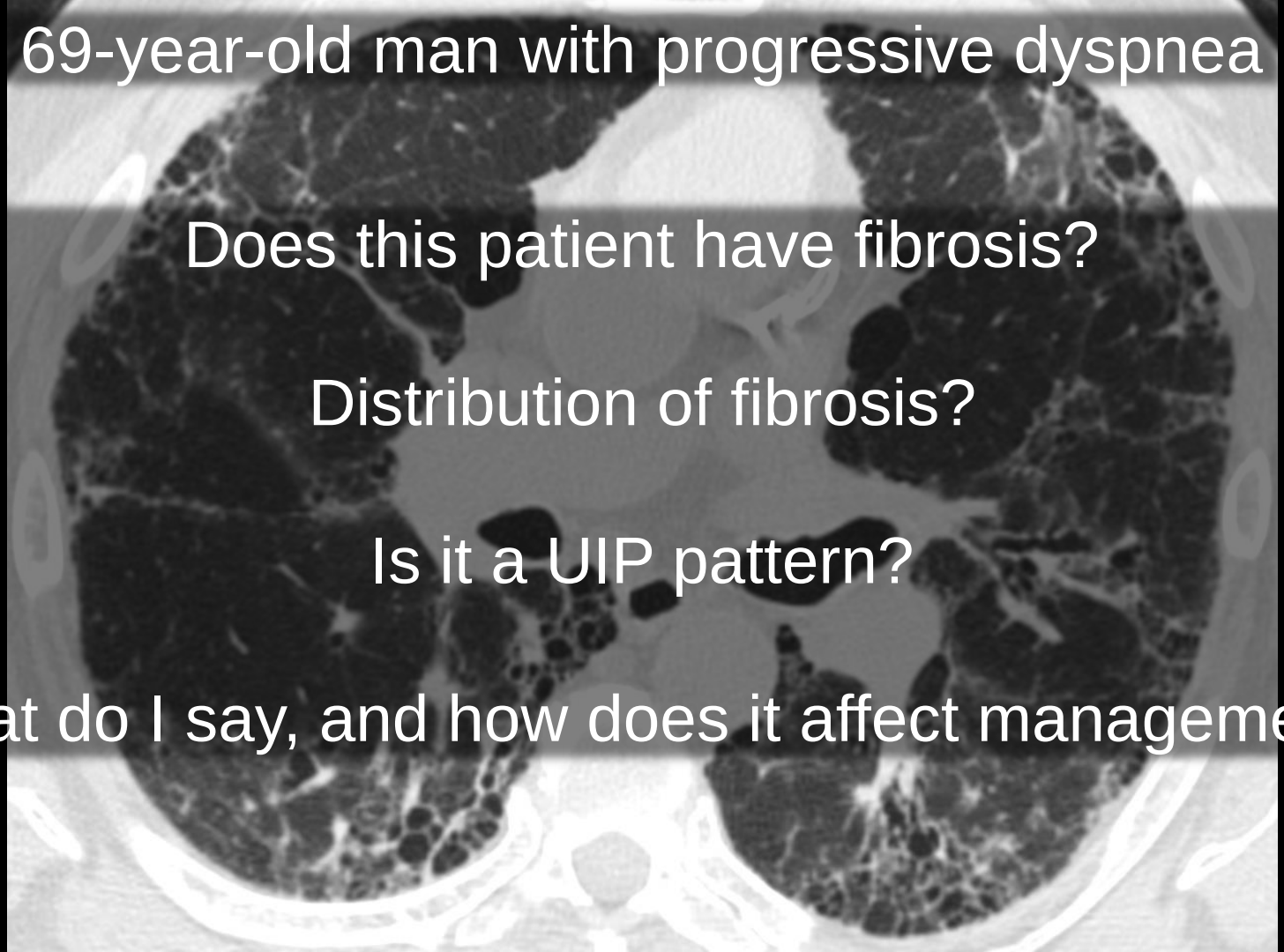
Usual Interstitial Pneumonia (UIP)

(UIP ≠ IPF)

American College of Radiology™

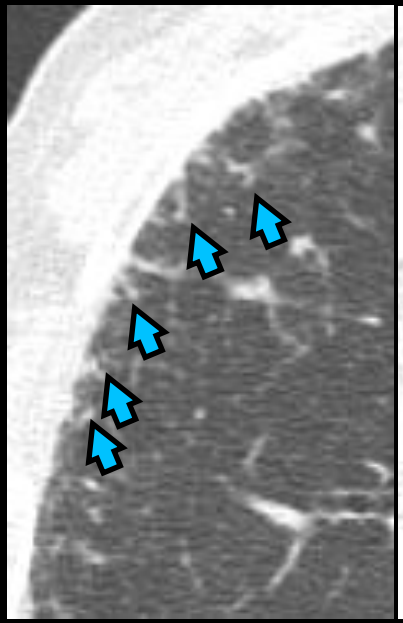
We Have No Relevant Disclosures


69-year-old man with progressive dyspnea
Does this patient have fibrosis?
Distribution of fibrosis?
Is it a UIP pattern?
What do I say, and how does it affect management?

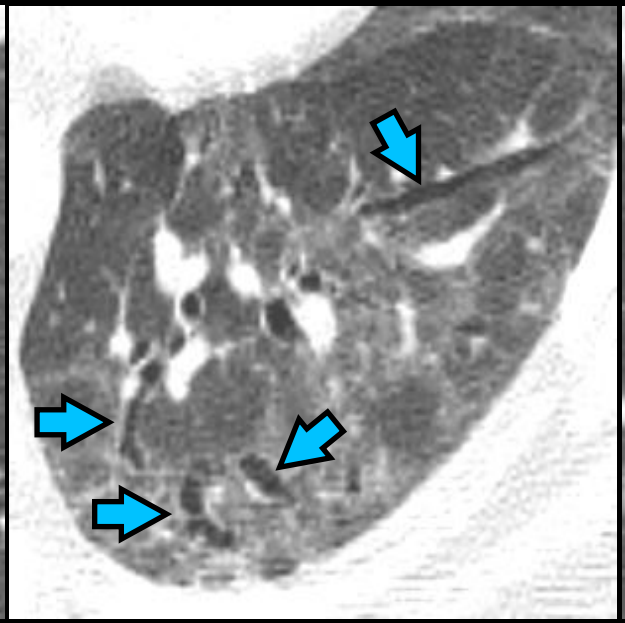
Objectives

- Terminology: Illustrate HRCT findings of lung fibrosis, and pitfalls
- Accurately (and concisely) describe HRCT findings of UIP focusing on patterns
- Discuss how integrating clinical and HRCT findings can obviate the need for surgical biopsy in some patients
- Pearls
- Review HRCT signs suggestive of CTD in patients with UIP pattern

