AT THE FOREFRONT
UChicago Medicine

A PRACTICAL APPROACH TO FIBROTIC LUNG DISEASE

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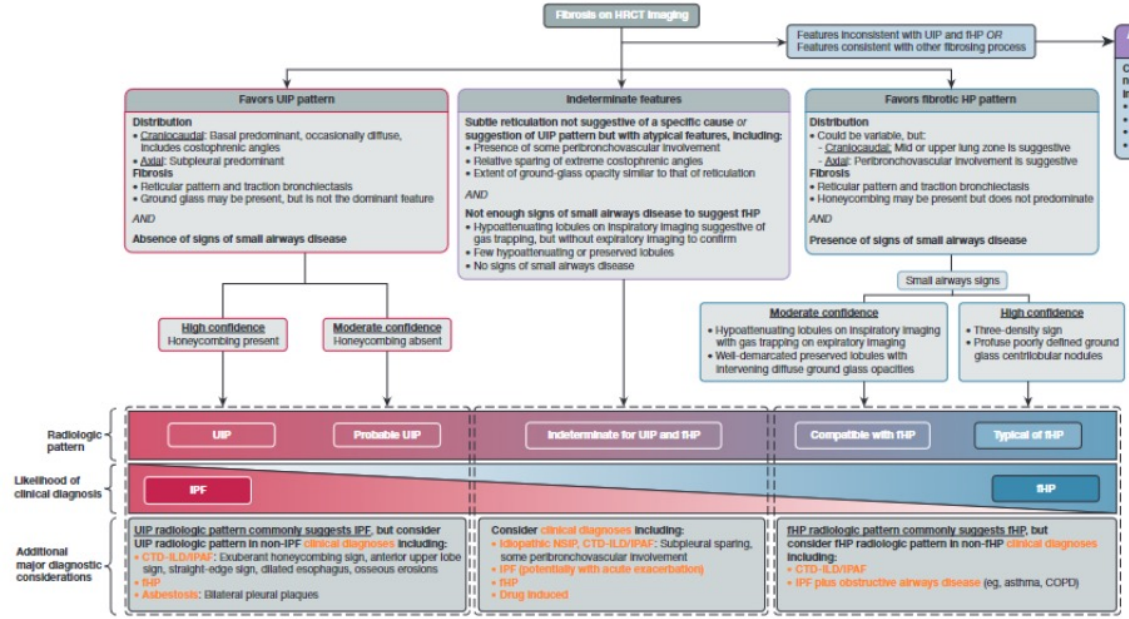
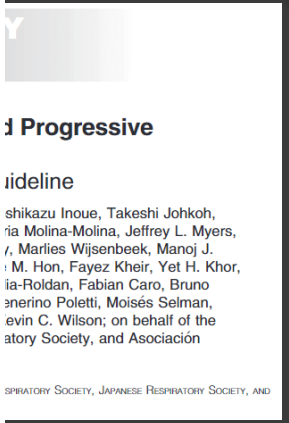
Disclosures

- Consultant:
  - Boehringer Ingelheim
  - Genentech
  - Riverain
- Speakers bureau:
  - Boehringer Ingelheim
  - Genentech

Outline

- Current classification systems
- Practical approach to pulmonary fibrosis
  - UIP
  - NSIP
  - Fibrotic HP (will not be discussed)
  - Sarcoidosis (will not be discussed)
- Brief: interstitial lung abnormality





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ia-Roldan, Fabian Caro, Bruno
enerino Poletti, Moisés Selman,
evin C. Wilson; on behalf of the
atory Society, and Asociación

spiratory Society, Japanese Respiratory Society, and

Margaret L. Salisbury, Moises Selman, Simon L. F. Walsh, Wim A. Wuyts, and Kevin C. Wilson; on behalf of the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax

This guideline is dedicated to the memory of Prof. Jean-Charles Dalphin† (June 2, 1956–October 17, 2019)

This official clinical practice guideline was approved by the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana de Tórax May 2020

[Diffuse Lung Disease Guidelines and Consensus Statements]

CHEST

Executive Summary

Diagnosis and Evaluation of Hypersensitivity Pneumonitis: CHEST Guideline and Expert Panel Report

Check for updates

Evans R. Fernández Pérez, MD, FCCP; William D. Travis, MD, FCCP; David A. Lynch, MB, BCh; Kevin K. Brown, MD, FCCP; Kerri A. Johannson, MD, MPH; Moisés Selman, MD; Jay H. Ryu, MD, FCCP; Athol U. Wells, MD; Yuh-Chin Tony Huang, MD, MHS, FCCP; Carlos A. C. Pereira, MD, FCCP; Mary-Beth Scholand, MD, FCCP; Ana Villar, MD, PhD; Naohiko Inase, MD, PhD; Richard B. Evans, MD, MPH, FCCP; Stephen A. Mette, MD, FCCP; and Lindsy Frazer-Green, PhD

HP ATS

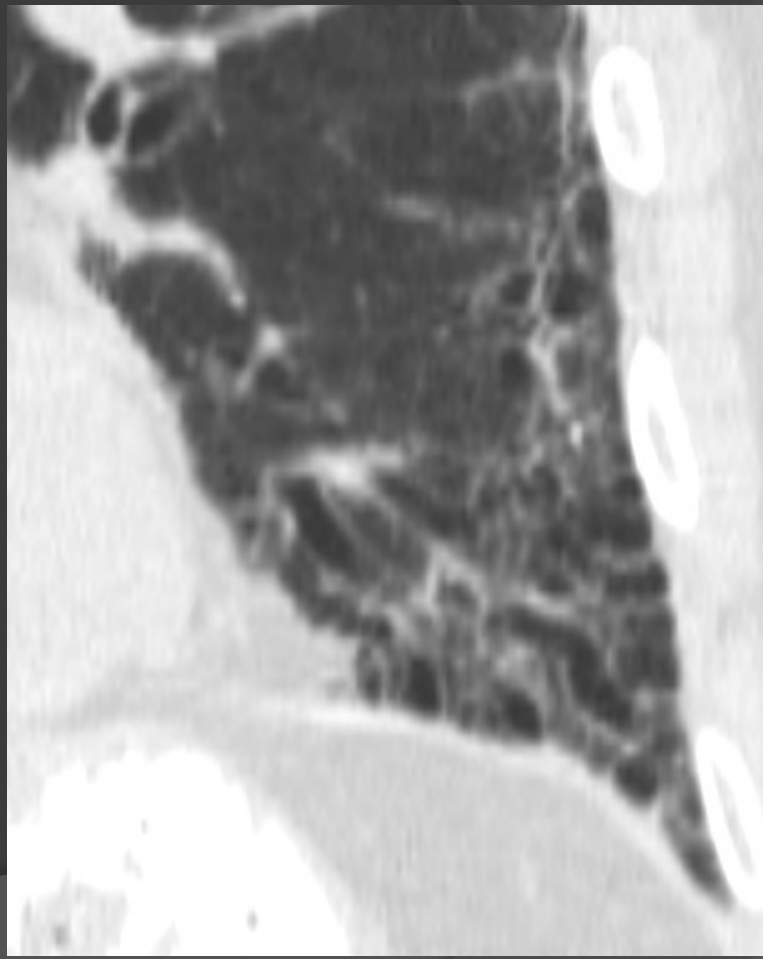
IPF/HP integration

IPF/PFF

HP CHEST

Pulmonary fibrosis

- UIP
  - Most cases IPF
- NSIP
- HP
- Sarcoidosis (not discussed)
- Other: Occupational lung disease, any chronic inflammatory lung disease



Pulmonary fibrosis: Practical approach

- 1. Does it have a UIP or probable UIP pattern on CT? If yes, you are done.
- 2. If not, then can you classify it as NSIP, HP, or sarcoidosis with high confidence? If yes, you are done.
- 3. If not, then probably best to label as non-IPF (”alternative”) diagnosis or indeterminate for UIP pattern (as per guidelines) and discuss in MDD.
  - Recall: MDD is gold standard in ILD; NOT pathology.

Pulmonary fibrosis

- **UIP**
- NSIP
- HP
- Sarcoidosis
- Other: Occupational lung disease, any chronic inflammatory lung disease

Fleischner CT UIP classification

	Typical UIP CT pattern	Probable UIP CT pattern	CT pattern indeterminate for UIP	CT features most consistent with non-IPF diagnosis
Distribution	Basal predominant (occasionally diffuse), and subpleural predominant; distribution is often heterogeneous	Basal and subpleural predominant; distribution is often heterogeneous	Variable or diffuse	Upper-lung or mid-lung predominant fibrosis; peribronchovascular predominance with subpleural sparing
Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; honeycombing is absent; absence of features to suggest an alternative diagnosis	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern	Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts

UIP=usual interstitial pneumonia. IPF=idiopathic pulmonary fibrosis. *Reticular pattern is superimposed on ground glass opacity, and in these cases it is usually fibrotic. Pure ground glass opacity, however, would be against the diagnosis of UIP or IPF and would suggest acute exacerbation, hypersensitivity pneumonitis, or other conditions.

Table 1: **Diagnostic categories of UIP based on CT patterns**

Lynch DA, et al. Lancet Respir Med. 2018 Feb;6(2):138-153.

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Typical UIP (formerly UIP)

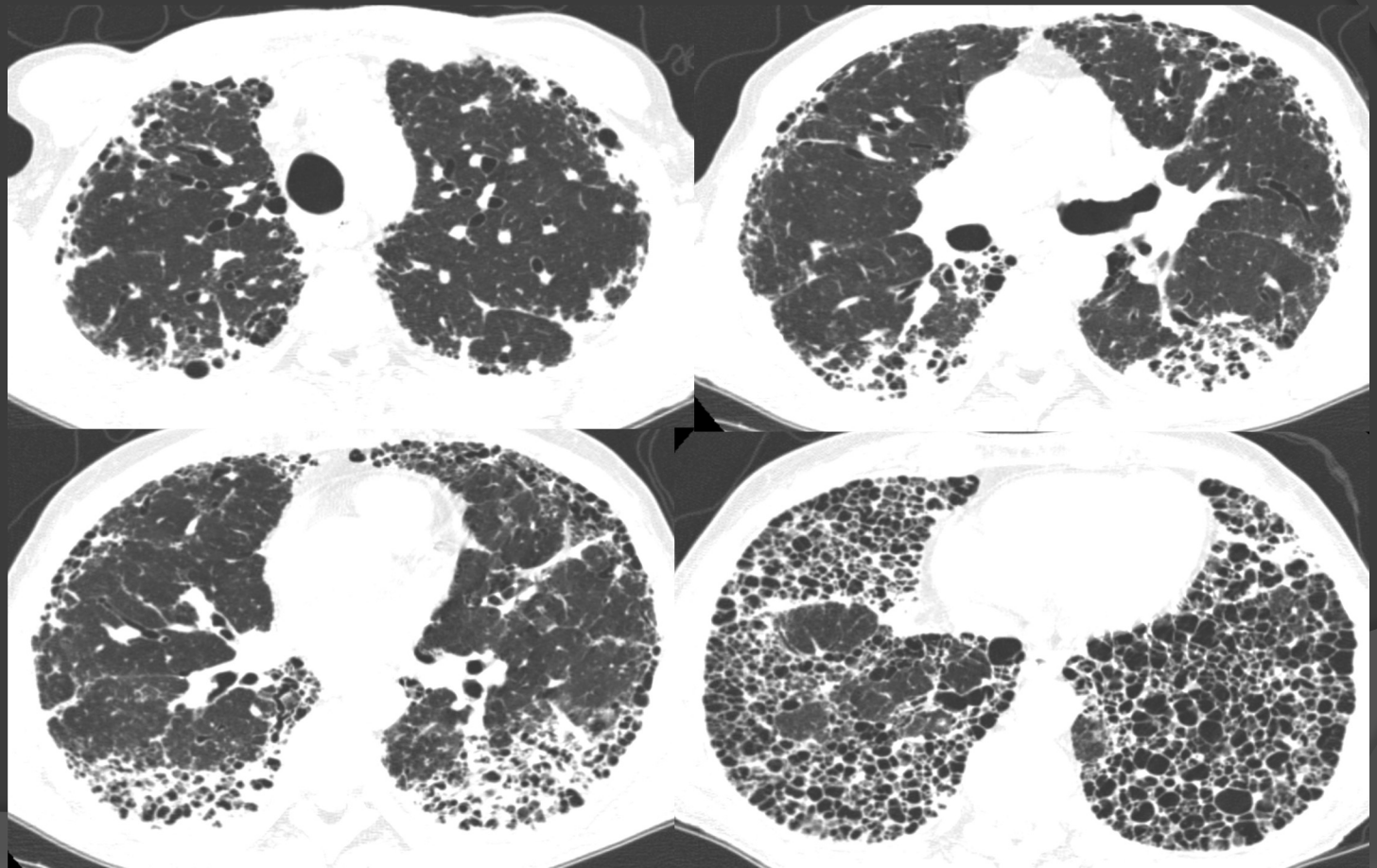
- Typical UIP pattern on HRCT
  - Basal/subpleural preponderance
    - May be zonally diffuse
  - Reticulation
  - Honeycombing with or without traction bronchiectasis
  - Absence of features listed as c/w non-IPF diagnosis
    - Including distribution

