

# Introduction of CT Approach and Semi-quantitation of ILD



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# 2013 ATS-ERS Classification of IIP

Interstitial lung disease

Known cause or association:

- Connective tissue diseases
- Occupational causes
- Drug side-effects

20%

Idiopathic interstitial pneumonias

Non-familial (> 80%)      Familial (2-20%)

Granulomatous:

- Sarcoidosis
- Hypersensitivity pneumonitis
- Infections

20%

20%

Other forms, e.g.:

- Lymphangioleiomyomatosis
- Histiocytosis X

Major

Unclassifiable

~5-10%

Rare

Chronic fibrosing

Smoking related

Acute and subacute

<1%

Idiopathic pleuroparenchymal fibroelastosis

Idiopathic lymphocytic interstitial pneumonia

~50%

Idiopathic pulmonary fibrosis

20%

~25%

Non-specific interstitial pneumonia

Desquamative interstitial pneumonia

~10%

Respiratory bronchiolitis-ILD

~5%

Cryptogenic organising pneumonia

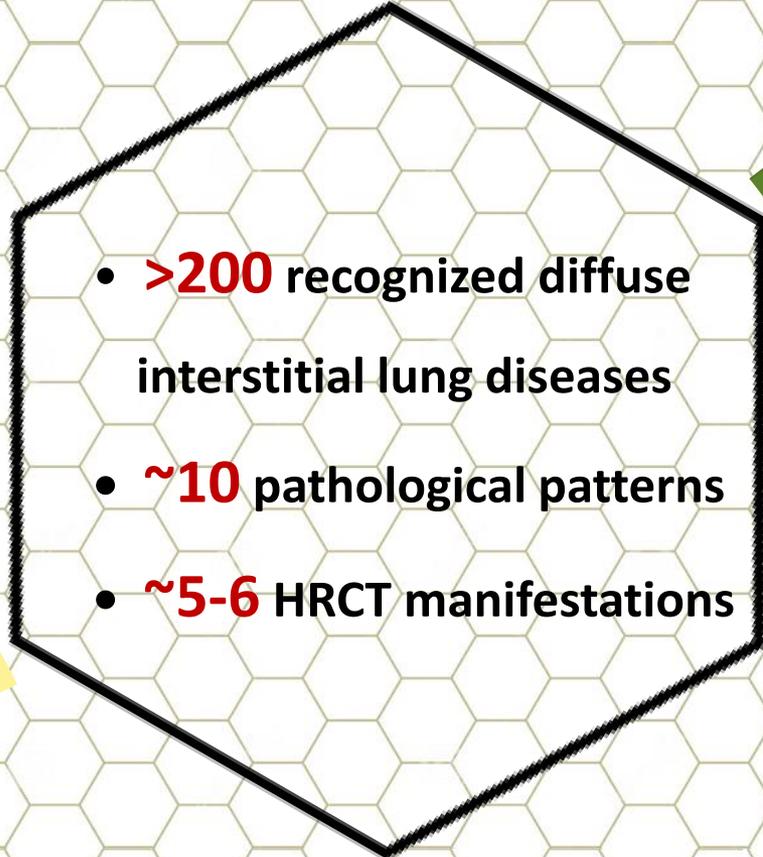
<2%

Acute interstitial pneumonia

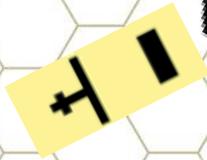
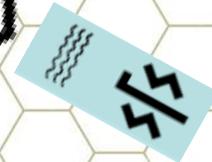
**UC**

Science?

Philosophy ?



- **>200** recognized diffuse interstitial lung diseases
- **~10** pathological patterns
- **~5-6** HRCT manifestations



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

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

|                                       | Probable UIP   | UIP   | Alternative Diagnosis   | Indeterminate for UIP  |
|---------------------------------------|--|---|---|--|
| Level of confidence for UIP histology |  |   |   |  |
| Distribution                          | Subpleural and basal predominant; distribution is often heterogeneous  | Subpleural and basal predominant; often heterogeneous   | Findings suggestive of another diagnosis, including:  | Subpleural and basal predominant   |
| CT features                           | <p>Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis</p> <p>May have mild GGO</p> <ul style="list-style-type: none"> <li>• Presence of irregular thickening of interlobular septa</li> <li>• Usually superimposed with a reticular pattern, mild GGO</li> <li>• May have pulmonary ossification</li> </ul> | <p>Honeycombing with peripheral traction bronchiectasis and bronchiolectasis</p> <ul style="list-style-type: none"> <li>• May have mild GGO</li> <li>• Absence of subpleural sparing</li> </ul> | <ul style="list-style-type: none"> <li>• CT features: <ul style="list-style-type: none"> <li>◦ Cysts</li> <li>◦ Marked mosaic attenuation</li> <li>◦ Predominant GGO</li> <li>◦ Profuse micronodules</li> <li>◦ Centrilobular nodules</li> <li>◦ Nodules</li> <li>◦ Consolidation</li> </ul> </li> <li>• Predominant distribution: <ul style="list-style-type: none"> <li>◦ Peribronchovascular</li> <li>◦ Perilymphatic</li> <li>◦ Upper or mid-lung</li> </ul> </li> <li>• Other: <ul style="list-style-type: none"> <li>◦ Pleural plaques (consider asbestosis)</li> <li>◦ Dilated esophagus (consider CTD)</li> <li>◦ Distal clavicular erosions (consider RA)</li> <li>◦ Extensive lymph node enlargement (consider other etiologies)</li> <li>◦ Pleural effusions, pleural thickening (consider CTD/drugs)</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>• Subtle reticulation; may have mild GGO or distortion ("early UIP pattern")</li> <li>• CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate") <ul style="list-style-type: none"> <li>◦ Mosaic attenuation or three-density sign (consider HP)</li> <li>◦ Predominant GGO (consider HP, smoking-related disease, drug toxicity, and acute exacerbation of fibrosis)</li> <li>◦ Profuse centrilobular micronodules (consider HP or smoking-related disease)</li> <li>◦ Nodules (consider sarcoidosis)</li> <li>◦ Consolidation (consider organizing pneumonia, etc.)</li> </ul> </li> <li>• Mediastinal findings <ul style="list-style-type: none"> <li>◦ Pleural plaques (consider asbestosis)</li> <li>◦ Dilated esophagus (consider CTD)</li> </ul> </li> </ul> |

# IPF on the basis of HRCT and biopsy patterns

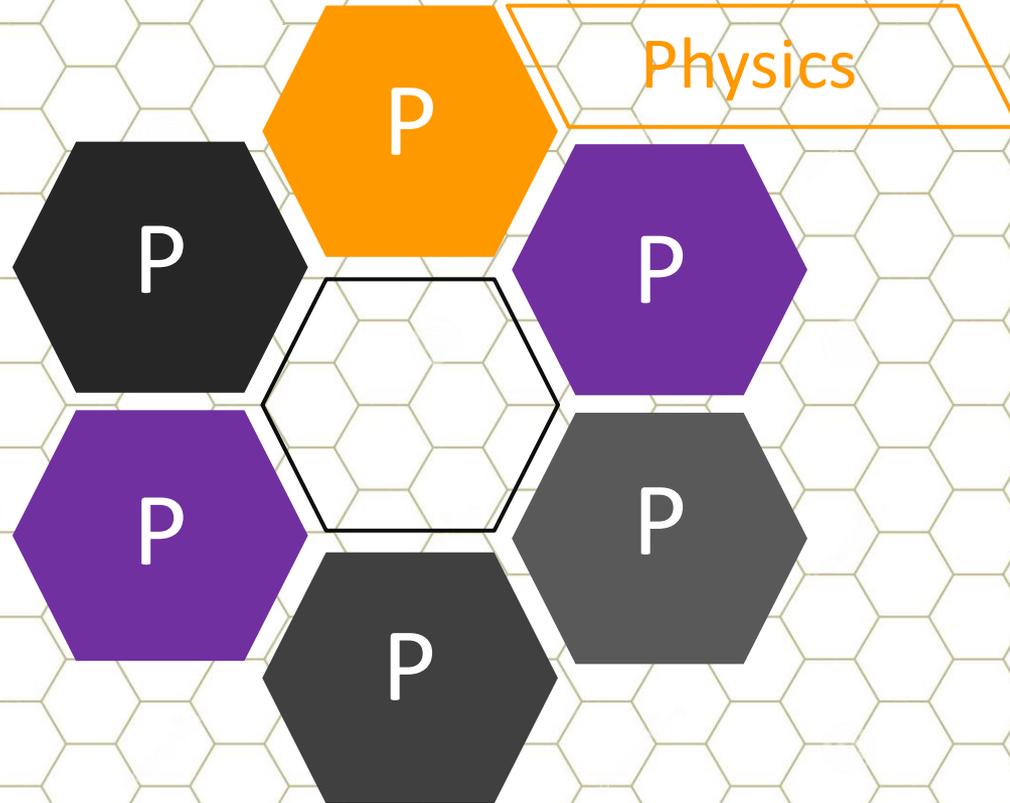
| IPF suspected* |                       | Histopathology pattern <sup>†</sup> |                            |   |                       |
|----------------|-----------------------|-------------------------------------|----------------------------|---|-----------------------|
|                |                       | 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) <sup>‡</sup>                     | Non-IPF dx            |
|                | Indeterminate         | IPF                                 | IPF (Likely) <sup>‡</sup>  | Indeterminate <sup>§</sup>                    | Non-IPF dx            |
|                | Alternative diagnosis | IPF (Likely) <sup>‡</sup>           | Indeterminate <sup>§</sup> | Non-IPF dx                                    | Non-IPF dx            |

| IPF suspected* |                       | Histopathology pattern     |                |                       |                       |
|----------------|-----------------------|----------------------------|----------------|-----------------------|-----------------------|
|                |                       | UIP                        | Probable UIP   | Indeterminate for UIP | 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)** /non-IPF dx | Non-IPF dx     | Non-IPF dx            | Non-IPF dx            |

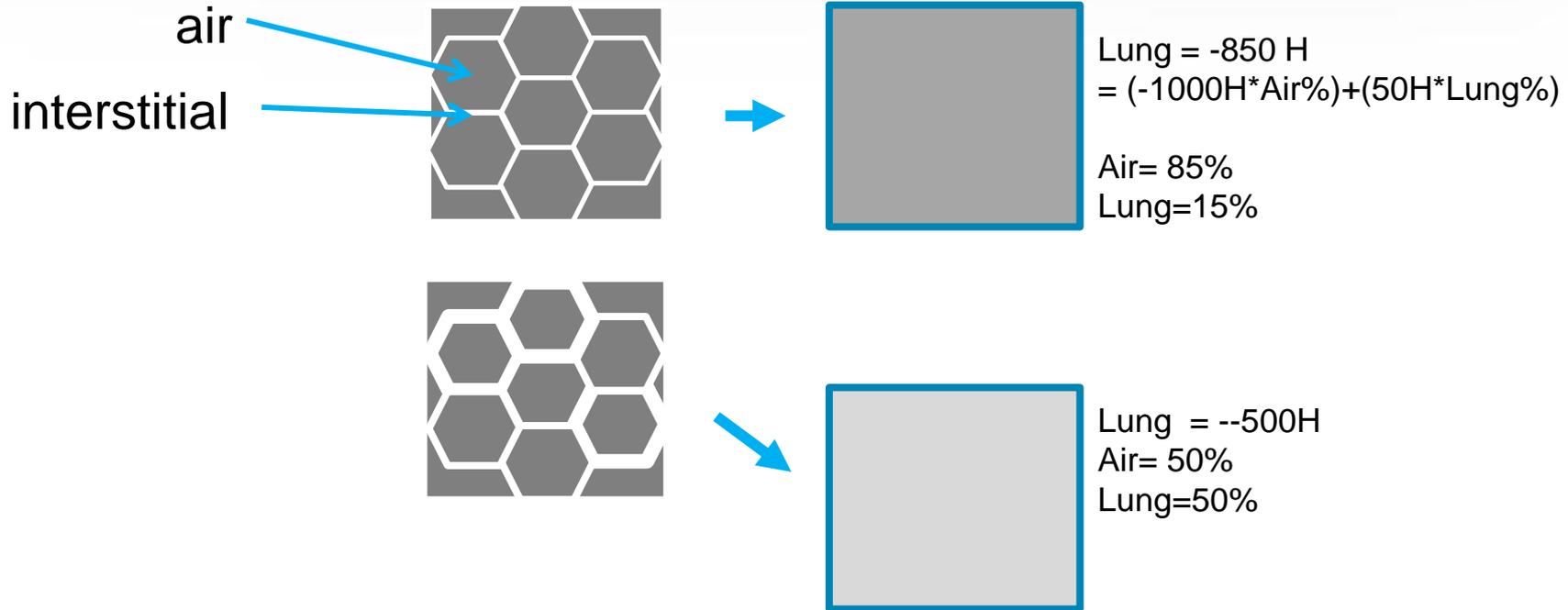
smaller biopsy size  
the following features  
bronchiectasis and  
in two or more lobes  
increased neutrophils  
IPF. § Indeterminate

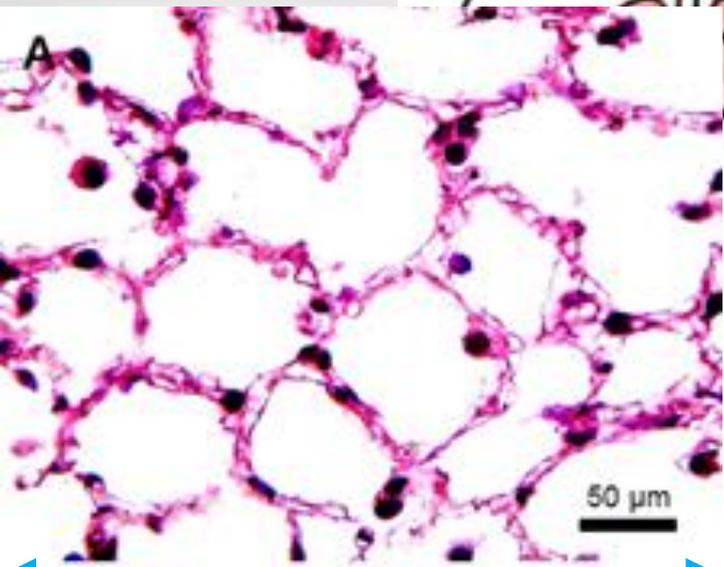
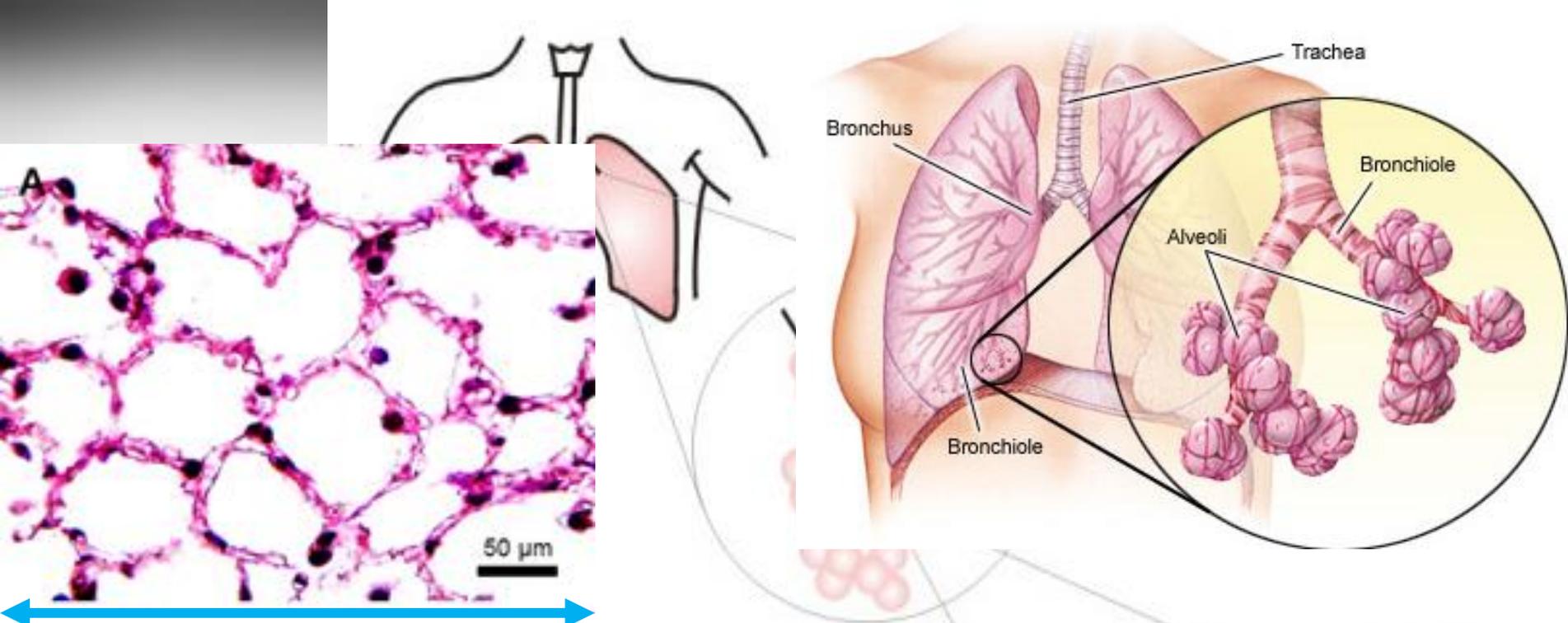
when any of  
on  
nchiectasis  
(70 yr, 3)  
diagnosis of

# 6 Perspectives

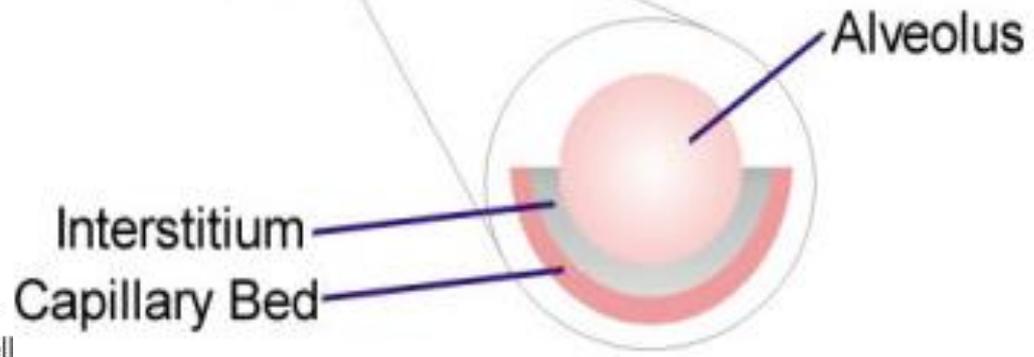
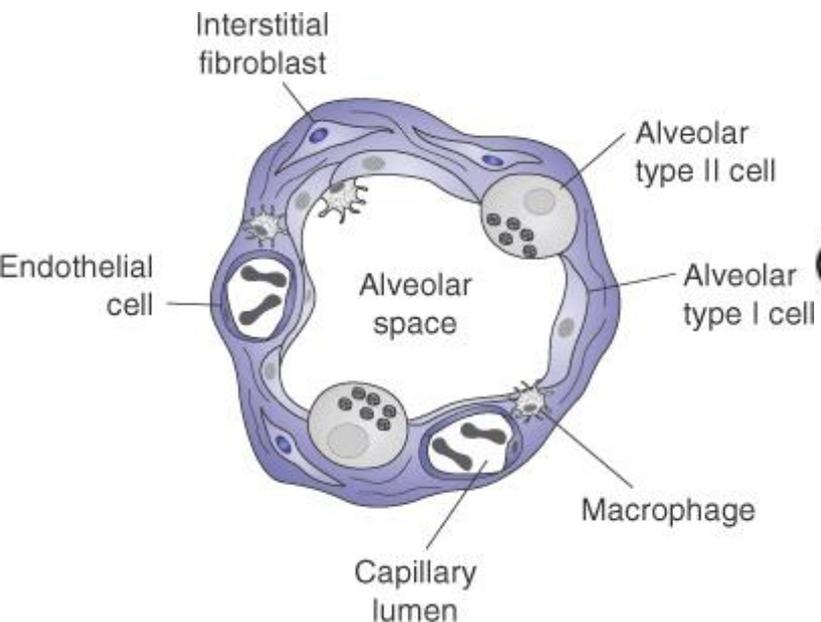


## Partial volume effect: Intra-voxel average

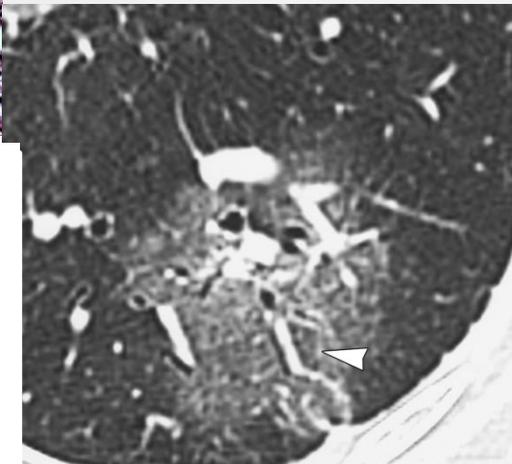
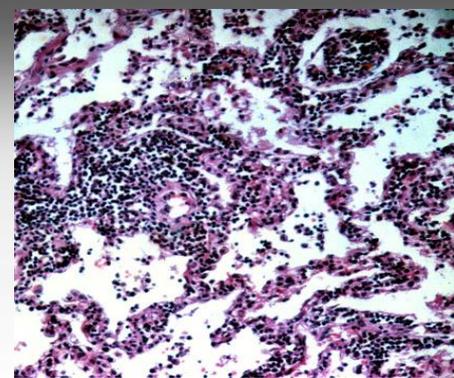
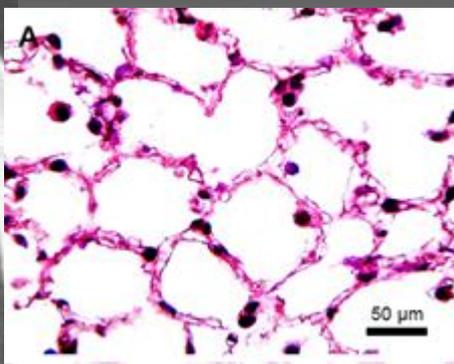
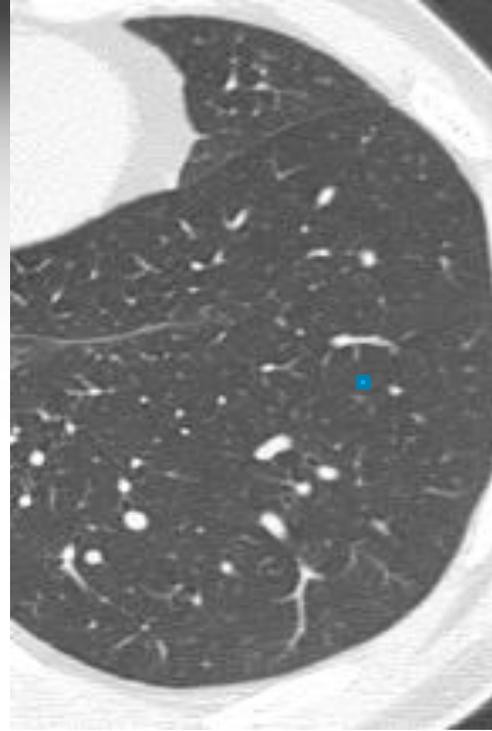