Terminology: Direct Findings of Fibrosis

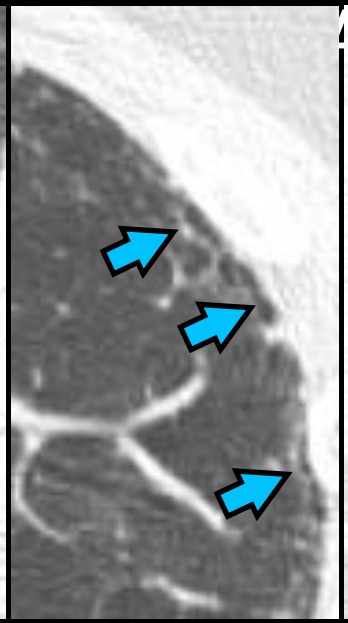


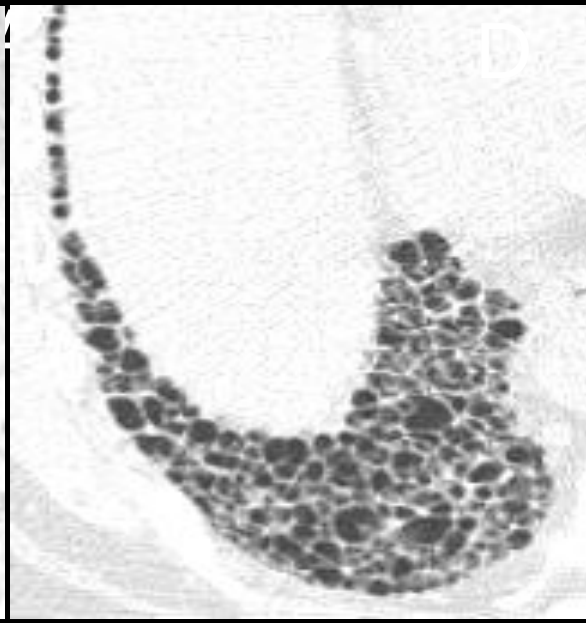
Reticulation



Traction bronchiectasis and bronchiolectasis

GGO**

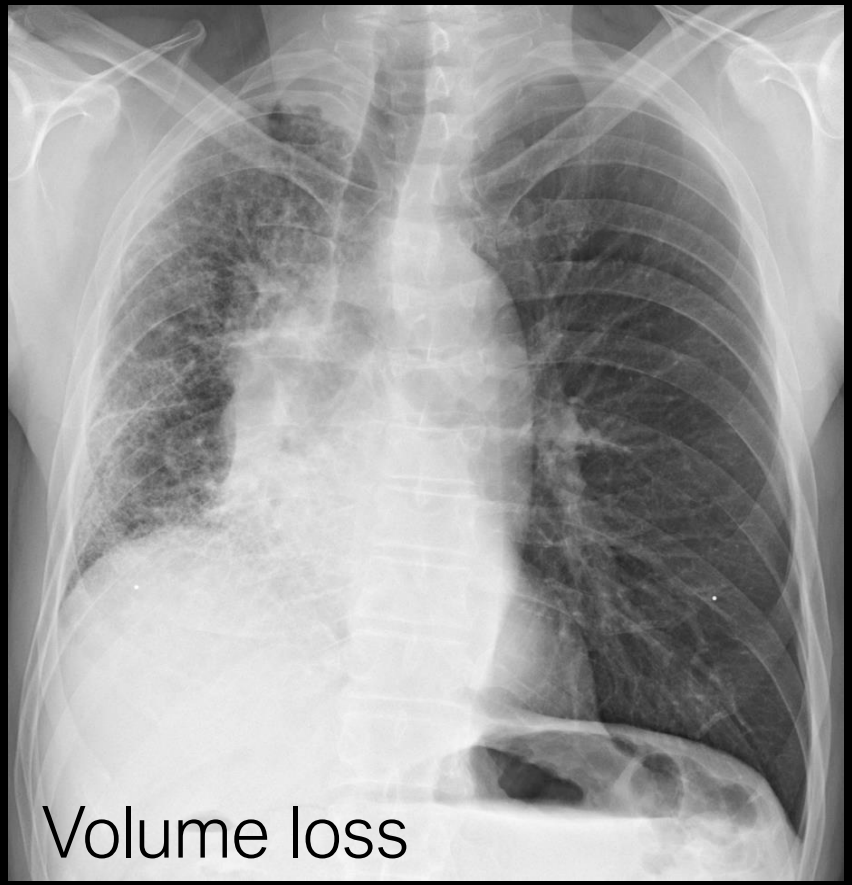


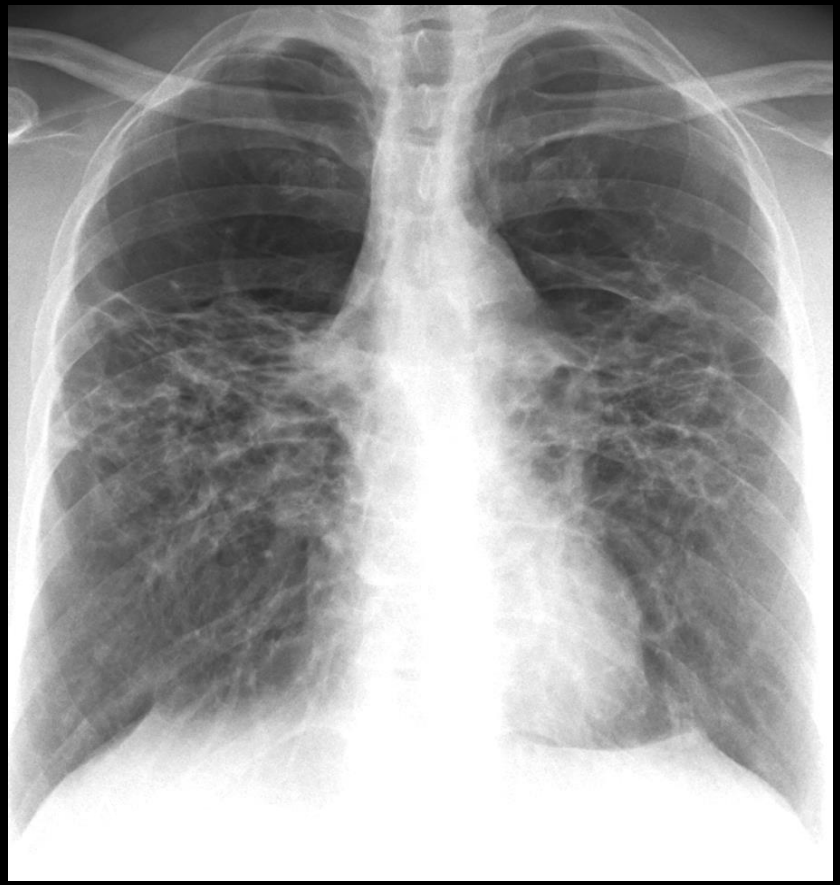


Honeycombing

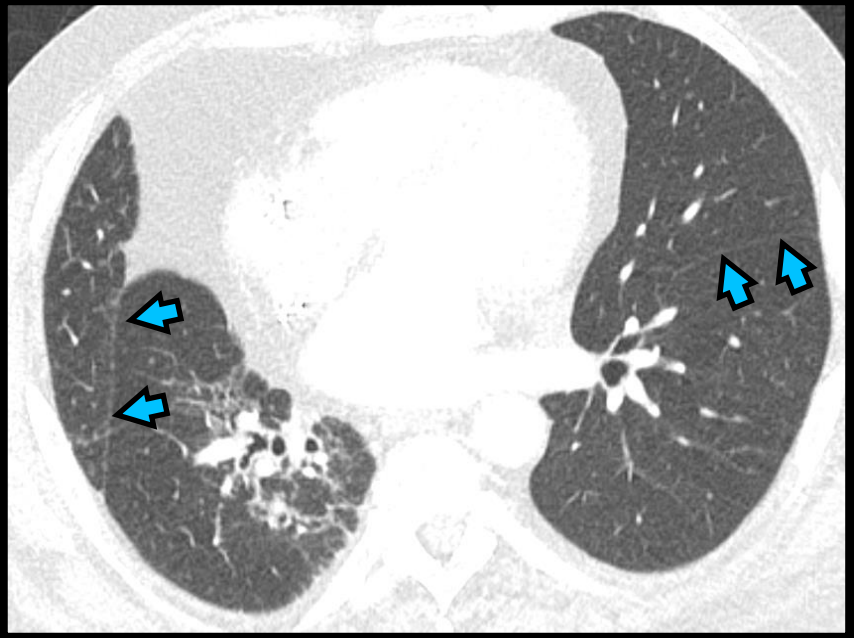
Details coming …

Indirect Findings of Fibrosis

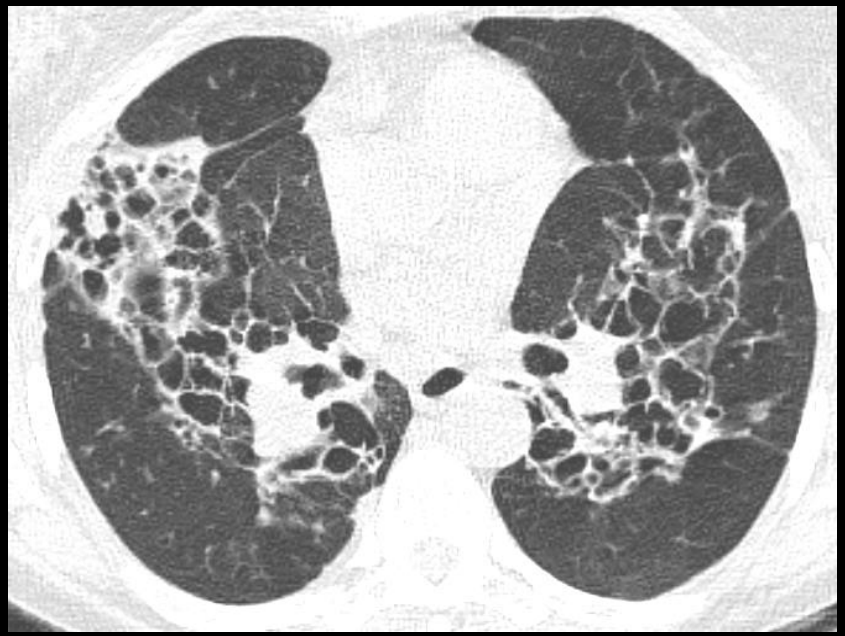




Indirect Findings of Fibrosis



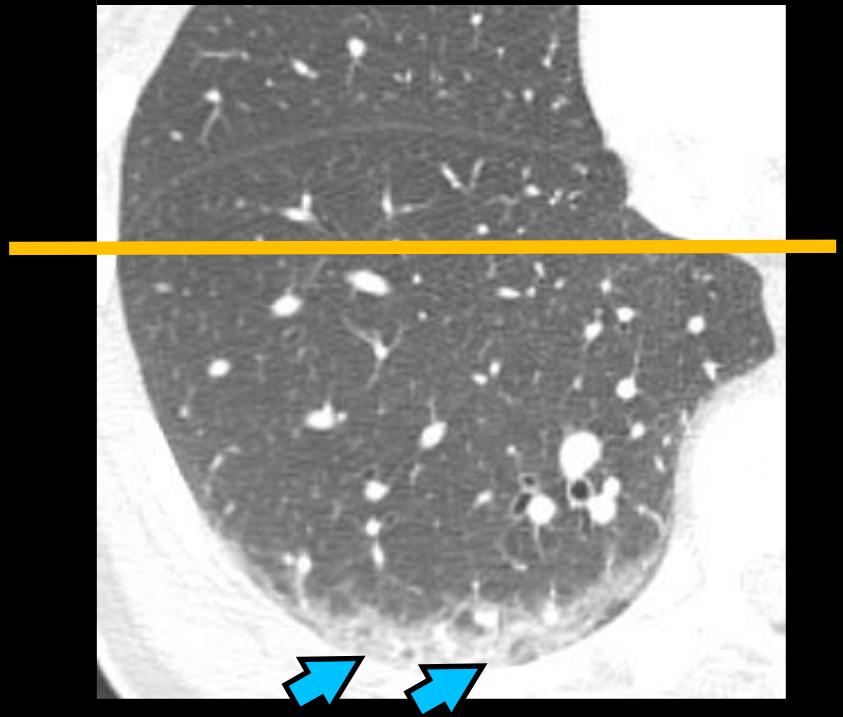
Volume loss

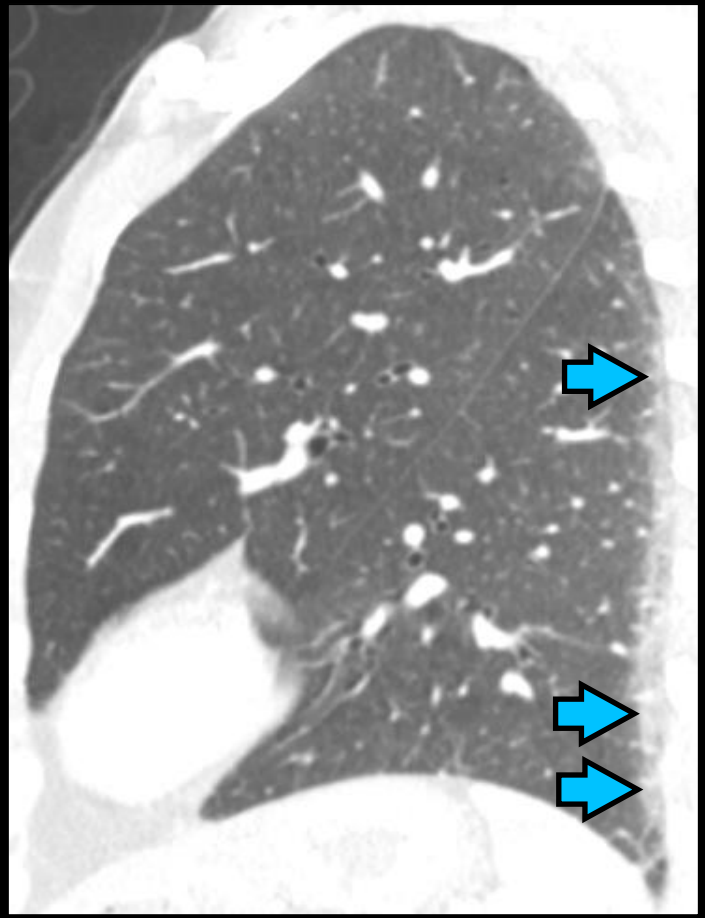


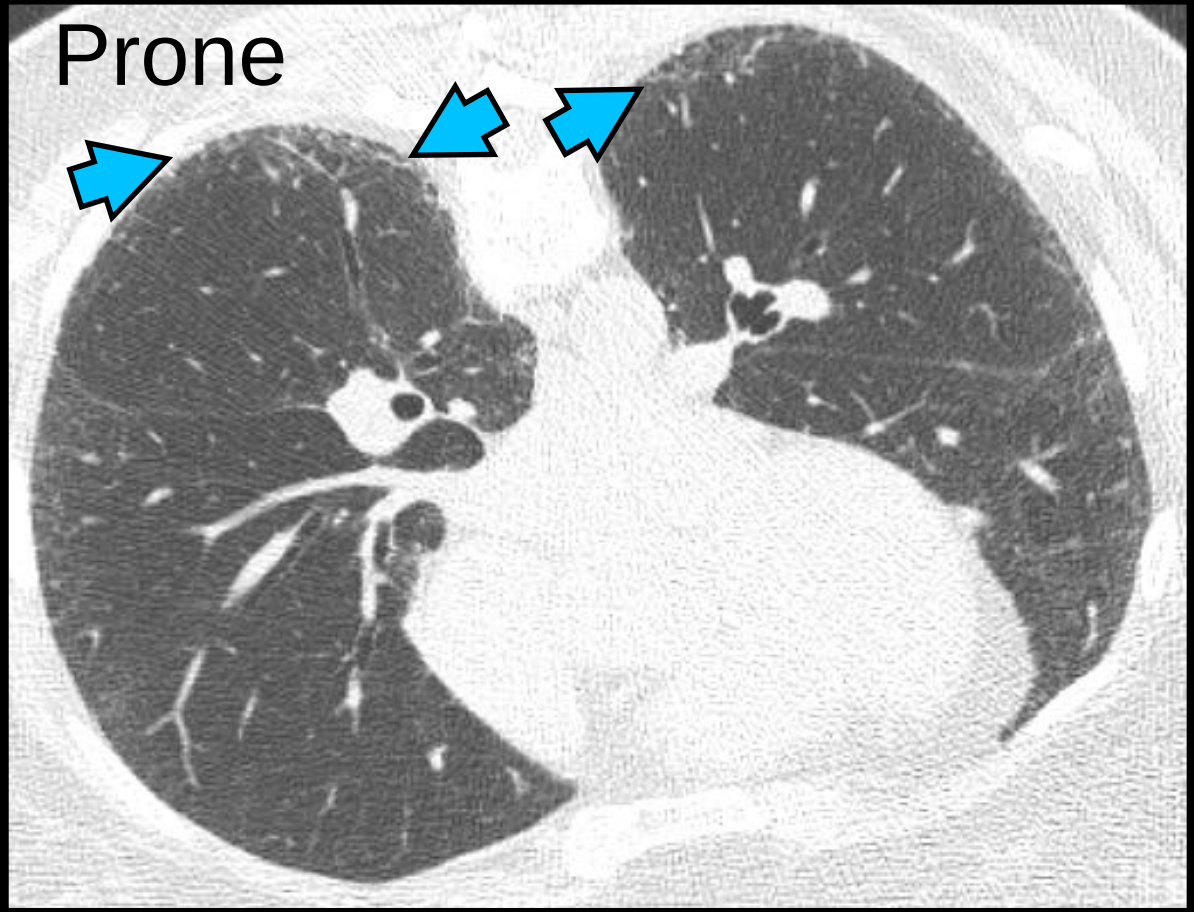
Architectural distortion

Fibrosis Pitfall

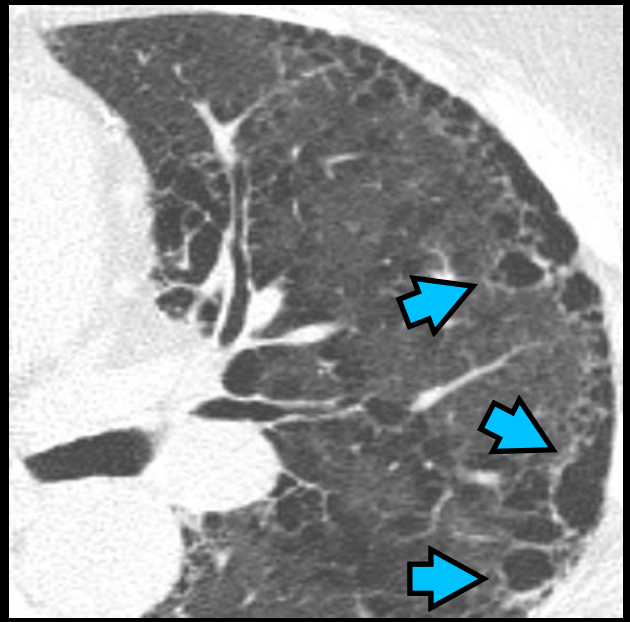
Atelectasis



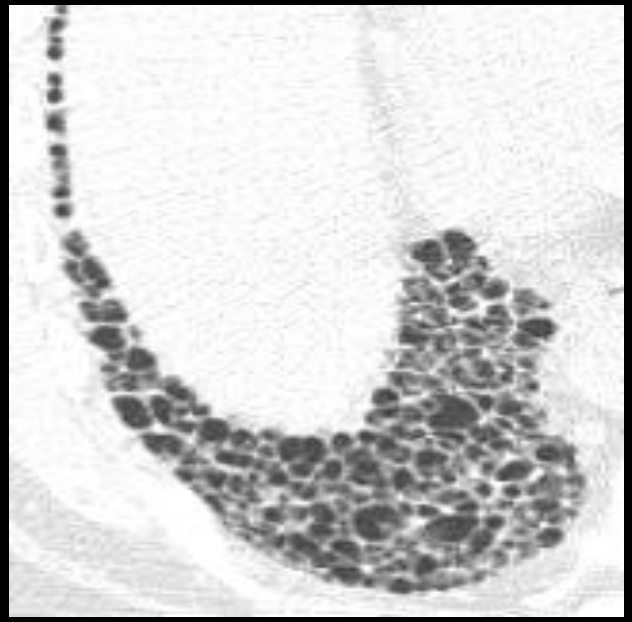



Prone

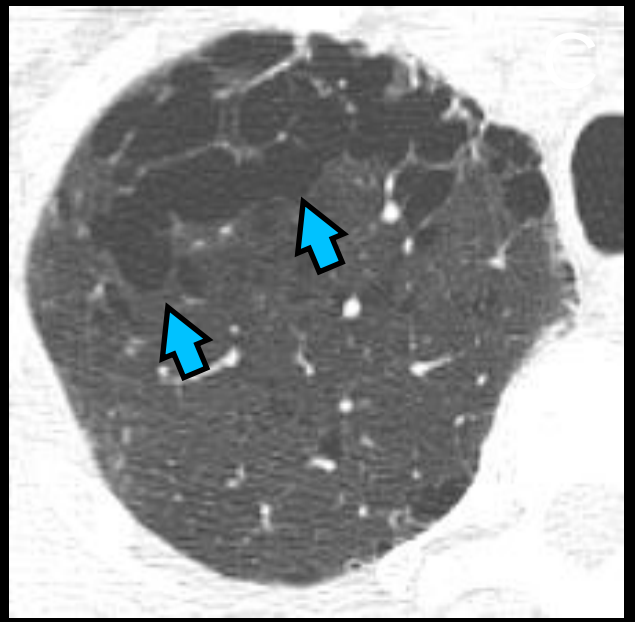
Fibrosis Pitfalls



Airspace Enlargement with Fibrosis



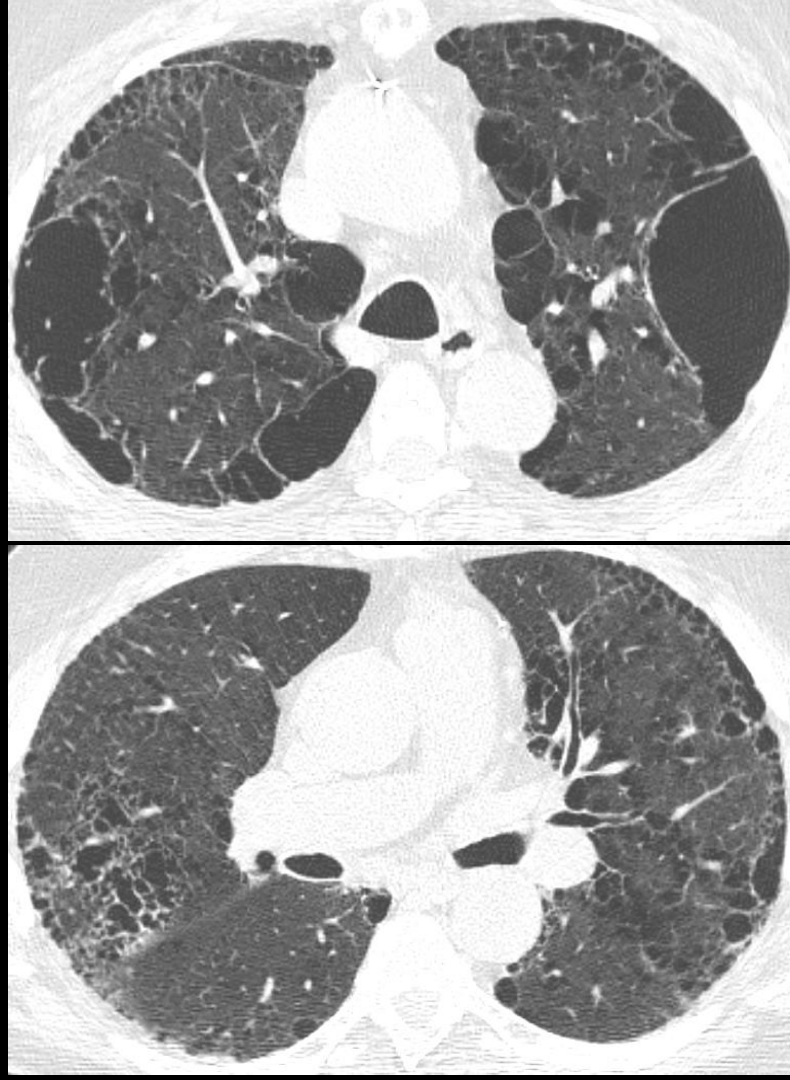
Honeycombing



Paraseptal Emphysema

Airspace enlargement with fibrosis (AEF)

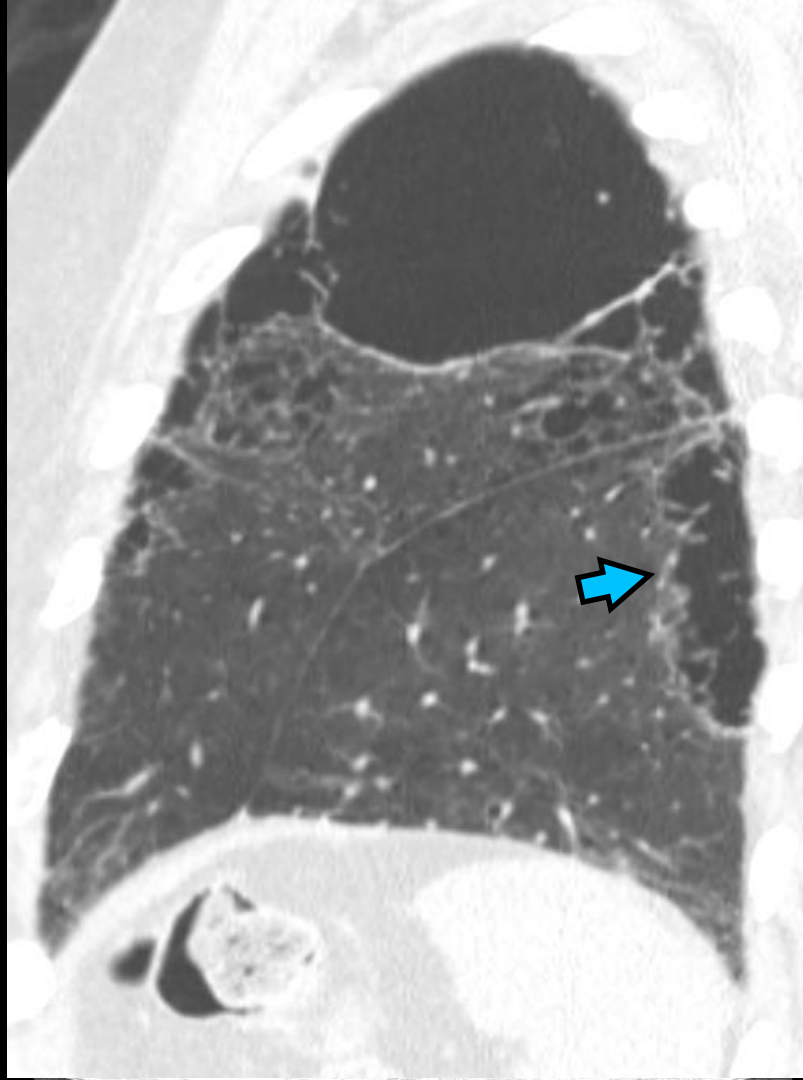
- Also called smoking-related interstitial fibrosis
- ≠ idiopathic interstitial pneumonia
- Greater amount of fibrosis than usually described in the classic definition of emphysema



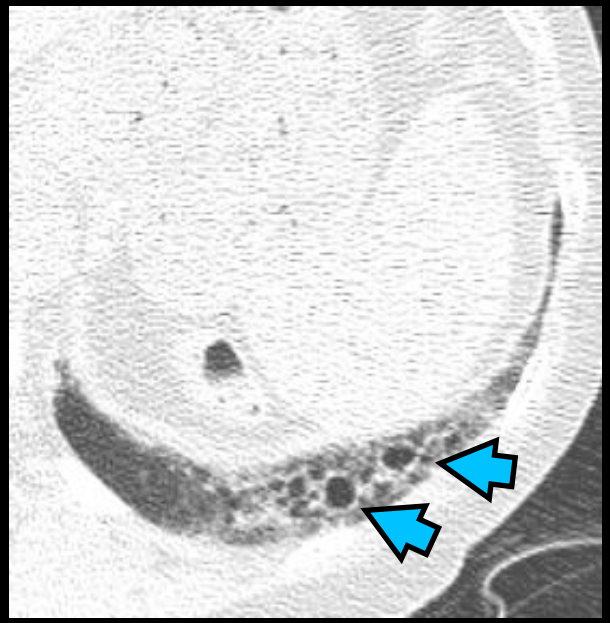
* Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med.* 2022.

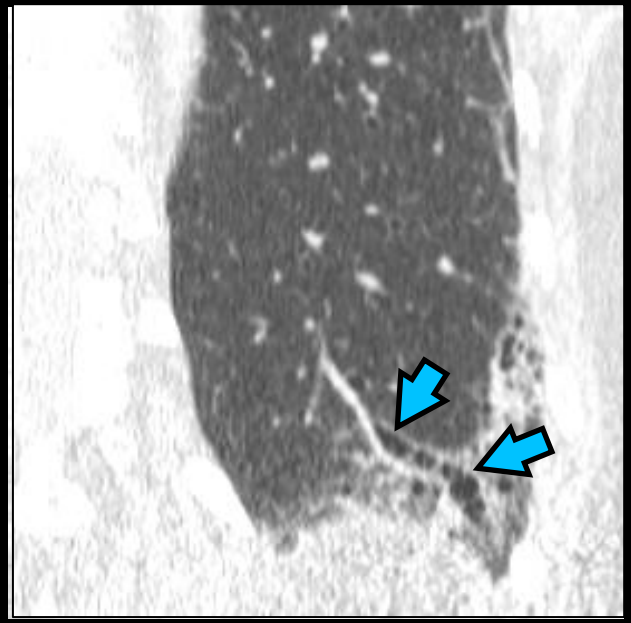
Airspace enlargement with fibrosis (AEF)

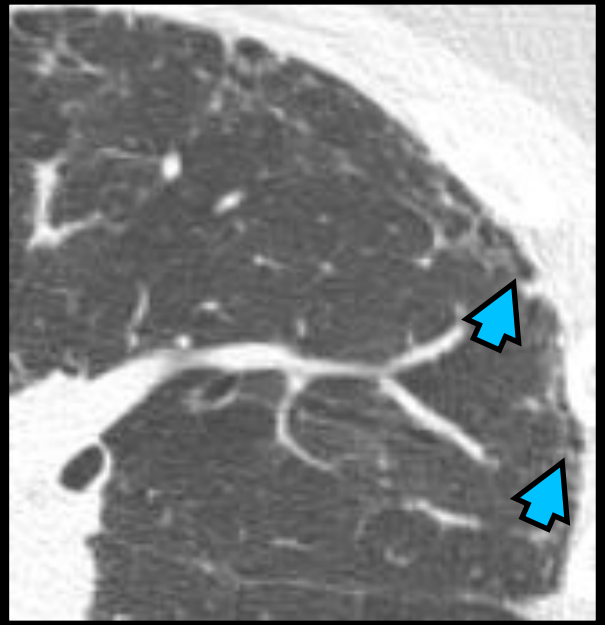
- Clustered asymmetric cysts, larger and more irregular than typical honeycomb cysts
- Can collapse on expiratory images
- No traction bronchiectasis or other signs of fibrosis
- + Emphysema



Honeycombing or bronchiectasis?







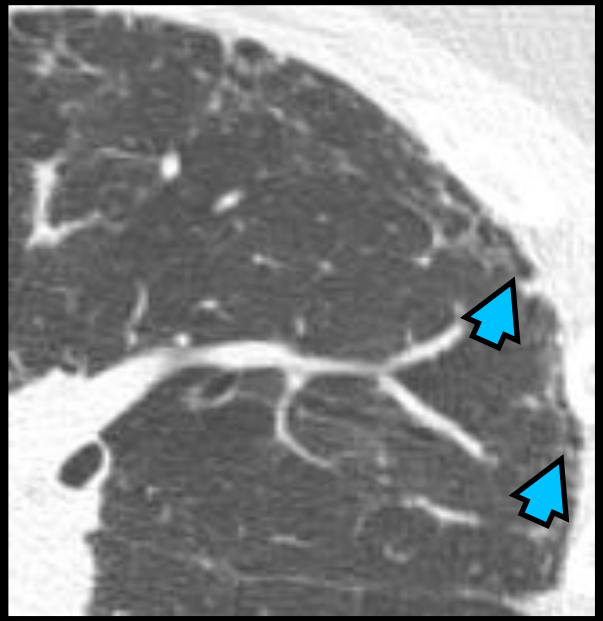
“irregular bronchial and bronchiolar dilatation caused by surrounding retractile pulmonary fibrosis”*

*Hansell DM, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008

**IPF (an Update) and Progressive Pulmonary Fibrosis in Adults. Am J Respir Crit Care Med. 2022.

Bronchiectasis ⟷ Honeycombing

"Recent observations have **underlined** that in IPF, the remodeling process appears to be a ***continuum*** from traction bronchiectasis to honeycombing and that conceptual separation of the two processes may be misleading"**



*Hansell DM, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008

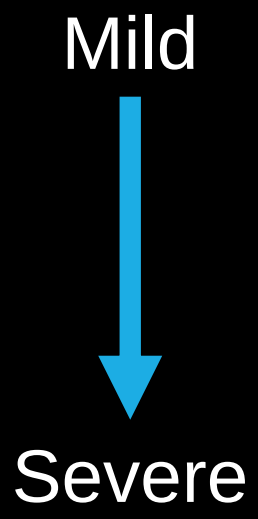
**IPF (an Update) and Progressive Pulmonary Fibrosis in Adults. Am J Respir Crit Care Med. 2022.

Three Direct Findings of Fibrosis

Reticulation

Traction bronchiectasis

Honeycombing



2011 2018 2022

AMERICAN THORACIC SOCIETY DOCUMENTS

Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults

An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline

Raghu G, et al. *Am J Respir Crit Care Med*. 2022

Idiopathic Pulmonary Fibrosis

- Progressive, chronic, fibrosing
- Most common idiopathic interstitial pneumonia
- Unknown cause
- Males, 6-7th decade

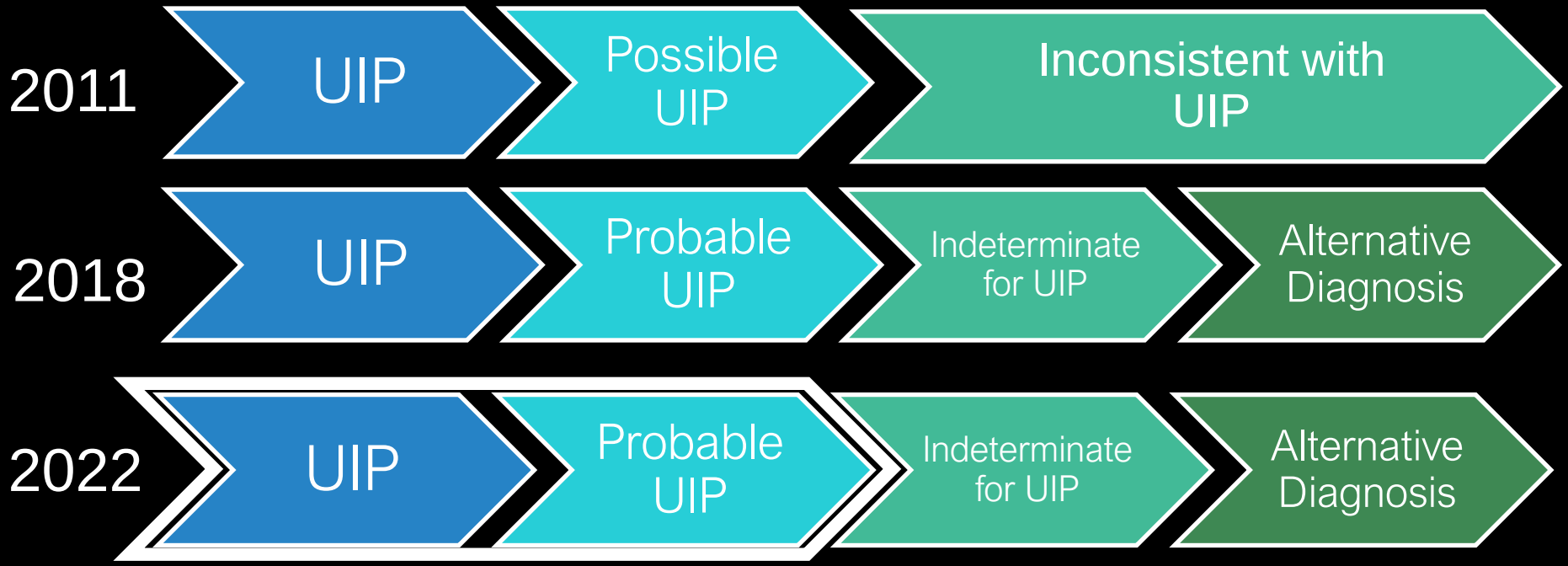
≠

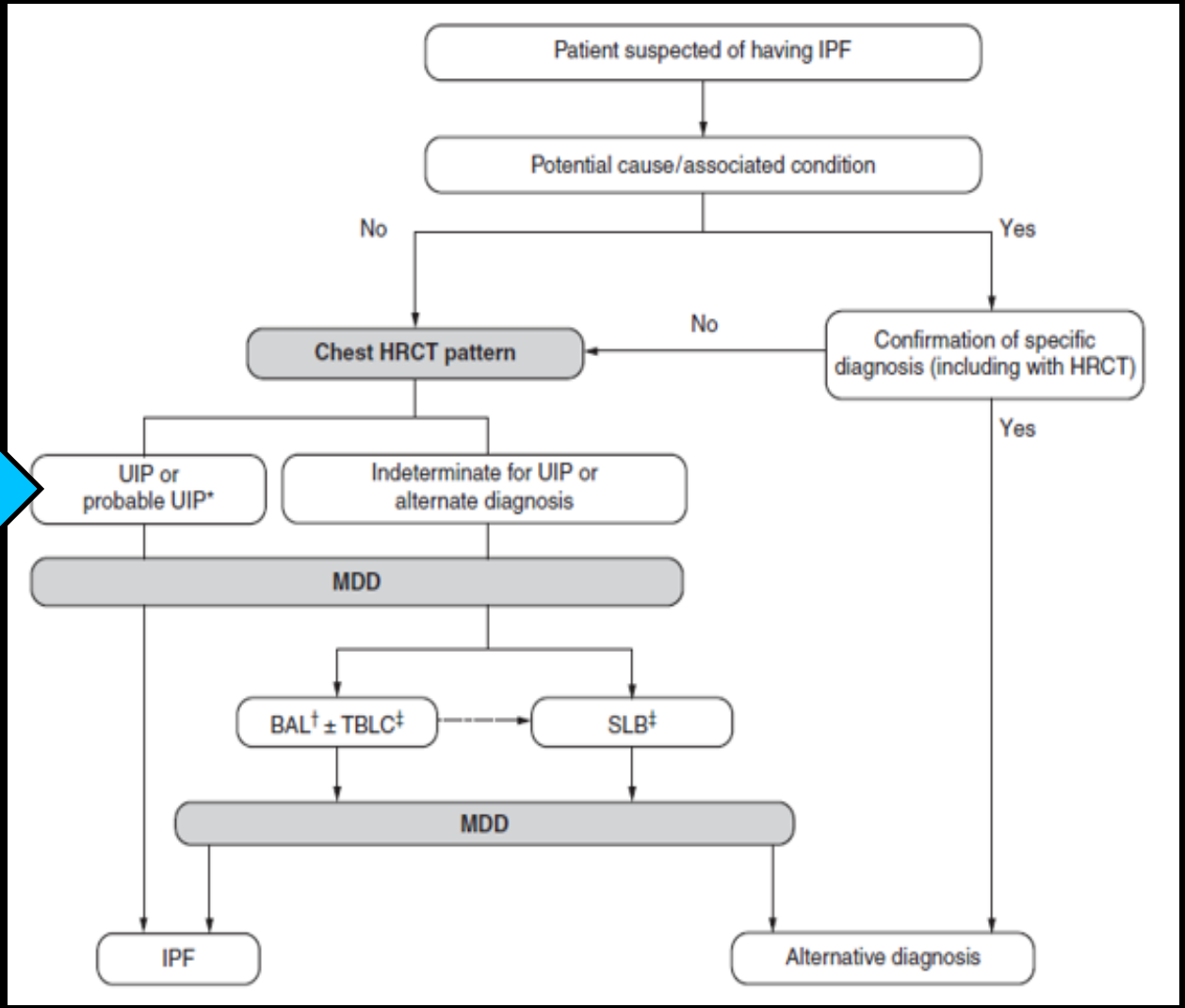
Usual Interstitial Pneumonia

- Pattern
- Pattern seen in patients with IPF
- Can be seen with other diseases that are not IPF*

* Connective Tissue Diseases (RA), fibrotic HP, familial, exposure-related.