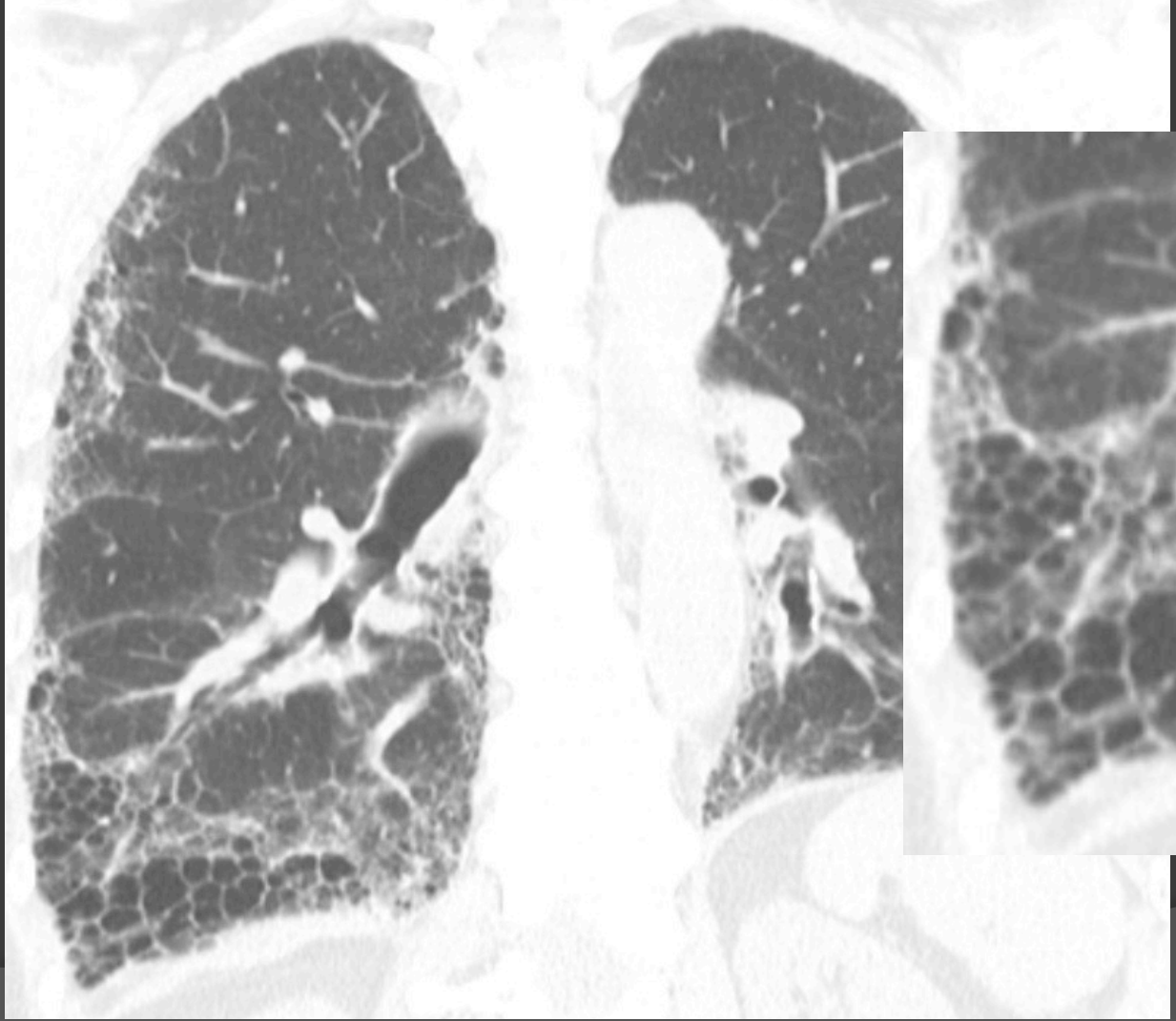
Lynch DA, et al. Lancet Respir Med. 2018 Feb;6(2):138-153.

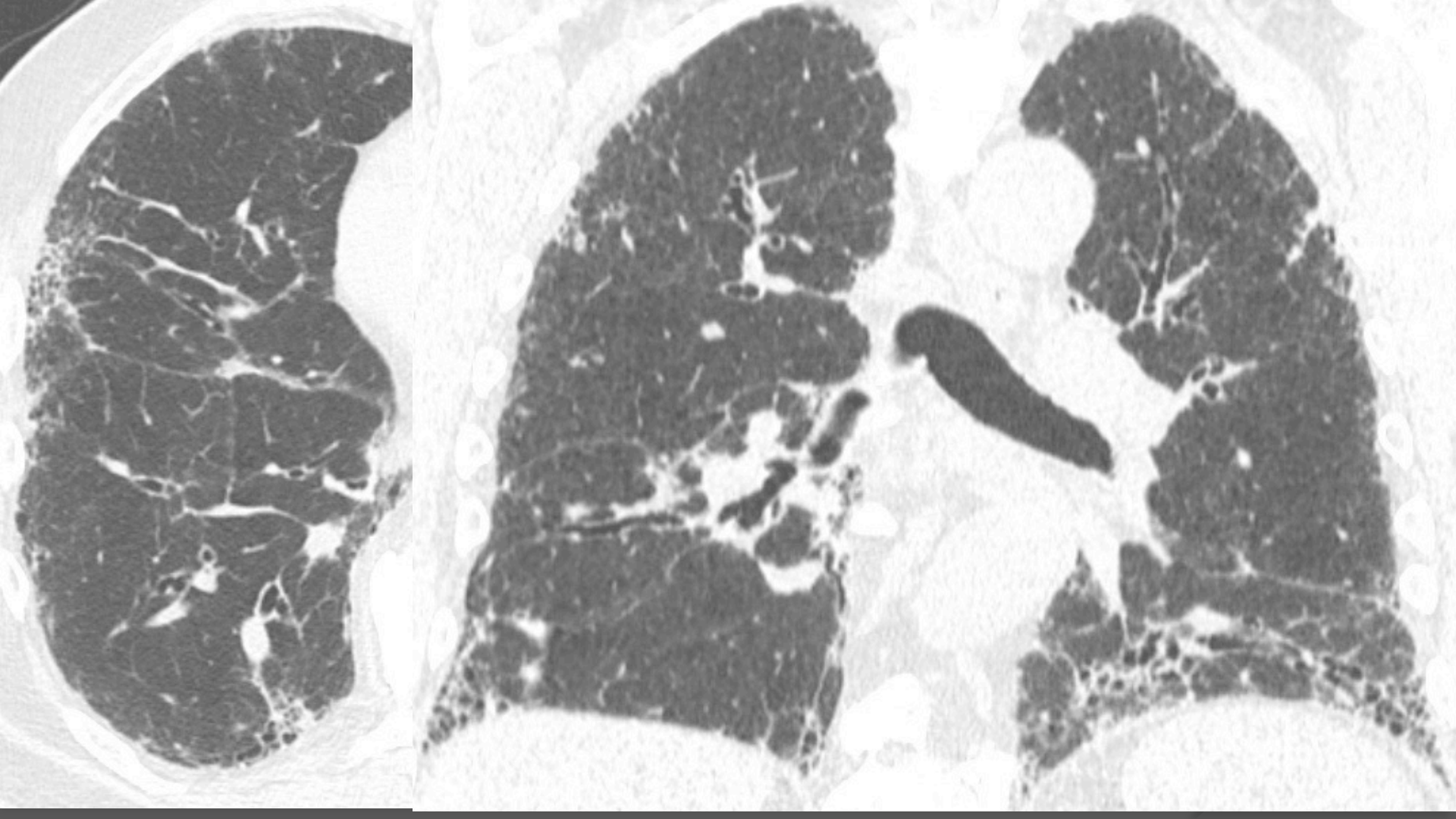
Accuracy of CT diagnosis of UIP

Study	Correctness of first choice diagnosis of UIP	Correctness of confident first choice diagnosis	% cases of UIP without confident CT diagnosis
Hunninghake	85%	96%	52%
Flaherty	100%	100%	63%
Tsubamoto	100%	91%	9%
Elliot	88%	88%	50%
Johkoh	71%	76%	44%
Silva	84%	100%	67%

Confident diagnosis UIP







Fleischner Society UIP classification

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Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; honeycombing is absent; absence of features to suggest an alternative diagnosis	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern	Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts

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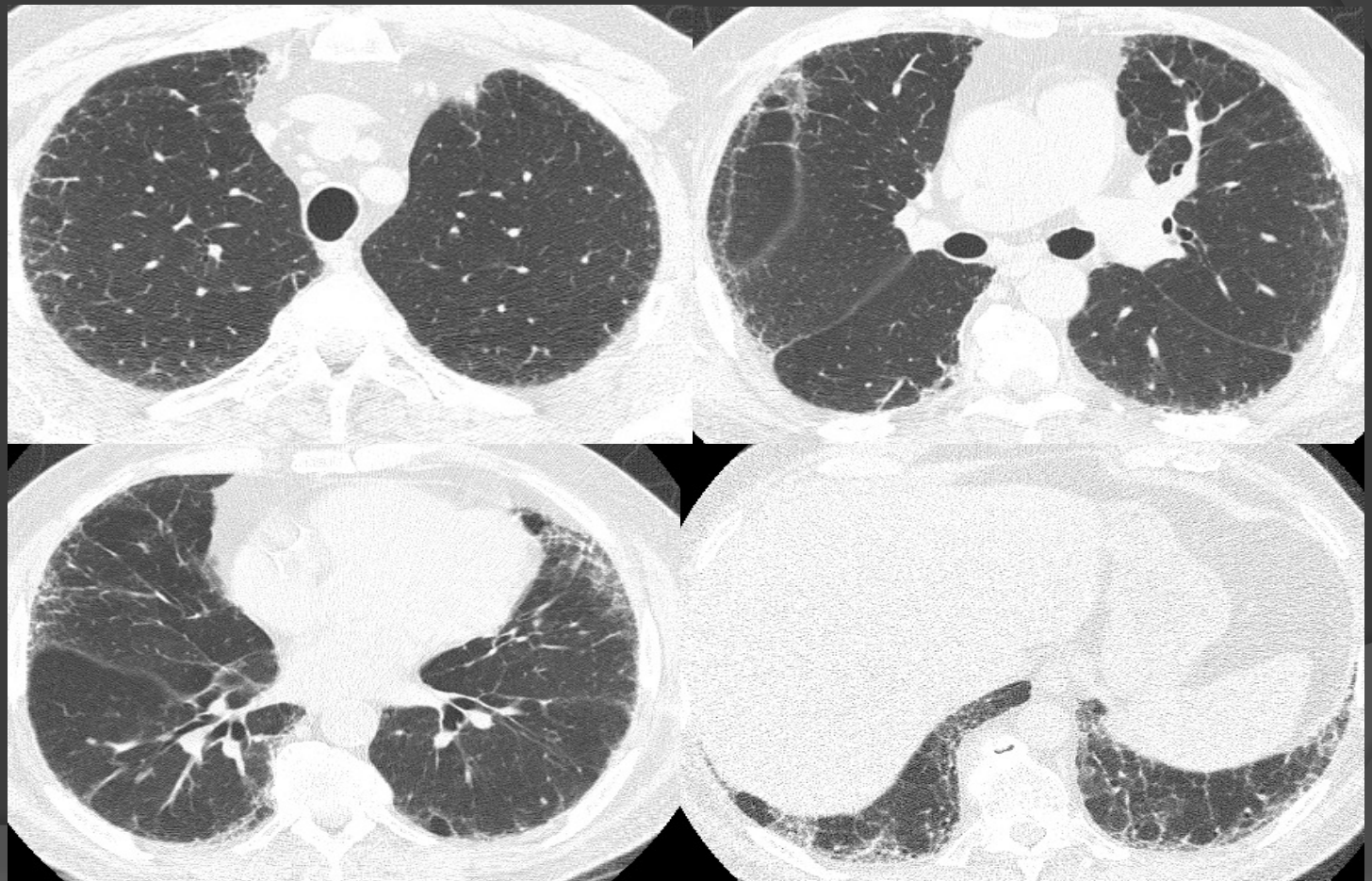
Probable UIP (formerly possible UIP)

- Probable UIP pattern on HRCT
  - Basal/subpleural preponderance
  - Reticulation with traction bronchiectasis or bronchiolectasis
  - Absence of features listed as c/w non-IPF diagnosis
  - *No honeycombing*

Lynch DA, et al. Lancet Respir Med. 2018 Feb;6(2):138-153.

