CT in the Diagnosis of Progressive Fibrosing Interstitial Lung Disease (PF-ILD)

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No Relevant Disclosures
Concept of PF-ILD

• “The response to lung injury includes the initial development of fibrosis that becomes progressive, self-sustaining, and independent of the original clinical association or trigger”


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Nintedanib PF-ILD Trial

- Enrolling patients with various fibrosing lung diseases (PF-ILDs)
- First trial to group patients based on the clinical behavior of their disease
- Need “scarring” on CT and clinical progression


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CT Findings of Fibrosis

- Reticulation
  - Interlobular septal thickening
  - Intralobular lines
  - Lobular distortion, irregular interfaces
- Traction bronchiectasis or bronchiolectasis
- Honeycombing (HC)

More severe, less reversible

GGO may also indicate fibrosis alone when superimposed on the above findings

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Interstitial Anatomy in Yellow
From Smithuis et al. in The Radiology Assistant, Radiologic Society of The Netherlands
Interlobular Septal Thickening
Reticulation: Intralobular Lines
Intralobular Lines: Onset of Fibrosis
Reticulation: Lobular Distortion
Traction Bronchiolectasis

“irregular dilatation caused by surrounding retractile pulmonary fibrosis seen as cysts (bronchi) or microcysts (bronchioles)”
Honeycombing (HC)

“Clustered cystic spaces, typically of comparable diameters on the order of 3-10 mm, but occasionally as large as 2.5 cm, usually subpleural and characterized by well-defined walls”

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Traction and HC: Advanced Fibrosis

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“Honeycombing and traction bronchiectasis/bronchiolectasis, previously defined separately, represent diverse aspect of a continuous spectrum”

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CT Findings of Fibrosis

- Reticulation
  - Interlobular septal thickening
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GGO without Fibrosis
GGO with Fibrosis

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GGO with Fibrosis

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GGO and Collimation

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Question

- Ground glass opacity (GGO) indicates
  - A. Interstitial disease
  - B. Airspace disease
  - C. Reversible disease
  - D. Irreversible disease
  - E. Something beneath the resolution of CT
CT Findings of Fibrosis

- Reticulation
  - Interlobular septal thickening
  - Intralobular lines
  - Lobular angulation, irregular interfaces
- Traction bronchiectasis or bronchiolectasis, honeycombing (HC)

More severe, less reversible

GGO may also indicate fibrosis alone when superimposed on the above findings

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Types of interstitial lung disease (ILD) most likely to have a progressive-fibrosing phenotype (indicated in bold)

PF-ILD

- Usual interstitial pneumonia (UIP)
- Chronic hypersensitivity pneumonitis (CHP)
- Nonspecific interstitial pneumonia (NSIP)
Patterns of PF-ILD

- UIP
- NSIP
- CHP

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PF-ILD: Causes

- Usual interstitial pneumonia (UIP)
- Chronic hypersensitivity pneumonitis (CHP)
- Nonspecific interstitial pneumonia (NSIP)
UIP Pattern

- Idiopathic (IPF)
- CVD
- Asbestosis
- Drug toxicity
- CHP

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2011 ATS/ERS/JRS/ALAT Statement
HRCT Criteria for UIP Pattern

- **Definite** UIP pattern (all 4 features):
  - Subpleural, basal predominance
  - Reticular abnormality
  - *Honeycombing* with or without traction bronchiectasis
  - Absence of features listed as inconsistent with UIP pattern (air trapping, cysts, others)
Definite UIP
Definite UIP: Coronal Reformats

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Definite UIP: Sagittal Reformats
Problems with the Guidelines

- Definite UIP pattern (all 4 features):
  - Subpleural, basal predominance
  - Reticular abnormality

Must have some upper lobe involvement, non-segmental distribution, and reticulation should include features of fibrosis, fibrosis should be heterogeneous
Heterogeneity of the Fibrosis in UIP

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Problems with the Guidelines

- Definite UIP pattern (all 4 features):
  - Honeycombing with or without traction bronchiectasis

Easy to confuse other pathology with HC and falsely diagnose definite UIP, HC occurs in other non-UIP ILD, and the distinction of traction bronchiectasis from HC is arbitrary and unnecessary.

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Clustered Subpleural Cystic Spaces

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Clustered Subpleural Cystic Spaces
Clustered Subpleural Cystic Airspaces

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HC Occurs on Other Fibrotic ILDs
Non-Definite UIP (Traction no HC)
Problems with the Guidelines

- Definite UIP pattern (all 4 features):
  - Absence of features listed as inconsistent with UIP pattern (air trapping, cysts, others)

  Air trapping can occur in any PF-ILD, does not always occur in CHP, and the degree of expiratory effort is completely variable
UIP Diagnosis: Modified Criteria

- UIP pattern (all features):
  - Peripheral reticulation with lobular distortion and intralobular lines
  - Subpleural, basal predominance but with some upper lobe involvement
  - Non-segmental
  - Traction bronchiectasis and/or HC
  - *Heterogenous* appearance to the fibrosis

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Advantages of These Criteria

- Better observer agreement, easy to teach
- Improves distinction of UIP from other entities (including non-PF-ILD diagnoses)
  - Reduce or eliminate false positives
- Enable earlier UIP diagnosis
Limitations of Existing Guidelines

“Based upon the results of this study, modification of these criteria may be necessary to improve observer agreement.”