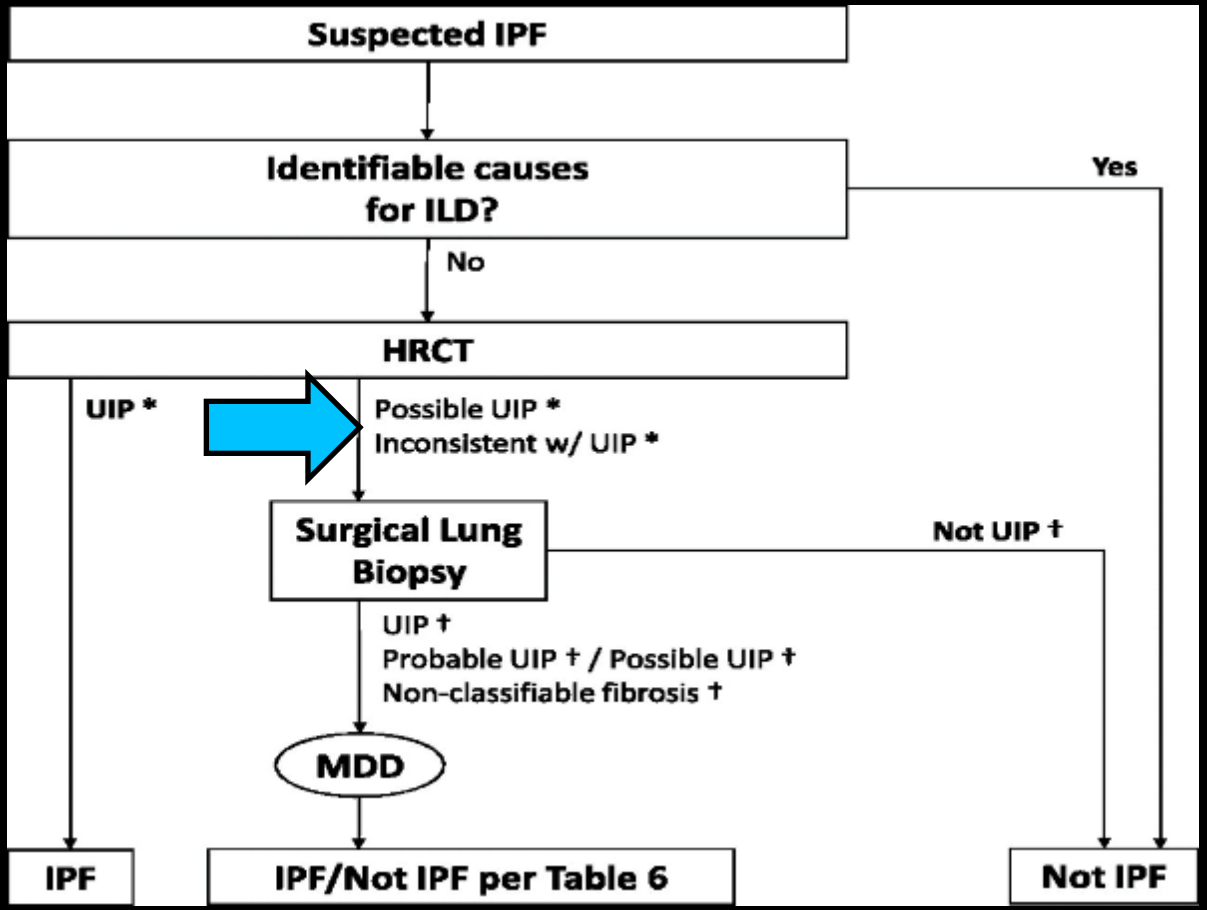
UIP: HRCT Pattern





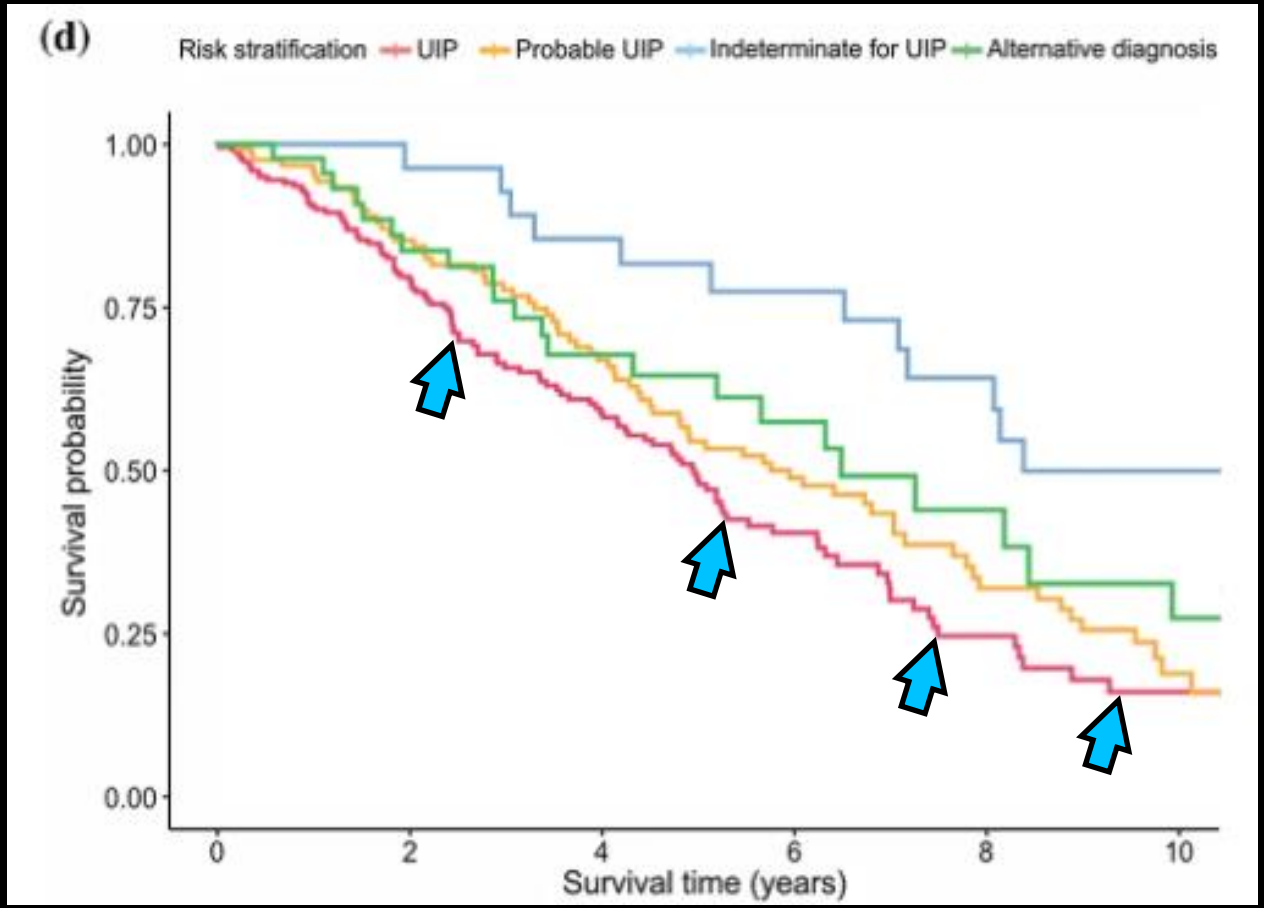
Raghu G, et al. *Am J Respir Crit Care Med*. 2022

Diagnosis of IPF



Am J Respir Crit Care Med 2011;183: 788–824.

Adjusted UIP Survival Curves – 2018 Classification

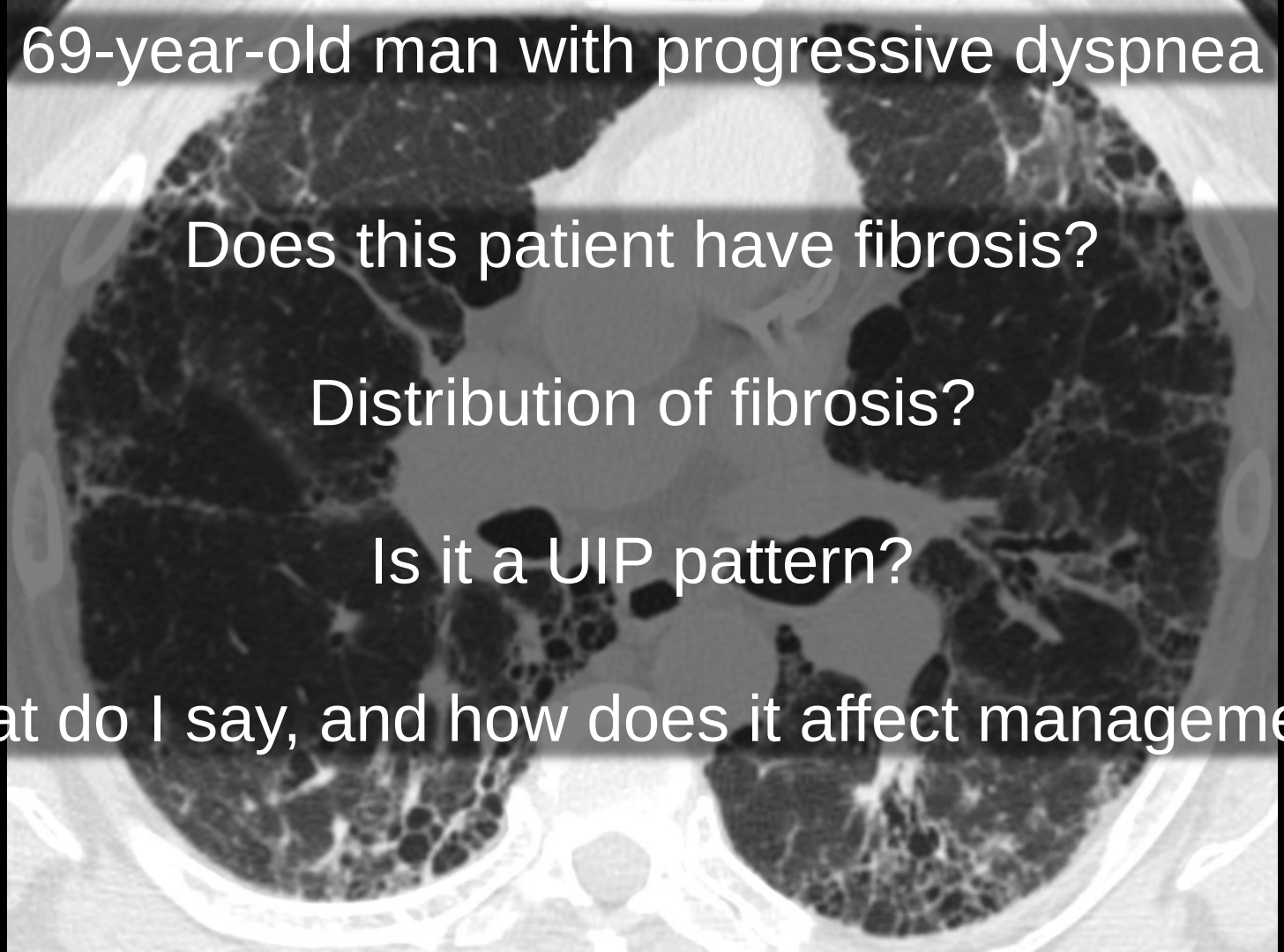


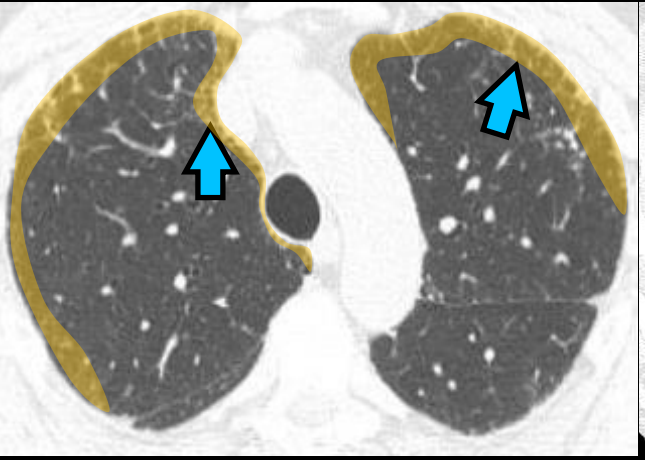
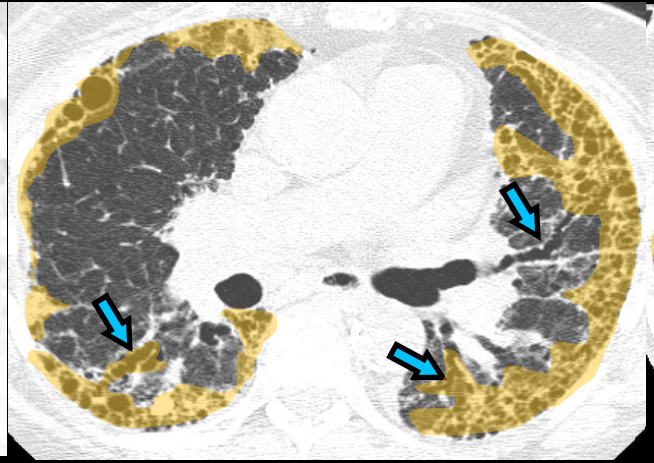
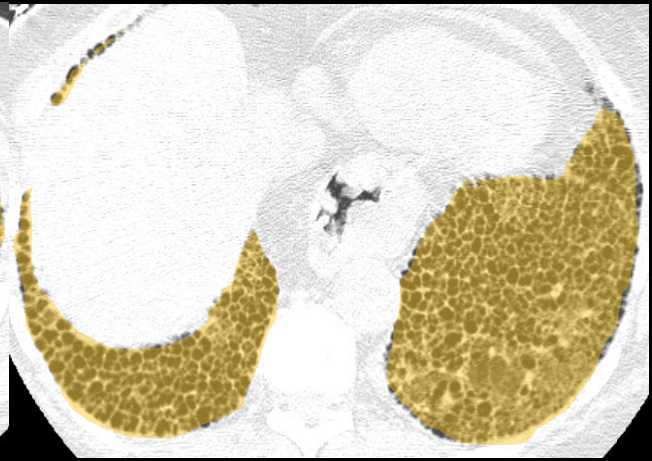
Choe, J. et al. *Sci Rep* 11, 16481 (2021)

One Reference - ATS 2022 IPF Update

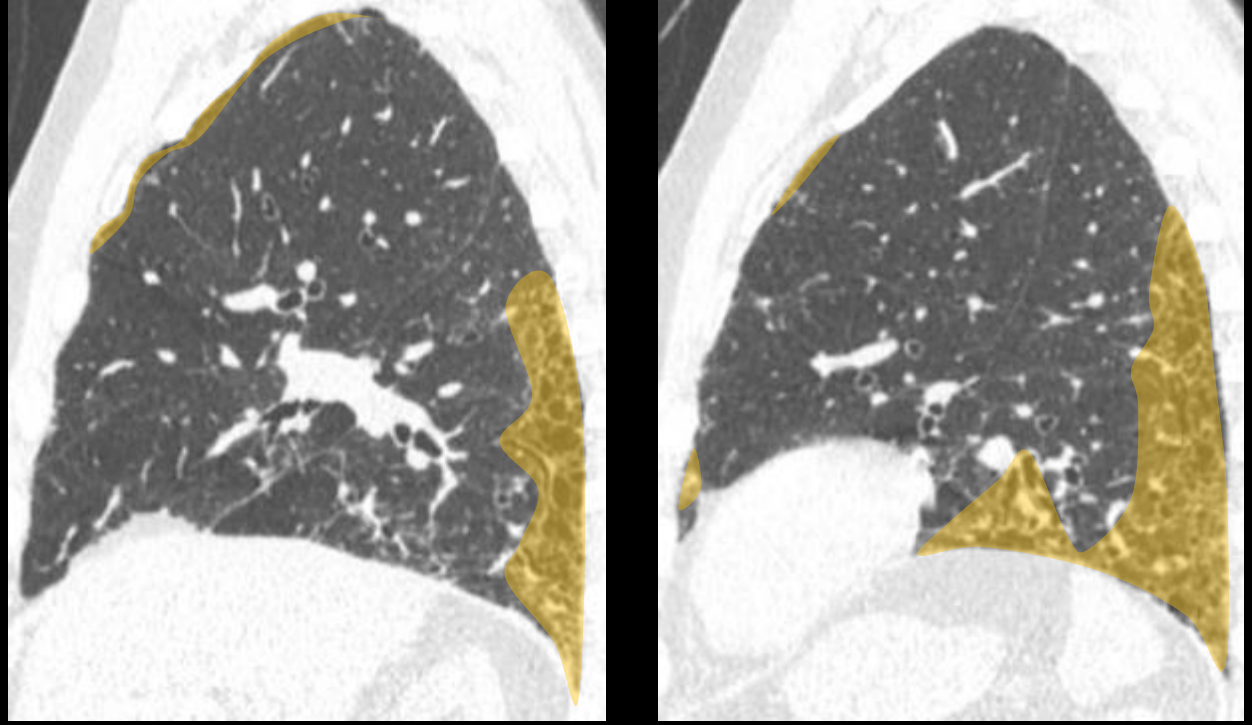
	UIP Pattern	Probable UIP Pattern	Indeterminate for UIP	CT Findings Suggestive of an Alternative Diagnosis
Level of confidence for UIP histology	Confident (>90%)	Provisional high confidence (70–89%)	Provisional low confidence (51–69%)	Low to very low confidence (≤50%)
Distribution	• Subpleural and basal predominant • Often heterogeneous (areas of normal lung interspersed with fibrosis) • Occasionally diffuse • May be asymmetric	• Subpleural and basal predominant • Often heterogeneous (areas of normal lung interspersed with reticulation and traction bronchiectasis/ bronchiolectasis)	• Diffuse distribution without subpleural predominance	• Peribronchovascular predominant with subpleural sparing (consider NSIP) • Perilymphatic distribution (consider sarcoidosis) • Upper or mid lung (consider fibrotic HP, CTD-ILD, and sarcoidosis) • Subpleural sparing (consider NSIP or smoking-related IP)
CT features	• Honeycombing with or without traction bronchiectasis/ bronchiolectasis • Presence of irregular thickening of interlobular septa • Usually superimposed with a reticular pattern, mild GGO • May have pulmonary ossification	• Reticular pattern with traction bronchiectasis/ bronchiolectasis • May have mild GGO • Absence of subpleural sparing	• CT features of lung fibrosis that do not suggest any specific etiology	• Lung findings ◦ Cysts (consider LAM, PLCH, LIP, and DIP) ◦ Mosaic attenuation or three-density sign (consider HP) ◦ Predominant GGO (consider HP, smoking-related disease, drug toxicity, and acute exacerbation of fibrosis) ◦ Profuse centrilobular micronodules (consider HP or smoking-related disease) ◦ Nodules (consider sarcoidosis) ◦ Consolidation (consider organizing pneumonia, etc.) • Mediastinal findings ◦ Pleural plaques (consider asbestosis) ◦ Dilated esophagus (consider CTD)

tions: CT = computed tomography; CTD = connective tissue disease; DIP = desquamative interstitial pneumonia; GGO = ground-glass opacity; pneumonitis; HRCT = high-resolution computed tomography; ILD = interstitial lung disease; IP = interstitial pneumonia; LAM = lymphangioleiomyomatosis; tial pneumonia; NSIP = nonspecific interstitial pneumonia; PLCH = pulmonary Langerhans cell histiocytosis; UIP = usual interstitial pneumonia


69-year-old man with progressive dyspnea
Does this patient have fibrosis?
Distribution of fibrosis?
Is it a UIP pattern?
What do I say, and how does it affect management?

