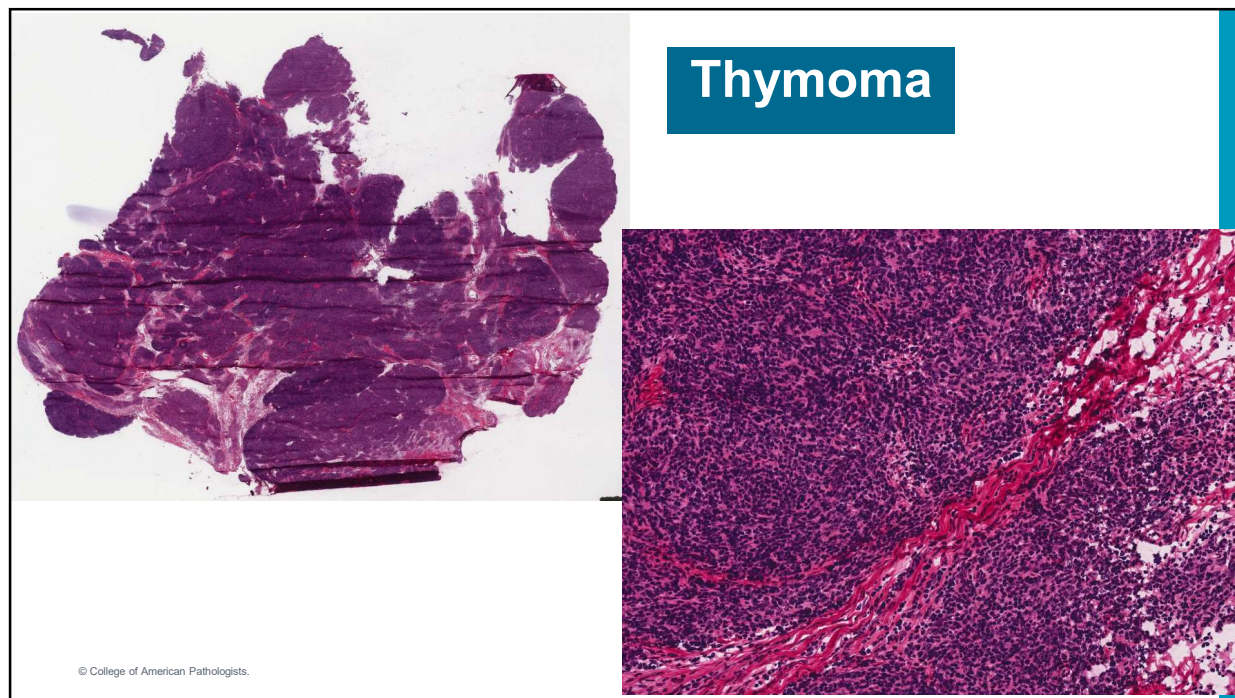




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10



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## THORACIC FROZEN SECTIONS

- Literature outlines the common issues

Mukhopadhyay S. Thoracic frozen section pitfalls: lung adenocarcinoma vs. selected mimics. *Arch Pathol Lab Med* 2025;149(4):e93-e99

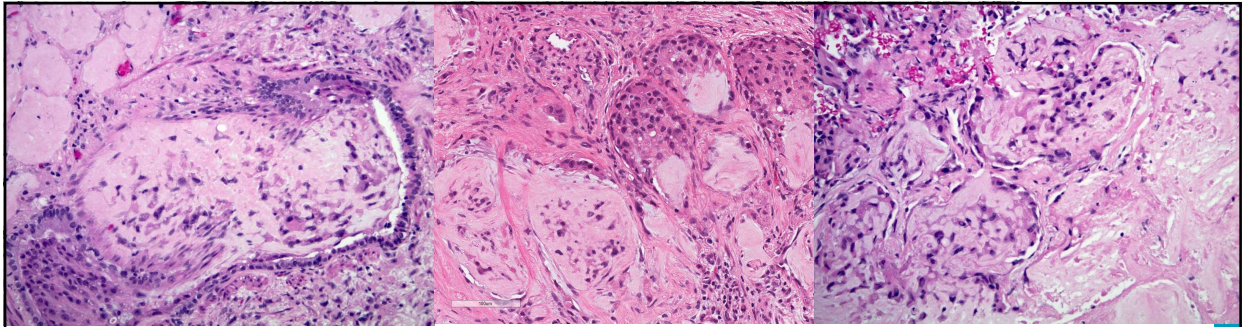
Mukhopadhyay S. Cecchini M. Approach to thoracic intraoperative consultation (frozen section). In: *Survival Guide to Thoracic Pathology*. 2023. Innovative Science Press. Pathology Survival Guides Series 1: pages 97-114

Borcuk AC. Challenges of frozen section in thoracic pathology: lepidic lesions, limited resections, and margins. *Arch Pathol Lab Med* 2017;141(7):932-939

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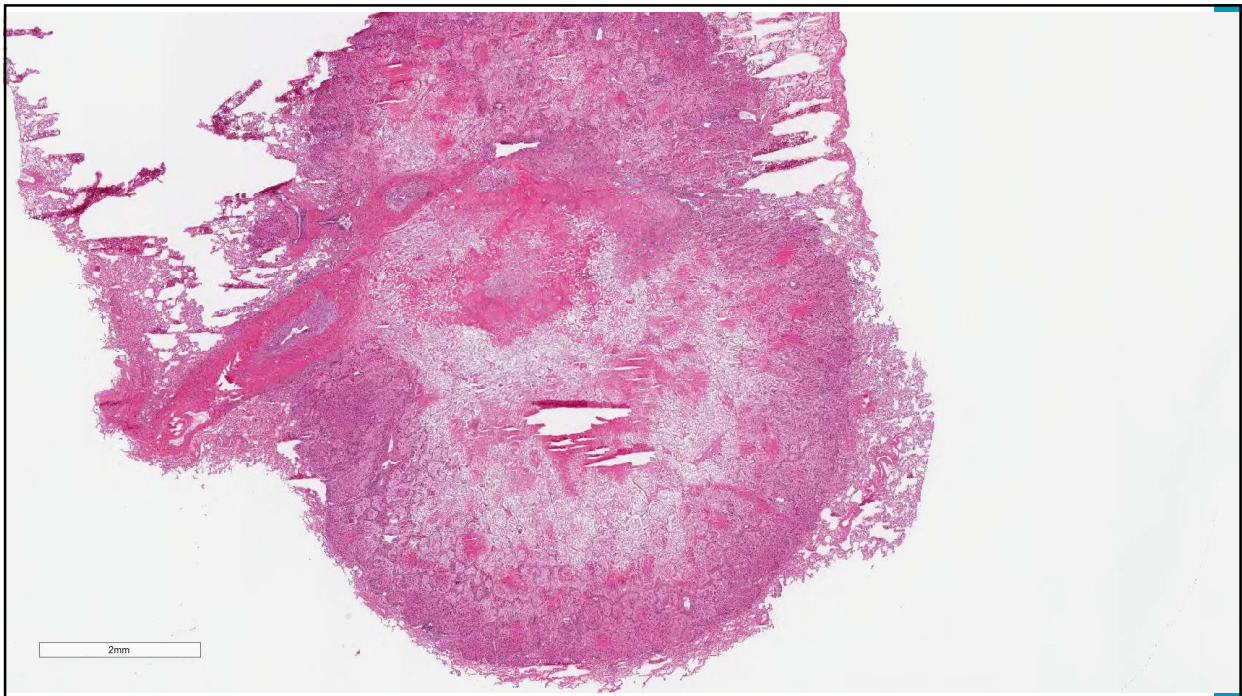




# FROZEN 1

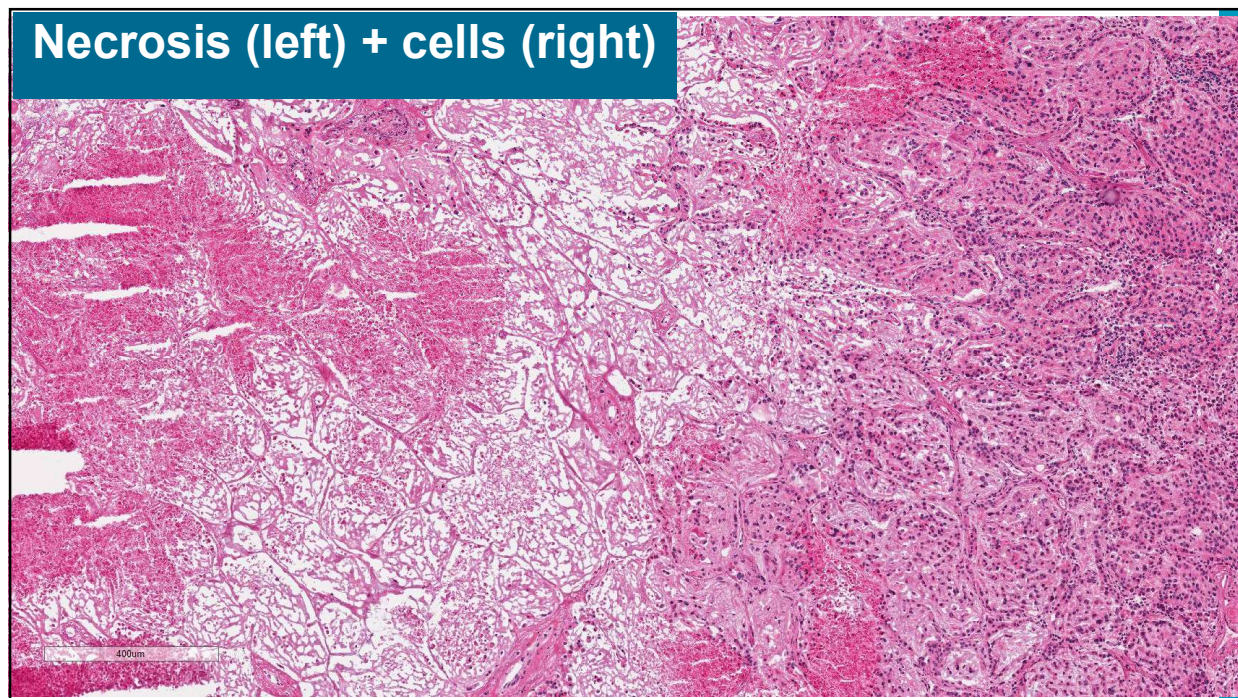
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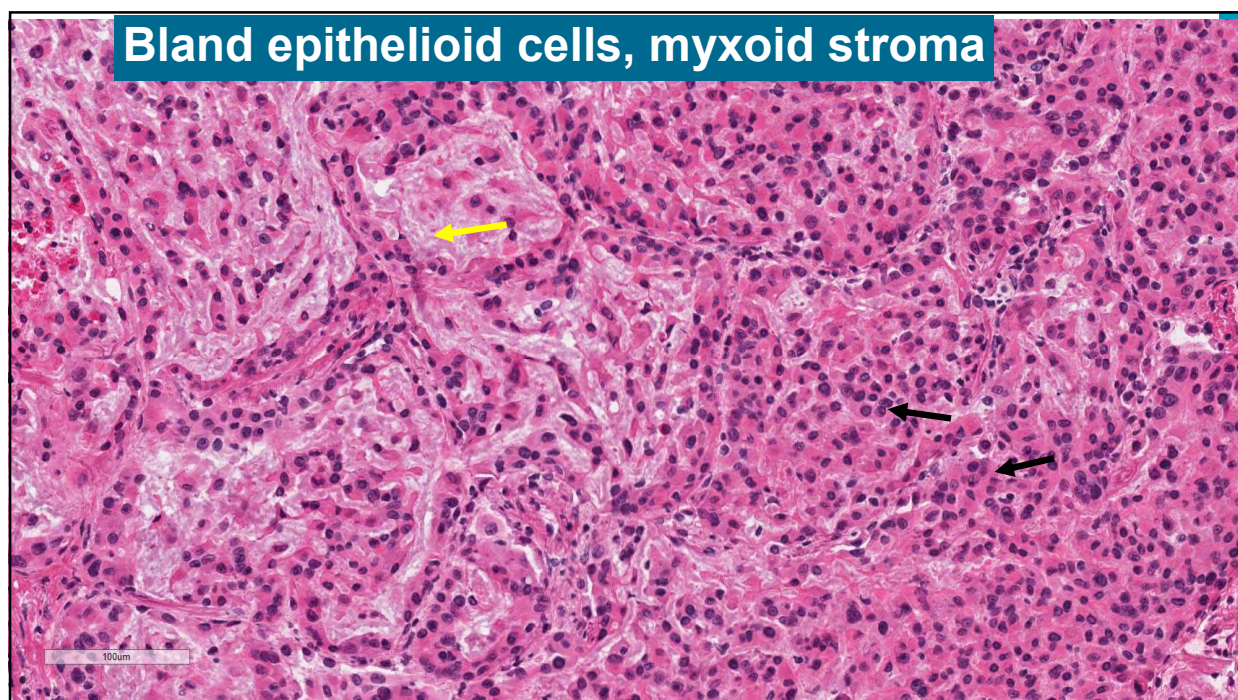


