ILD 진단하기 – 임상적 접근

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Interstitial Lung Disease

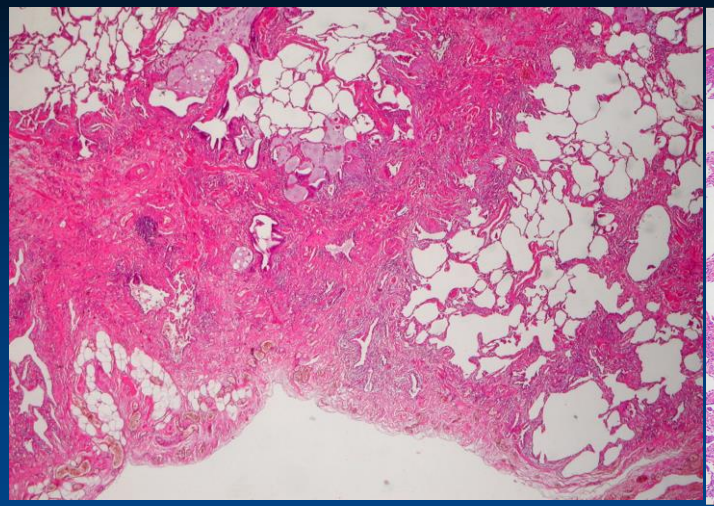
- Diverse group of disorders that involve the distal pulmonary parenchyma

- Patients typically presented with
  - Progressive dyspnea and cough
  - Abnormal pulmonary physiology
  - Abnormal CXR and/or HRCT

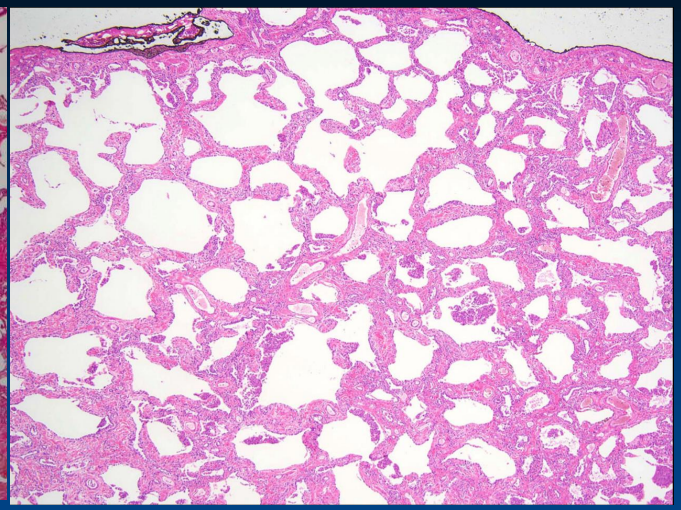
- Idiopathic or associated with systemic diseases (CTDs) or enviromental exposures

American Thoracic Society; European Respiratory Society. *Am J Respir Crit Care Med*. 2002;165:277-304.

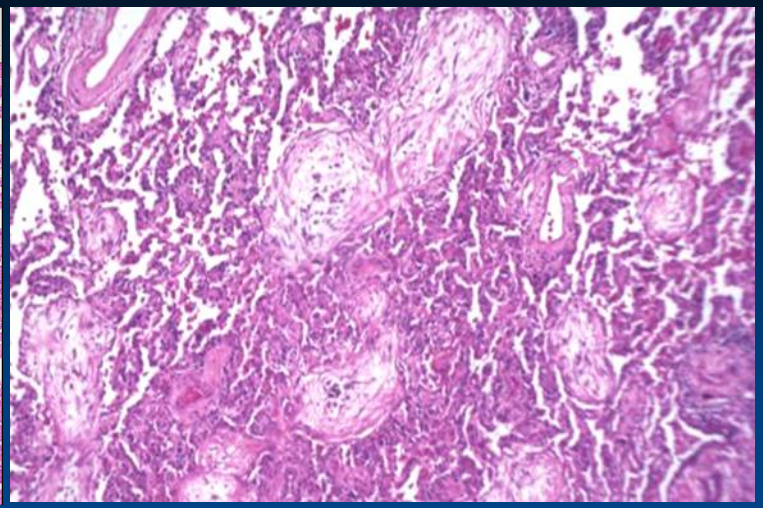
- UIP pattern



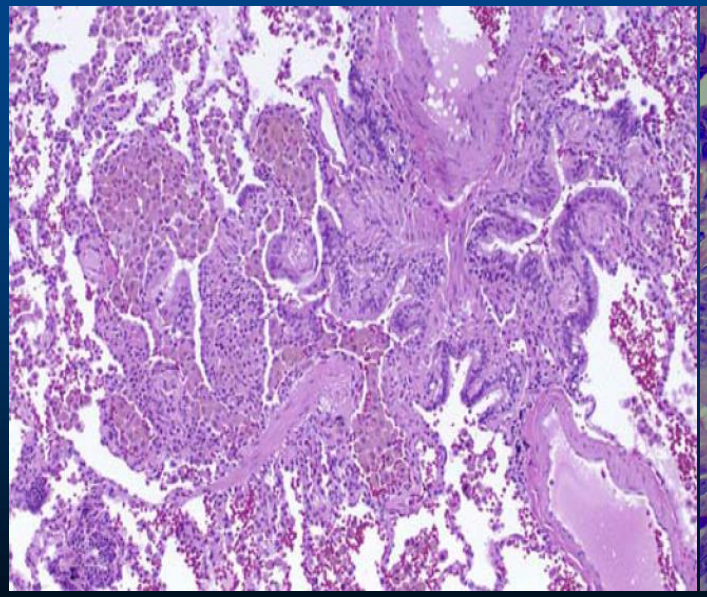
- NSIP pattern



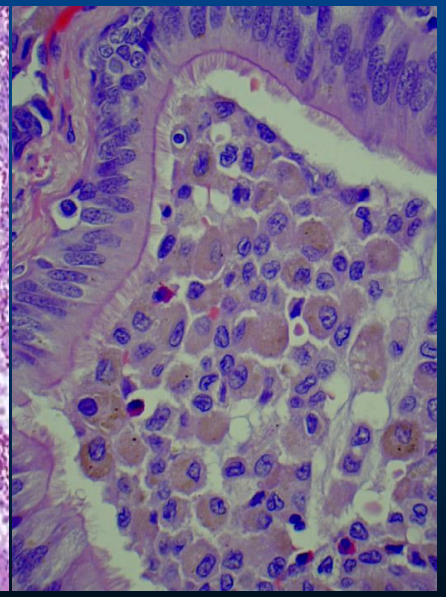
- OP pattern



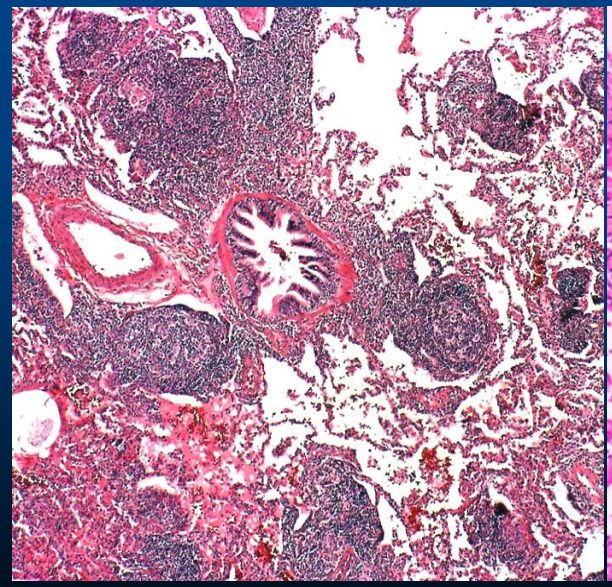
- DIP pattern



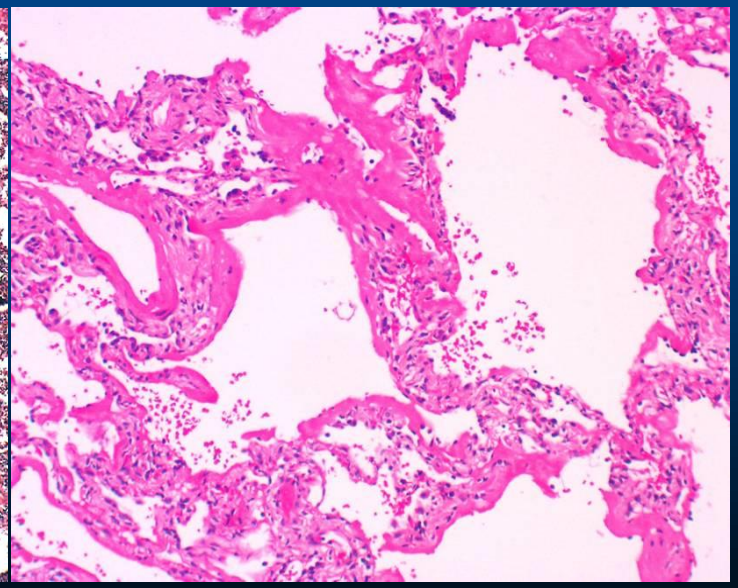
- RB pattern



- LIP pattern

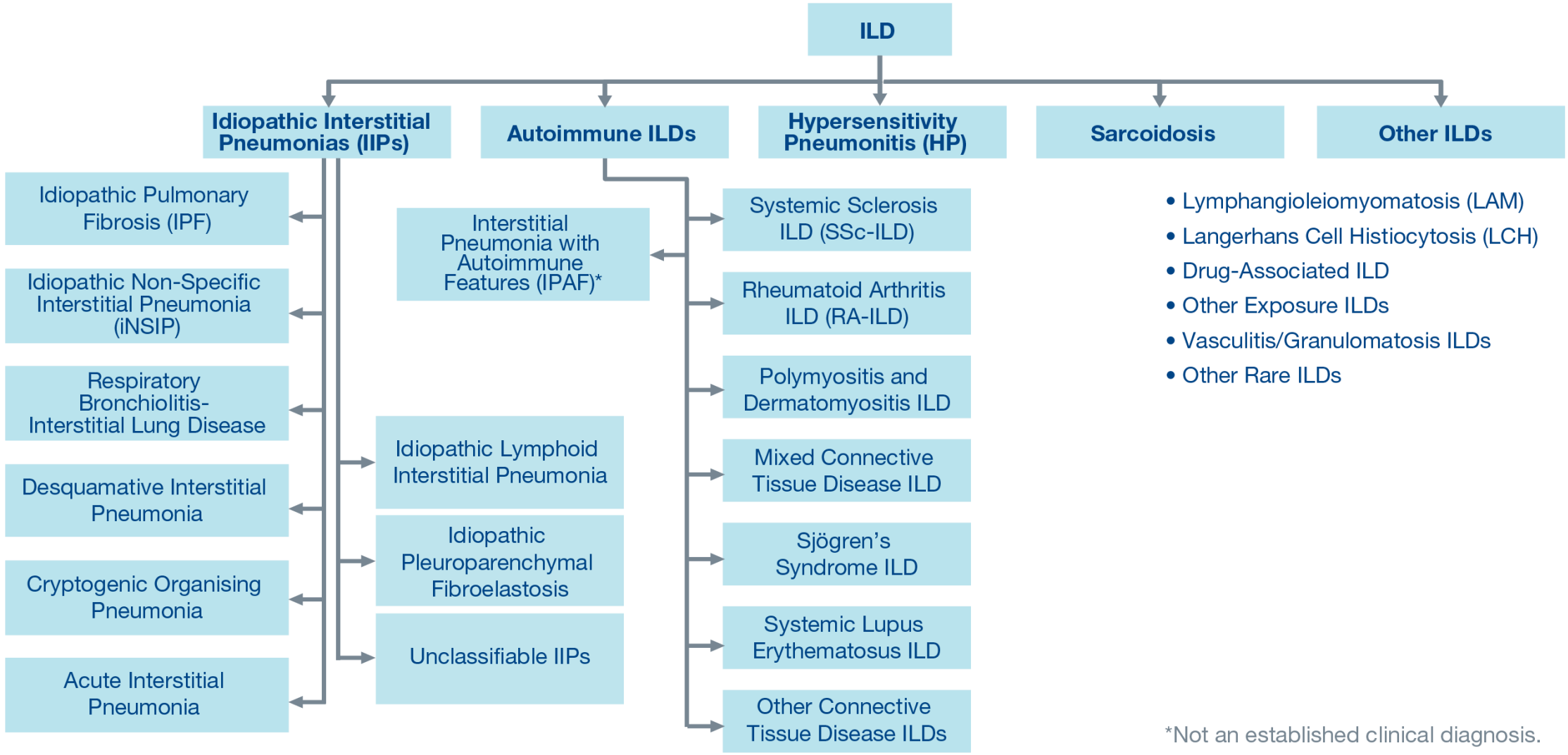


- DAD pattern



American Thoracic Society; European Respiratory Society. *Am J Respir Crit Care Med*. 2002;165:277-304.

Splitting in ILD: classification

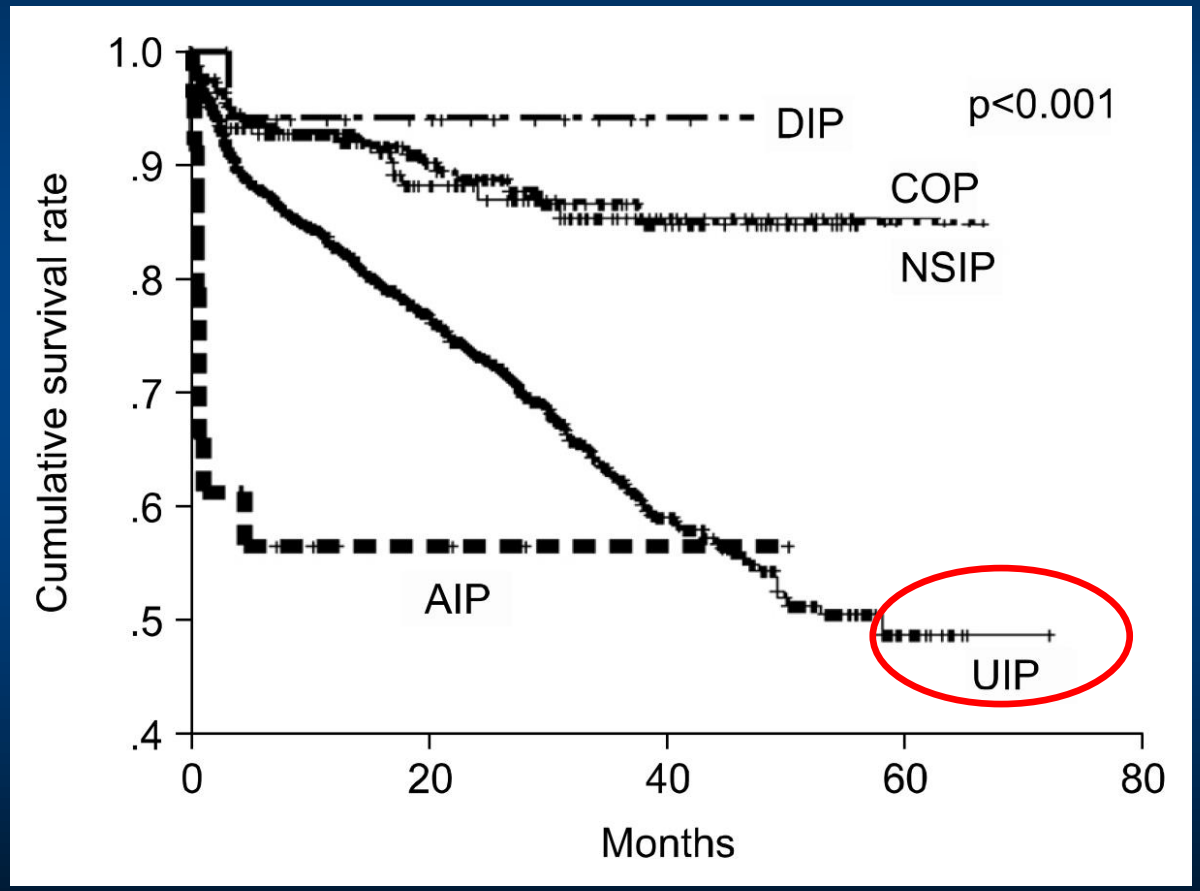


*Not an established clinical diagnosis.

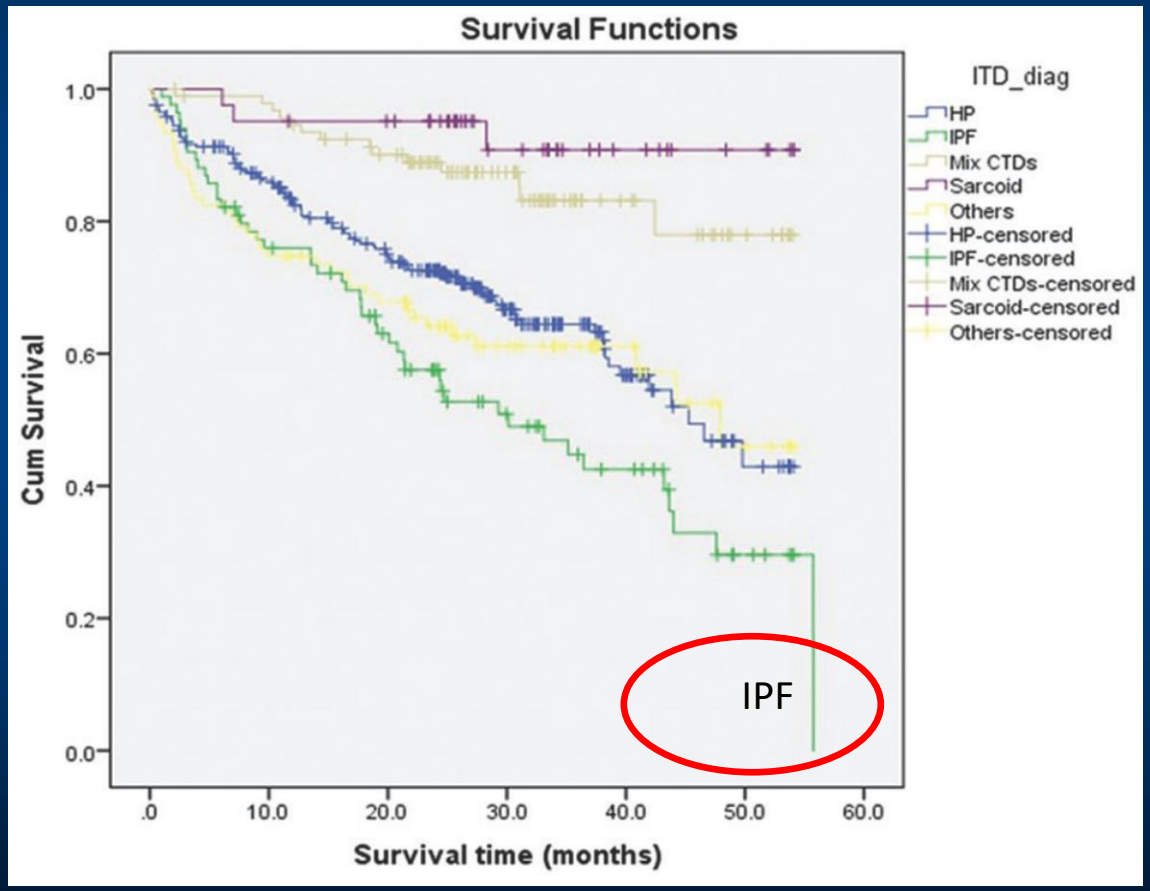
Travis WD, et al. *Am J Respir Crit Care Med*. 2013;188(6):733-48.

