ILD School
2025

Optimizing HRCT in ILDs: From diagnosis to monitoring

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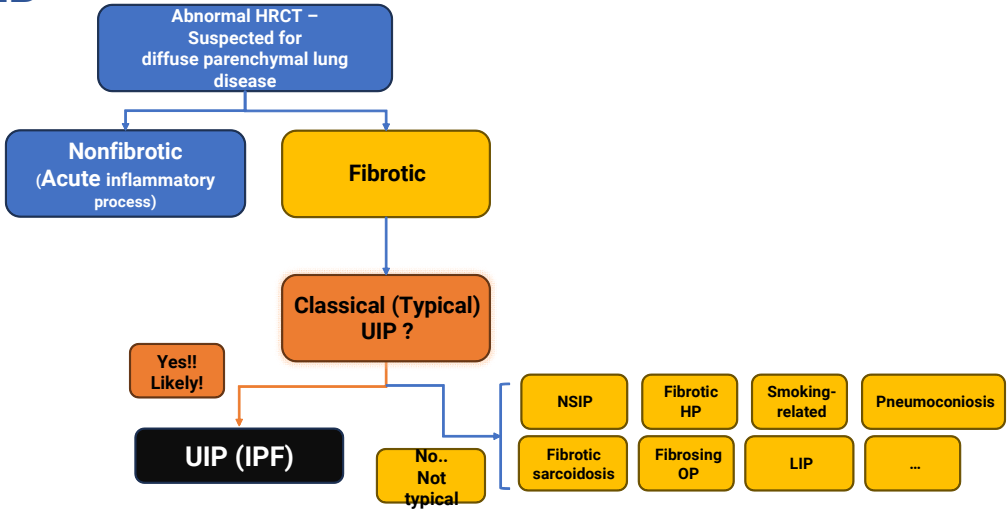
Contents

- Diagnosis
  - Radiologic findings for ILD
  - HRCT pattern – UIP
  - Other CT patterns – clue for diagnosis

- Follow-up
  - PPF criteria
  - Quantitative CT
  - Monitoring complications of pulmonary fibrosis

Diagnosis

HCRT interpretation algorithms for suspected ILD

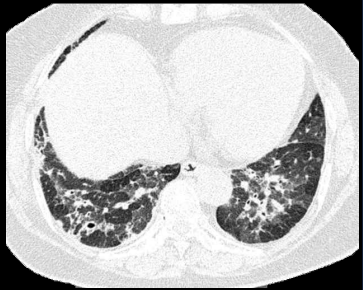


Fibrosing ILD

65/M

62/M

70/F



UIP? NSIP? Fibrotic HP?

Radiologic findings for ILD

CT features

- **Ground-glass opacity**
- **Reticulation**
- **Traction bronchiectasis**
- **Honeycombing cysts**
- **Volume decrease and lung distortion**
- **Three density sign**
- **Nonemphysematous cysts (airspace enlargement with fibrosis)**

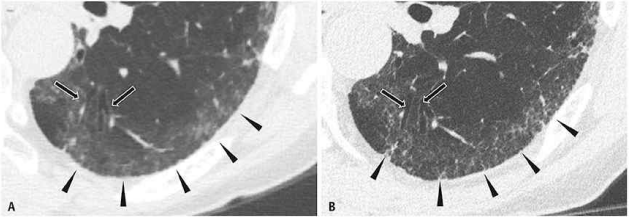
Distribution

- **Upper-/Upper to mid- or lower**
- **Central/peribronchovascular or subpleural**
- **Anterior or posterior**
- **Diffuse or focal**

Radiologic findings for ILD

CT features

- **Ground-glass opacity**
  - **represent reversible inflar**



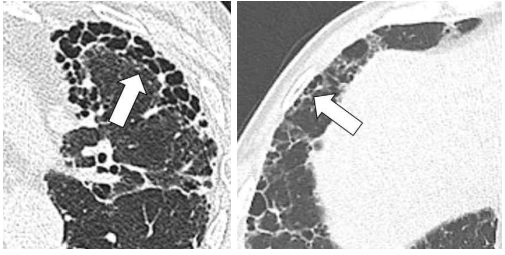
- **Reticulation**
- **Traction bronchiectasis**
- **Honeycombing cysts**
- **Volume decrease and lung distortion**

- **Three density sign**
- **Nonemphysematous cysts (airspace enlargement with fibrosis)**

Esquivel A, et al. KJR 2022.

CT features

- **Honeycombing cysts**
  - **Consist of both dilatation of peripheral airspaces due to surrounding alveolar septal fibrosis and tangentially viewed traction bronchiolectasis**
  - **Most commonly represents advanced traction bronchiolectasis with surrounding alveolar collapse on histopathology ~ continuum from traction bronchiectasis to honeycombing**



- **Higher predictive value for UIP compared with traction bronchiectasis**
- **Multi-layered or single layered**

Raghu G, et al. AJRCCM 2022.

Table 3. High-Resolution Computed Tomography Patterns in Idiopathic Pulmonary Fibrosis

HRCT patterns–diagnostic criteria for IPF

	HRCT Pattern			
	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)
		• 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)

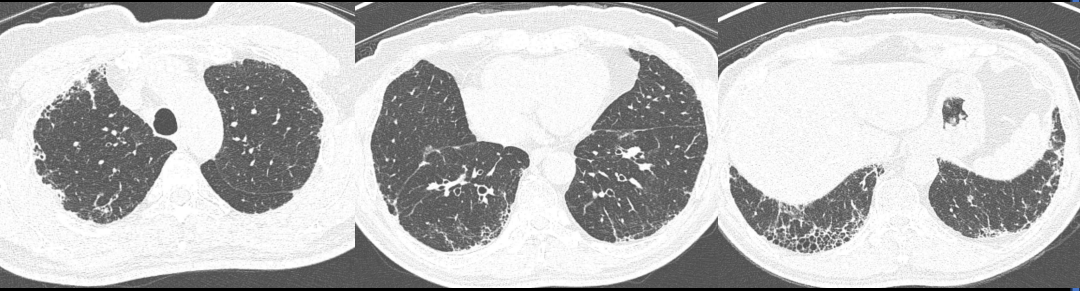
Probable UIP	Indeterminate for UIP
Subpleural and basal predominant; distribution is often heterogeneous	Subpleural and basal predominant
	Subtle reticulation; may have mild GGO or distortion ("early UIP pattern")
Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis	
May have mild GGO	CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")

Raghu G, et al. AJRCCM 2018

Definition of abbreviations: CT = computed tomography; CTD = connective tissue disease; DIP = desquamative interstitial pneumonia; GGO = ground-glass opacity; HP = hypersensitivity pneumonitis; HRCT = high-resolution computed tomography; ILD = interstitial lung disease; IP = interstitial pneumonia; LAM = lymphangioleiomyomatosis; LIP = lymphoid interstitial pneumonia; NSIP = nonspecific interstitial pneumonia; PLCH = pulmonary Langerhans cell histiocytosis; UIP = usual interstitial pneumonia.
The previous term, "early UIP pattern," has been eliminated to avoid confusion with "interstitial lung abnormalities" described in the text. The term "indeterminate for UIP" has been retained for situations in which the HRCT features do not meet UIP or probable UIP criteria and do not explicitly suggest an alternative diagnosis. Adapted from Reference 2.