0.5 mm

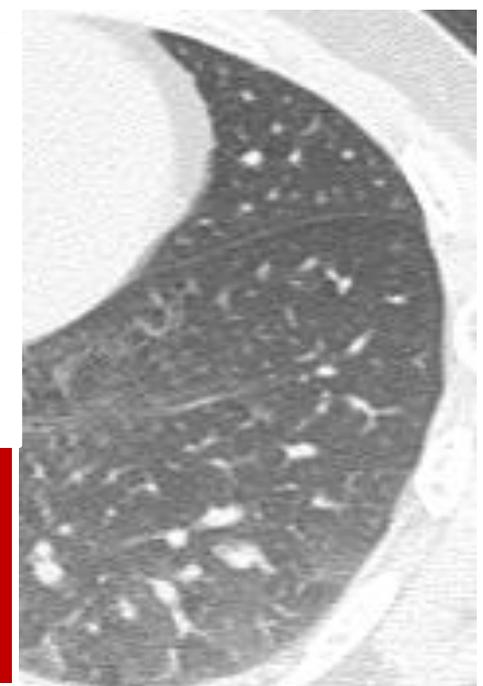


Interstitial compartment is the portion of the lung sandwiched between the epithelial and endothelial basement membrane

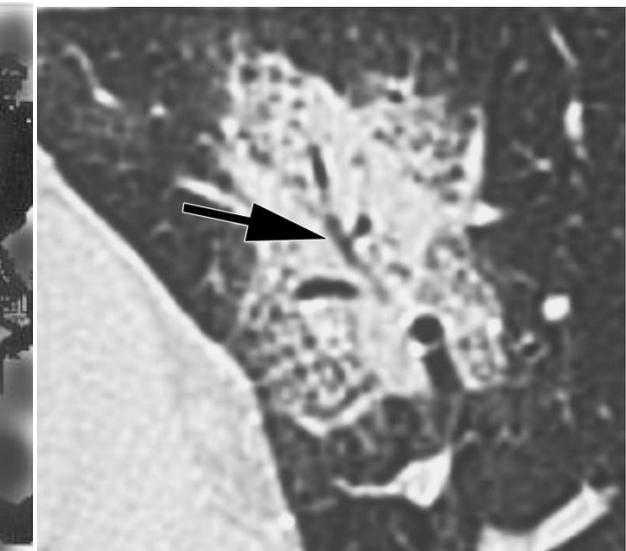
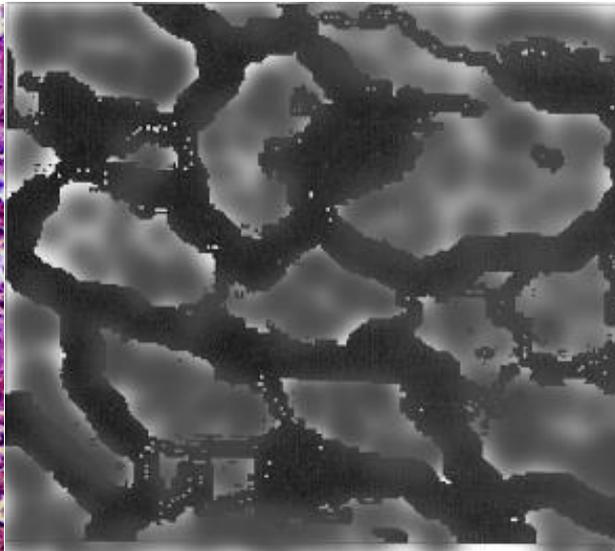
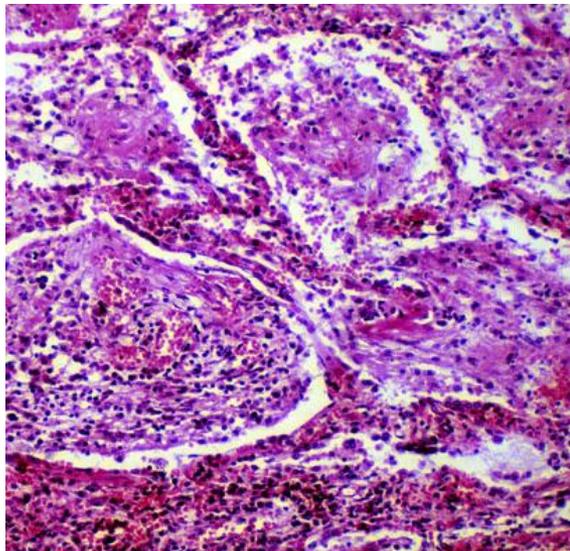
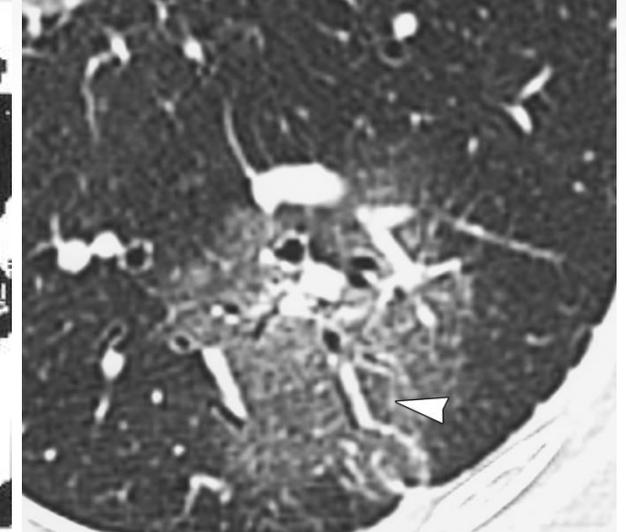
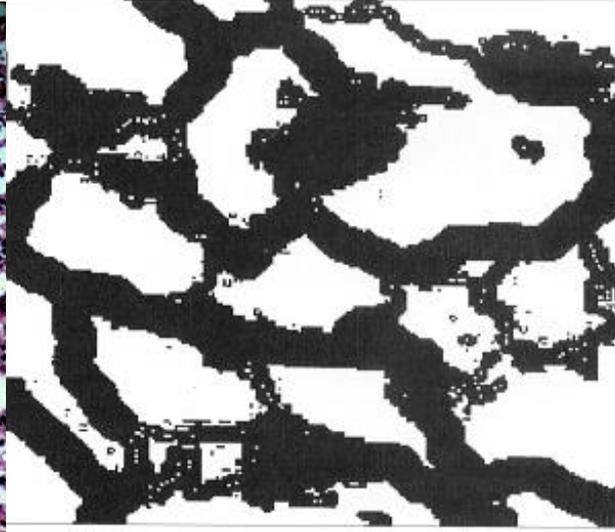
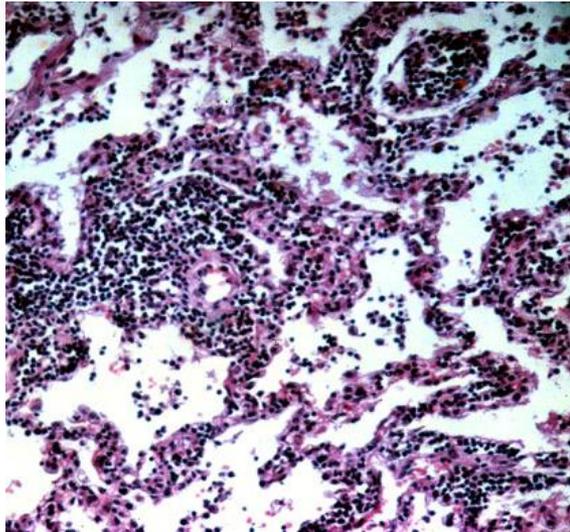


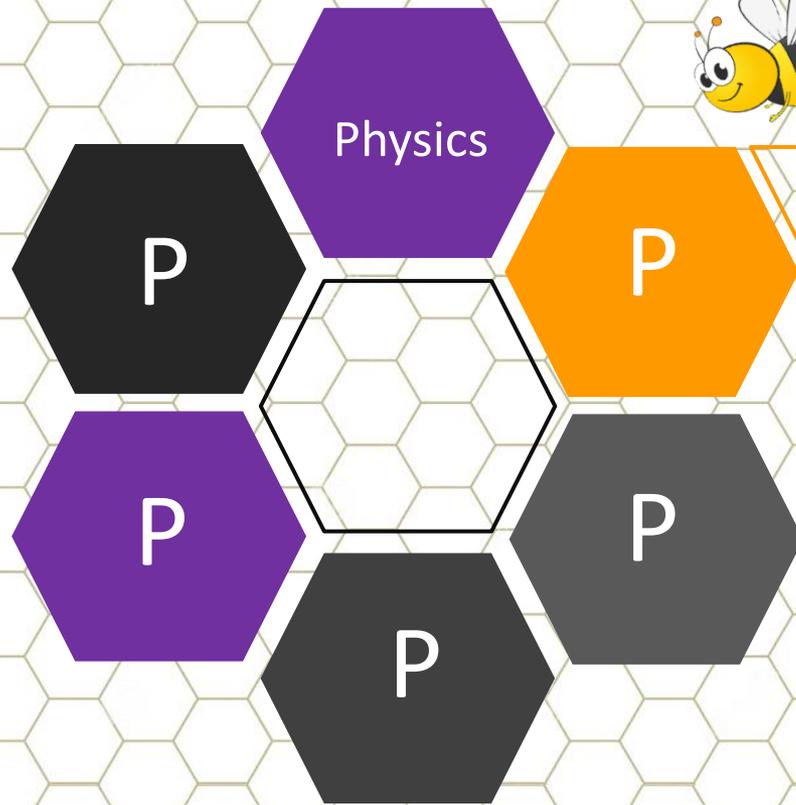
**edema,  
perfusion**

**ground-glass opacity  
can be an interstitial process!**



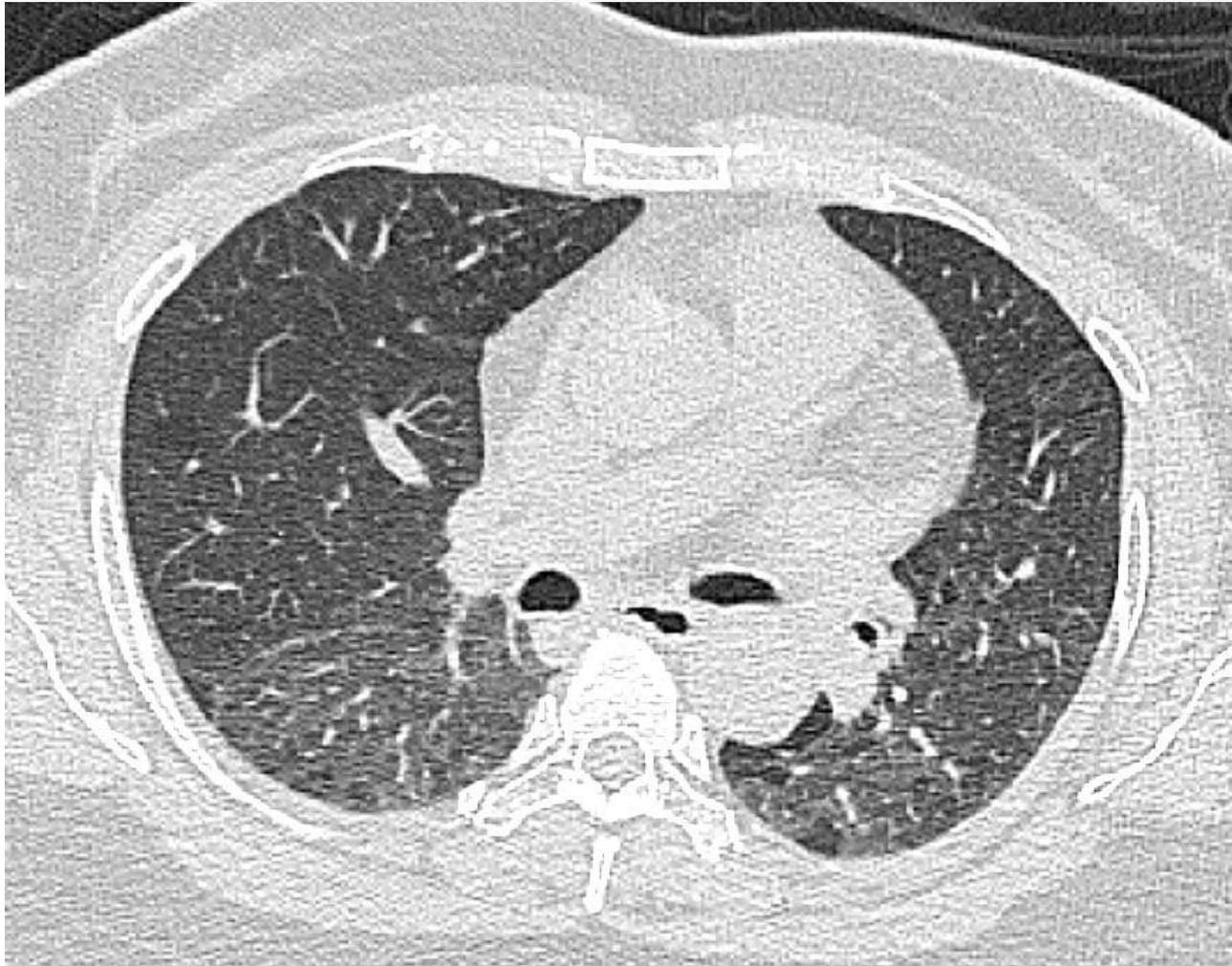
# Ground-glass opacity vs. consolidation (underlined vessels + vs. -)





Physiology

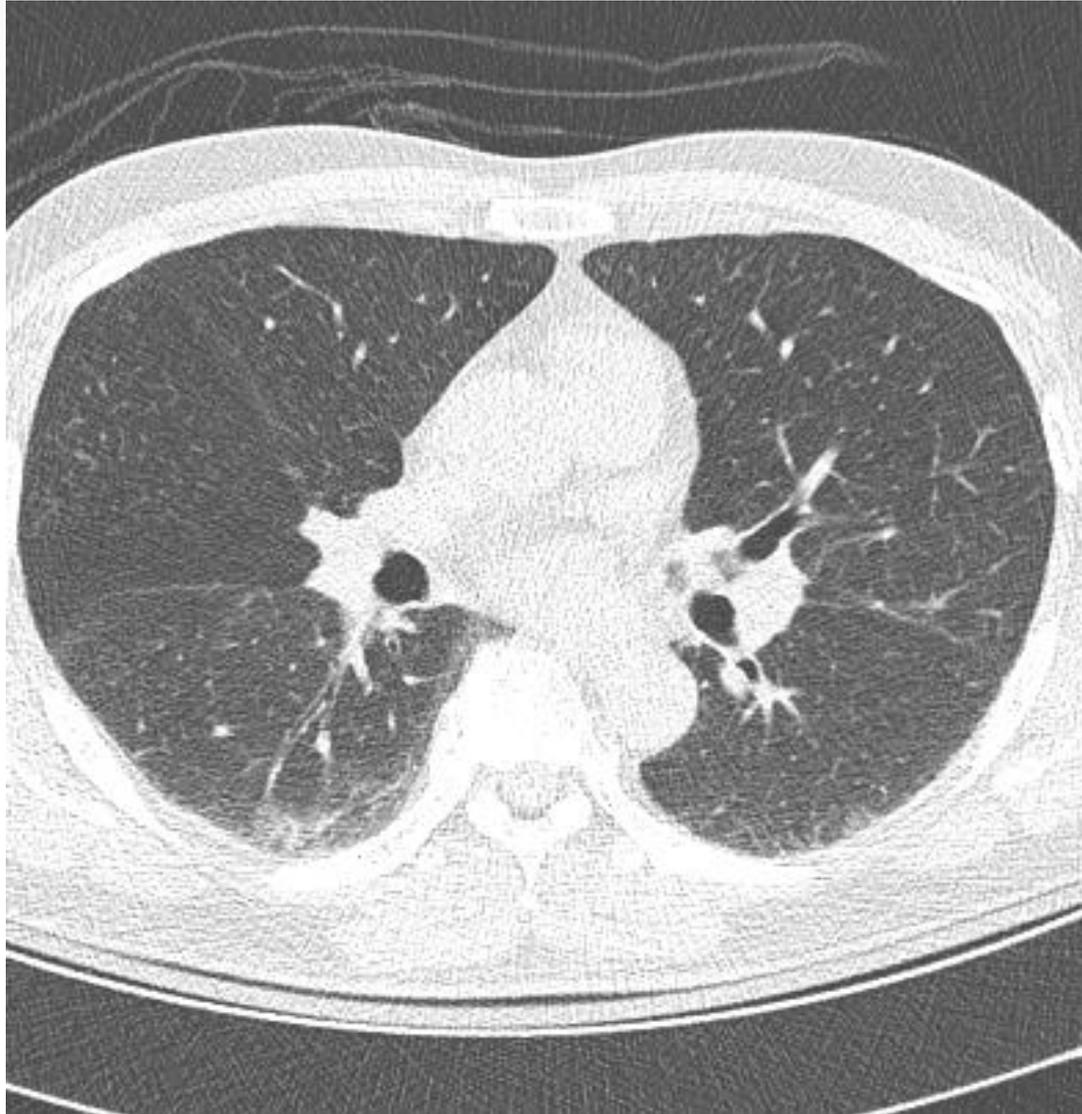
**Is there GGO?**



# The Influence of Expiratory phase

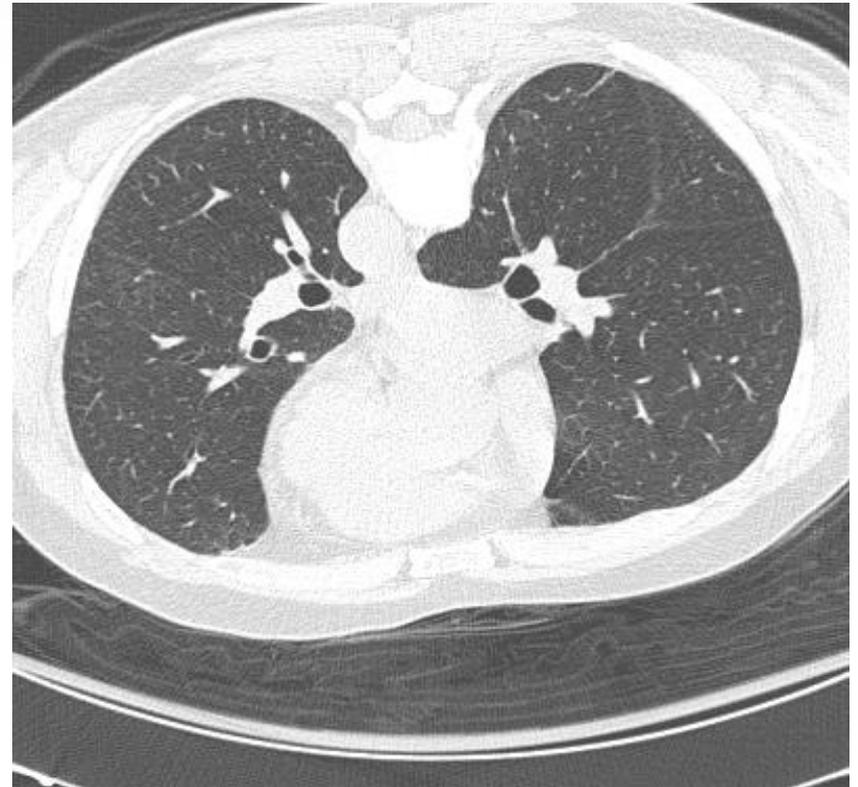


**Is there ILA?** (interstitial lung abnormality)  
**Is it NSIP? indeterminate UIP?**

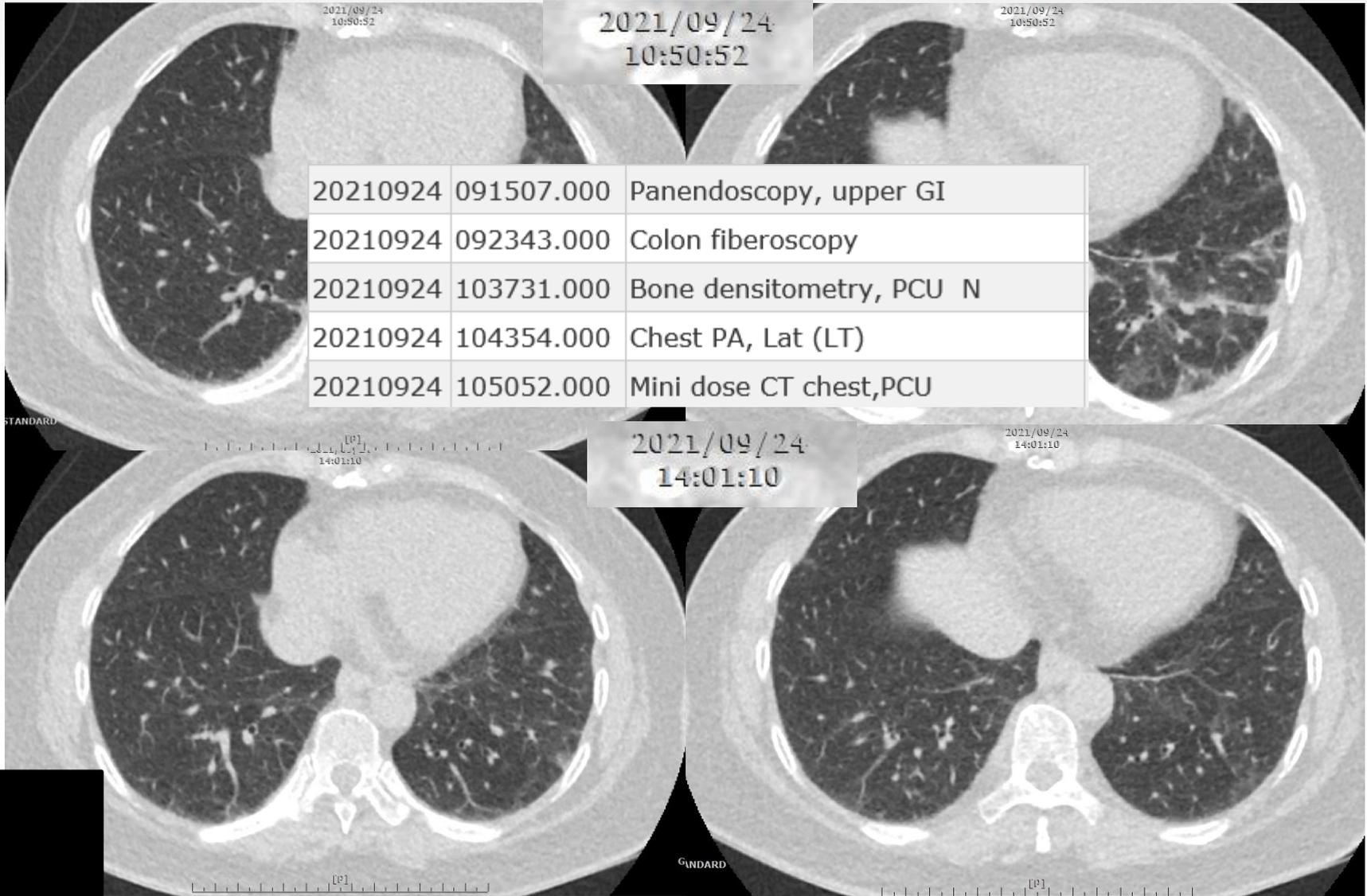


# Effect of gravity

Why some centers prefer Prone HRCT routinely



# Post-scope Atelectasis



# 53 YOF SOB for months

102

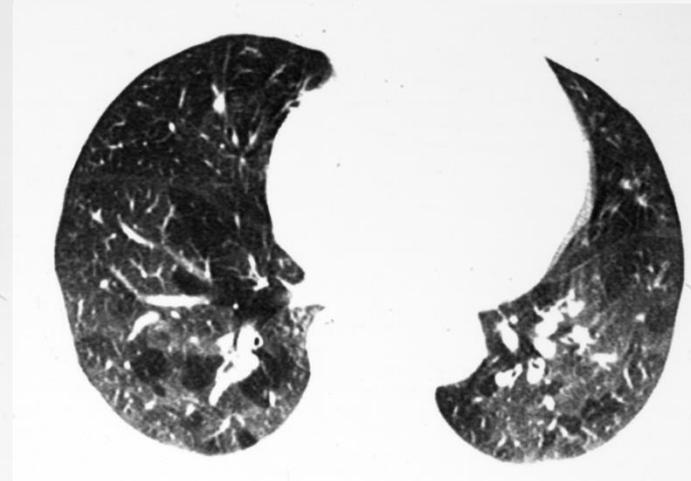
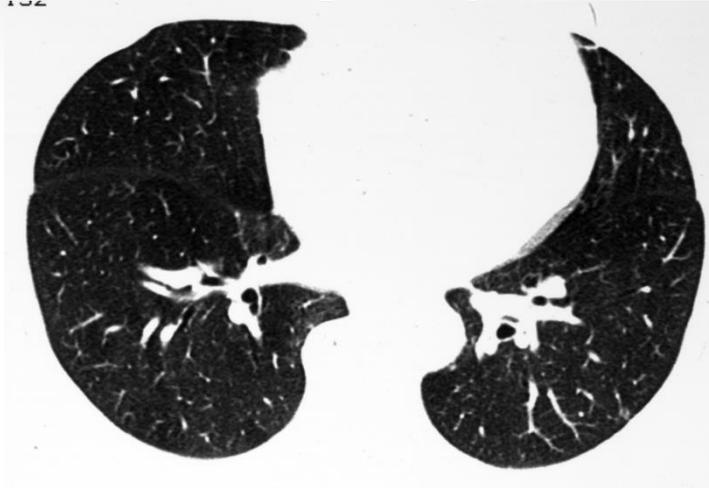