1. Are there findings of fibrosis?
2. Axial distribution
3. CC distribution



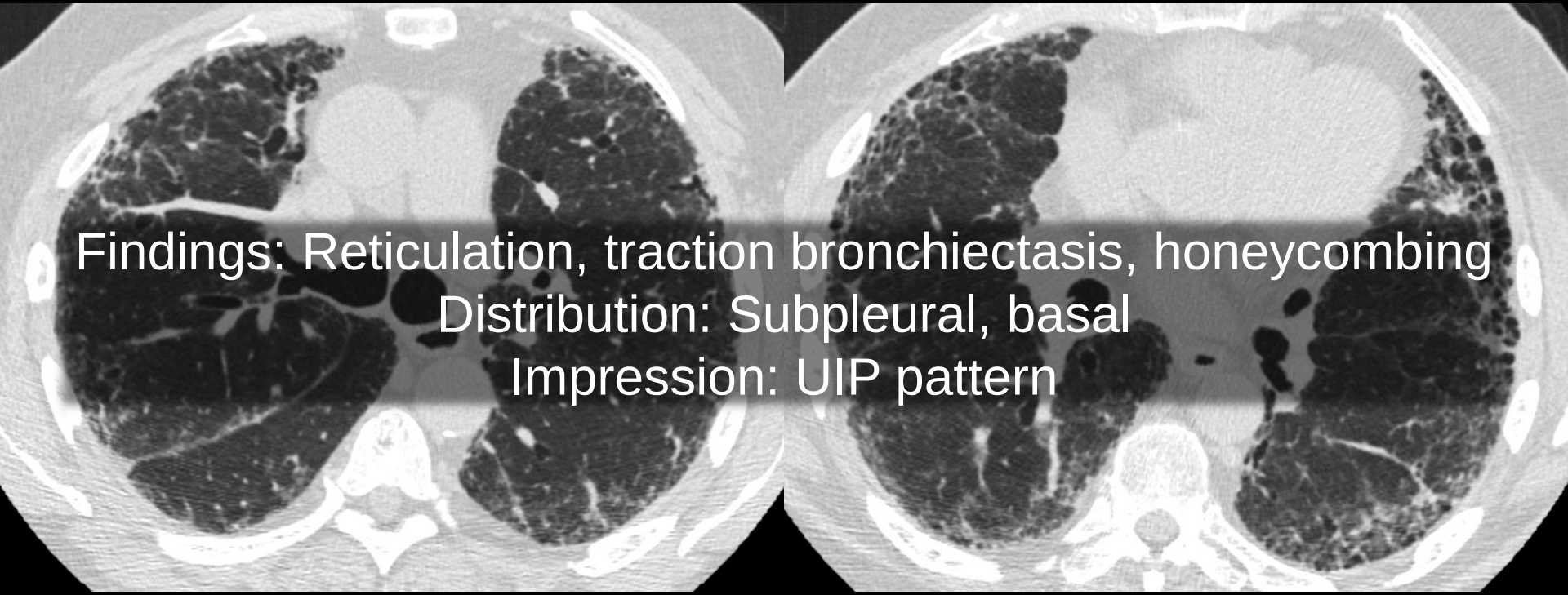
3. CC Distribution

UIP Pattern (> 90% confidence)

Distribution	Findings
Subpleural Basal predominant*	**Honeycombing** +/- traction +/- reticulation +/- pulmonary ossification +/- mild ggo

* Often heterogeneous
* Occasionally diffuse craniocaudal
* May be asymmetric

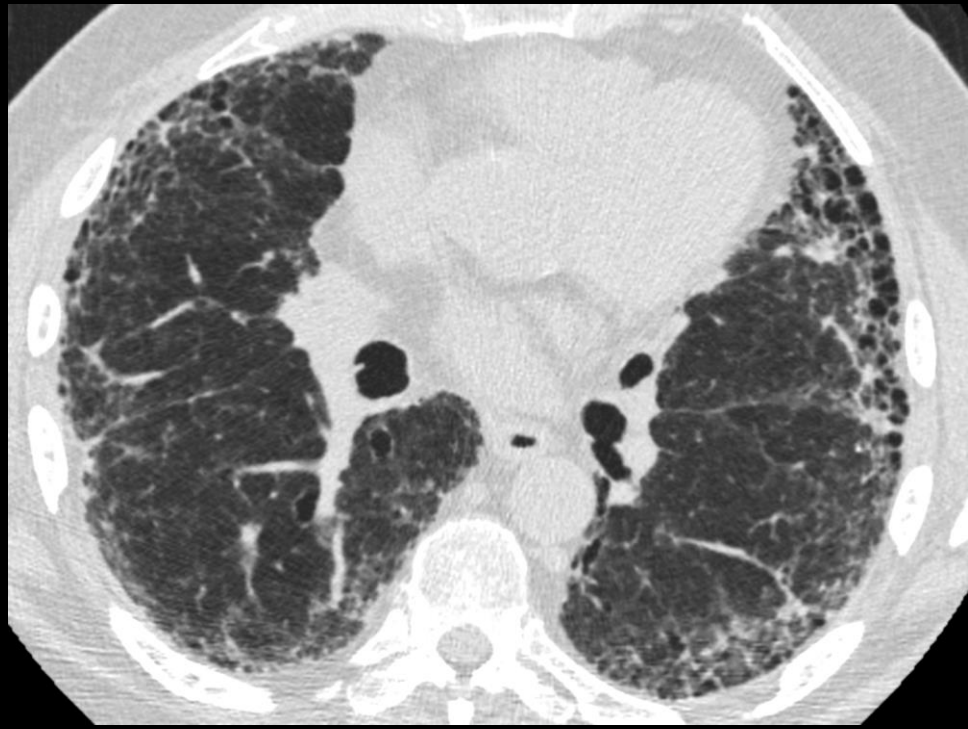
73-year-old male



Findings: Reticulation, traction bronchiectasis, honeycombing
Distribution: Subpleural, basal
Impression: UIP pattern

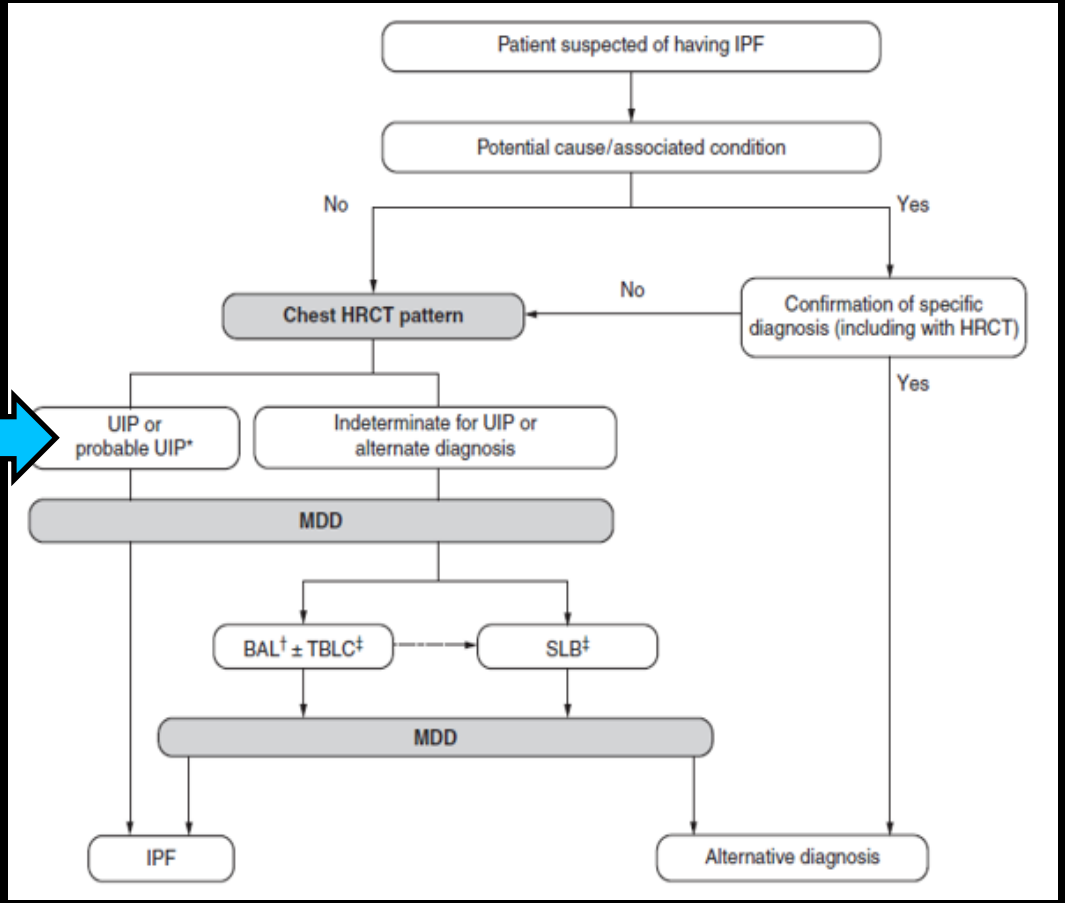
UIP Pattern ≠ IPF

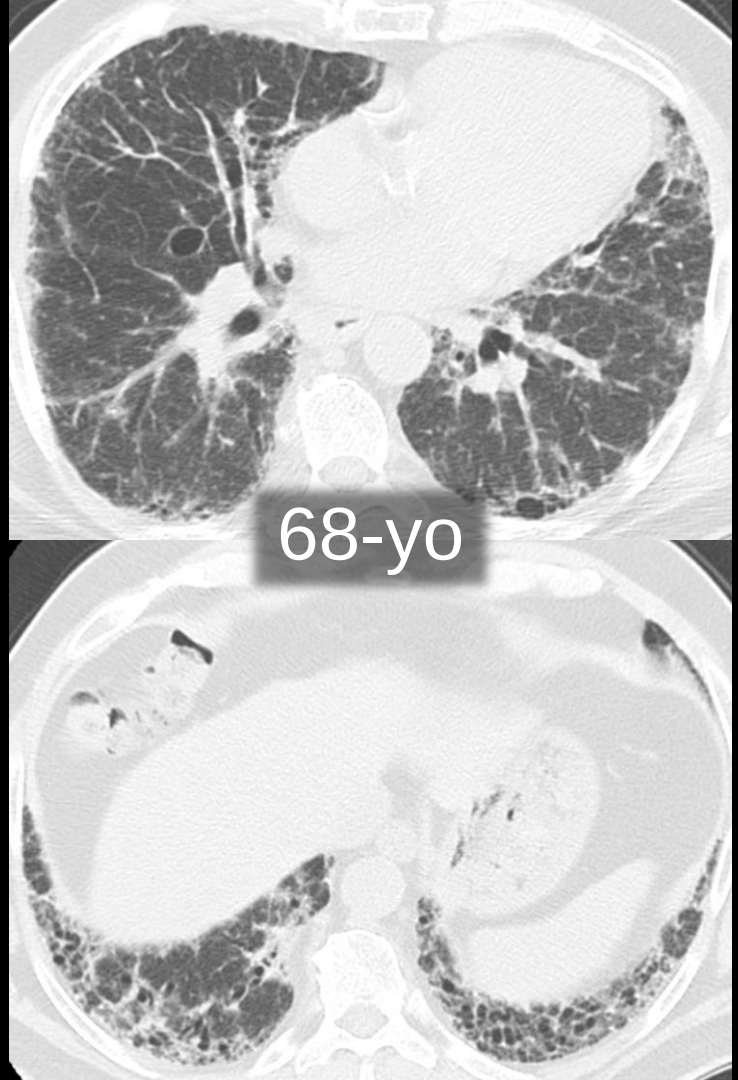
IPF is a multidisciplinary diagnosis

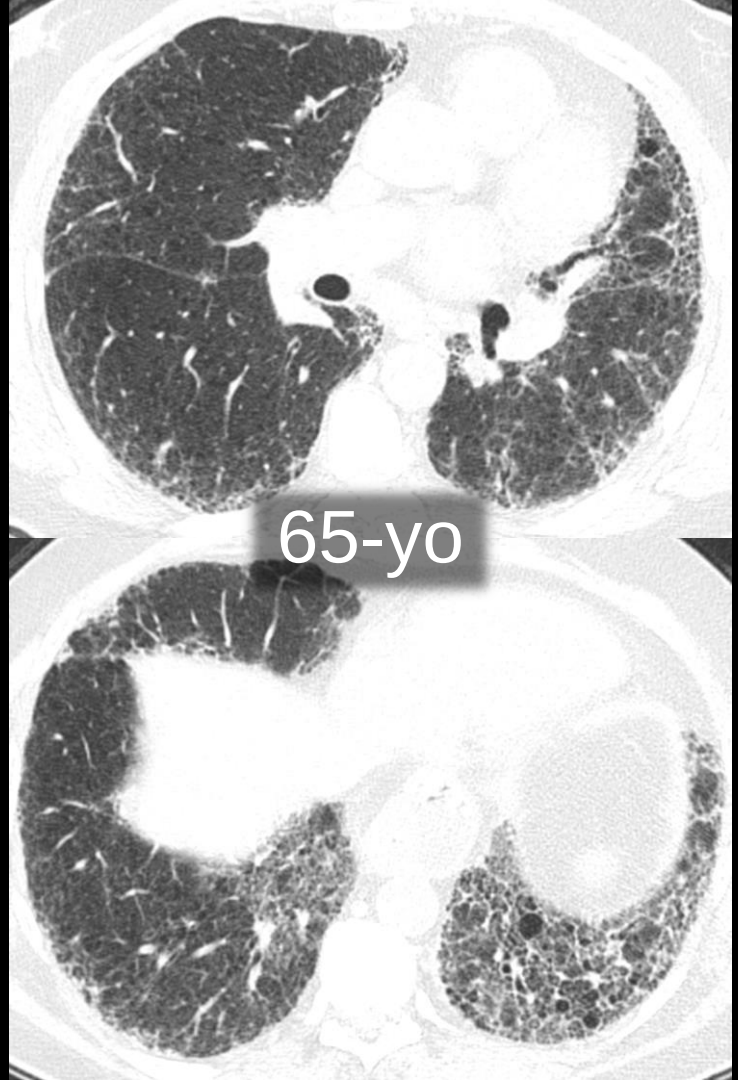


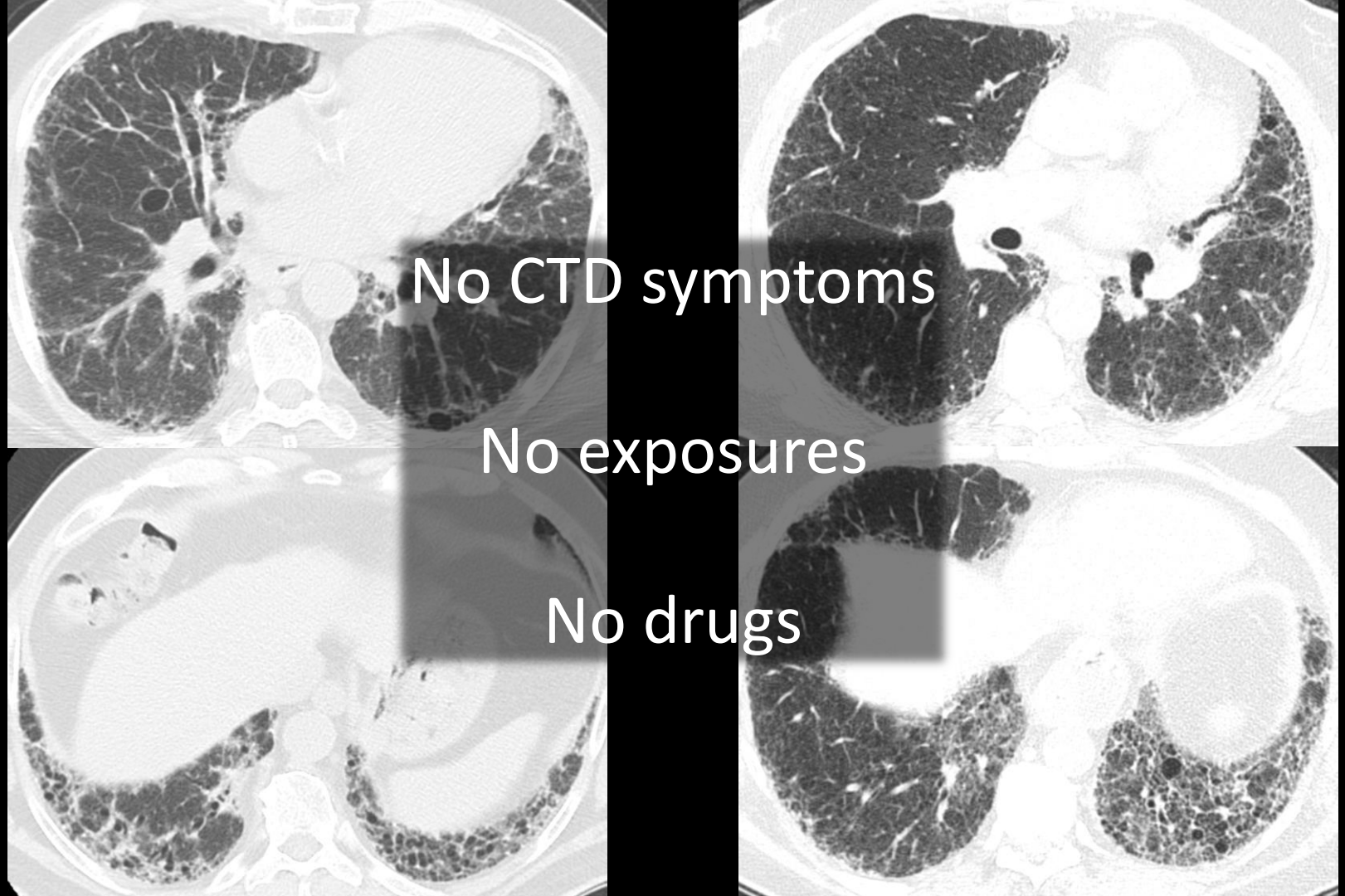
What does a UIP pattern mean?