Survival difference according to ILD subtypes

- Korean IIP registry

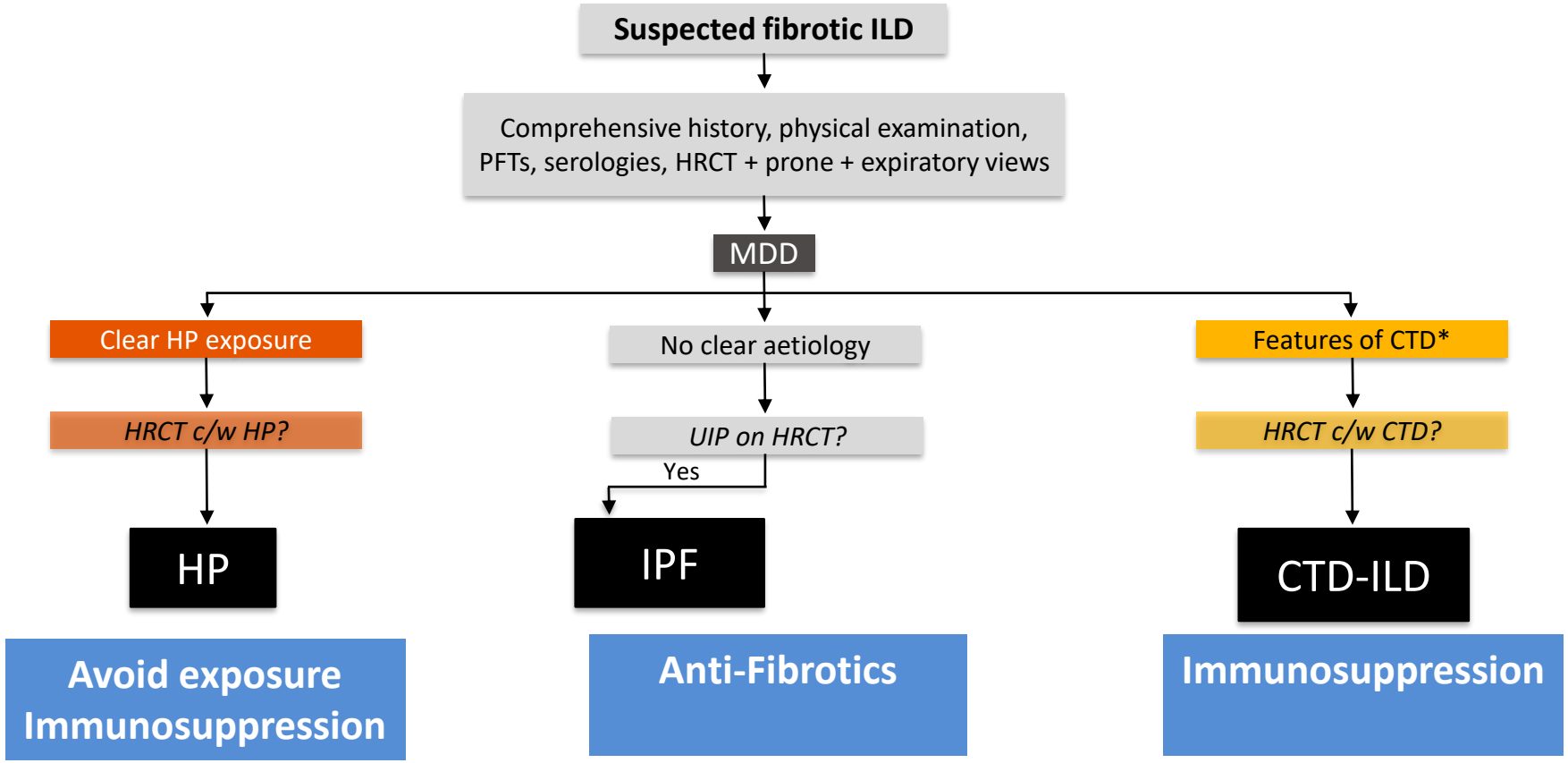


- Indian ILD registry



Scientific Committee of the Korean Academy of Tuberculosis and Respiratory Diseases *Tuberc Respir Dis* 2009;66:141-151.; Singh S et al. *Lung india* 2021;38:5-11

Management of fibrosing-ILD



Steroid – harmful

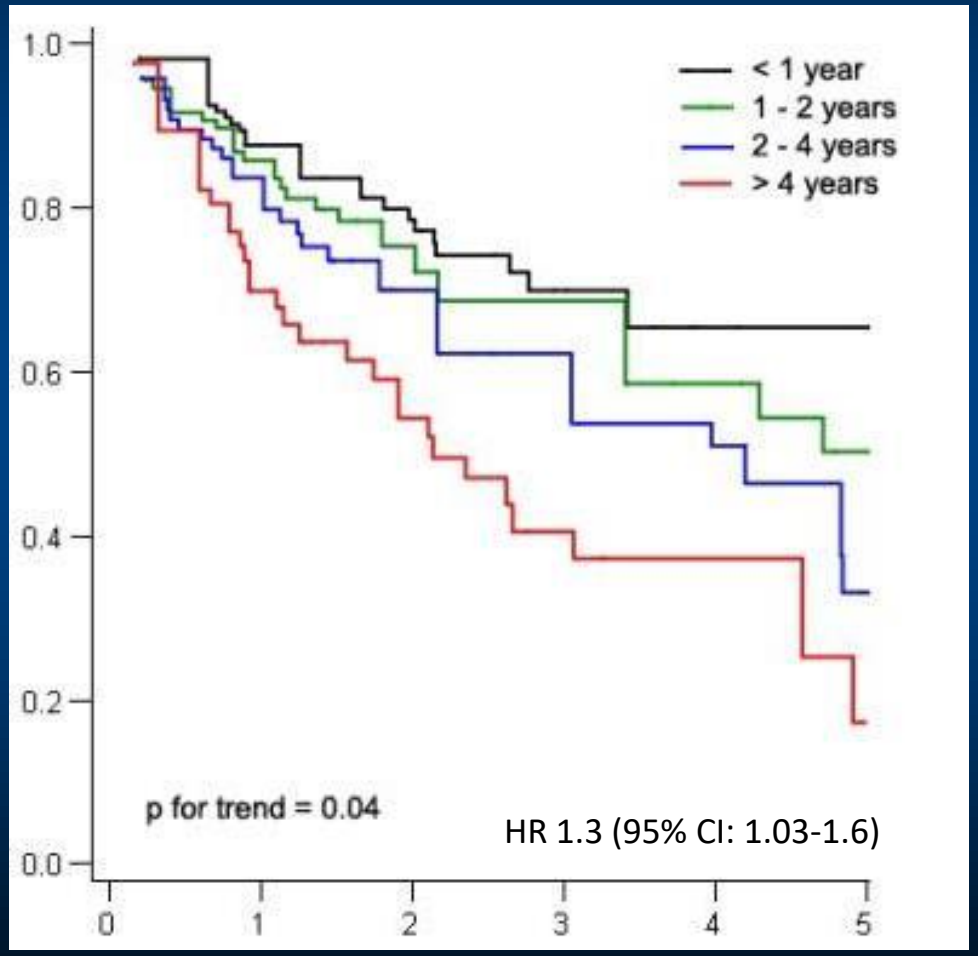
May stable patients

CTD, connective-tissue disease; c/w, consistent with; HP, hypersensitivity pneumonitis; HRCT, high-resolution computed tomography; ILD, interstitial lung disease; MDD, multidisciplinary discussion; PFTs, pulmonary function tests; UIP, usual interstitial pneumonia

Johannson KA, et al. *Can J Resp Crit Care Sleep Med* 2017;1(3):133-141.

Higher mortality is associated with delays in accessing care

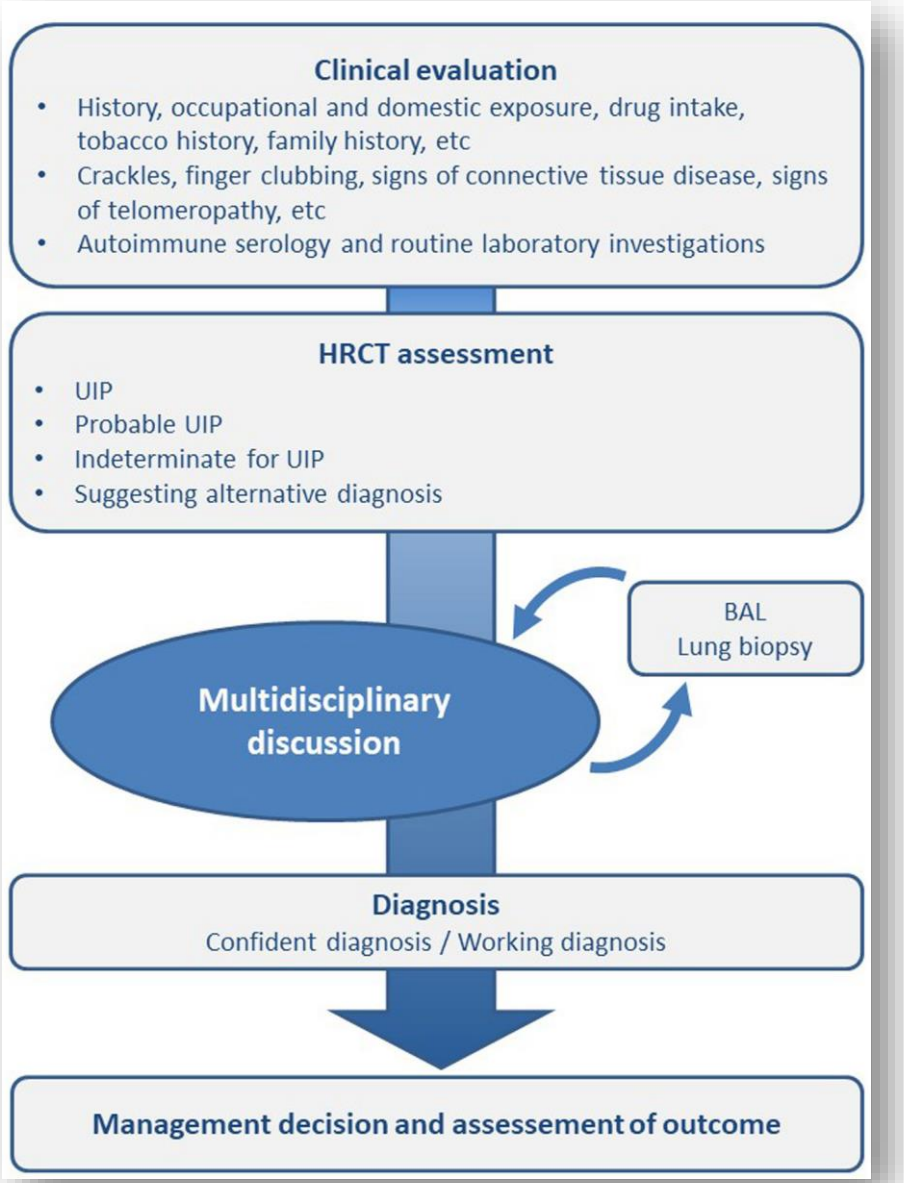
- Survival from the time of evaluation (adjusted for age, sex and FVC)



- Prospective IPF cohort (n=129); median delay from the onset of dyspnea to the date of initial evaluation: 2.2 years (IQR .0-3.8 yeasr)

Lamas DJ et al. *Am J Respir Crit Care Med*. 2011;184:842

Algorithm for the diagnosis of ILD



Cottin V et al. *Presse Med 2020;49:104021*

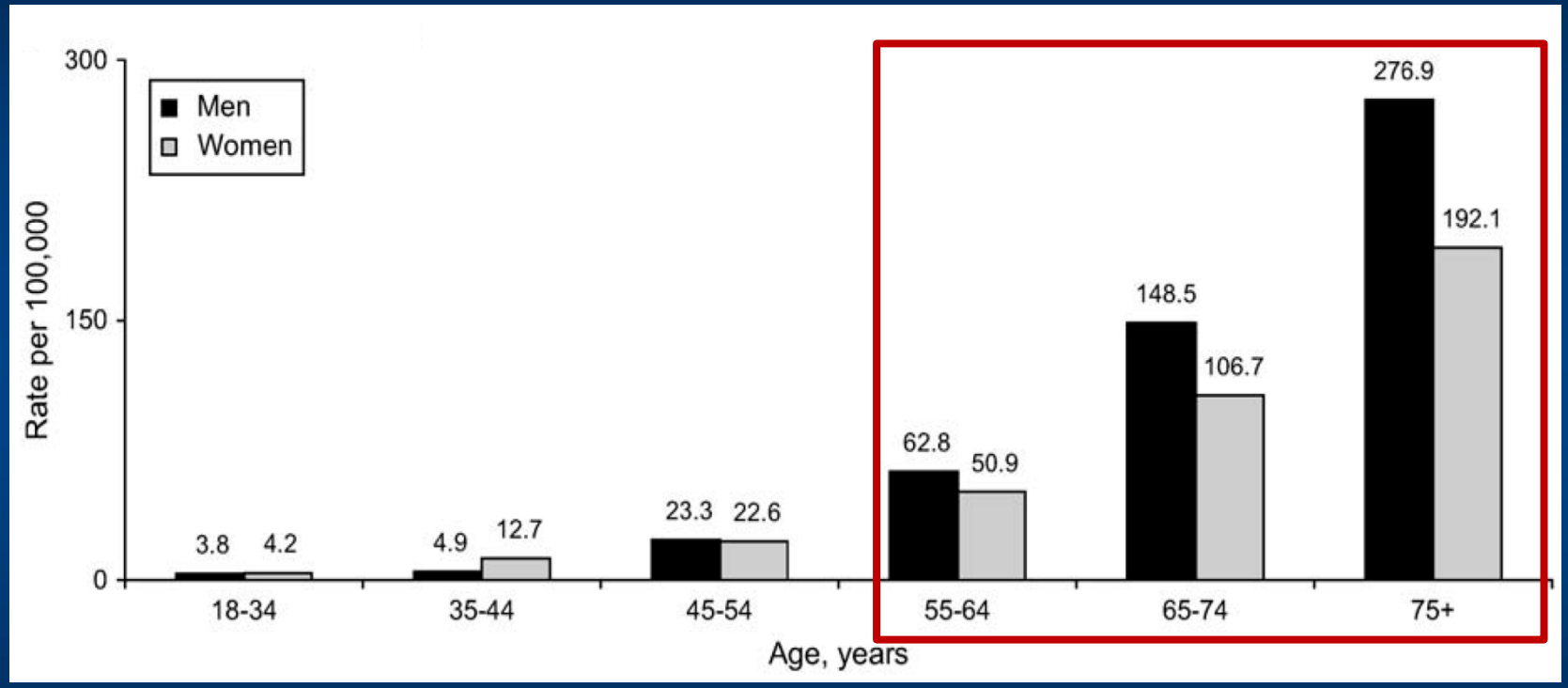
ILD: clinical manifestations

Similarities	Differences

• Dyspnea
  – Progressive
  – Exertional
• Cough
  – Non-productive
• Bibasilar crackles
• Finger clubbing
• Restrictive ventilatory defect
• Exertional desaturation
	• Demographics
	• Duration of symptoms
	• Prior/current exposures
	• Extrapulmonary findings
	  – Sarcoidosis
	  – Connective tissue disease
	  – Joint involvement
	• Serologies

IPF: prevalence by age and sex stratification

Old people's disease



- Men > women
- > 50 years of age
- Average age of diagnosis: 66 years

Raghu G et al. *Am J Respir Crit Care Med*. 2006;174:810

Differences : IPF vs. other ILDs

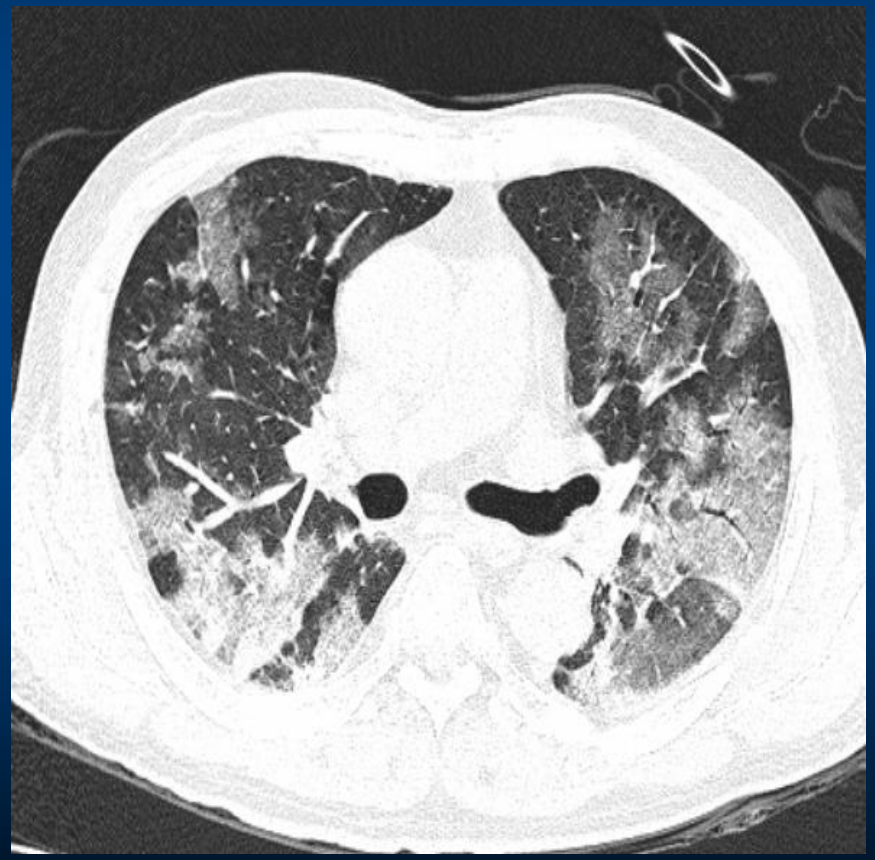
	IPF	fHP	fNSIP	SJS-IP	RA-IP	COP
Patient Number	1114	101	72	62	310	76
Age	65.7(8.2)	60.4(12.8)	54.3(10.1)	59.8(11.4)	61.7(10.3)	56.0(11.5)
Male	897(80.5)	50(49.5)	23(31.9)	10(16.1)	137(44.2)	31(40.8)
Ever-smokers	846(75.9)	38(37.6)	21(29.2)	14(22.6)	139(44.8)	21(26.7)