Raghu G, et al. AJRCCM 2022.

64/M



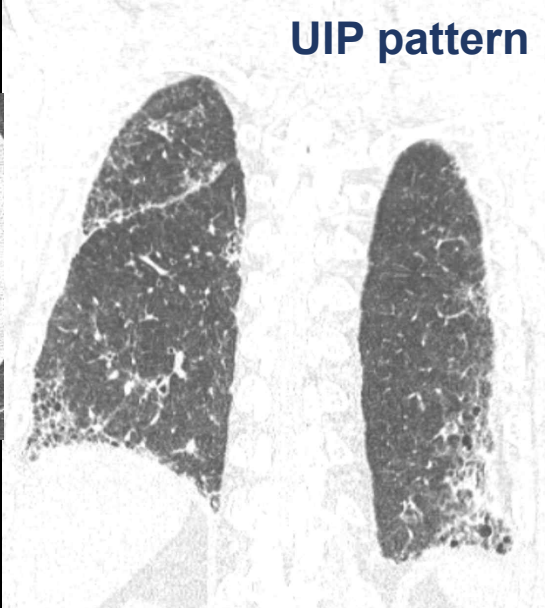
- Subpleural basal predominant
- Honeycombing
- Superimposed with reticulation and mild GGO

UIP pattern

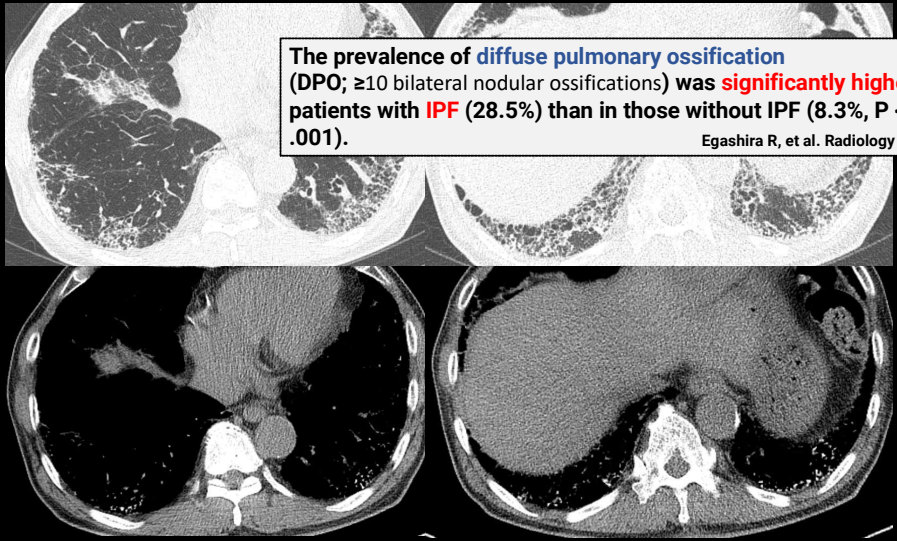
64/M

- Subpleural basal predominant
- Honeycombing

UIP pattern



UIP CT pattern with pulmonary ossification



The prevalence of diffuse pulmonary ossification (DPO; ≥10 bilateral nodular ossifications) was significantly higher in patients with IPF (28.5%) than in those without IPF (8.3%, P < .001).

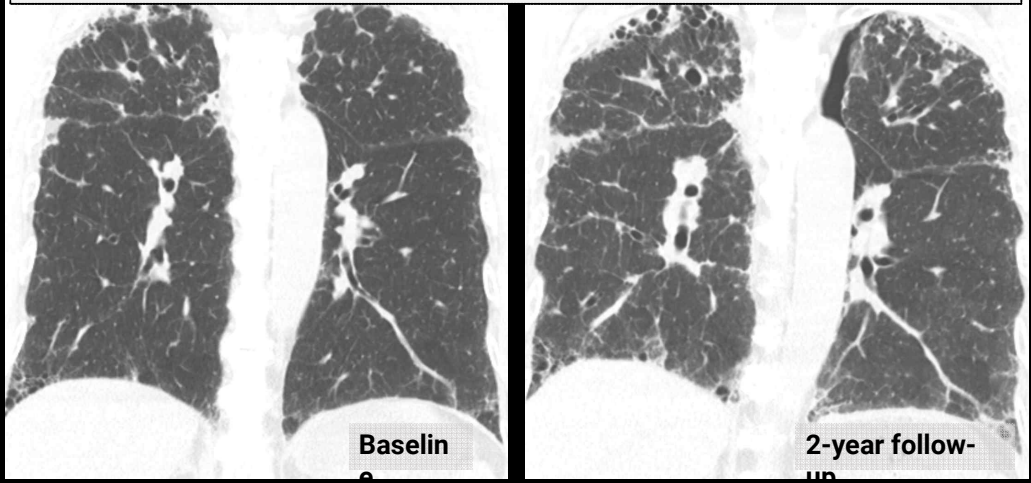
Egashira R, et al. Radiology 2017.

71/M

UIP pattern with PPFE
(Pleuroparenchymal fibroelastosis)
in upper lobes

IPF with PPFE: Lower BMI, more rapid decline in lung function, higher risk of pneumothorax and pneumomediastinum, and poorer survival

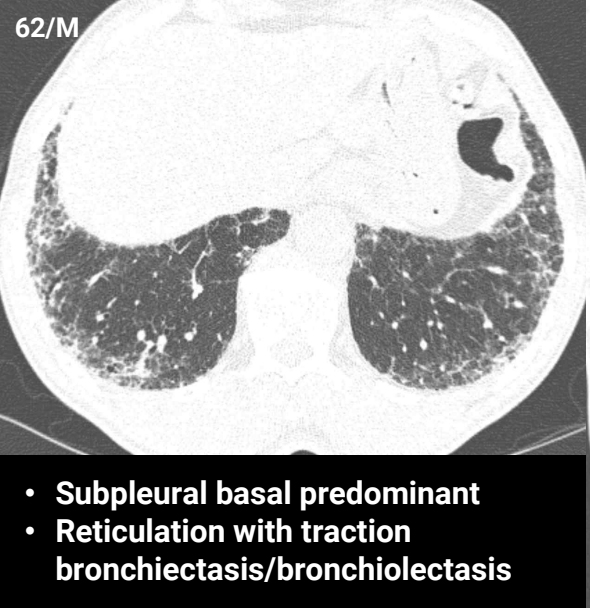
Song JW, et al. Respirology 2020



62/M

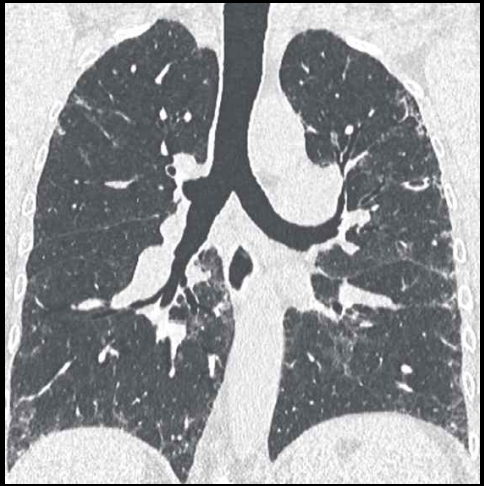
- Subpleural basal predominant
- Reticulation with traction bronchiectasis/bronchiolectasis
- No overt honeycombing
- Absence of subpleural sparing