Probable UIP (formerly possible UIP)



Probable UIP (formerly “possible” UIP) on CT

Study	**UIP on pathology**
Yagihashi	94%
Chung (AJR)	82%
Chung (CHEST)	82%
Raghu	94%
Brownell	63-94%*

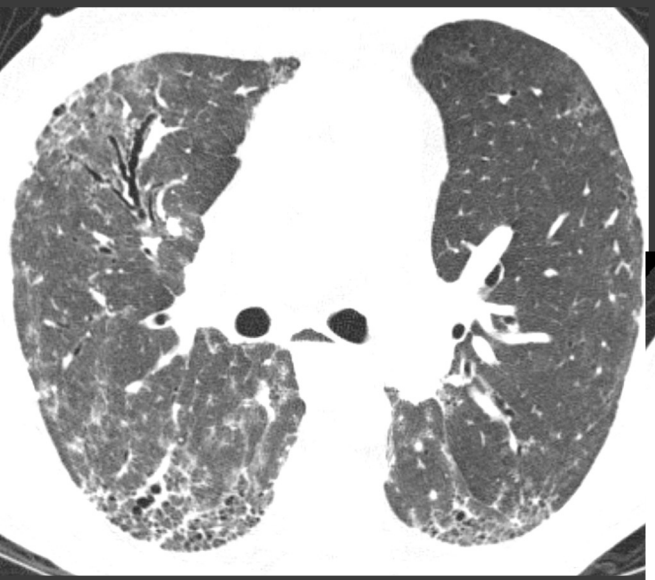
*Dependent on UIP prevalence on pathology

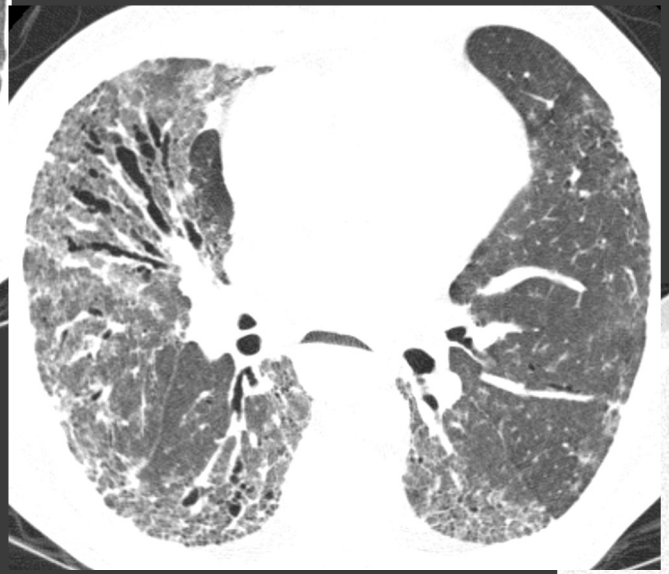
Yagihashi K, et al. Eur Respir J. 47:1189-1197, 2016
Chung JH, et al. AJR Am J Roentgenol 210:1034-1041, 2018
Chung JH, et al. Chest 147:450-459, 2015
Raghu G, et al. Lancet Respir Med 2:277-284, 2014
Brownell R, et al. Thorax 72:424-429, 2017

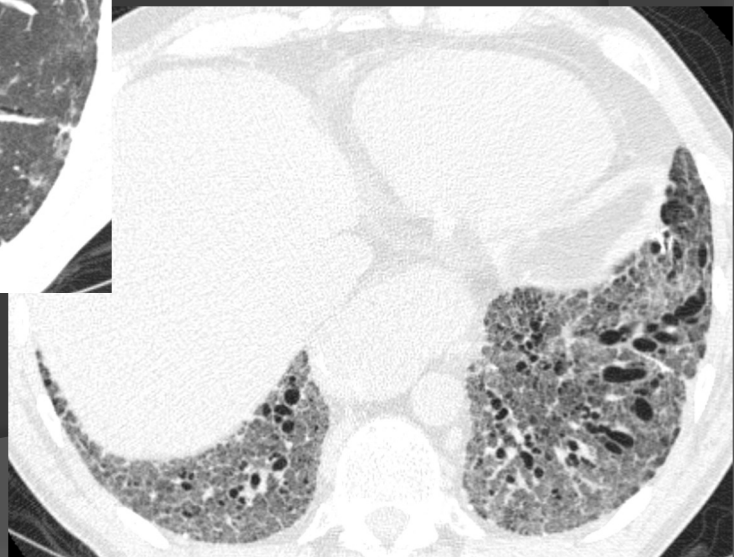
NSIP

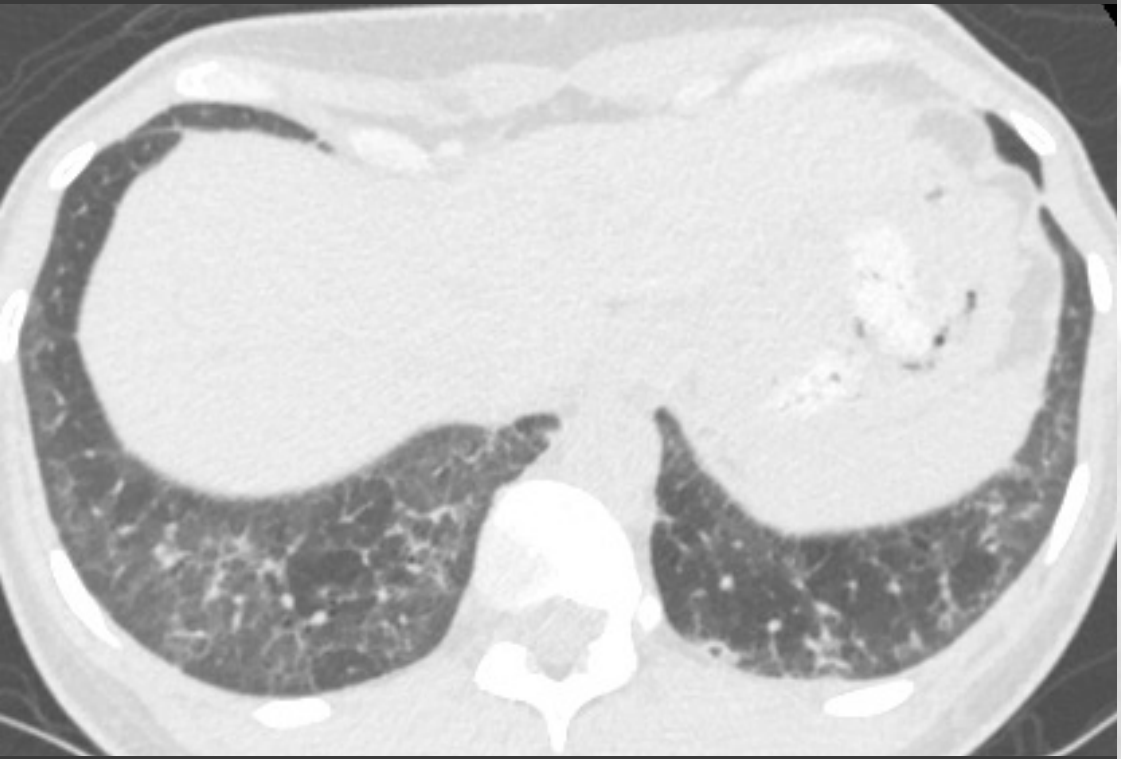
- Usually secondary as opposed to UIP (usually idiopathic): CTD, HP, Drugs
  - Ground-glass
  - Traction bronchiectasis
  - Reticulation
  - No honeycombing (or limited)
  - Distribution
    - Almost always basilar
    - Axial distribution: variable but subpleural sparing or central specific (around 1/3 of cases)