# Mosaic perfusion due to small airway disease

## Constrictive bronchiolitis = bronchiolitis obliterans

inspiratory

expiratory



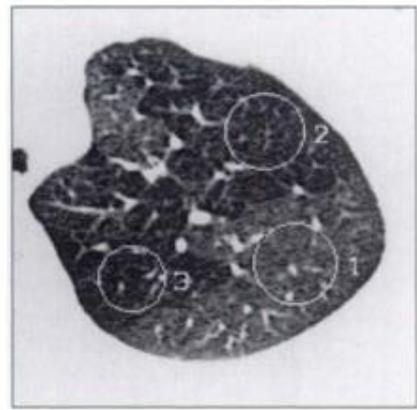
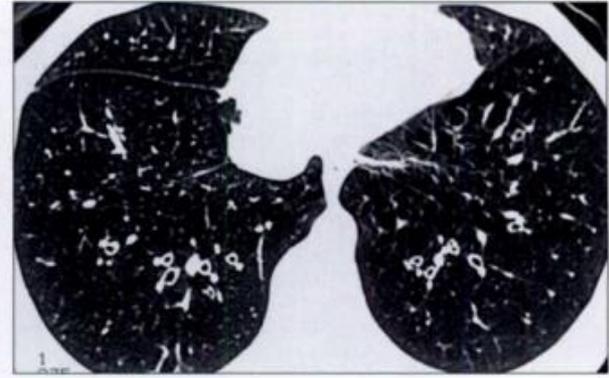
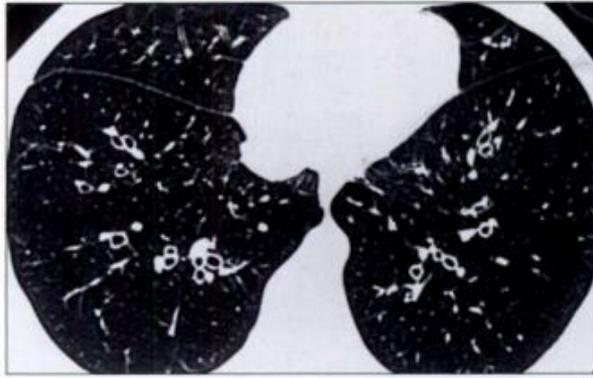
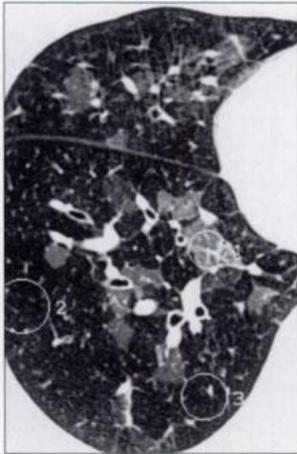
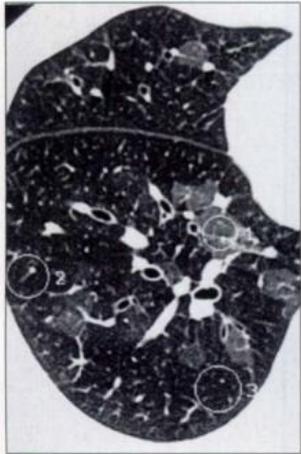
CASE A.  
FEV1 =  
50% pred

The contrast between light and dark is accentuated on the expiratory image.



CASE B.  
FEV1 =  
20% pred

# Correlation of High-Resolution CT and Pulmonary Function in Bronchiolitis Obliterans: A Study Based on 24 Patients Associated with Consumption of *Sauropus Androgynus*

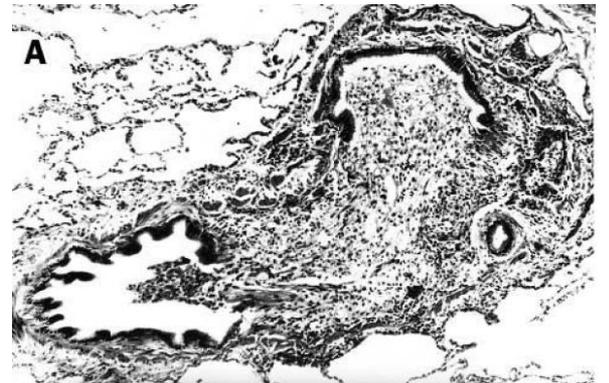


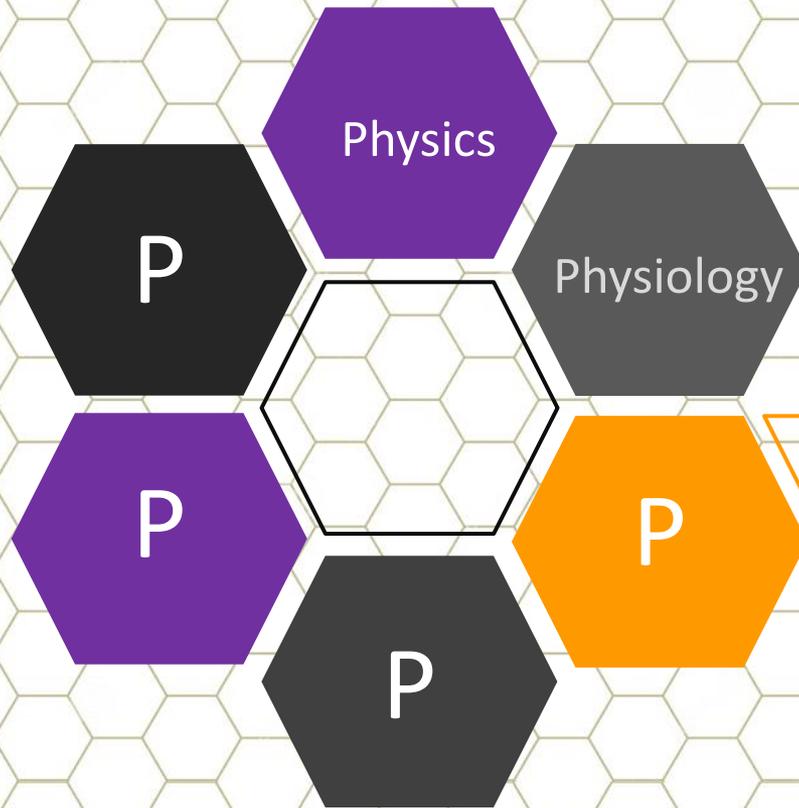
| Score                    | FEV <sub>1</sub>   | FVC                | DL <sub>CO</sub>   |
|--------------------------|--------------------|--------------------|--------------------|
| Bronchial dilatation     | -0.41 <sup>a</sup> | -0.31              | -0.24              |
| Extent of bronchiectasis | -0.42 <sup>a</sup> | -0.29              | -0.29              |
| Extent of air-trapping   | -0.73 <sup>b</sup> | -0.48 <sup>a</sup> | -0.43 <sup>a</sup> |
| Dynamic attenuation      | 0.85 <sup>b</sup>  | 0.71 <sup>b</sup>  | 0.66 <sup>b</sup>  |

THE LANCET

**Outbreak of bronchiolitis obliterans associated with consumption of *Sauropus androgynus* in Taiwan**

278 Pt with SABO, 8 lung transplants





Pattern

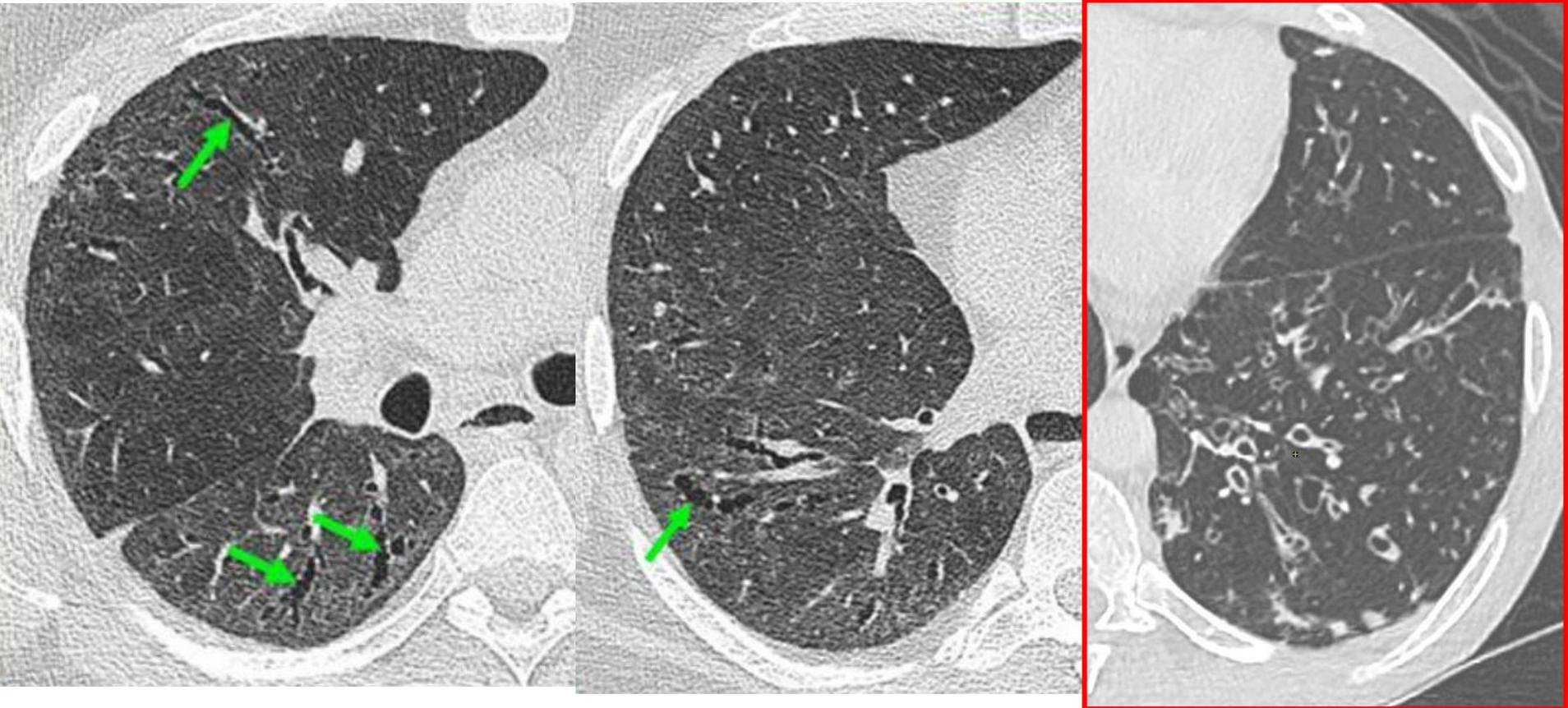
**6 Patterns**

# 6 Patterns

- Ground Glass
  - Mosaic
  - Honeycomb
  - Reticulation
- Traction bronchiectasis
  - Distribution

# Traction bronchiectasis

Infectious  
bronchiectasis

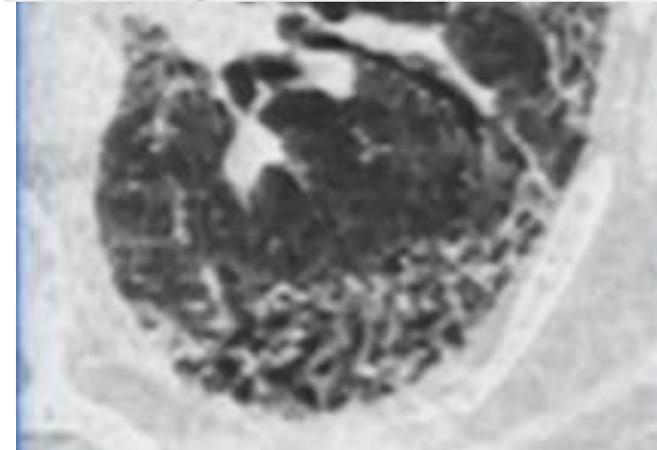
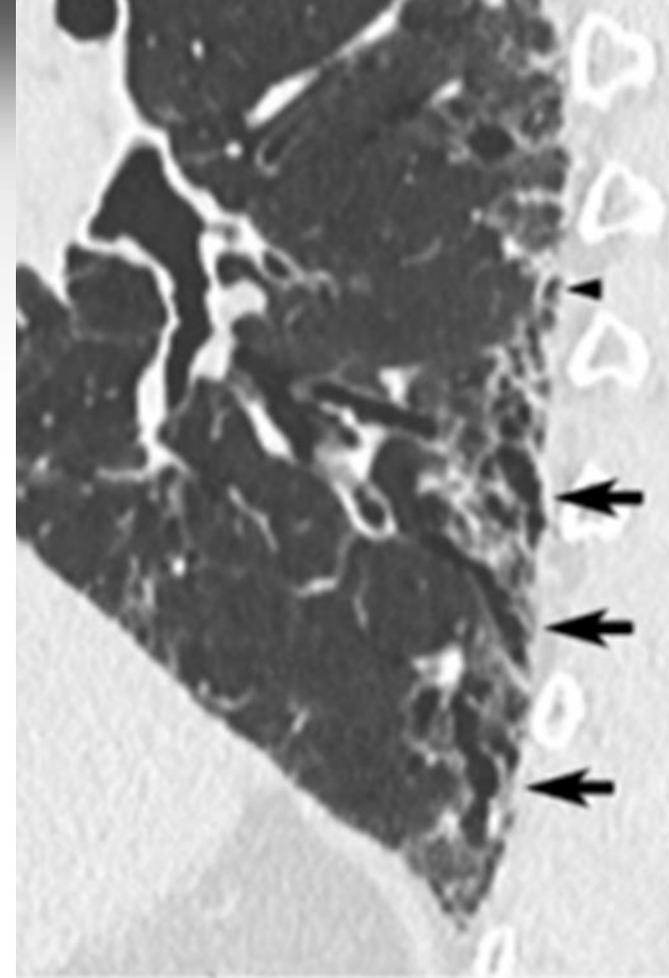


Traction is a surrogate **marker** of the **burden of fibroblastic foci** in the adjacent lung parenchyma which is a known indicator of poor prognosis

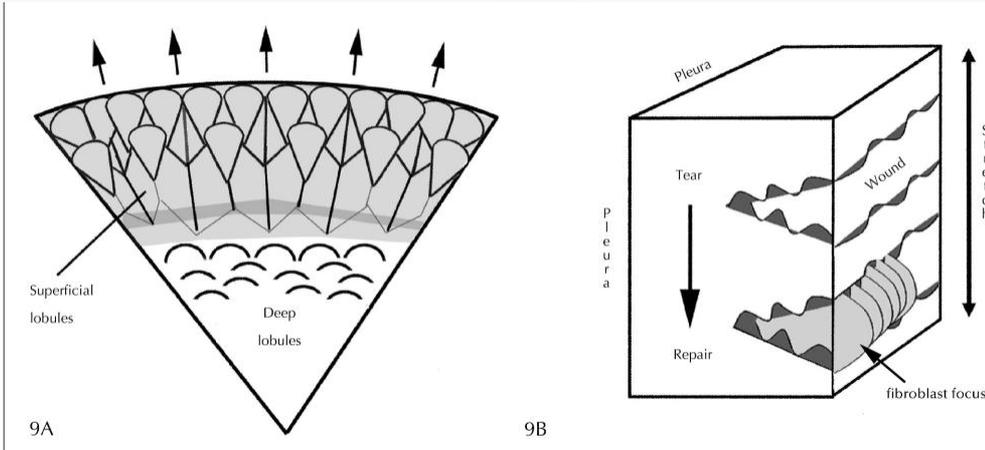
# Traction bronchiectasis: Central vs. peripheral

- **False positive identification**
  - honeycombing
  - dilated bronchi within OP/DAD
  - conspicuous, but not dilated bronchi within GGO
- **False negative**
  - Within honeycombing (advanced)

*Kappas* = 0.58-0.69

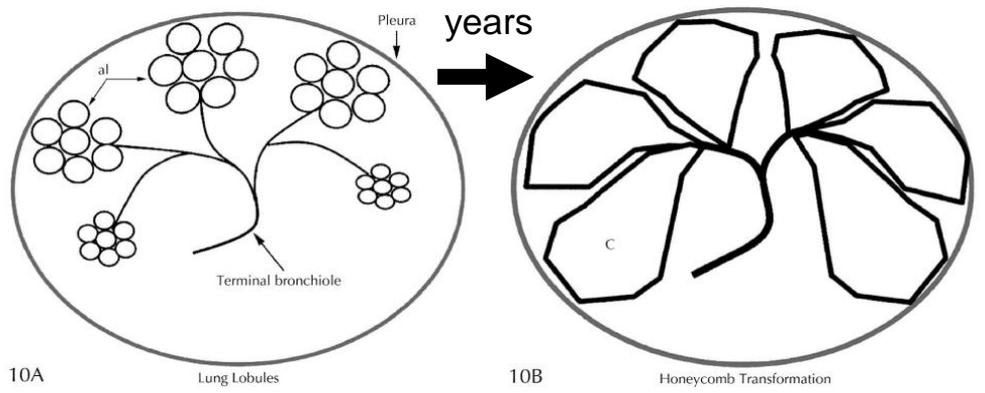


# Traction -Repair Injury Hypothesis



A, the structural relationships between the **superficial and deep lung lobules** are important in the mechanics of lung **ventilation**

B, **shear forces** in the peripheral lung lead to tears in the epithelium, followed by prolonged fibroblastic repair.

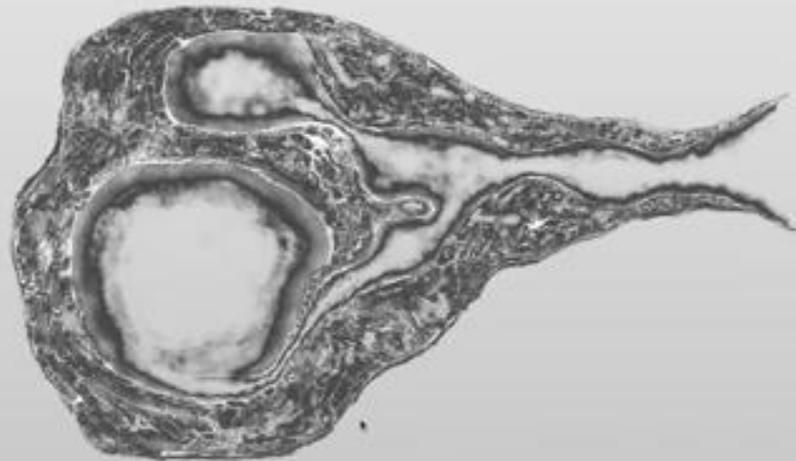
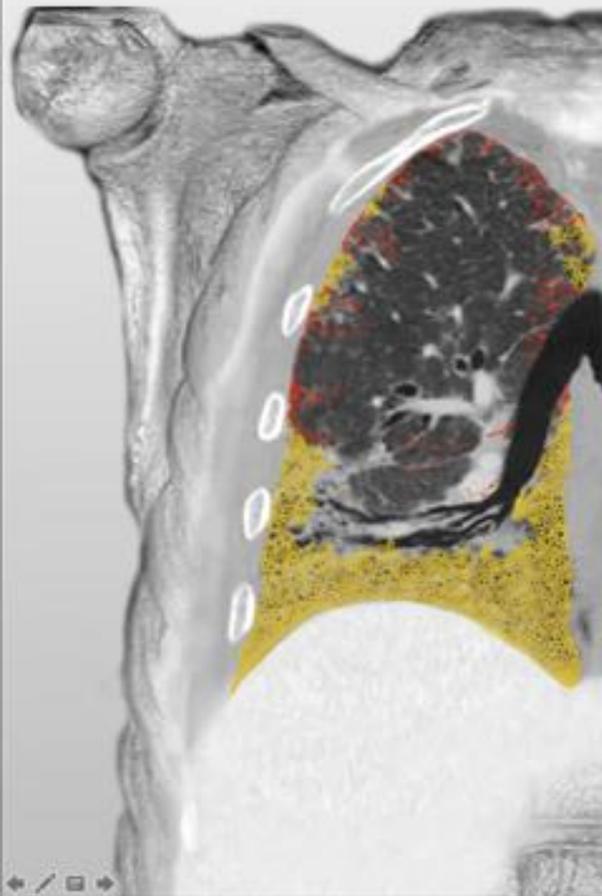


The alveoli (al) in the involved lobules (A) become obliterated in scar, and the terminal ends of the **respiratory bronchioles** and alveolar ducts expand to form (B) aggregations of **mucous-filled cysts** (C)

- **Microscopic honeycombing cyst:**  
Lining: airway respiratory mucosa;  
Walls: smooth muscle of the terminal airway
- Continued respiratory motion caused progressive dilatation of residual respiratory bronchioles... years...
- **Grossly, CT honeycombing**

# Traction bronchiectasis to Honeycombing

Honeycombing: bronchiolar dilatation/flap valve formation



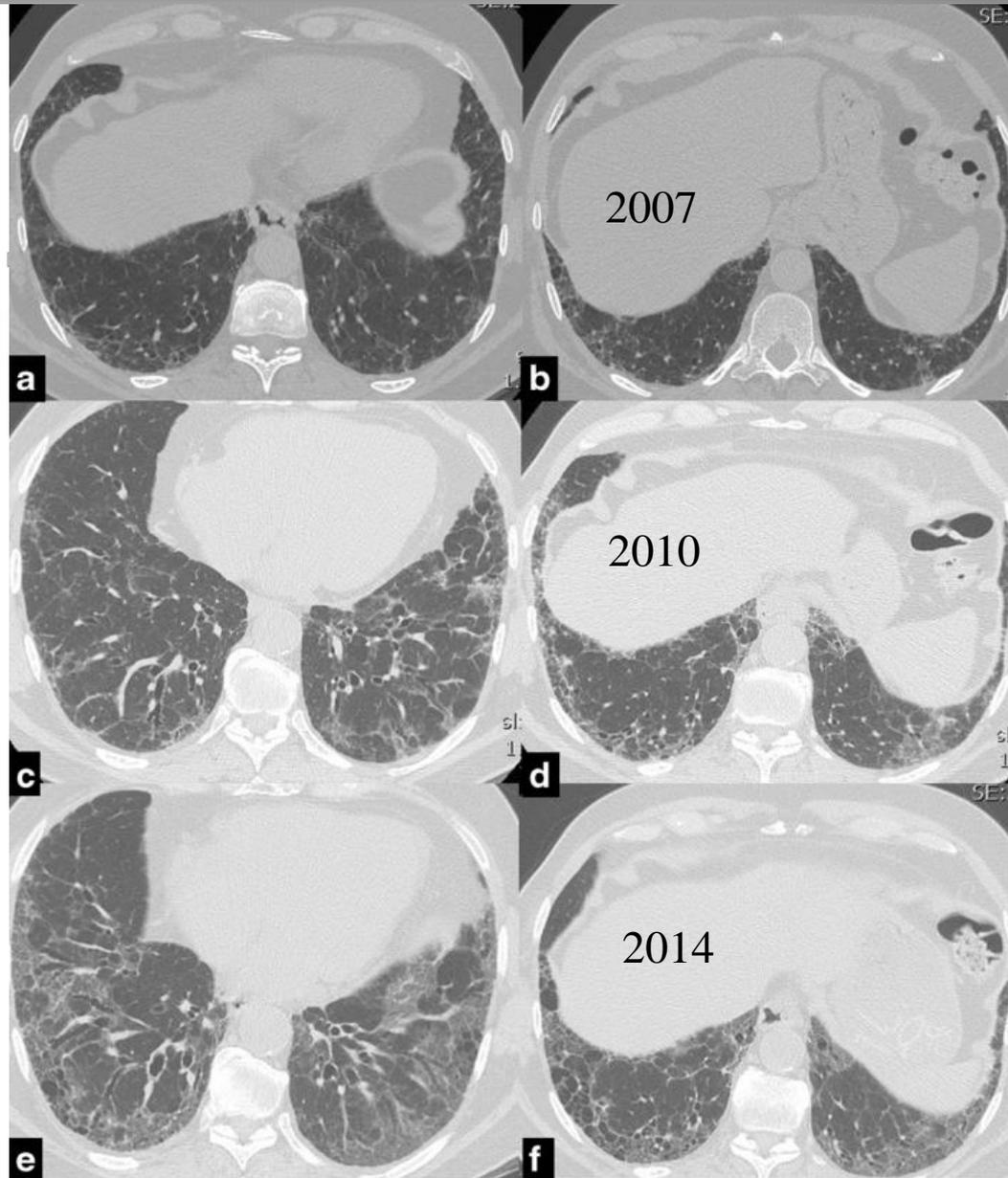
# From “traction bronchiectasis” to honeycombing in idiopathic pulmonary fibrosis: A spectrum of bronchiolar remodeling also in radiology?

