New guidelines for the diagnosis of Idiopathic Pulmonary Fibrosis

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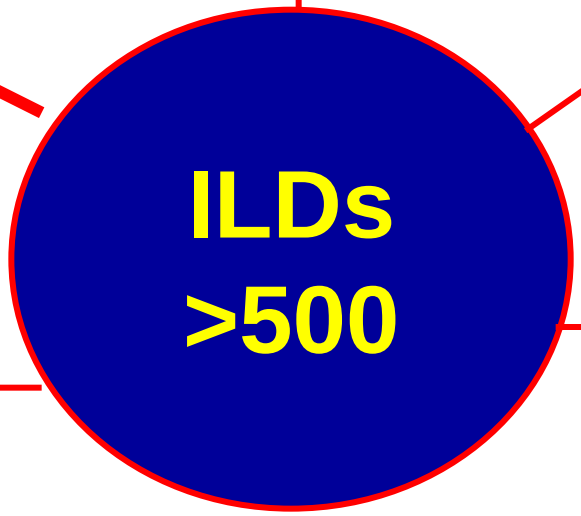
Conflicts of Interest

I declare

NO conflicts of interest

CLASSIFICATION OF ILDs



ACUTE
[AIP, EAA, VASCULITIS]

CHRONIC WITHOUT SYSTEMIC DISEASE
(*Idiopathic interstitial Pneumonias, PAP, PVOD, IPHsid)*

SUBACUTE
[DIP, COP, EAA]

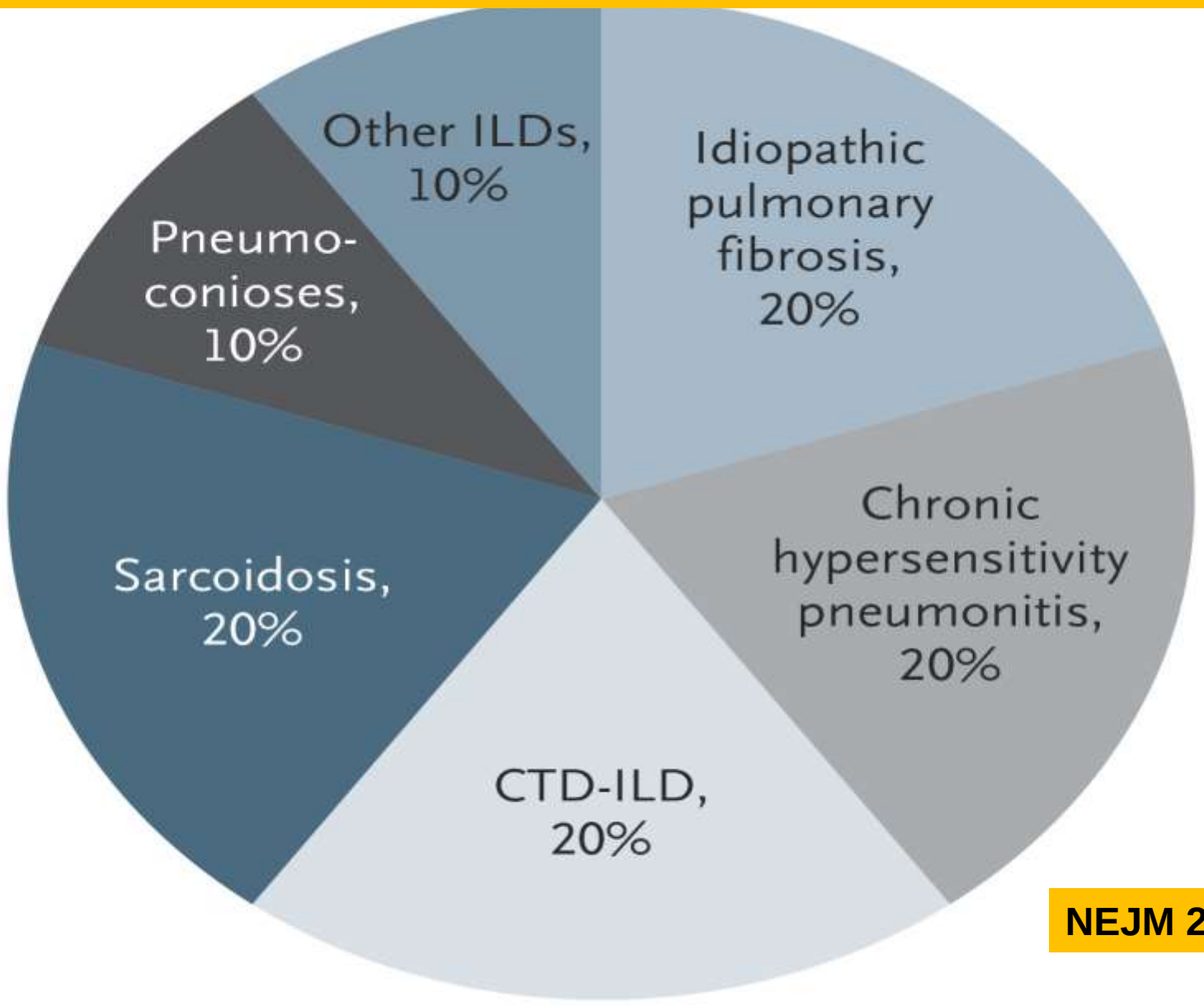
EPISODIC
[EP, EAA, VASCULITIS, COP]

CHRONIC WITH SYSTEMIC DISEASE
[CVD, VASCULITIS, SARCOIDOSIS, TS, IBD, HES, COP*,LCH*]

CHRONIC KNOWN ETIOLOGY
(Environmental, Occupational, Drugs)

Slide courtesy of Demosthenes Bouros

Estimated Relative Distribution of Specific ILDs in the US



NEJM 2018

American Thoracic Society Documents

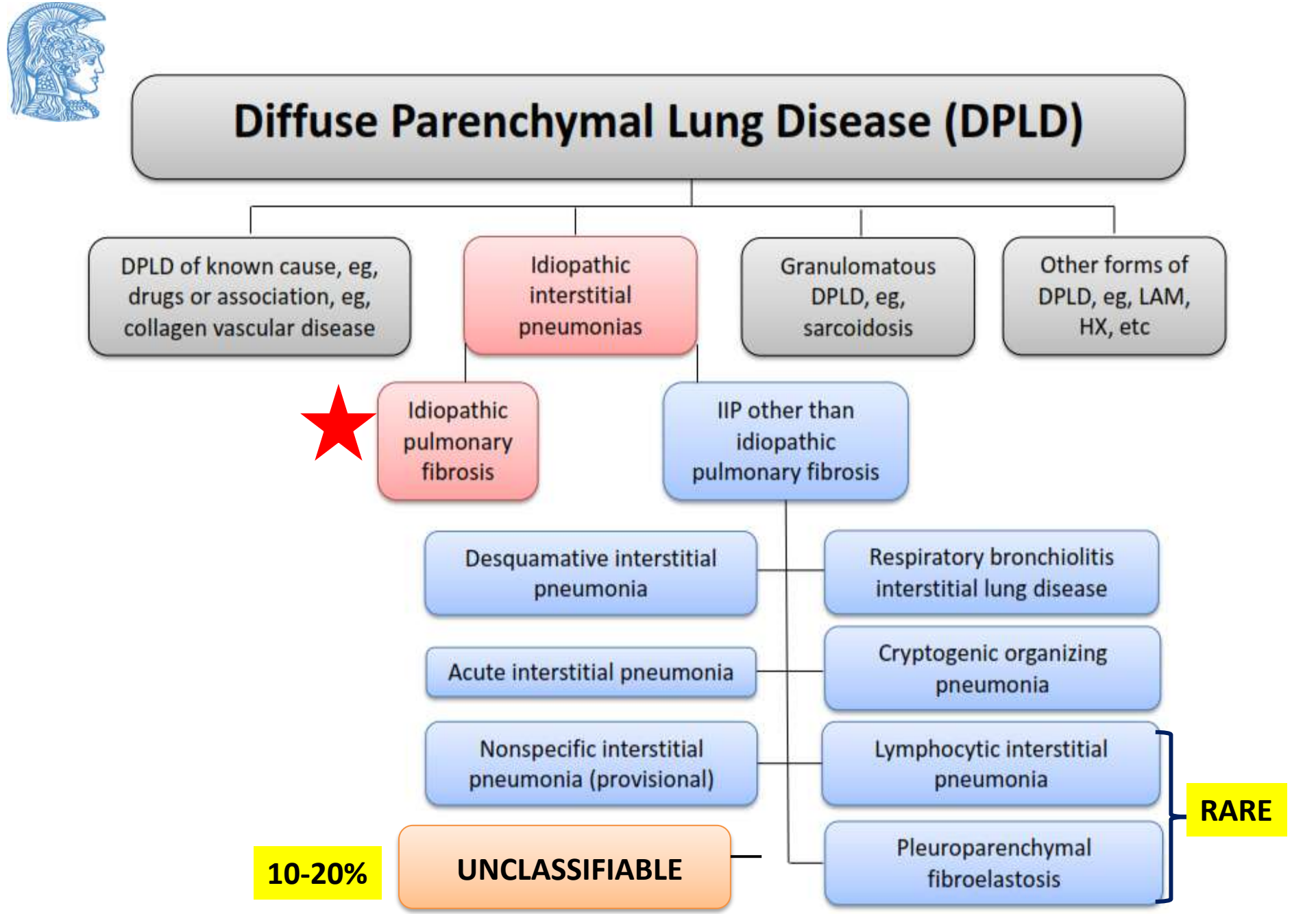
An Official American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias

AJRCCM 2013

William D. Travis, Ulrich Costabel, David M. Hansell, Talmadge E. King, Jr., David A. Lynch, Andrew G. Nicholson, Christopher J. Ryerson, Jay H. Ryu, Moisés Selman, Athol U. Wells, Jurgen Behr, Demosthenes Bouros, Kevin K. Brown, Thomas V. Colby, Harold R. Collard, Carlos Robalo Cordeiro, Vincent Cottin, Bruno Crestani, Marjolein Drent, Rosalind F. Dudden, Jim Egan, Kevin Flaherty, Cory Hogaboam, Yoshikazu Inoue, Takeshi Johkoh, Dong Soon Kim, Masanori Kitaichi, James Loyd, Fernando J. Martinez, Jeffrey Myers, Shandra Protzko, Ganesh Raghu, Luca Richeldi, Nicola Sverzellati, Jeffrey Swigris, and Dominique Valeyre; on behalf of the ATS/ERS Committee on Idiopathic Interstitial Pneumonias

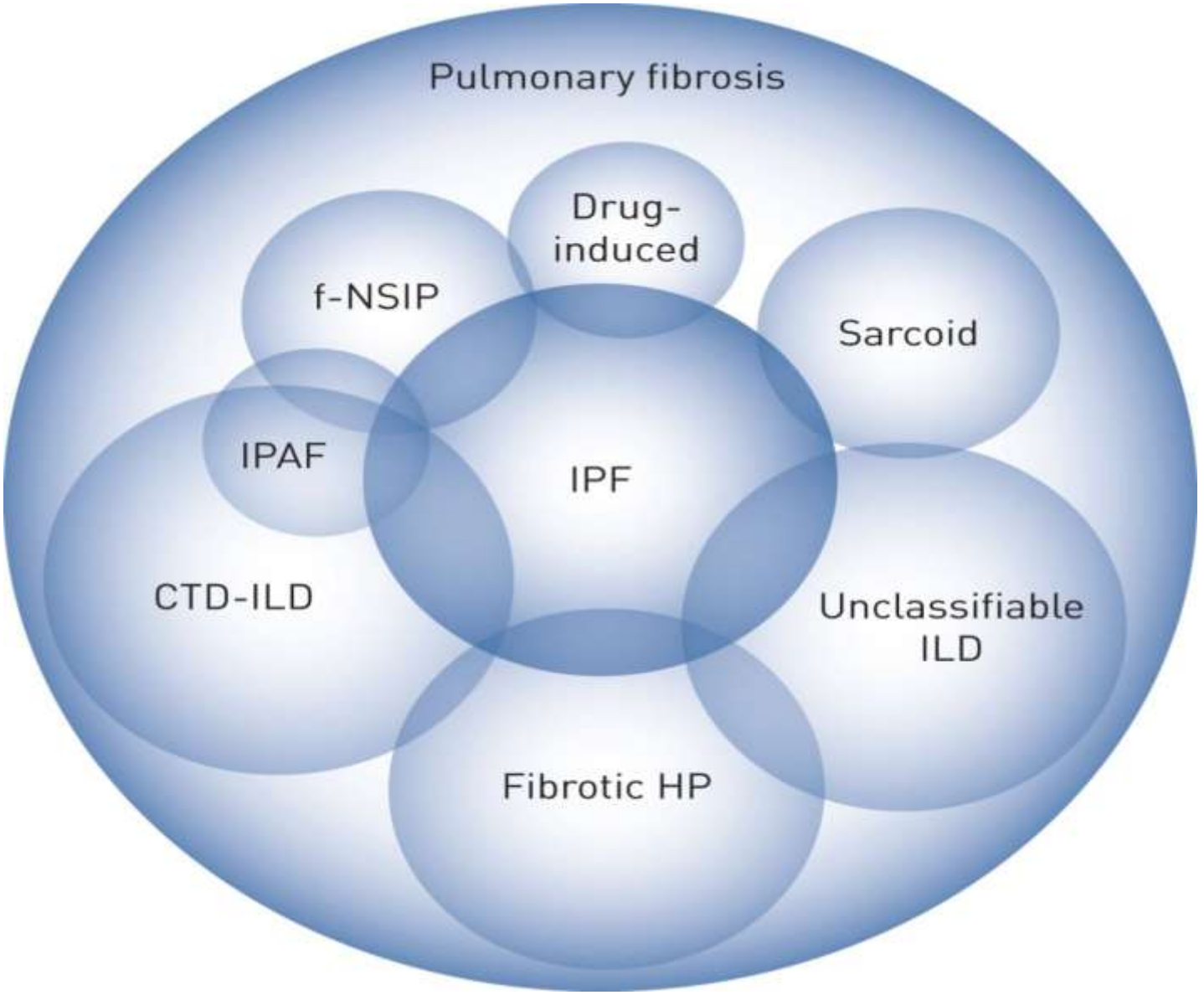
Idiopathic interstitial pneumonias (IIP)

Idiopathic pulmonary fibrosis/Usual interstitial pneumonia (IPF/UIP)	Nonspecific interstitial pneumonia (NSIP)	Cryptogenic organizing pneumonia (COP/OP)	Desquamative interstitial pneumonia (DIP)	Respiratory bronchiolitis-associated interstitial lung disease (RBILD)	Acute interstitial Pneumonia (AIP)	RARE IIPs • LIP • PPFE
55%	25%	3%	15%		3%	



Travis WD, et al; ATS/ERS Committee on Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med*. 2013;188(6):733-748.

The overlap in longitudinal disease behavior between IPF and other progressive fibrotic disorders .



American Thoracic Society Documents

2011

An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management

Ganesh Raghu, Harold R. Collard, Jim J. Egan, Fernando J. Martinez, Juergen Behr, Kevin K. Brown, Thomas V. Colby, Jean-François Cordier, Kevin R. Flaherty, Joseph A. Lasky, David A. Lynch, Jay H. Ryu, Jeffrey J. Swigris, Athol U. Wells, Julio Ancochea, Demosthenes Bouros, Carlos Carvalho, Ulrich Costabel, Masahito Ebina, David M. Hansell, Takeshi Johkoh, Dong Soon Kim, Talmadge E. King, Jr., Yasuhiro Kondoh, Jeffrey Myers, Nestor L. Müller, Andrew G. Nicholson, Luca Richeldi, Moisés Selman, Rosalind F. Dudden, Barbara S. Griss, Shandra L. Protzko, and Holger J. Schünemann, on behalf of the ATS/ERS/JRS/ALAT Committee on Idiopathic Pulmonary Fibrosis

This Official Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Japanese Respiratory Society (JRS), and the Latin American Thoracic Association (ALAT) Was Approved by the ATS Board of Directors, November 2010, the ERS Executive Committee, September 2010, the JRS Board of Directors, December 2010, and the ALAT Executive Committee, November 2010

This Statement has been formally endorsed by the Society of Thoracic Radiology and by the Pulmonary Pathology Society

Am J Respir Crit Care Med 2011; 183: 788-824

2011 ATS/ERS Diagnostic Criteria for IPF

Exclusion of known causes of ILD*

AND

UIP pattern on HRCT without surgical biopsy

OR

Definite/possible UIP pattern on HRCT with a surgical lung biopsy showing definite/probable UIP

*also known as diffuse parenchymal lung disease, DPLD

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

Most common first symptoms of ILD
(600 US residents responded to the survey)

77% Shortness of breath

53% Cough

38% Fatigue

Patients diagnosed with IPF
(47% of respondents)

Median time to diagnosis: 7 months
For 28% of patients, the diagnostic process took over 2 years

Median number of physician visit: 3
14% of patients saw more than 6 physicians

56% of patients were initially misdiagnosed
most frequent misdiagnoses: asthma, pneumonia, bronchitis and allergies.

Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper

David A Lynch, Nicola Sverzellati, William D Travis, Kevin K Brown, Thomas V Colby, Jeffrey R Galvin, Jonathan G Goldin, David M Hansell, Yoshikazu Inoue, Takeshi Johkoh, Andrew G Nicholson, Shandra L Knight, Suhail Raoof, Luca Richeldi, Christopher J Ryerson, Jay H Ryu, Athol U Wells

This Review provides an updated approach to the diagnosis of ic pulmonary fibrosis (IPF), based on a systematic search of the medical literature and the expert opinic bers of the Fleischner Society. A checklist is provided for the clinical evaluation of patients with suspect nterstitial pneumonia (UIP). The role of CT is expanded to permit diagnosis of IPF without surgical lun n select cases when CT shows a probable UIP pattern. Additional investigations, including surgical lun should be considered in patients with either clinical or CT findings that are indeterminate for IPF. A plinary approach is particularly important when deciding to perform additional diagnostic assessments, g biopsy results with clinical and CT features, and establishing a working diagnosis of IPF if lung tissue i able. A working diagnosis of IPF should be reviewed at regular intervals since the diagnosis might cha ia are presented to establish confident and working diagnoses of IPF.

Introduction

The approval of medical treatments for c pulmonary fibrosis (IPF) marks a new era in ng this deadly disease: offering hope to pati their physicians, a clearer path forward for comp rested in the development of new treatments, otential for new biological insights. This n so offers clinicians the opportunity to re roaches to diagnosis. The diagnostic criteria fo lished by the American Thoracic Society (ATS an Respiratory Society (ERS), Japanese Respi ciety (JRS), and Latin American Thoracic Asso LAT) in 2011[1] have been crucial for defining eria and ensuring appropriate recruitment fo ive clinical trials.[2–7] In turn, these trials, with la s of well characterised patients, have provided le new clinically relevant information about dise ntation and its longitudinal behaviour.[8,9] The sp usion and exclusion criteria used in these studi so highlighted the limitations of current di guidelines, and indicated opportunities fo ement.[9,10]

The diagn PF requires the collaboration of multiple s , the ability to interpret and communi plex clinical data patterns, and to integrate or sometimes conflicting information. The interprets the history and physical exam the patient to develop a clinical context, the tho ologist interprets the pattern present on high-re CT images of the chest and, if needed, the st interprets the histopathological pattern seen biopsy samples. All the information gained must be shared in a common language to enable clinical de ion making. Since so-called classic clinical stories and patterns are uncommon, some degree of clinical uncertainty is often present, and acknowledgment of this limitation and a clear plan to address it are essential.

For this Review, we identified specific questions pertaining to the diagnosis of IPF (panel 1), and did a search of the medical literature to identify evidence related to the topics identified and that had been published after the 2011 ATS/ERS/JRS/ALAT guidelines.[1] Using this research and the expert opinion of members of the Fleischner Society, we provide IPF diagnostic criteria that we believe will be useful for clinicians, clinical trialists, trial sponsors, and other interested groups.

Systematic review

An international multidisciplinary committee, including 17 members of the Fleischner Society with expertise in interstitial lung disease (ILD) and evidence-based medicine (eight pulmonologists, six radiologists, and three pathologists), and a medical librarian expert (SLK), developed the key questions believed to be important for the diagnosis of IPF (panel 1). Several face-to-face meetings were held, in addition to monthly conference calls. We did a literature search with the assistance of a medical librarian (search strategy and selection criteria and appendix). The committee was divided into subgroups assigned to specific

Key messages

- A confident diagnosis of IPF (idiopathic pulmonary fibrosis) can be made in the correct clinical context when CT imaging shows a pattern of typical or probable UIP (usual interstitial pneumonia)
- If the clinical context is indeterminate for IPF, or the CT pattern is not indicative of typical or probable UIP, biopsy should be considered to confirm the presence of a UIP histological pattern, and a confident diagnosis of IPF could then be made on the basis of a multidisciplinary evaluation
- If diagnostic tissue is not available, a working diagnosis of IPF could be made after a careful multidisciplinary evaluation
- All patients with an IPF diagnosis, particularly those with a working diagnosis, should have this diagnosis reviewed at regular intervals

AMERICAN THORACIC SOCIETY DOCUMENTS

2018

Diagnosis of Idiopathic Pulmonary Fibrosis

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

Ganesh Raghu, Martine Remy-Jardin, Jeffrey L. Myers, Luca Richeldi, Christopher J. Ryerson, David J. Lederer, Juergen Behr, Vincent Cottin, Sonye K. Danoff, Ferran Morell, Kevin R. Flaherty, Athol Wells, Fernando J. Martinez, Arata Azuma, Thomas J. Bice, Demosthenes Bouros, Kevin K. Brown, Harold R. Collard, Abhijit Duggal, Liam Galvin, Yoshikazu Inoue, R. Gisli Jenkins, Takeshi Johkoh, Ella A. Kazerooni, Masanori Kitaichi, Shandra L. Knight, George Mansour, Andrew G. Nicholson, Sudhakar N. J. Pipavath, Ivette Buendía-Roldán, Moisés Selman, William D. Travis, Simon Walsh, and Kevin C. Wilson; on behalf of the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE OF THE AMERICAN THORACIC SOCIETY (ATS), EUROPEAN RESPIRATORY SOCIETY (ERS), JAPANESE RESPIRATORY SOCIETY (JRS), AND LATIN AMERICAN THORACIC SOCIETY (ALAT) WAS APPROVED BY THE ATS, JRS, AND ALAT MAY 2018, AND THE ERS JUNE 2018

***Am J Respir Crit Care Med* 2018; 198: Sept 1st.**

ATS/ERS/JRS/ALAT Diagnosis of IPF Guidelines-2018

GUIDELINES ATS 2018

ΕΡΩΤΗΣΕΙΣ-ΠΡΟΤΑΣΕΙΣ ΟΔΗΓΙΩΝ

- **ΓΕΝΙΚΕΣ-MOTHERHOOD**
- **EVIDENCE BASED**

Am J Respir Crit ***Care*** *Med* 2018; 198: Sept 1st.

TABLE 1 Diagnosis of idiopathic pulmonary fibrosis (IPF): similarities and differences between the 2018 ATS/ERS/JRS/ALAT clinical practice guideline and the 2018 Fleischner white paper

	ATS/ERS/JRS/ALAT clinical practice guideline [1]		Fleischner white paper consensus statement [2]
Number of authors	34		17
Overlapping authors		8	
Endorsing scientific societies	Multiple		Single
Multidisciplinary nature	Yes		Yes
Question-based structure	Yes		Yes
Systematic search of the literature	Yes		Yes
Evidence-based approach (Institute of Medicine standards)	Yes		No
PICO questions/format	Yes		No
Expert opinion-based approach	No		Yes
Grading of recommendations	Yes		No
Published in a peer-reviewed journal	Yes		Yes
Implementation and interest to all stakeholders (policy makers, regulating agencies, IPF community-at-large)	Yes		?

Eur Respir J 2018; 52: 1801485

The new guidelines for IPF diagnosis (ATS/ERS/JRS/ALAT 2018)

Committee decision after voting

- ***Strong for***
- ***Conditional for***
- ***Strong against***
- ***Conditional against***
- ***Abstain***

Table 2. Implications of Strong and Conditional Recommendations

	Strong Recommendation ("We recommend . . .")
For patients	The overwhelming majority of individuals in this situation would want the recommended course of action and only a small minority would not.
For clinicians	The overwhelming majority of individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
For policy makers	The recommendation can be adapted as policy in most situations, including for use as performance indicators.

Conditional Recommendation
("We suggest . . .")