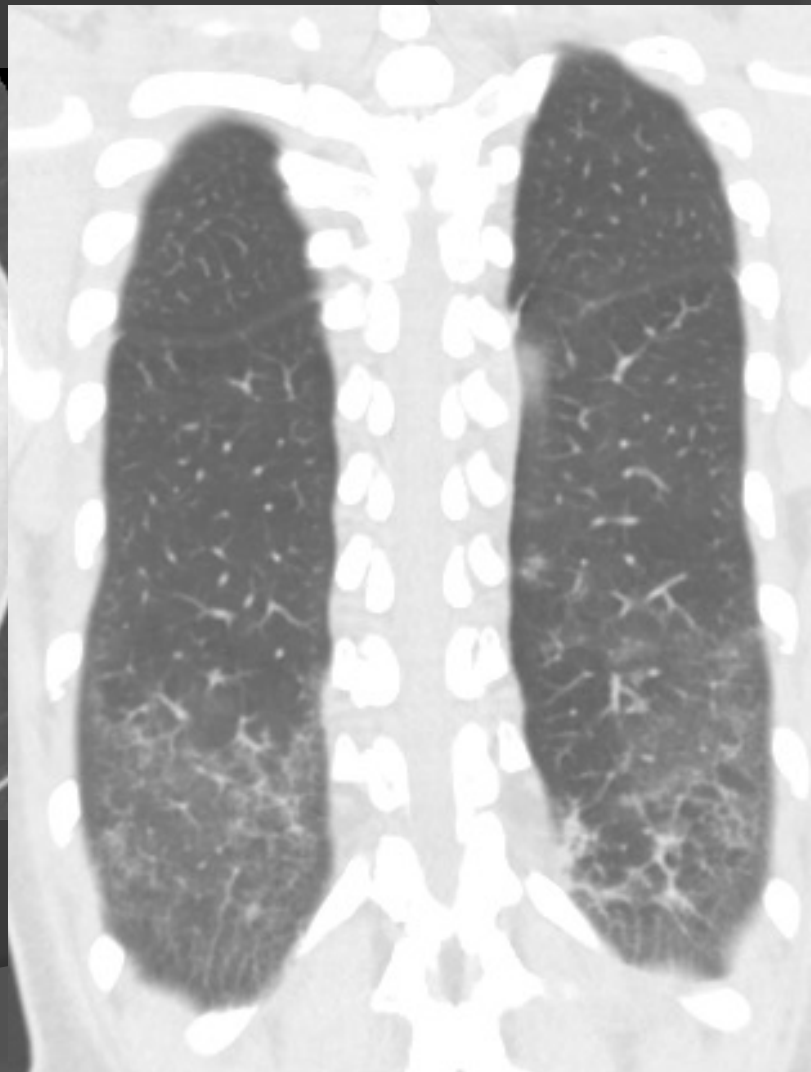
NSIP: Scleroderma



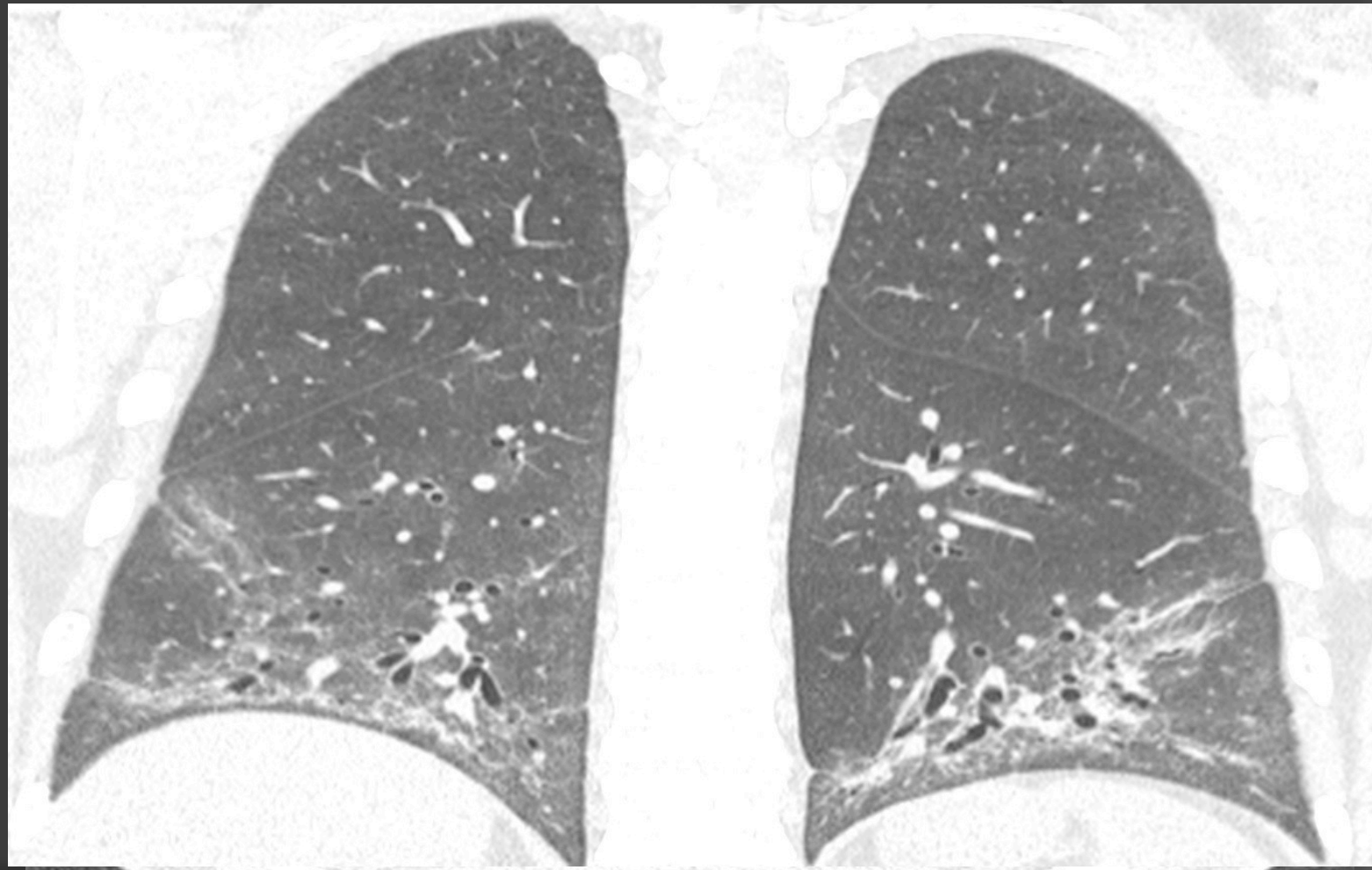


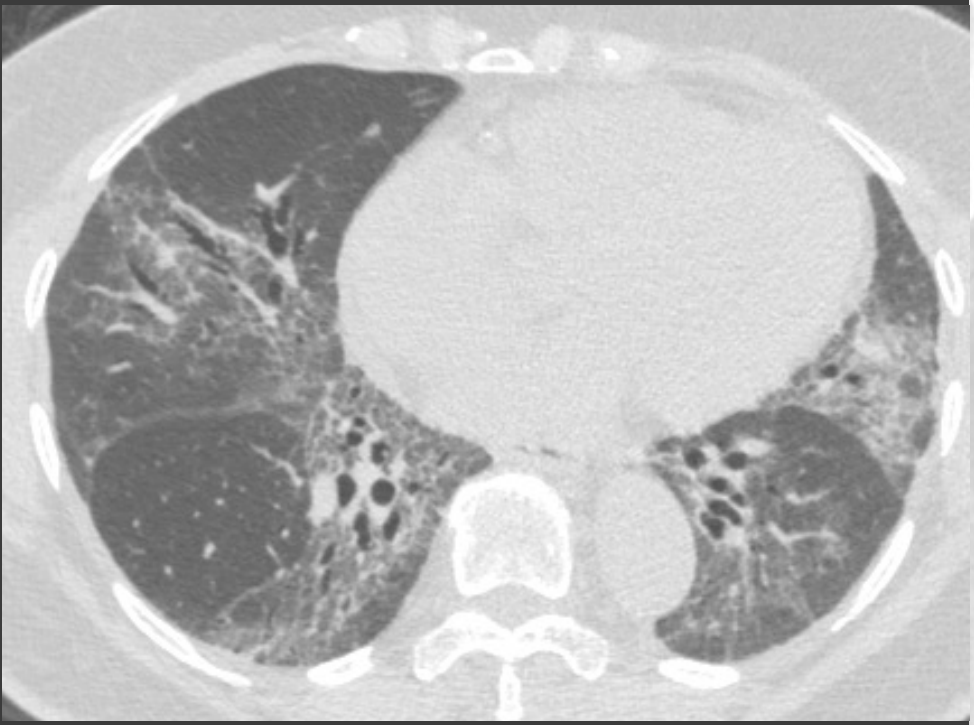


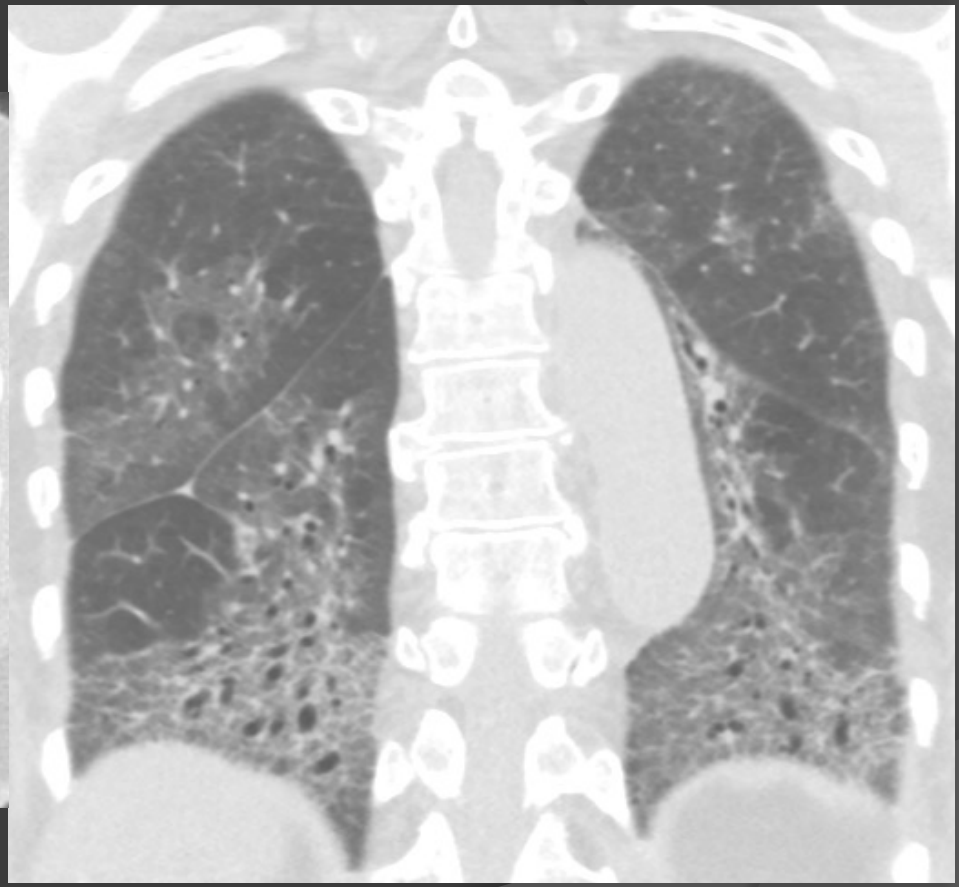


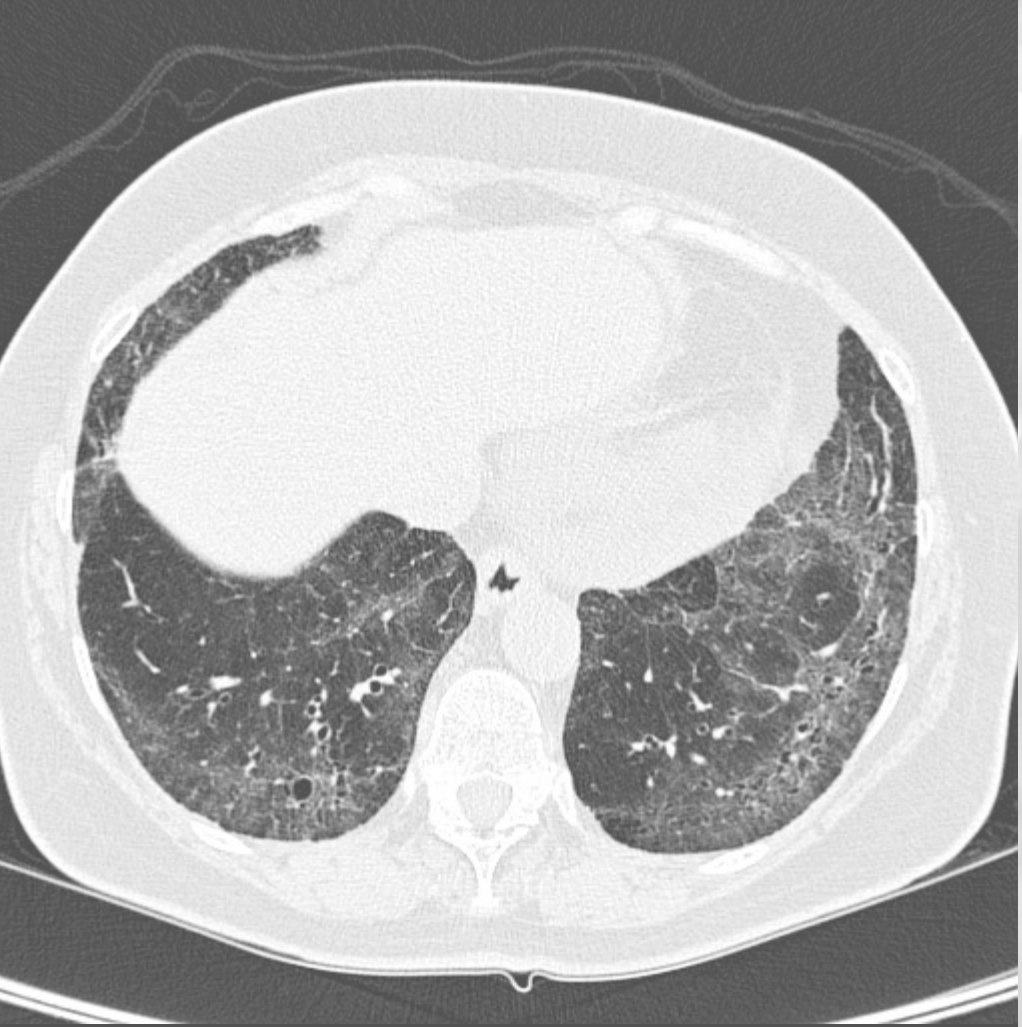


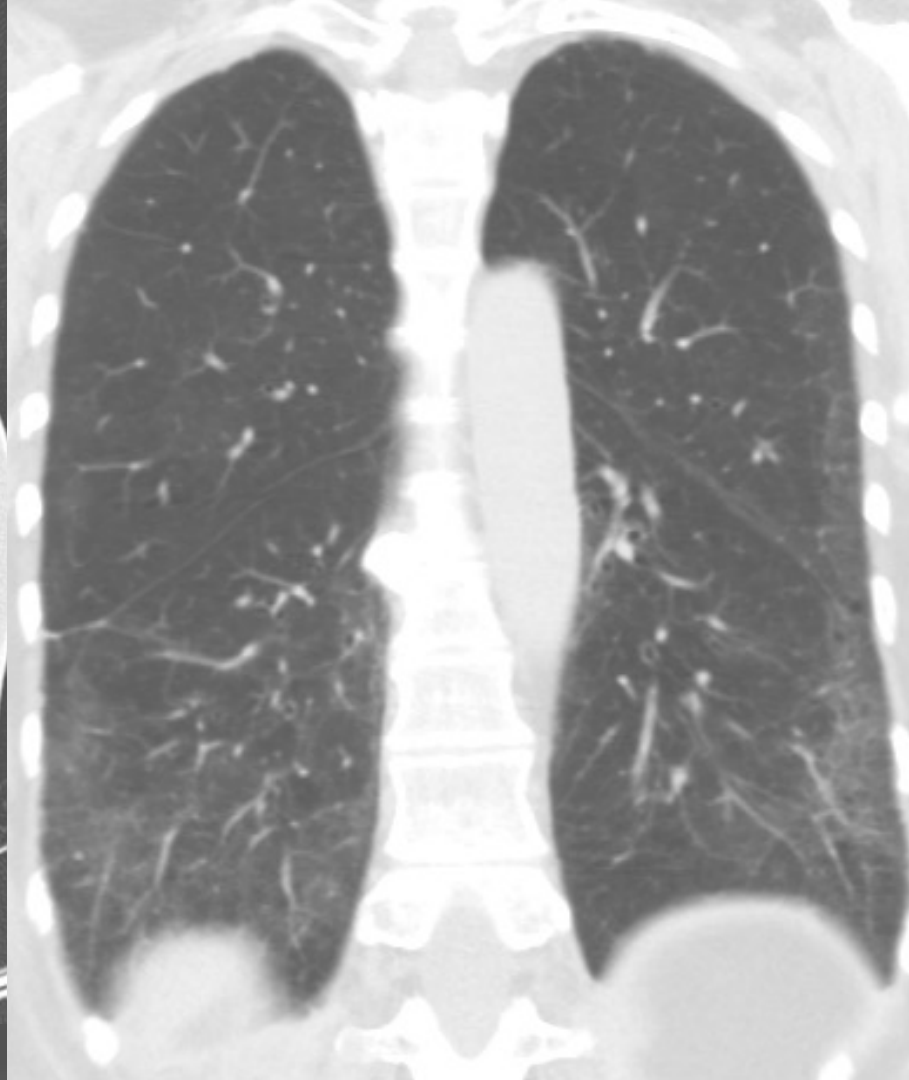
NSIP: HP

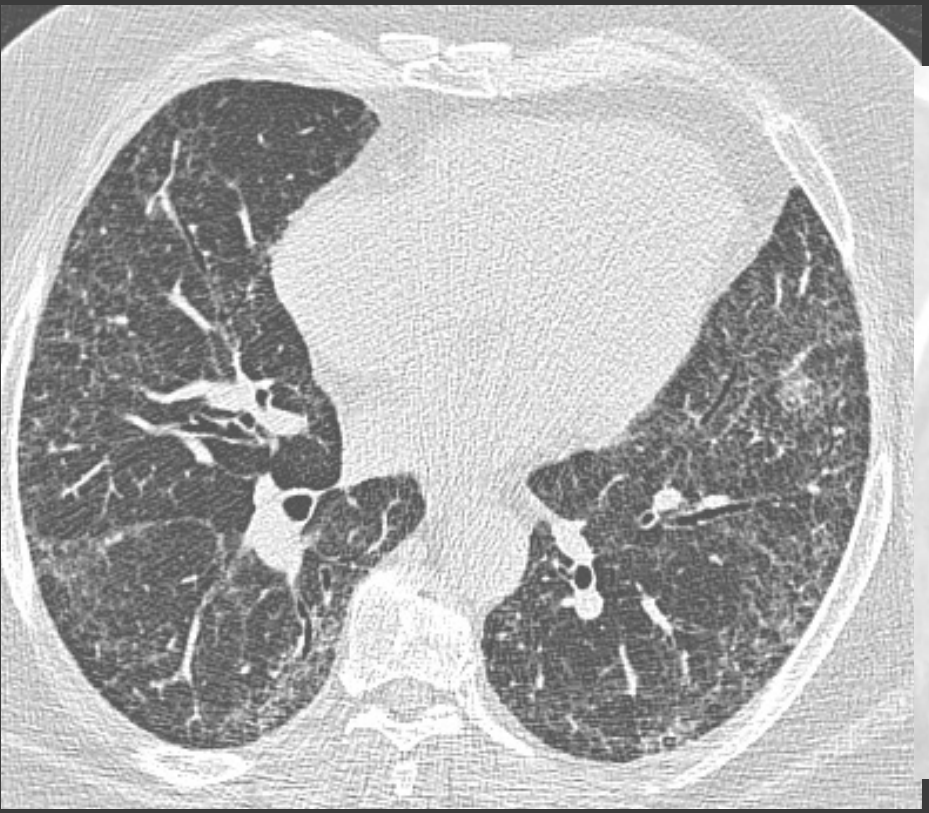