Sara Piciocchi<sup>1\*</sup>, Sara Tomassetti<sup>2</sup>, Claudia Ravaglia<sup>2</sup>, Christian Gurioli<sup>2</sup>, Carlo Gurioli<sup>2</sup>, Alessandra Angelo Carloni<sup>4</sup>, Marco Chilosi<sup>5</sup>, Thomas V Colby<sup>6</sup> and Venerino Poletti<sup>2,7</sup>

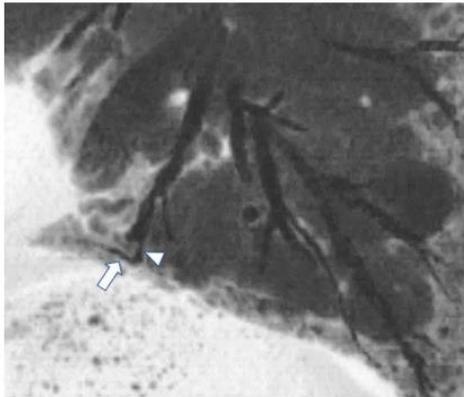
- TXB in IPF is better interpreted as resulting from **bronchiolar proliferation rather than from pure mechanical traction** of a single airway by scarring tissue.

## UIP

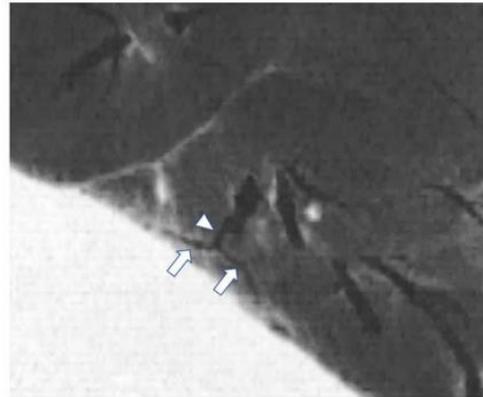
- TXB and honeycombing is a unique and **continuous** process of **bronchiolar dysplastic proliferation** and to interpret accordingly the HRCT features.



# Right-Angled Traction Bronchiectasis in Differentiating Idiopathic Pulmonary Fibrosis Without Honeycombing From Idiopathic Nonspecific Interstitial Pneumonia

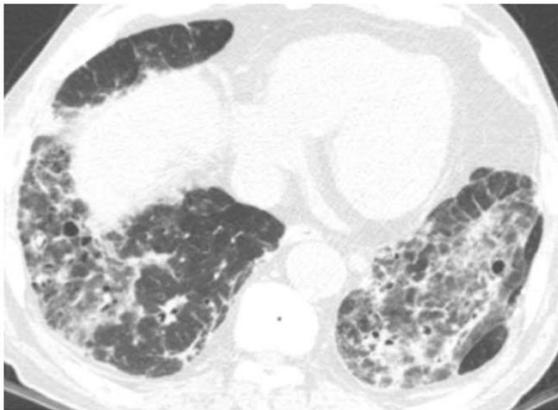


A

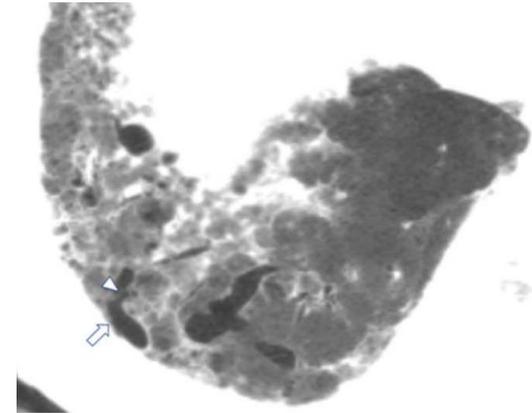
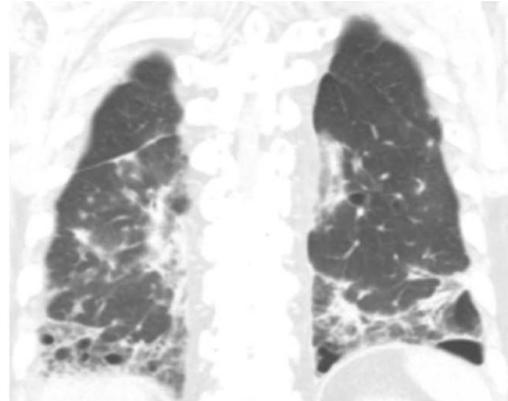


B

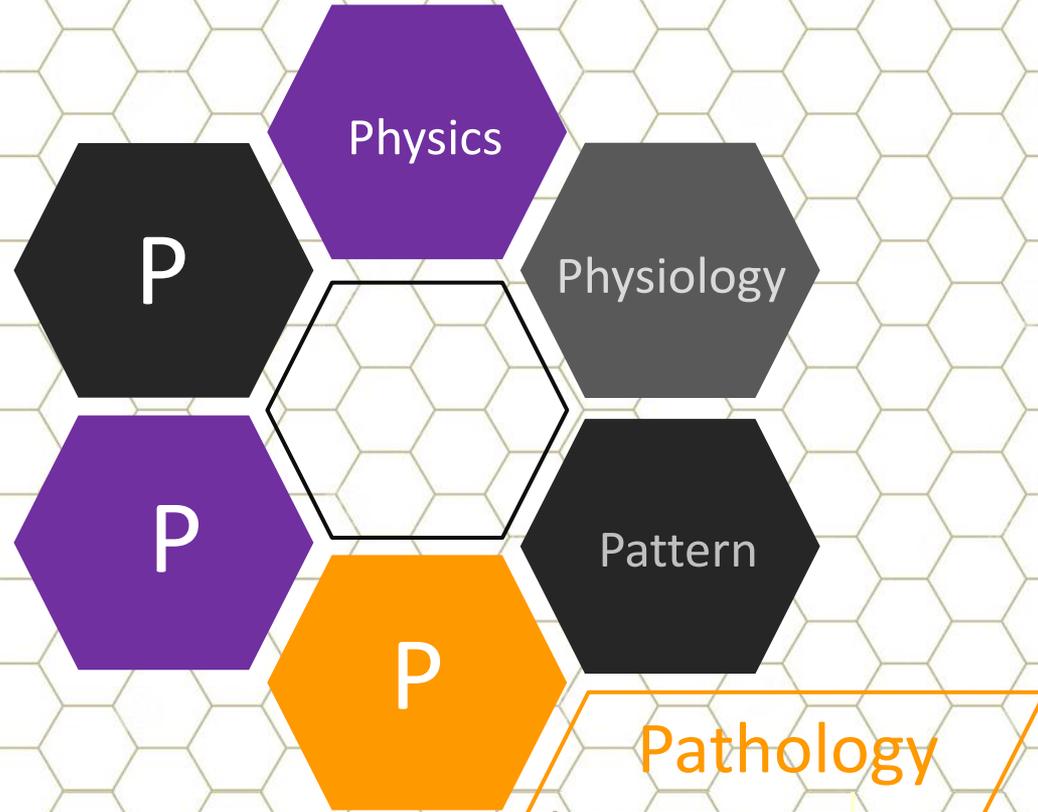
- mIP: 20 mm slab/5 mm increment
- 90 degree between the proximal and distal bronchus (usu. parallel to pleura) in the background of fibrosis
- The mean kappa value for 90°-TxB was  $0.49 \pm 0.19$



A



68 YOM. A.B heterogenous reticulation, GGO and bronchovascular involvement => alternative dx. C. mIP 90°-TxB. Patho. = UIP



# 2013 ATS-ERS Classification of IIP

Interstitial lung disease

Known cause or association:

- Connective tissue diseases
- Occupational causes
- Drug side-effects

20%

Idiopathic interstitial pneumonias

Non-familial (> 80%)      Familial (2-20%)

Granulomatous:

- Sarcoidosis
- Hypersensitivity pneumonitis
- Infections

20%

20%

Other forms, e.g.:

- Lymphangioleiomyomatosis
- Histiocytosis X

Major

Unclassifiable

~5-10%

Rare

Chronic fibrosing

Smoking related

Acute and subacute

Idiopathic pleuroparenchymal fibroelastosis

Idiopathic lymphocytic interstitial pneumonia

<1%

~50%

Idiopathic pulmonary fibrosis

20%

~25%

Non-specific interstitial pneumonia

Desquamative interstitial pneumonia

~10%

Respiratory bronchiolitis-ILD

~5%

Cryptogenic organising pneumonia

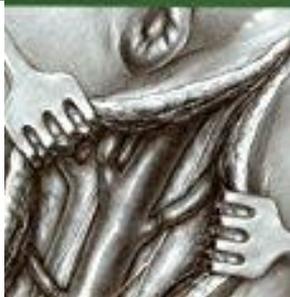
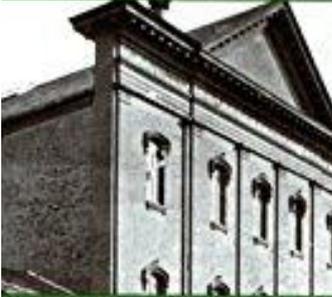
<2%

Acute interstitial pneumonia

# Fibrosing Alveolitis = UIP

PAUL STONE

Legacy of Excellence  
THE ARMED FORCES INSTITUTE OF PATHOLOGY, 1862-2011



**AIRP**<sup>TM</sup>  
AMERICAN INSTITUTE FOR  
RADIOLOGIC PATHOLOGY

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A PROGRAM OF THE  
AMERICAN COLLEGE OF RADIOLOGY

A R



**Protocol**

**P**

**P**

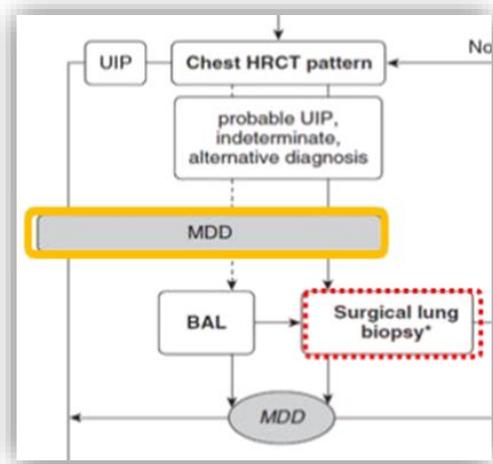
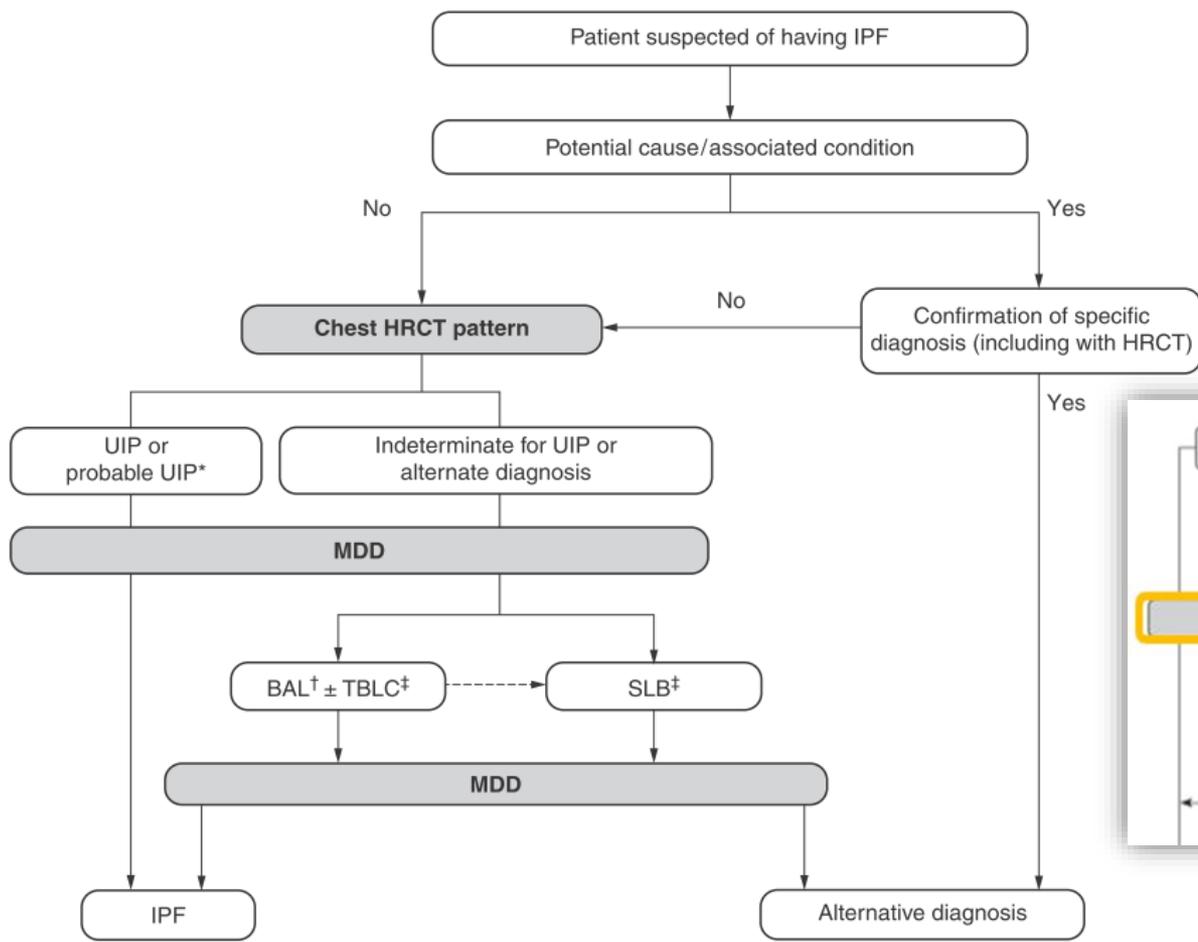
Physics

Physiology

Pattern

Pathology

# Diagnostic algorithm for idiopathic pulmonary fibrosis (IPF)



TBLC: transbronchial lung cryobiopsy SLB: surgical lung bx

# Multicentre evaluation of multidisciplinary team meeting agreement on diagnosis in diffuse parenchymal lung disease: a case-cohort study

*SLF Walsh et al Lancet Respir Med 2016; 4: 557*

- 70 cases of ILD from Royal Brompton
- 7 MDT across Euro

|   | % of 1 <sup>st</sup> choice | Clinicians ( $\kappa$ w) | Radiologists ( $\kappa$ w) | Pathologists ( $\kappa$ w) | MDTM ( $\kappa$ w) |
|---|-----------------------------|--------------------------|----------------------------|----------------------------|--------------------|
| Idiopathic pulmonary fibrosis                               | 18%                         | 0.72 (0.67–0.76)         | 0.60 (0.46–0.66)           | 0.58 (0.45–0.66)           | 0.71 (0.64–0.77)   |
| Connective tissue disease-related interstitial lung disease | 30%                         | 0.76 (0.70–0.78)         | 0.17 (0.08–0.31)           | 0.21 (0.06–0.36)           | 0.73 (0.68–0.78)   |
| Non-specific interstitial pneumonia                         | 9%                          | 0.31 (0.27–0.41)         | 0.32 (0.26–0.41)           | 0.30 (0.00–0.53)           | 0.42 (0.37–0.49)   |
| Hypersensitivity pneumonitis                                | 9%                          | 0.42 (0.30–0.47)         | 0.35 (0.29–0.43)           | 0.26 (0.10–0.45)           | 0.29 (0.24–0.40)   |

Data are median (IQR). MDTM=multidisciplinary team meeting.

**Table 4: Weighted kappa values ( $\kappa$ w) for estimation of diagnostic likelihood for individual diagnoses of diffuse parenchymal lung disease**

UC

金

木

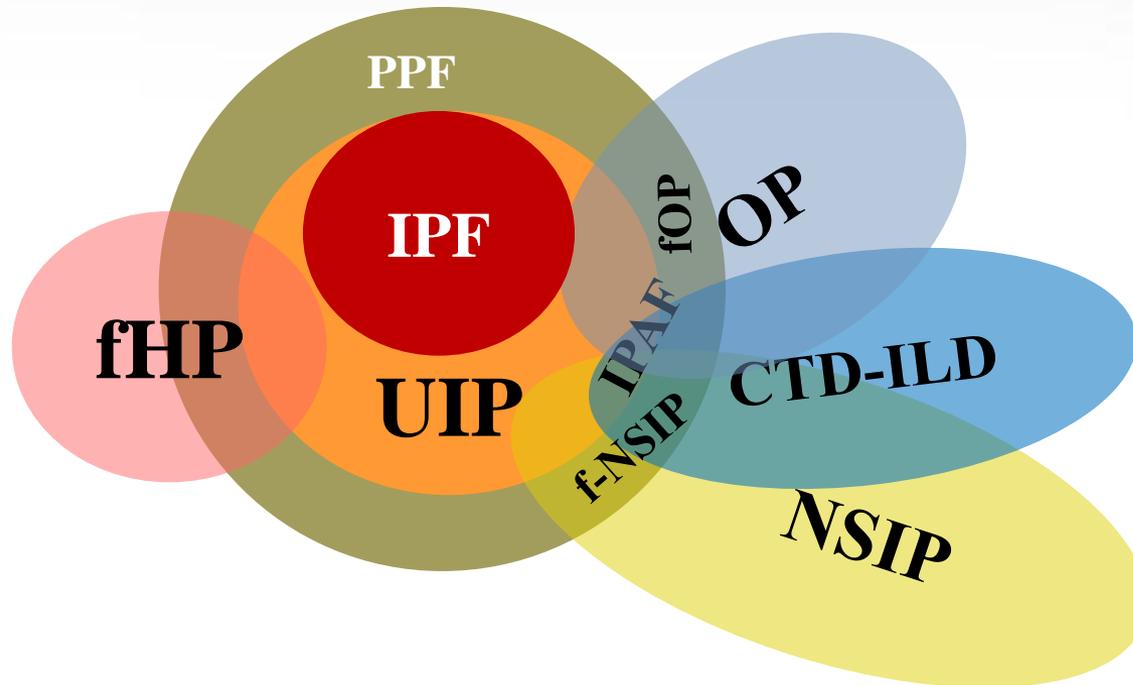
土

水

火



# The HRCT Diagram



PF-ILD: Progressive fibrosis ILD

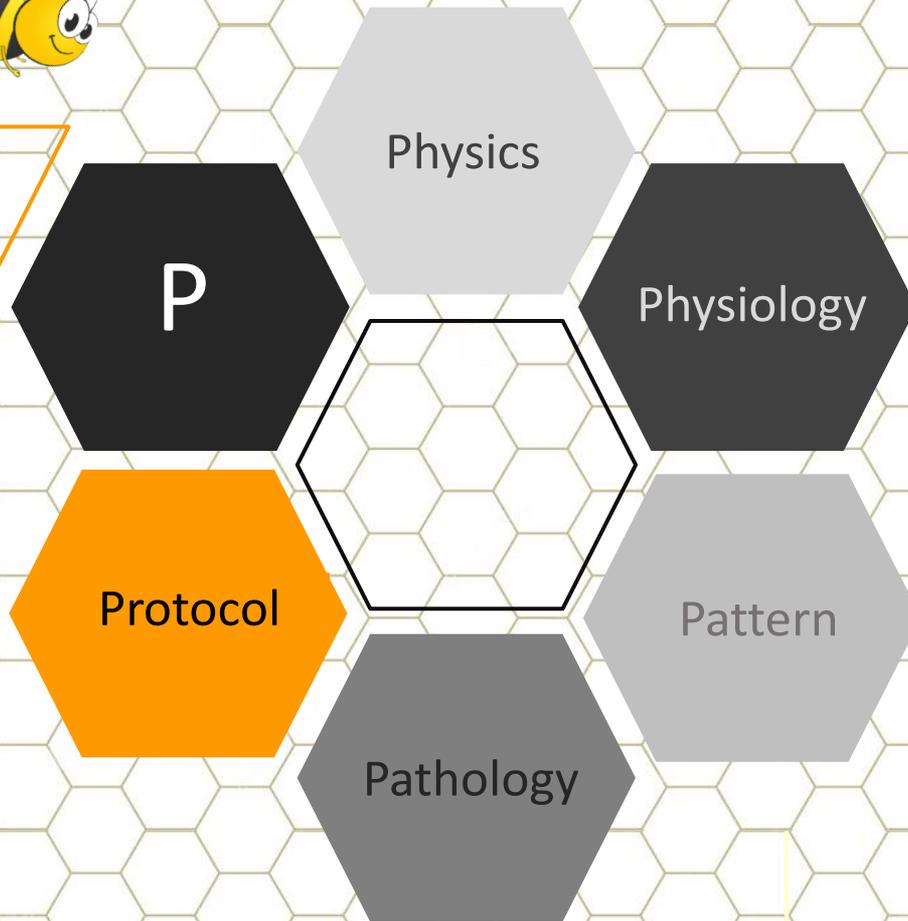
PPF-ILD: Progressive fibrosis phenotype ILD