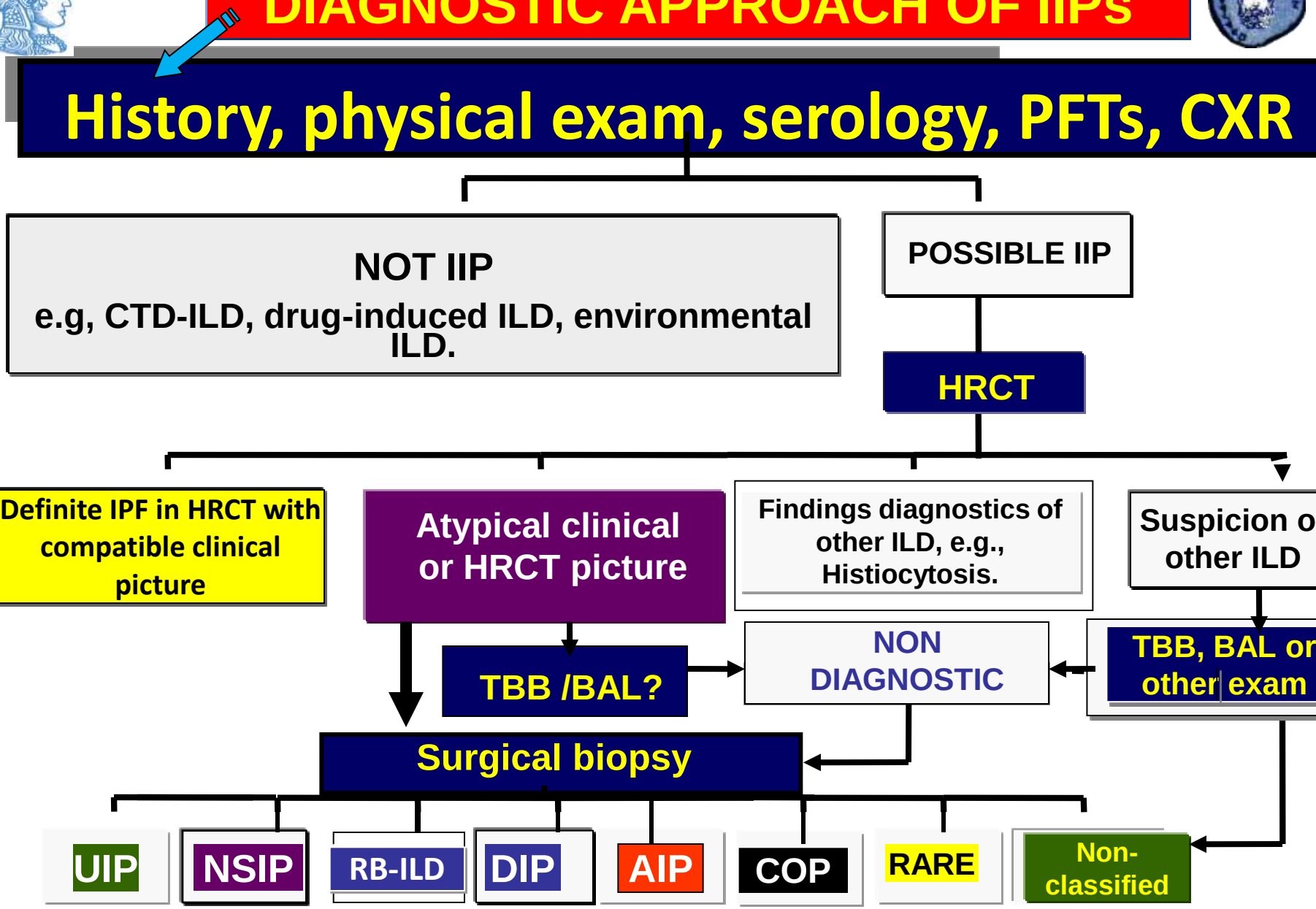
For patients	The majority of individuals in this situation would want the suggested course of action, but a sizeable minority would not.
For clinicians	**Διαφορετικές επιλογές θα είναι κατάλληλες για διαφορετικούς ασθενείς, και πρέπει να βοηθήσεις τον κάθε ασθενή να αποφασίσει ανάλογα με τις αξίες του και τις προτιμήσεις του.** **Ο γιατρός αναμένεται να αφιερώσει περισσότερο χ** **με τους ασθενείς προκειμένου να αποφασίσουν.**
For policy makers	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

DEFINITION

- IPF is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause.
- It occurs primarily in older adults, is limited to the lungs, and is defined by the histopathologic and/or radiologic pattern of UIP.
- It should be considered in all adult patients with unexplained chronic exertional dyspnea, cough, bibasilar inspiratory crackles, and/or digital clubbing, that occur without constitutional or other symptoms that suggest a multisystem disease.

Am J Respir Crit Care Med 2018; 198: Sept 1st.

DIAGNOSTIC APPROACH OF IIPs



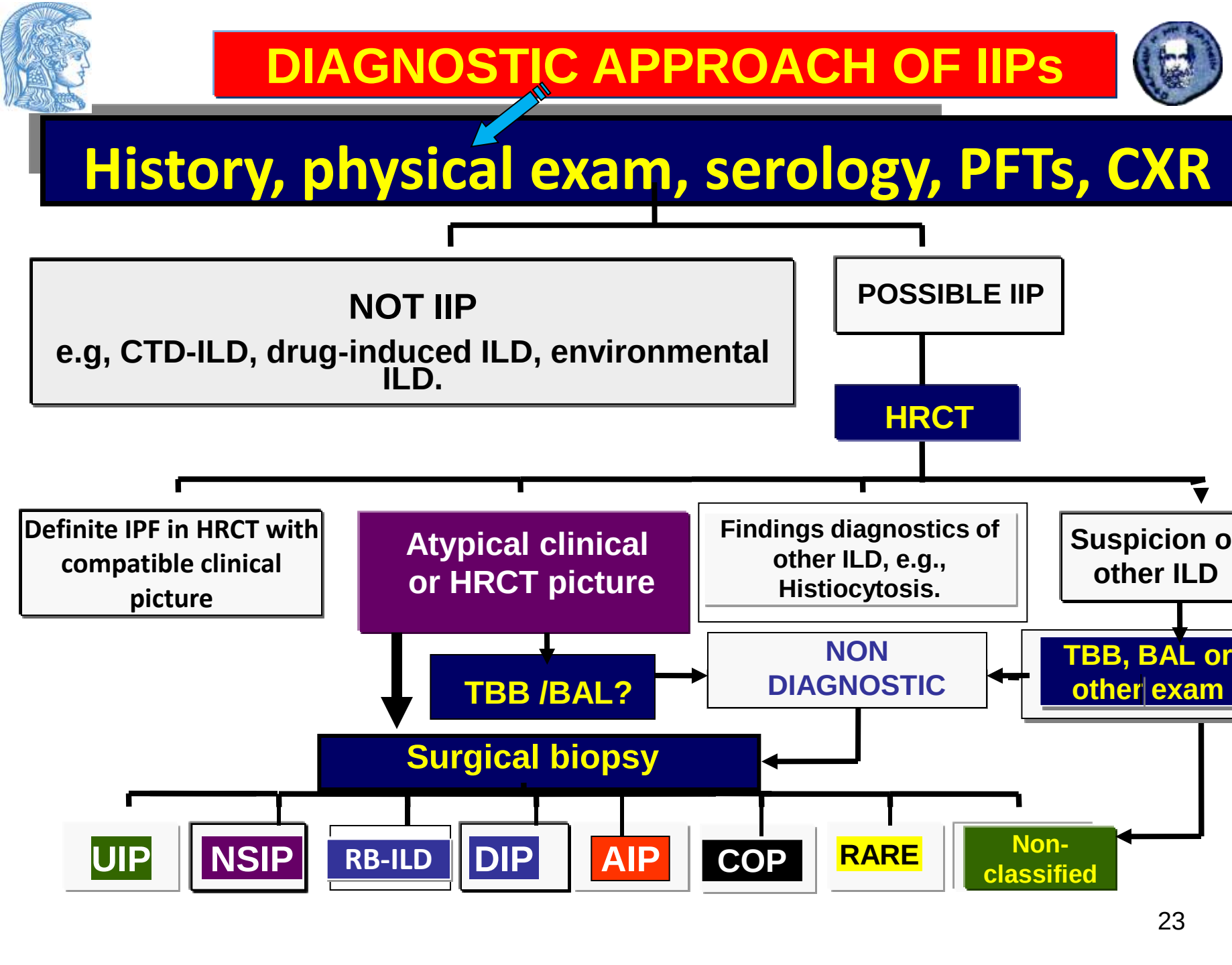
HISTORY

We recommend taking a detailed history of both medication use and environmental exposures at home, work, and other places the patient frequently visits to exclude potential causes of ILD (*motherhood statement*).

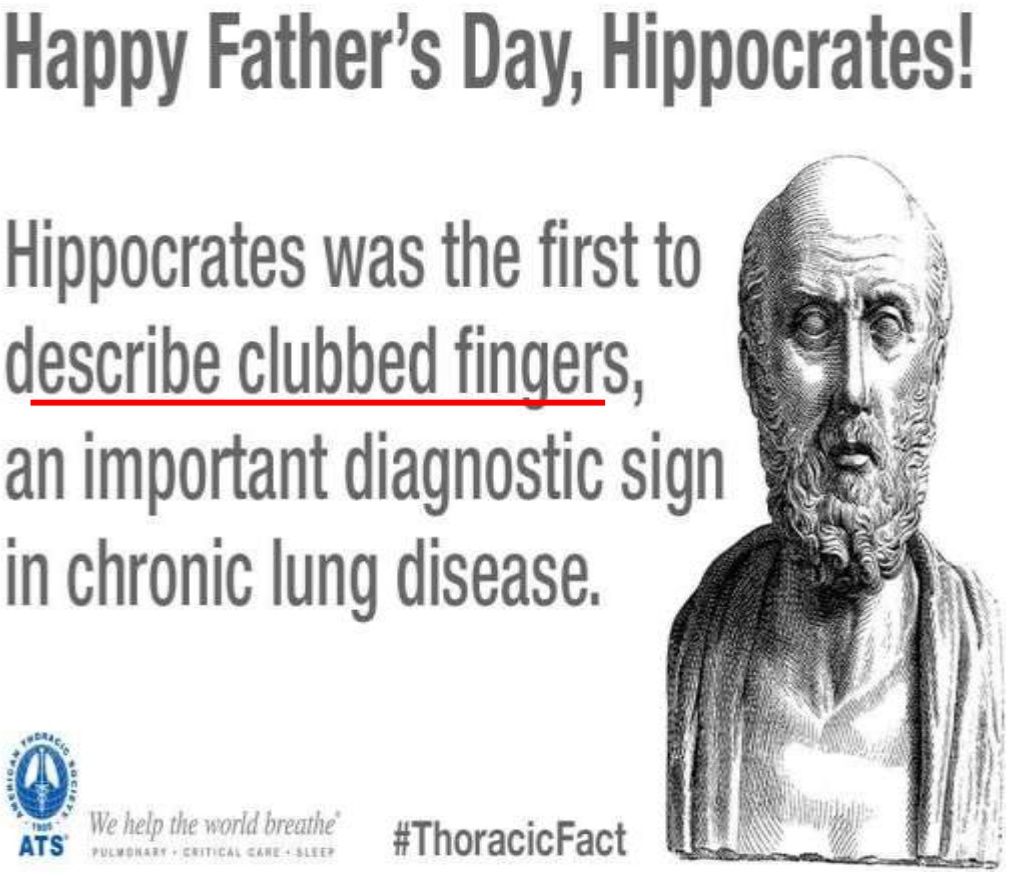
- **AGE** (*>50 years*)
- **GENDER** (*male>female*)
- **SMOKING** (*frequently*)
- **DRUGS** (*exclude*)
- **Sx DURATION** (*months-years*)
- **EXPOSURE** (organic/*inorganic dust*)
- **FAMILIAL PULMONARY FIBROSIS** (*5-8%*)