Yoon HY et al. *Eur Respir J* 2021;57(5):2001877, Kang J et al. *Respir Res* 2021;22(1):152, Park IN et al. *Eur Respir J* 2009;33(1):68-76, Kim YJ et al. *Sci Rep* 2021;11(1):12827, Kwon BS et al, *CHEST* 2022, Yoo JW et al, *Rheumatology* 2011;50(5):932-8

Onset of disease: subacute, acute

- COP

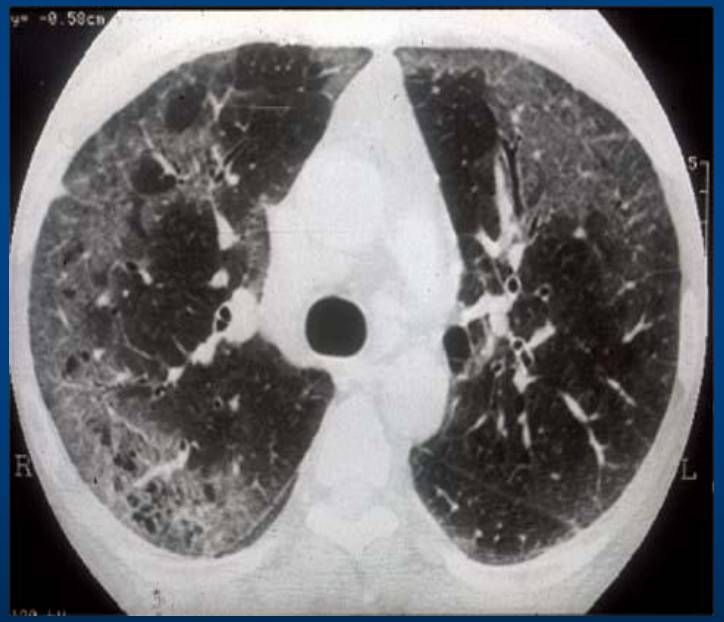
- AIP



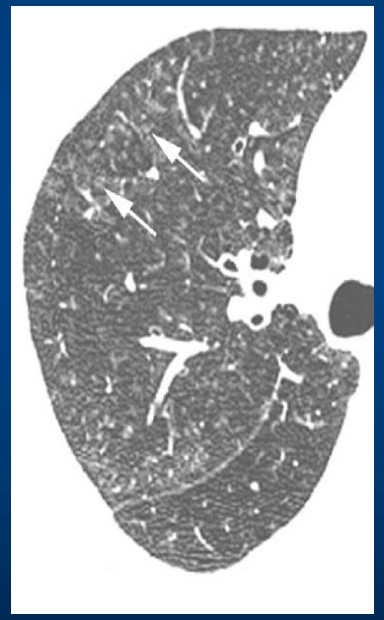
- AE of IPF

Exposure: smoking

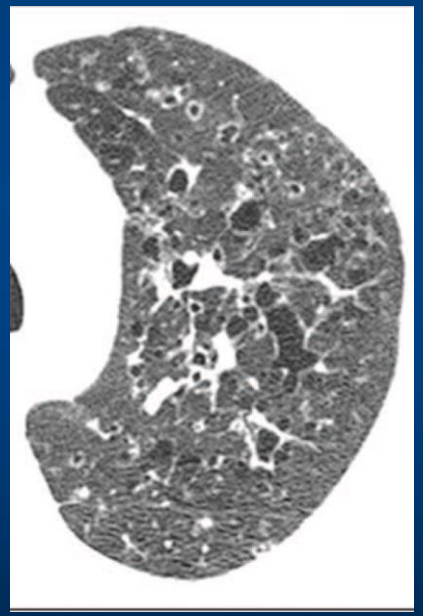
- DIP



- RB-ILD



- PLCH



- IPF, RA-ILD

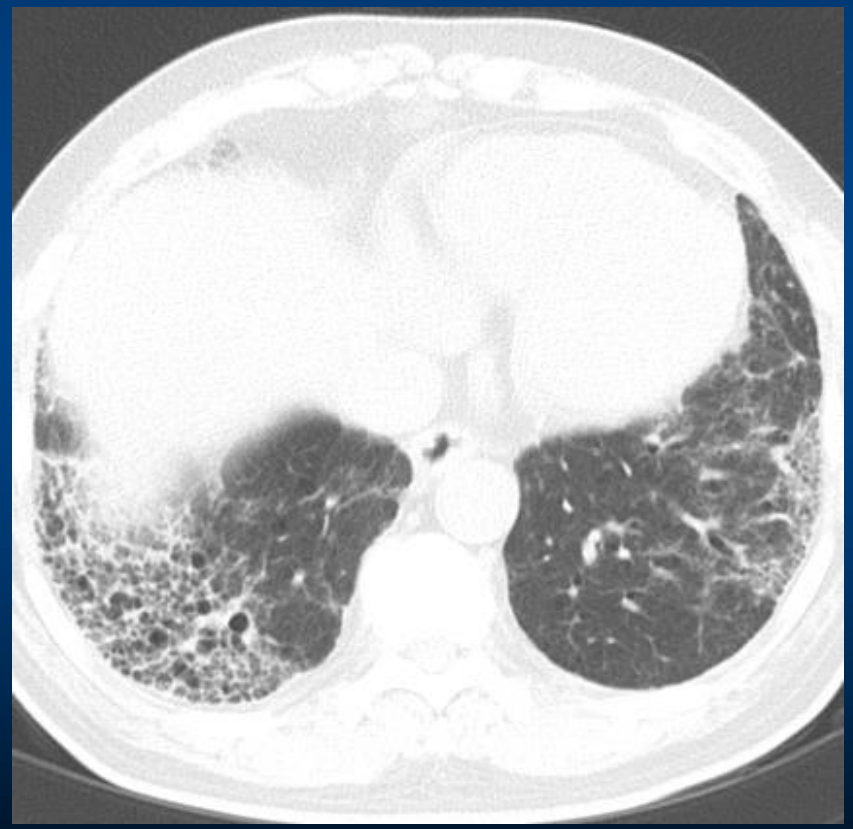
Known causes of ILD

- Occupational/Environmental
  - Inorganic antigens (Pneumoconioses)
    - Asbestosis
    - Coal worker's pneumoconiosis
    - Silicosis
  - Organic antigens (Hypersensitivity Pneumonitis)
    - Birds
    - Mold
  - www.hplung.com
- Drugs
  - eg, Amiodarone, bleomycin, nitrofurantoin
  - www.pneumotox.com
- Radiation
  - External beam radiation therapy to thorax
- Connective Tissue Diseases
  - Rheumatoid arthritis
  - Systemic sclerosis (scleroderma)
  - Idiopathic inflammatory myopathies
  - Vasculitis

Pneumoconiosis

- Silicosis, Coal worker's pneumoconiosis

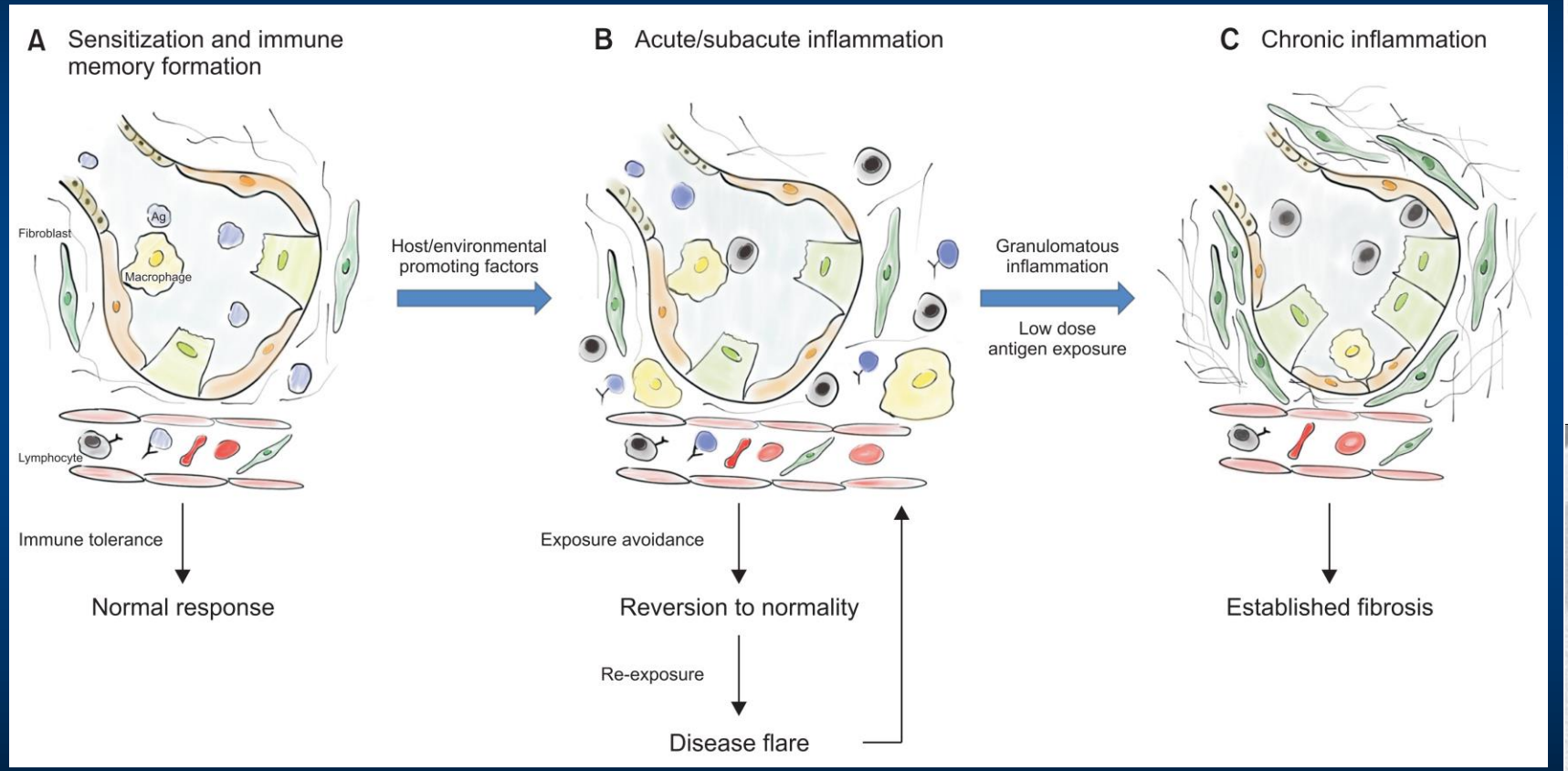
- Asbestosis

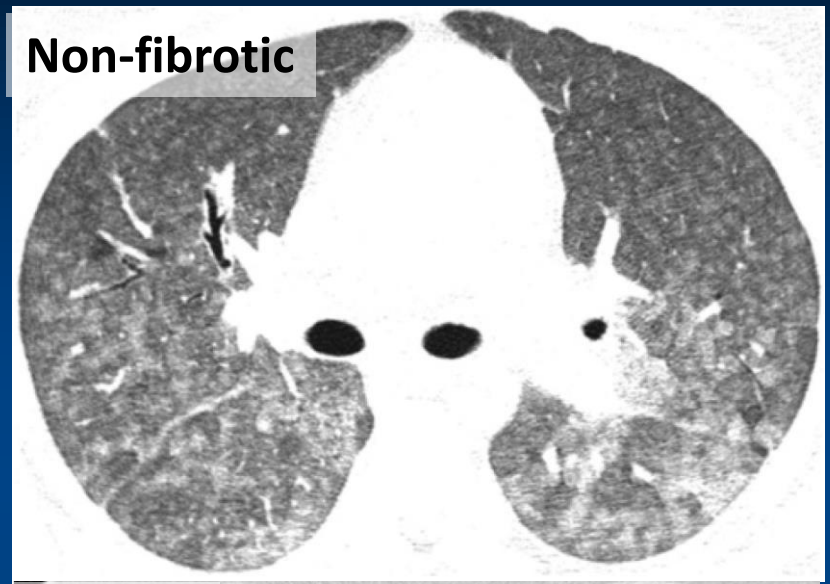


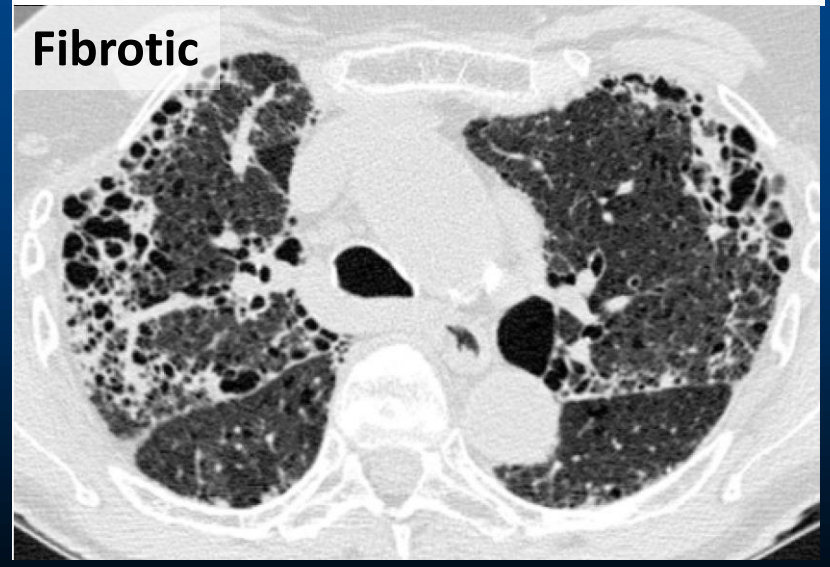
Exposure: Silica

Exposure: Asbestos

Pathogenesis of HP







Leone PM, et al. *Tuber Respir Dis* 2020 Apr;83(2):122-131.

Sauces of antigens known to cause HP

Matter	Matter	Typical Sources	HP "Disease"
Organic particulate matter			
I. Microbes			
Fungi/molds			
Aspergillus spp.			
Alternaria alternata, *Aureobasid* spp.			
Botrytis cinerea			
Cephalosporium spp.			
Cladosporium spp.			
Cryptococcus spp.			
Fusarium spp.			
Graphium spp.			
Mucor spp.			
Penicillium spp.			
Rhizopus spp.			
Trichoderma spp.			
Phytase (enzyme from *Aspergillus Trichoderma*)			
Yeasts			
Candida spp.			
Geotrichum candidum			
Saccharomyces cerevisiae			
Saccharomonospora viridis			
Saccharopolyspora rectivirgula			
	II. Pharmaceutical agents		
	Penicillins, cephalosporins	Antibiotics	Drug-induced HP
	Methotrexate	Immunosuppressive agents	
	α-IFN	Immunomodulatory agents	
	Lenalidomide	Hypolipidemics	
	Pravastatin	Antidepressants	
	Venlafaxine	Alkylating agents	
	Temozolomide		
	III. Metals		
	Cobalt	Hard metals, alloys	Giant cell pneumonitis
	Zinc (tungsten and alloys)	Zinc fumes	Zinc-fumes alveolitis
	Zirconium	Zircon	Zirconium alveolitis
	Beryllium	Batteries, computers, neons	Beryllium HP
	TMI	Organometallic compound for semiconductors used in industry	—
	Shell protein (oyster, sea snail, mussels)	Oyster-shell powder	Shellfish alveolitis, oyster-shell HP, mollusk-shell HP
	Pig pancreas	Animal extracts	—
	Pituitary proteins	Pituitary powder	Pituitary snuff-taker's lung
	Rat and desert mouse (gerbil) urine, serum, pelts	Rats, gerbils	Alveolitis due to rat and mouse proteins
	Silkworm proteins	Dust from silkworm larvae and cocoon	Silkworm rearer's lung
	Weevils (corn, wheat) (*Sitophilus* spp.)	Contaminated grain or flour	Corn (wheat)–weevil lung
	Plant proteins		
	Alginate	Seaweed	—
	Argan cake	Cosmetics, unsaturated fatty acids, phytosterol	—
	Catechin	Green-tea powder	—
	Esparto dust	Esparto grass	Esparto lung, plasterer's lung

Raghu G, et al. *Am J Respir Crit Care Med* 2020. 202:e36-69.

Exposure: HP

- Farmer's lung (Aspergillus sp.)

- Hot-tub lung (NTM)

- Bird-breeder's lung, Feather-duvet lung (Avian droppings, serum, feathers)

Exposure: HP

- Mouldy walls, Steam iron alveolitis (Iron's steam), Humidifier lung (Alternaria alternate, Candida)




- Saxophone player's lung (Ulocladuim botrytis, Penicilium), Trombone player's lung


Raghu G, et al. *Am J Respir Crit Care Med* 2020. 202:e36-69.

HP: exposure history to causative antigens

Characteristics	Total
Patients, number	101
Microbes (mold, humid hay, cotton)	50 (49.5)
Chemical (insecticides, cement, dye, fertilizers)	18 (17.8)
Animal protein (birds' feather)	8 (7.9)
Enzymes (mushrooms)	1 (1.0)
Metal (fumes)	1 (1.0)
Pharmaceutical agents (drugs)	1 (1.0)
Plant proteins (flour, vegetable processing)	7 (6.9)
Unidentifiable antigen	15 (14.9)

- AMC fibrotic HP cohort (n=101)

Kang JE, et al. *Respir Res* 2021;22:152159.