Design by Wu Ming-Ting

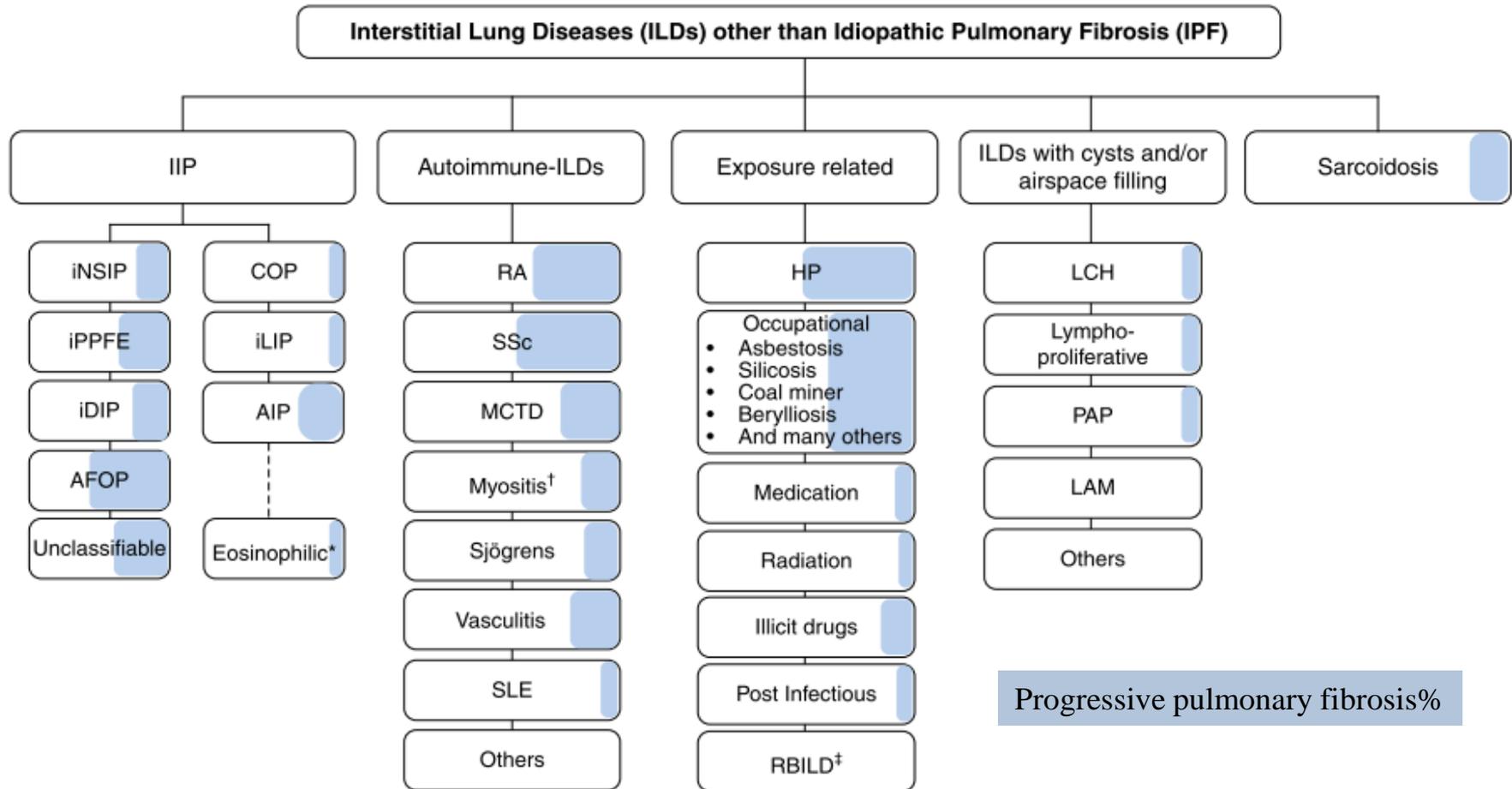
\*\*One-third of non-IPF ILD patients are at risk of developing a progressive fibrosing phenotype



Progression



# ILD (PPF%) other than IPF



# Progressive Pulmonary Fibrosis (PPF, PF-ILD)

## 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  $\geq 5\%$  predicted within 1 yr of follow-up
  - b. Absolute decline in DL<sub>CO</sub> (corrected for Hb)  $\geq 10\%$  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

# Example of types of ILD that may likely be associated with a progressive fibrosing phenotype

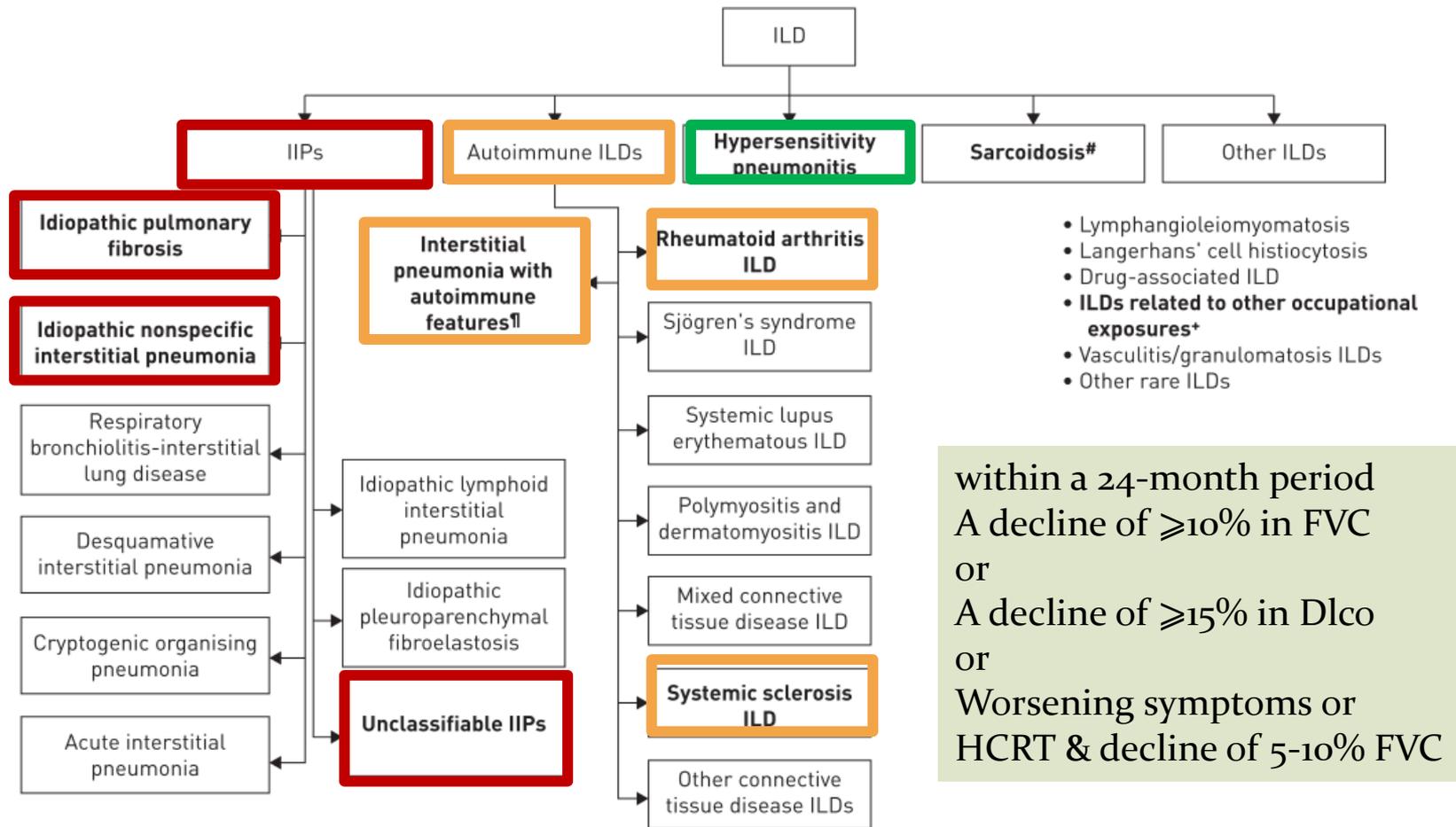
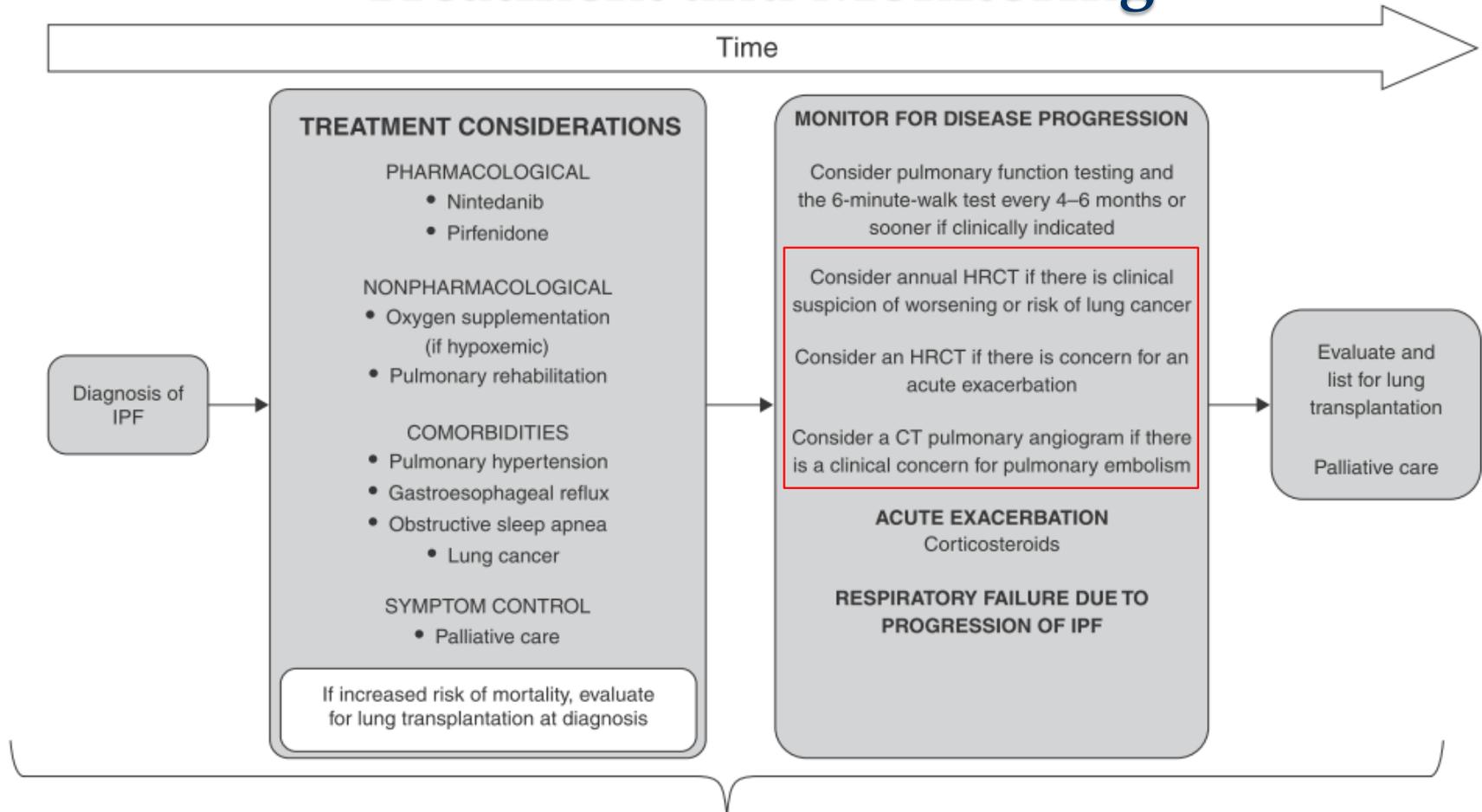


FIGURE 1 Types of interstitial lung disease (ILD) most likely to have a progressive-fibrosing phenotype (indicated in bold). IIPs: idiopathic interstitial pneumonias. #: stage IV sarcoidosis only; ¶: not an established clinical diagnosis; +: e.g. asbestosis, silicosis.

# Treatment and Monitoring



Patients should be made aware of available clinical trials for possible enrollment at all stages

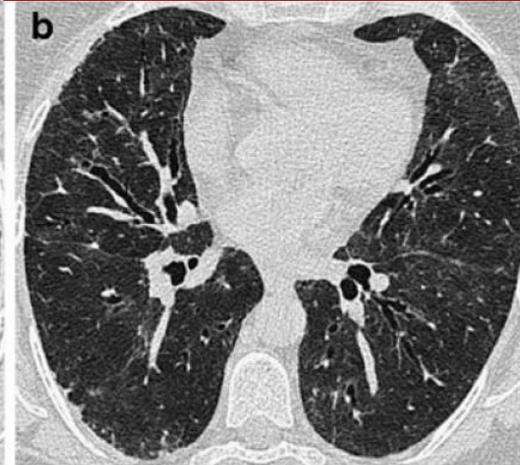
# Fibrotic idiopathic interstitial pneumonias: HRCT findings that predict mortality

## Traction Bronchiectasis

Grade I,  
mild  
(peripheral)



grade II,  
moderate  
(central)



grade III,  
severe  
(both)



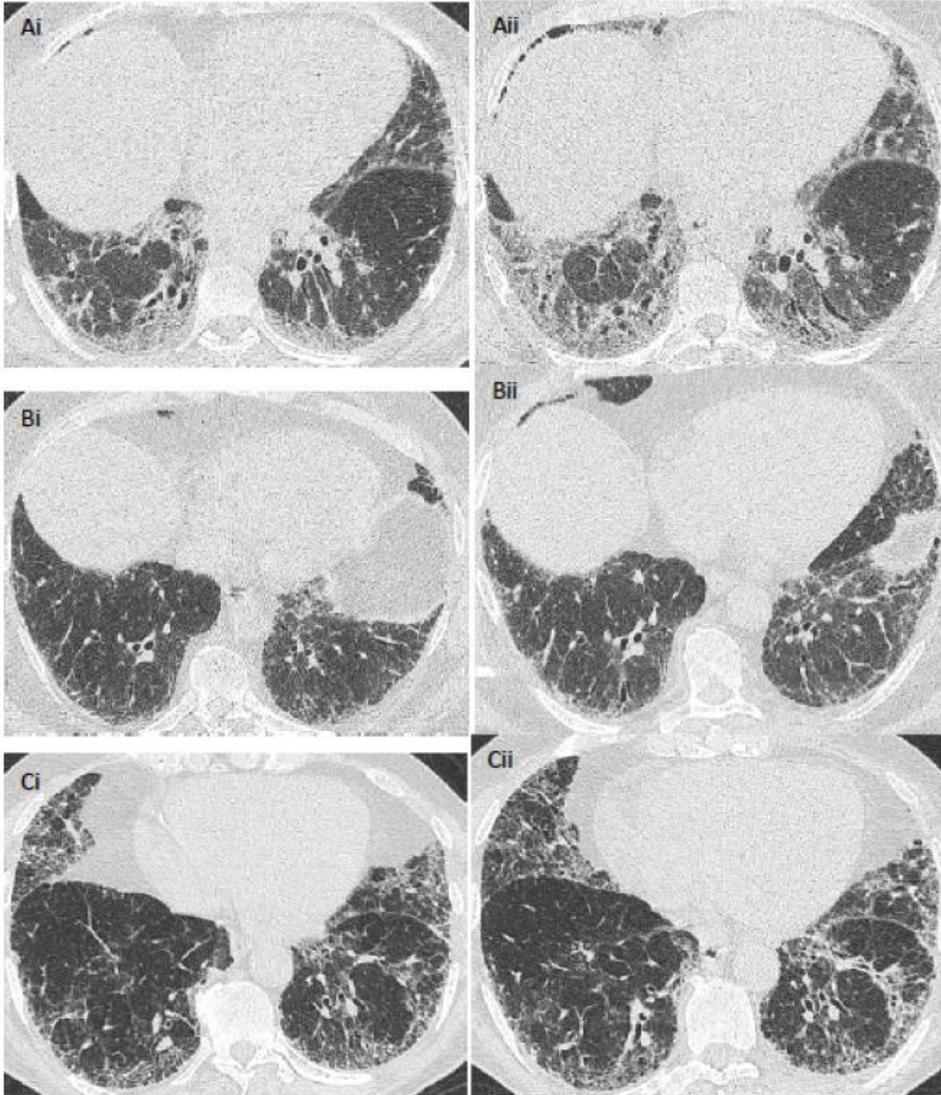
Grade I,  
mild  
(peripheral)



- **Poor Prognosis: Traction Bronchiectasis**, corrected for extent score, regardless of the background on reticulation or honeycomb

Serial CT analysis in idiopathic pulmonary fibrosis:  
comparison of visual features that determine  
patient outcome

**ΔTraction Bronchiectasis**



A: 50 YOM, antifibrotic (-) 6 M apart

FVC decline: >10% /yr,

**TxBx change:** markedly worsened (score=5)

Score 1=markedly improved, 2=slightly improved,  
3=no change, 4=slightly worsened and 5=markedly  
worsened.

B: 62 YOM, antifibrotic (+)\_13 M apart.

FVC decline 5.0% - 9.9%,

**TxBx change:** mildly worsened (score=4).

C: 77 YOM, antifibrotic (-) 15 M apart,

**TxBx change:** Score=3, stable)

FVC decline (-5.0% to 4.9%)

stable. Parenchymal changes visible on the  
CT may reflect disease maturation rather than  
disease progression.

# Visual and Automated CT Measurements of Lung Volume Loss in Idiopathic Pulmonary Fibrosis

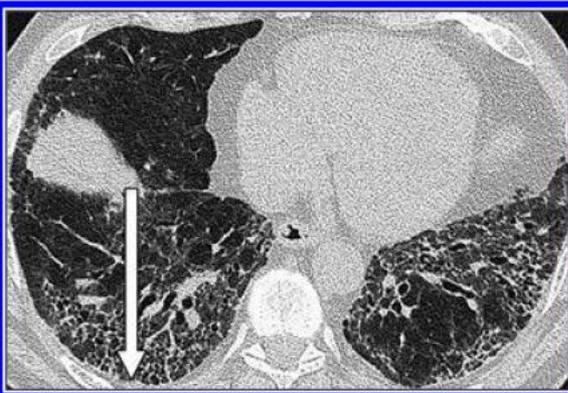
Lung Volume



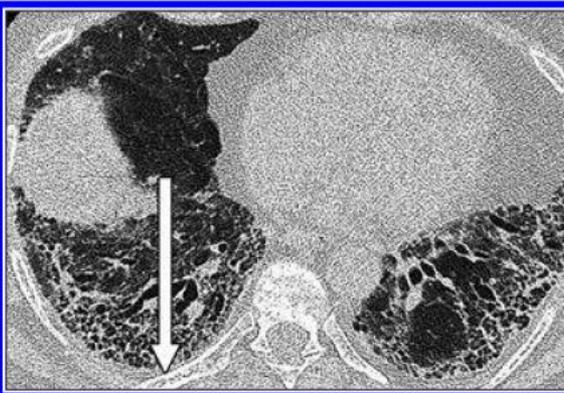
A



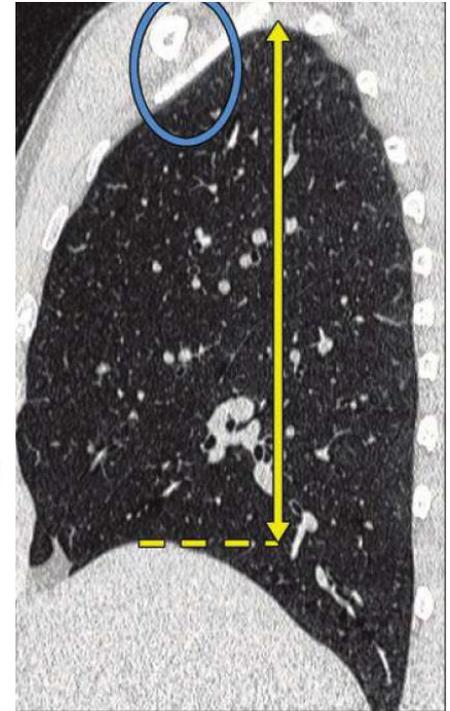
B



C

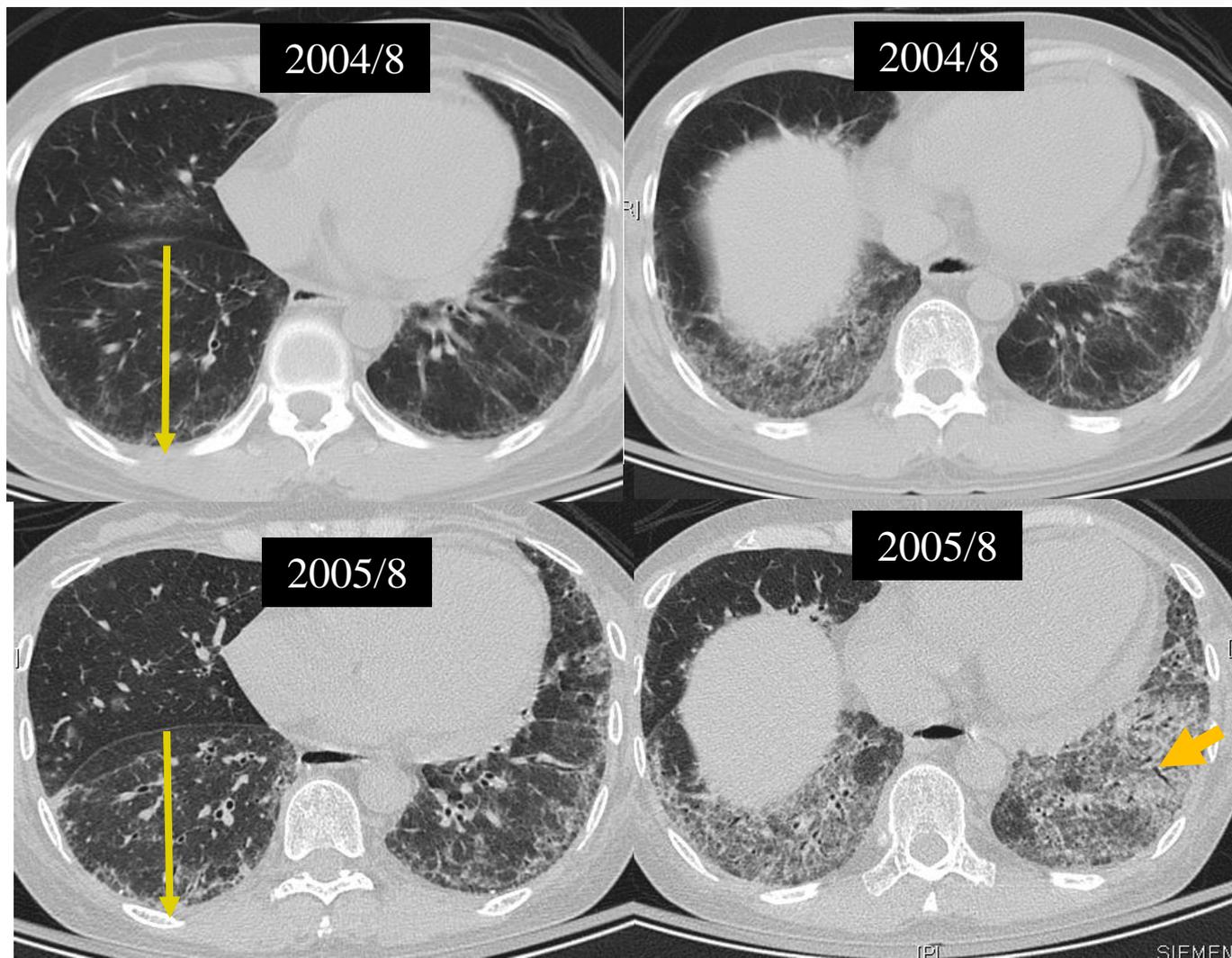


D

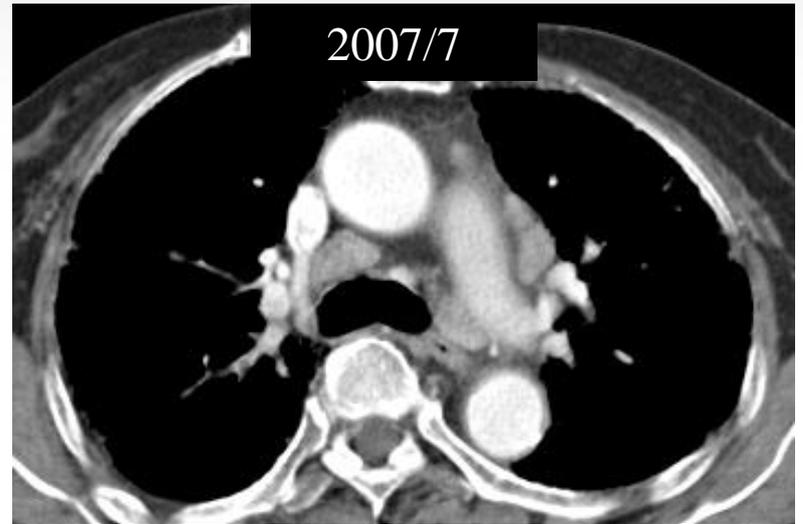
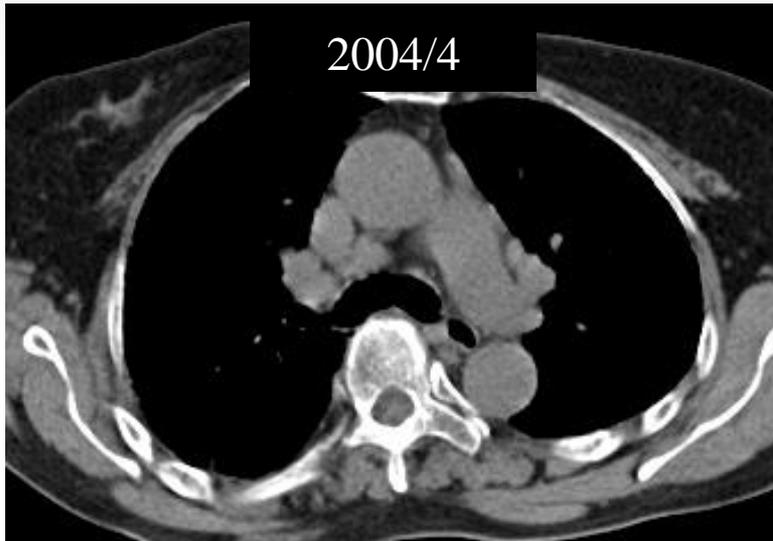