Am J Respir Crit Care Med 2018; 198: Sept 1st.

DIAGNOSTIC APPROACH OF IIPs



Digital clubbing



> 50% OF THE PATIENTS

Fine end inspiratory basal crackles (velcro).
Λεπτοί τελοεισπνευστικοί μη μουσικοί ρόγχοι

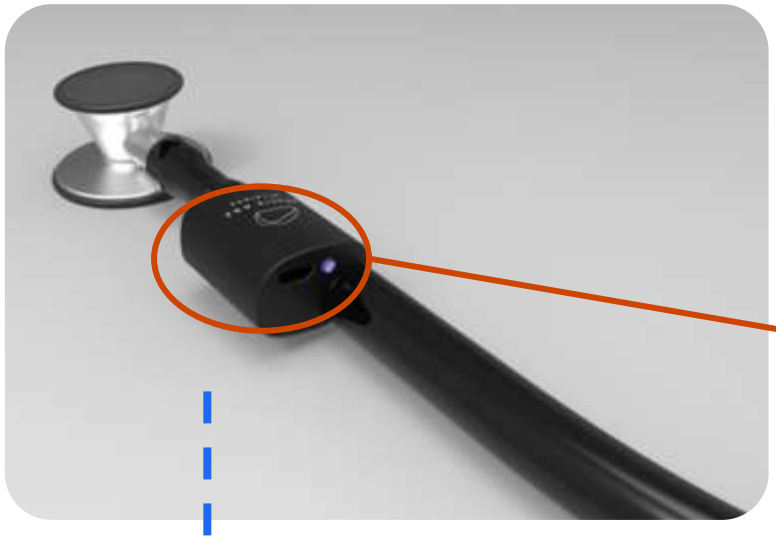
Eur Respir J 2012; 40: 519–521
DOI: 10.1183/09031936.00001612

EDITORIAL

Velcro crackles: the key for early diagnosis of idiopathic pulmonary fibrosis?

Vincent Cottin and Jean-François Cordier

How Does the Digital Stethoscope Work?



LiPo Rechargeable Battery

1-Button User Interface

BLE 5 iOS & Droid

100 hours between charges

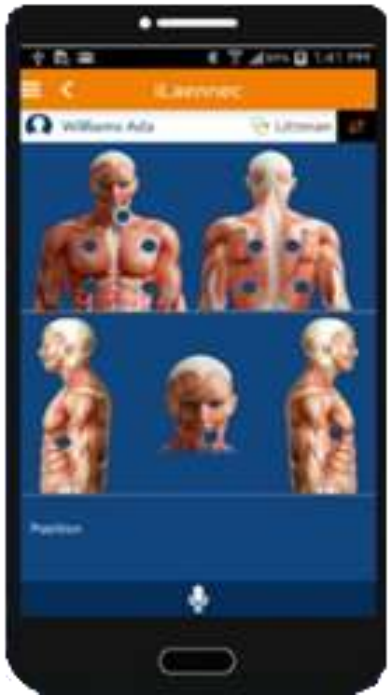
Send lung sound to apps

AI analyses the sound and shows the results on apps

Digital Auscultation Aids

Data sources

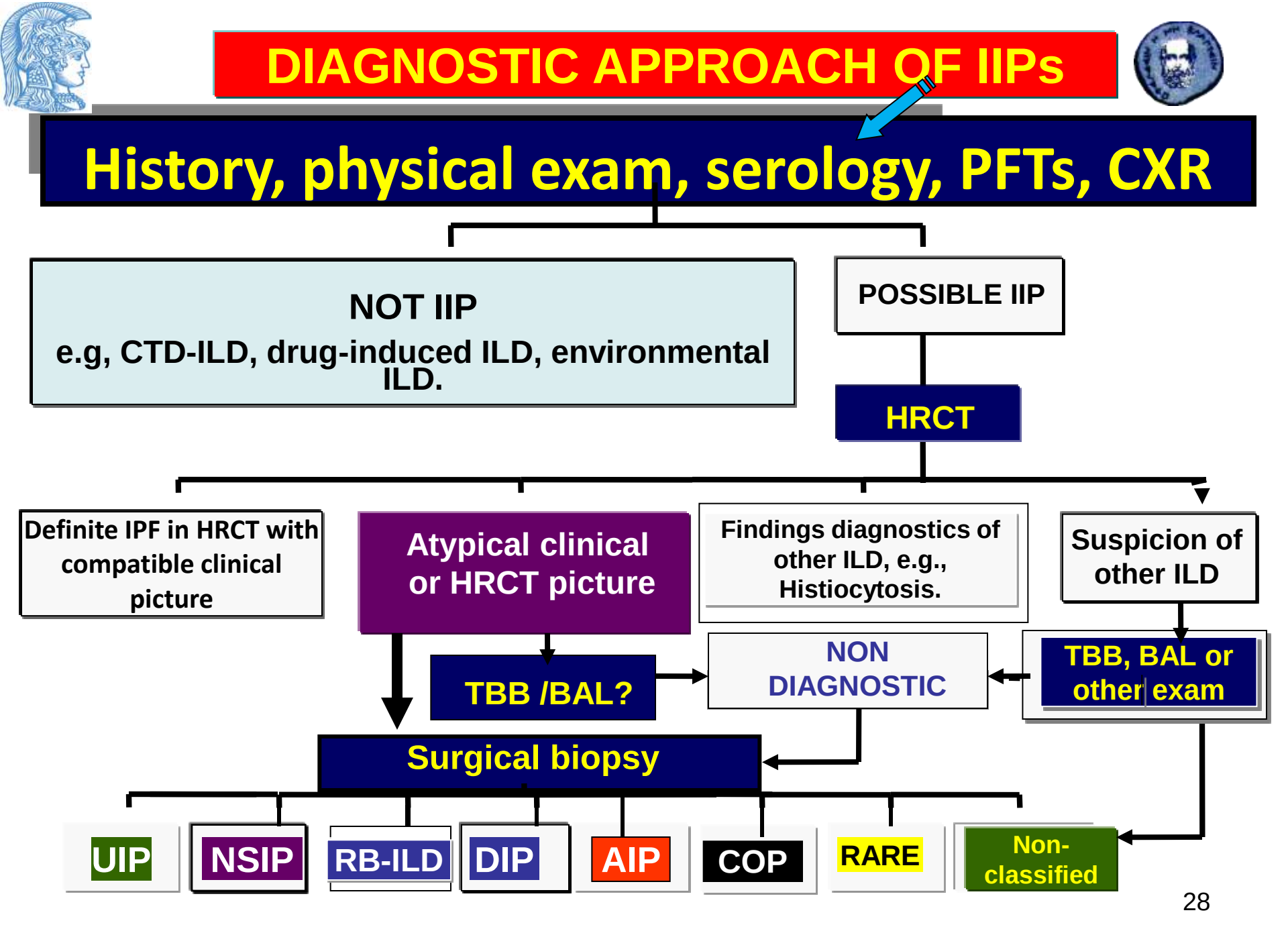
- Patient demographics
- Medical history
- Patient-reported symptoms
- Lung auscultation (4-6 points)



Probabilistic scores for all compatible diagnostic hypotheses
Pulmonary fibrosis, COPD, asthma, CHF, etc…

AT THE CORE OF CARE

DIAGNOSTIC APPROACH OF IIPs



Serologic Tests Can Help Identify Other Conditions

We recommend serological testing to exclude connective tissue disease (CTD) as a potential cause of the ILD (*motherhood statement*).