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UIP: CT Diagnosis

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UIP: CT Diagnosis

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“Definite UIP” Without HC
UIP Diagnosis Without Honeycombing

- UIP pattern (5 features):
  - Peripheral reticulation with lobular distortion and intralobular lines
  - Subpleural, basal predominance but with some upper lobe involvement
  - Non-segmental
  - Traction bronchiectasis and/or HC
  - Heterogenous appearance to the fibrosis

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PF-ILD: Causes

- Usual interstitial pneumonia (UIP)
- Chronic hypersensitivity pneumonitis (CHP)
- Nonspecific interstitial pneumonia (NSIP)
CHP: Overview

- CHP implies fibrosis, which carries a worse prognosis (by CT or histology)
- Can be difficult to separate CHP and UIP on OLB (especially in advanced disease)
- Many patients (at least 50%) have no recognizable antigen exposure
- Some previous UIP/IPF now reclassified as CHP

Churg A, Arch Pathol Lab Med 142, January 2018

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• Peribronchiolar (centrilobular) fibrosis, upper zone
• Extends from centrilobular region to adjacent bronchiole, interlobular septum, or pleura ("bridging fibrosis") (intralobular lines)
• Fibrotic NSIP in areas, granulomata may be absent
CHP: CT Appearance

- GGO superimposed on reticulation
  - Intralobular lines often prominent
- Peribronchovascular, upper-mid zone
- Variable secondary lobule size, many hyperlucent, air trapping *variable*
  - “Headcheese sign”
- Centrilobular nodules absent when no antigen
CHP: Mold
CHP: Mold
CHP: Headcheese Sign
CHP: Headcheese Sign
CHP: Headcheese Sign
Sarcoidosis and Headcheese
CHP: Intralobular Lines
CHP: Expiratory Scanning
Question 2

- The biggest problem with expiratory CT is
  - A. Instructions are complicated
  - B. Technologists are not uniformly trained
  - C. Variable patient expiratory effort
  - D. Non contiguous scans
  - E. Lack of reader agreement
CT-Biopsy Discordance

Radiologic–pathologic discordance in biopsy-proven usual interstitial pneumonia

Kumihiro Yagihashi¹,²,³, Jason Huckleberry⁴, Thomas V. Colby⁵, Henry D. Tazelaar⁵, Jordan Zach⁶, Baskaran Sundaram⁶, Sudhakar Pipavath⁷, Marvin L. Schwarz⁸ and David A. Lynch⁹ for the Idiopathic Pulmonary Fibrosis Clinical Research Network (IPFnet)⁹

Top reason (70%): multifocal air trapping on CT as “inconsistent” with UIP
CHP on CT, UIP on Biopsy

Yagihashi K et al. Eur Respir J 2016;47:1189-1197
Copyright European Respiratory Society 2016

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Is idiopathic CHP a distinct entity? Should it be included in IPF?

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PFIELD: Causes

- Usual interstitial pneumonia (UIP)
- Chronic hypersensitivity pneumonitis (CHP)
- Nonspecific interstitial pneumonia (NSIP)
NSIP Pattern

- CVD (often with OP)
  - can precede CVD diagnosis (IPAF)
- Drug reaction
- HP
- Post DAD or post OP/COP
- Idiopathic
Cellular NSIP
Fibrotic NSIP

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NSIP Pattern: CT Features

- GGO superimposed on reticulation
  - Traction bronchiolectasis, HC in the fibrotic form
- Often lower zone predominant, can be only lower but should be non-segmental (aspiration ddx)
- Homogeneous
- Subpleural sparing
- Inferior central RML involvement
NSIP Pattern: Rheumatoid Arthritis

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NSIP Pattern: Scleroderma
NSIP: The Bottom of the RML

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NSIP and Subpleural Sparing: MCTD
NSIP and Subpleural Sparing: MCTD
NSIP: Predated Scleroderma Onset

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Idiopathic NSIP
2 Years Later: Fibrotic NSIP Pattern
Summary Case

UIP

NSIP

CHP

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2010: NSIP/UIP
2014: Fibrotic NSIP

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2018: Clear PF-ILD

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PF-ILD Dictation Template

- “The imaging features are consistent with (progressive) fibrotic interstitial lung disease (PF-ILD) with a (definite UIP, CHP, fibrotic NSIP, overlapping, or other) pattern
PF-ILD Dictation Template

• “The imaging features are consistent with (progressive) fibrotic interstitial lung disease (PF-ILD) with a (definite UIP, CHP, fibrotic NSIP, overlapping, or other) pattern”
• Attempt to quantify and specify fibrosis extent, severity
Concept of PF-ILD: Questions

• Does every PF-ILD carry a poor prognosis? Should all be treated with anti-fibrotic agents?
• Is it reasonable to expand “IPF” to include cases of CHP with no clear inciting antigen?
• How to group patients on treatment (according to CT pattern, severity of fibrosis) and what CT criteria are important to follow (if any)?
• Fibrosis quantification, which findings may respond to therapy, overall role of CT unclear

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