Probable UIP pattern



- **Subpleural basal predominant**
- **Reticulation with traction bronchiectasis/bronchiolectasis**

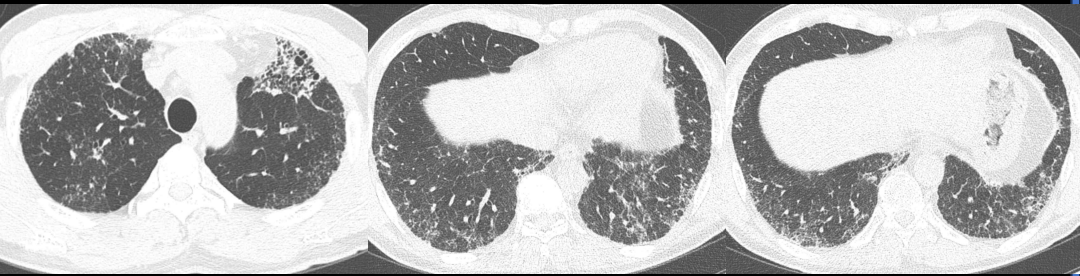
CT pattern indeterminate for UIP



- **Diffuse distribution without subpleural predominance**
- **CT features of lung fibrosis that do not suggest any specific etiology *"truly indeterminate"***

Raghu G, et al. AJRCCM 2022.

57/M



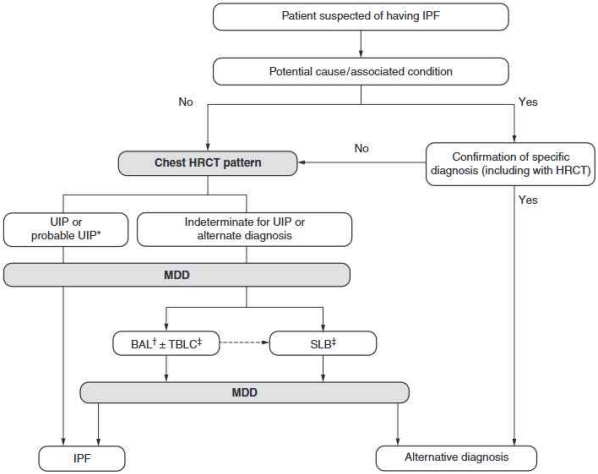
CT pattern indeterminate for UIP

CT pattern and probability of histologic UIP

CT pattern	UIP on histology
UIP	~90%
Probable UIP	~80%
Indeterminate for UIP	~50%
Alternative diagnosis	~50%

Chung JH, et al. Chest 2015

Diagnostic algorithm for IPF



Raghu G, et al. AJRCCM 2022.

IPF suspected*		Histopathology pattern†			
		UIP	Probable UIP	Indeterminate for UIP or biopsy not performed	Alternative diagnosis
HRCT pattern	UIP	IPF	IPF	IPF	Non-IPF dx
	Probable UIP	IPF	IPF	IPF (Likely)‡	Non-IPF dx
	Indeterminate	IPF	IPF (Likely)‡	Indeterminate§	Non-IPF dx
	Alternative diagnosis	IPF (Likely)‡	Indeterminate§	Non-IPF dx	Non-IPF dx

Raghu G, et al. AJRCCM 2022.

CT findings suggestive of alternative diagnosis

Distribution

- **Peribronchovascular predominant with subpleural sparing (NSIP)**
- **Perilymphatic distribution (sarcoidosis)**
- **Upper or mid lung (fibrotic HP, CTD-ILD, and sarcoidosis)**
- **Subpleural sparing (NSIP or smoking-related IP)**

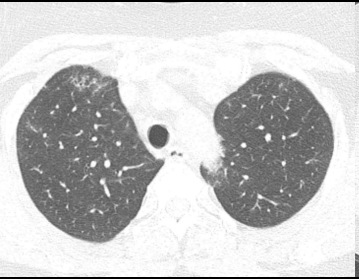
Lung findings

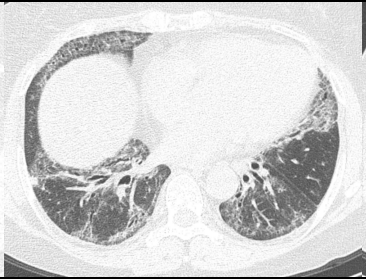
- **Cyst (LAM, PLCH, LIP and DIP)**
- **Mosaic attenuation or three density sign (HP)**
- **Predominant GGO (Smoking, NSIP, HP, ..)**
- **Centrilobular nodules (HP, smoking, ..)**
- **Consolidation (OP, ..)**