HP: online repository of potential cause

hpLung

EXPOSURES ANTIGENS ABOUT

Browsing Exposures

Or search... Go

A	Cases
Air Conditioners	48
Argan Cake	2
B	
Bagasse	16
Baker's Yeast	1
Bathtubs	2
Bats	1
Bed Cleaner	1
Birds, Mixed or NOS	181
Blackbirds	8
Blacksmiths	1
Broom Grass	1
Budgerigars	103

Birds, Mixed or NOS

Also described as bird fancier's lung, bird fancier's disease
There are **181 cases** described in **29 citations**

Citation	Antigens	Cases
2019 Moasaic attenuation Marchiori, E., et al. *Jornal Brasileiro De Pneumologia: Publicacao Oficial Da Sociedade Brasileira De Pneumologia E Tisilogia.*		1
2018 [A Case of Acute Exacerbation of Chronic Birdrelated Hypersensitivity Pneumonitis with a Remarkable Elevation of Environmental Avian Antigen Levels] Suzuki, T., et al. *Arerugi.*	Pigeon Droppings	1
2015 Hypersensitivity pneumonitis associated to birds care González-Zúñiga, A. M., et al. *Revista Facultad de Medicina.*		1
2015 Identical Twins, Matching Symptoms: Hypersensitivity Pneumonitis Chen, C., et al. *American Journal of Medicine.*		2
2015 Pneumomediastinum: a rare manifestation of hypersensitivity pneumonitis in a patient presenting with unexplained breathlessness at the Borders General Hospital Grecian, R., et al. *BMJ Case Reports.*	Avian antigens	1
2015 [Chronic form of bird breeder's disease: about one observation] Frikha, F., et al. *The Pan African Medical Journal.*		1
2014 [Hypersensitivity pneumonitis in the school environment] Callero, A., et al. *Anales De Pediatria.*	Aspergillus spp., Canary droppings	1
2013 Bird fancier's lung complicated by pulmonary nocardiosis Komiya, K., et al. *Jornal Brasileiro De Pneumologia.*		1

Drug-induced interstitial lung disease

Antibiotics
- Nitrofurantoin, acute and chronic
- Sulfsalazine

Anti-inflammatory agents
- Aspirin
- Gold
- Pencillamine

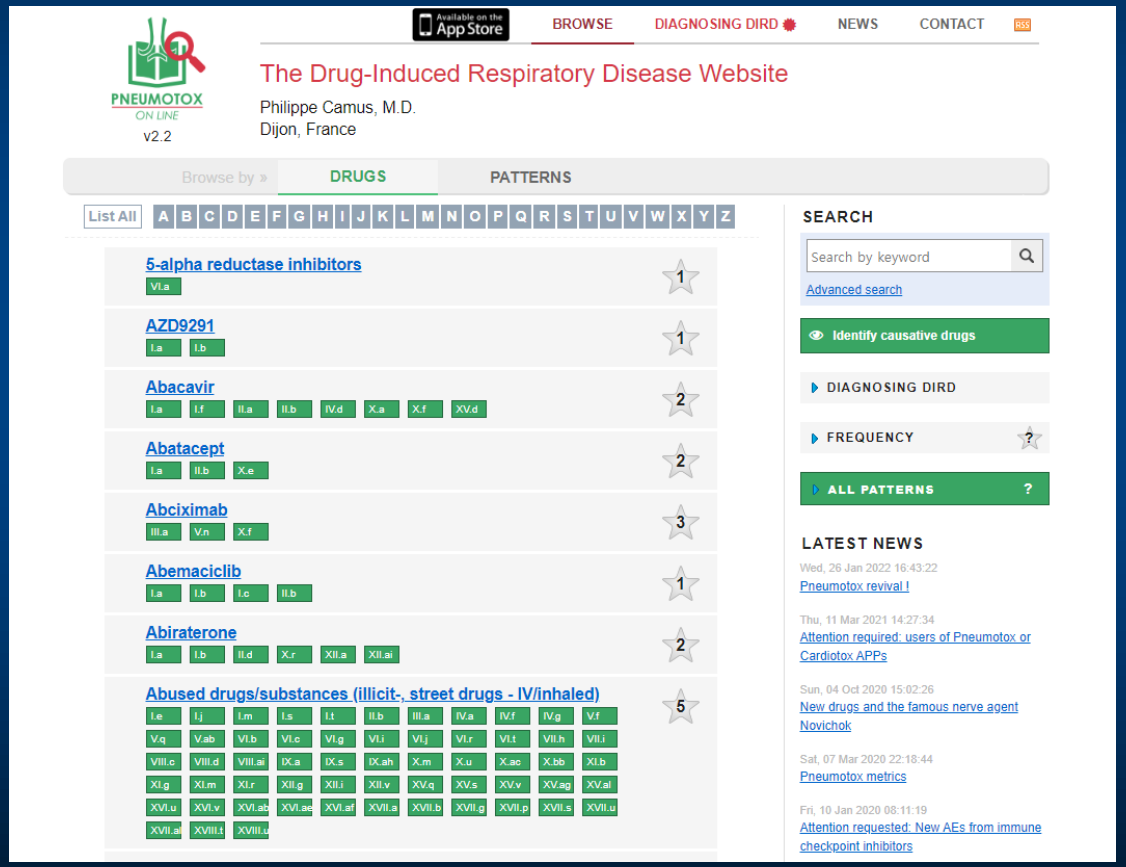
Chemotherapeutic agents
- Antibiotics
  - Bleomycin sulfate
  - Mitomycin C
- Alkylating agents
  - Busulfan
  - Cyclophosphamide
  - Chlorambucil
  - Melphalan
- Antimetabolites
  - Azathioprine
  - Cytosine arabinoside
  - Methotrexate

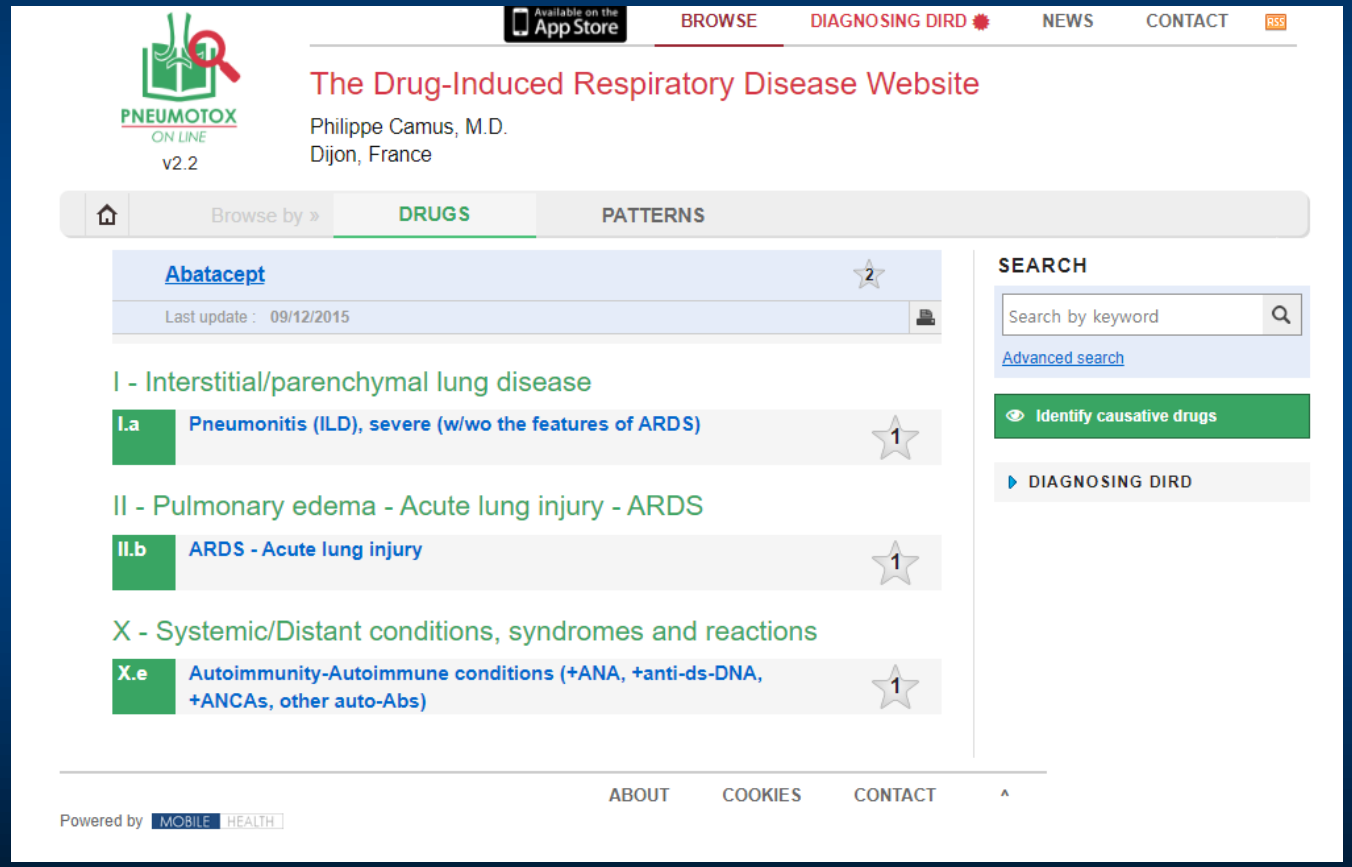
Miscellaneous
- O2
- Drugs inducing pulmonary infiltrates and eosinophilia
- Radiation
- L-tryptophan

Drug-induced systemic lupus erythematosus
- Procainamide hydrochloride
- Isoniazid
- Hydralazine hydrochloride
- The hydantoins
- Pencillamine

Illicit drugs
- Heroin
- Methadone hydrochloride
- Propoxyphene hydrochloride (Darvon)
- Talc

Drug-ILD: online repository of potential cause





ACCP: ILD patient questionnaire

15. Have you lived or worked in environment where you were exposed to heavy smoke or dust? ☐ Yes ☐ No

16. Occupational history: *Please include all occupations in your life.*

Occupation	Years worked	Exposures *(Dust, metal, paint, fine particles, etc)*

17. Have you ever performed any of the following occupations?

- ☐ Farm work
- ☐ Painter
- ☐ Sand blaster
- ☐ Pipe fitter
- ☐ Automotive mechanic
- ☐ Welder
- ☐ Insulator
- ☐ Vineyard worker
- ☐ Carpenter
- ☐ Laboratory worker
- ☐ Longshoreman

18. Have you ever worked in any of the following locations?

- ☐ Mine
- ☐ Quarry
- ☐ Pulp mill
- ☐ Bakery
- ☐ Foundry
- ☐ Railroad
- ☐ Paper mill
- ☐ Smelting
- ☐ Plastic factory
- ☐ Tunnel construction

19. Have you ever been exposed to the following at work/ home/ elsewhere?

Animals and farming
- ☐ Birds
- ☐ Feathers
- ☐ Fishmeal
- ☐ Insecticide
- ☐ Fertilizer

Metals/rocks
- ☐ Beryllium
- ☐ Cobalt
- ☐ Tin
- ☐ Iron oxide
- ☐ Aluminum
- ☐ Mica
- ☐ Silica
- ☐ Asbestos
- ☐ Coal

Food/ plant Production
- ☐ Cheese
- ☐ Maple Bark
- ☐ Wheat
- ☐ Coffee/ tea
- ☐ Mushroom
- ☐ Oil
- ☐ Sugar cane
- ☐ Malt
- ☐ Meat

Miscellaneous
- ☐ Cotton
- ☐ Wood
- ☐ Industrial strength cleaning solution
- ☐ Oily Nosedrops

Skilled
- ☐ Cork
- ☐ Detergent *(isocyanates)*
- ☐ Pottery
- ☐ Talc
- ☐ Paint
- ☐ Cement
- ☐ Pipes
- ☐ Brakes
- ☐ Tile *(ceramic)*

16. 다음 직업 중 종사한 적이 있는 직업이 있으시면 표시해주십시오.

농부	○ 네	○ 아니오
도장공(페인트칠)	○ 네	○ 아니오
샌드블라스터(모래분사기)작업	○ 네	○ 아니오
배관공	○ 네	○ 아니오
자동차 정비	○ 네	○ 아니오
용접공	○ 네	○ 아니오
절연(전기 통하지 않도록) / 단열 / 방음 처리	○ 네	○ 아니오
과수원	○ 네	○ 아니오
목수	○ 네	○ 아니오
실험실 업무	○ 네	○ 아니오
부두 노동자	○ 네	○ 아니오

17. 다음 장소에서 근무한 적이 있으십니까?

광산	○ 네	○ 아니오
주조(주물)공장	○ 네	○ 아니오
제련(용광로)공장	○ 네	○ 아니오
채석장	○ 네	○ 아니오
철로	○ 네	○ 아니오
플라스틱 제조 공장	○ 네	○ 아니오
펄프 제작소	○ 네	○ 아니오
제지 공장	○ 네	○ 아니오
터널 건설 현장	○ 네	○ 아니오
제과점(제과 제빵업)	○ 네	○ 아니오

18. 집 / 작업장 등에서 다음에 노출된 적이 있으시면 표시해주십시오.

동물 / 농업 관련

새	○ 네	○ 아니오	깃털	○ 네	○ 아니오
어분(말린 생선가루)	○ 네	○ 아니오	살충제	○ 네	○ 아니오
비료	○ 네	○ 아니오			

https://foundation.chestnet.org/wp-content/uploads/2020/04/Interstitial-Diffuse-Lung-Disease-Patient-Questionnaire.pdf

ILD is the most common pulmonary manifestation in Autoimmune disease

	SSc	RA	Sjögren's	MCTD	PM/DM	SLE
Airways	-	++	++	+	-	+
ILD	+++	++	++	++	+++	+
Pleural	-	++	+	+	-	+++
Vascular	+++	+	+	++	+	+
DAH	-	-	-	-	-	++

Lauretis AD et al. *Chron Respir Dis*. 2011;8(1):53-82

Raynaud’s phenomenon

Puffy fingers in early scleroderma or mixed CTD

Advanced sclerodactyly

Gottron’s papules in dermatomyositis

Mechanic’s hands in anti-synthetase syndrome

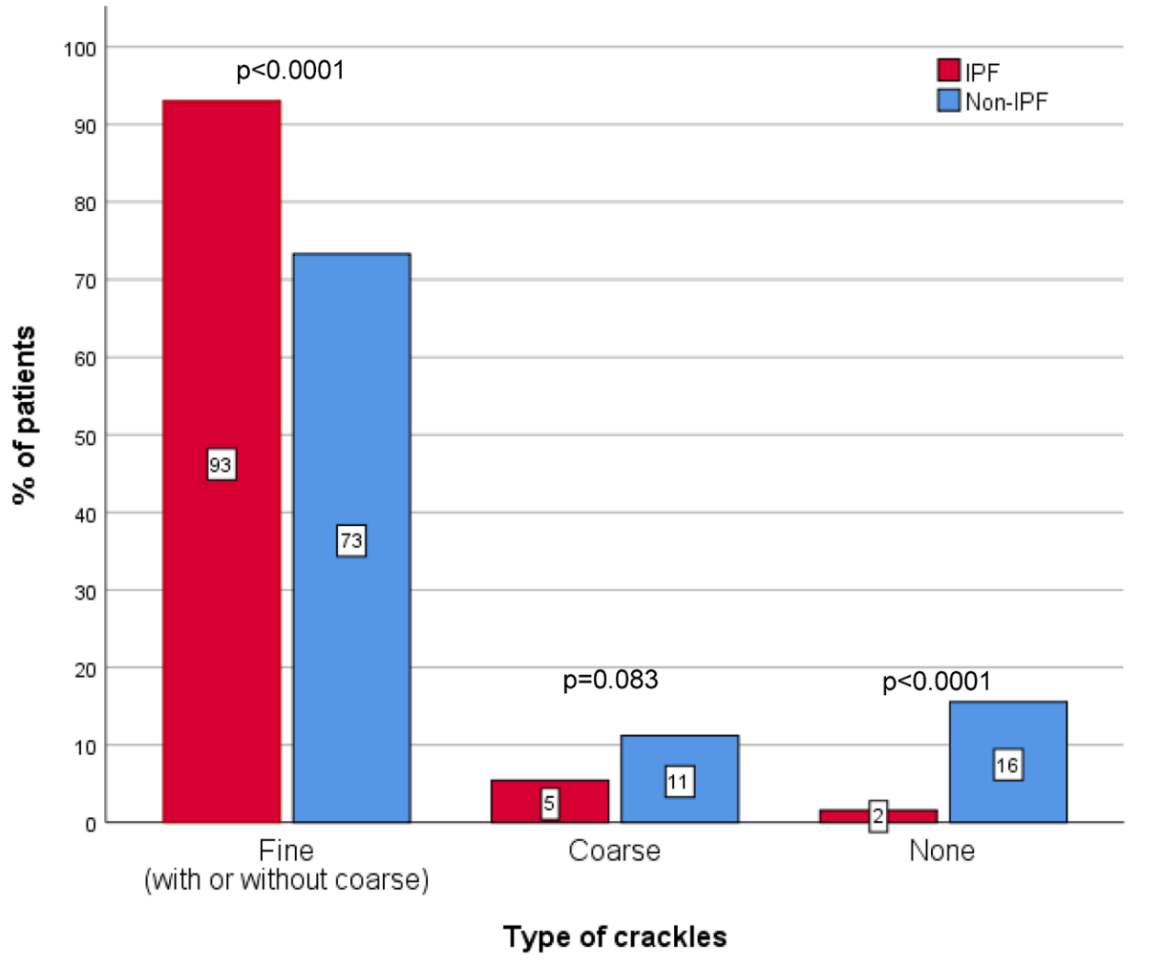
Serological evaluation

- Minimum: CRP, ESR, ANA, RF, anti-CCP, *myositis panel*

- Based on history & physical exam, consider:
  - Enzyme (CK, aldolase, myoglobin)
  - Antisynthetase antibodies (Jo-1 and others if available)
  - Anti-MDA5, anti-Mi-2, anti-NXP2, anti-TIF1-r, anti-SRP, anti-HMGCR, anti-SAE, anti-U1RNP, anti-PM/Scl75, anti-PM/Scl100, anti-Ku
  - SSc (suspected): anti-Scl-70/topoisomerase-1, anti-centromere, anti-RNA polymerase III, anti-U1RNP, anti-Th/To, anti-PMScl, U3 RNP, anti-Ku
  - SjS: anti-SSA/Ro, anti-SSB/La
  - Vasculitis: anti-cytoplasmic antibodies

Raghu G et al. *Am J Respir Crit Care Med*. 2018;198:e44-e68

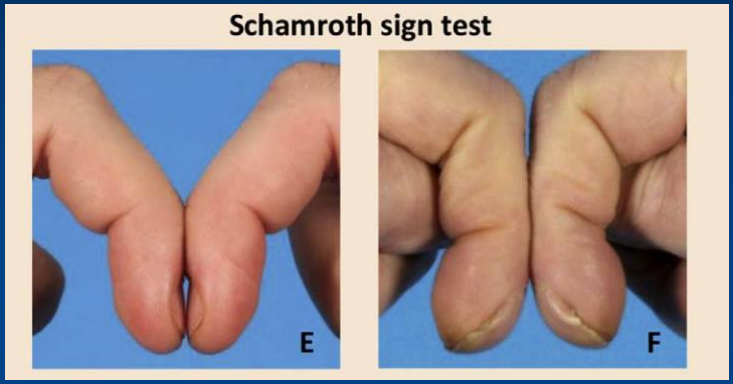
Fine crackles on chest auscultation in the diagnosis of ILD



	None	Fine crackles
IPF n (%)	2 (1.6%)	97 (75.2%)
Non-IPF n (%)	25 (15.5%)	98 (60.9%)
CTD-related ILD	5 (9.8%)	34 (66.7%)
HP	6 (15.8%)	25 (65.8%)
NSIP	1 (5.0%)	14 (70.0%)
Others	13 (24.5%)	25 (47.2%)
Drug-related ILD	3 (25.0%)	6 (50.0%)
Non-specific PF	2 (18.2%)	6 (54.5%)
Unclassifiable ILD	1 (9.1%)	5 (45.5%)
Smoking-related ILD	4 (50%)	2 (25.0%)
Other	3 (30.0%)	6 (60.0%)

Moran-Mendoza O et al *BMJ Open Resp Res* 2021;8:e000815

Clubbing in patients with fibrotic IP



	Digital index	Phalangeal depth ratio		Schamroth sign	At sight	
N (%)	≥10.2	Left	Right	Positive	Physician	Investigator
Total group	10 (7)	50 (33)	47 (31)	12 (8)	63 (41)	64 (42)
IPF	5 (7)	21 (31)	19 (28)	6 (9)	35 (52)	27 (40)
Others	5 (6)	29 (34)	28 (33)	6 (7)	28 (33)	37 (44)
Underlying CVD	1 (5)	3 (16)	3 (16)	2 (11)	7 (37)	8 (42)
CHP	0 (0)	6 (50)	5 (42)	1 (8)	5 (42)	6 (50)
Fibrosing pulmonary sarcoïdose	0 (0)	4 (27)	3 (20)	0 (0)	3 (20)	5 (33)
Unclassifiable PF	0 (0)	6 (35)	7 (41)	1 (6)	6 (35)	8 (47)
Various fibrotic ILDs	4 (18)	10 (46)	10 (46)	2 (9)	7 (32)	10 (46)