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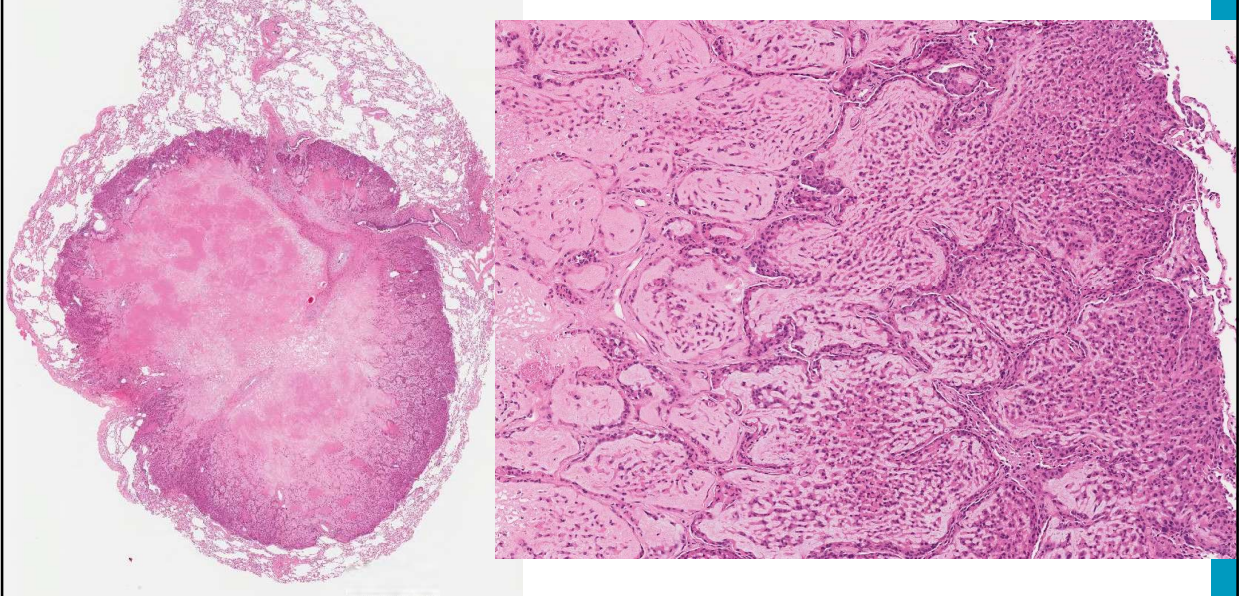
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## Typical pink center, myxohyaline stroma: déjà vu!



17



FIG. 2. A typical chest radiograph with multiple widespread bilateral small nodules in a 14-year-old girl (Case 3).

...dendronized tumor was noted by bronchoscopy.<sup>13)</sup>

### Microscopic Pathologic Findings

Even when a limited number of nodules was documented by x-ray, many more nodules were generally present at open biopsy and on pathologic exam. Low power microscopic examination showed round to oval nodules with pale pink acellular centers surrounded by rims of viable tumor. The degree of cellularity at the

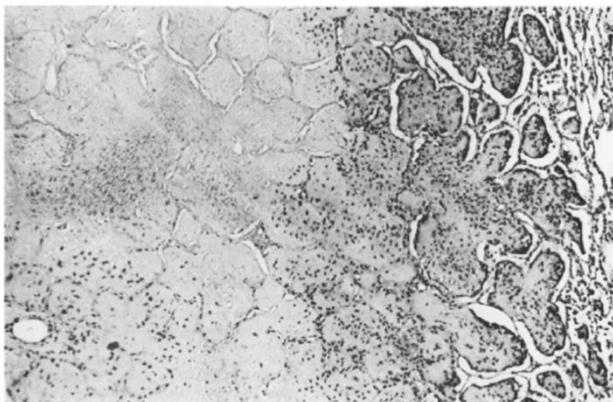


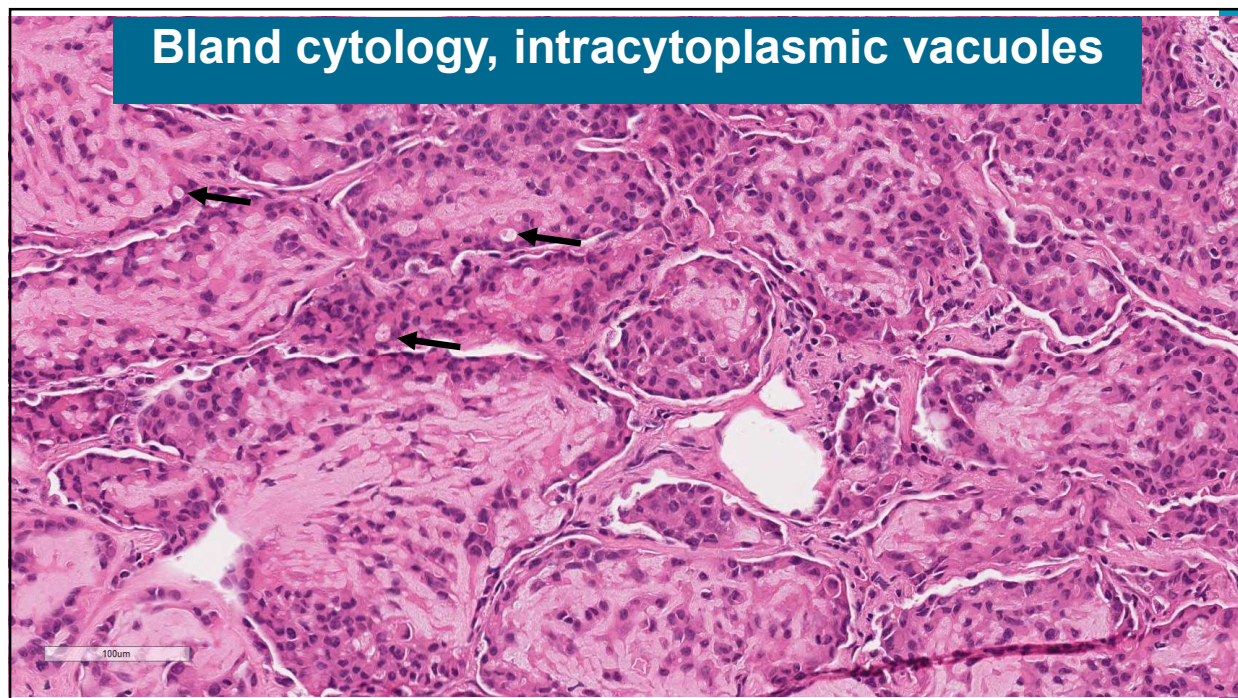
FIG. 3. Border of typical lung nodule shows the more active cellular growth zone extending in a micropolyoid fashion at right. Note retraction artifact. There is some preservation of viable cells around a small patent vessel in the left lower edge. The remaining tumor has undergone coagulative necrosis with remnant dense stroma, empty cellular or nuclear lacunae and ghosts of architecturally well preserved infarcted alveolar septa (Case 1, H & E, x50).

“pale pink  
acellular centers  
surrounded by  
rims of viable  
tumor”

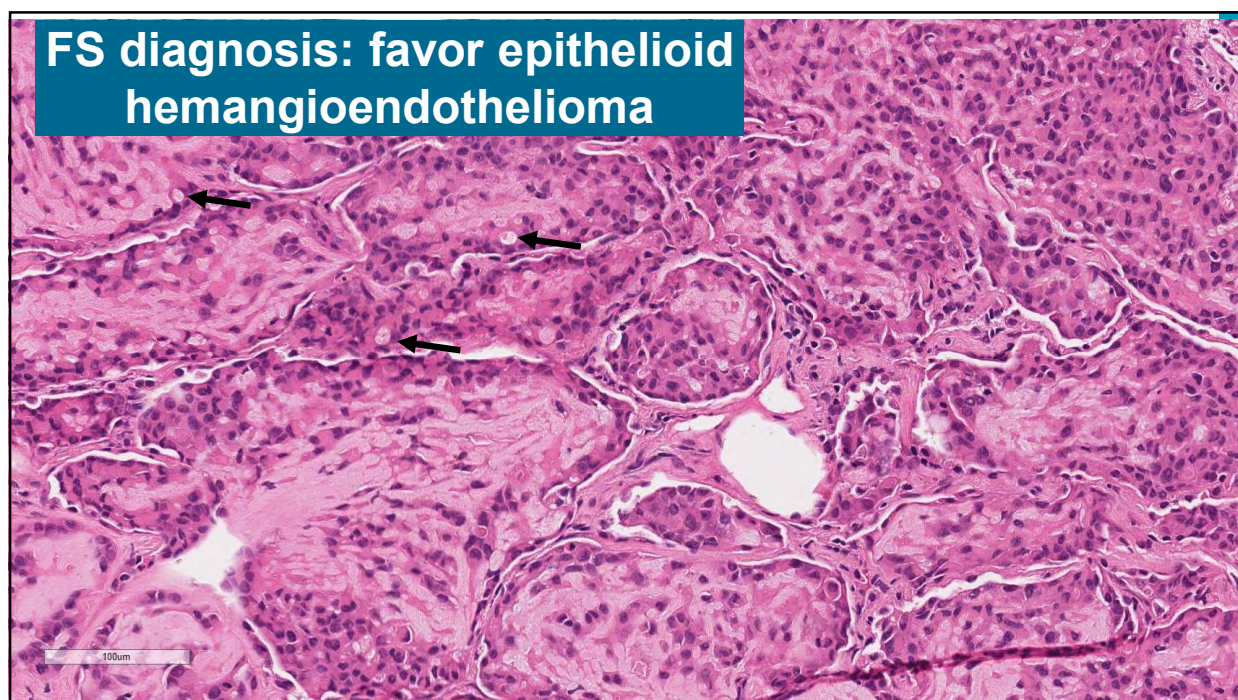
Dail DH, et al. *Cancer* 1983;51(3):452-64