A

# PF-SSc-ILD



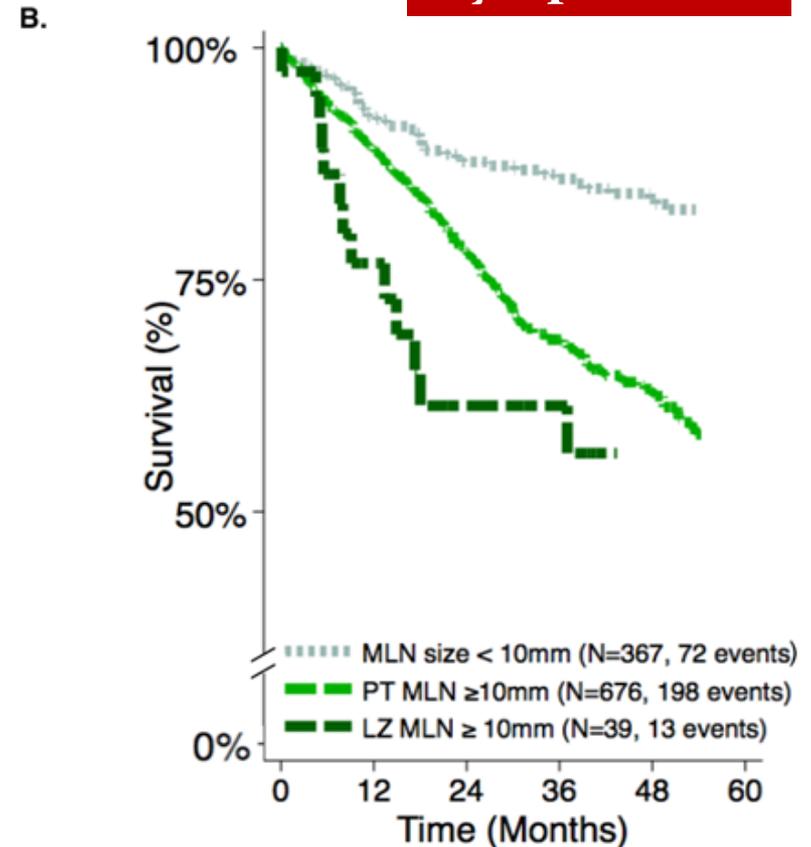
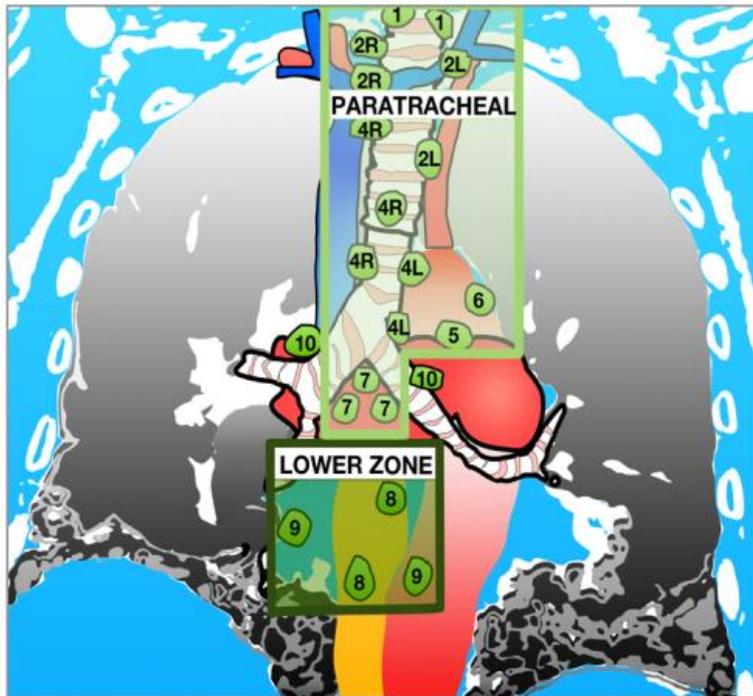
# PF-ILD+progressive LNE



# Prognosticating Outcomes in Interstitial Lung Disease by Mediastinal Lymph Node Assessment: An Observational Cohort Study with Independent Validation

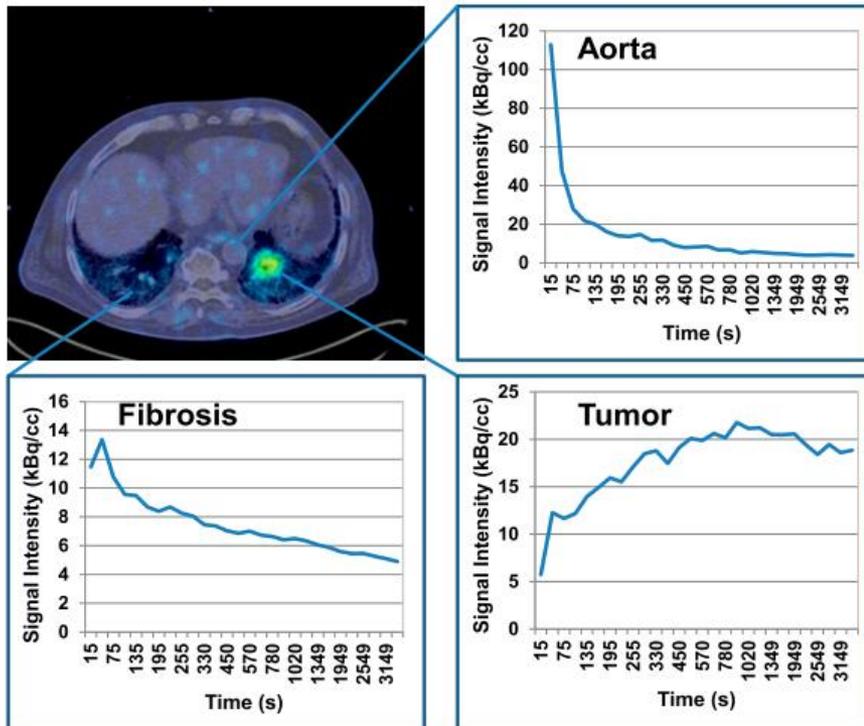
## Lymph Node

- 1094 Pt (53%M); f/u 10 years
- MLN > 10 mm (66% Pt ) predict
  - TRS (Transplant-free survival )
  - all-cause mortality
  - hospitalization risk



|               |     |     |     |     |     |     |
|---------------|-----|-----|-----|-----|-----|-----|
| MLN < 10mm    | 367 | 277 | 210 | 173 | 145 | 124 |
| PT MLN ≥ 10mm | 676 | 461 | 318 | 222 | 164 | 123 |
| LZ MLN ≥ 10mm | 39  | 22  | 13  | 12  | 7   | 6   |

# Fibroblast Activation Protein–Specific PET/CT Imaging in Fibrotic Interstitial Lung Diseases and Lung Cancer: A Translational Exploratory Study



- $^{68}\text{Ga}$ -labeled dynamic fibroblast activation protein (FAP) inhibitor  $^{68}\text{Ga}$ -FAPI PET/CT
- 15 patients with fILD with suspected lung cancer
- Histology validation: 4 human biopsy and *Nedd4-2<sup>-/-</sup>* mice with fibrotic lungs: patchy expression esp in the transition zone.
- Pattern specific to fibroblast activity

# Quantitation of ILD

Visual scoring

**Semi-quantitative score**

Full (auto) quantitative maps

# Semi-QCT

## 台灣間質性肺病影像半定量化 評估標準與結構式報告 使用說明

**SSc-ILD extent >10%? 健保給付**



中華民國放射線醫學會  
Taiwan Radiological Society

地址：103 台北市大同區重慶北路三段63號2樓  
電話：02-25865331  
Email：office@rsroc.org.tw

## ▶▶ 台灣間質性肺病影像半定量化評估步驟與說明

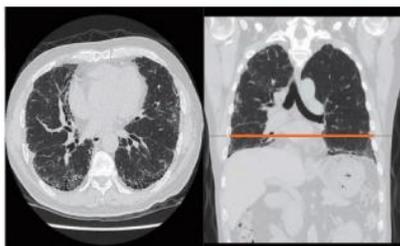
### 步驟 1. 將肺部分成六個截面：

如圖一所示，依照六項解剖學標的之橫切面做 HRCT 影像之評估，即主動脈弓上緣切面 (level 1)、隆凸下 1 公分 (level 2)、肺靜脈匯合處 (level 3)、level 3 至中點 (level 4)、右橫膈上方 1 公分 (level 5)、右橫膈下方 2 公分 (level 6)。

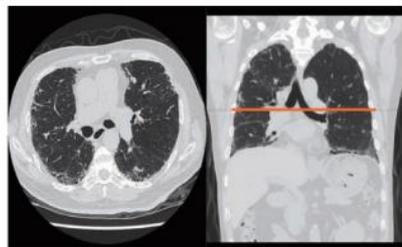
圖一



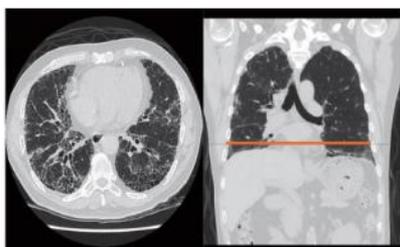
1 主動脈弓上緣切面 (aortic arch)



4 3 與 5 的中間 (halfway between 3<sup>rd</sup> and 5<sup>th</sup> section)



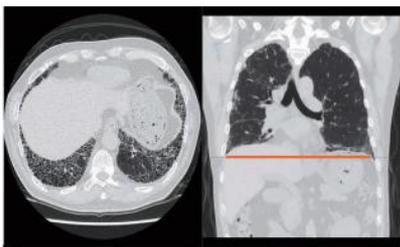
2 隆凸下 1 公分 (1 cm below the carina)



5 右橫膈肌上方 1 公分 (1 cm above the right hemidiaphragm)



3 肺靜脈匯合處 (pulmonary venous confluence)



6 右橫膈肌下方 2 公分 (2 cm below the right hemidiaphragm)

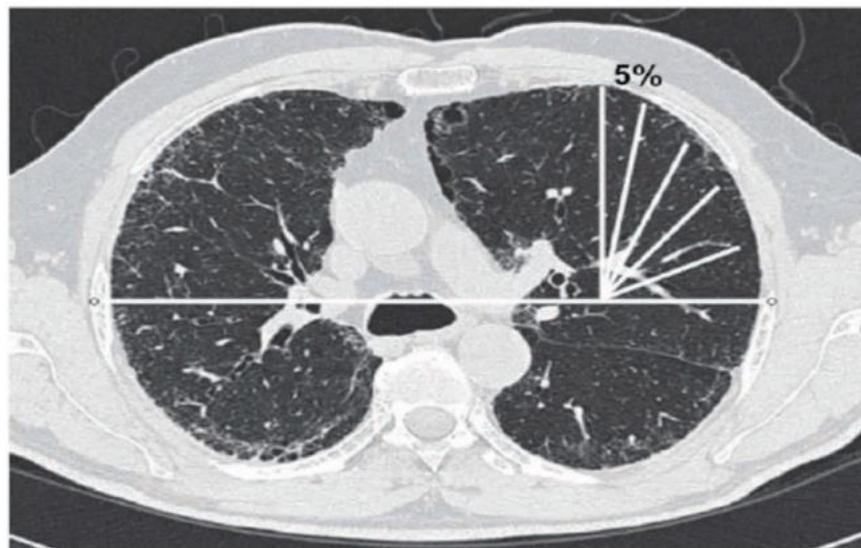
### 步驟 2. 纖維化侵犯肺野計算(異常部位估算)：

觀察上述六截面之橫切面影像裡是否含有代表肺纖維化的 CT 表徵，如蜂窩狀組織 (honeycombing)、網狀組織 (reticulation)、拉扯性支氣管擴張 (traction bronchiectasis) 及其伴隨之毛玻璃狀陰影 (ground-glass opacity wit traction bronchiectasis)。找出上述四項 CT 表徵並確定分佈位置與範圍之後，準備進行視覺半定量化評估。

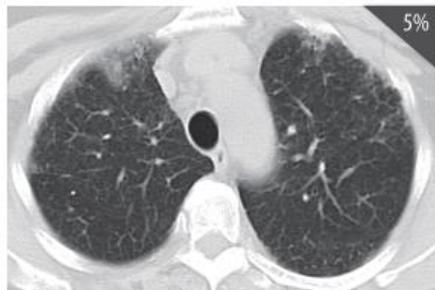
### 步驟 3. 視覺半定量化評估方法：

將上述六個截面符合肺纖維化之 CT 表徵範圍，以視覺評估方式(肉眼)來估算侵犯範圍百分比。估算數值以 5% 作為最小級距。進行視覺評估時，將每一位置之 CT 影像中央劃出一條水平線並留下 50% 的可測量區域；再劃出第二條線垂直線與水平線交錯，留下每個肺 25% 的可評估區域。每 25% 又細分為 5 個部分，每個部分對應 5% 的面積。依上述方式分別估算六個截面的異常部位，取其六個截面估算結果的平均值，即是該名患者纖維化影響肺野範圍(異常部位範圍)百分比。

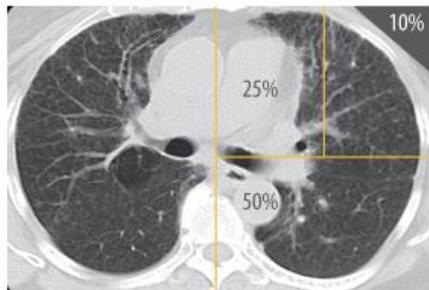
圖二



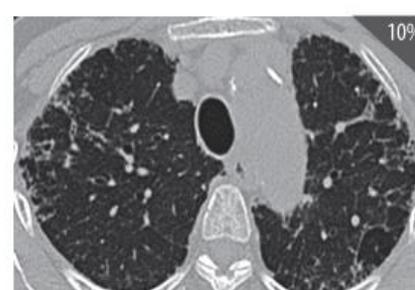
# Q: Is the ILD extent > 10%



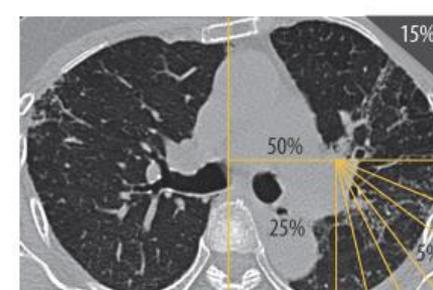
1 aortic arch



2 1 cm below the carina



1 aortic arch



2 1 cm below the carina



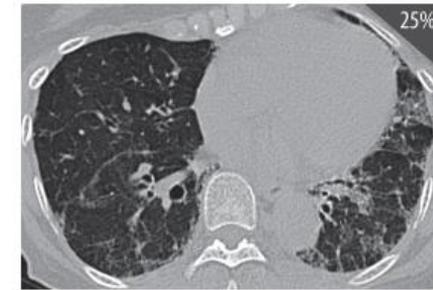
3 right pulmonary venous confluence



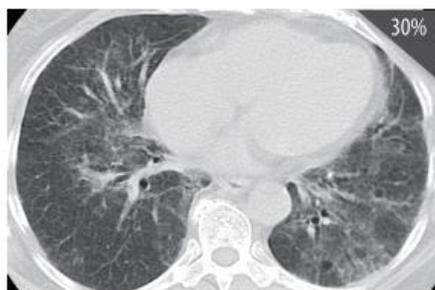
4 halfway between the third and fifth section



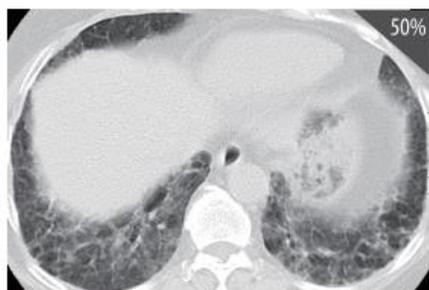
3 right pulmonary venous confluence



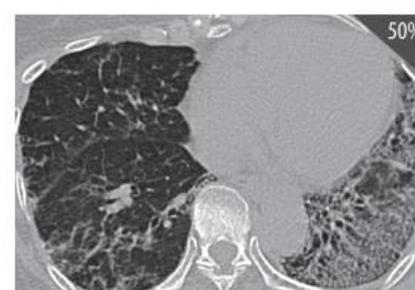
4 halfway between the third and fifth section



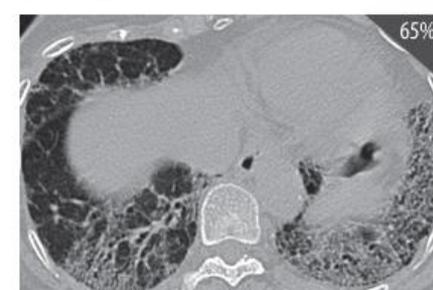
5 1 cm above the right hemidiaphragm



6 2 cm below the right hemidiaphragm



5 1 cm above the right hemidiaphragm



6 2 cm below the right hemidiaphragm

如果經視覺估算六個位置的 fibrosis extent，分別為 5%、10%、15%、15%、20%、30%、50%，則整體之纖維化比例為上述總額之平均： $(5+10+15+20+30+50)/6=21.6\%$

如果經視覺估算六個位置的 fibrosis extent，則整體纖維化比例為： $(10+15+15+25+50+65)/6=30\%$

# Structure Report

下方表格為根據 2018 ATS/ERS/JRS/ALAT 共同發表的 IPF 臨床診斷指引中的【影像診斷標準與定義】內容所設計的結構性報告，提供放射線影像報告含健保審查要項。由於健保審查以  $\geq 10\%$  之纖維化為藥物給付條件，若  $<10\%$  可能僅為 interstitial lung abnormality (ILA)，因此必須在報告中提及。

《標準 HRCT 判讀 ILD 應該為 non-contrast enhanced, standard dose, thin section  $\leq 1.5\text{mm}$ , sharp or lung kernel, supine position in full inspiration。若在其他狀況，則勾選下方 scanning parameters(詳細請參考原始文獻<sup>3</sup>之 Table 3 : HRCT screening parameters, 及 Table 4 : HRCT Scanning Pattern) 》

## CT scanning parameters

| Dose            | Standard ( )    | Low dose ( )   | Note   |
|-----------------|-----------------|----------------|--|
| Slice thickness | ( ) mm          |                | For visual assessment in clinical practice, it is suggested to use sharp or lung kernel in thin slice thickness ( $\leq 1-1.25$ mm) with or without gap, while for computer aided quantification, please use standard kernel in contiguous thin slices ( $\leq 1-1.25$ mm) to avoid noise from edge enhancement. |
| Kernel          | ( ) sharp       | ( ) standard   |  |
| Respiration     | ( ) inspiration | ( ) expiration |  |
| Position        | ( ) supine      | ( ) prone      |  |

## HRCT Findings

| HRCT features            |     |  | Absence | Presence   | Note |
|--------------------------|-----|--|---------|--|------|
| Predominant distribution | ( ) | Subpleural   |         |  |      |
|                          | ( ) | Basal  |         |  |      |
|                          | ( ) | Peribronchovascular  |         |  |      |
|                          | ( ) | Perilymphatic  |         |  |      |
|                          | ( ) | Upper or mid-lung  |         |  |      |
| Findings                 | ( ) | Ground glass opacity (GGO)   |         |  |      |
|                          | ( ) | Reticulation   |         |  |      |
|                          | ( ) | Traction bronchiolectasis  |         |  |      |
|                          | ( ) | Honeycombing   |         |  |      |
|                          | ( ) | Cysts  |         |  |      |
|                          | ( ) | Dilated esophagus  |         |  |      |
|                          | ( ) | Emphysema  |         |  |      |
|                          | ( ) | Others   |         |  |      |
| Fibrosis extent          | ( ) | Honeycombing + Reticulation+ Traction bronchiolectasis+ Ground glass opacity with traction bronchiolectasis ('GGO+TB'; taken to signify fine fibrosis) |         | <input type="checkbox"/> $\geq 10\%$<br><input type="checkbox"/> $<10\%$ |      |

| HRCT patterns             | Description  |
|---------------------------|--|
| ( ) UIP                   | *Subpleural and basal predominant; distribution is often heterogeneous<br>*Honeycombing with or without peripheral traction bronchiolectasis or bronchiolectasis   |
| ( ) Probable UIP          | *Subpleural and basal predominant; distribution is often heterogeneous<br>*Reticular pattern with peripheral traction bronchiolectasis or bronchiolectasis<br>*May have mild GGO   |
| ( ) Indeterminate for UIP | *Subpleural and basal predominant<br>*Subtle reticulation; may have mild GGO or distortion ("early UIP pattern")<br>*CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")  |
| ( ) Alternative diagnosis | Findings suggestive of another diagnosis, including:<br>*CT features:<br>✓ Cysts<br>✓ Marked mosaic attenuation<br>✓ Predominant GGO <input type="checkbox"/> Profuse micronodules <input type="checkbox"/> Centrilobular nodules <input type="checkbox"/> Nodules <input type="checkbox"/> Consolidation<br>*Predominant distribution:<br>✓ Peribronchovascular<br>✓ Perilymphatic<br>✓ Upper or mid-lung<br>*Other:<br>✓ Pleural plaques (consider asbestosis)<br>✓ Dilated esophagus (consider CTD)<br>✓ Distal clavicular erosions (consider RA)<br>✓ Extensive lymphadenlargement (consider other etiologies)<br>✓ Pleural effusions, pleural thickening (consider CTD/drugs) |