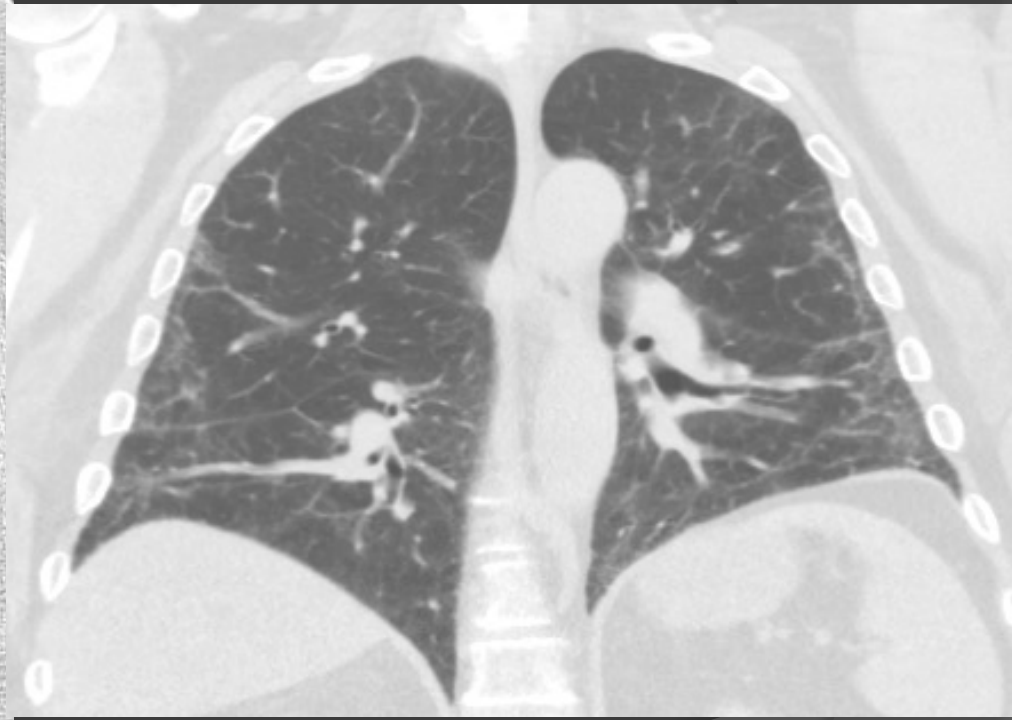












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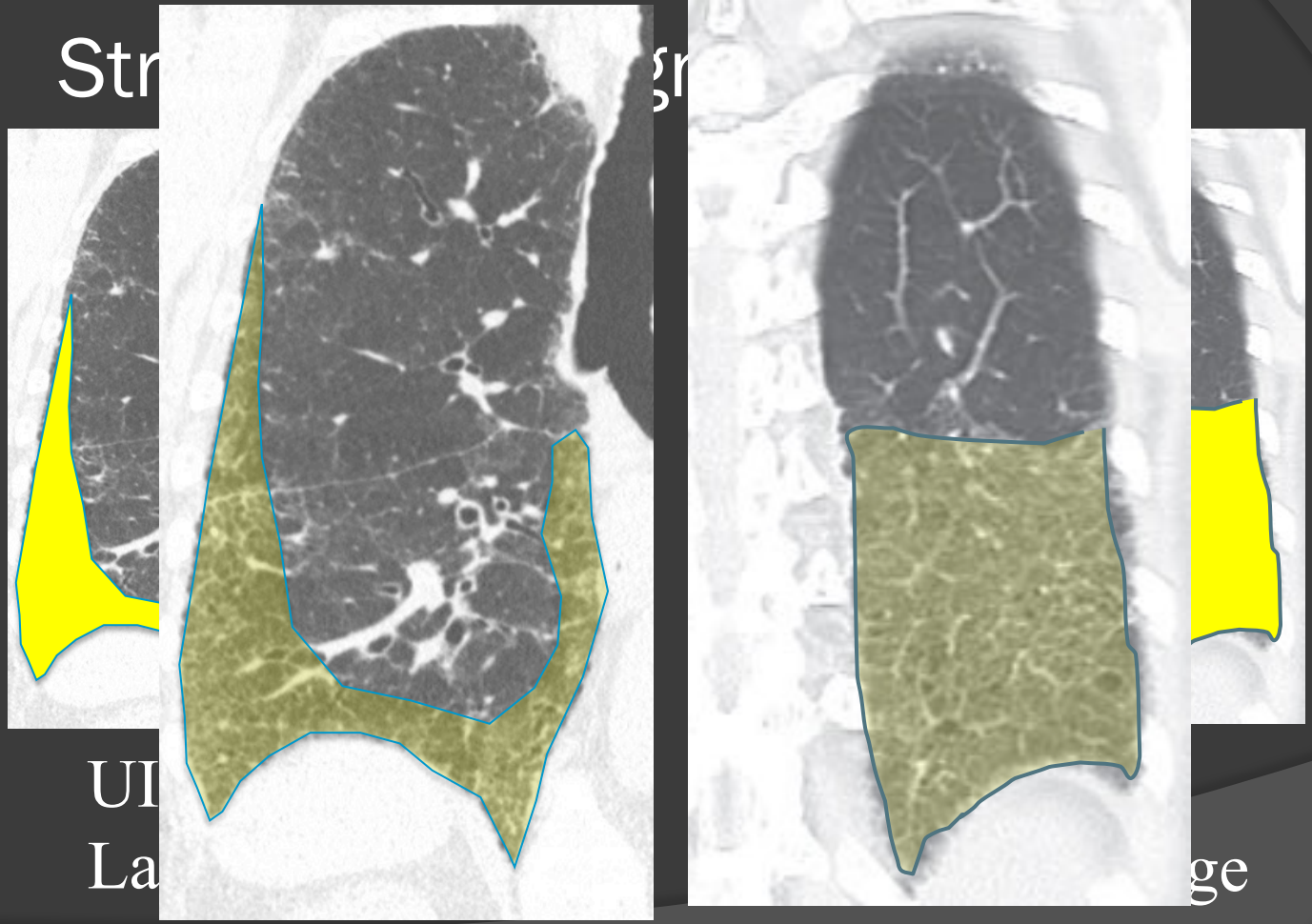

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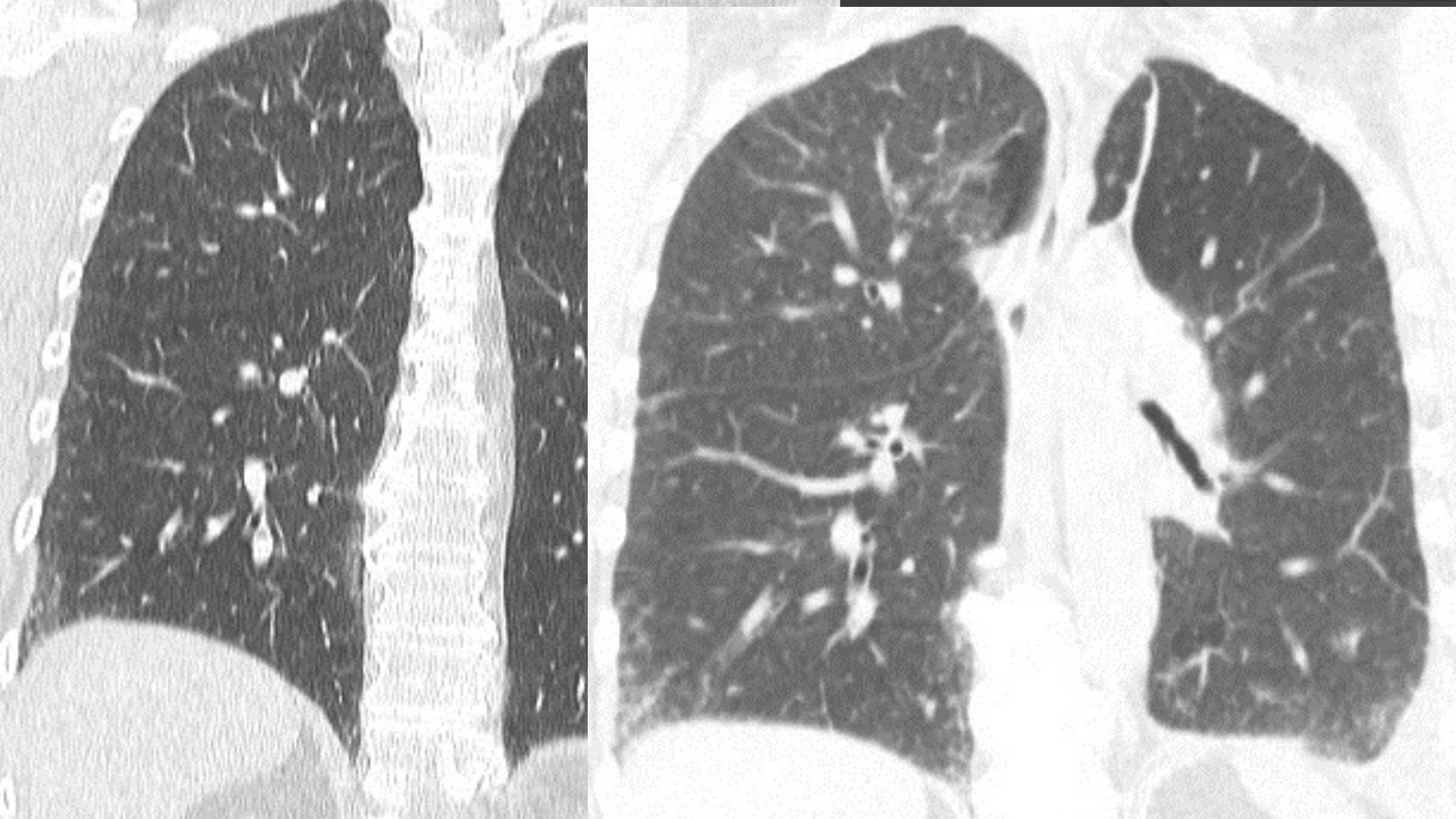
HP and Sarcoid will be discussed in other talks today