18



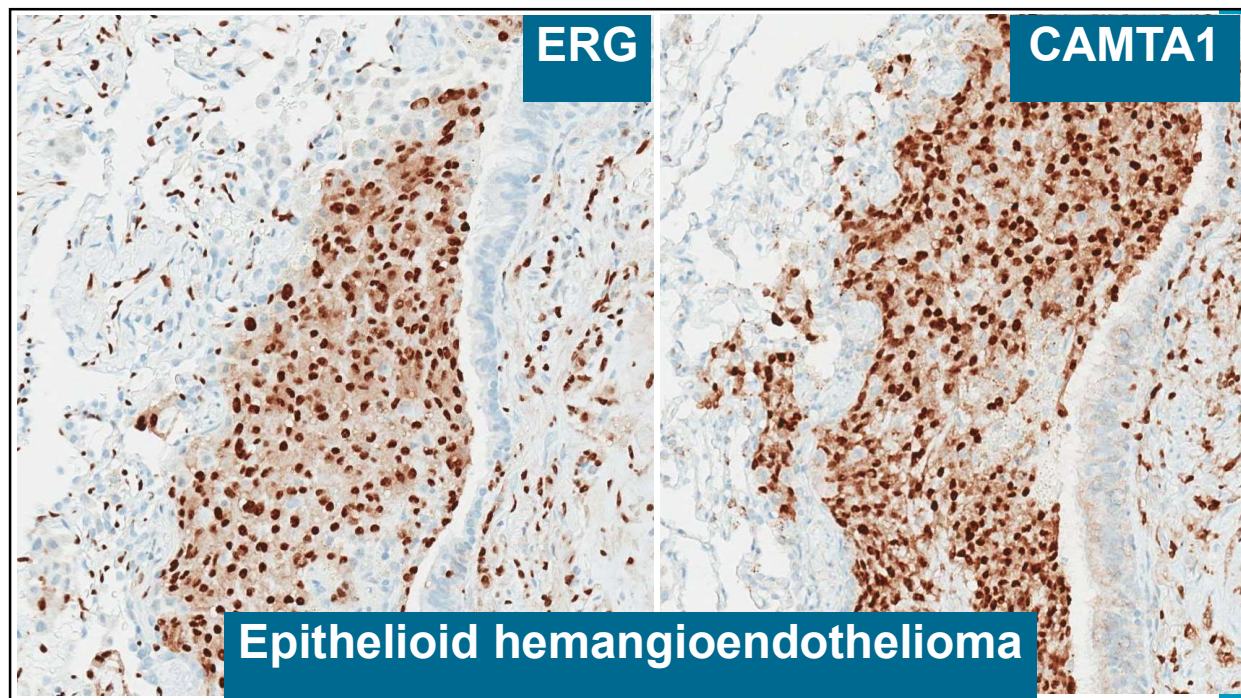


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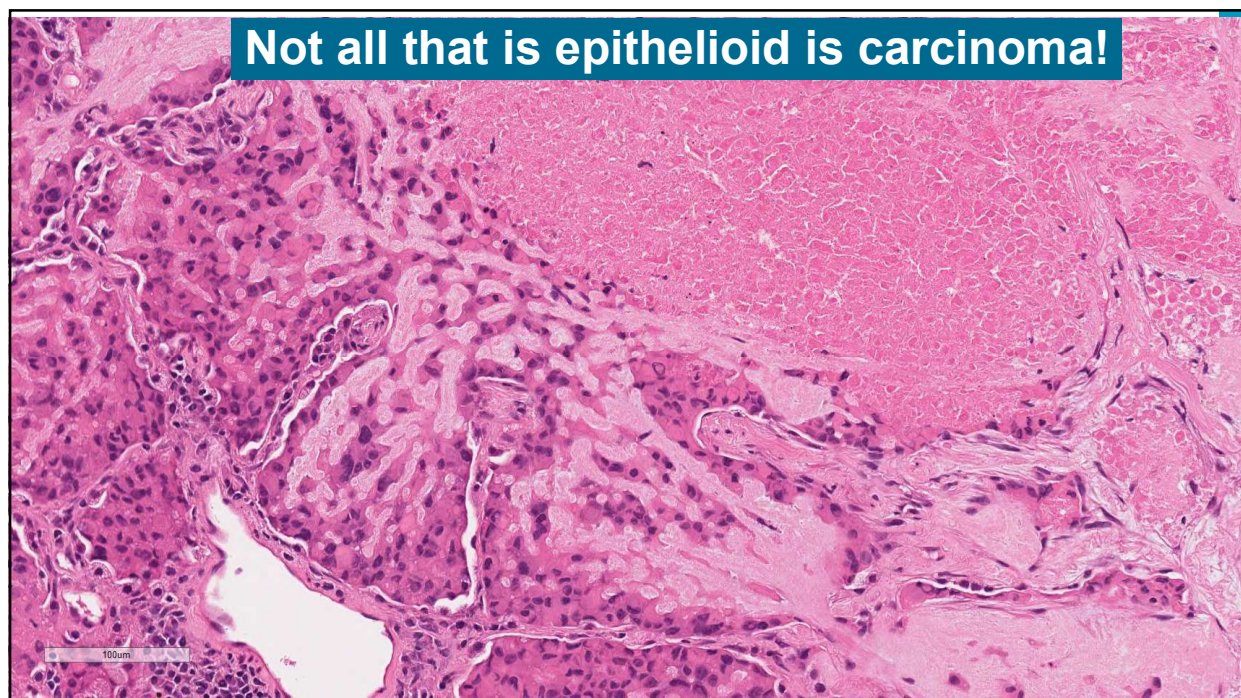


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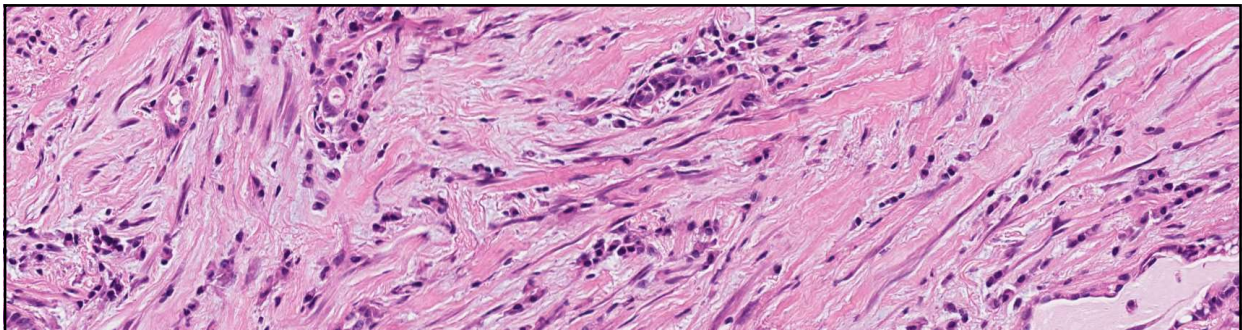
## EPITHELIOID HEMANGIOENDOTHELIOMA

- **Clinical:** Lung nodule(s), pleural thickening, patients can be young (median age for pulm EHE = 38 y)
- **H&E:** Bland epithelioid cells, vacuoles, myxohyaline stroma
- **Immunohistochemistry:** ERG +, CAMTA1 + CD31/34 +
- **How to confirm? FISH or NGS:** *WWTR1::CAMTA1* or *YAP1::TFE3*

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Dail DH, et al. *Cancer* 1983;51(3):452-64

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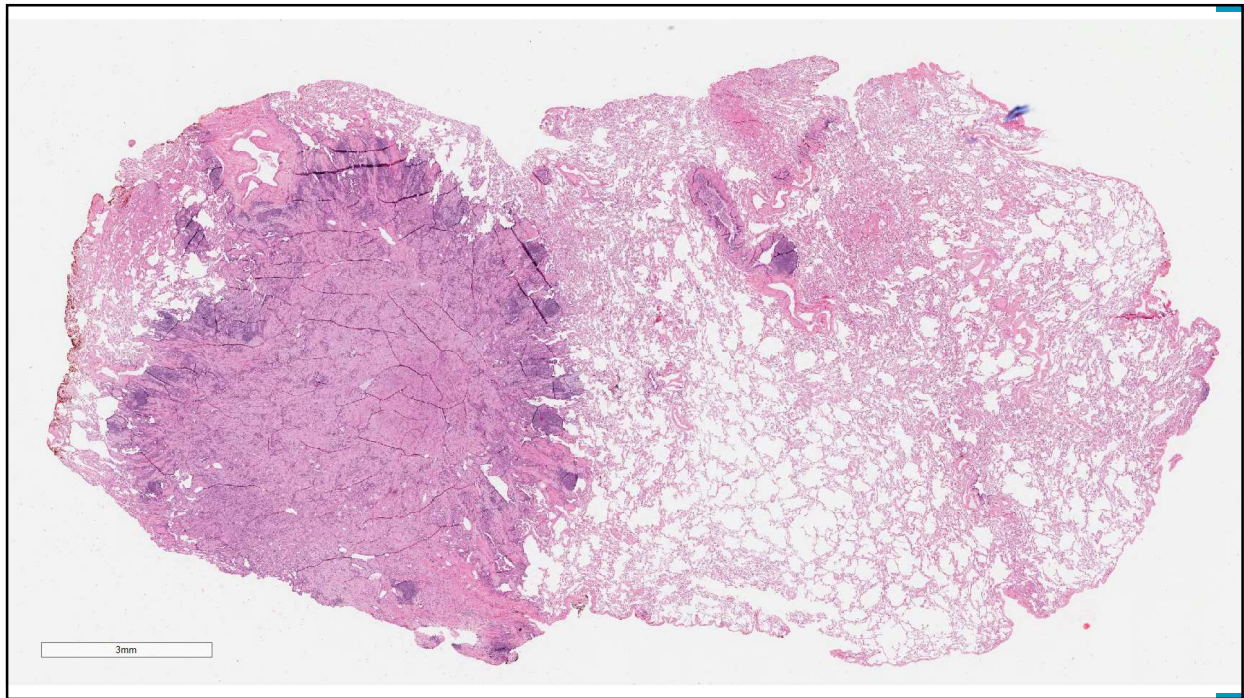


## FROZEN 2

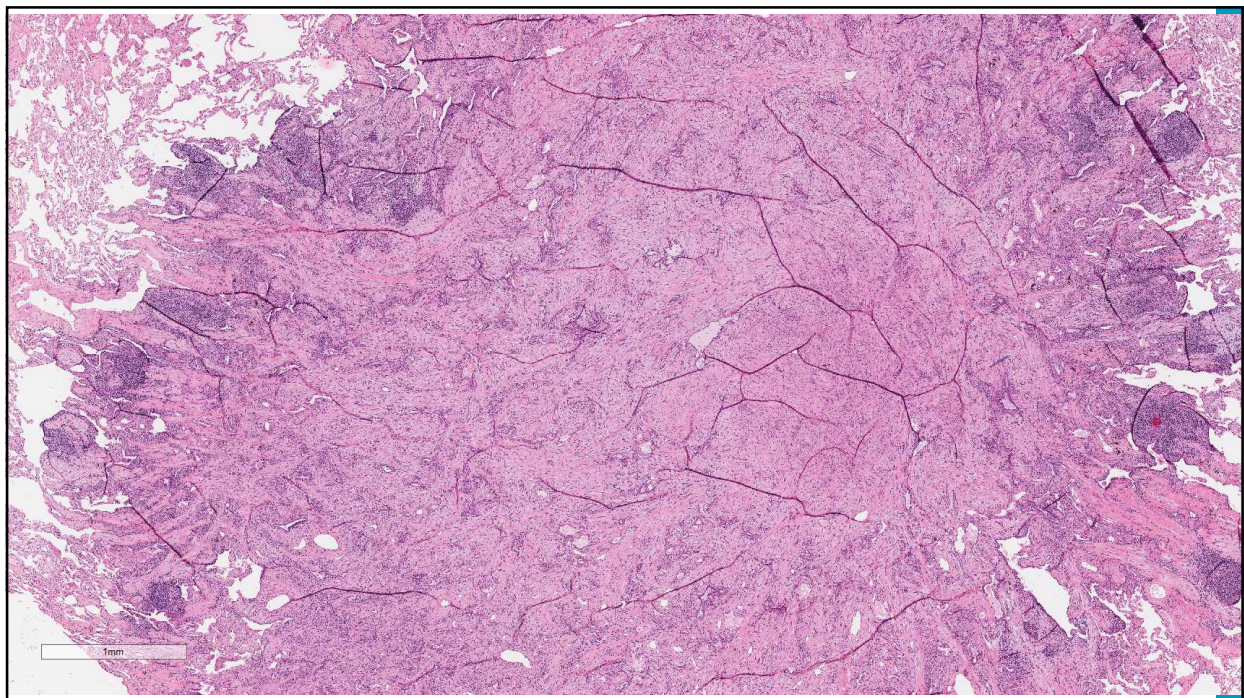
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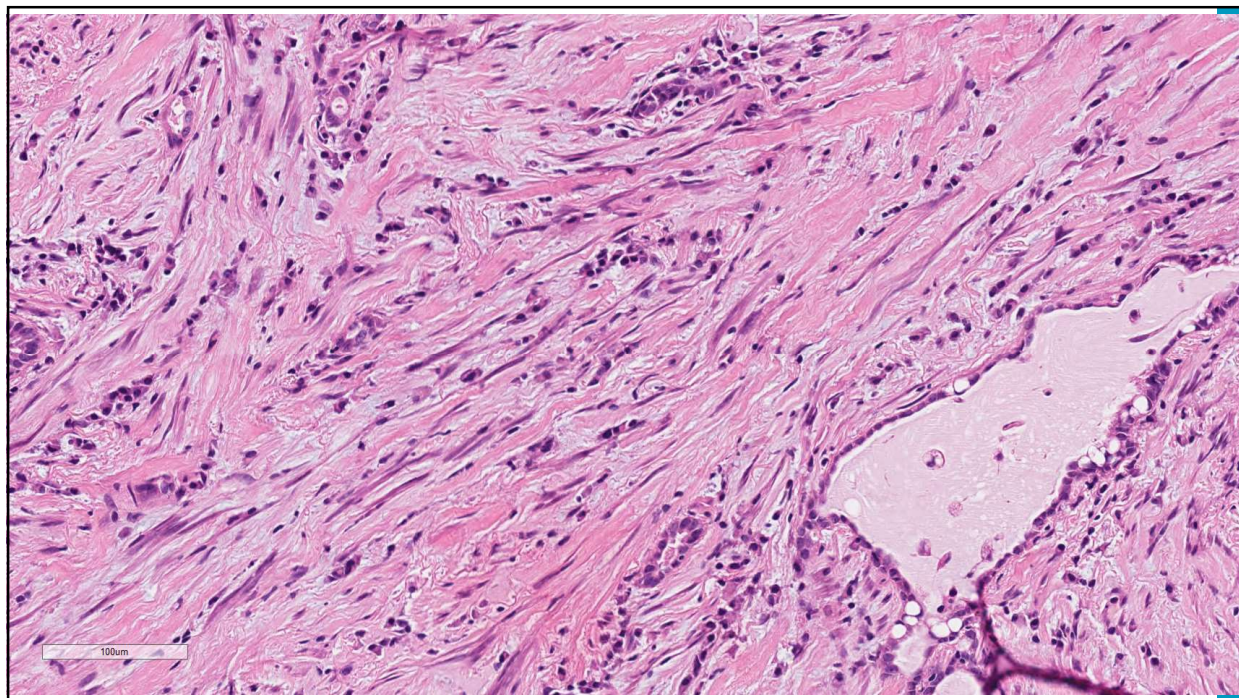