Connective tissue diseases

ANA, RF & anti-CCP (ERS/ATS guidelines)
CK and aldolase
Anti-myositis panel with Jo-1 antibody
ENA panel
- **Scl-70, ACA**
- **Ro (SSA), La (SSB)**
- **MPO/PR3 (ANCA)**
- **Smith, RNP**
- **ESR, CRP**

Hypersensitivity pneumonitis

Hypersensitivity panel (*if exposure history*)

ATS/ERS/JRS/ALAT Statement. *Am J Respir Crit Care Med*. 2011 & 2018.

Respiratory Medicine (2013) 107, 249–255

Available online at www.sciencedirect.com

SciVerse ScienceDirect

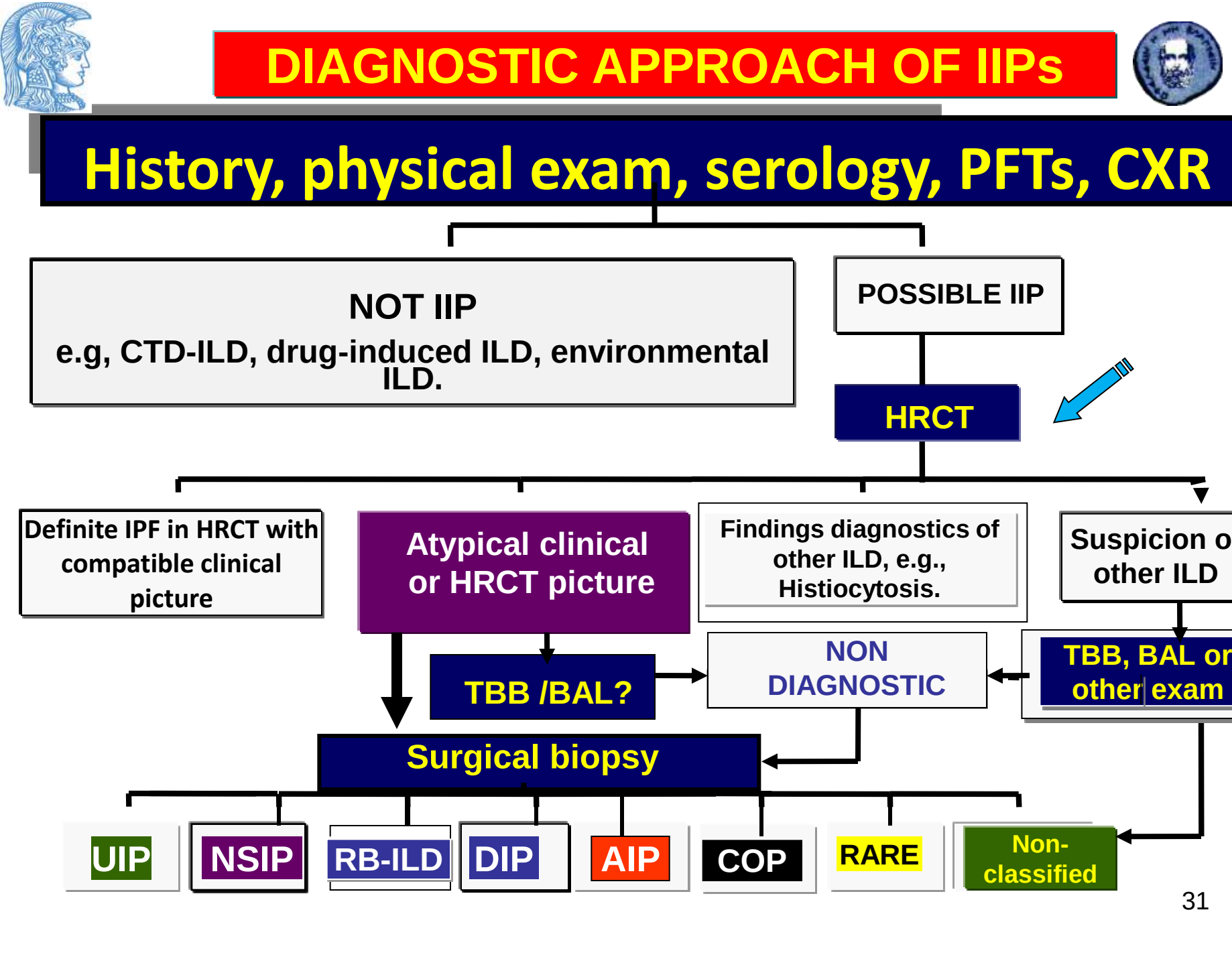
journal homepage: www.elsevier.com/locate/rmed

Prevalence and clinical significance of circulating autoantibodies in idiopathic pulmonary fibrosis

Joyce S. Lee [a,*,g], Eunice J. Kim [a,g], Kara L. Lynch [b], Brett Elicker [c], Christopher J. Ryerson [e], Tamiko R. Katsumoto [a], Anthony K. Shum [a], Paul J. Wolters [a], Stefania Cerri [f], Luca Richeldi [f], Kirk D. Jones [d], Talmadge E. King Jr [a], Harold R. Collard [a]

Positive autoantibodies were found in 22% of patients with IPF and 21% of healthy controls. There were no differences in the types of autoantibodies found between patients with idiopathic pulmonary fibrosis and healthy controls.

DIAGNOSTIC APPROACH OF IIPs



What are the features of an HRCT?