Interstitial lung abnormalities: Definition

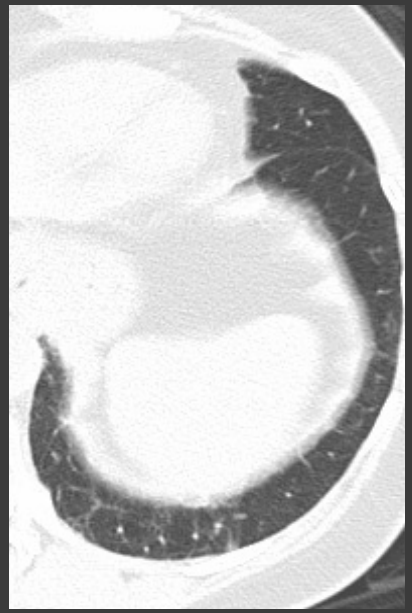
- Incidental identification of non-dependent abnormalities, including
  - ground-glass abnormality
  - reticular abnormality
  - lung distortion
  - traction bronchiectasis
  - honeycombing
  - nonemphysematous cysts
- Involving at least 5% of a lung zone
- In individuals in whom interstitial lung disease is not suspected

Fleischner Society Position Paper: Lancet Respir Med 2020;8:726-37

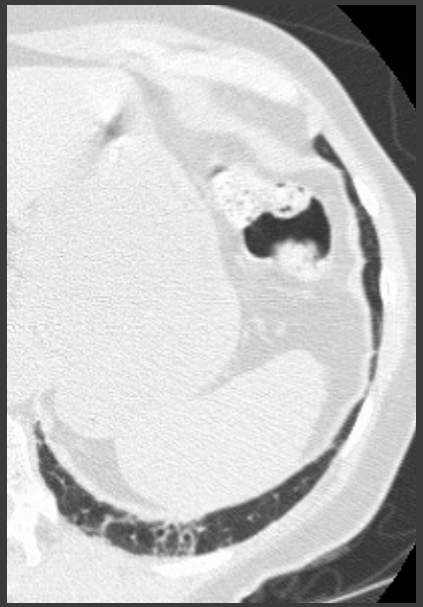
Courtesy of David Lynch, MBBS



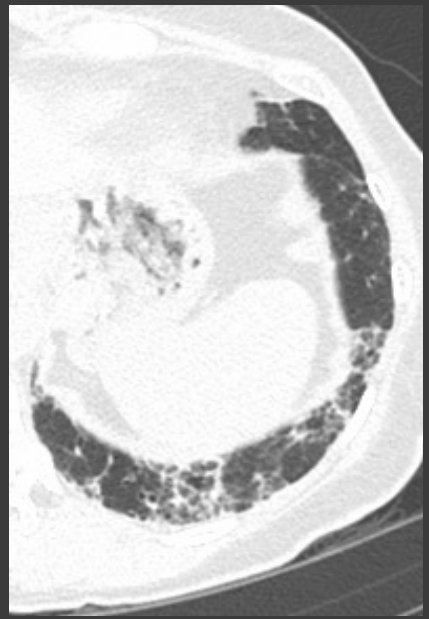
2003



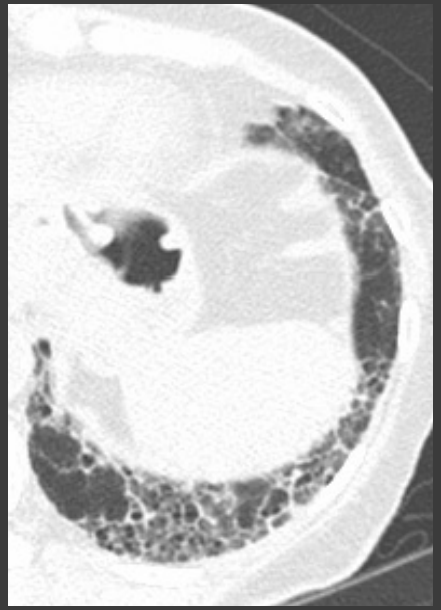
2007



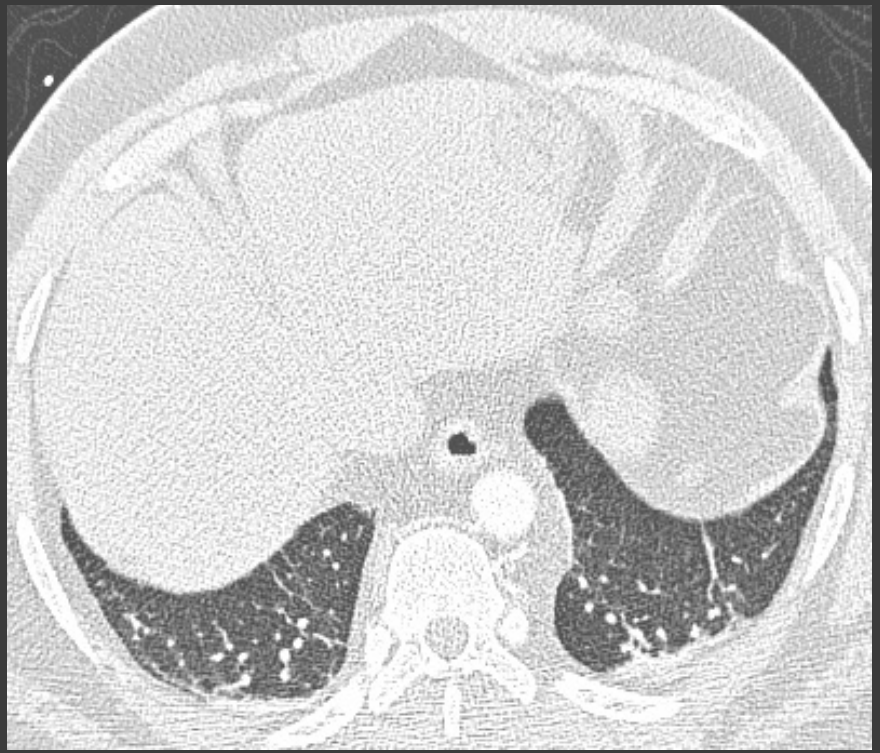
2010



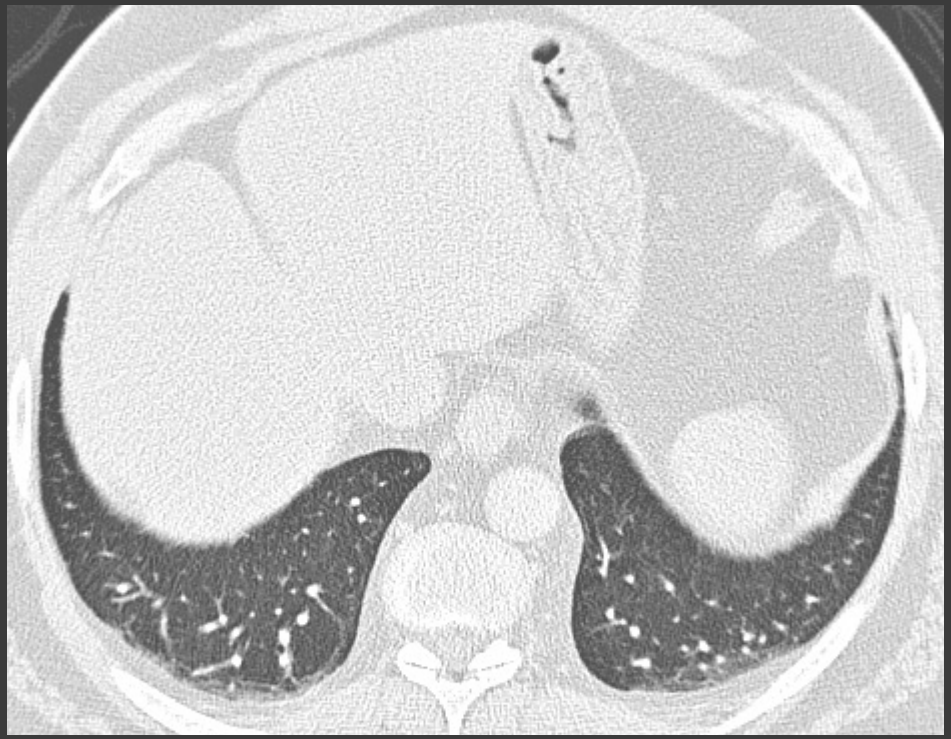
2015



2011



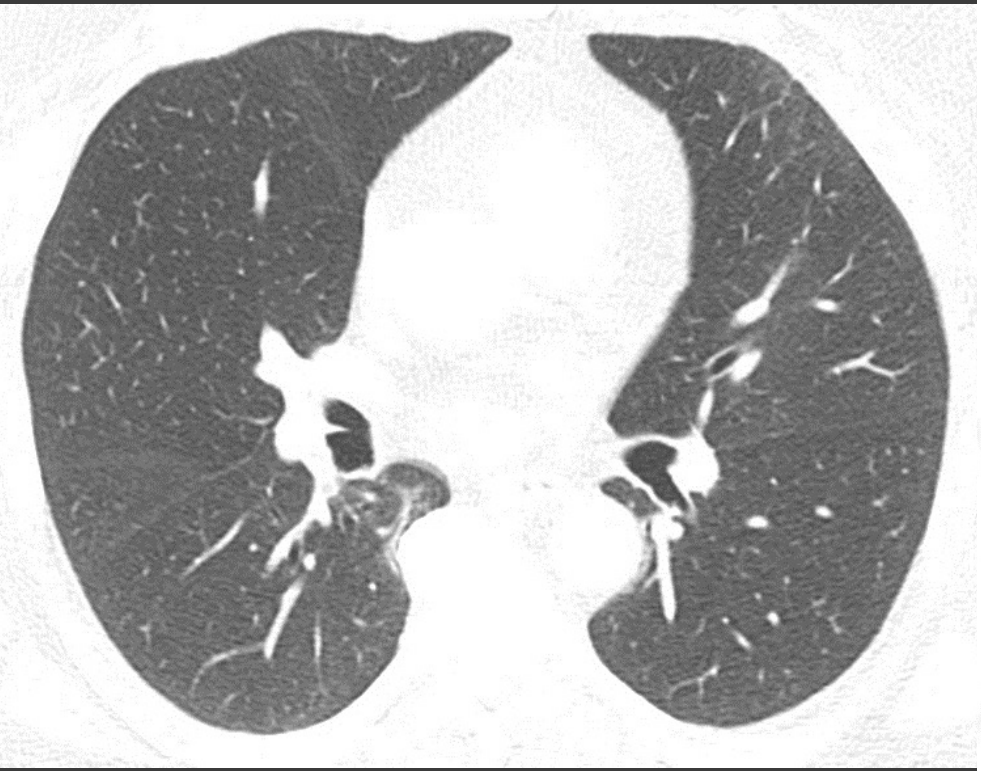
2013

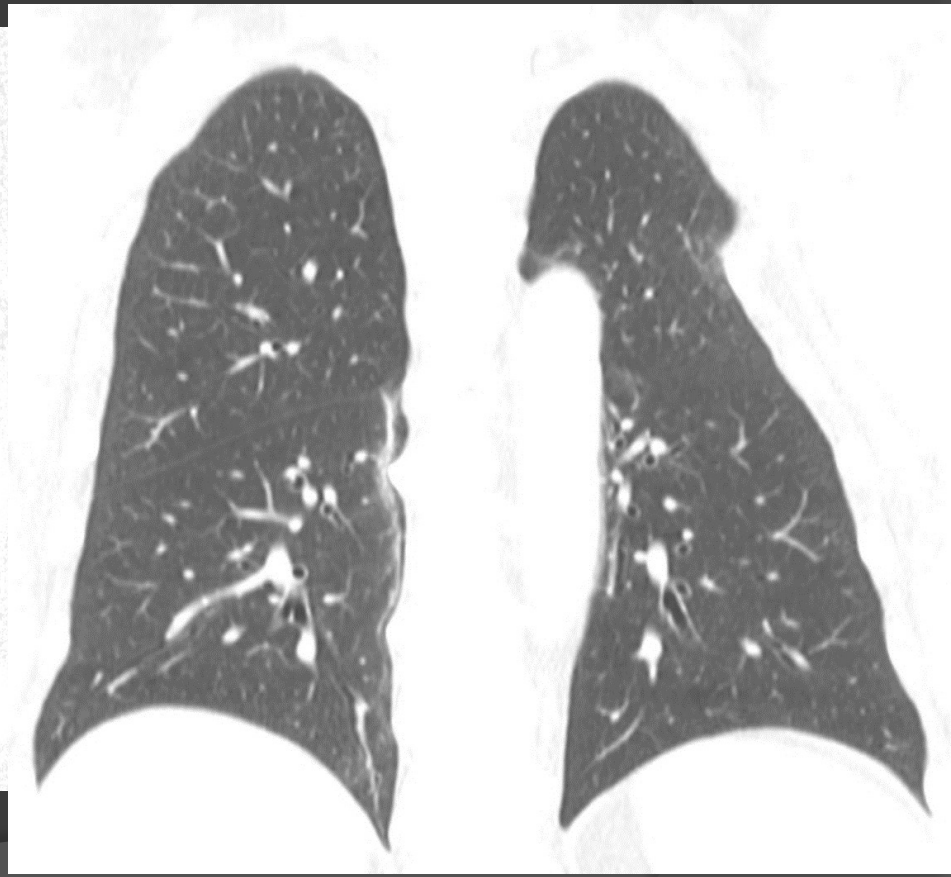


What is **NOT** ILA

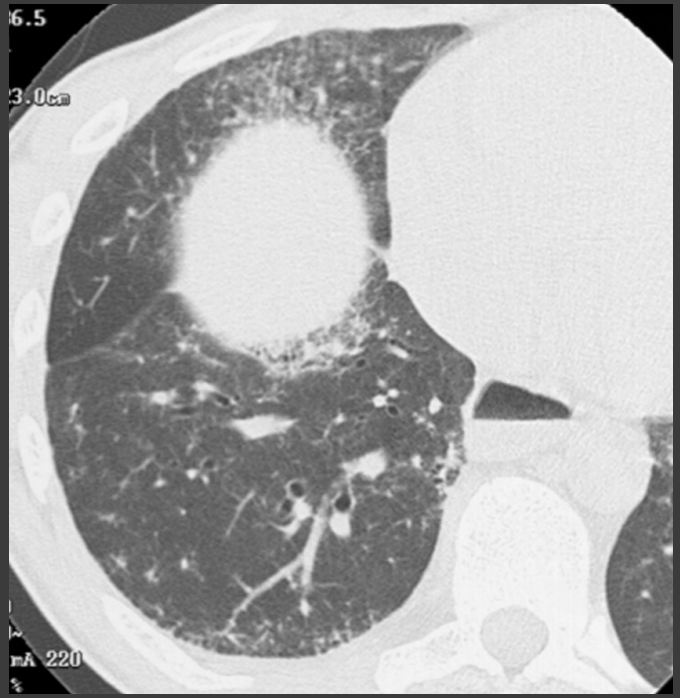
- Findings limited to the following:
  - Dependent lung atelectasis
  - Focal paraspinal fibrosis in close contact with thoracic spine osteophytes
  - Mild focal or unilateral abnormality
  - Smoking-related centrilobular nodularity in the absence of other findings
  - Interstitial edema (e.g. in heart failure)
  - Findings of aspiration (patchy ground glass, tree in bud)
- Preclinical interstitial abnormalities identified during screening of high risk subjects (e.g. rheumatoid arthritis, scleroderma, occupational exposure, familial)
- Findings in patients with known clinical ILD