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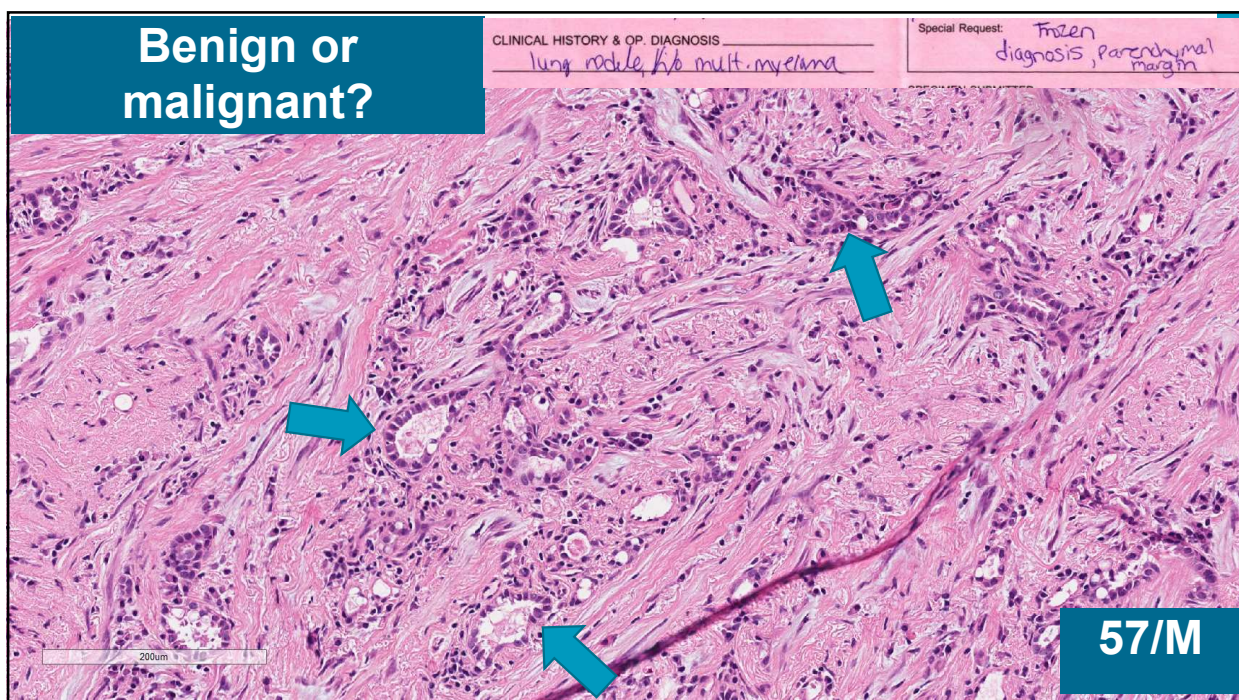


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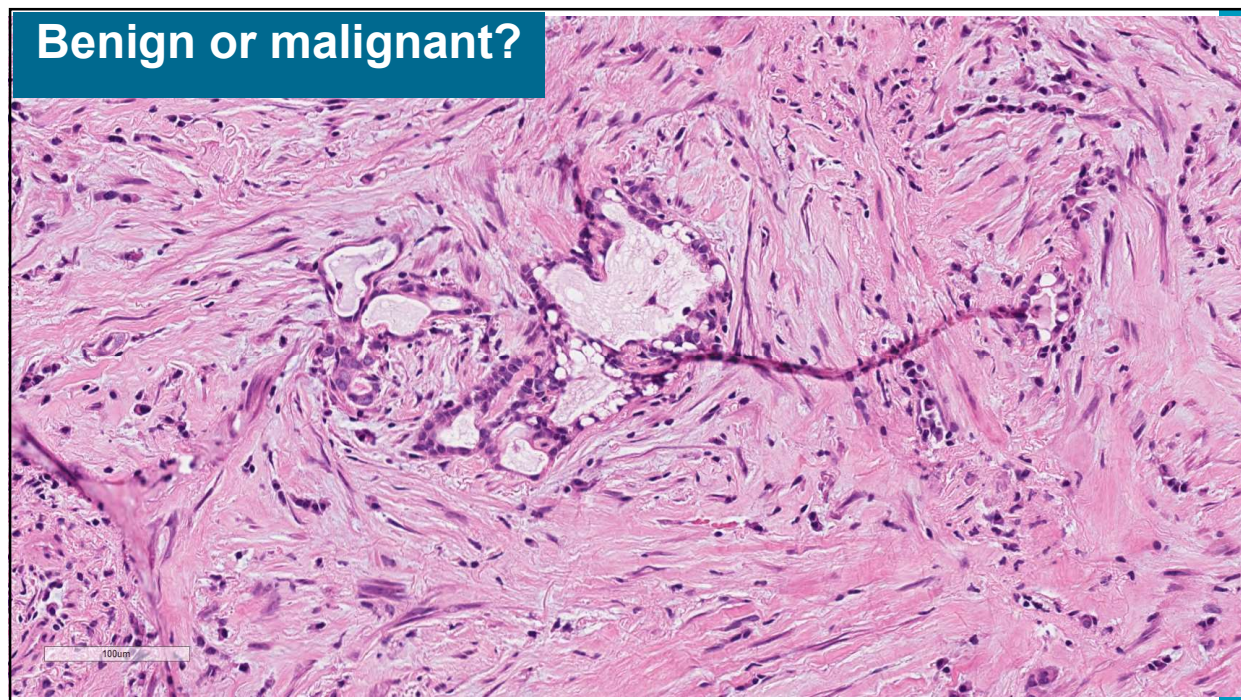


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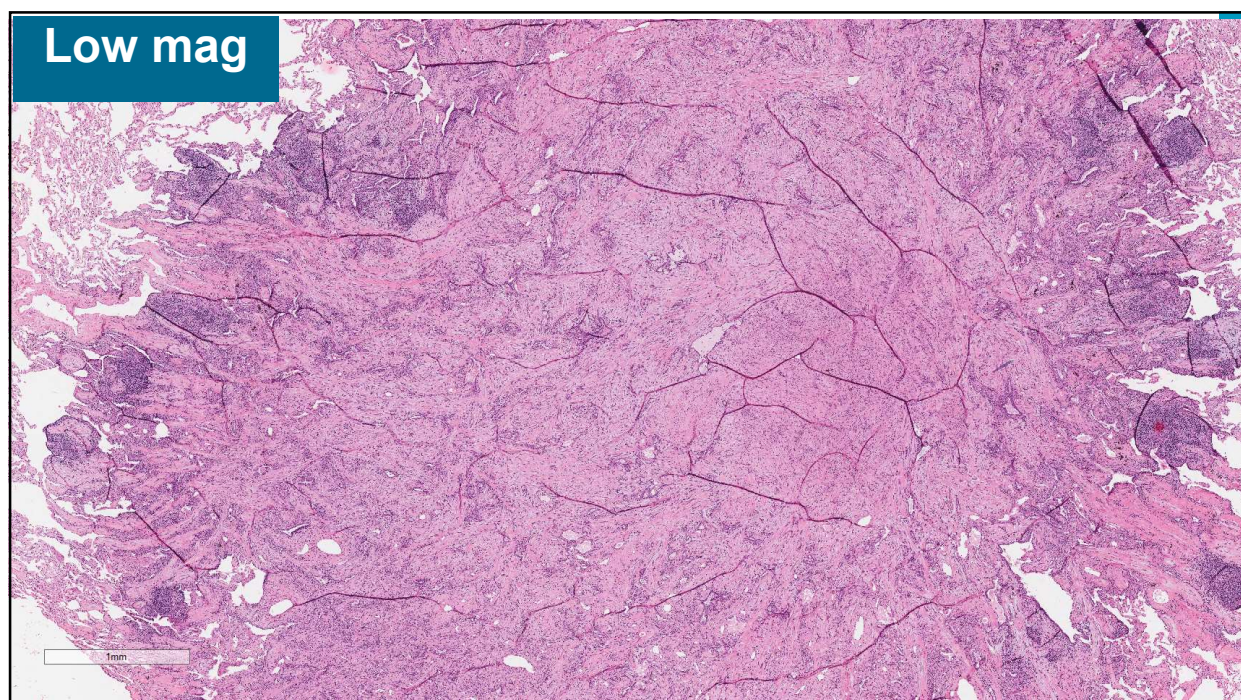


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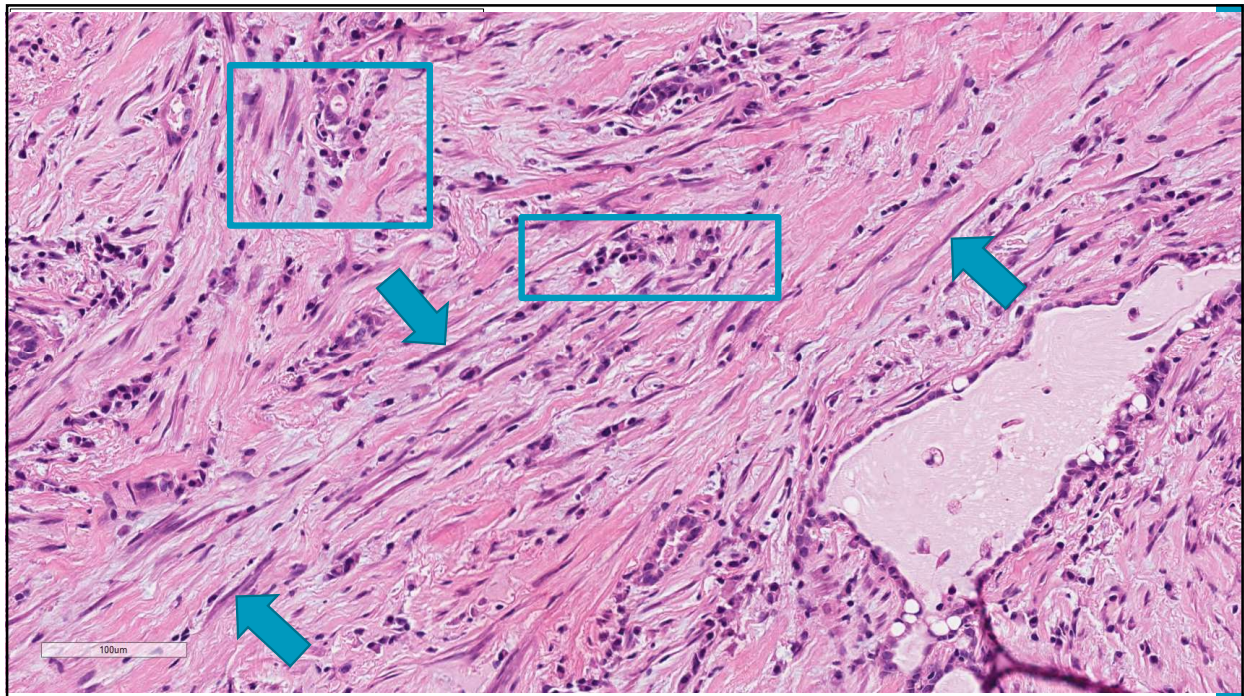