Van Manen M.J.G. et al *Repiratory Medicine 2017;132:226-231*

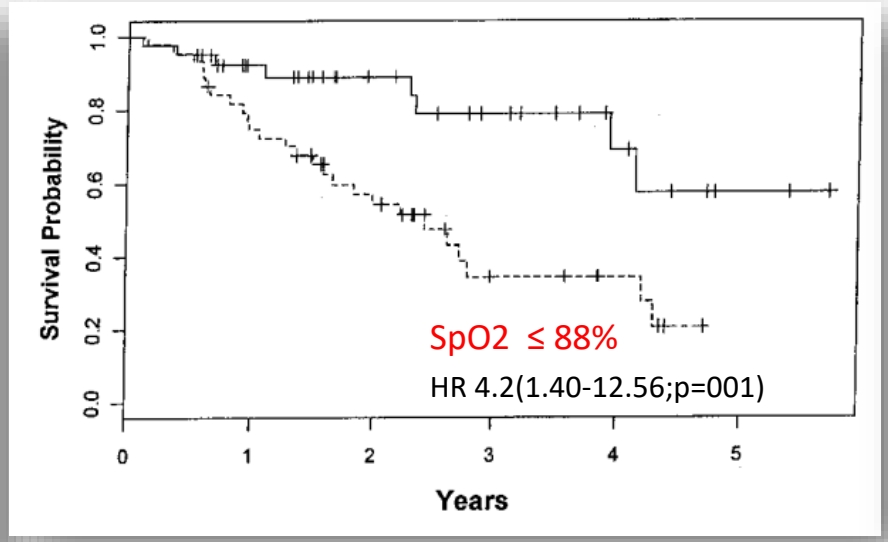
Pulmonary function test

- Spirometry
  - Reduced FVC (and TLC)
  - Normal or increased FEV_1/FVC ratio
- Restriction often accompanied by some obstruction
- Impaired gas exchange
  - Decreased DL_{CO}, PaO_2
  - Increased A-aPO_2 gradient
  - Disproportionately reduced: Emphysema, Pulmonary HTN
- Normal PFTs (FVC) do not exclude ILD
  - Emphysema + Interstitial Lung Disease

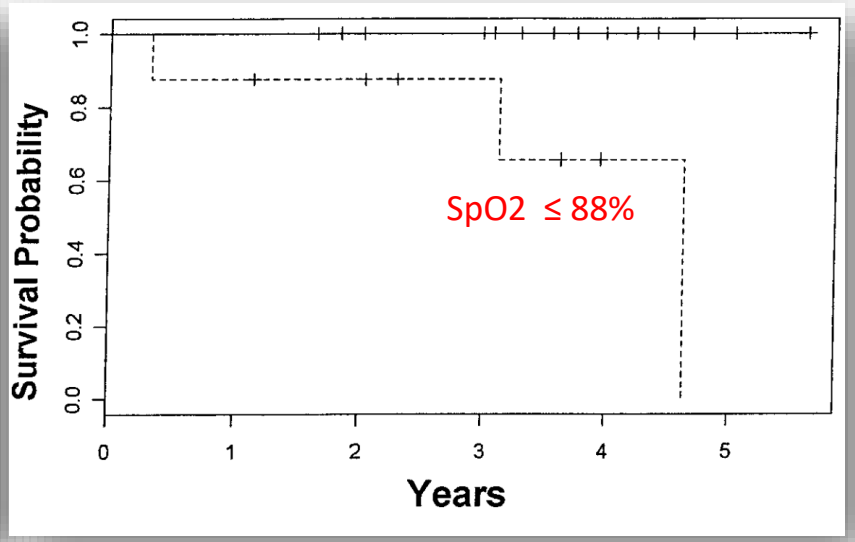
6MWT in ILD: prognostic value of desaturation

진료구분	외래			진료기간
상병명				투약내용
TEST(I) O2 ____ LPM				TIME
Pulse	SaO_2	DISTANCE	RPE	
96	94			resting
				_
				test
100	94			30"
103	86			1'
103	82			1'30"
102	81			2'
97	85			2'30"
98	86			3'
101	88			3'30"
100	91			4'
100	91			4'30"
101	89			5'
102	90			5'30"
102	87	203	5	6'

- IPF

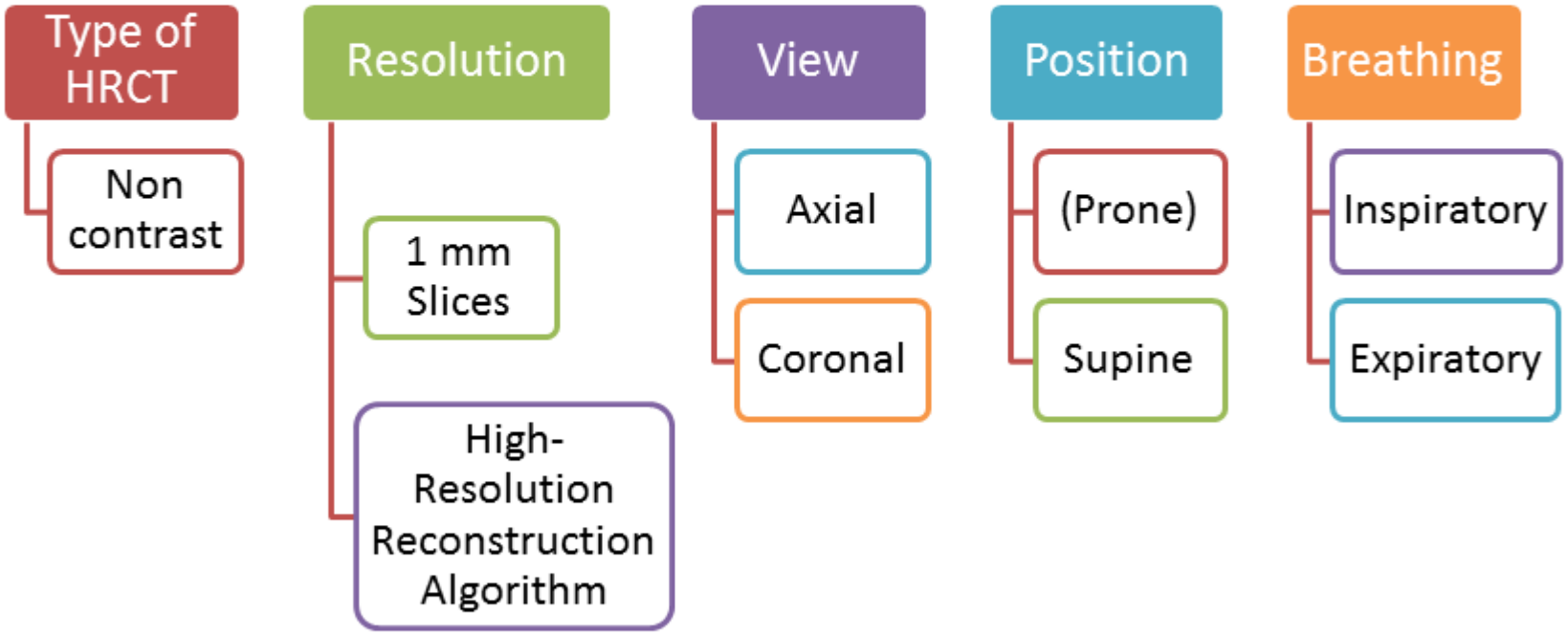


- iNSIP



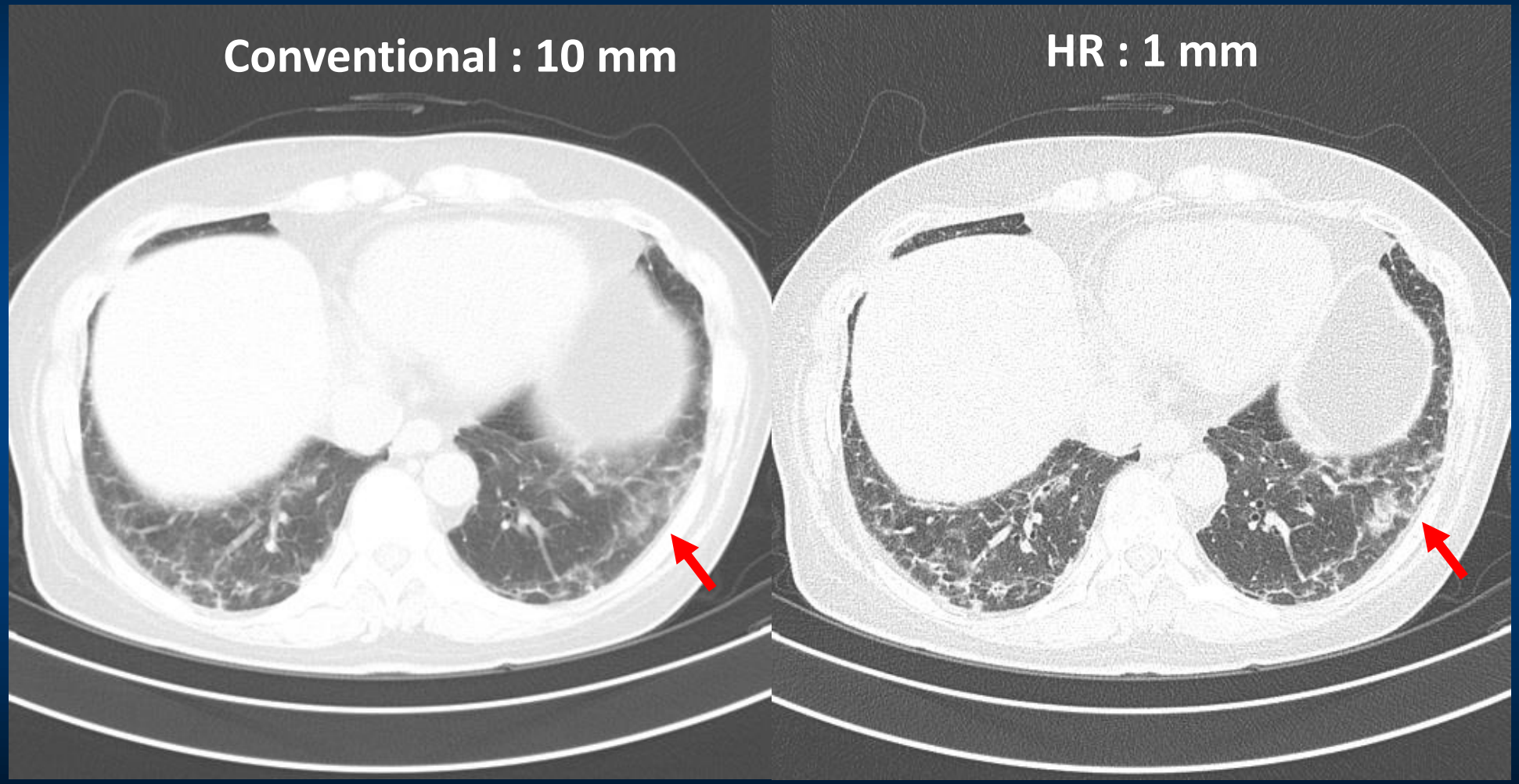
Lama VN et al. *Am J Respir Crit Care Med*. 2003;168:1084

What are the features of an HRCT?



Raghu G et al. *Am J Respir Crit Care Med*. 2018;198:e44-e68

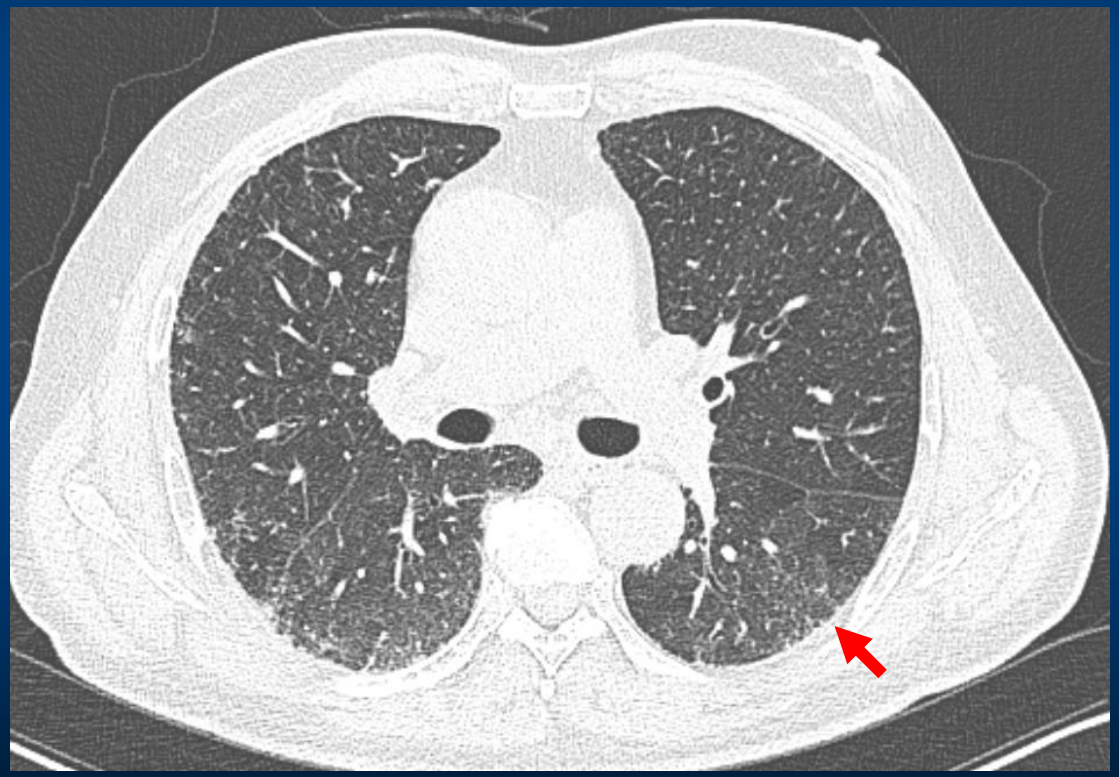
High Resolution Computed Tomography



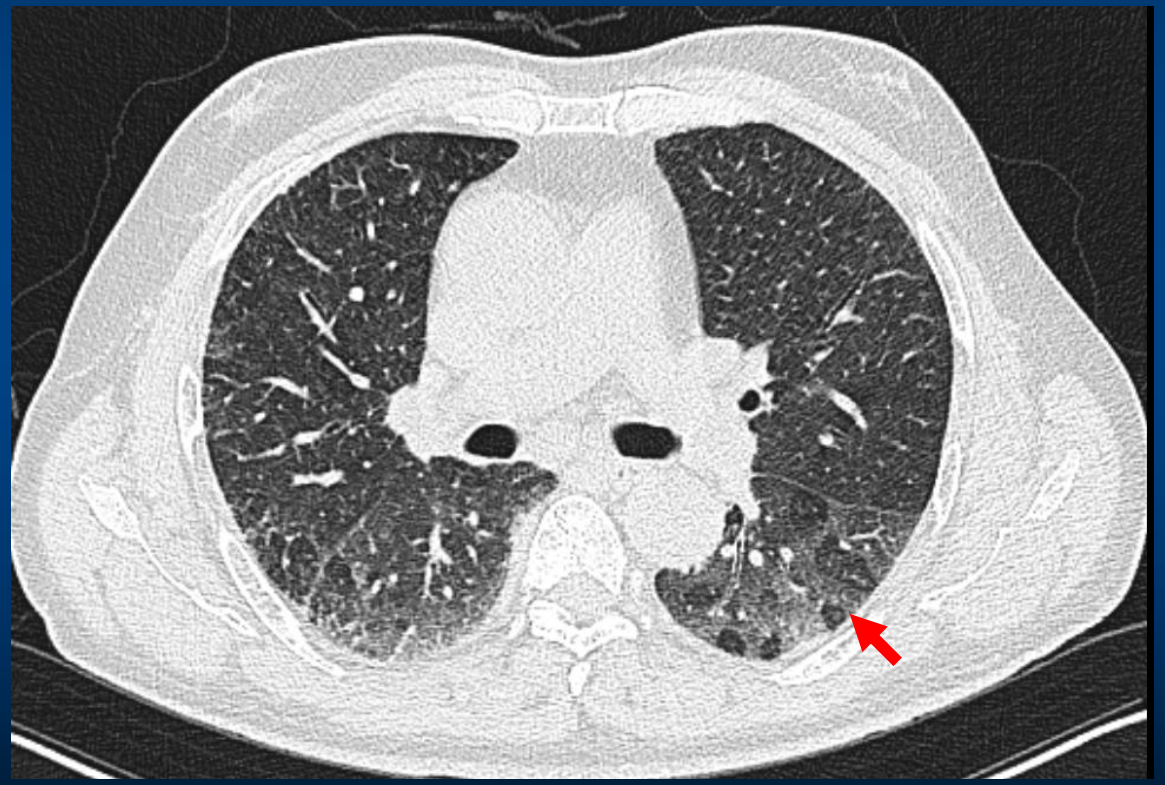
- HRCT help to detect more detailed parenchymal changes in ILD.