Fleischner Society Position Paper: Lancet Respir Med 2020;8:726-37

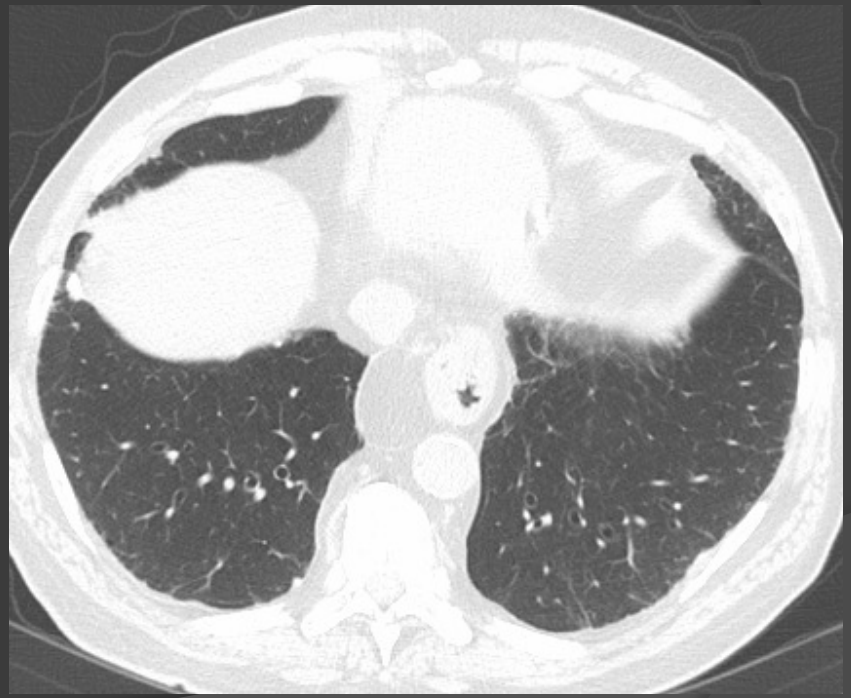


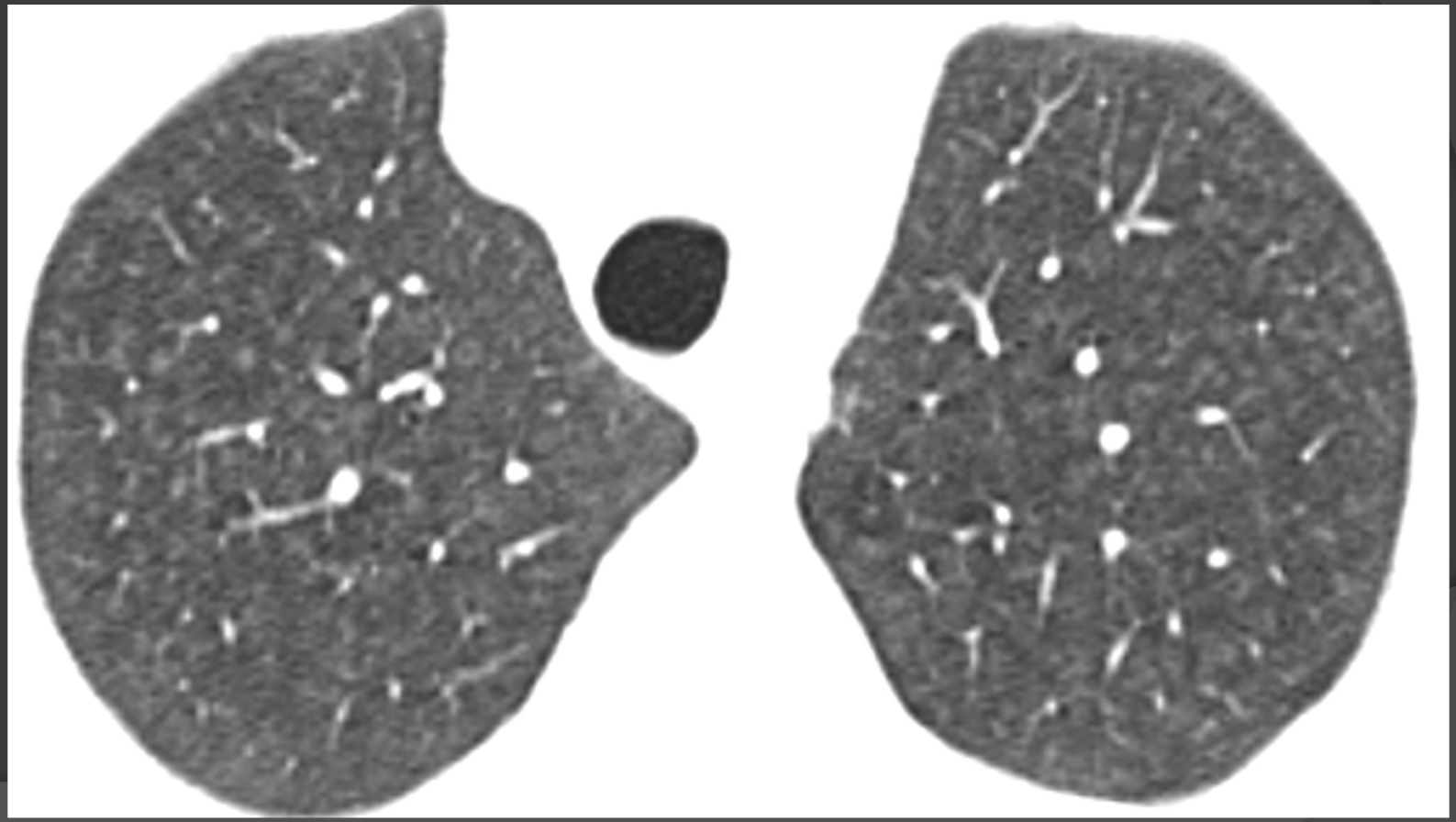


Systemic sclerosis



Asbestosis



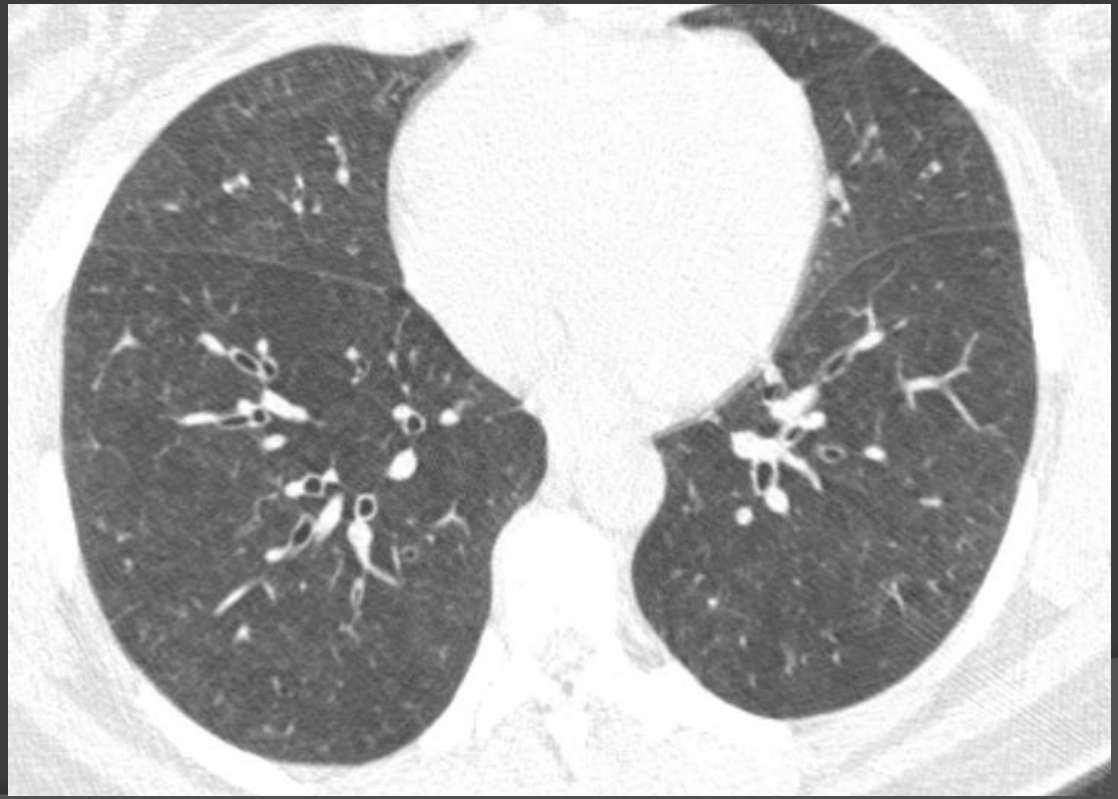


Imaging categories in ILAs

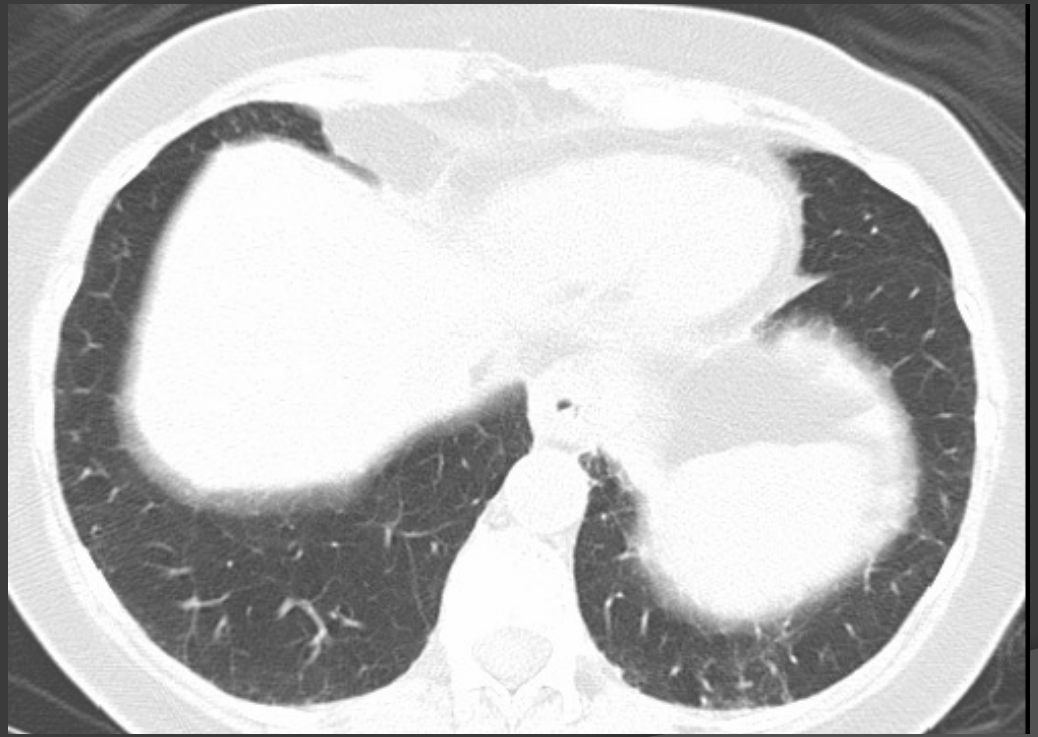
- Non–subpleural
  - Not associated with increased mortality or progression
- Subpleural and nonfibrotic
  - Higher likelihood of progression
- Subpleural and fibrotic
  - Increased mortality and progression risk
  - Classify per typical UIP imaging classification
    - UIP and probable UIP associated with progression and mortality

Fleischner Society Position Paper: Lancet Respir Med 2020;8:726-37

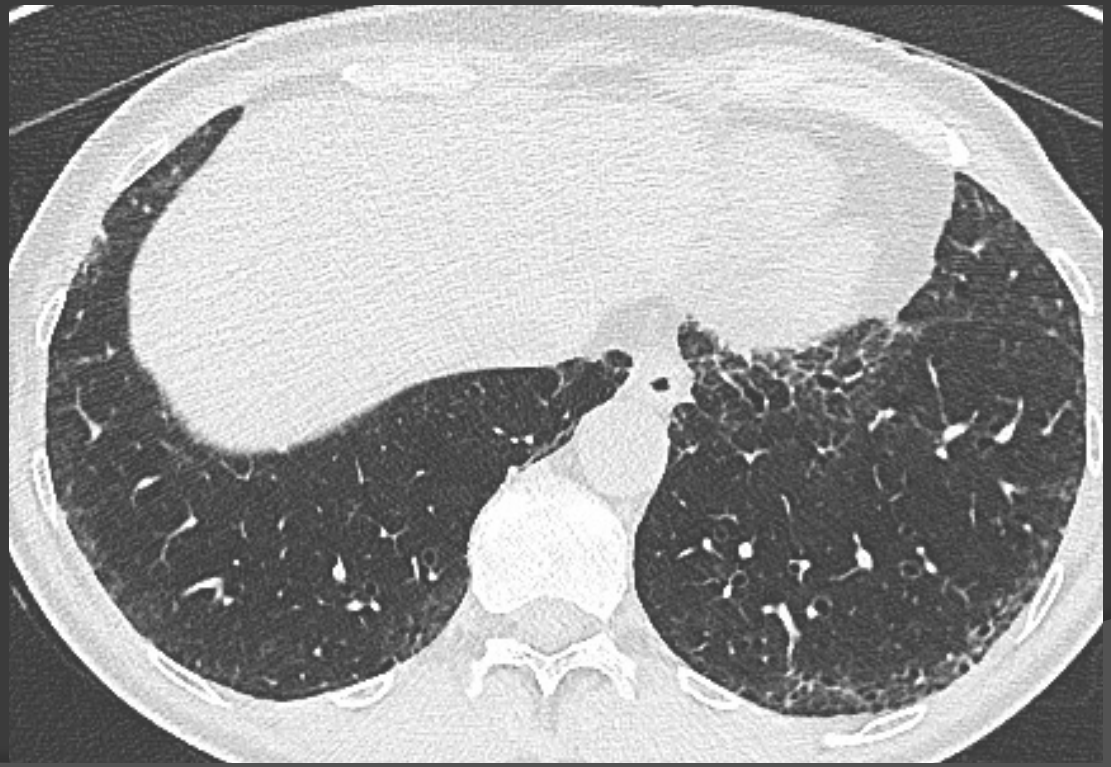
Non-subpleural



Subpleural non-fibrotic



Subpleural fibrotic

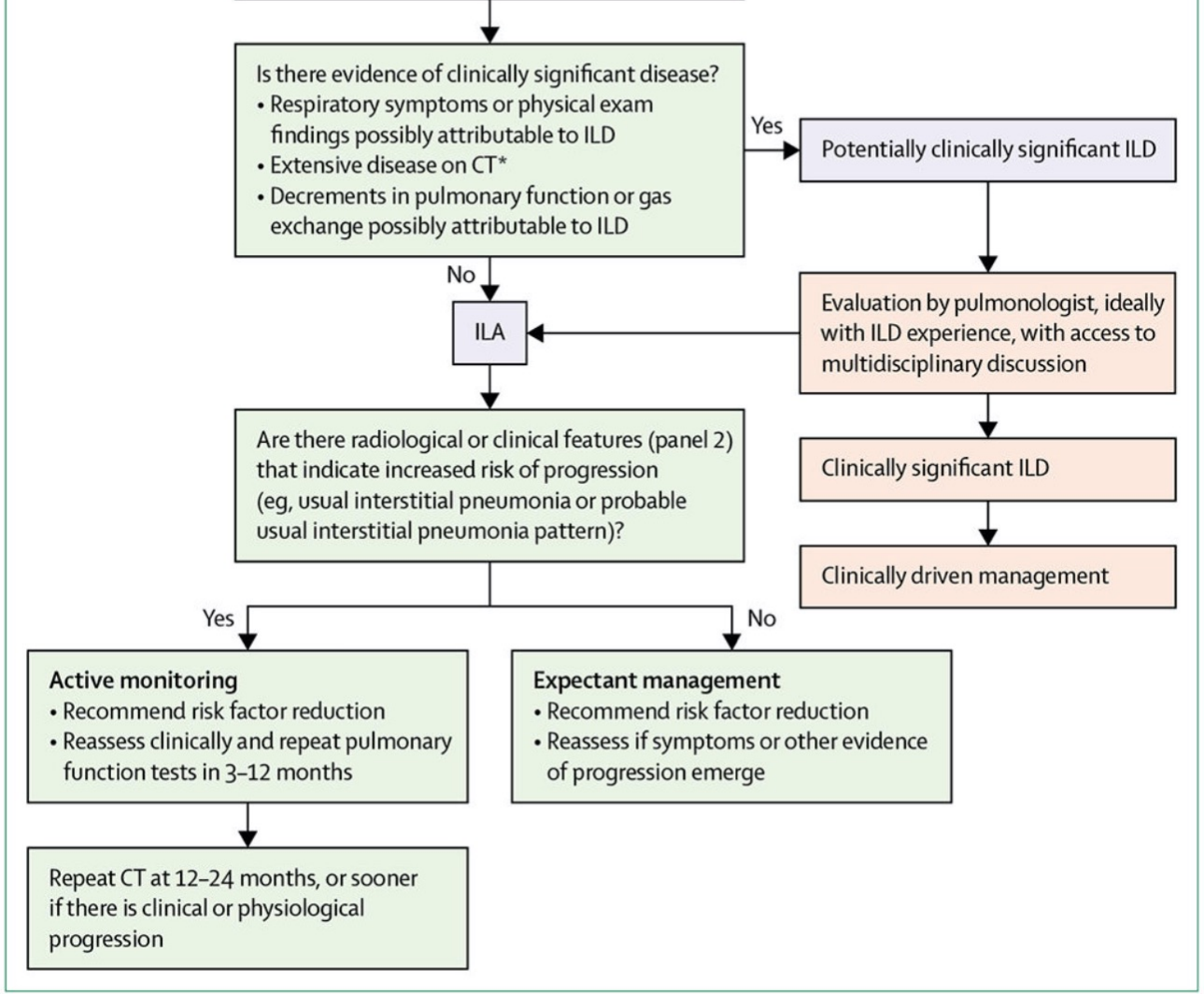


Non-imaging risk factors for progression

- Cigarette smoking
- Increased age
- Inhalational exposures
- Medications (e.g. chemo, immunotherapy)
- MUC5B promoter site polymorphism
- Radiation therapy
- Thoracic surgery
- Physiological or gas exchange findings at lower limits of normal