## Frozen Section Diagnosis

- “Adenocarcinoma”
- This prompted completion lobectomy

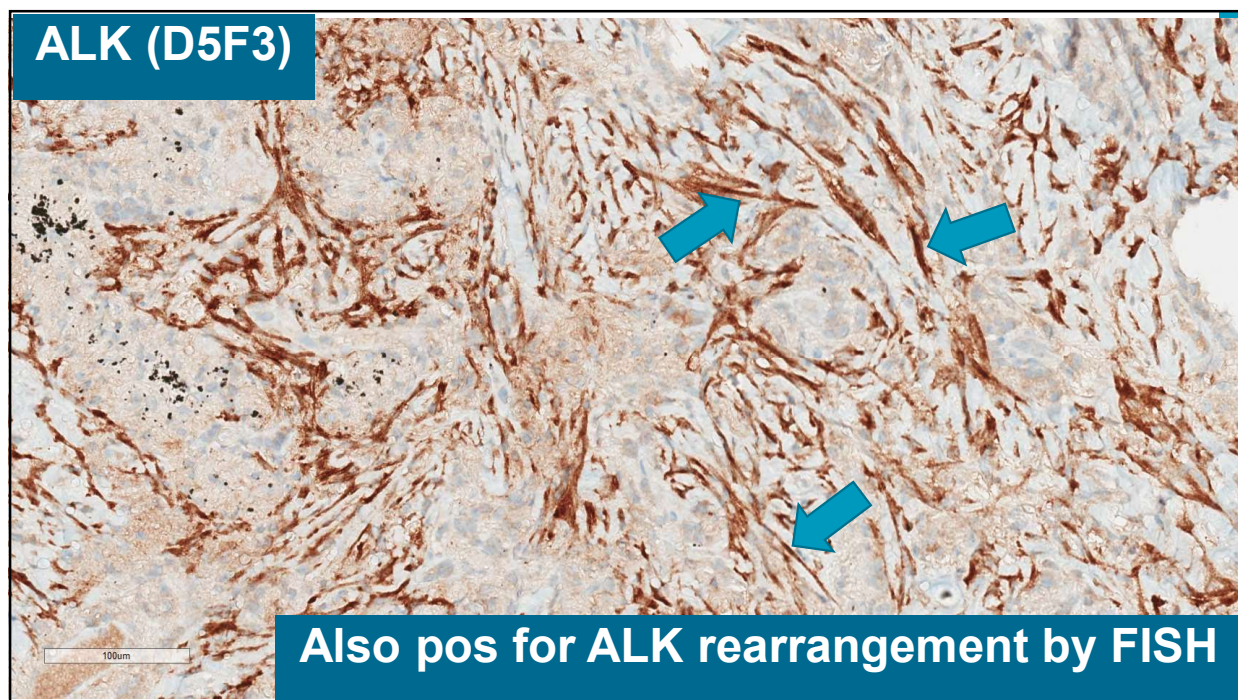
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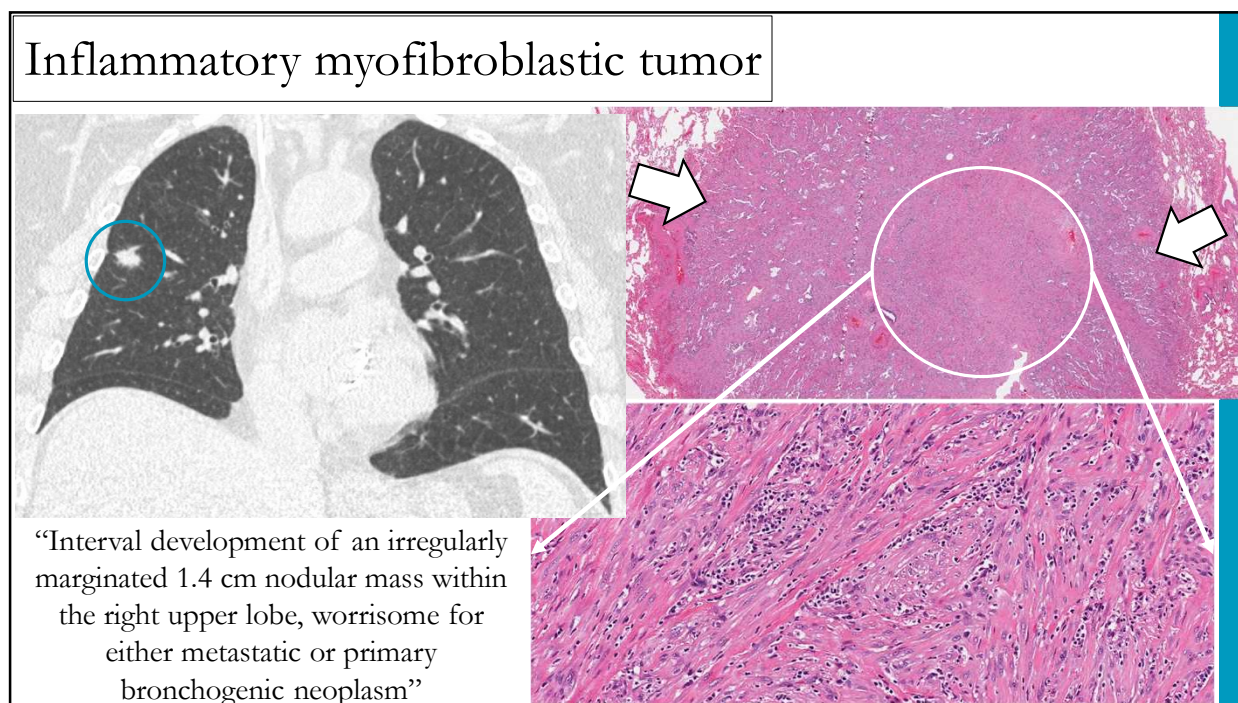


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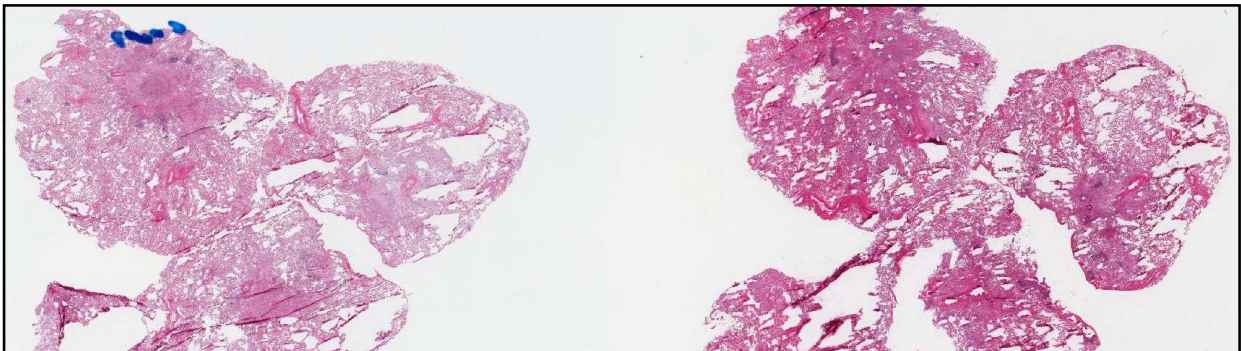
## INFLAMMATORY MYOFIBROBLASTIC TUMOR

- **Clinical:** Lung mass in young patient (most cases)
- **H&E:** Bland elongated spindle cells (spindle cell neoplasm) + many plasma cells
- **Immunohistochemistry:** ALK + (try D5F3!), SMA +, IgG4 + cells common
- **How to confirm?** ALK (D5F3) IHC or ALK FISH

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Chang JC, et al. *J Thorac Oncol* 2019;14(5):825-834

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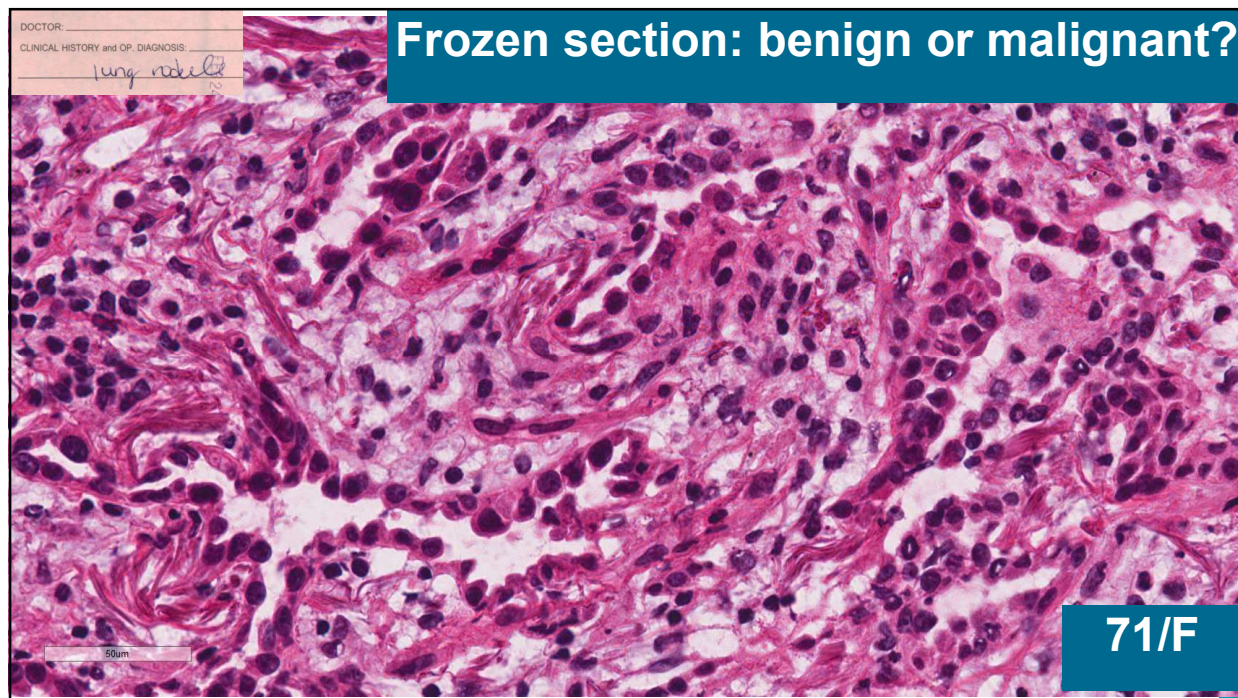


# FROZEN 3

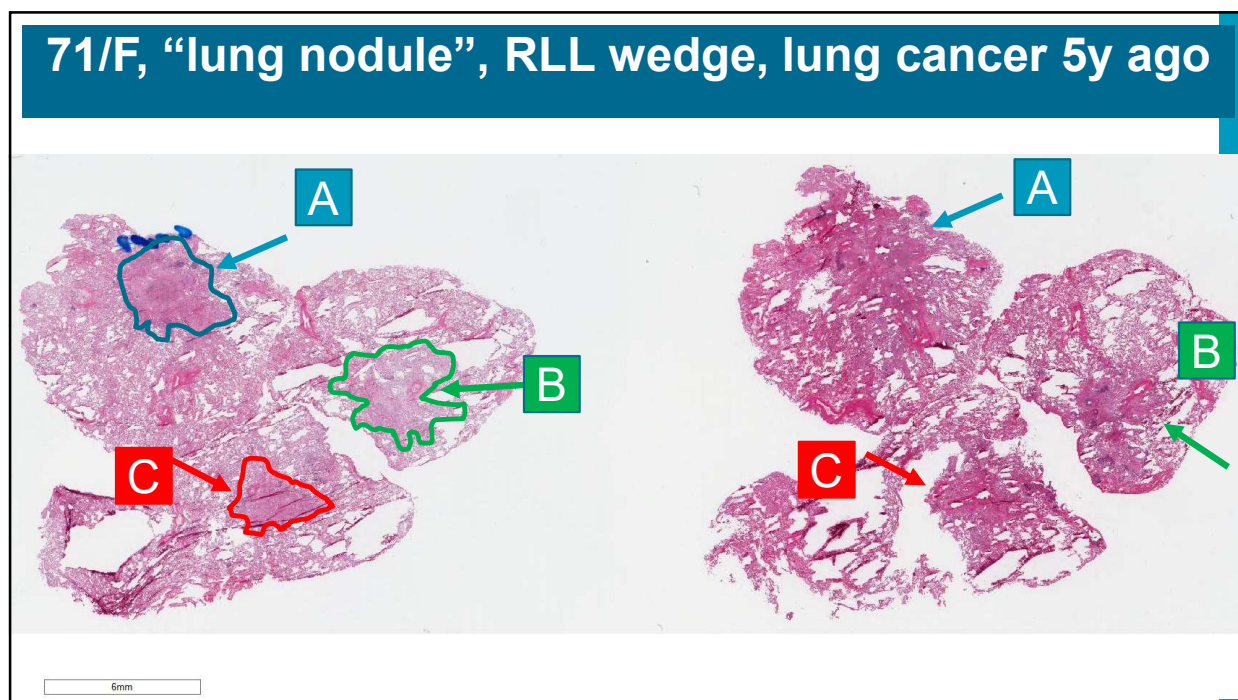
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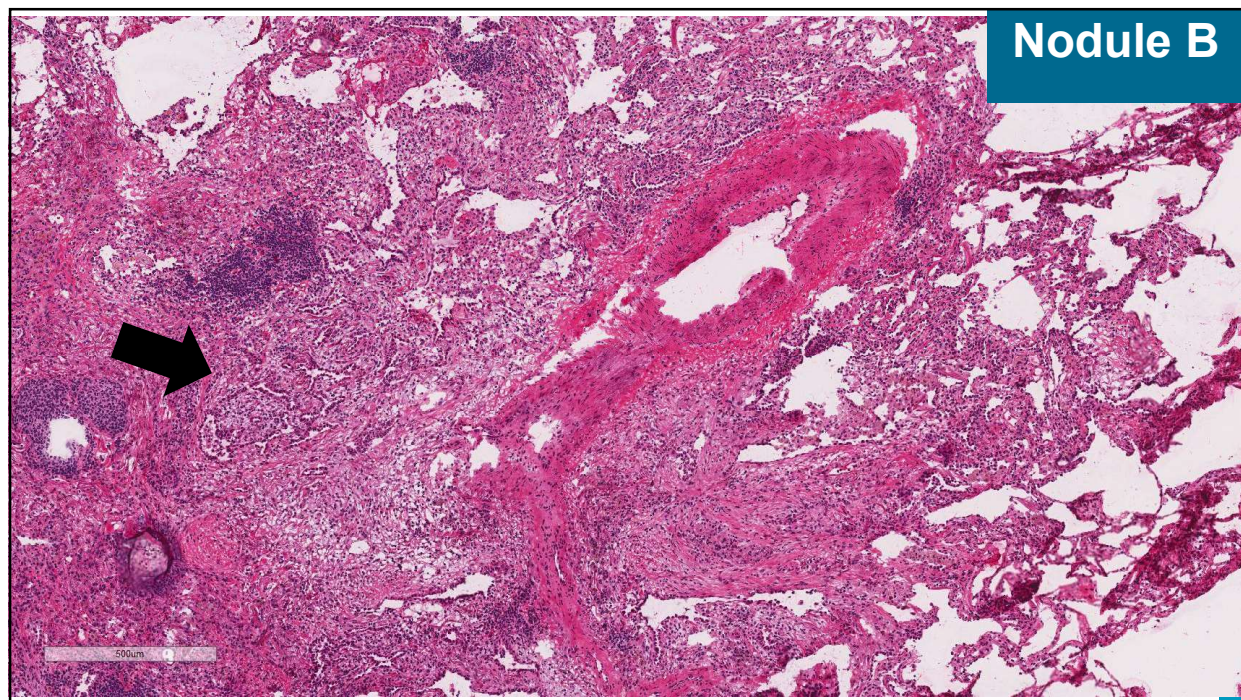