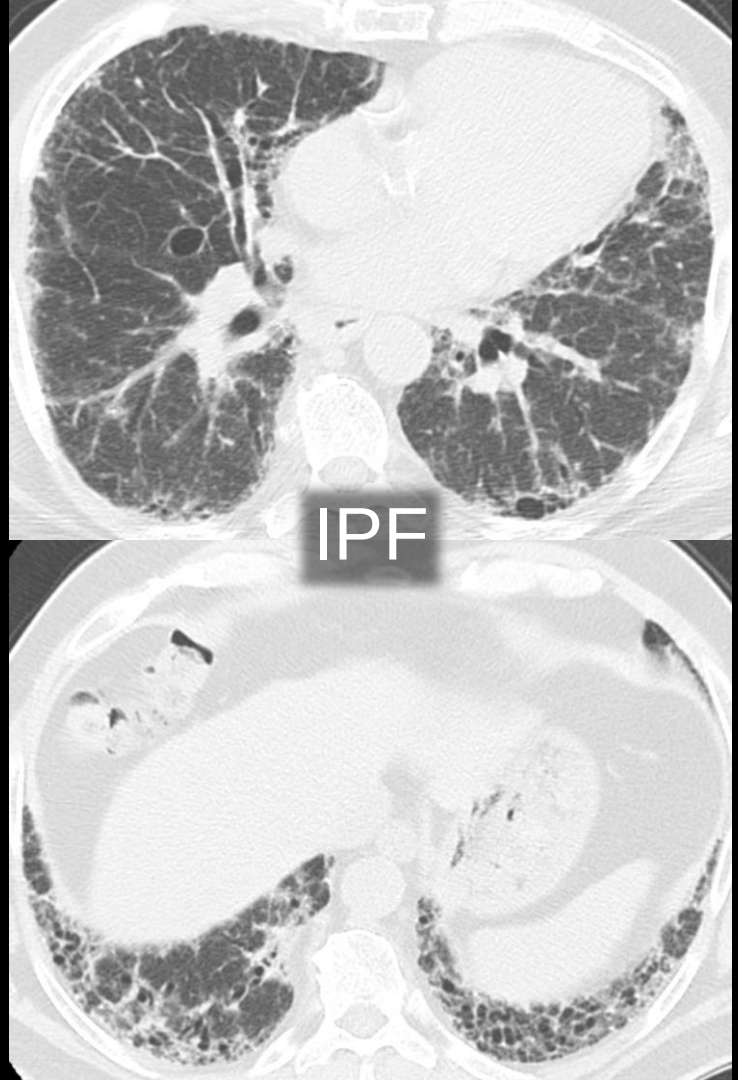
Treat without biopsy

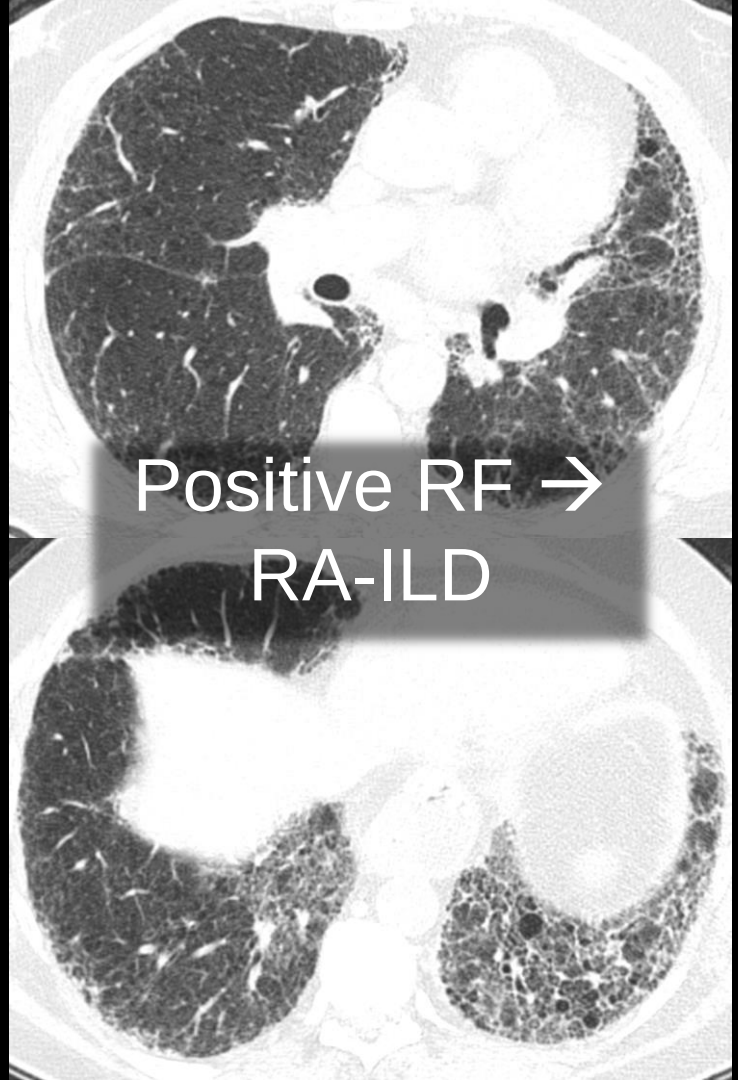



68-yo

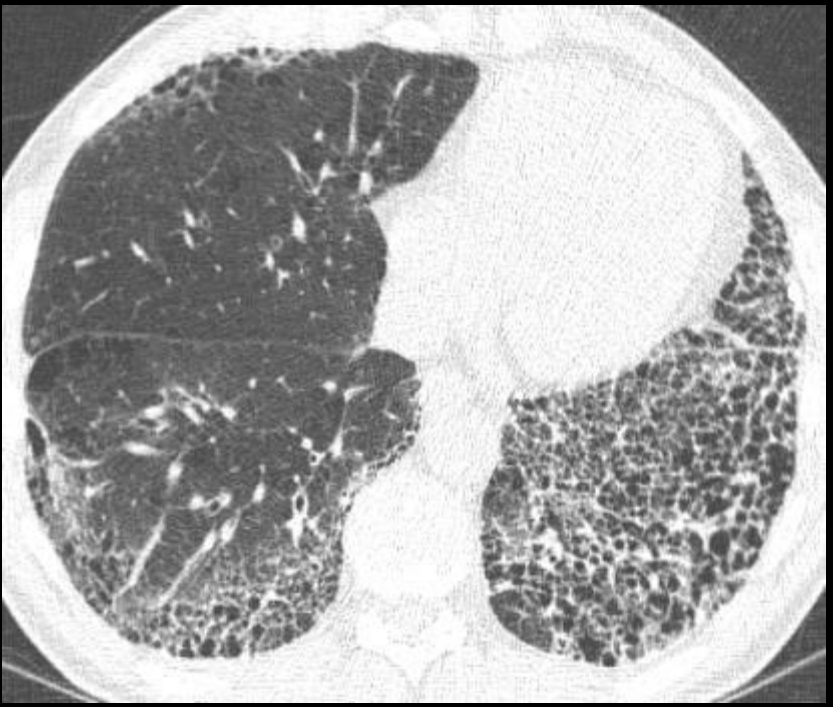

65-yo


No CTD symptoms
No exposures
No drugs

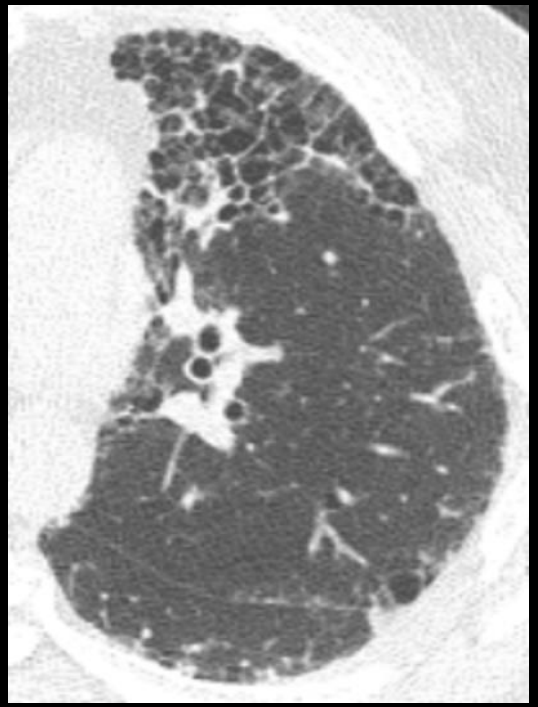

IPF


Positive RF →
RA-ILD

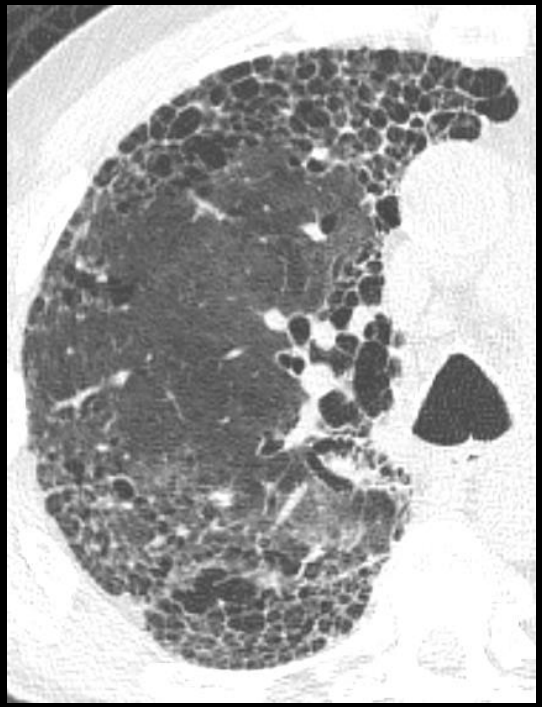
UIP: Distribution variants



Asymmetric ~25 %



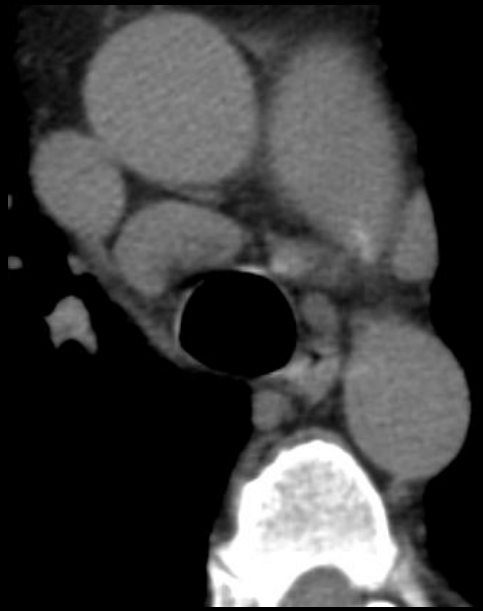
Upper lobe involvement



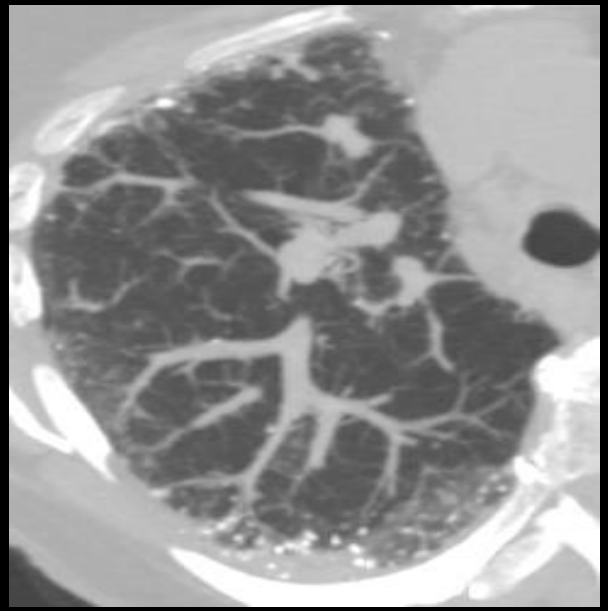
Diffuse (CC)

* Diagnosis of Idiopathic Pulmonary Fibrosis. Am J Respir Crit Care Med. 2018.

UIP: Other findings

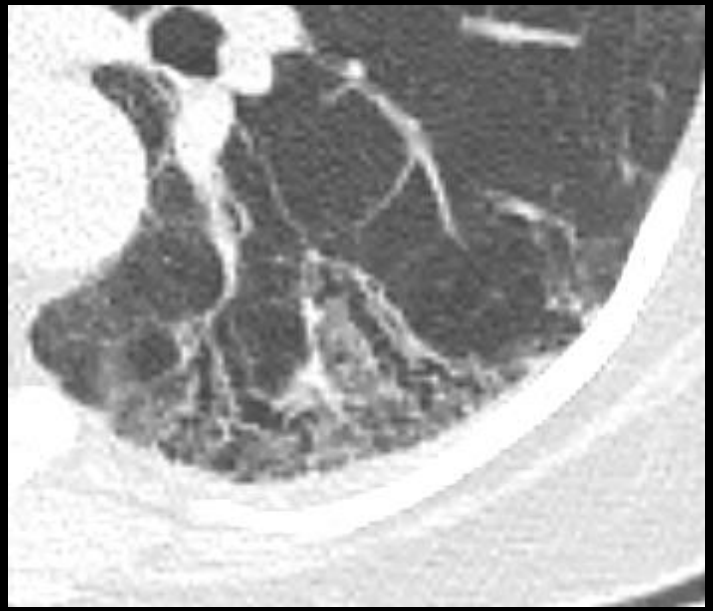


Lymph nodes



Pulmonary Ossification up to 19%

UIP (29%) > NSIP > HP*



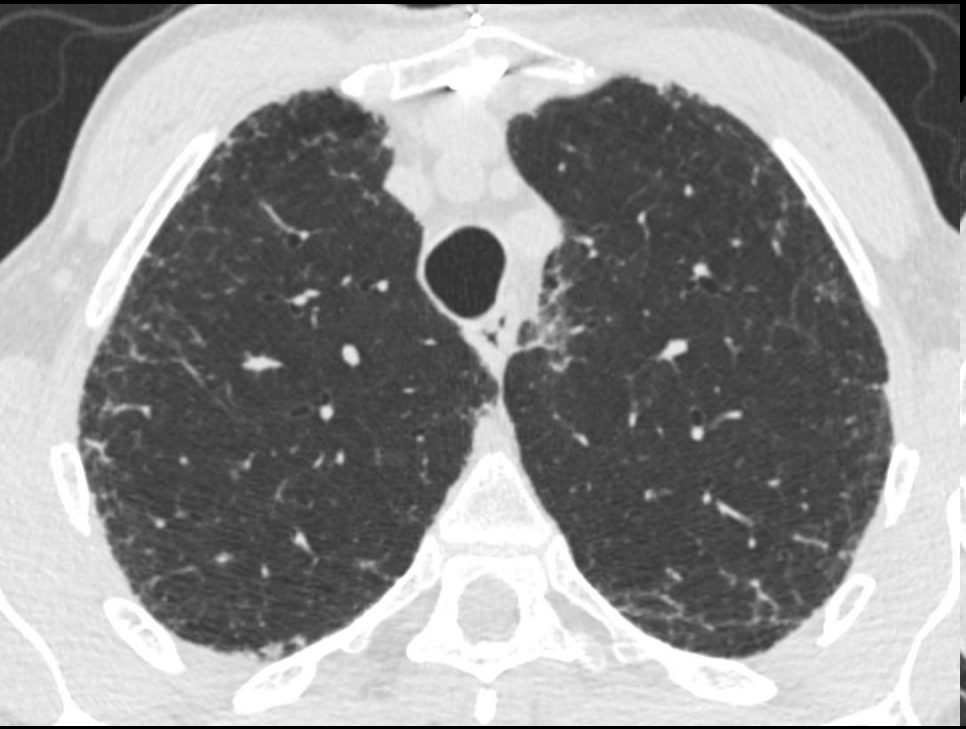
Mild GGO

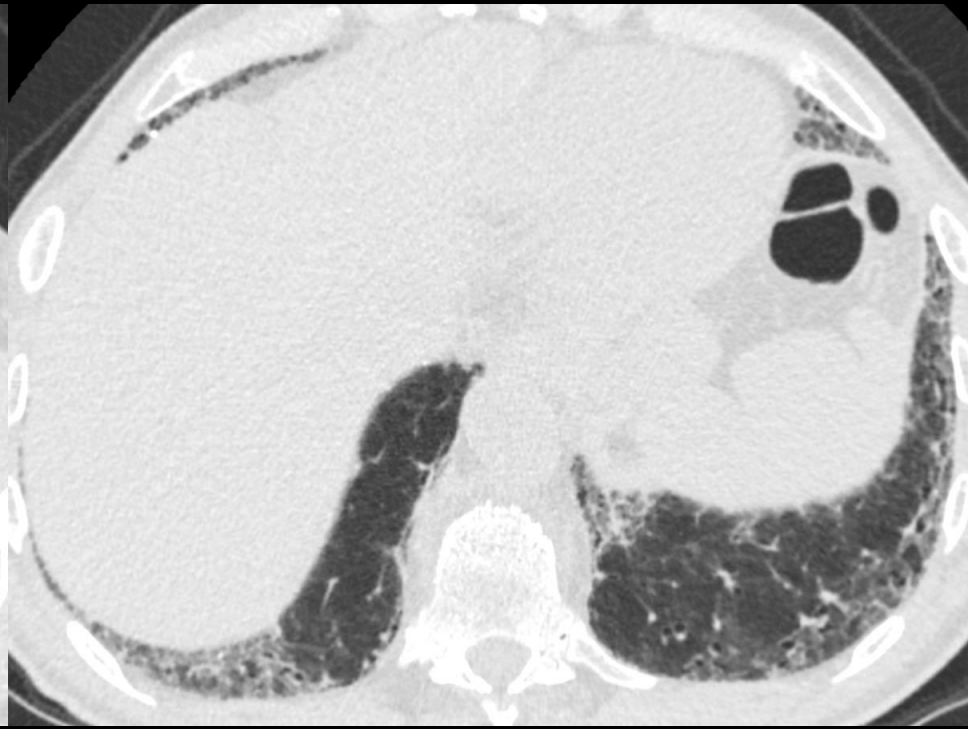
(limited to areas of fibrosis)

* Egashira R et al. Diffuse Pulmonary Ossification in Fibrosing Interstitial Lung Diseases: Prevalence and Associations. *Radiology*. 2017.

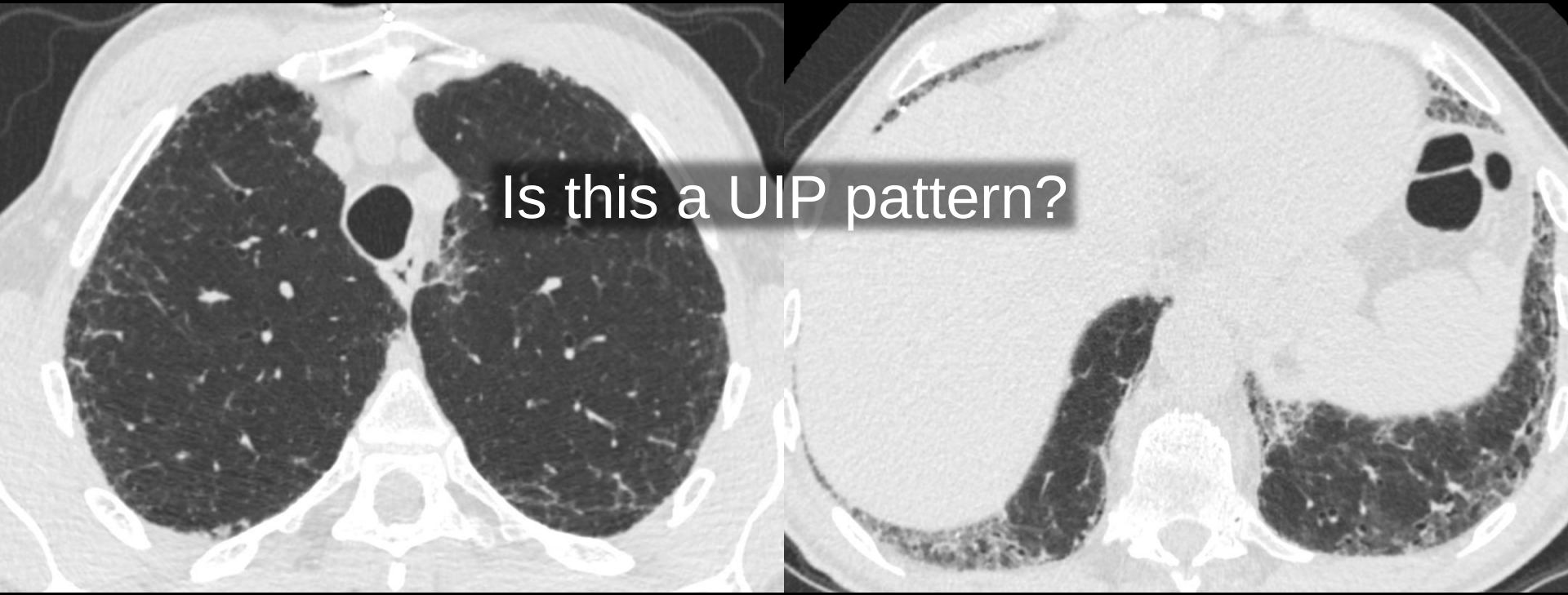
What if there is no honeycombing?

Findings → Reticulation and traction





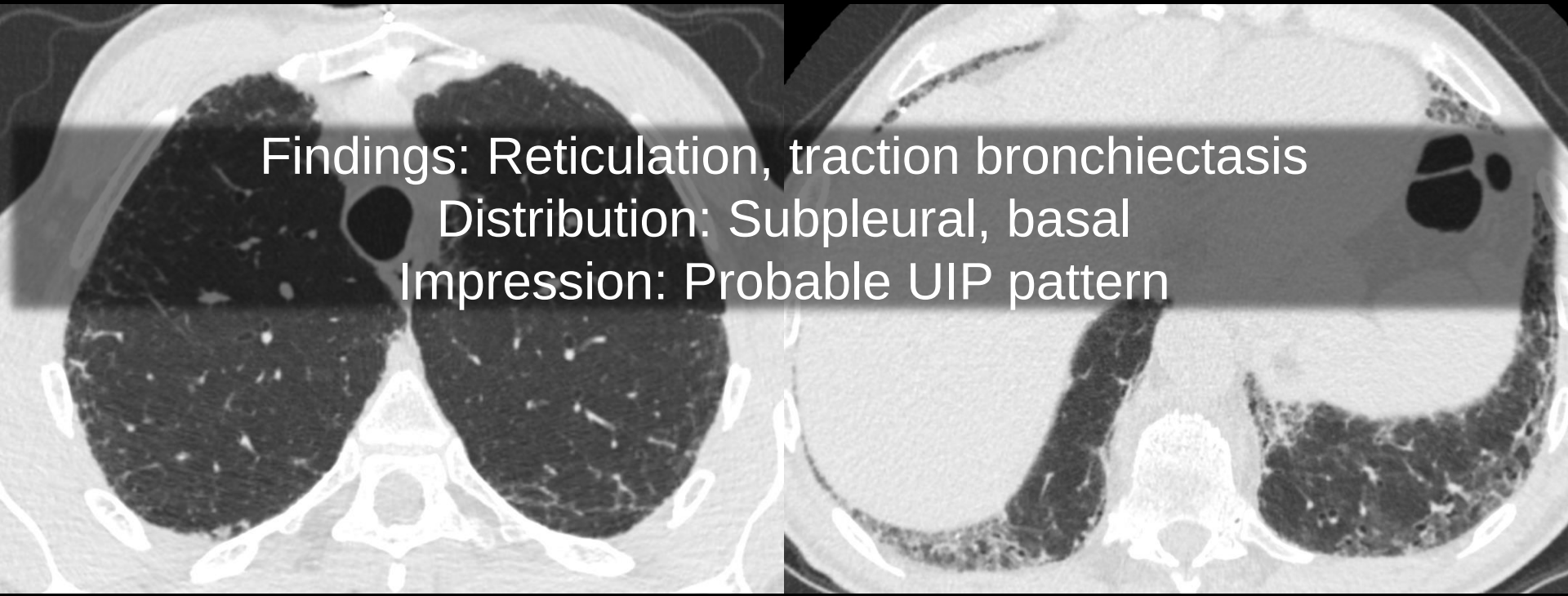
Distribution → Basal and peripheral



Probable UIP Pattern (70-89% confidence)