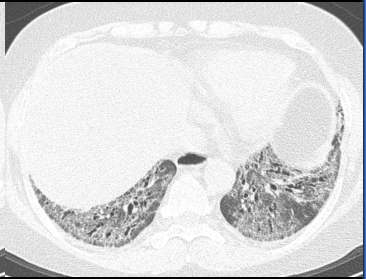
Mediastinal findings

- **Pleural plaques (asbestosis)**
- **Dilated esophagus (CTD)**

62/F







- Subpleural sparing
- Peribronchovascular distribution

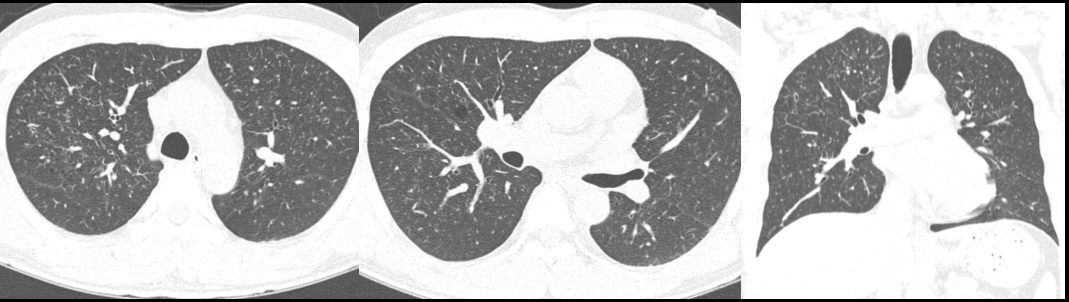
NSIP pattern SSc-ILD

72/F

- Cysts
- Peribronchovascular distribution

Sjogren syndrome with LIP on right lung wedge resection

43/M

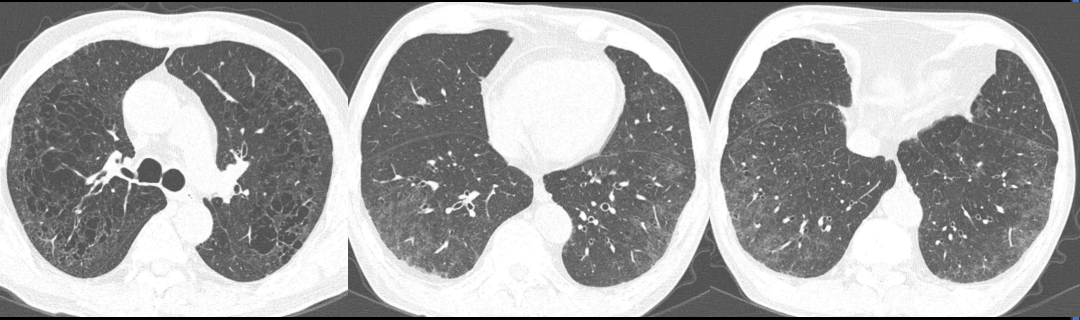


- **Cysts**
- **Nodules**

Langerhans cell histiocytosis

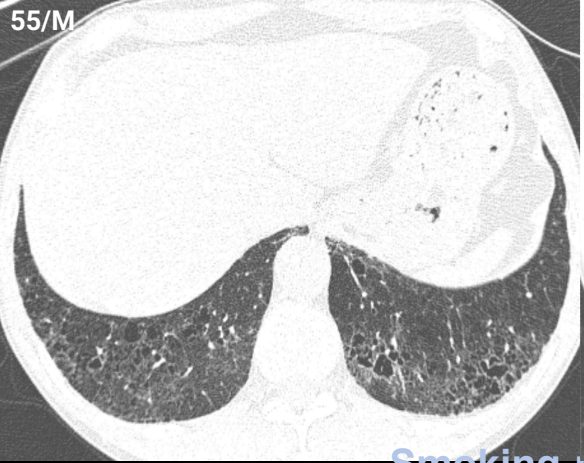
- Multifocal variable sized small nodules and cyst with bizarre shape in both lungs with sparing of the costophrenic recesses

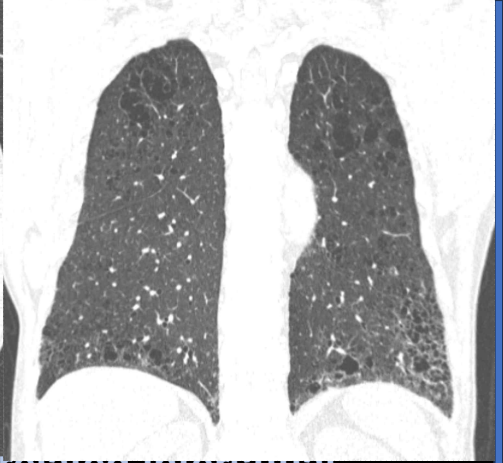
41/M



- GGOs
- Ill-defined nodules
- Subpleural sparing

Respiratory bronchiolitis-ILD





Smoking-related interstitial fibrosis

- GGOs
- Nonemphysematous cysts
  - Thin- or thick-walled irregular cysts; clustered, confluent or layered
- Subpleural sparing

CT findings of airspace enlargement with fibrosis (or SRIF), honeycombing, and paraseptal emphysema

Chae KJ, et al. Radiology 2024

Table 1: CT Findings of Airspace Enlargement with Fibrosis, Honeycombing, and Paraseptal Emphysema

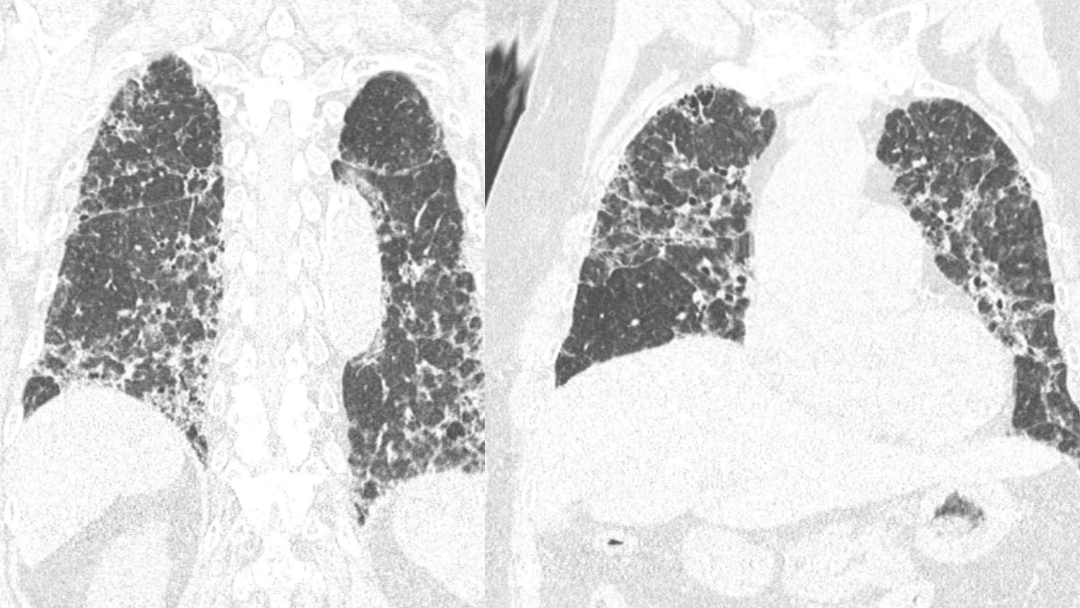
CT Feature	Honeycombing	Paraseptal Emphysema	AEF/SRIF
Characteristic appearance	Clustered cystic airspaces, typically of comparable diameters Multilayered cysts, which tend to share walls	Well-demarcated rounded or cystlike juxtapleural lucencies up to 1 cm in size Usually larger than cysts of honeycombing Usually single-layered cysts without stacking	Variably sized thin-walled cysts, which are mostly multilayered, confluent, or separated by normal lung parenchyma
Signs of fibrosis	Usually present (in addition to honeycombing)	Absent	Usually sparse or absent
Location on coronal view	Mainly the basal area of the lower lobe	Predominantly the upper lobe	Upper lobe, upper and middle portions of the lower lobe
Location on axial view	Usually subpleural location	Juxtapleural location, sometimes including along an interlobar fissure	Often sparing the immediate subpleural lung
Cyst diameter	Usually ≤5 mm	Often >1 cm	Usually >5 mm

- *AEF/SRIF: often spare the immediate subpleural lung, asymmetry, heterogeneous cyst size*
- *CPFE → Emphysema with UIP pattern / Emphysema with non-UIP pattern (NSIP, SRIF ..)*

78/F

- Multifocal (profound) mosaic attenuation
- Peribronchovascular distribution
- Diffuse distribution

Fibrotic HP (hypersensitivity pneumonitis)