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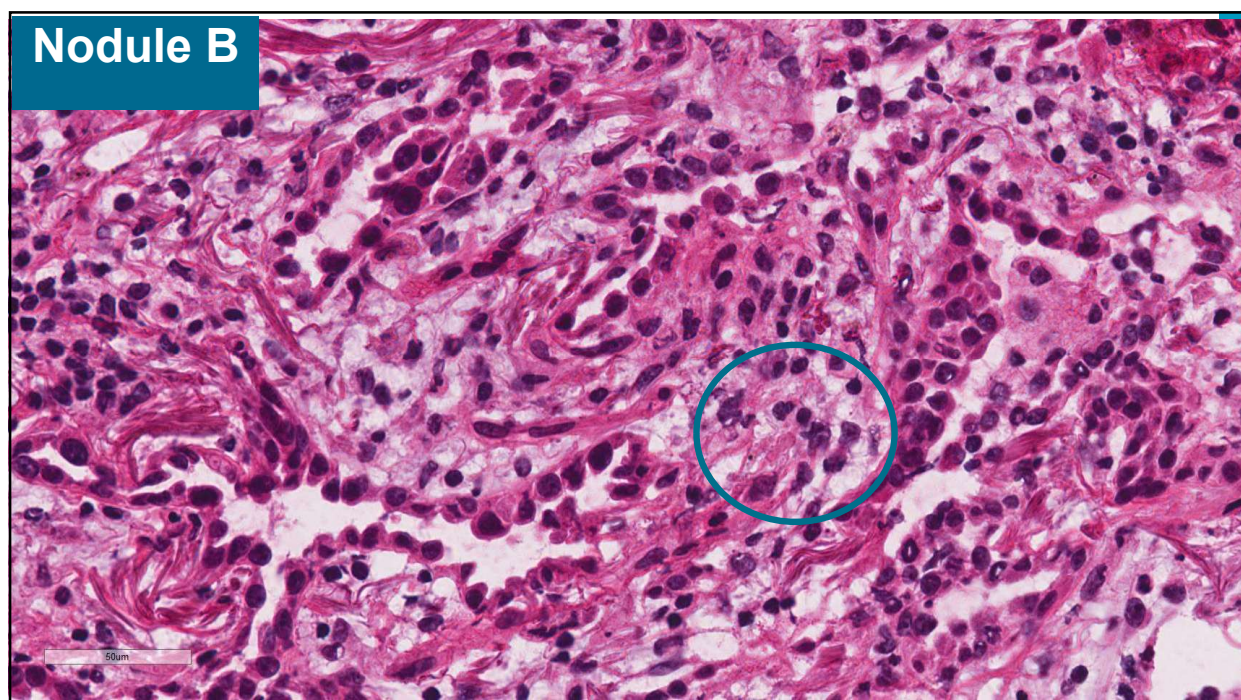


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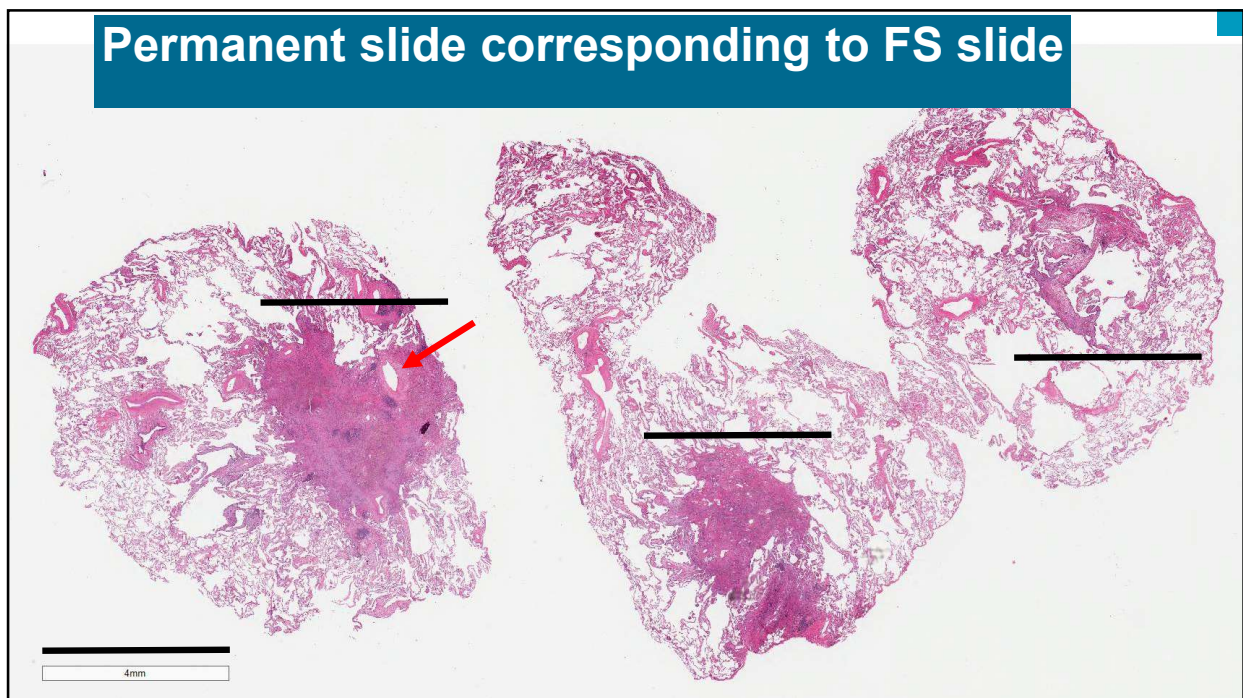
## Frozen Section Diagnosis

- “No definitive malignancy”
- “Architectural changes suggestive of Langerhans, defer to permanent”
- There was no further surgical intervention

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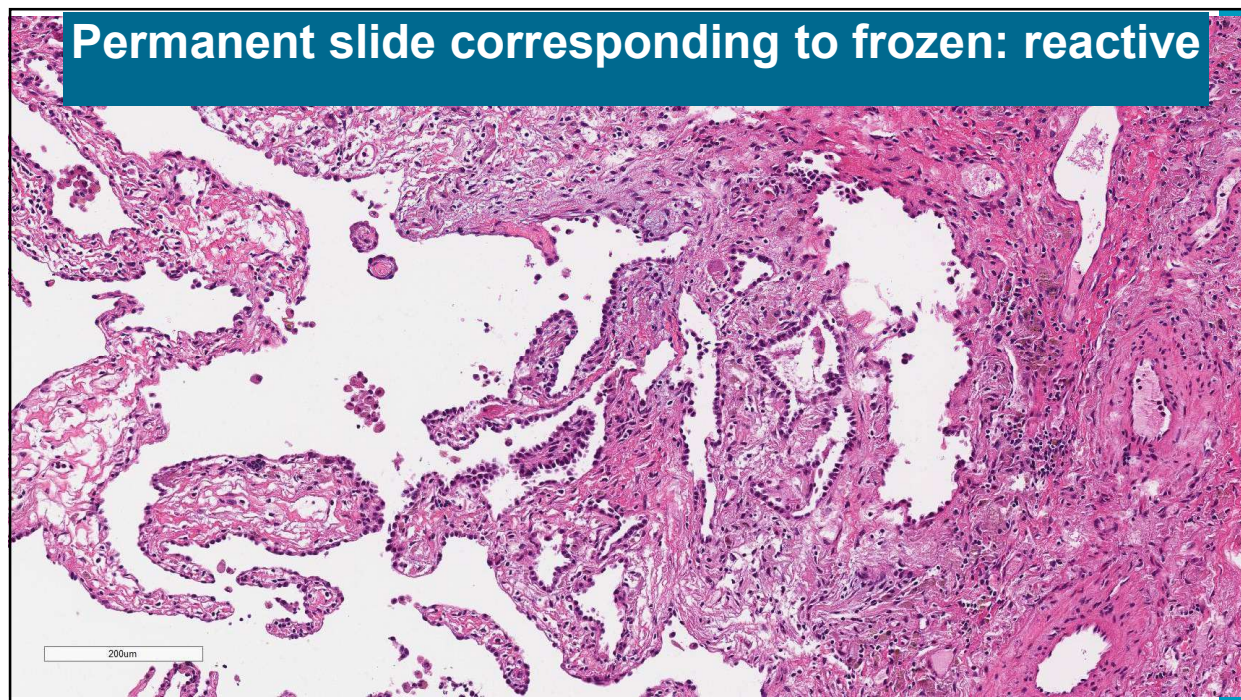
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## Permanent slide corresponding to FS slide

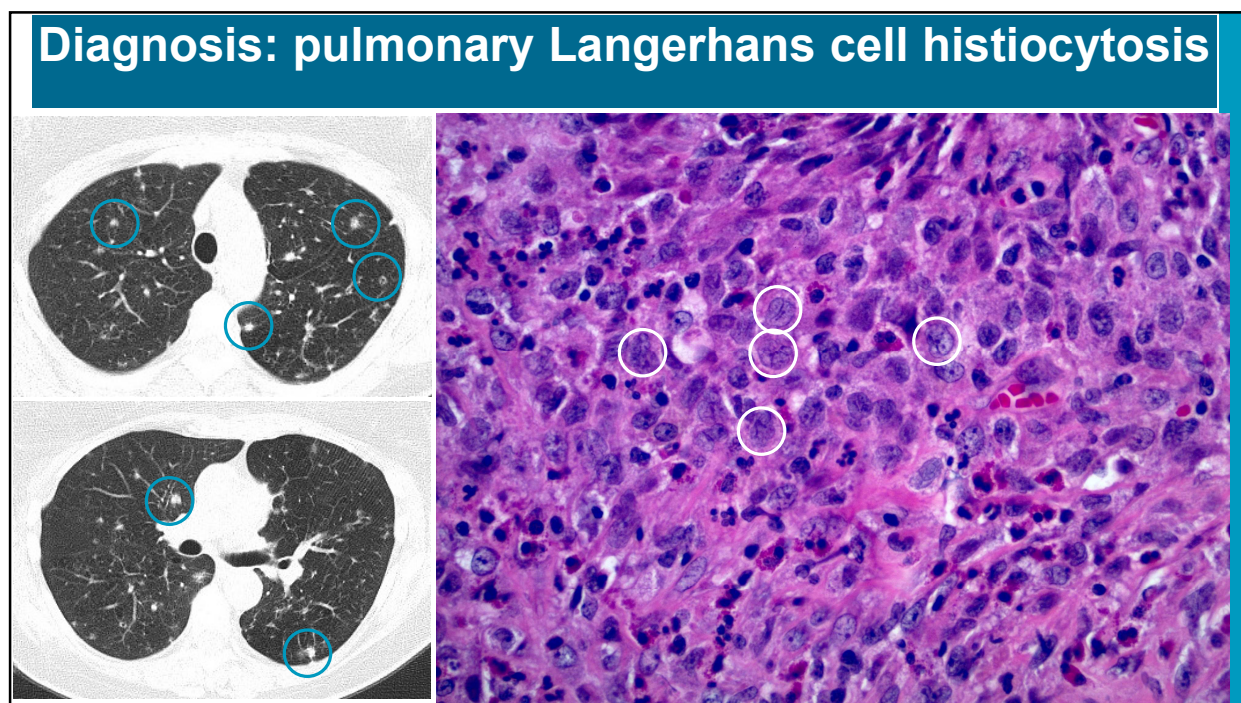


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## Pulmonary Langerhans cell histiocytosis is smoking-related

CT1 8M after smoking cessation CT2

Pigmented airspace macrophages, smoking-related

Smoking-related interstitial fibrosis (SRIF)

© College of American Pathologists. Mukhopadhyay S, Sansano I. *Surg Pathol Clin* 2024;17(2):159-171