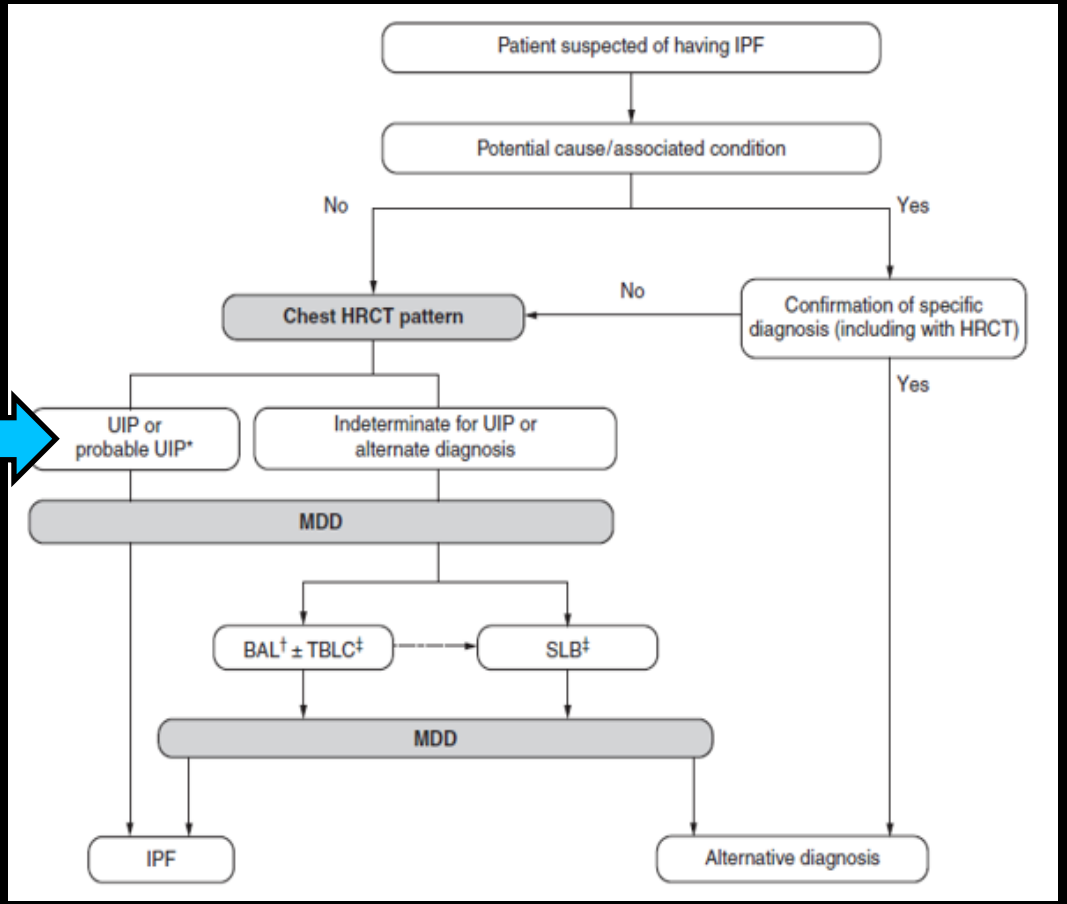
Distribution	Findings**
Subpleural Basal*	Reticulation with traction bronchiectasis +/- mild GGO ***No honeycombing***

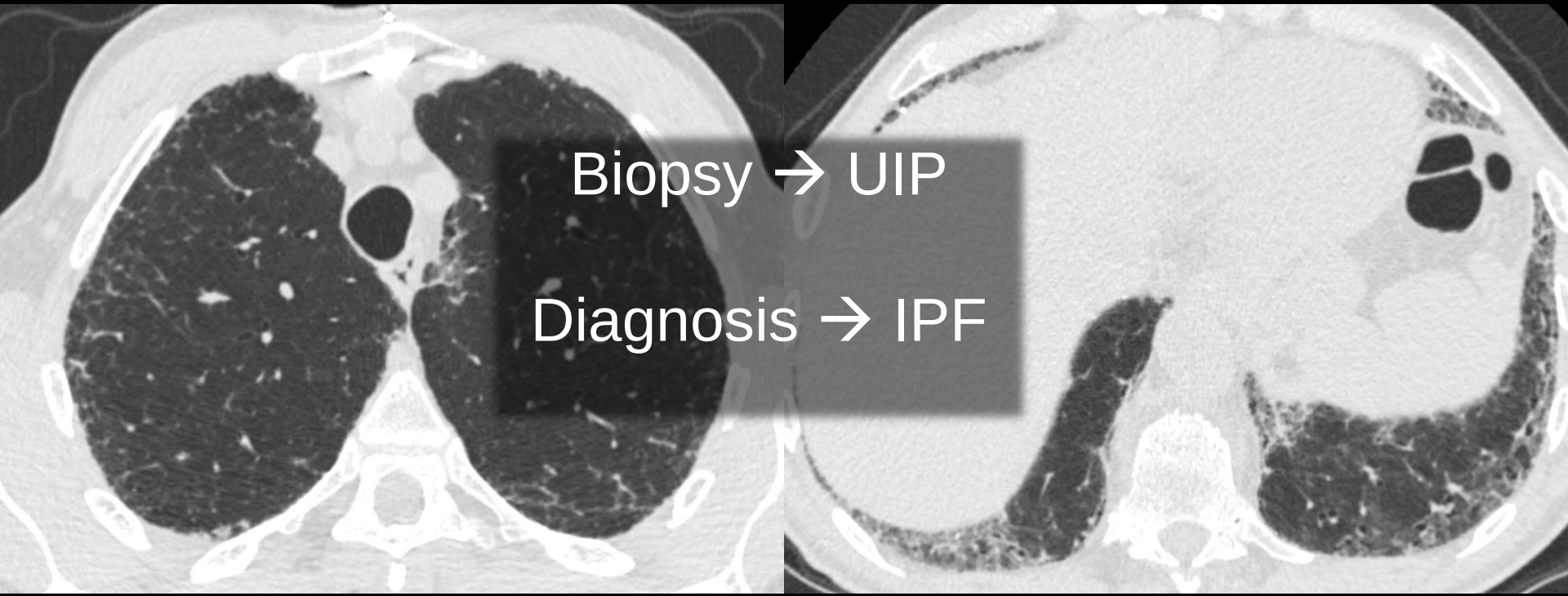
* Occasionally diffuse craniocaudal
** Absence of subpleural sparing


Findings: Reticulation, traction bronchiectasis
Distribution: Subpleural, basal
Impression: Probable UIP pattern

What does a probable UIP pattern mean?

- Biopsy = 80-85% UIP
- Similar disease behavior and clinical course than UIP
- Might have better survival

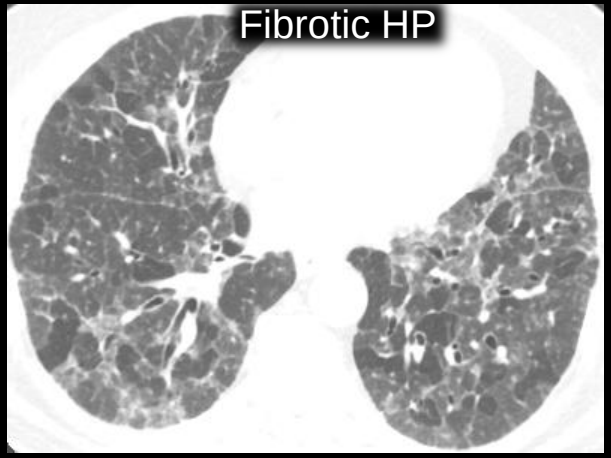



Biopsy → UIP
Diagnosis → IPF

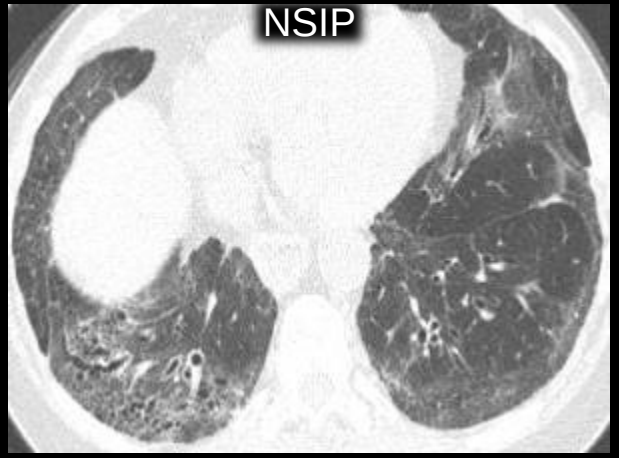
CT Findings of Alternative Diagnosis (≤ 50%)

Distribution	Findings
Perilymphatic Peribronchovascular Subpleural sparing Upper or mid-lung	Mosaic Attenuation Three Density sign Predominant GGO Consolidation Cysts Nodules Centrilobular GGO

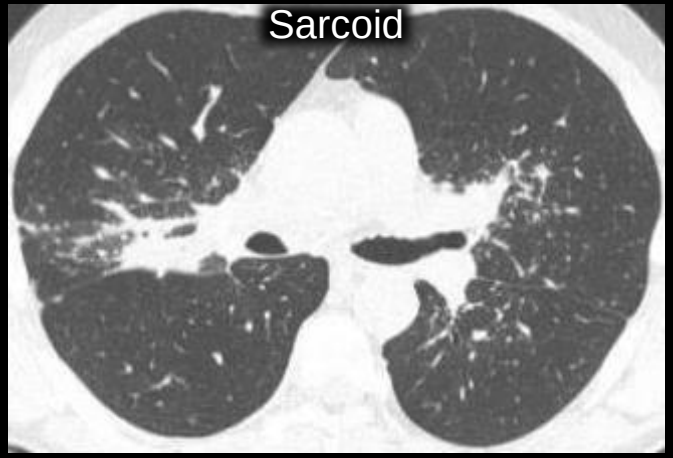
Alternative Diagnosis



Air trapping
GGO
Diffuse

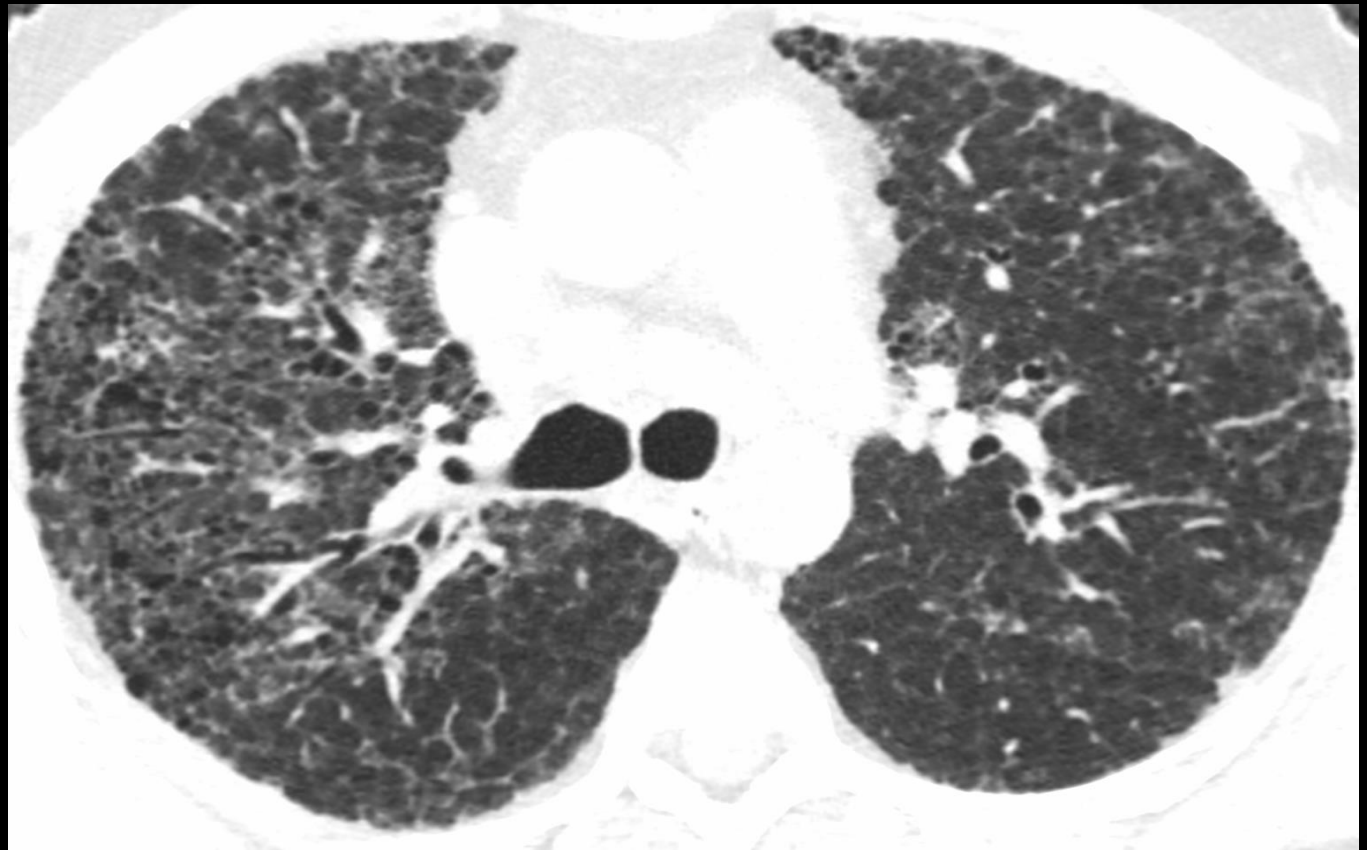


Peribronchovascular
GGO

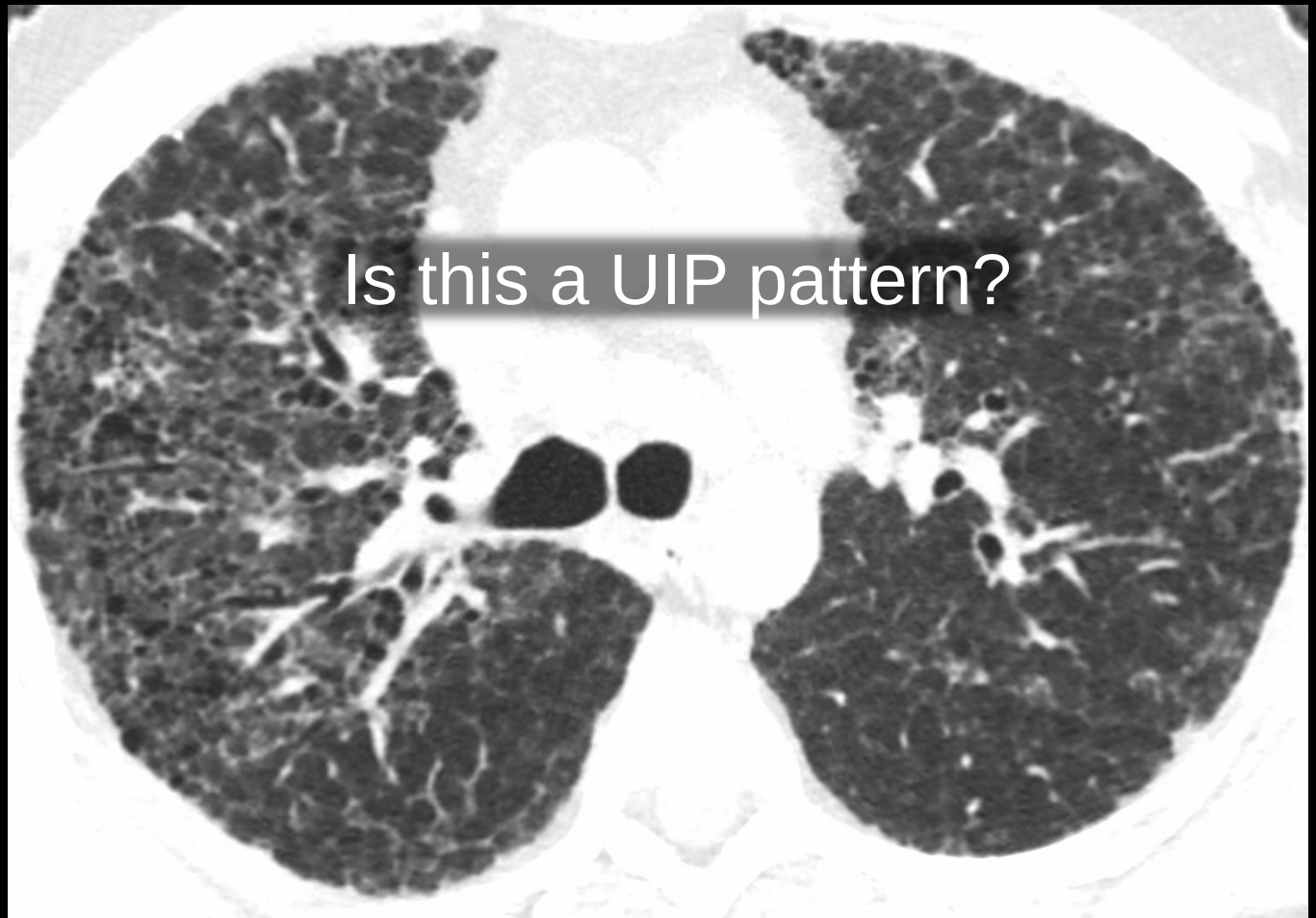


Perilymphatic
Nodules

Findings → Reticulation, traction bronchiectasis, GGO, cysts, honeycombing

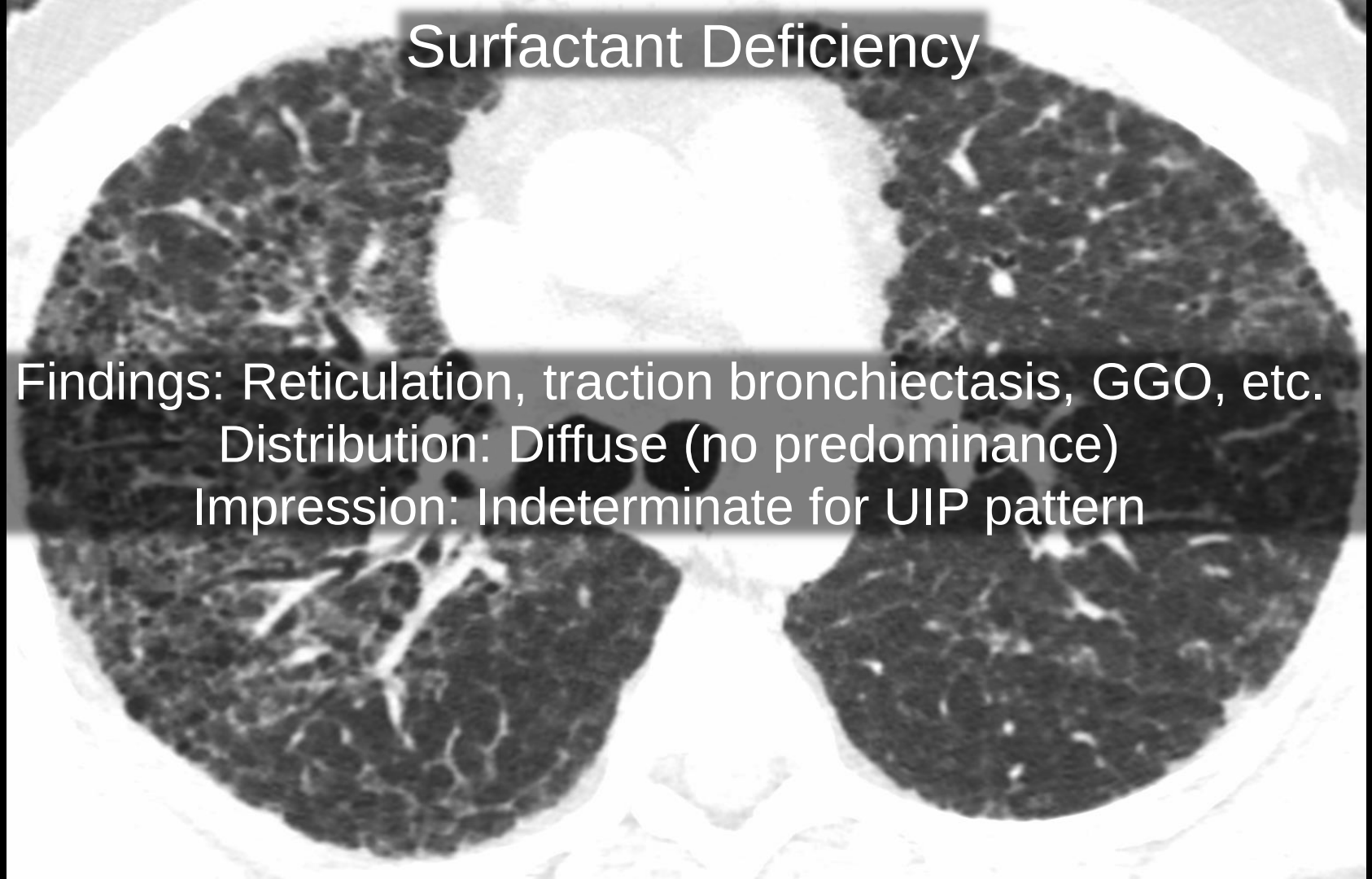


Distribution → Diffuse



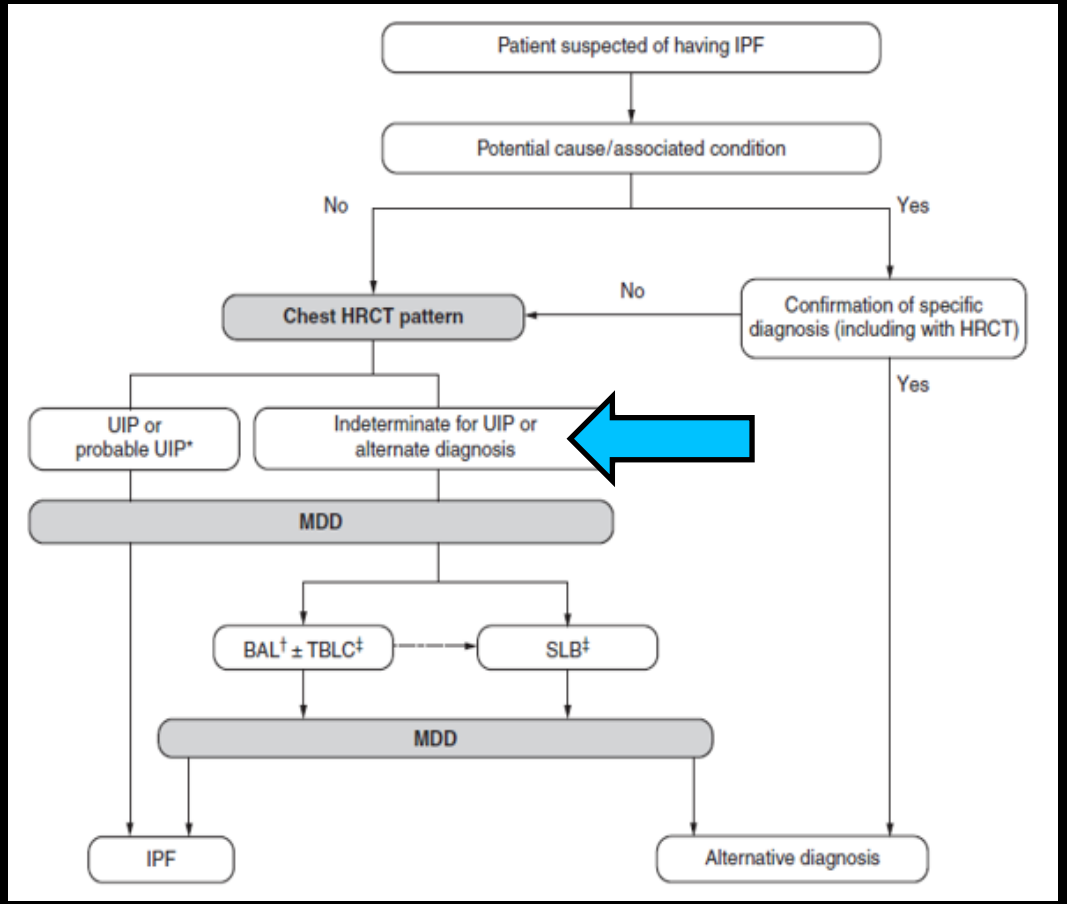
CT Findings Indeterminate for UIP (51-69%)

Distribution	Findings
Diffuse No subpleural predominance	CT features that do not suggest any specific etiology


Surfactant Deficiency
Findings: Reticulation, traction bronchiectasis, GGO, etc.
Distribution: Diffuse (no predominance)
Impression: Indeterminate for UIP pattern

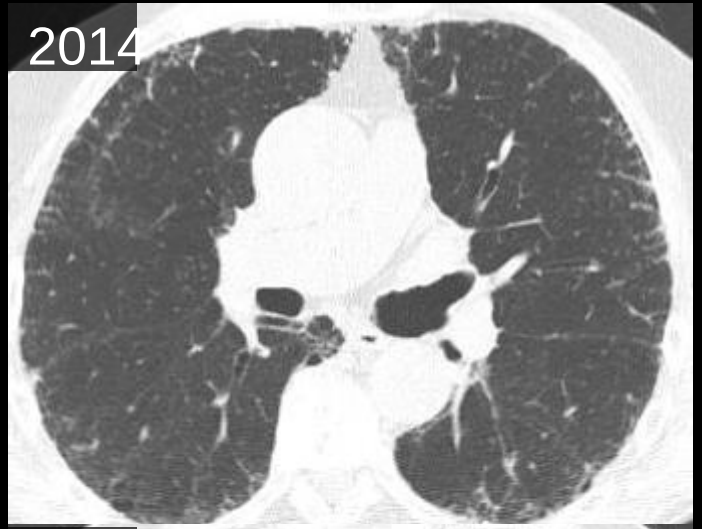
What does an indeterminate for UIP pattern mean?