### Final impression based on HRCT findings

| HRCT patterns            |   |  |
|--------------------------|---|--|
| <input type="checkbox"/> | UIP   |  |
| <input type="checkbox"/> | Probable UIP                                      |  |
| <input type="checkbox"/> | Indeterminate for UIP                             |  |
| <input type="checkbox"/> | Alternative diagnosis                             |  |
| <input type="checkbox"/> | NSIP  |  |
| <input type="checkbox"/> | Suspicious for CTD-ILD                            |  |
| <input type="checkbox"/> | Suspicious for chronic hypersensitivity pneumonia |  |
| <input type="checkbox"/> | Suspicious for organizing pneumonia (OP)          |  |
| <input type="checkbox"/> | Other   |  |

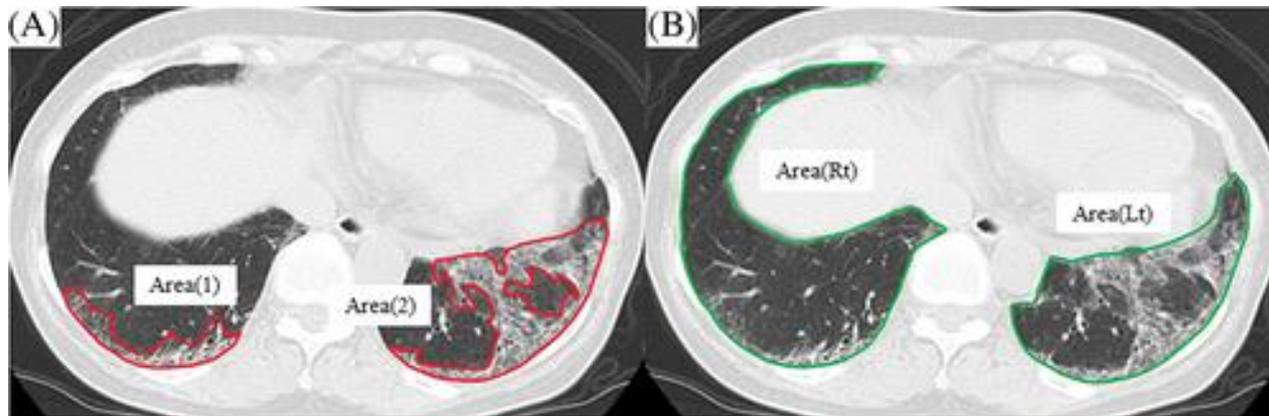
### References:

1. Fraser E, St Noble V, Hoyles RK, et al. Readily accessible CT scoring method to quantify fibrosis in IPF. *BMJ Open Res* 2020;7:e000584. doi:10.1136/bmjresp-2020-000584  
<https://bmjopenrespres.bmj.com/content/7/1/e000584>
2. Sánchez RP, Fernández-Fabrellas E, Samper GJ, Montañana MLD, Vilar LN (2018) Visual HRCT Score to Determine Severity and Prognosis of Idiopathic Pulmonary Fibrosis. *Int J Respir Pulm Med* 5:084.  
doi.org/10.23937/2378-3516/1410084  
<https://clinmedjournals.org/articles/ijrpm/international-journal-of-respiratory-and-pulmonary-medicine-ijrpm-5-084.php?jid=ijrpm>
3. Ganesh Raghu, Martine Remy-Jardin, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med* Vol 198, Iss 5, pp e44–e68, Sep 1, 2018. DOI: 10.1164/rccm.201807-1255ST  
<https://www.atsjournals.org/doi/full/10.1164/rccm.201807-1255ST>

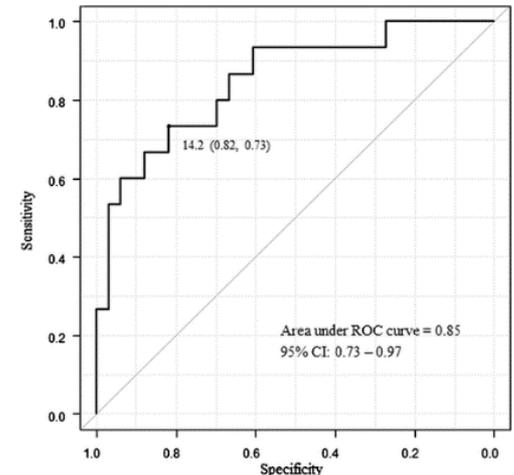
# Q: Is the ILD extent > 10%

## Simplified Quantification

- 48 patients, SSc-ILD
- Six anatomical levels :
  1. arch of the aorta
  2. carina
  3. pulmonary venous confluence
  4. a point halfway between level 3 and level 5
  5. 1 cm above the dome of the right hemidiaphragm
  6. 2 cm below the dome of the right hemidiaphragm
- \* Cut-off value for fibrosis score to overall survival (OS) was 14.2%, with moderate accuracy.

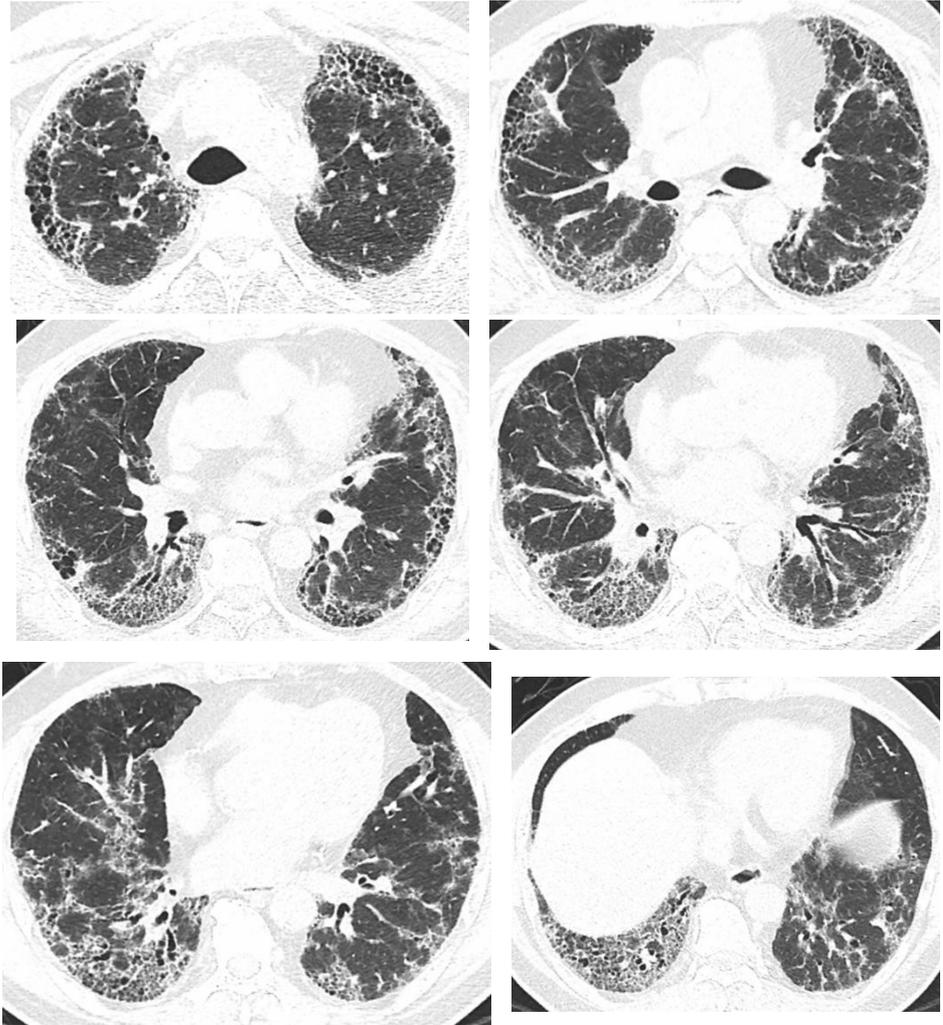
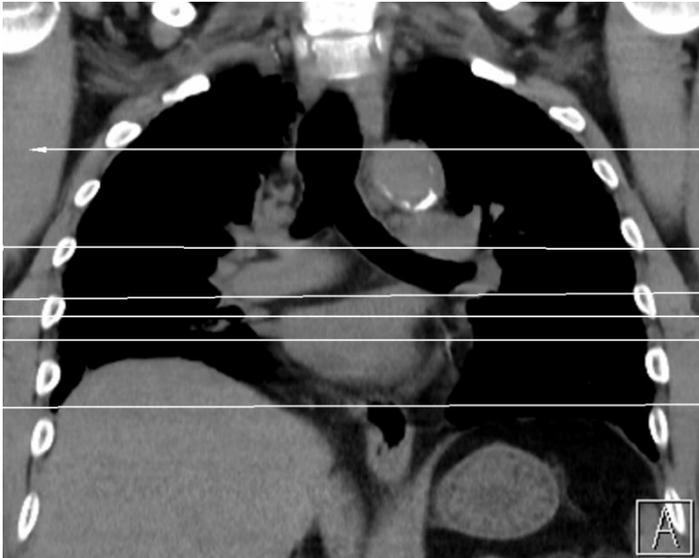


2 cm below the dome of the right hemidiaphragm



**One lung of one slice = one score, total score = 12.**

59 Y/O male, CTD-ILD pattern  
Immune factor negative



**12 scores x 10% = 1.2 If total score > 1.2  
pass the criteria**

$$0.8+0.28+0.43 = 1.51 > 1.2 \#$$

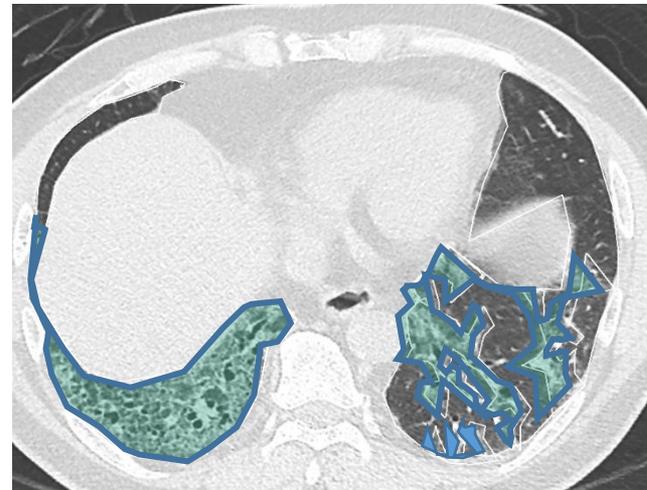
0.43



S5

0.8

0.28



S6

# Quantitation of ILD

Visual scoring

Semi-quantitative score

Simplified quantitative score

**Full (auto) quantitative maps**

Texture Pattern \* Extent

LN Enlargement

Vessel-related score

Lung Volume

# Use of Quantitative CT to Predict Postoperative Lung Function in Patients with Lung Cancer<sup>1</sup>

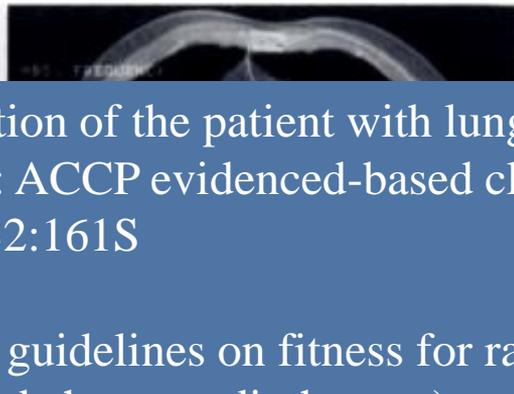
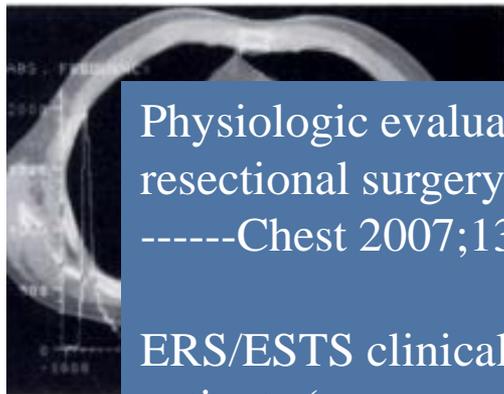
Ming-Ting Wu, MD • Jinn-Ming Chang, MD • Ambrose A. Chiang, MD • Jau-Yeong Lu, MD  
Hon-Ki Hsu, MD • Wen-Hu Hsu, MD • Chien-Fang Yang, MD

# Prediction of Postoperative Lung Function in Patients with Lung Cancer: Comparison of Quantitative CT with Perfusion Scintigraphy

AJR:178, March 2002

Ming-Ting Wu<sup>1,2</sup>  
Huay-Ben Pan<sup>1,2</sup>  
Ambrose A. Chiang<sup>3-5</sup>  
Hon-Ki Hsu<sup>2,6</sup>  
Huang-Chou Chang<sup>2,6</sup>  
Nan-Jing Peng<sup>2,7</sup>  
Ping-Hong Lai<sup>1,2</sup>  
Huei-Lung Liang<sup>1,2</sup>  
Chien-Fang Yang<sup>1,2</sup>

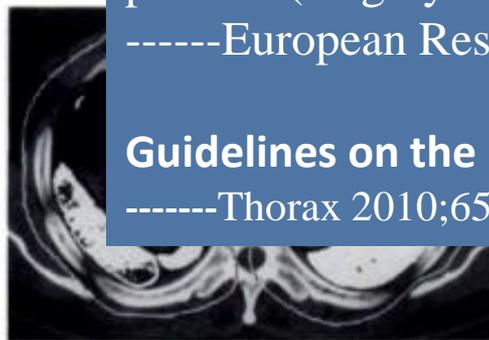
Radiology 1994; 191:257-262



Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: ACCP evidenced-based clinical practice guidelines  
-----Chest 2007;132:161S

ERS/ESTS clinical guidelines on fitness for radical therapy in lung cancer patients (surgery and chemo-radiotherapy)  
-----European Respiratory Journal 2009 34: 17-41

Guidelines on the radical management of patients with lung cancer  
-----Thorax 2010;65, iii1-27



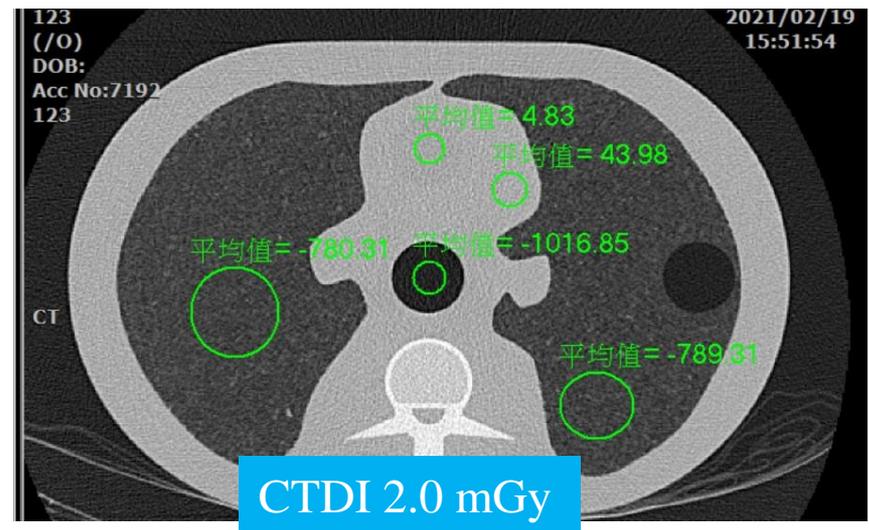
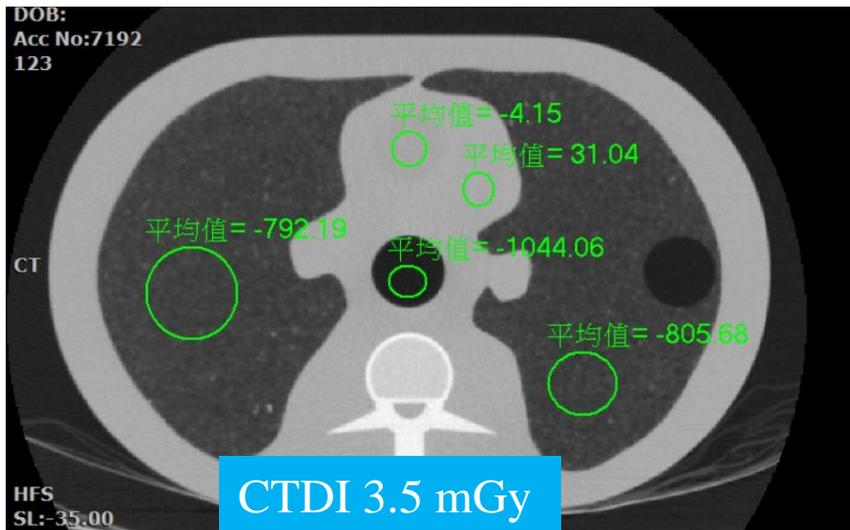
a.

b.

c.

# Pulmo Phantom

- The H value varies in different exposure and recon setting

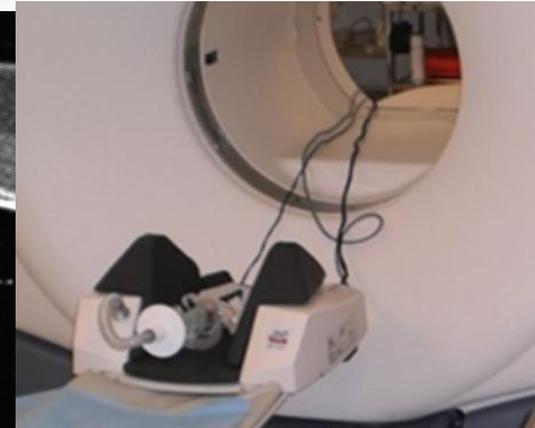
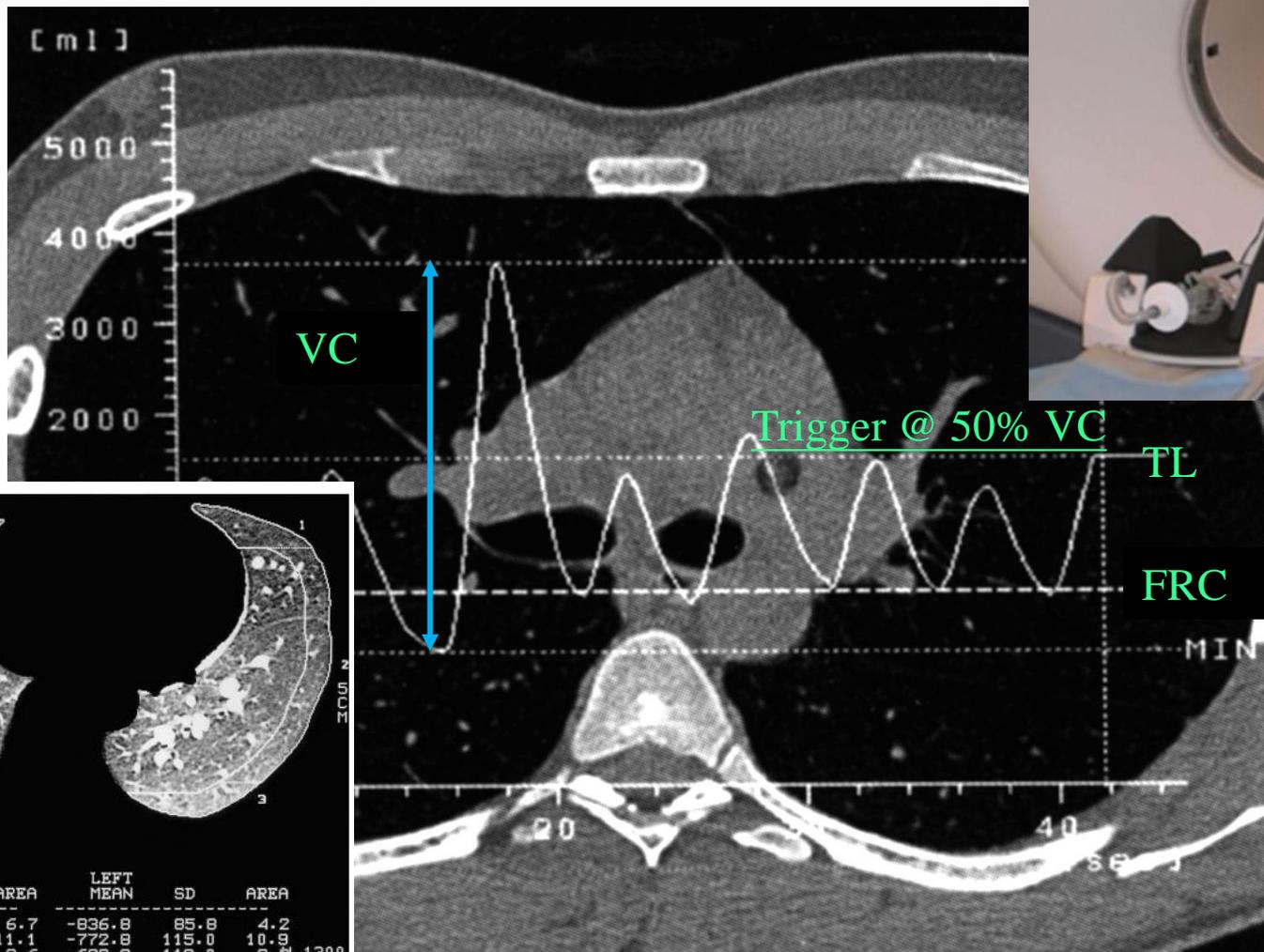