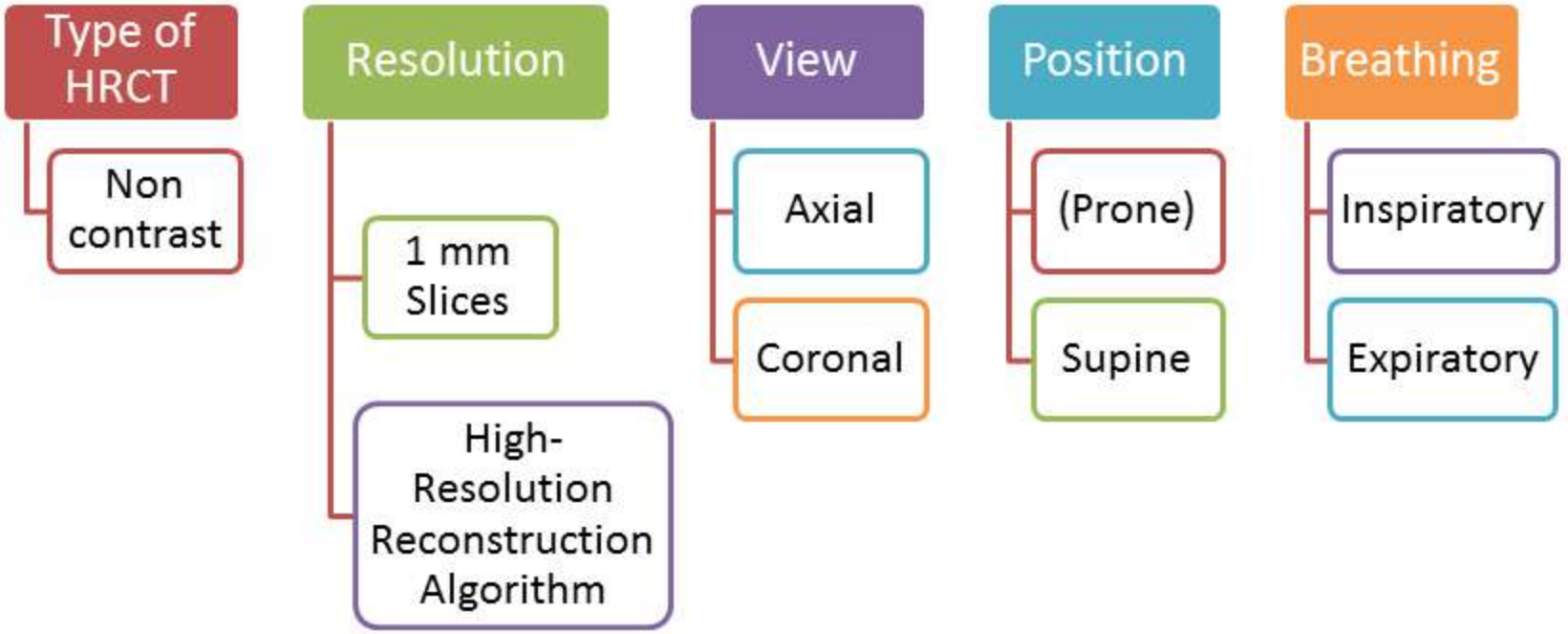


Table 3. High-Resolution Computed Tomography Scanning Parameters

Recommended Scanning Protocol	Advantages of Updated Recommendations
1. Noncontrast examination	—
2. Volumetric acquisition with selection of: • Sub-millimetric collimation • Shortest rotation time • Highest pitch • Tube potential and tube current appropriate to patient size: ° Typically 120 kVp and 9240 mAs ° Lower tube potentials (e.g., 100 kVp) with adjustment of tube current encouraged for thin patients • Use of techniques available to avoid unnecessary radiation exposure (e.g., tube current modulation)	A. Acquisition covering the entire lung volume (vs. analysis of 10% of lung volume with sequential scanning) • No risk of missing subtle infiltrative abnormalities • Possibility of multiplanar reformations, helpful for analysis of the ILD pattern and predominant distribution of lung changes • Possibility of post-processing to optimize detection of subtle hypoattenuated lesions (minimum intensity projection) and micronodular infiltration (maximum intensity projection) • Possibility of detection of additional lesions (e.g., incidental identification of lung nodule or focal consolidation in lung fibrosis that may correspond to lung carcinoma) • Optimal to assess progression or improvement in patient's follow-up B. Dramatic increase in temporal resolution and speed of data acquisition • Motion-free images C. Availability of numerous dose-reduction tools
3. Reconstruction of thin-section CT images (≤1.5 mm): • Contiguous or overlapping • Using a high-spatial-frequency algorithm • Iterative reconstruction algorithm if validated on the CT unit (if not, filtered back projection)	—
4. Number of acquisitions: • Supine: inspiratory (volumetric) • Supine: expiratory (can be volumetric or sequential) • Prone: only inspiratory scans (can be sequential or volumetric); optional (*see text*) • Inspiratory scans obtained at full inspiration	A. Expiratory scans useful to detect air trapping B. Prone scans allow analysis of peripheral lung changes without dependent lung atelectasis that may be mistaken for abnormal lung infiltration or mimic disease (e.g., pseudohoneycombing when combined with paraseptal emphysema) C. Inadequate inspiration increases lung attenuation (which should not be interpreted as ground-glass attenuation) and is responsible for dependent lung atelectasis (which may mimic abnormal lung infiltration or mask subtle abnormalities)
5. Recommended radiation dose for the inspiratory volumetric acquisition: • 1–3 mSv (i.e., "reduced" dose) • Strong recommendation to avoid "ultralow-dose CT" (<1 mSv)	A. Considerable dose reduction compared to sequential scanning

Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper

David A Lynch, Nicola Sverzellati, William D Travis, Kevin K Brown, Thomas V Colby, Jeffrey R Galvin, Jonathan G Goldin, David M Hansell, Yoshikazu Inoue, Takeshi Johkoh, Andrew G Nicholson, Shandra L Knight, Suhail Raoof, Luca Richeldi, Christopher J Ryerson, Jay H Ryu, Athol U Wells

- **CRITERIA ARE PRESENTED TO ESTABLISH CONFIDENT AND WORKING DIAGNOSIS OF IPF.**
- **IF A DIAGNOSTIC TISSUE IS NOT AVAILABLE, A WORKING DIAGNOSIS OF IPF COULD BE MADE AFTER A CAREFUL MDD.**
- **ALL PATIENTS ESPECIALLY THOSE WITH A WORKING DIAGNOSIS SHOULD HAVE THIS DIAGNOSIS REVIEWED AT REGULAR INTERVALS.**

FLEISCHNER society 2017 white paper Diagnostic criteria for IPF. Lancet RM 2017

- **HRCT categories**
  - **Typical UIP**
  - **Probable UIP *("possible" in ATS/ERS 2011*)**
  - **Indeterminate for UIP**
  - **Consistent with alternative diagnosis *(inconsistent with UIP)***
- **Histopathologic categories**
  - **UIP**
  - **Probable UIP**
  - **Indeterminate for UIP**
  - **Consistent with alternative diagnosis**

THE LANCET
Respiratory Medicine

V. Tzilas, D. Valeyre, A. Tzouvelekis,*D. Bouros

Taking a giant step in the diagnosis of idiopathic pulmonary fibrosis

Lancet Respir Med 2017

Published Online
November 10, 2017
http://dx.doi.org/10.1016/PII

See Online/Review
http://dx.doi.org/10.1016/PII

Diagnostic categories of UIP based on CT patterns

	Typical UIP CT pattern
Distribution	Basal predominant (occasionally diffuse), and subpleural predominant; distribution is often heterogeneous
Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; absence of features to suggest an alternative diagnosis

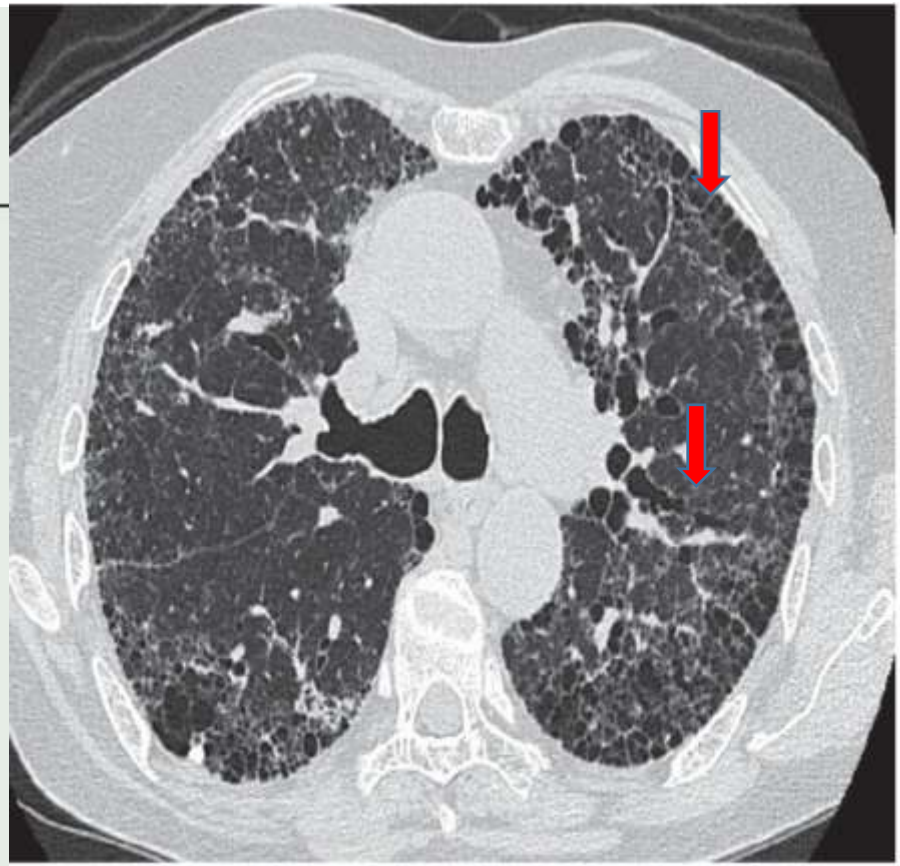


Figure 4: High-resolution computer tomography in idiopathic pulmonary fibrosis. Predominantly basal and subpleural reticular fibrosis with honeycombing