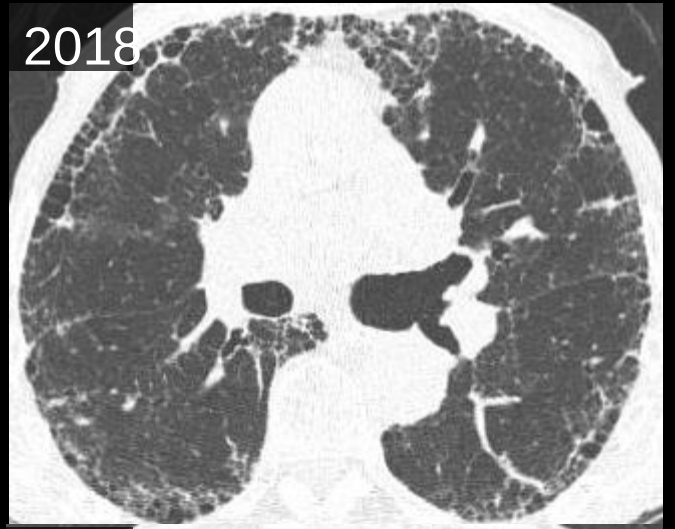
Potential more invasive workup

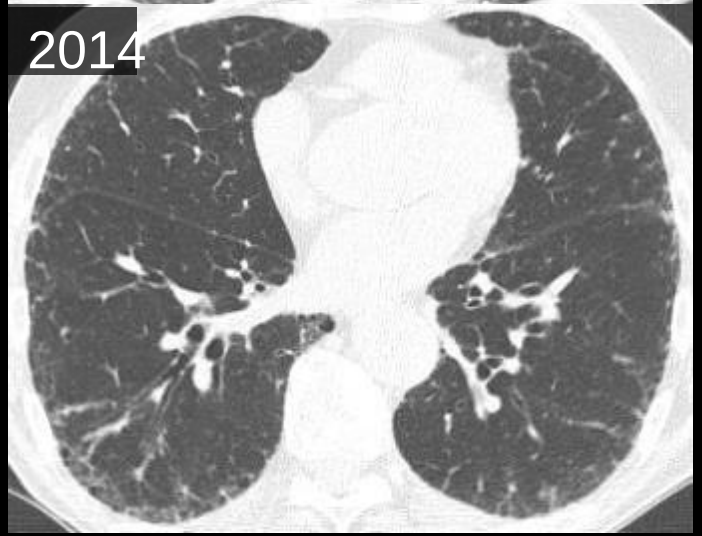


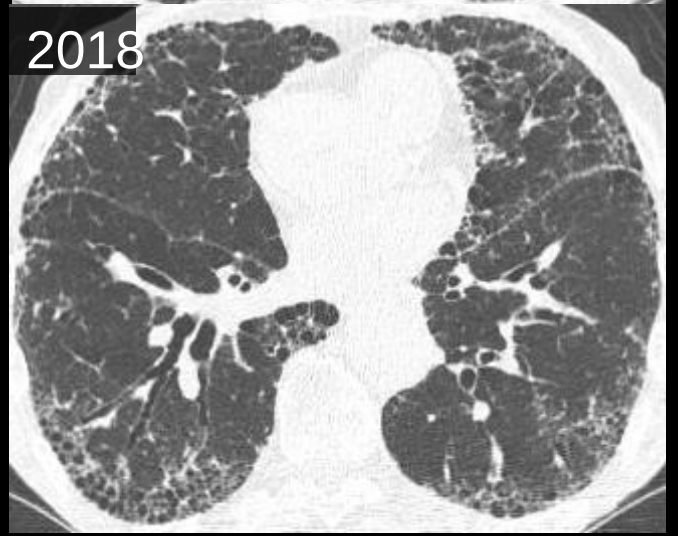
Three pearls when reading UIP cases

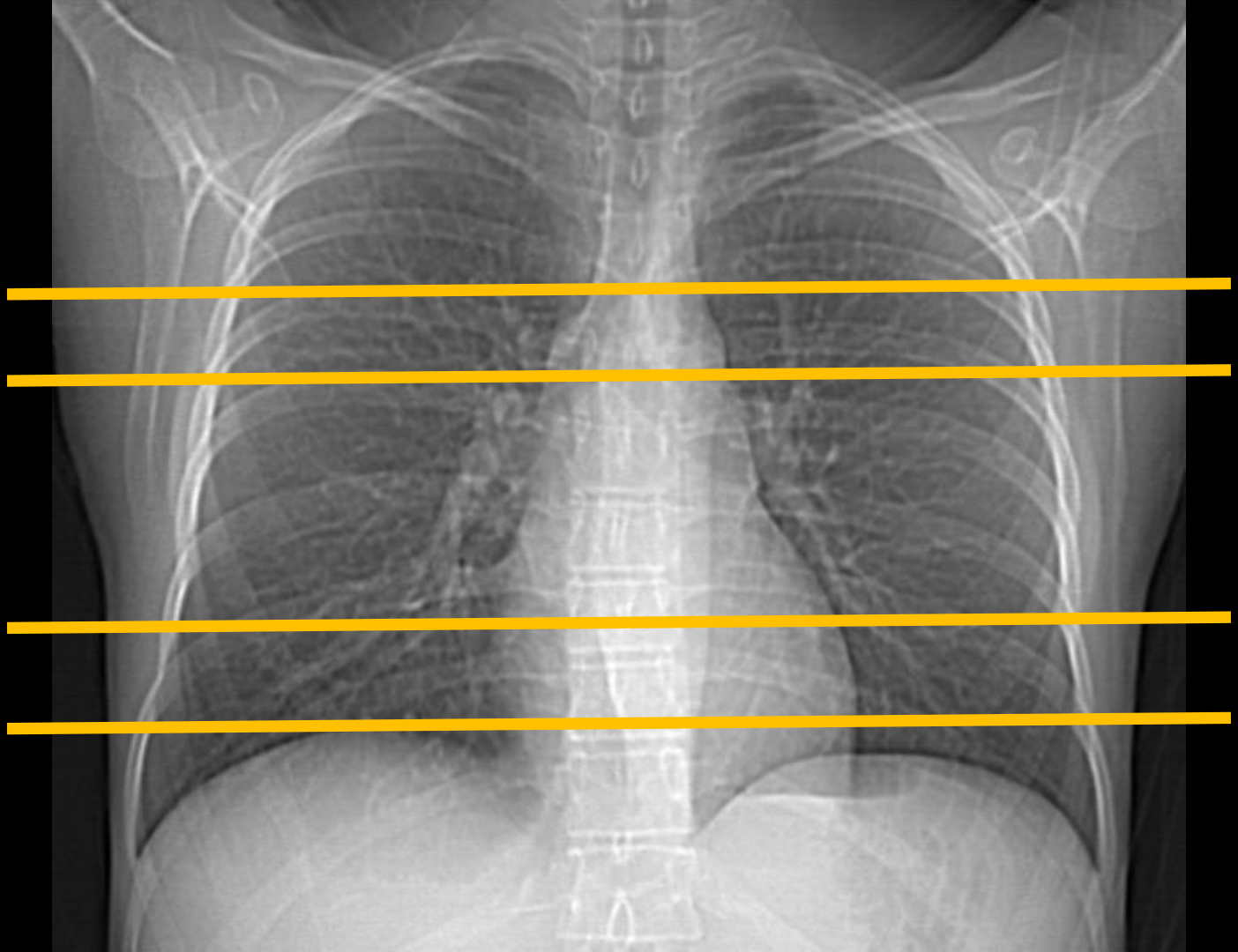
1. Discuss Progression



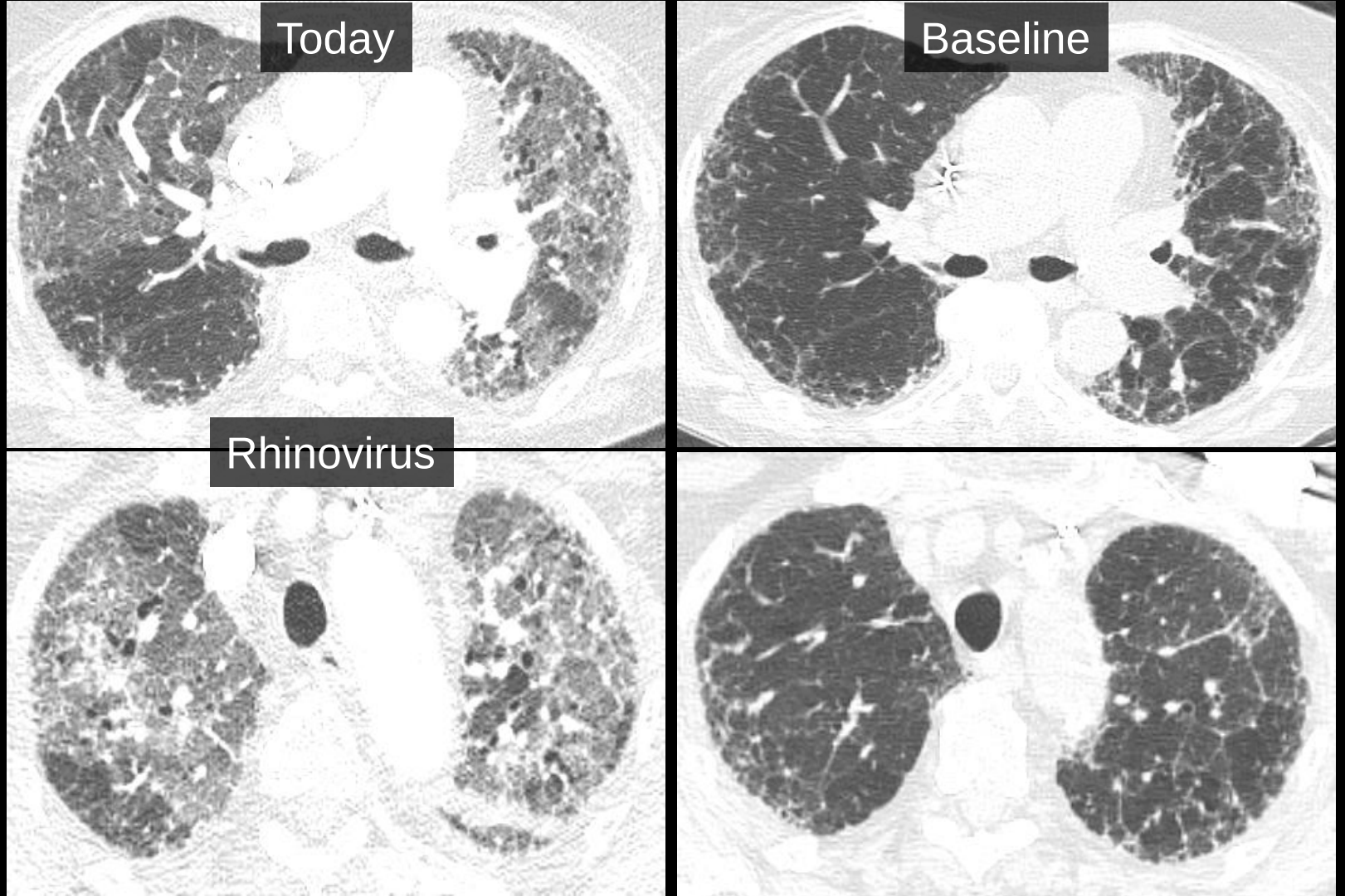








“Drop in PFTs”

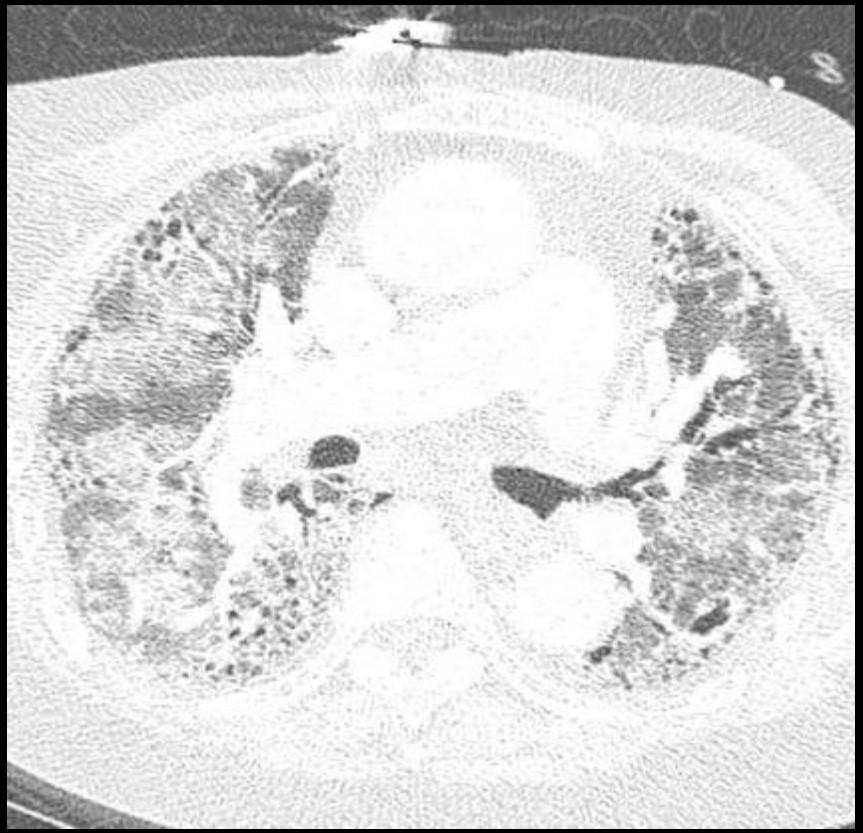


2. Acute Exacerbation

- Acute deterioration in patients with underlying fibrosing lung disease
- Most often associated with IPF but can occur with non-IPF UIP, NSIP, and fibrotic HP
- Organizing pneumonia and diffuse alveolar damage common patterns of injury
- High mortality rate

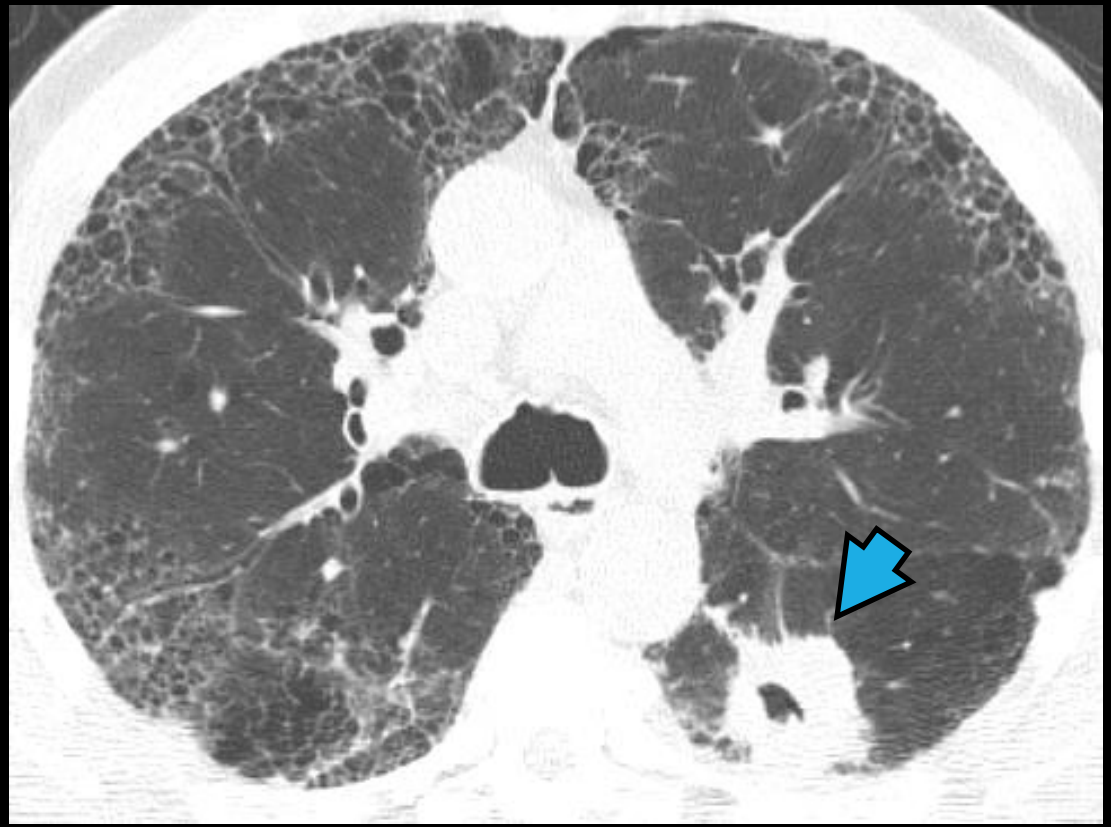
2. Acute Exacerbation

- New ground-glass opacity
- New consolidation
- Background of fibrosis
- Differential diagnosis
  - Infection
  - Drug toxicity
  - Congestive heart failure
  - Aspiration

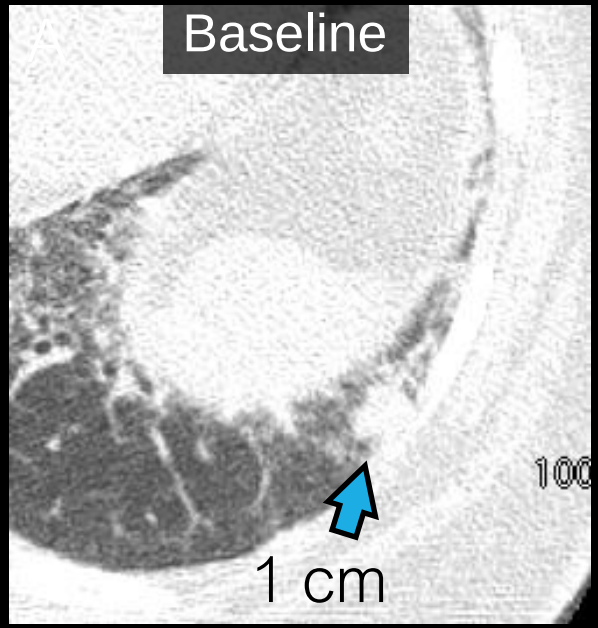


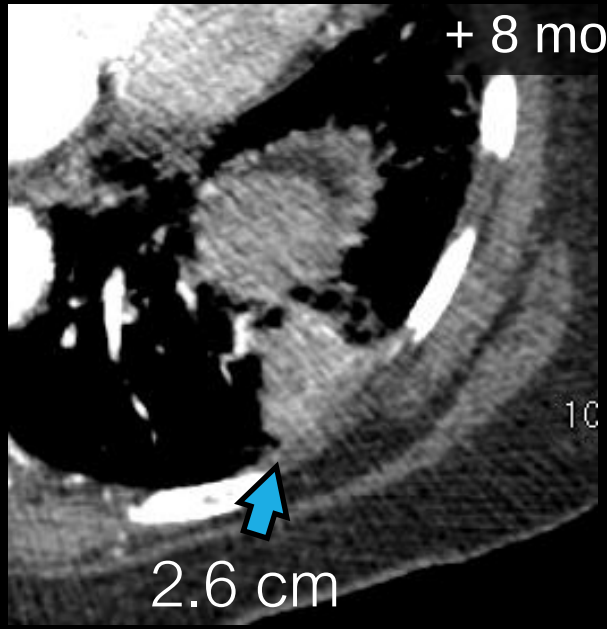
Acute Exacerbation

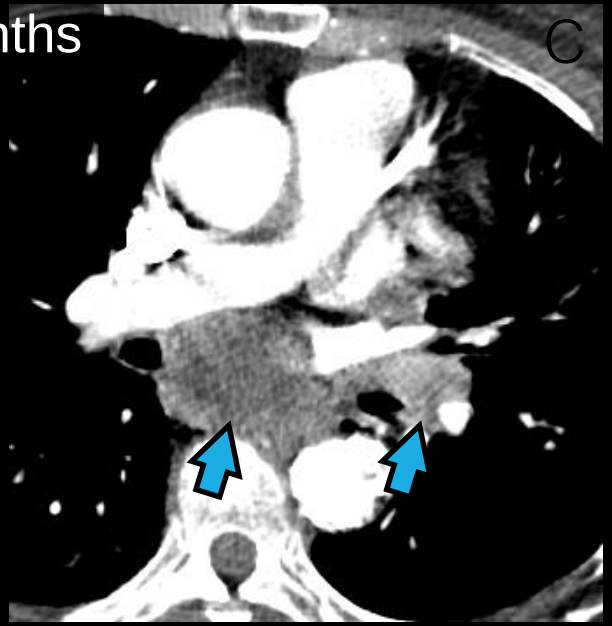
3. Lung Cancer: median delay in diagnosis= 409 days*



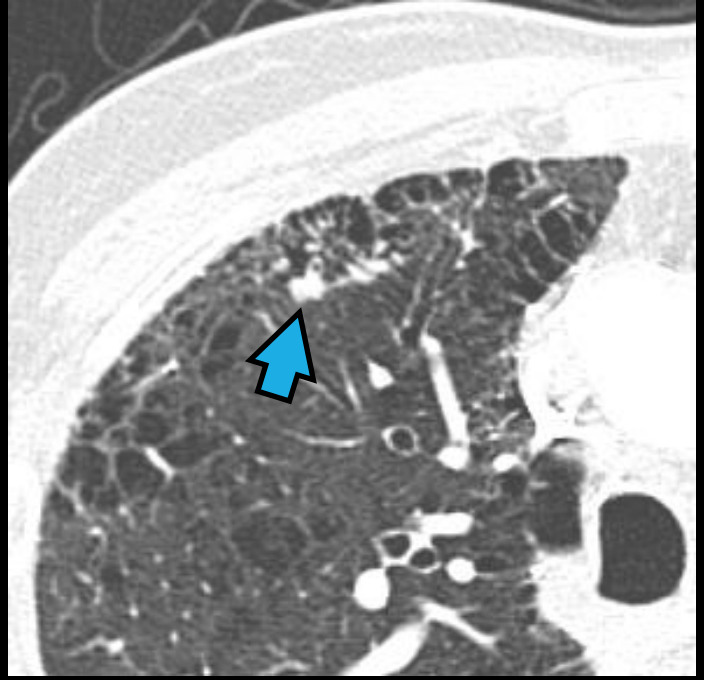
* Yoshida R, et al. Lung cancer in chronic interstitial pneumonia: early manifestation from serial CT observations. Am J Roentgenol. 2012;199(1):85-90.