HRCT: inspiration vs. expiration images

Inspiration

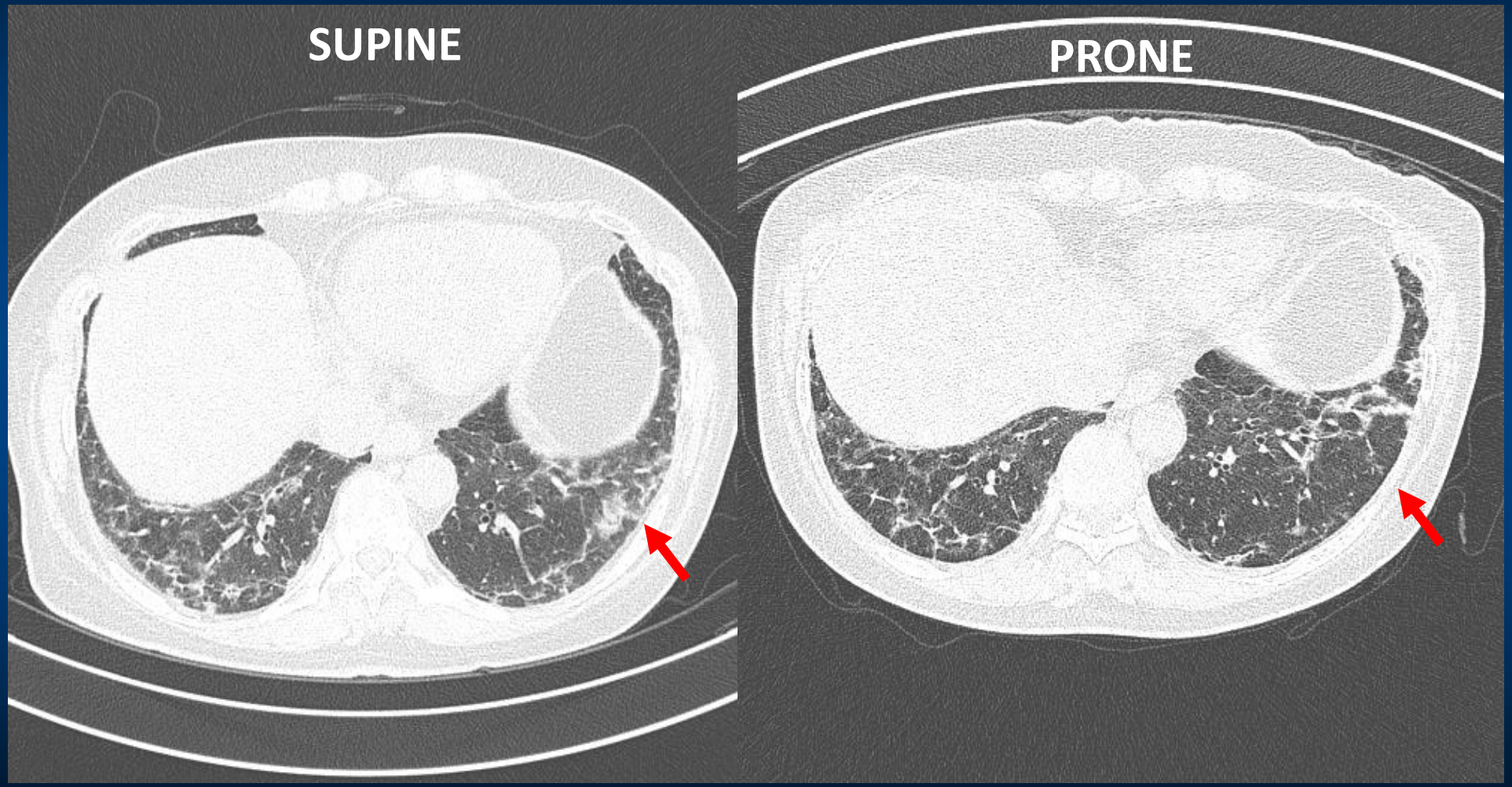


Expiration



- Expiratory image help to detect air-trapping seen in HP or BO.

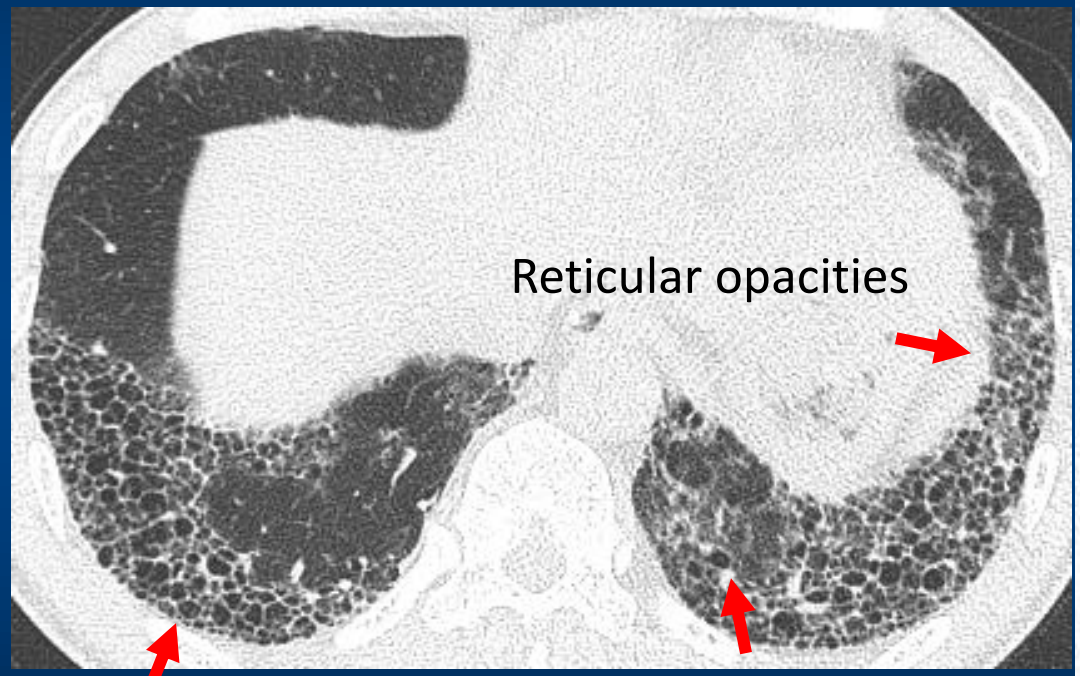
HRCT: supine vs. prone images

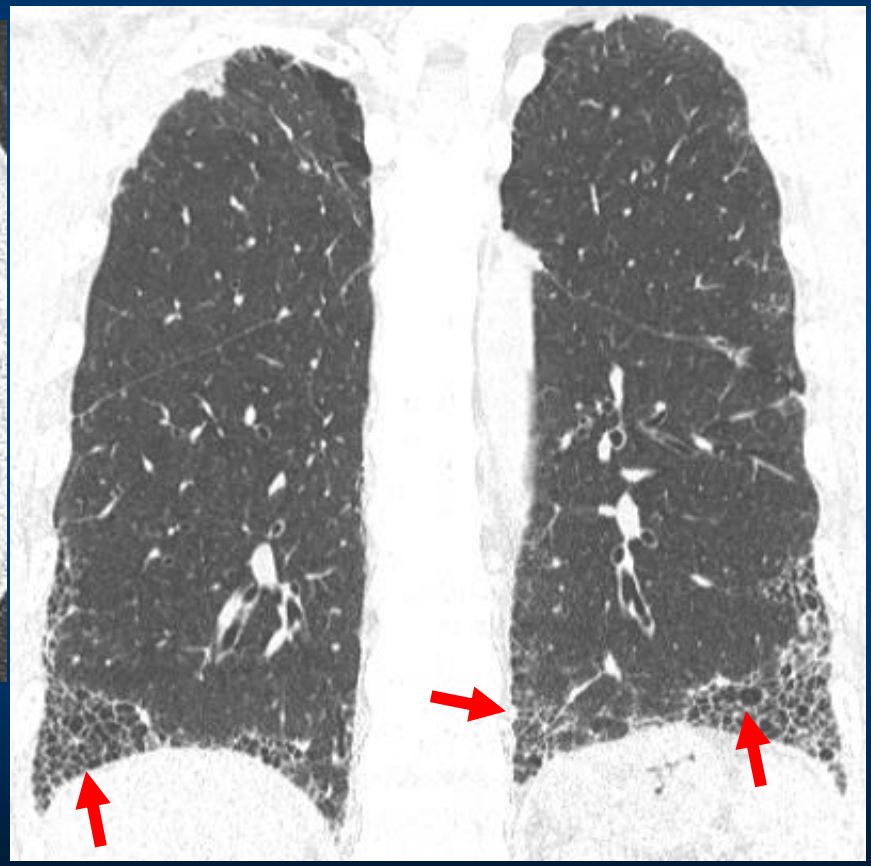


- Prone image help to differentiate GGO/CON from pseudolesion.

UIP pattern

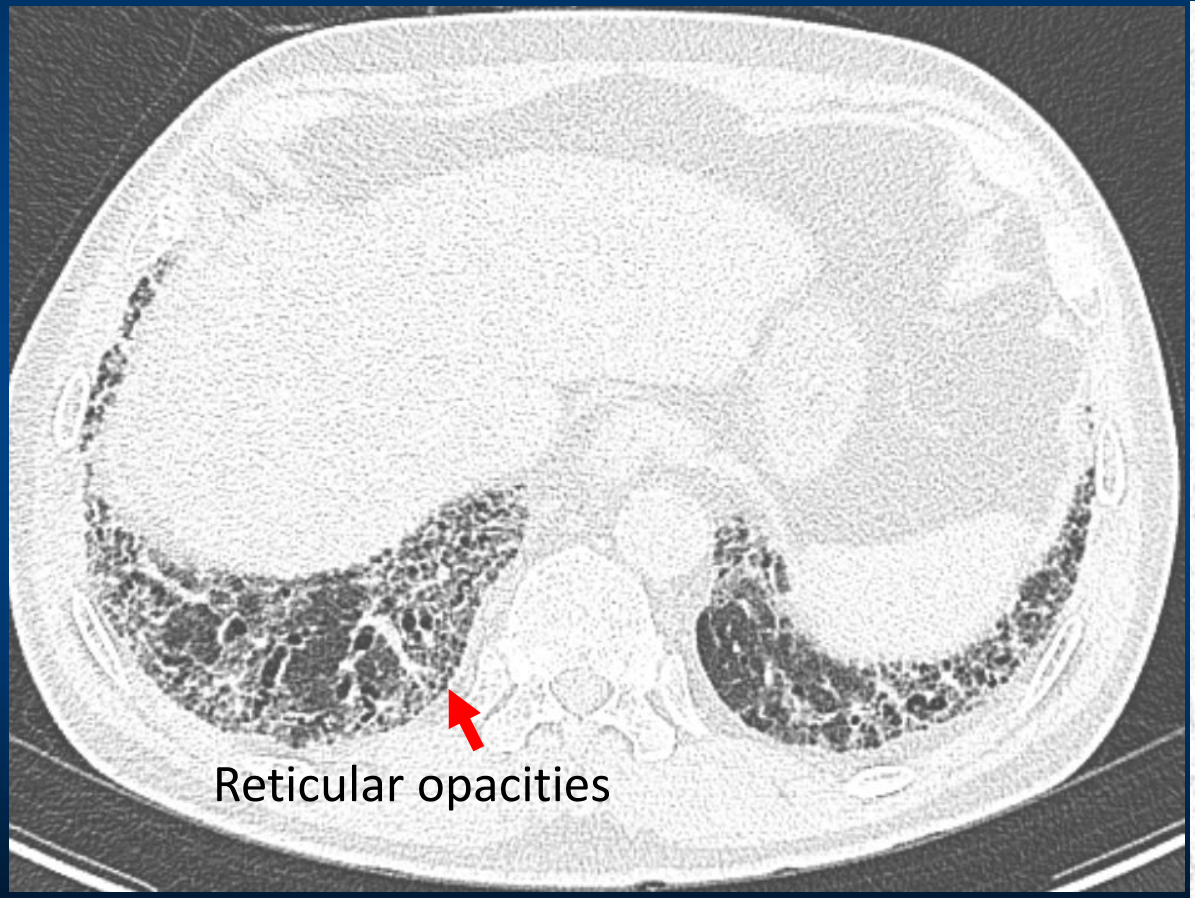
Basal and subpleural predominance





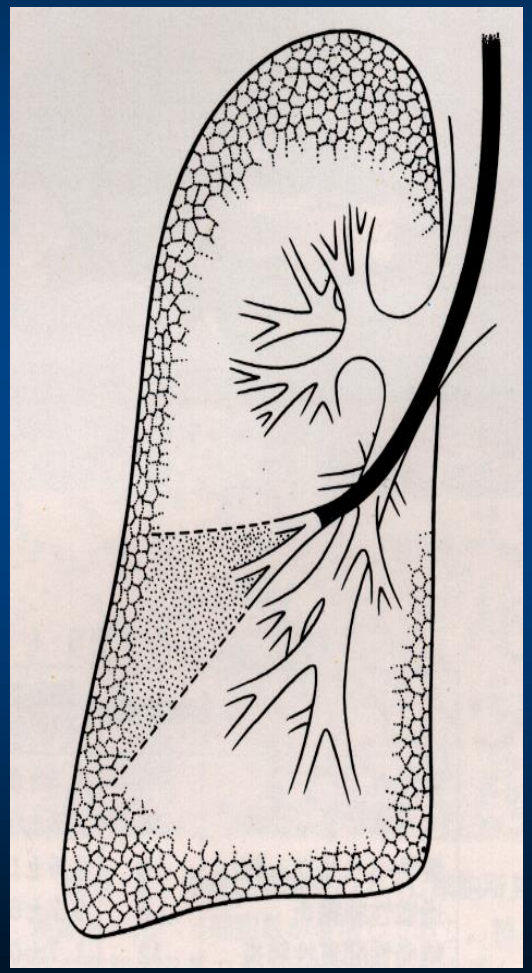
Probable UIP pattern

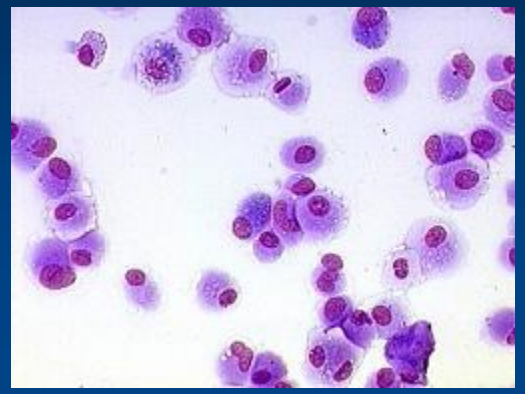
Basal and subpleural predominance



- No honeycombing; level of confidence for UIP histology (70-89%); IPF diagnosis without biopsy is possible after MDD in the appropriate clinical setting (eg. 60 yr old, male, smoker)

Bronchoalveolar lavage





Description	결과값	단위
Others fluid Color	Colorless	
Turbidity	Mild tubid	
Specific gravity	1.020	
RBC	20	mm³
WBC	400	mm³
Lymphoctyte	79	%
Alveolar macrophage	21	%
pH - Other Fluid	5.0	

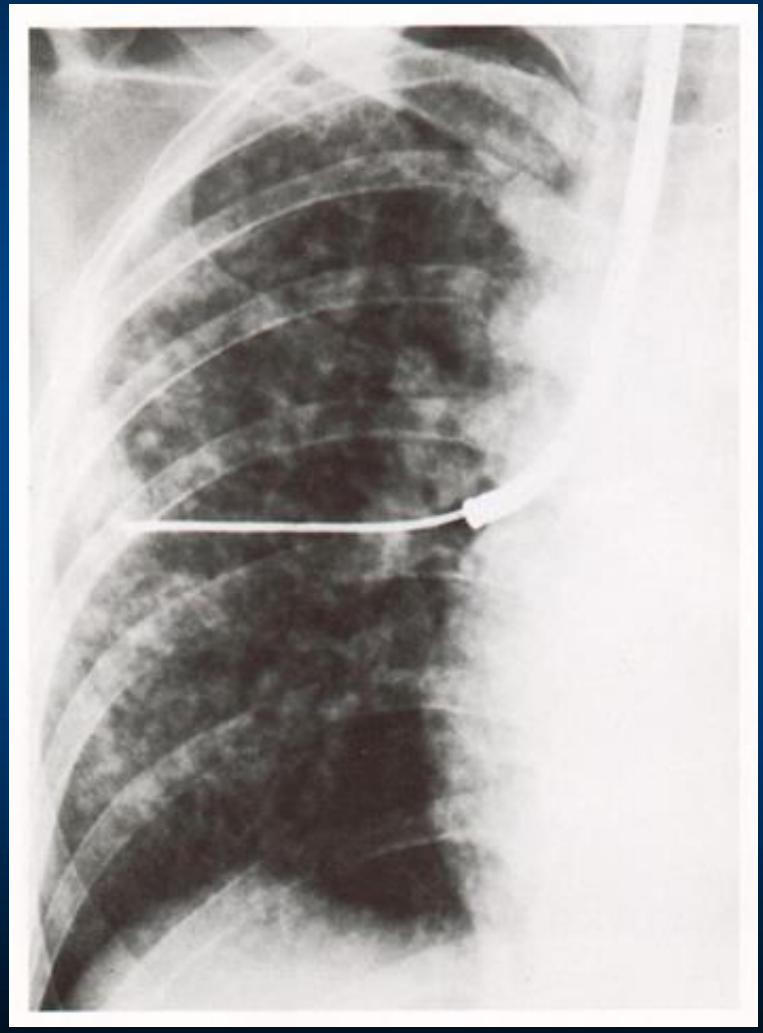
Description	결과값	단위
T-cell %	94.6	%
T helper/inducer cell %	84.4	%
T helper/inducer cell N	-	/uL
T suppressor/cytotoxic	6.5	%
T suppressor/cytotoxic	-	/uL

- Patients with ILD who do not have a UIP pattern on HRCT

- Usefulness:
  - Eosinophilic pneumonia (>25% Eo),
  - Lymph (>20%): sarcoidosis, HP, NSIP
  - Others: PAP, Lipoid Pn, DAH, Smoking-IP, drug-IP, PLCH, infection, malignancy

Raghu G et al. *Am J Respir Crit Care Med*. 2018;198:e44-e68

Bronchial biopsy



	Endobronchial biopsies	Forceps transbronchial biopsies
Very useful	Sarcoidosis Lymphangitic carcinomatosis	Sarcoidosis Lymphangitic carcinomatosis Berylliosis Organising pneumonia Bronchiolo-alveolar carcinoma
Often or occasionally useful	Granulomatosis with polyangiitis Some infections	Diffuse alveolar damage √ Alveolar lipoproteinosis Eosinophilic pneumonia √ Lymphangioleiomyomatosis √ Pulmonary Langerhans cell histiocytosis Silicosis Diffuse lymphoma Some infections Amyloidosis √ Hypersensitivity pneumonitis

Cottin V et al . *Presse Med 2020;49:104021*

Video-Assisted Thoracic Surgery (VATS)

- High diagnostic accuracy (~90%)
- Is it safe ? : ~1.7% for elective procedures
- Ideal biopsy
  - Preoperative targeting
  - Two or more surgical wedge biopsies with areas of normal lung taken from different areas of the lung
  - Samples should measure 3–5 cm in length and 2–3 cm in depth

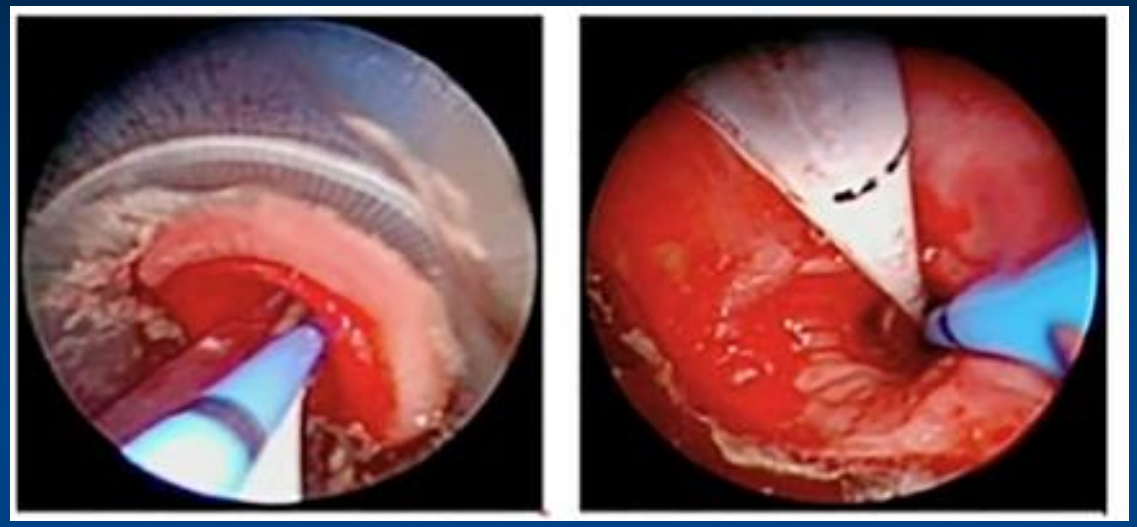
Rena O et al. *Eur J Cardiothorac Surg*. 1999;16:624-7, Chang AC et al. *Ann Thorac Surg. 2002*;74:1942-6