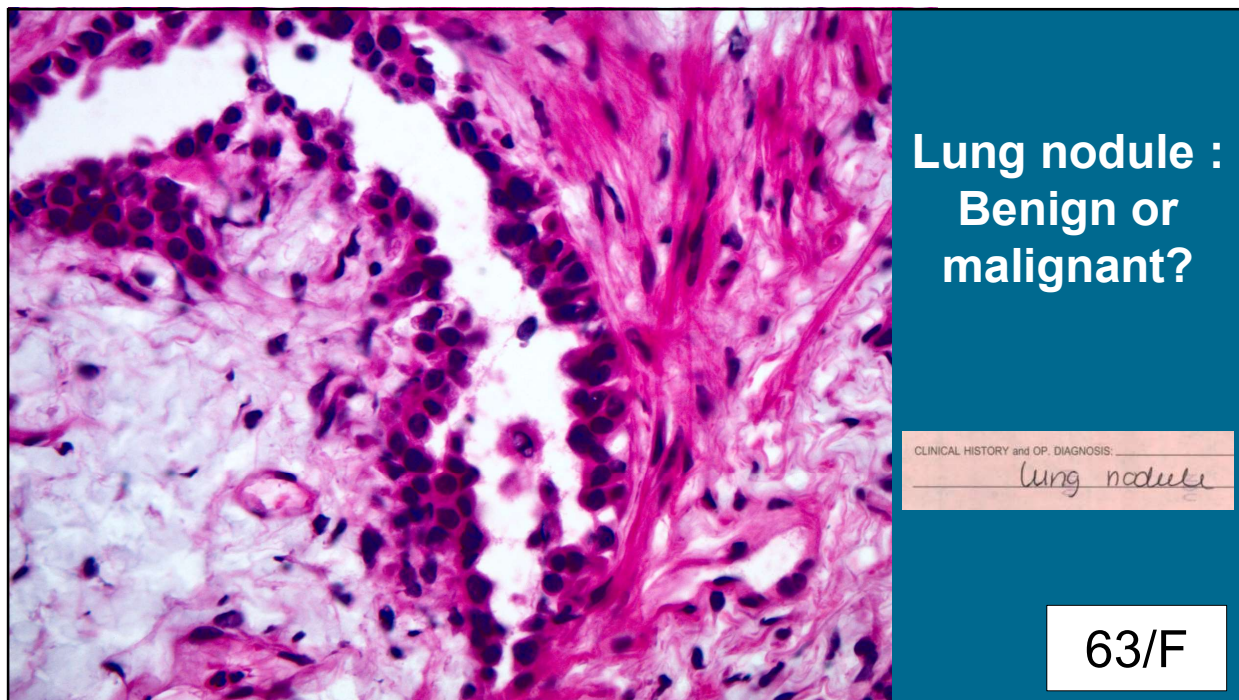
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# FROZEN 4

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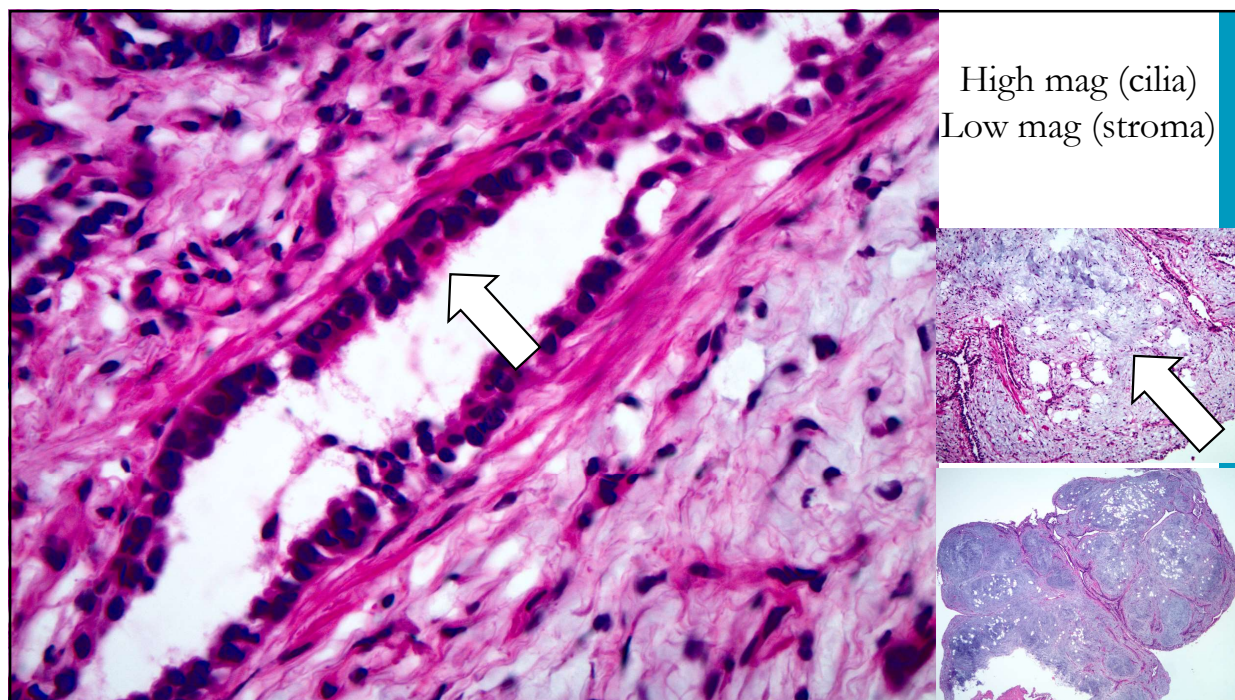
## Frozen Section Diagnosis

- “Adenocarcinoma”
- This prompted mediastinal lymph node sampling but no lobectomy was performed

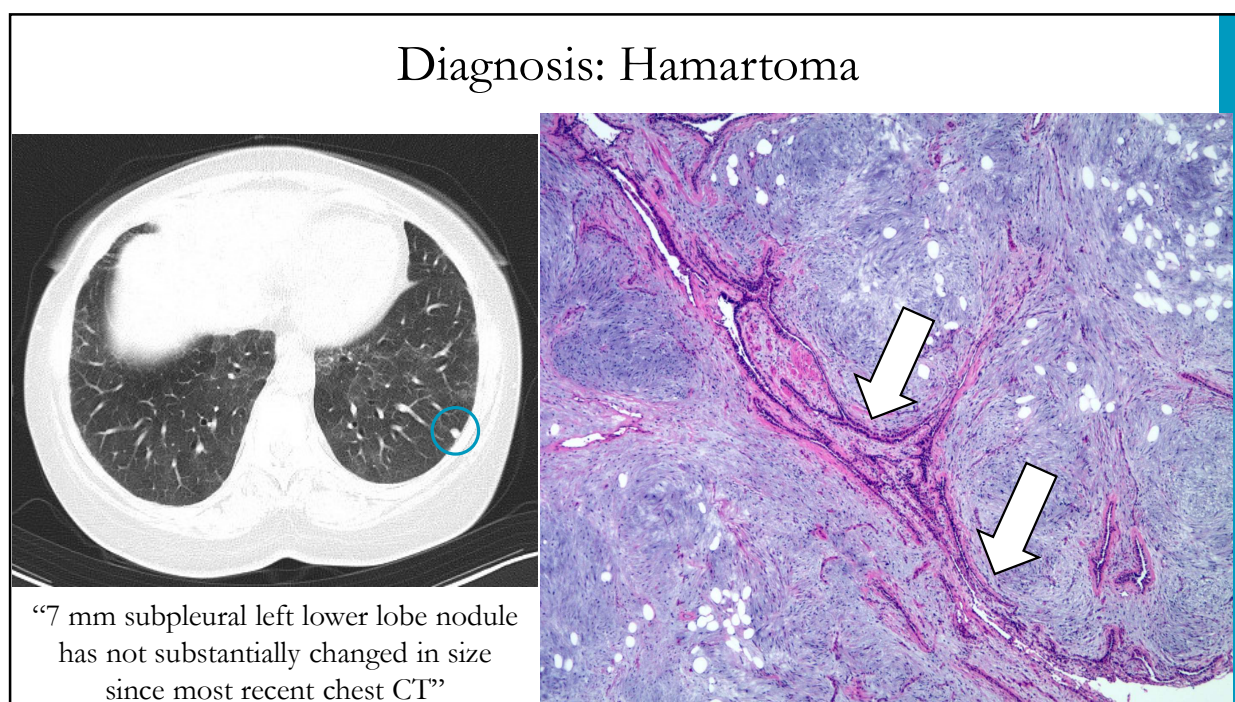
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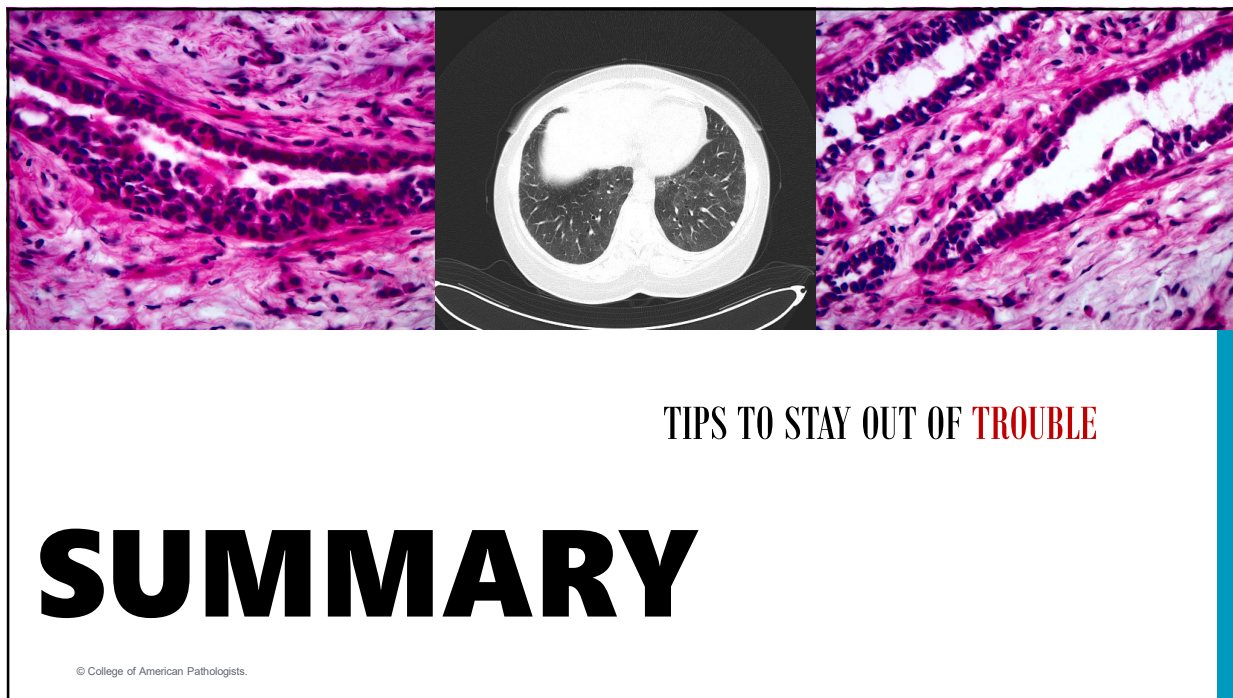


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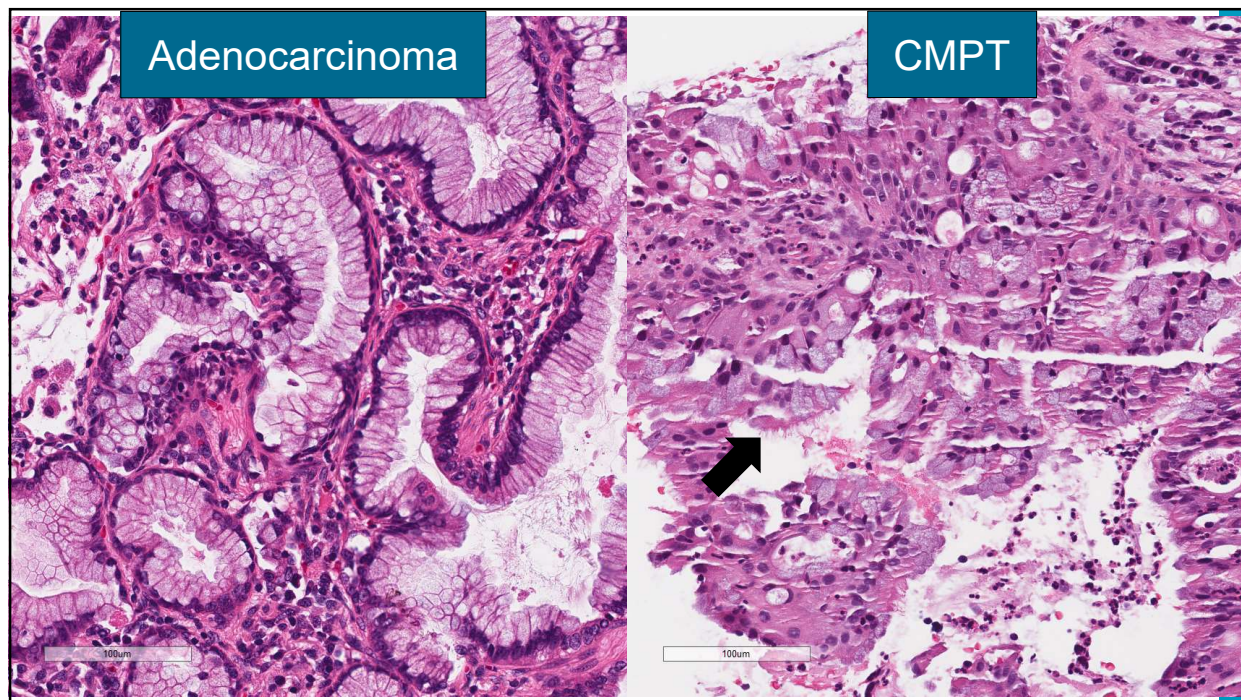
### Pathology Tip 1: Hunt for Cilia