Fleischner Society Position Paper: Lancet Respir Med 2020;8:726-37
Radiol Clin N Am 60 (2022) 889–899
Radiology 2021; 301:19–34

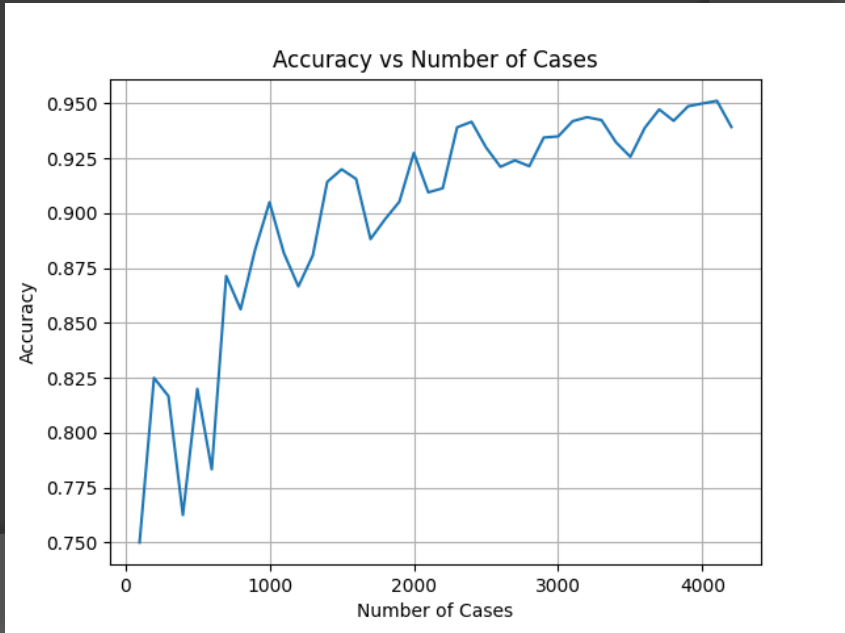
Management



Fleischner Society Position Paper: Lancet Respir Med 2020;8:726-37

How can we help guide ILA patients into the ILA pathway?

- At most centers in the US, most CTs read by general radiologists
- Education key, but even this is limited
- Potential strategies
  - Dedicated reporting templates
  - Quantitative imaging and/or AI
  - NLP tool to screen report
    - A combination likely the answer



Take-home points

- Currently, there are multiple published guidelines
  - Need to be reviewed to understand current state of ILD
- Pulmonary fibrosis practical approach
  - UIP centric approach most logical
  - If not UIP, decide if imaging supports NSIP, HP, or sarcoidosis
  - If not, label as non-IPF (”alternative”) diagnosis or indeterminate for UIP pattern and discuss in MDD
- ILA research is the next big question in ILD

Thank You

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