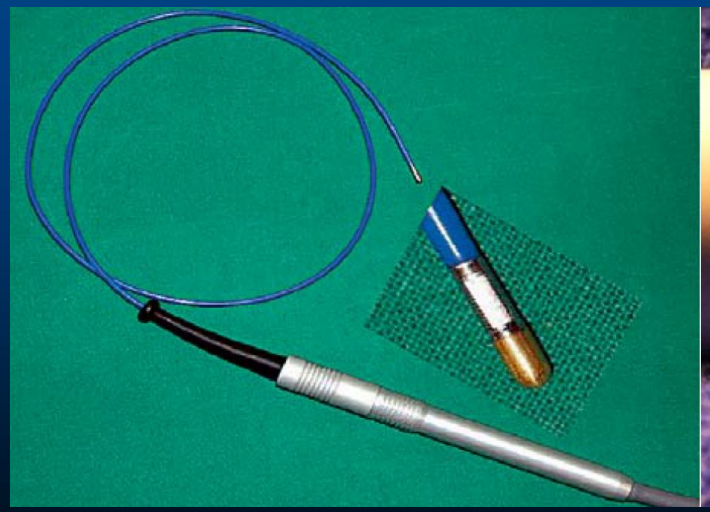
VATS: main contraindications

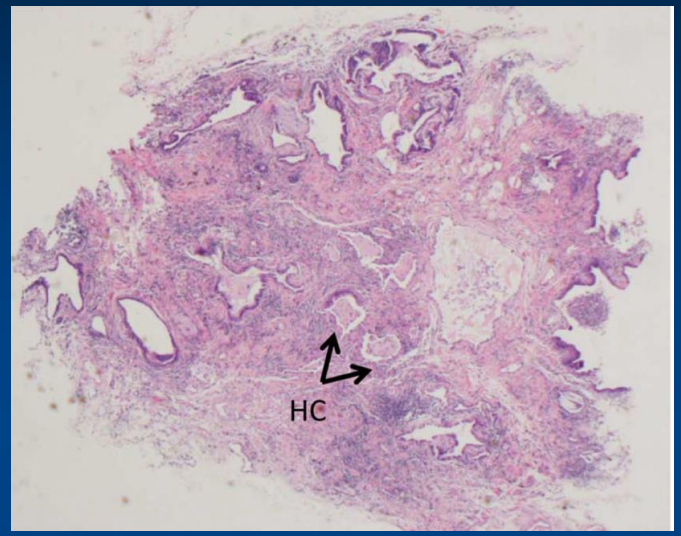
Age (physiologic) > 75 years
Rapid worsening or acute exacerbation (non-elective biopsy)
Low pulmonary reserve (FVC < 60–70%, DLco < 35–40% of predicted)
Supplementary oxygen at rest
Pulmonary hypertension
Major comorbidities
Immunodepression

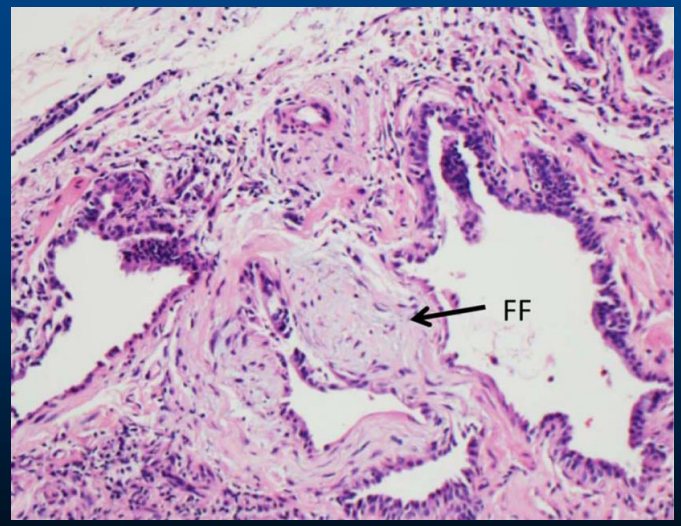
Cottin V et al. *Presse Med 2020;49:104021*

Cryobiopsy







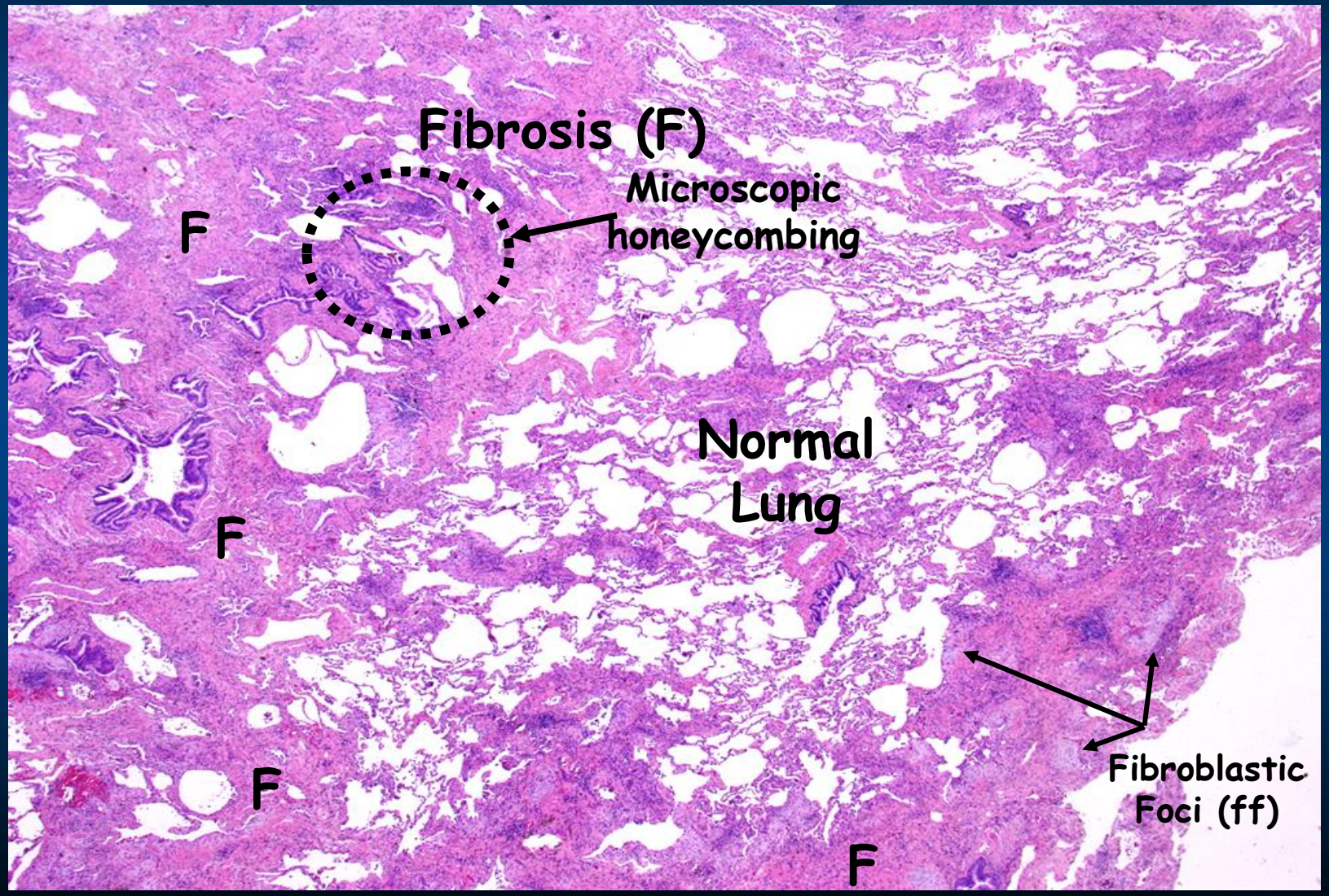


- Diagnostic yield in ILD: 79%
- Conditional recommendation in experienced centers

Raghu G et al. *Am J Respir Crit Care Med*. 2022;205:e18-e47

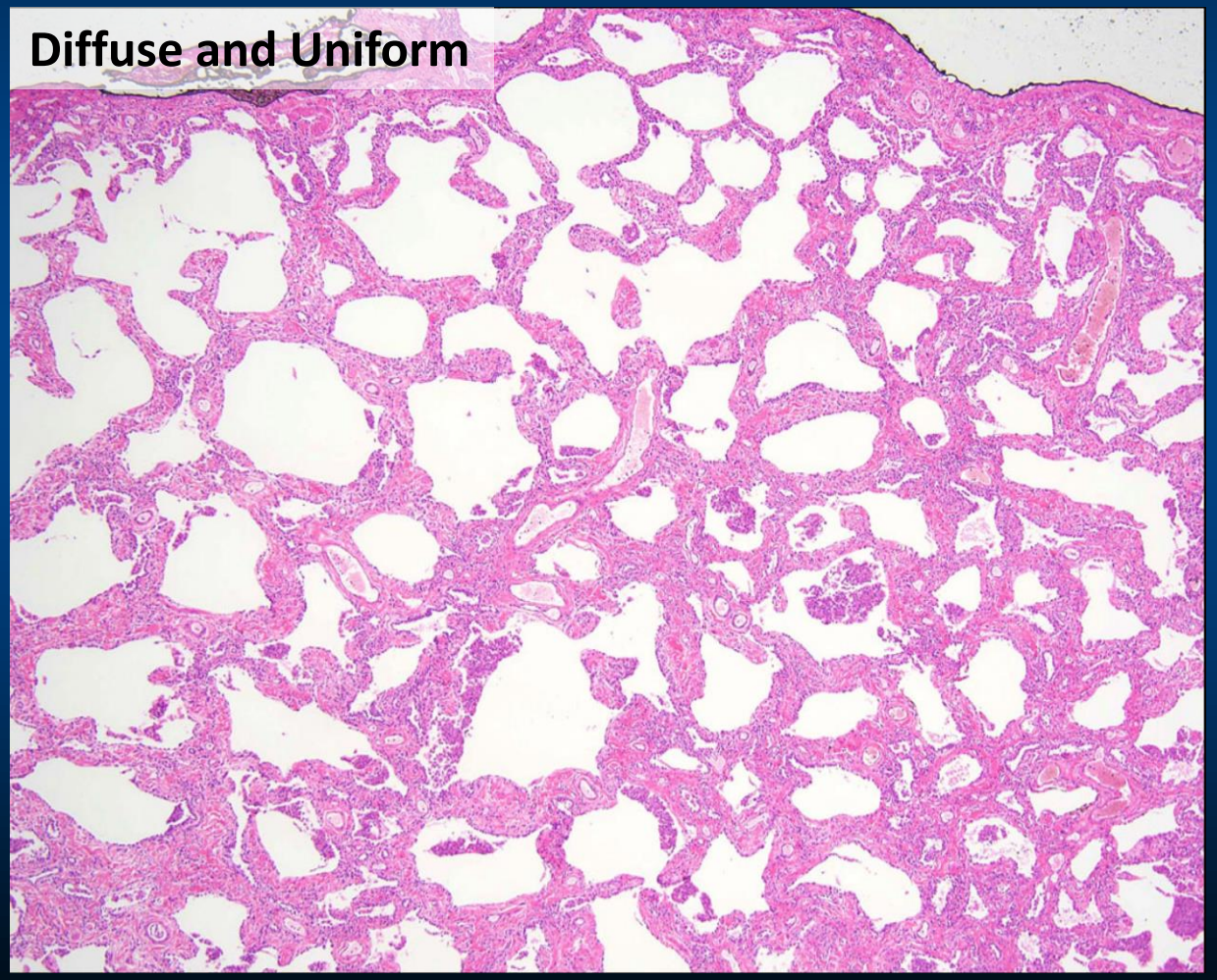
UIP is the histologic hallmarks of IPF

- Spatial and temoproal heterogeniety

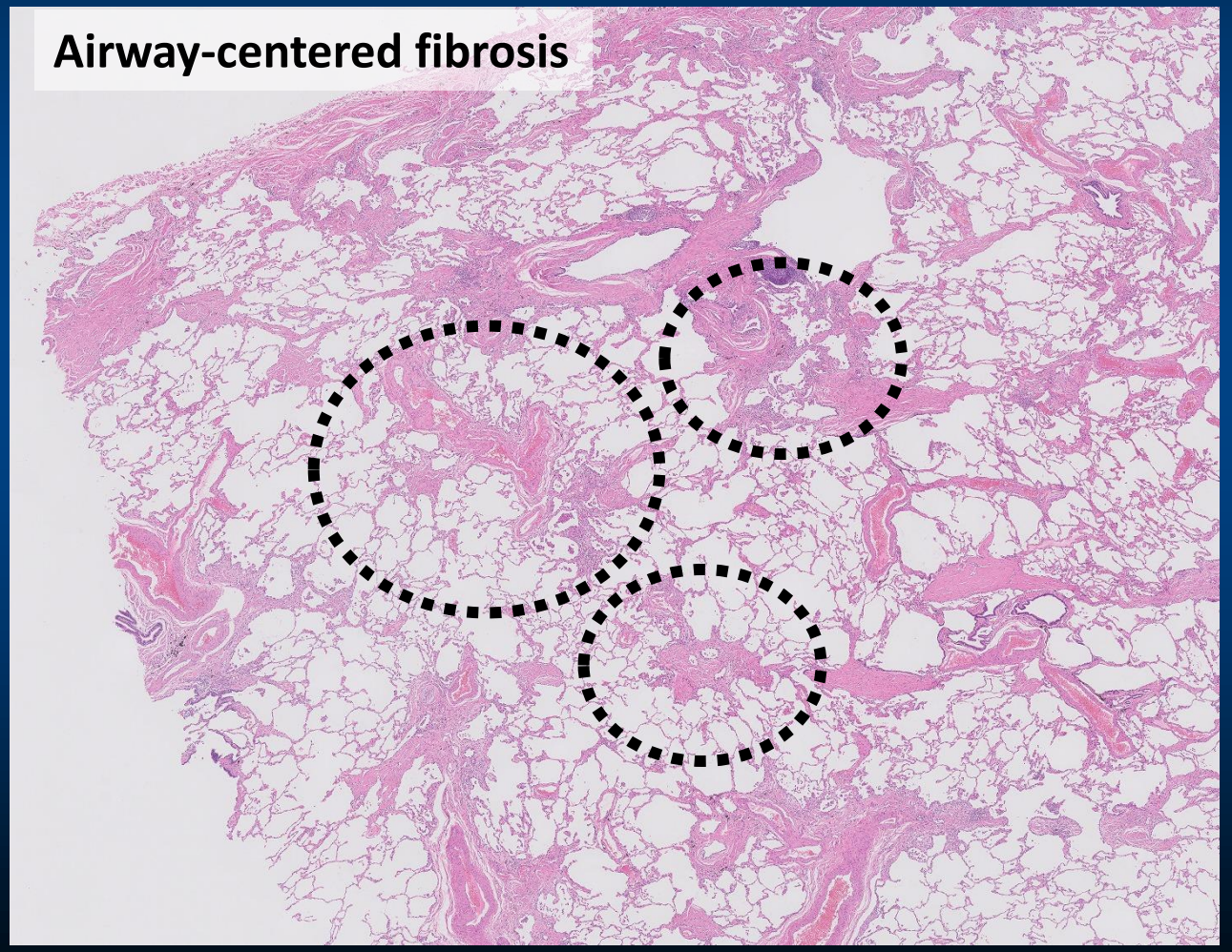


UIP vs. other fibrosing ILD

- fNSIP



- fHP



Histopathologic diagnosis in ILD
An Ailing Gold Standard

Using histology alone as the “gold standard” for diagnosis can be complicated by difficulties with..

1. interrater agreement (*low kappa value*)
2. the potential for sampling error (*intra-patient heterogeniety*)
3. The combination of HRCT and histologic features better predicts prognosis compared with either.