- Siemens Somatom HQ, KSVGH, 1995*

# The Influence of Expiratory phase



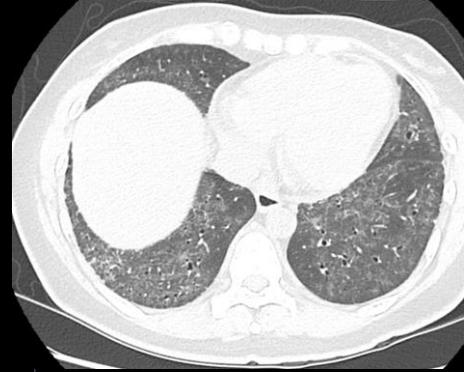
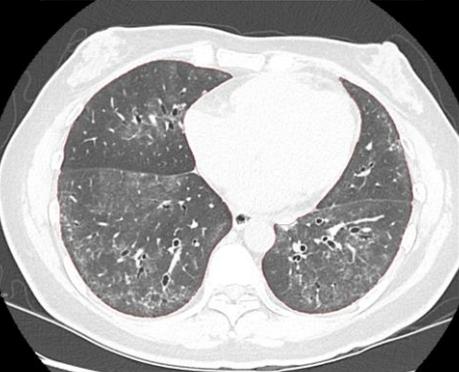
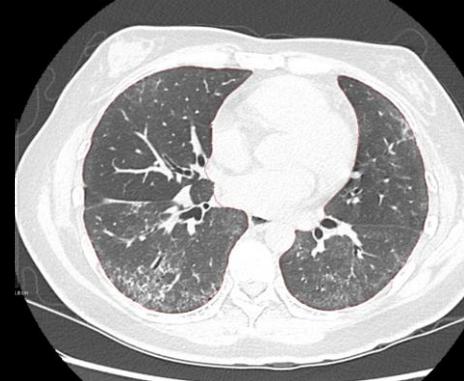
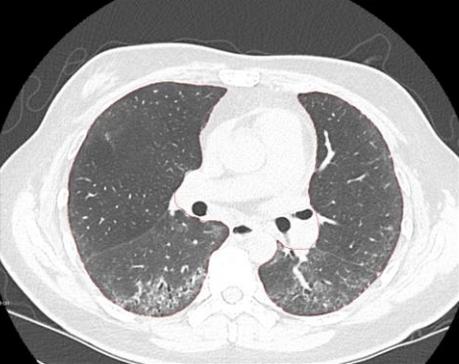
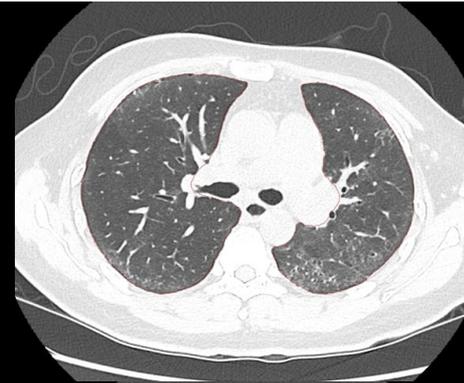
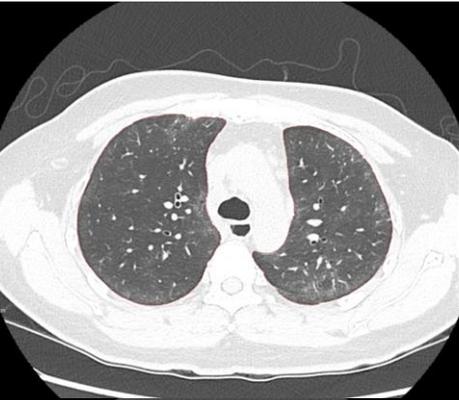
# Spirometry-gated CT (PulmoCT)



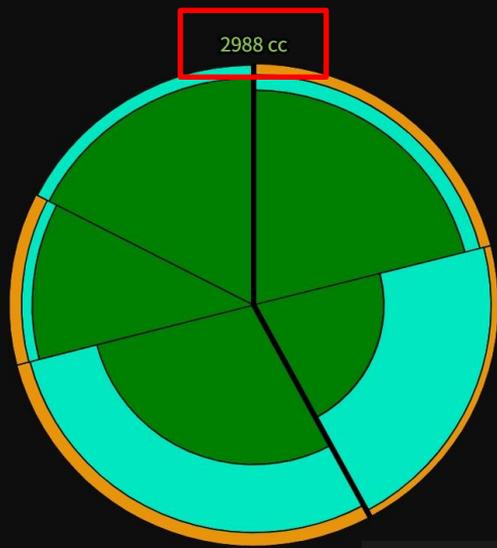
# AI-3D Camera Method



# Visual.semi- vs Auto.full-QCT



# 39 YOF PSS



- Pattern H
- Pattern R
- Pattern G
- Pattern C
- Pattern E
- Pattern N

| Regions     | Volume (cc) | Pattern H (%) | Pattern R (%) | Pattern G (%) | Pattern C (%) |
|-------------|-------------|---------------|---------------|---------------|---------------|
| Whole Lungs | 2988        | 0             | 4             | 20            |               |
| Rt. Lung    | 1730        | 0             | 4             | 17            |               |
| Lt. Lung    | 1258        | 0             | 4             | 25            |               |
| RUL         | 521         | 0             | 0             | 5             |               |
| RML         | 346         | 0             | 5             | 4             |               |
| RLL         | 863         | 0             | 6             | 28            |               |
| LUL         | 629         | 0             | 5             | 6             |               |
| LLL         | 629         | 0             | 3             | 44            |               |

| Pattern N (%) |
|---------------|
| 76            |
| 79            |
| 71            |
| 94            |
| 90            |
| 66            |
| 89            |
| 53            |

|                     |        | PRED | ACTUAL        | %PRED        |
|---------------------|--------|------|---------------|--------------|
| FVC                 | Liters | 3.80 | 1.92 *        | <b>050.5</b> |
| FEV1                | Liters | 3.30 | 1.74 *        | 052.7        |
| FEV1/FVC            | %      |      | 90.62         |              |
| LUNG VOLUMES (BTSP) |        |      |               |              |
| VC                  | Liters | 3.80 | 1.92 *        | 049.4        |
| TLC                 | Liters | 5.69 | <b>3.14 *</b> | 055.2        |
| DLCO                |        | 09.5 | 03.2 *        | 33.6         |
| DLCO/VA             |        | 01.7 | 01.2 *        | 68.7         |

# Radiomics for the Prediction of Response to Antifibrotic Treatment in Patients with Idiopathic Pulmonary Fibrosis: A Pilot Study

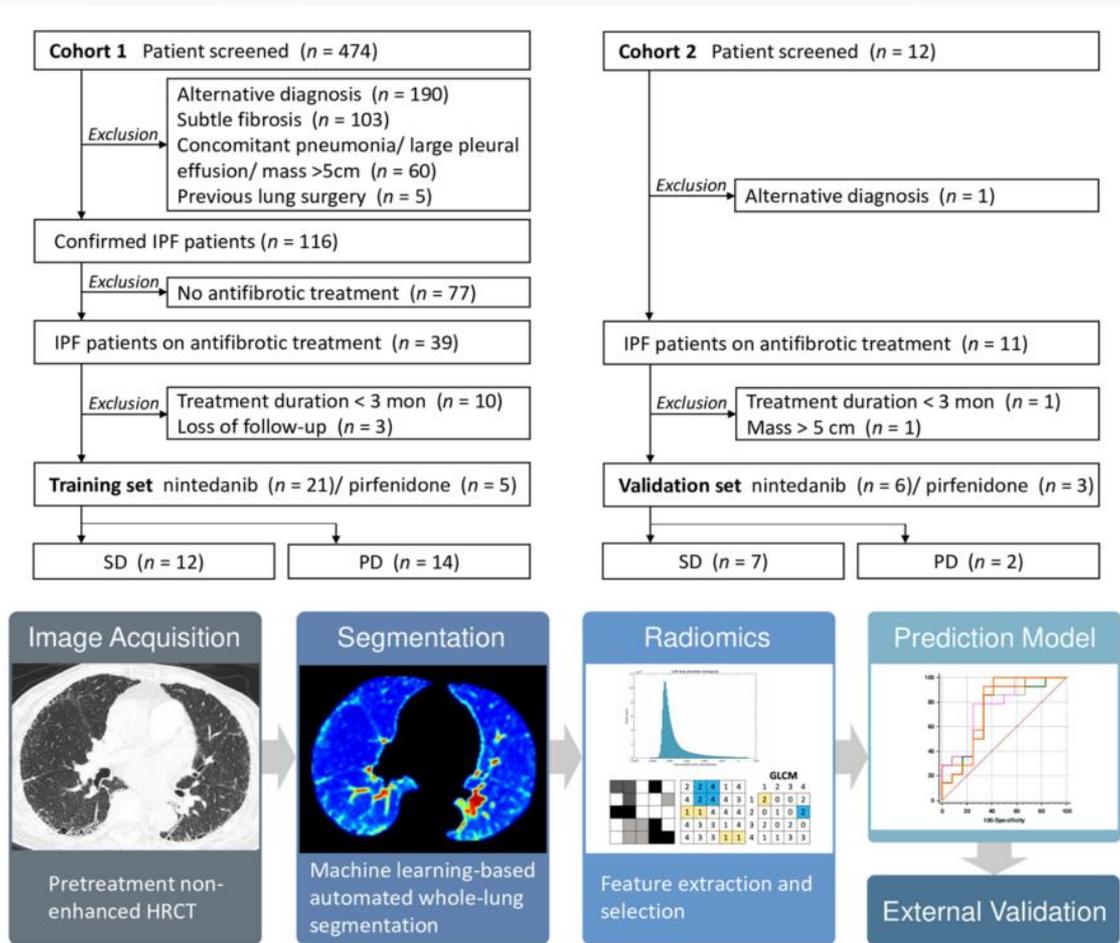


Figure 2. Flow diagrams of patient selection process and radiomics workflow.

# Radiomics of the lungs

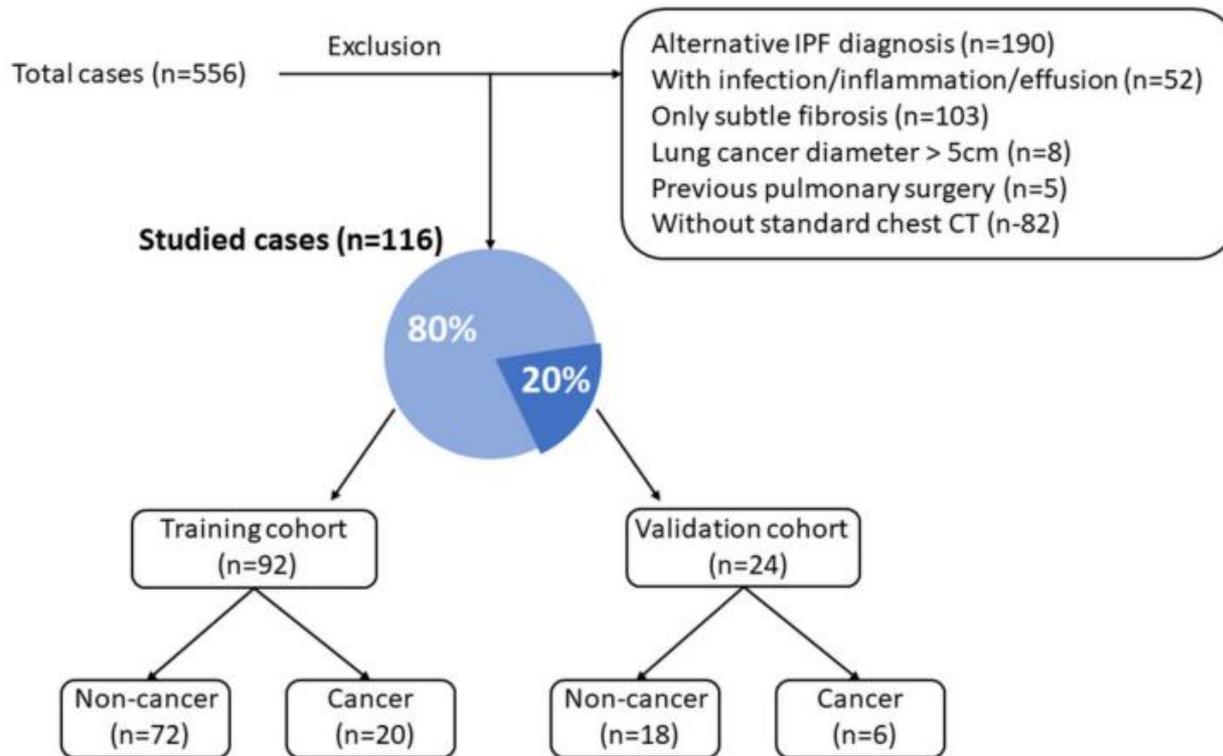
(QUIBIM Precision 2.8, QUIBIM SL, Valencia, Spain)

**Table 2.** Comparison of Radiomic Features of Stable Disease (SD) and Progressive Disease (PD) Groups in the Training Set.

| Metrics         | Features                       | SD     | PD         | n-Value                          |                       |                             |        |
|-----------------|--------------------------------|--------|------------|----------------------------------|-----------------------|-----------------------------|--------|
| Characteristics | Univariate Regression Analysis |        |            | Multivariate Regression Analysis |                       |                             |        |
|                 | OR                             | 95% CI | p-Value    | OR                               | 95% CI                | p-Value                     |        |
|                 | Entropy                        | 4.37   | 1.05–18.30 | 0.04 *                           | $3.42 \times 10^{75}$ | $0.02-5.94 \times 10^{153}$ | 0.06   |
|                 | Difference entropy             | 8.15   | 0.99–66.94 | 0.05 *                           | $1.67 \times 10^{16}$ | $0.01-4.14 \times 10^{40}$  | 0.19   |
|                 | Sum entropy                    | 3.93   | 1.01–15.32 | 0.05 *                           | 0.01                  | 0.01–0.22                   | 0.04 * |
|                 | Kurtosis                       | 0.85   | 0.73–1.01  | 0.04 *                           | 0.90                  | 0.25–3.25                   | 0.87   |
|                 | Skewness                       | 0.40   | 0.16–0.95  | 0.04 *                           | 0.01                  | 0.01–63.14                  | 0.29   |
|                 | Dissimilarity                  | 2.30   | 0.97–5.48  | 0.06 *                           | 0.01                  | 0.01–525.21                 | 0.16   |
|                 | Inverse difference             | 0.03   | 0.01–0.95  | 0.05 *                           | $1.40 \times 10^{61}$ | $0.35-5.58 \times 10^{122}$ | 0.05   |
|                 | Maximum probability            | 0.02   | 0.01–0.47  | 0.04 *                           | 0.01                  | $0.01-2.21 \times 10^{42}$  | 0.58   |
|                 | GGO%                           | 1.04   | 0.97–1.09  | 0.09 *                           | 1.10                  | 0.99–1.22                   | 0.07   |
|                 | Honeycombing%                  | 0.75   | 0.21–2.73  | 0.67                             |                       |                             |        |
|                 | Reticulation%                  | 1.06   | 0.84–1.34  | 0.62                             |                       |                             |        |
|                 | Emphysema%                     | 1.04   | 0.89–1.13  | 0.92                             |                       |                             |        |
|                 | Age                            | 1.08   | 0.98–1.19  | 0.13                             |                       |                             |        |
|                 | Sex                            | 4.29   | 0.65–28.26 | 0.13                             |                       |                             |        |
|                 | Smoking                        | 1.40   | 0.30–6.62  | 0.67                             |                       |                             |        |

\* Indicates statistical significance.

# Quantification of Cancer-Developing Idiopathic Pulmonary Fibrosis Using Whole-Lung Texture Analysis of HRCT Images

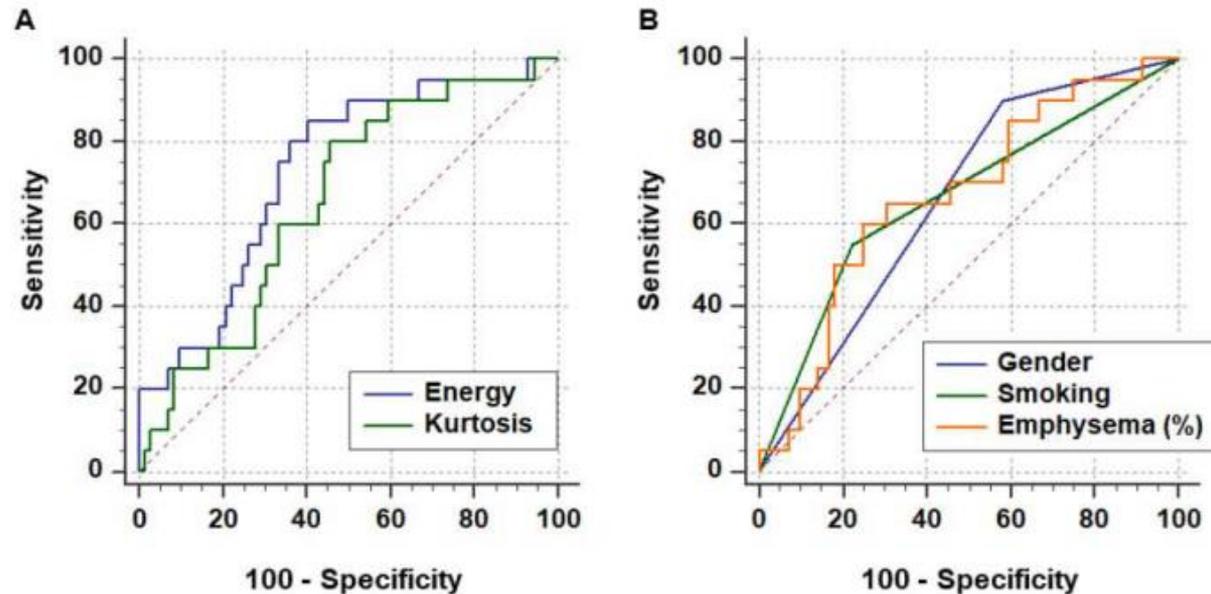


**Figure 2.** Patient selection flowchart for the training and validation cohorts.

**Table 3.** Univariate and multivariate logistic regression model to differentiate cancer-developing ILD from non-cancer ILD in the training cohort.

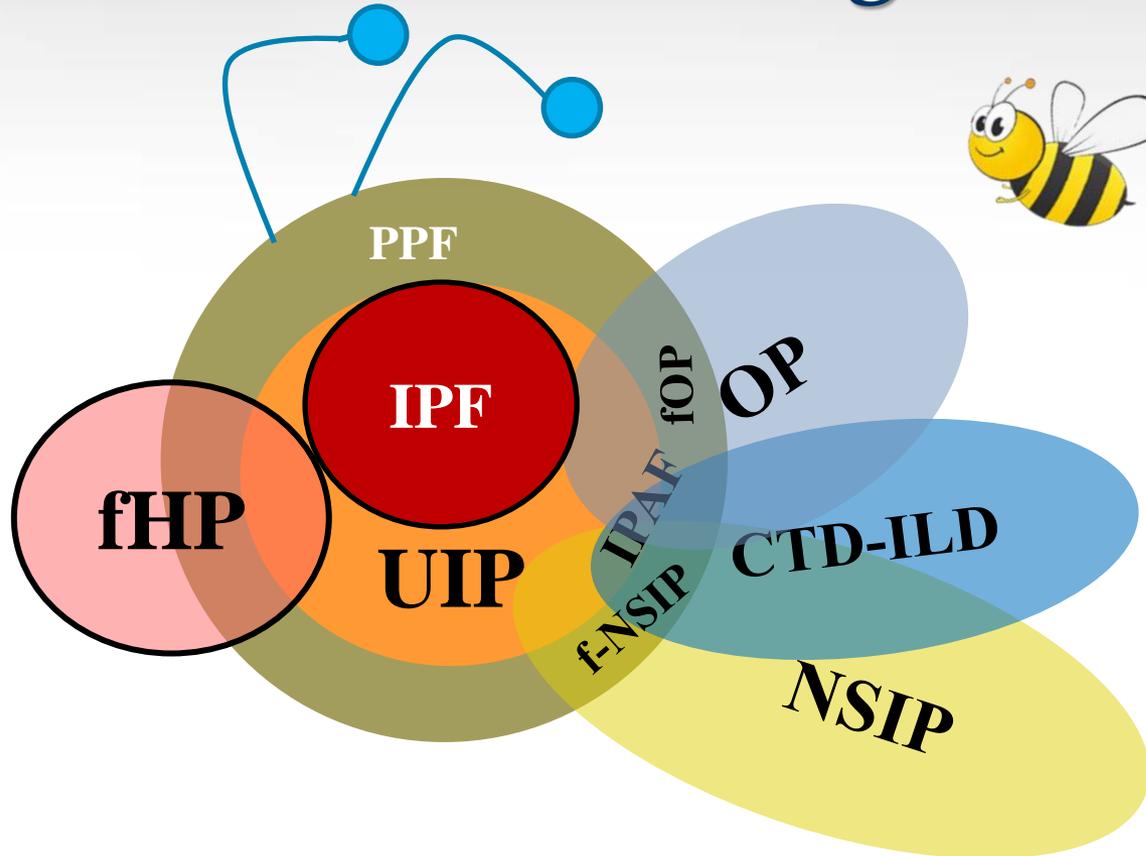
| Characteristic | Univariate Regression Analysis |              |                | Multivariate Regression Analysis |             |                |
|----------------|--------------------------------|--------------|----------------|----------------------------------|-------------|----------------|
|                | OR                             | (95% CI)     | <i>p</i> Value | OR                               | (95% CI)    | <i>p</i> Value |
| Smoke          | 4.28                           | (1.51–12.12) | 0.006          | 3.22                             | (1.05–9.87) | 0.041 *        |
| Energy         | 1.52                           | (1.14–2.05)  | 0.001          | 1.02                             | (0.93–1.11) | 0.012 *        |
| Kurtosis       | 1.08                           | (1.01–1.15)  | 0.034          | 1.03                             | (0.95–1.11) | 0.508          |

OR: odd ratio; CI: confidence interval. \* with significant difference.



**Figure 5.** ROC curve for differentiating cancer-associated and non-cancer IPF. (A) Radiomics features (energy and kurtosis) demonstrated acceptable performance, with an AUC of 0.66–0.73, which was not inferior to (B) the performance of traditional risk factors (gender, smoke, and emphysema), with an AUC of 0.66–0.67.

# The HRCT Diagram



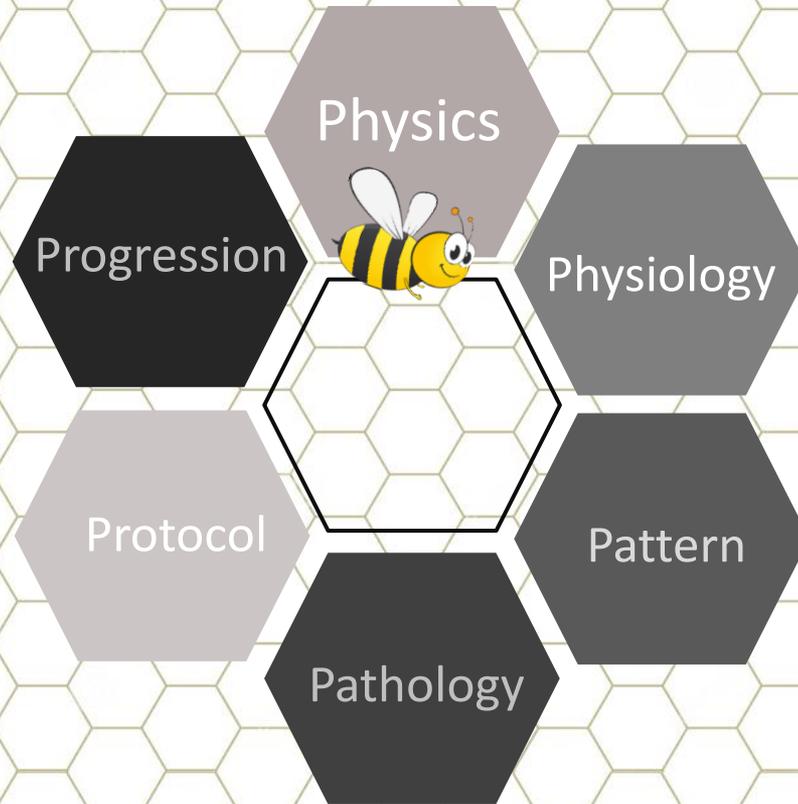
PF-ILD: Progressive fibrosis ILD

PPF-ILD: Progressive fibrosis phenotype ILD

Design by Wu Ming-Ting

\*\*One-third of non-IPF ILD patients are at risk of developing a progressive fibrosing phenotype

# Professionalism



## 6 Professionals

- Pulmonologist
  - Radiologist
- Rheumatologist
  - Cardiologist
- Thoracic Surgeon
  - Pathologist

# 6 P<sup>3</sup>-app<sup>®</sup>



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wu.mingting@gmail.com