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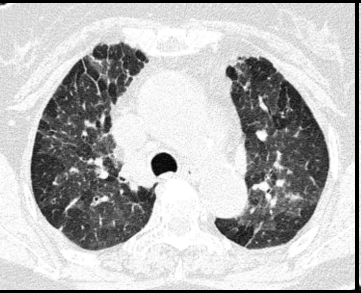
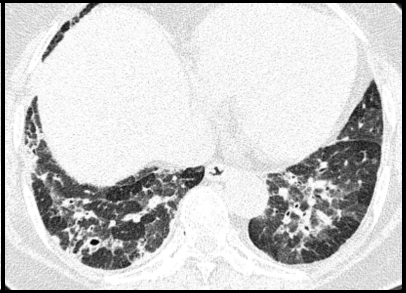
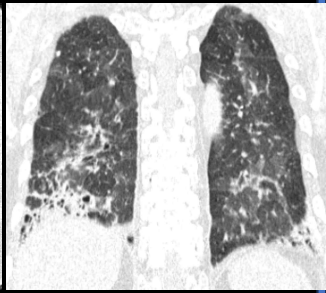






Fibrotic HP (hypersensitivity pneumonitis)

- Combination of three findings on inspiratory image: normal / low attenuation / GGO
- Sharply demarcated from each other
- Indicative of a mixed obstructive (low-attenuation) and infiltrative (GGO) process
- Highly specific for fibrotic HP; has not been shown HP

= Headcheese sign

Three-density pattern

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis of Hypersensitivity Pneumonitis in Adults

An Official ATS/JRS/ALAT Clinical Practice Guideline

Ganesh Raghu, Martine Remy-Jardin, Christopher J. Ryerson, Jeffrey L. Myers, Michael Kreuter, Martina Vasakova, Elena Bargagli, Jonathan H. Chung, Bridget F. Collins, Elisabeth Bendstrup, Hassan A. Chami, Abigail T. Chua, Tamera J. Corte, Jean-Charles Dalphin[1], Sonye K. Danoff, Javier Diaz-Mendoza, Abhijit Duggal, Ryoko Egashira, Thomas Ewing, Mridu Gulati, Yoshikazu Inoue, Alex R. Jenkins, Kerri A. Johannson, Takeshi Johkoh, Maximiliano Tamae-Kakazu, Masanori Kitaichi, Shandra L. Knight, Dirk Koschel, David J. Lederer, Yolanda Mageto, Lisa A. Maier, Carlos Matiz, Ferran Morell, Andrew G. Nicholson, Setu Patolia, Carlos A. Pereira, Elisabetta A. Renzoni, 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

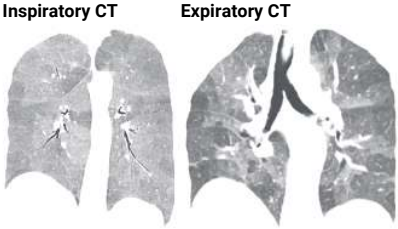
Raghu G, et al. AJRCCM 2020.

Acute, Subacute, or Chronic ➡

- **Nonfibrotic HP**
- **Fibrotic HP**

Typical HRCT features of nonfibrotic HP pattern

- At least one, both in a diffuse distribution
  - HRCT abnormality indicative of parenchymal infiltration
    - GGOs
    - Mosaic attenuation (inspiratory image)
  - HRCT abnormality indicative of small airway disease
    - Ill-defined, centrilobular nodules
    - Air trapping



Raghu G, et al. AJRCCM 2020.

HRCT features of the fibrotic HP pattern

HRCT Pattern	Typical HP	Compatible with HP	Indeterminate for HP
Description	The "typical HP" pattern is suggestive of a diagnosis of HP. It requires *a*) an HRCT pattern of lung fibrosis (as listed below) in one of the distributions and *b*) at least one abnormality that is indicative of small airway disease	"Compatible-with-HP" patterns exist when the HRCT pattern and/or distribution of lung fibrosis varies from that of the typical HP pattern; the variant fibrosis should be accompanied by signs of small airway disease	The "indeterminate-for-HP" pattern exists when the HRCT is neither suggestive nor compatible with a typical and probable HP pattern
Relevant radiological findings	HRCT abnormalities indicative of lung fibrosis are most commonly composed of irregular linear opacities/ coarse reticulation with lung distortion; traction bronchiectasis and honeycombing may be present but do not predominate The distribution of fibrosis may be: • Random both axially and craniocaudally or • Mid lung zone–predominant or • Relatively spared in the lower lung zones HRCT abnormalities indicative of small airway disease: • Ill-defined, centrilobular nodules and/or GGOs • Mosaic attenuation, three-density pattern,* and/or air trapping (*often in a lobular distribution*)	Variant patterns of lung fibrosis: • UIP pattern: basal and subpleural distribution of honeycombing with/without traction bronchiectasis (*per 2018 diagnosis of IPF guidelines* [20]) • Extensive GGOs with superimposed subtle features of lung fibrosis Variant (predominant) distributions of lung fibrosis: • Axial: penbronchovascular, subpleural areas • Craniocaudal: upper lung zones HRCT abnormalities indicative of small airway disease: • Ill-defined centrilobular nodules, or • Three-density pattern* and/ or air trapping	Lone patterns (i.e., not accompanied by other findings suggestive of HP) of: • UIP pattern (*as per 2018 IPF diagnosis guidelines* [20]) • Probable UIP pattern (*as per 2018 IPF diagnosis guidelines* [20]) • Indeterminate pattern for UIP (*as per 2018 IPF diagnosis guidelines* [20]) • Fibrotic NSIP pattern • Organizing pneumonia–like pattern • Truly indeterminate HRCT pattern

Raghu G, et al. AJRCCM 2020.

Connective tissue disease (CTD)-related ILD

Table 1
Frequency of Pulmonary Disease Involvement in Various Collagen Vascular Diseases

Pulmonary Disease	Systemic Lupus Erythematosus	Rheumatoid Arthritis	Progressive Systemic Sclerosis	Polymyositis or Dermatomyositis	Sjögren Syndrome	Mixed Connective Tissue Disease
Usual interstitial pneumonia	+	++	++	++	+	++
Nonspecific interstitial pneumonia	+	+	++++	++++	+	+++
Diffuse alveolar damage	++	+	+	+	. . .	. . .
BOOP	+	. . .	+	++	+	. . .
Lymphocytic interstitial pneumonia	. . .	. . .	. . .	. . .	+++	+
Hemorrhage	+++	. . .	. . .	. . .	. . .	. . .
Airway disease	. . .	++	. . .	. . .	++	. . .

Note.—Plus signs (+) indicate relative frequency of pulmonary disease involvement (+ = lowest frequency, ++++ = highest frequency). Empty cells (. . .) indicate no pulmonary disease involvement.

Kim EA, et al. RadioGraphics 2002.