Flaherty KR et al. *Am J Respir Crit Care Med*. 2001;164(9):1722, Flaherty KR et al. *Am J Respir Crit Care Med*. 2004;170:904-10, Flaherty KR et al. *Thorax* 2003;58:143-8

Histopathologic diagnosis in ILD

- Agreement between pathologists

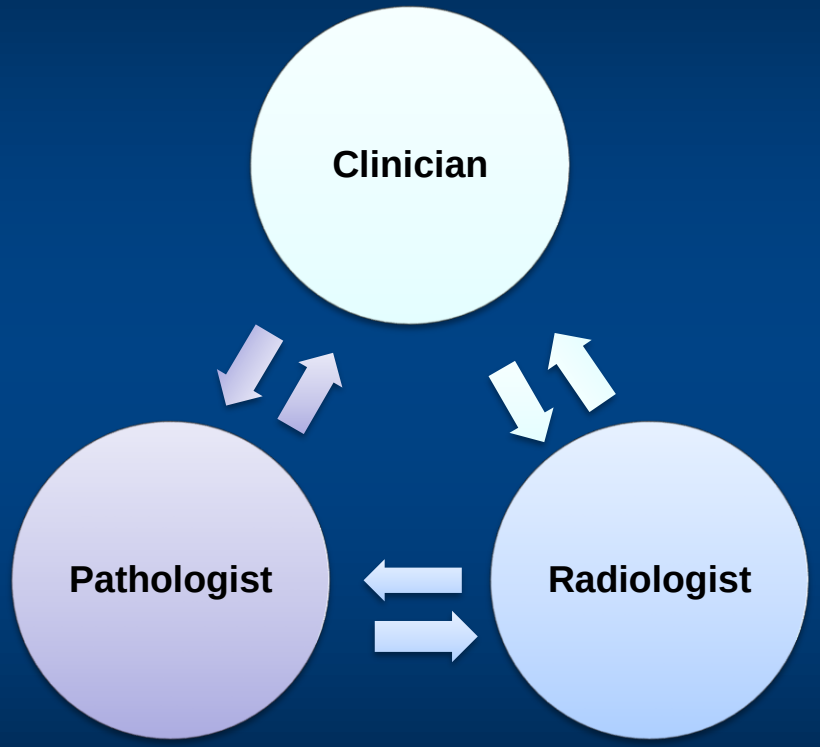
Histologic diagnosis	**Lobar diagnosis (n = 98)***	**Final diagnosis (n = 48)***
Usual interstitial pneumonia	0.40 (Moderate)	0.49 (Moderate)
Nonspecific interstitial pneumonia	0.32	0.32
Organizing pneumonia	0.59	0.67
Hypersensitivity pneumonitis	0.39	0.35
Sarcoidosis	0.76	0.82
Overall	0.39 (Fair)	0.43 (Moderate)

*kappa coefficients

Nicholson AG et al. *Thorax*. 2004;59:500-5

ILD diagnostic team

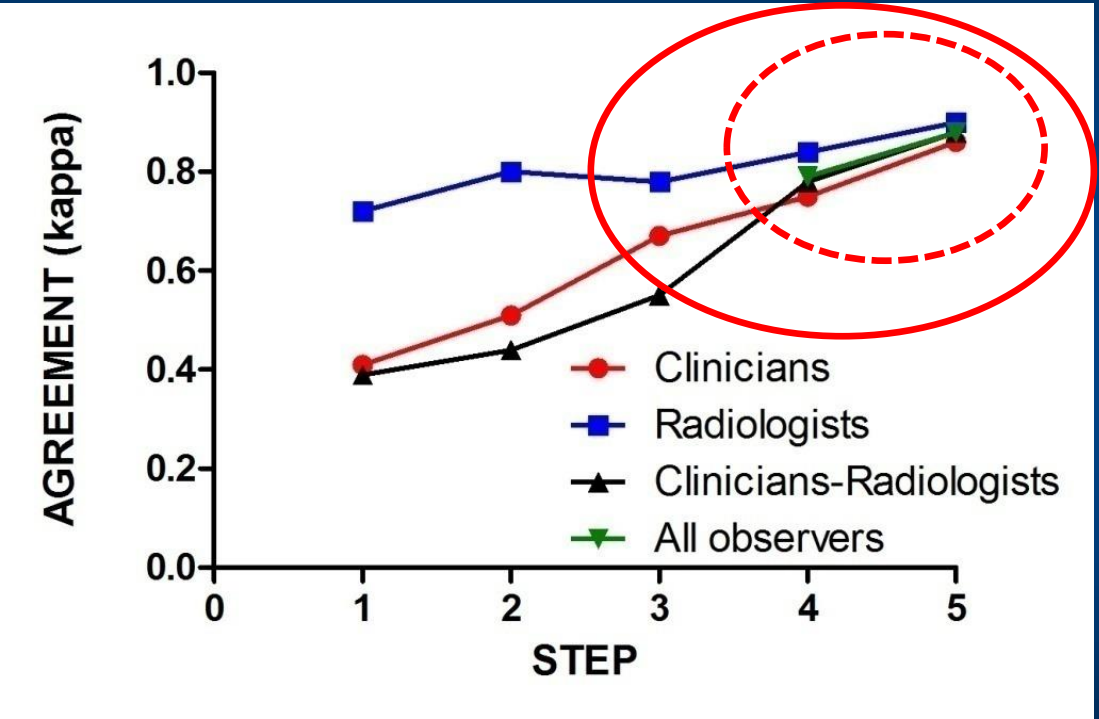
Multidisciplinary Discussion

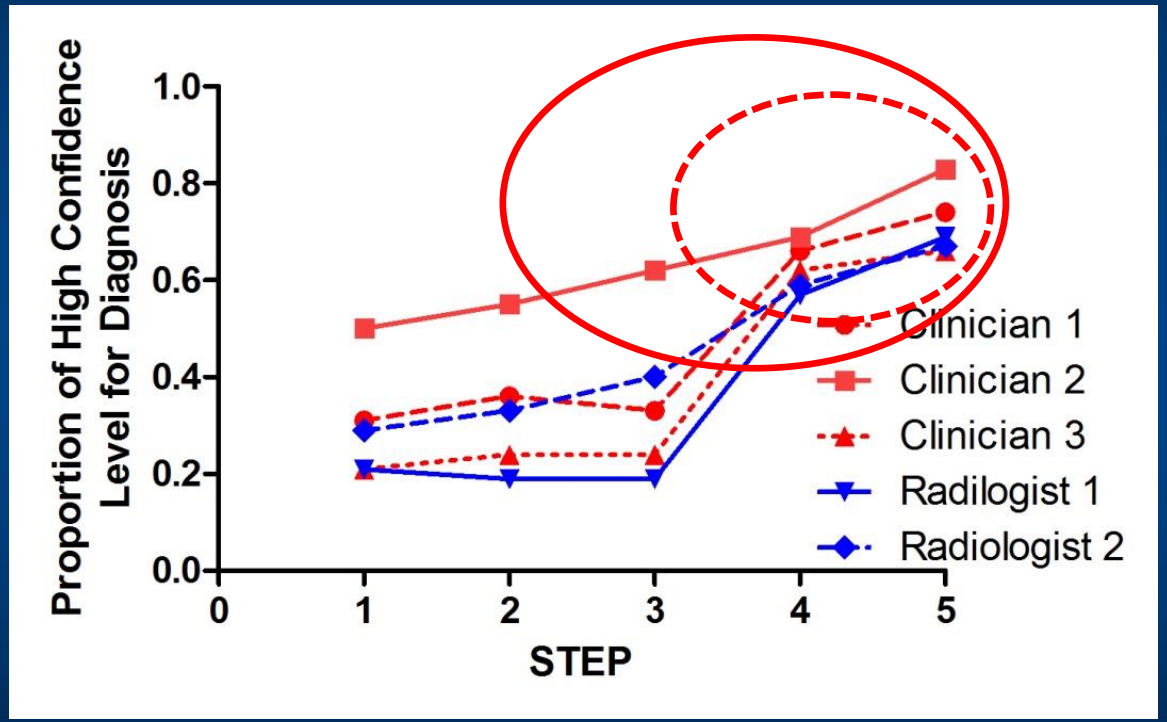


The current gold standard for the diagnosis of IIP is a dynamic integrated process that requires direct interaction between clinicians and radiologists as well as pathologists.

Raghu G et a. *Am J Respir Crit Care Med*. 2011;183:788-824

Multidisciplinary approach improve diagnostic agreement and confidence





- More information and multidisciplinary interactions improve diagnostic agreement and confidence.

Flaherty KR et al. *Am J Respir Crit Care Med*. 2004;170:904-10

Cases in which initial and final pathologic interpretation changed

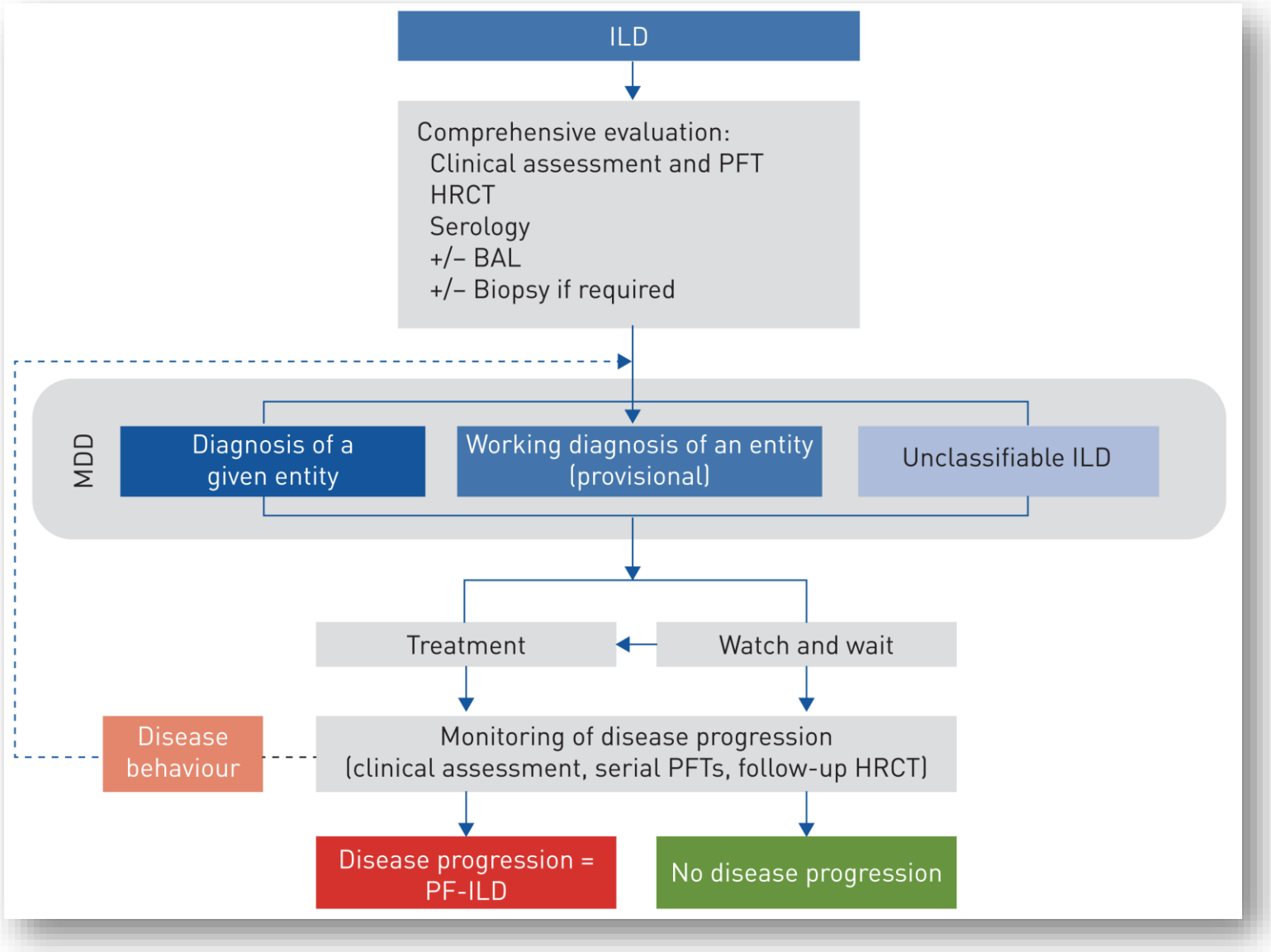
Thomas V. Colby, William D. Travis,

Initial Diagnosis	Final Diagnosis
Hypersensitivity pneumonitis	NSIP*
Organizing pneumonia	NSIP
UIP	ILD associated with CVID
Bronchiolar disease	Pulmonary veno-occlusive disease
End-stage lung	IPF
End-stage lung	IPF
End-stage lung	IPF
UIP	NSIP*
UIP	NSIP
Bronchiolar disease	RBILD
Bronchiolar disease	RBILD

- Diagnosis of 19% (11/58) was changed after C-R-P discussion.

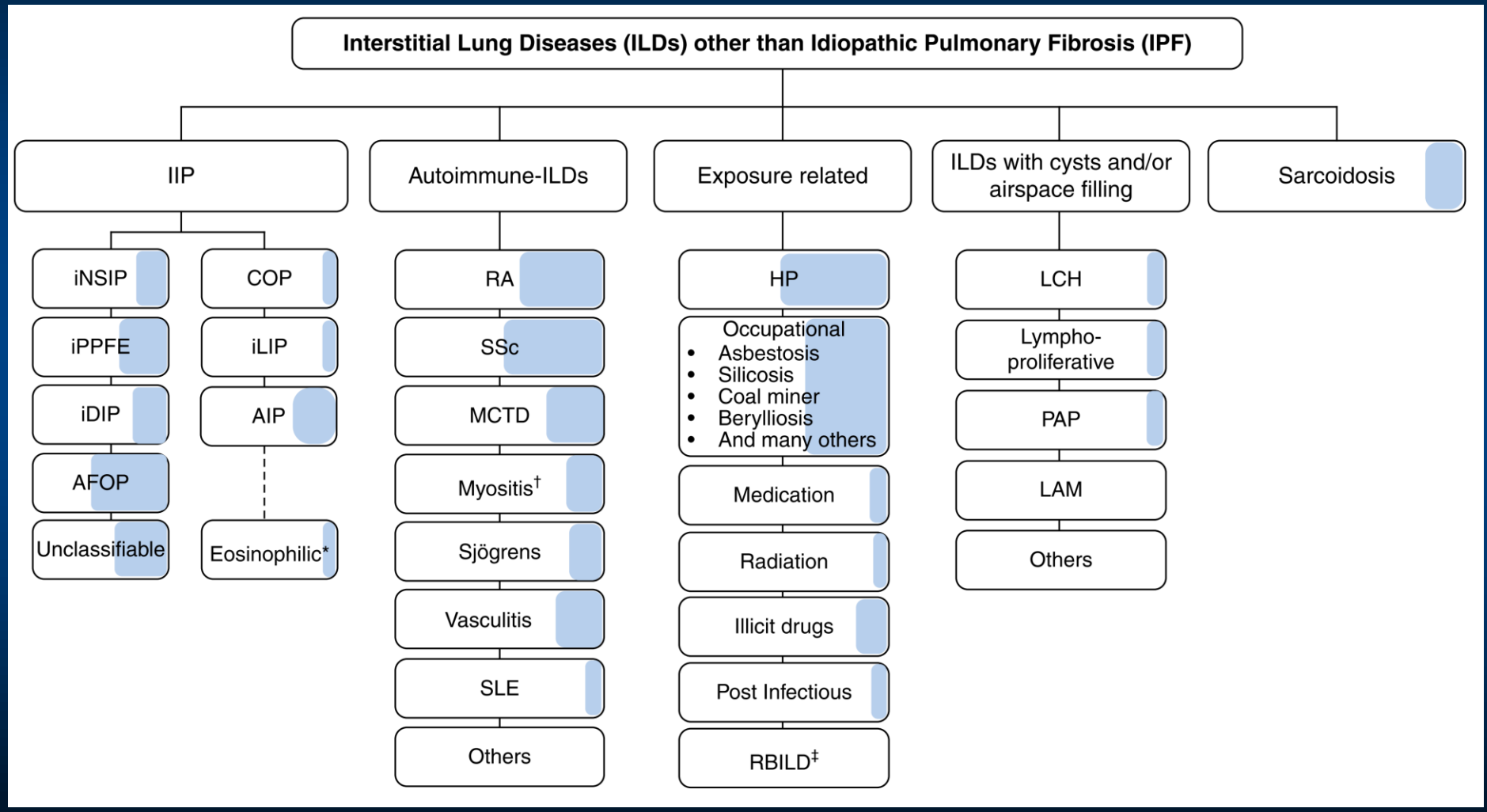
Flaherty KR et al. *Am J Respir Crit Care Med*. 2004;170:904-10

Diagnosis of fibrosing-ILD that may present a progressive phenotype



Cottin V. *Eur Respir Rev* 2019;28:190109

Proportion of Progressive Pulmonary FIbrosis



Raghu G et al. *Am J Respir Crit Care Med*. 2022;205:e18-e47

ATS/ERS/JRS/ALAT guideline: PPF

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*:

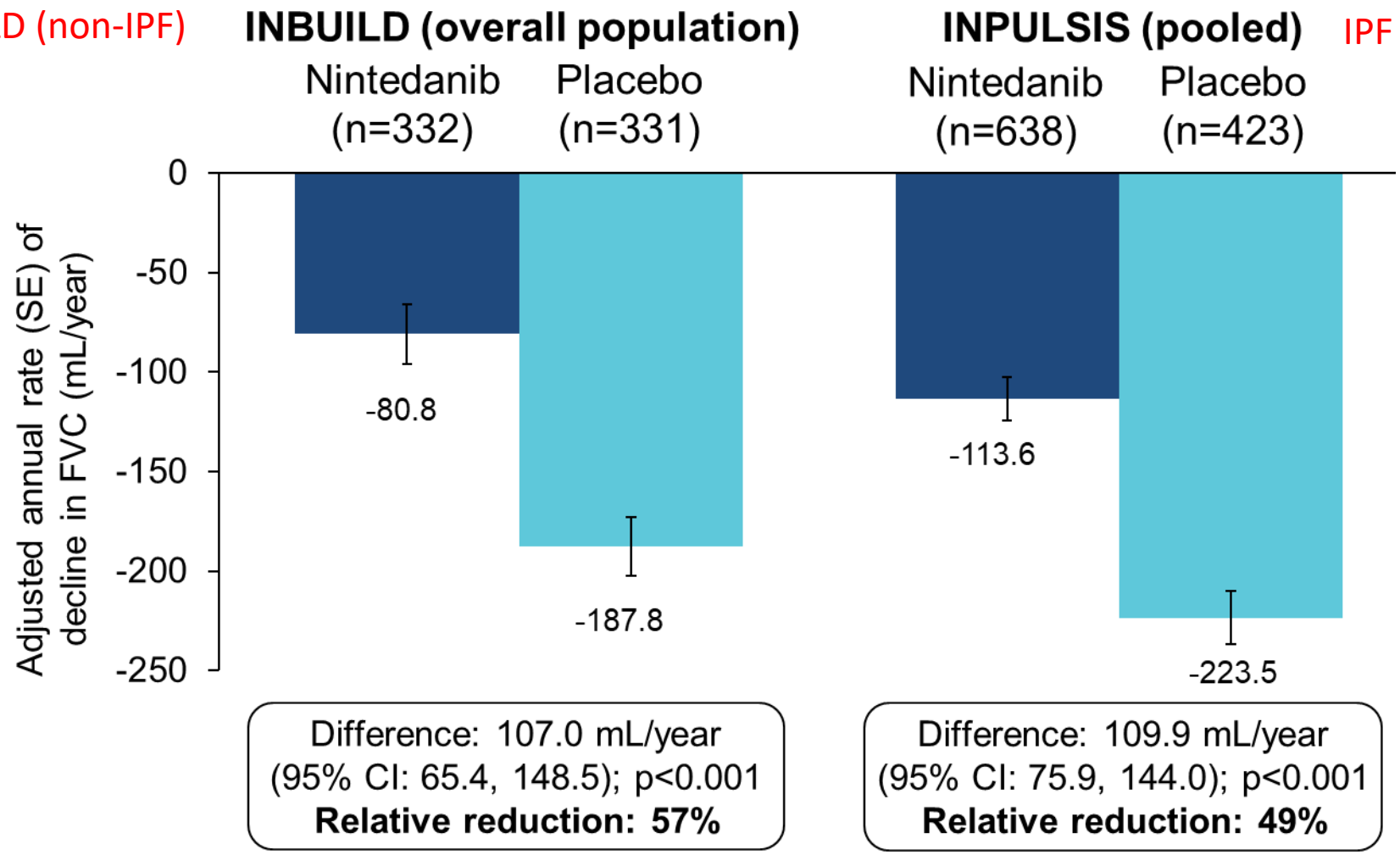
1 Worsening respiratory symptoms

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. *Am J Respir Crit Care Med*. 2022;205:e18-e47

Adjusted annual rate of decline in FVC (mL/year) over 52 weeks



Flaherty KR, et al. *N Engl J Med*. 2019;381(18):1718-1727.

Summary

- Clinical approach in ILD diagnosis

  - How thoroughly the patient's history and possible exposures are assessed, determine the possibility of an accurate diagnosis.
  - HRCT is the key of initial diagnostic approach.
  - MDD is the gold standard in diagnosing ILD.
  - Monitoring is important for early detection of PPF.