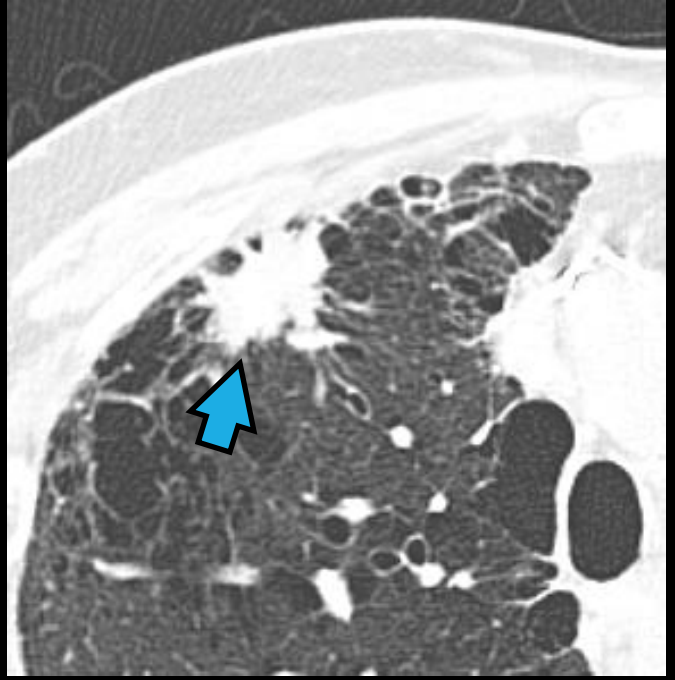






Average of 1.1 cm at presentation, 2.2 cm at diagnosis





65 % Interface

17% GGO

Last but not least…

Kono et al recognized that almost 10% of patients initially diagnosed as IPF subsequently developed CTD.

Kono et al. Usual interstitial pneumonia preceding collagen vascular disease: a retrospective case control study of patients initially diagnosed with idiopathic pulmonary fibrosis. PLoS One. 2014;9:1–10.

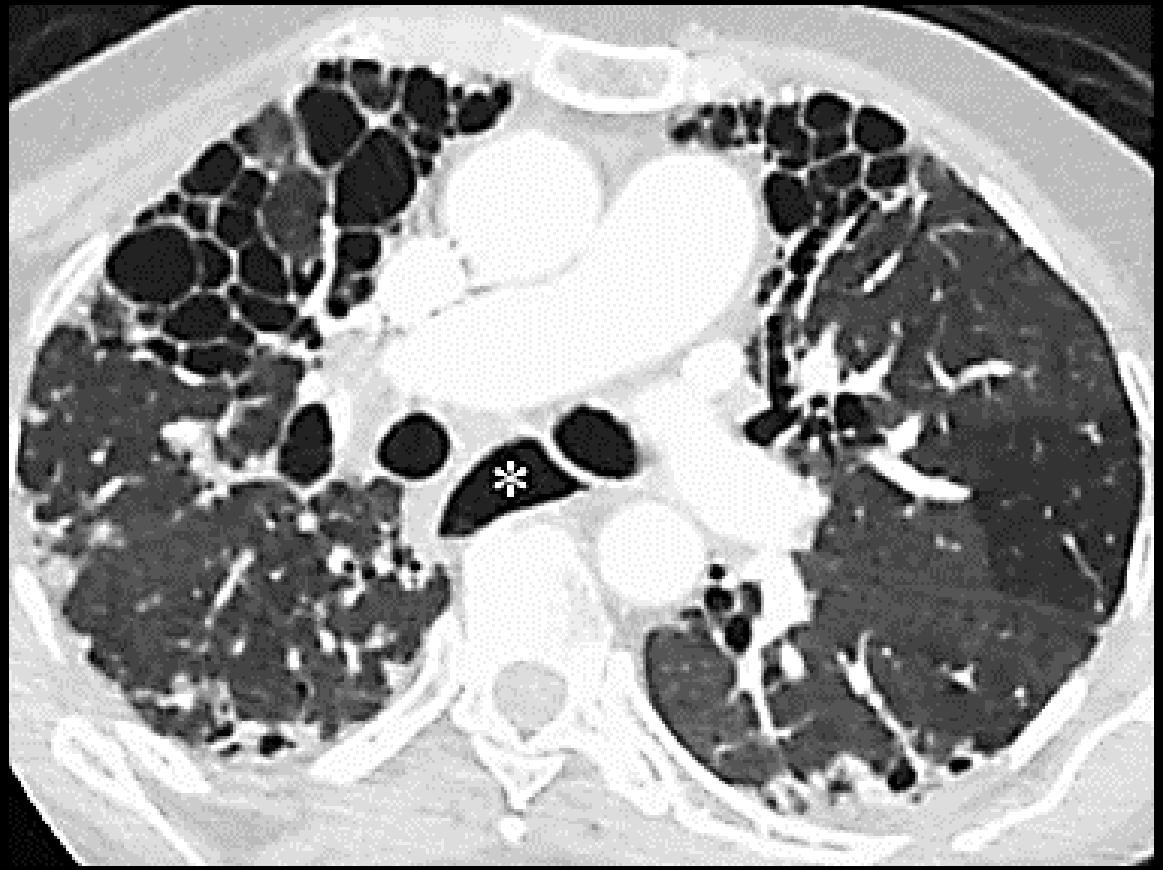
Signs suggestive of **underlying CTD** in patients with **UIP Pattern**

- Chung *et al*. CT Features of UIP Pattern: Differentiating CTD–ILD From IPF. 2018
  - Anterior upper lobe sign
  - Exuberant honeycombing
  - Straight edge sign

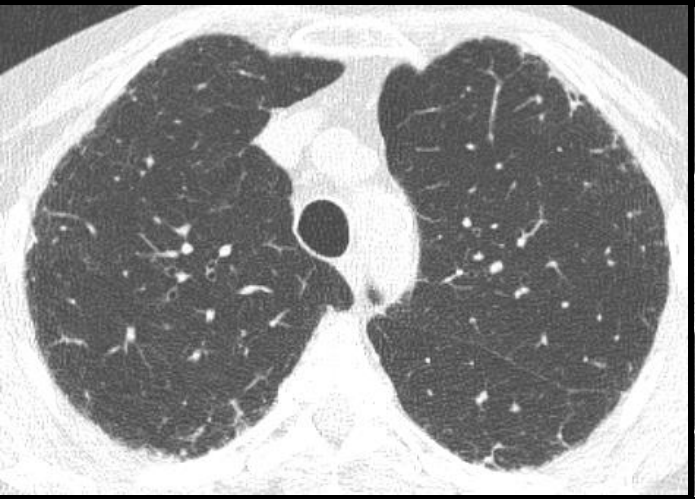
- Walkoff *et al.* The Four Corners Sign: A Specific Imaging Feature in Differentiating Systemic Sclerosis-related ILD From IPF. 2018

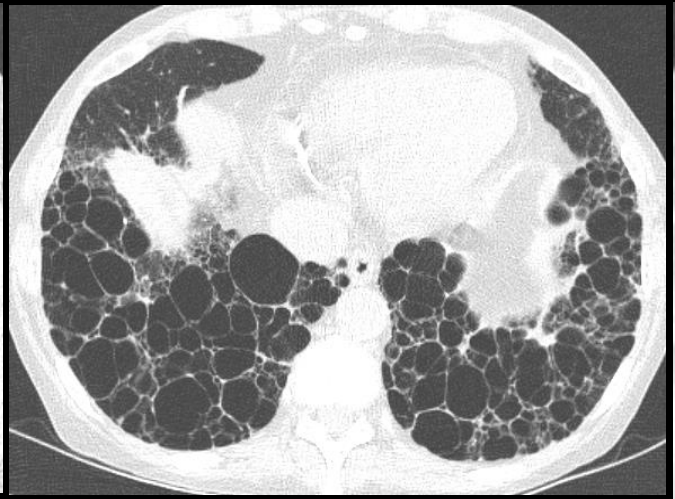
Anterior Upper Lobe Sign - SSc

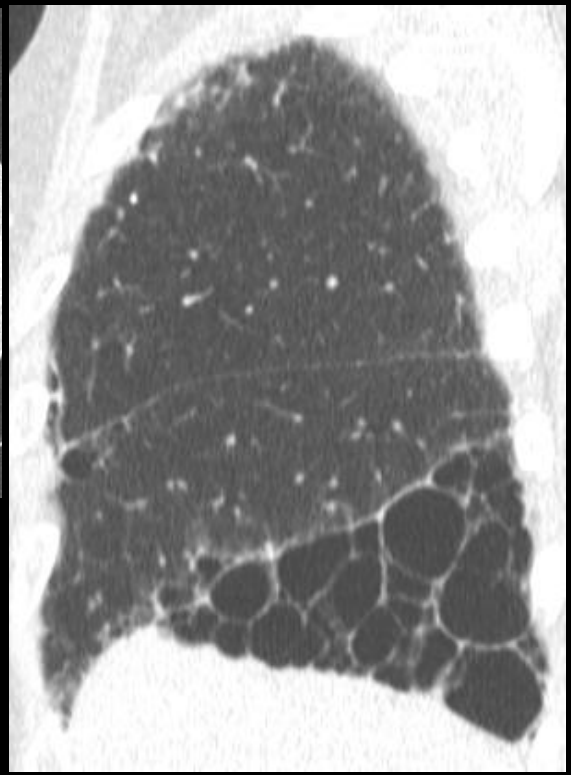
Fibrosis concentrated in the anterior aspect of the upper lobes with relative sparing of the adjacent upper lobe parenchyma and coexistent lower lobe fibrosis



Exuberant Honeycombing - RA



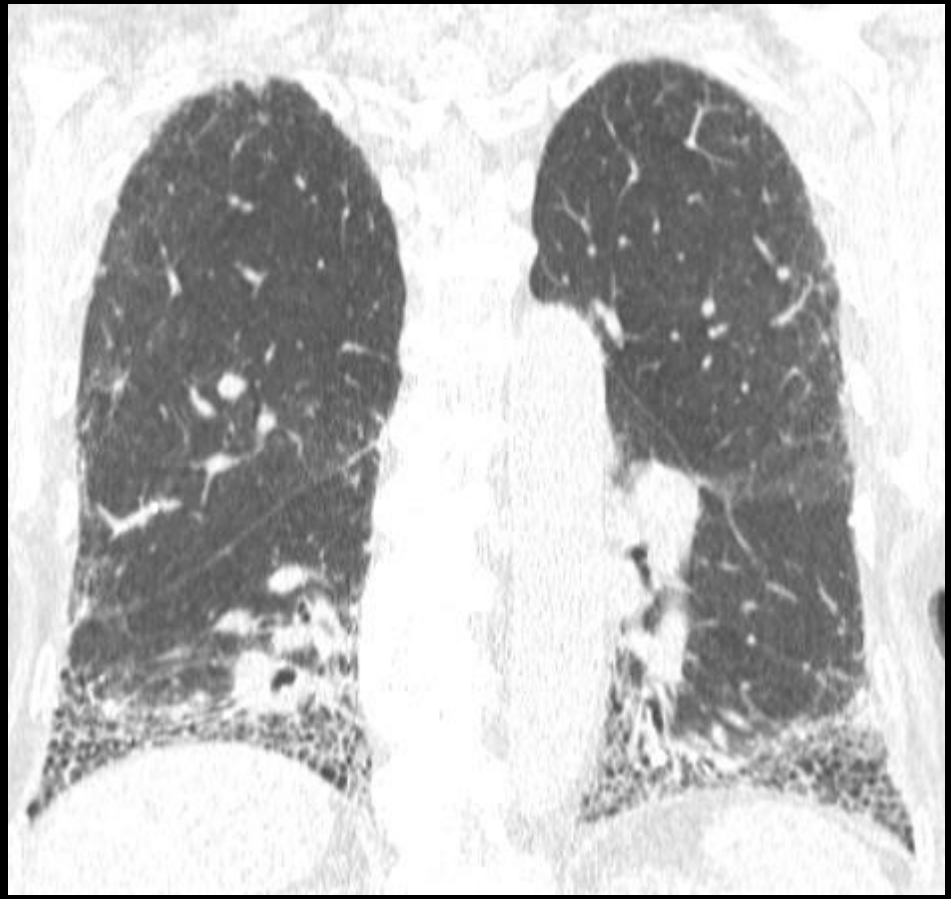




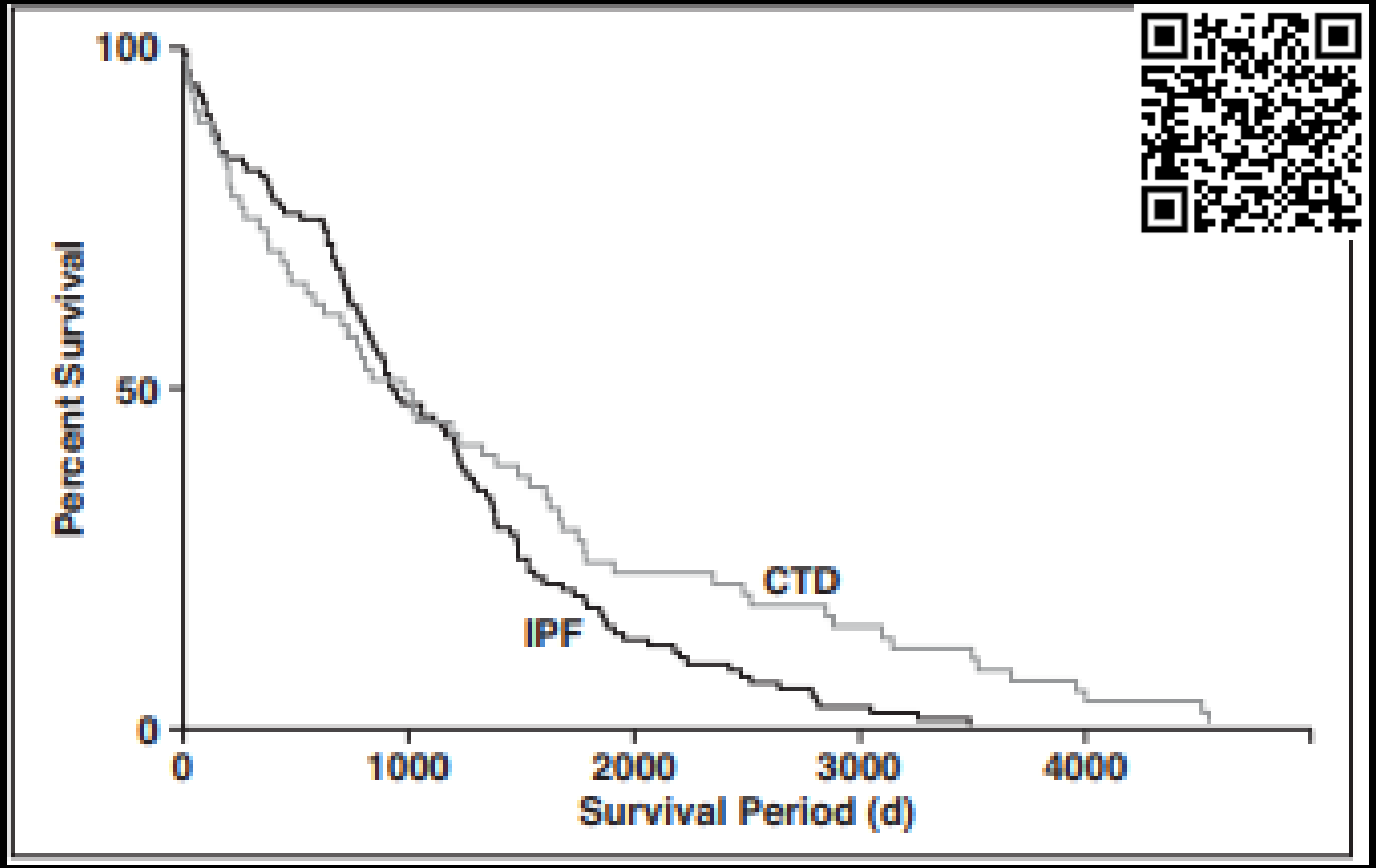
Extensive honeycomb change occupying greater than 70% of the fibrotic portions of the lung

Straight Edge Sign - SSc

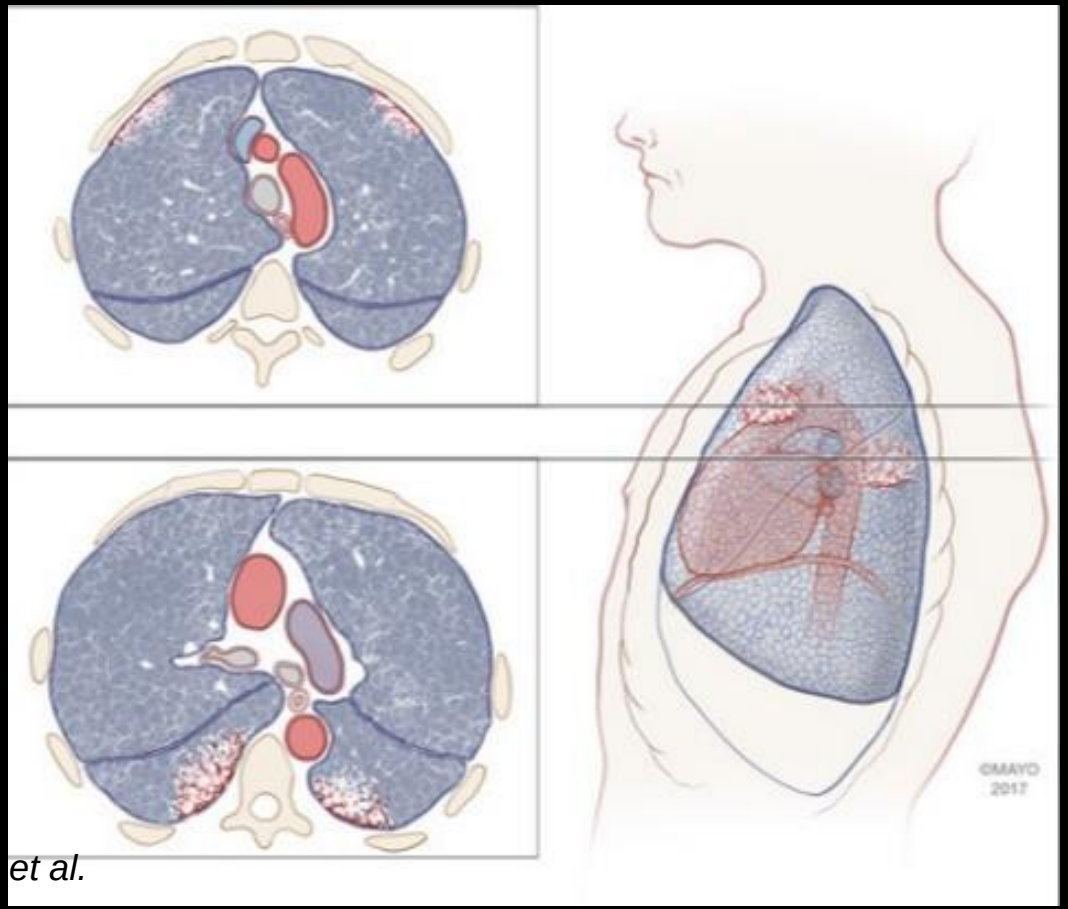
Sharply demarcated basal lung fibrosis with adjacent relatively normal lung on coronal reformatted images and no significant superior extension of fibrosis along the lateral portions of the lung



Survival curves for connective tissue disease (CTD) and idiopathic pulmonary fibrosis (IPF)



Four Corners Sign



et al.

Take home points

- Three questions:
  - Is there fibrosis?
  - What is the distribution?
  - Is the pattern UIP?
- “Flexible” definition of honeycombing
- Probable UIP on HRCT very likely reflects histopathologic UIP in most patients
- Avoid biopsies
- Pearls
- Signs in patients with UIP might point to CTD

Usual Interstitial Pneumonia (UIP)
(UIP ≠ IPF)

Questions ?