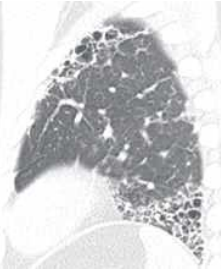
Connective tissue disease (CTD)-related ILD

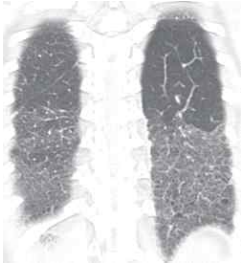
Clues to think of CTD >> IIP on imaging:

- **Presence of other thoracic manifestation**
  - **Pleural/pericardial effusion, thickening**
  - **Esophageal dilatation (scleroderma)**
  - **Airway involvement**
  - **Pulmonary artery dilatation**
  - **Musculoskeletal: bone erosion, soft tissue calcification**

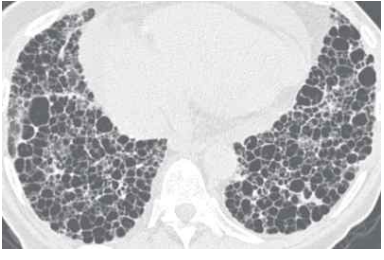
- **NSIP, OP, LIP >> UIP**
- **CTD-UIP pattern** *Chung HJ, et al. AJR 2018*

Connective tissue disease (CTD)-related UIP





Anterior upper lobe sign **Straight edge sign**

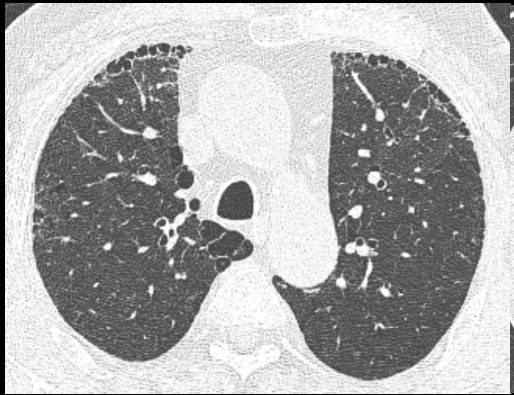


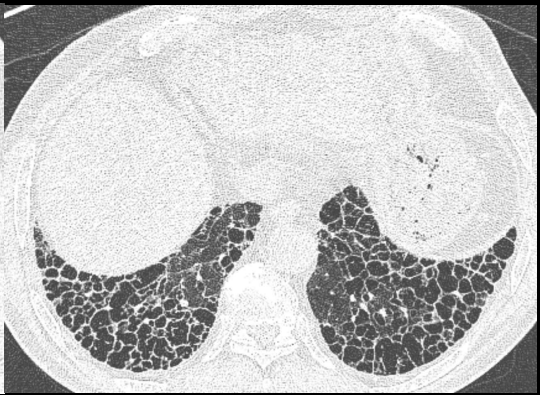
CT Sign	Percentage of Patients With IPF With CT Sign ($n = 133$)	Percentage of Patients With CTD-ILD With CT Sign ($n = 63$)	Sensitivity (%)	Specificity (%)	Positive Likelihood Ratio	Negative Likelihood Ratio	p
Anterior upper lobe	12.8 (17)	25.4 (16)	25.4	87.2	1.99	0.86	0.028[a]
Exuberant honeycombing	6.0 (8)	22.2 (14)	22.2	94.0	3.69	0.83	< 0.001[a]
Straight edge	6.0 (8)	25.4 (16)	25.4	94.0	4.22	0.79	< 0.001[a]
More than one sign	4.5 (6)	23.8 (15)	23.8	95.5	5.28	0.80	< 0.001[a]
Any CT sign	19.5 (26)	42.9 (27)	42.9	80.5	2.19	0.71	< 0.001

Exuberant honeycombing sign

Chung JH, et al. AJR 2018

Connective tissue disease (CTD)-related UIP





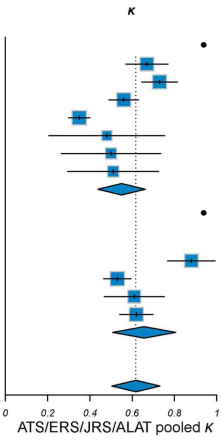
51/M RA-associated ILD

- Anterior upper lobe sign
- Exuberant honeycombing sign

Interreader agreement

Study / Subgroup	Size	Number of observers	κ	95%–CI	Weight
2011 ATS/ERS/JRS/ALAT					
Assayag 2014	69	2	0.67	[0.57; 0.77]	9.9%
Brownell 2017	385	2	0.73	[0.64; 0.81]	10.3%
Choe 2021	535	3	0.56	[0.49; 0.63]	10.6%
Kim 2017	86	5	0.35	[0.30; 0.40]	10.9%
Walsh 2016	150	22	0.48	[0.21; 0.75]	5.5%
Walsh 2016	150	42	0.50	[0.26; 0.74]	6.4%
Walsh 2016	150	27	0.51	[0.29; 0.73]	6.8%
Random effects model			0.55	[0.44; 0.66]	60.5%
Heterogeneity: I^2 = 92%, τ^2 = 0.0172, p < 0.001					
2018 ATS/ERS/JRS/ALAT					
Alnaghy 2022	65	2	0.88	[0.77; 0.99]	9.6%
Choe 2021	535	3	0.53	[0.46; 0.59]	10.7%
Westphalen 2022	44	4	0.61	[0.47; 0.75]	8.8%
Widell 2020	126	2	0.62	[0.54; 0.70]	10.4%
Random effects model			0.66	[0.51; 0.81]	39.5%
Heterogeneity: I^2 = 89%, τ^2 = 0.0204, p < 0.001					
Three-level random effects model			**0.61**	**[0.48; 0.74]**	**100.0%**

Heterogeneity: I^2 = 92%, τ^2 = 0.0185, p < 0.001
Test for subgroup differences: χ^2_1 = 1.27, df = 1 (p = 0.26)



- **Moderate interobserver agreement for ILD findings (traction bronchiectasis, honeycombing, reticulation): pooled κ of 0.56.**
- **Moderate interobserver agreement for IPF diagnostic categories: pooled κ of 0.61.**

Delaney L, et al. Radiology 2024

Follow-up

Progressive pulmonary fibrosis

Definition of PPF

In a patient with ILD of known or unknown etiology other than IPF who has radiological evidence of pulmonary fibrosis, PPF is defined as at least two of the following three criteria occurring within the past year with no alternative explanation*:

1 Worsening respiratory symptoms

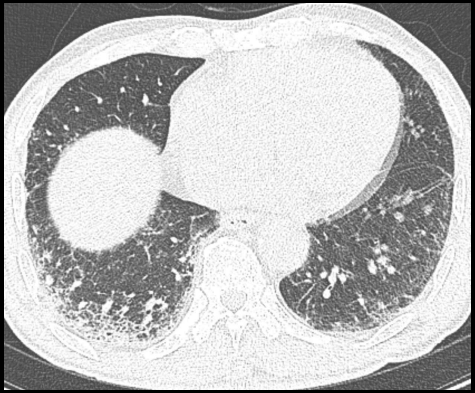
2 Physiological evidence of disease progression (either of the following):
- a. Absolute decline in FVC ⩾5% predicted within 1 yr of follow-up
- b. Absolute decline in D_{LCO} (corrected for Hb) ⩾10% predicted within 1 yr of follow-up

3 Radiological evidence of disease progression (one or more of the following):
- a. Increased extent or severity of traction bronchiectasis and bronchiolectasis
- b. New ground-glass opacity with traction bronchiectasis
- c. New fine reticulation
- d. Increased extent or increased coarseness of reticular abnormality
- e. New or increased honeycombing
- f. Increased lobar volume loss

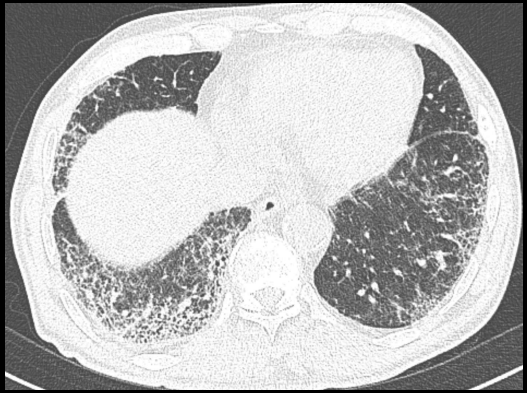
Raghu G, et al. AJRCCM 2022.