- Cells with true cilia are always benign
- Fuzz at apex of cell is not the same as true cilia

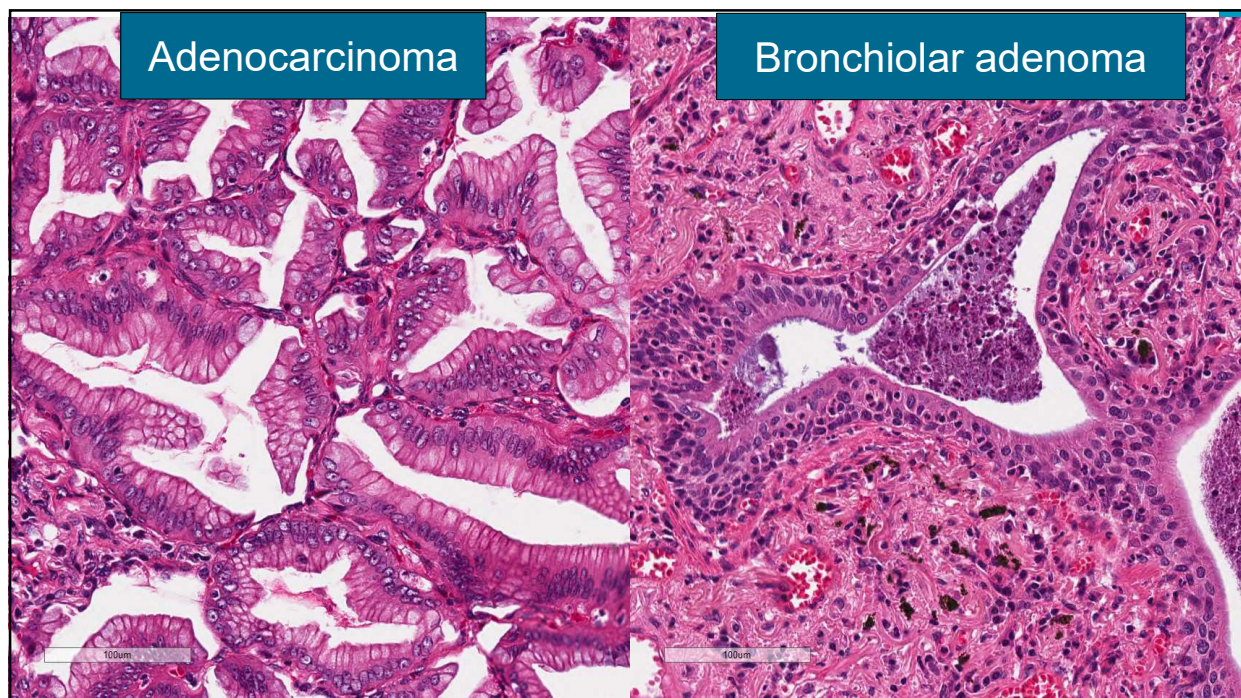
Mukhopadhyay S. *Arch Pathol Lab Med* 2025;149(4):e93-e99

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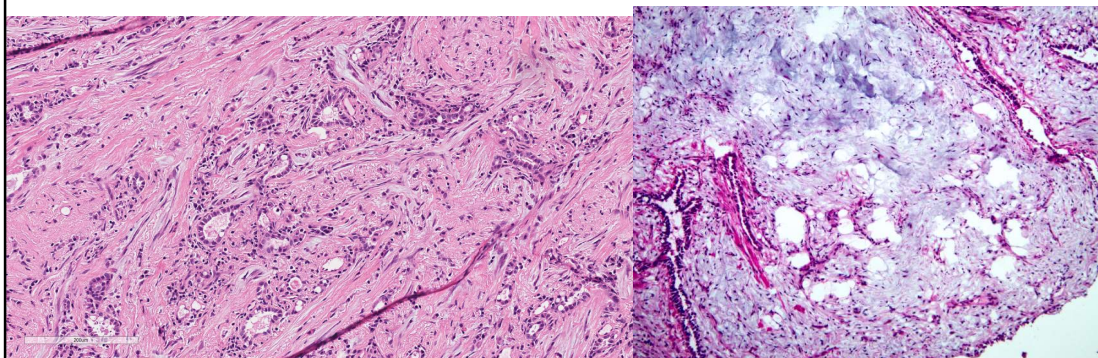


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## Pathology Tip 2: Evaluate Background

- Is the lesion a mesenchymal lesion with entrapped lung epithelium?
- Is there inflammation or acute lung injury?
- Is this Langerhans cell histiocytosis?



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## Pathology Tip 3: Ask for Help

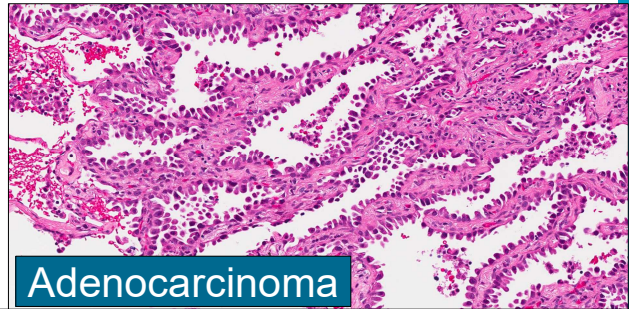
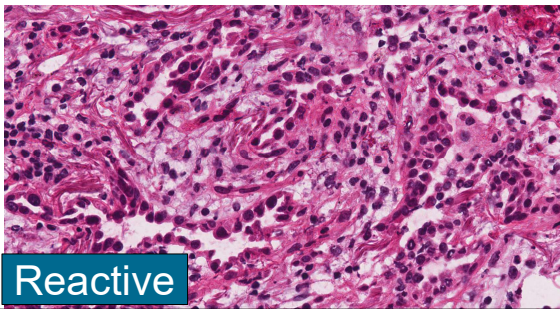
- Use clinical info: Slow growing? Small? Young person?
- Show slide to another pathologist.
- Talk to your surgeon. What does imaging look like? Will a malignant diagnosis lead to lobectomy?

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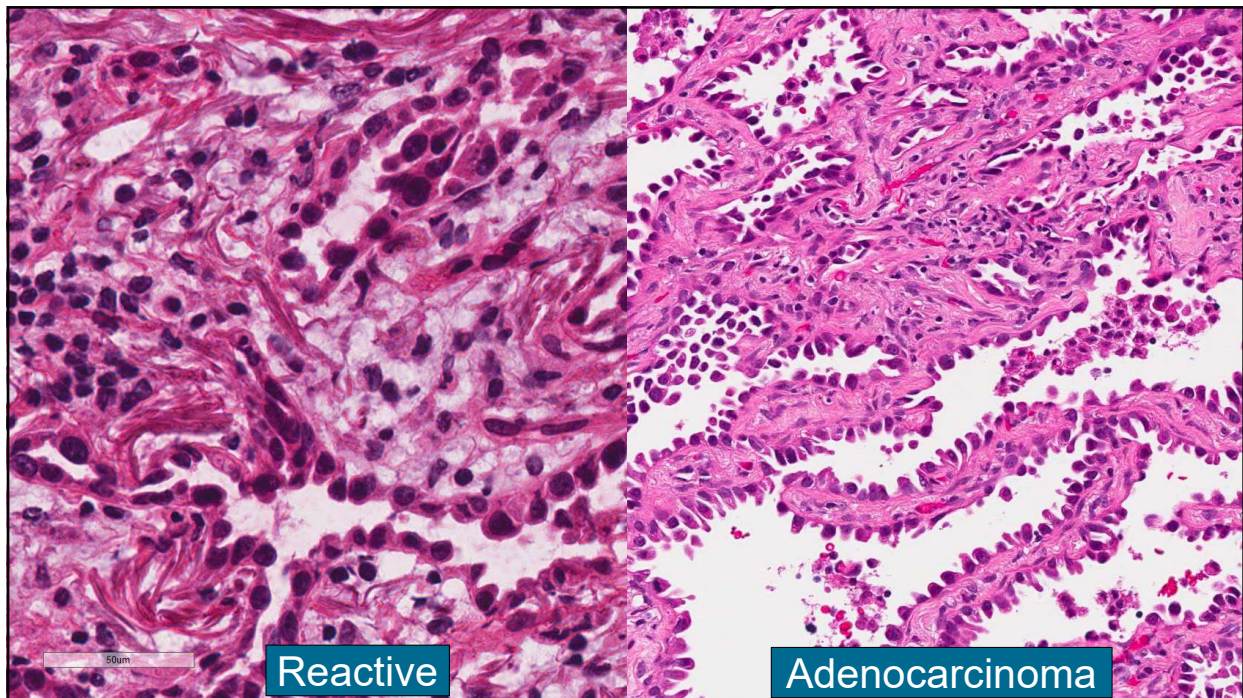


## Pathology Tip 4: Focus on the issue

- Key issue for the surgeon: benign or malignant?
- Don't get hung up on "lepidic"
- Lung adenocarcinomas can be very bland and often do not show invasion of the type that occurs in other organs (e.g., colon)



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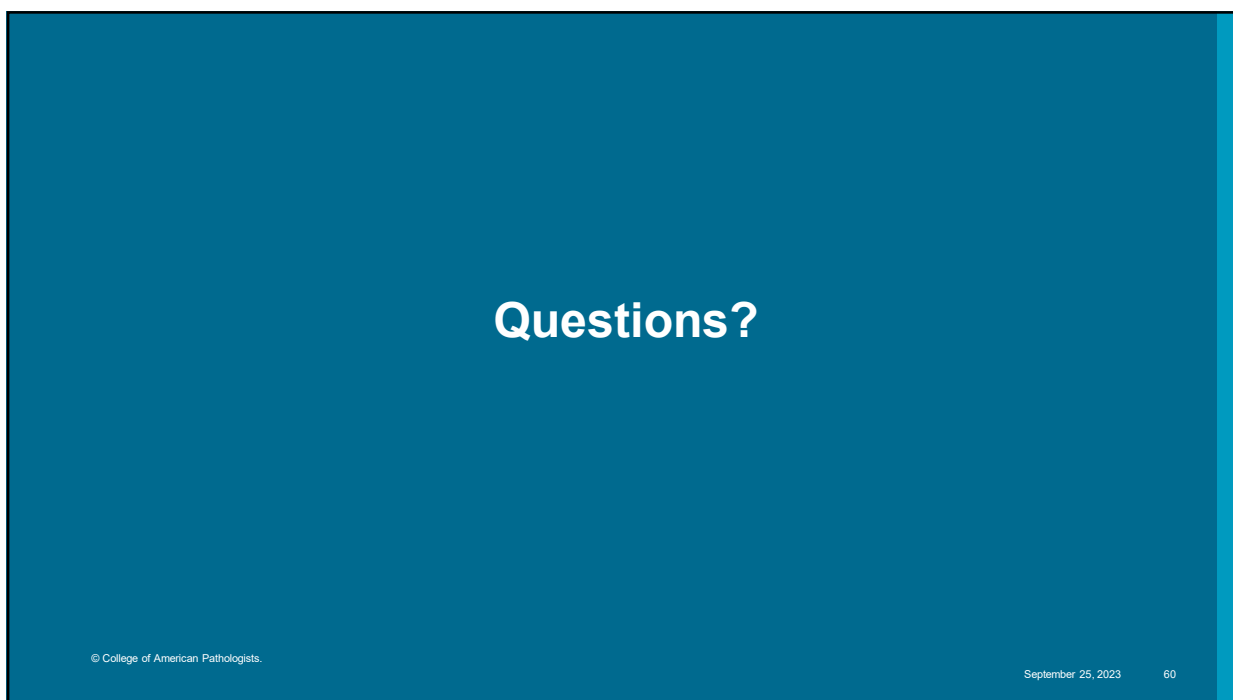


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