Radiologic criterion for fibrotic progression

Baseline



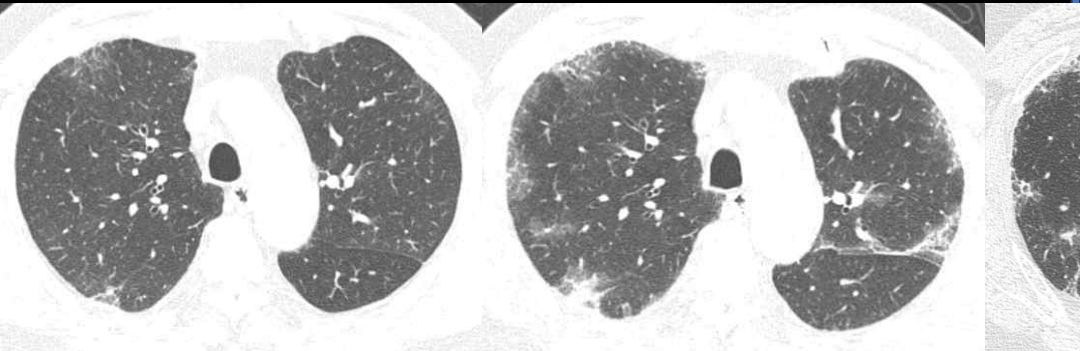
1 year follow-up



Baseline

12-month follow-up CT

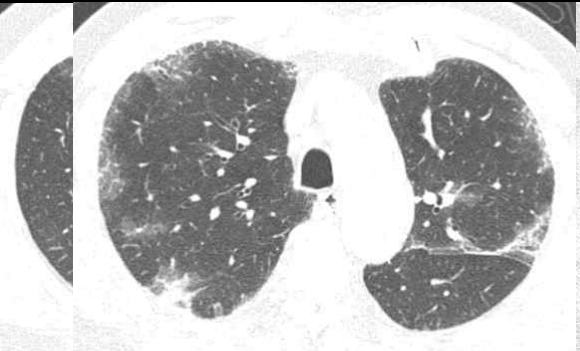
68/M



Baseline

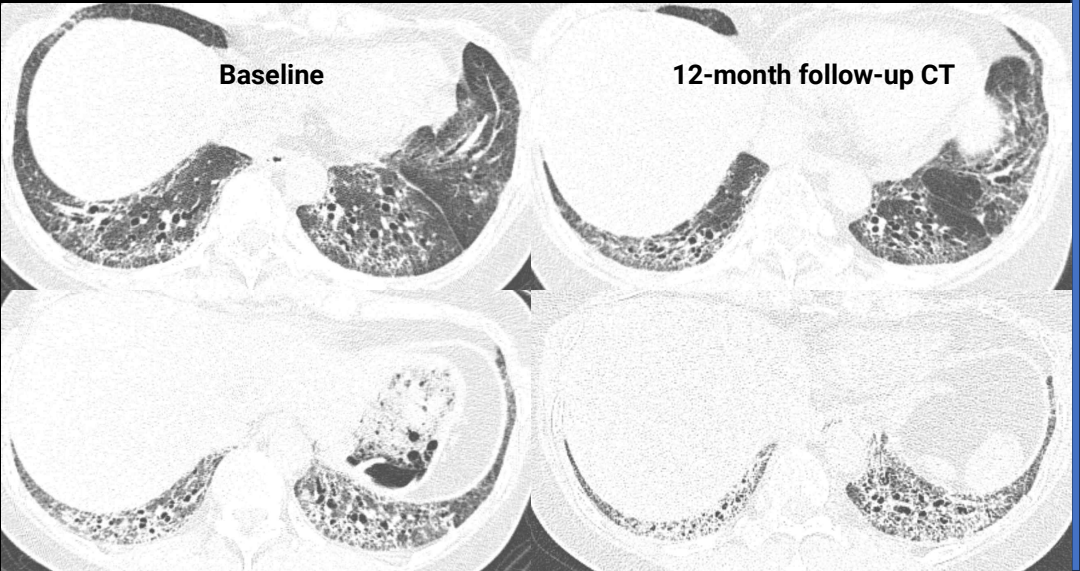
15 month follow-up

68/M

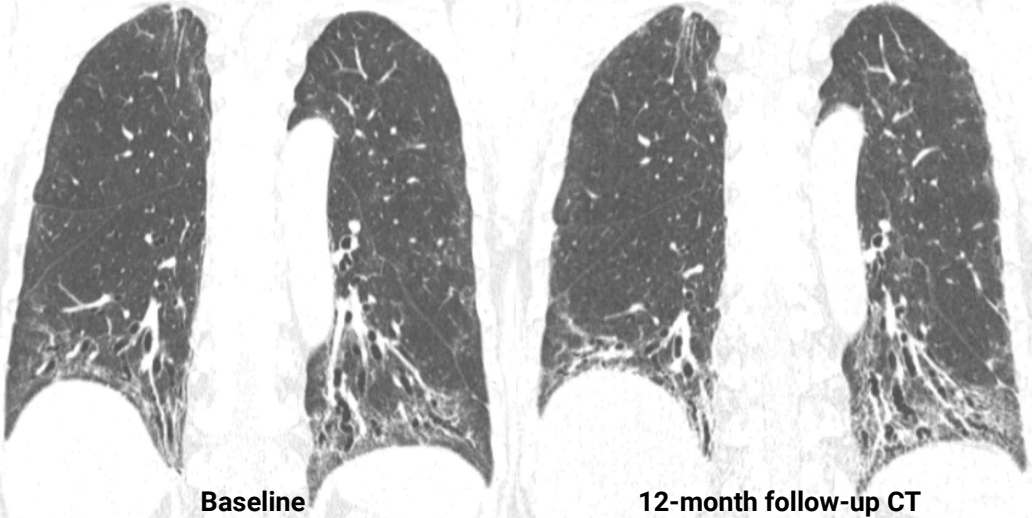


15 month follow-up

36 month follow-up


Baseline
12-month follow-up CT

53/F idiopathic nonspecific interstitial pneumonia



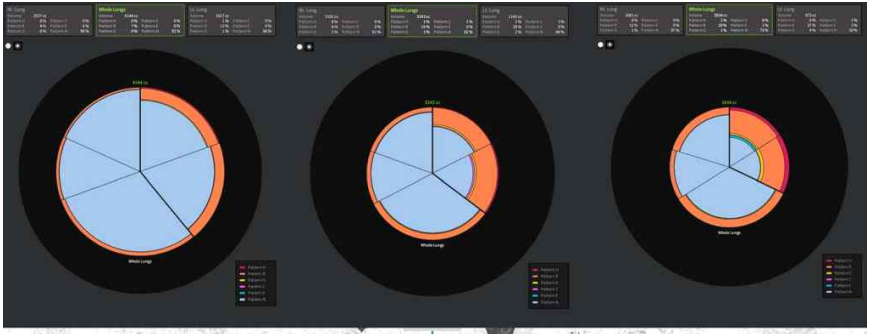
Baseline

12-month follow-up CT

Why we need automated quantification for follow-up evaluation?

- **Minimize/remove inter-reader variability**
- **Objective assessment of different components of disease (GGO, reticulation, honeycombing…)**
- **Detection of early disease**
- **Objective assessment of follow-up changes**
  - Structural report for disease extent and its change
- **Measure/predict treatment effect**
  - Select patients for trial enrolment based on extent of fibrosis

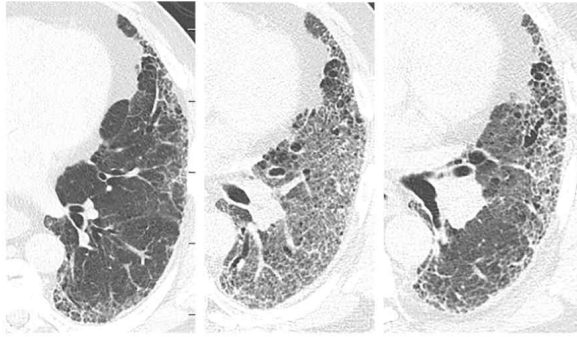
Flaherty KR, et al. AJRCCM 2003
Choe J, et al. Invest Radiol 2025



Choe J, et al.
Invest Radiol 2025

Monitoring complications of pulmonary fibrosis

- Pulmonary hypertension
- Acute exacerbation (AE)
- Infection
- Lung cancer
- Pulmonary thromboembolism
- Pneumothorax ..



AE in patients with IPF

Hobbs S, et al. Radiology: Cardiothoracic imaging 2021

Monitoring complications of pulmonary fibrosis

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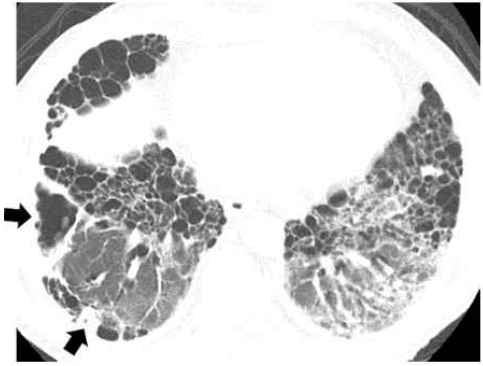


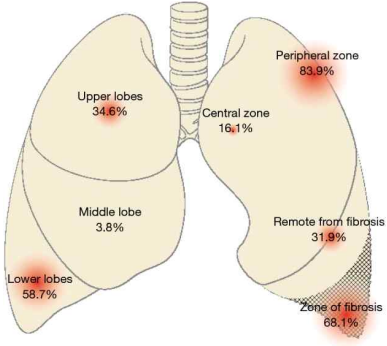
Mycobacterium avium-intracellulare complex in patients with IPF

Chae KJ, et al. Radiology 2024

Surveillance of lung cancer in lung fibrosis

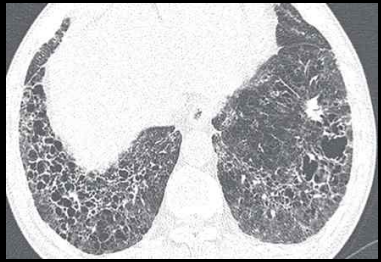
- **3.5- to 7.3-times higher in ILD with 10-20% develop lung cancer**
- **Increase in risk of lung cancer in CPFE**

  (Squamous cell carcinoma > adenocarcinoma)
- **Frequent location**
  - Mostly manifests as peripheral tumors (83.9%) developing within/near fibrotic areas (68.1%)
  - Indistinct interface between the mass and adjacent honeycombing on CT
  - *Comparison with previous imaging is important!*
- **Challenges in accurate Tumor (T) and Nodal (N) staging**



Kazuma K, et al. JCAT 2006
Lloyd CR, et al. BJR 2011
Naccache JM, et al. JTD 2018

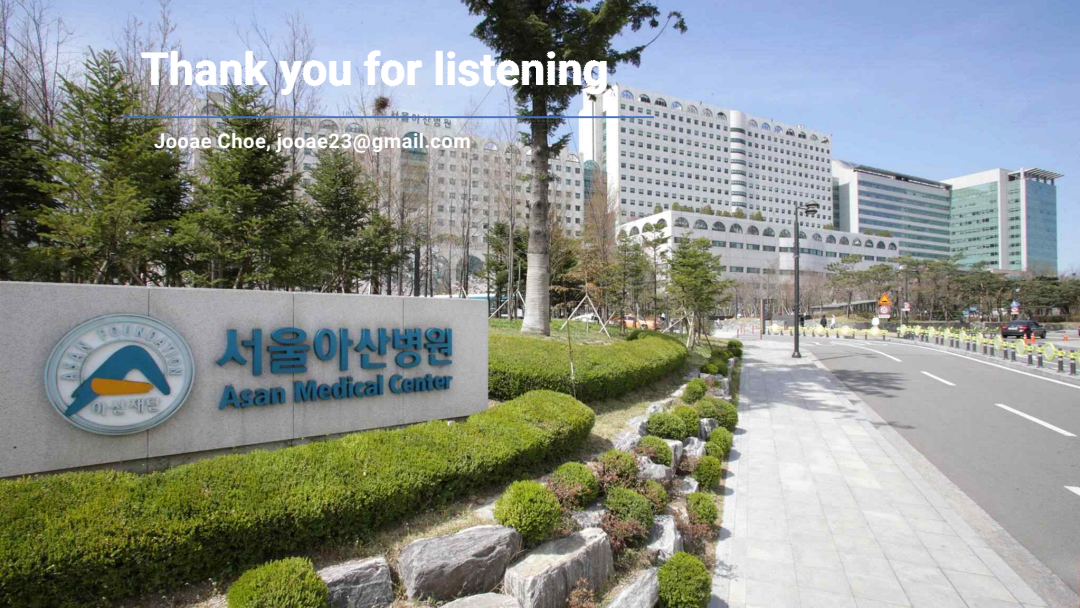
Surveillance of lung cancer in lung fibrosis



Oh SY, et al AJR 2014

Summary

- Key CT findings and diagnostic approach to ILD
  - Nonfibrotic vs. fibrotic
  - Identify key features (specific disease patterns) and anatomic distributions
- HCRT patterns in IPF
- Differentiating points for common alternative diagnoses to IPF
- Follow-up evaluation of ILD
  - Defining PPF: criteria for radiologic progression
  - Complication: AE, lung cancer ..



Thank you for listening

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