www.thelancet.com/respiratory Published online November 15, 2017

Diagnostic categories of UIP based on CT patterns

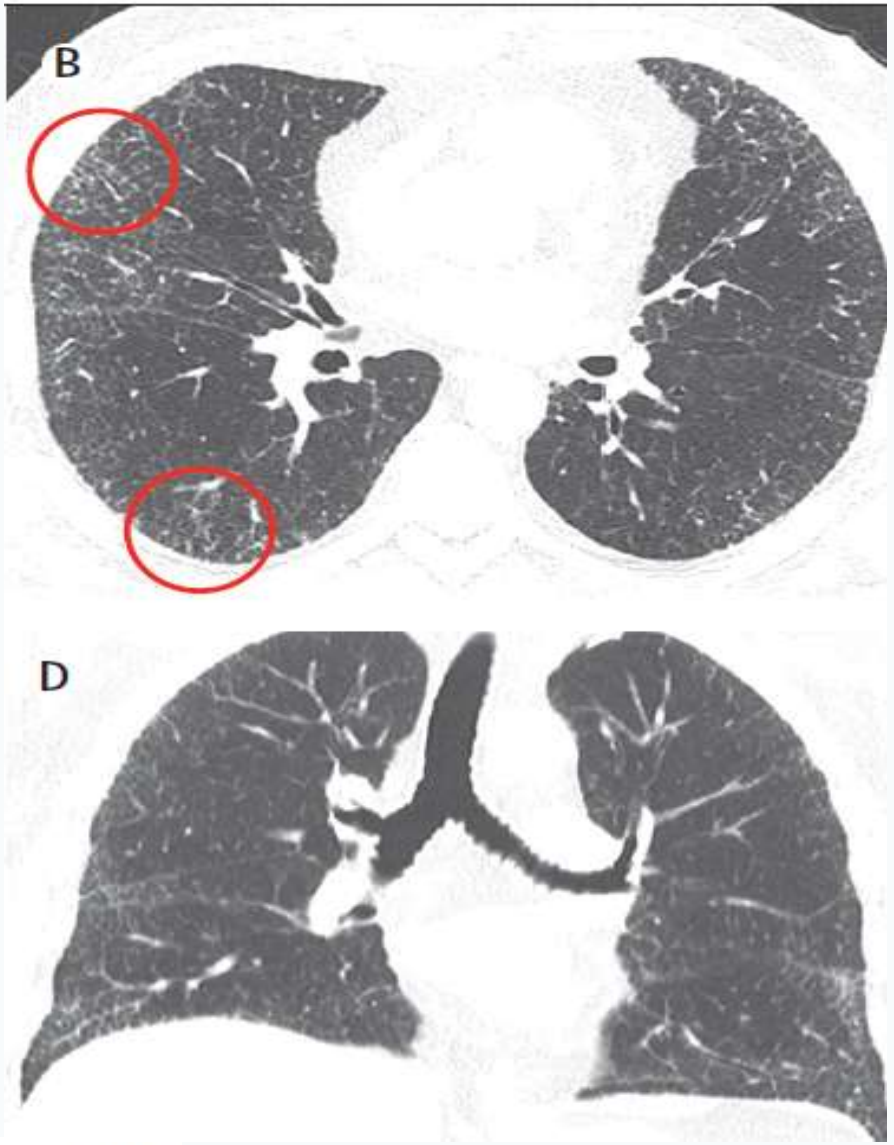
Probable UIP CT pattern

Distribution

Basal and subpleural predominant; distribution is often heterogeneous

Features

Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; honeycombing is absent; absence of features to suggest an alternative diagnosis



www.thelancet.com/respiratory Published online November 15, 2017

THE LANCET
Respiratory Medicine

Usual interstitial pneumonia pattern in the diagnosis of idiopathic pulmonary fibrosis?

Probable UIP has high positive predictive value for IPF

*Vasilios Tzilas, *Demosthenes Bouros*
First Academic Department of Pneumonology, Hospital for Diseases of the CHEST "SOTIRIA", Medical School, National and Kapodistrian University of Athens, Athens, 11527, Greece (VT, DB)
dbouros@med.uoa.gr.

www.thelancet.com/respiratory Vol 4 October 2016

Diagnostic categories of UIP based on CT patterns

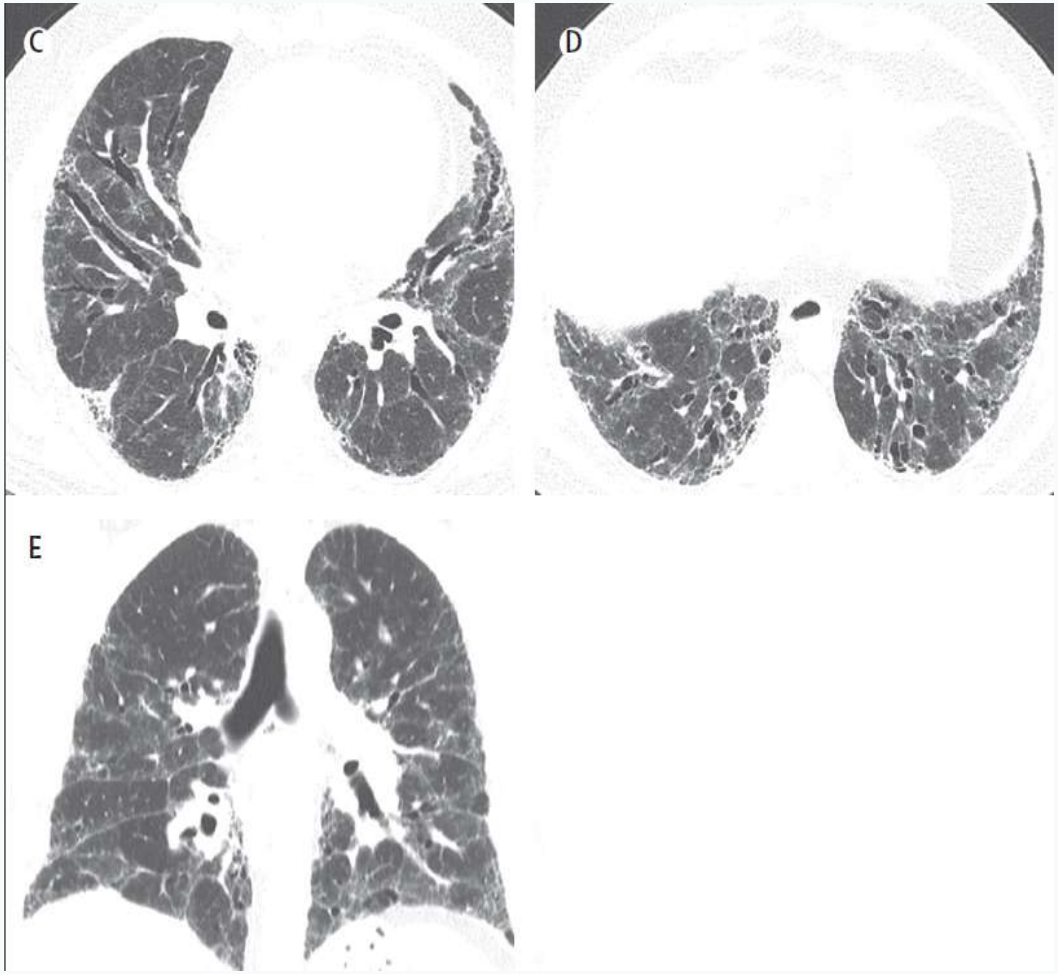
CT pattern indeterminate for UIP

Distribution

Variable or diffuse

Features

Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern



www.thelancet.com/respiratory Published online November 15, 2017

Diagnostic categories of UIP based on CT patterns

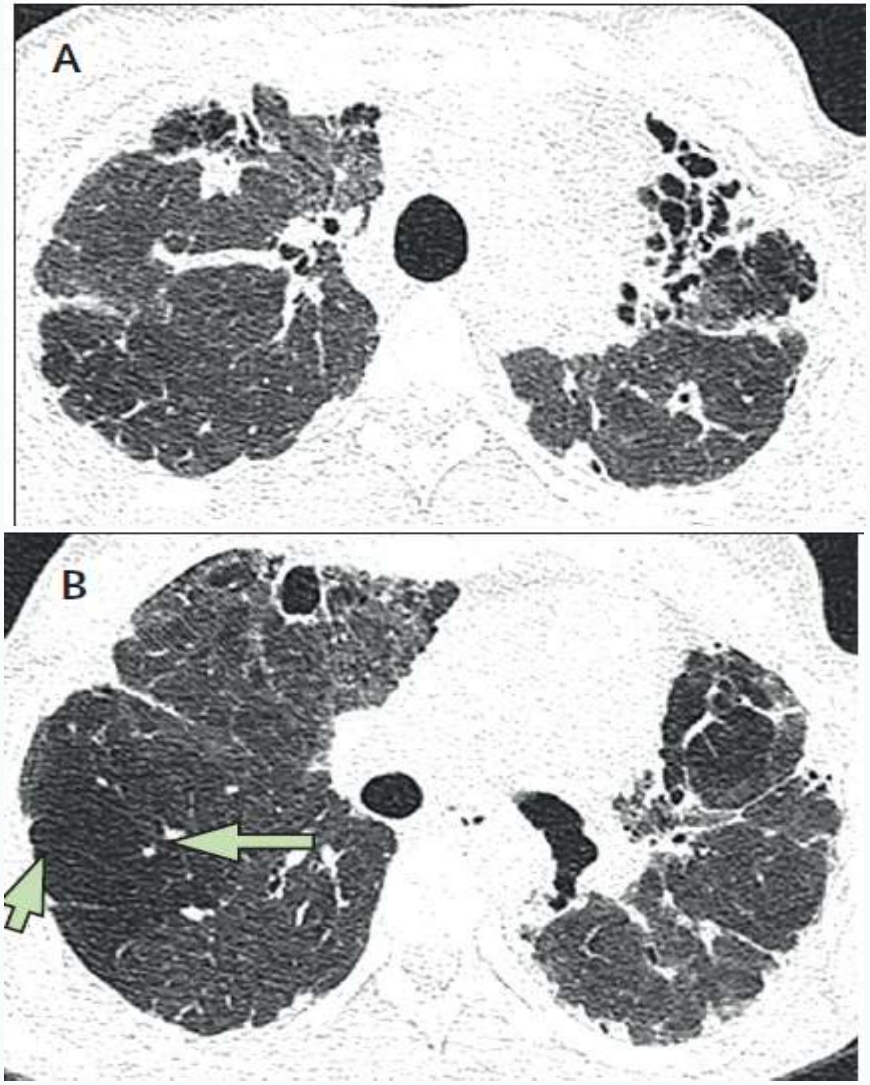
CT features most consistent with non-IPF diagnosis

Distribution

Upper-lung or mid-lung predominant fibrosis; peribronchovascular predominance with subpleural sparing

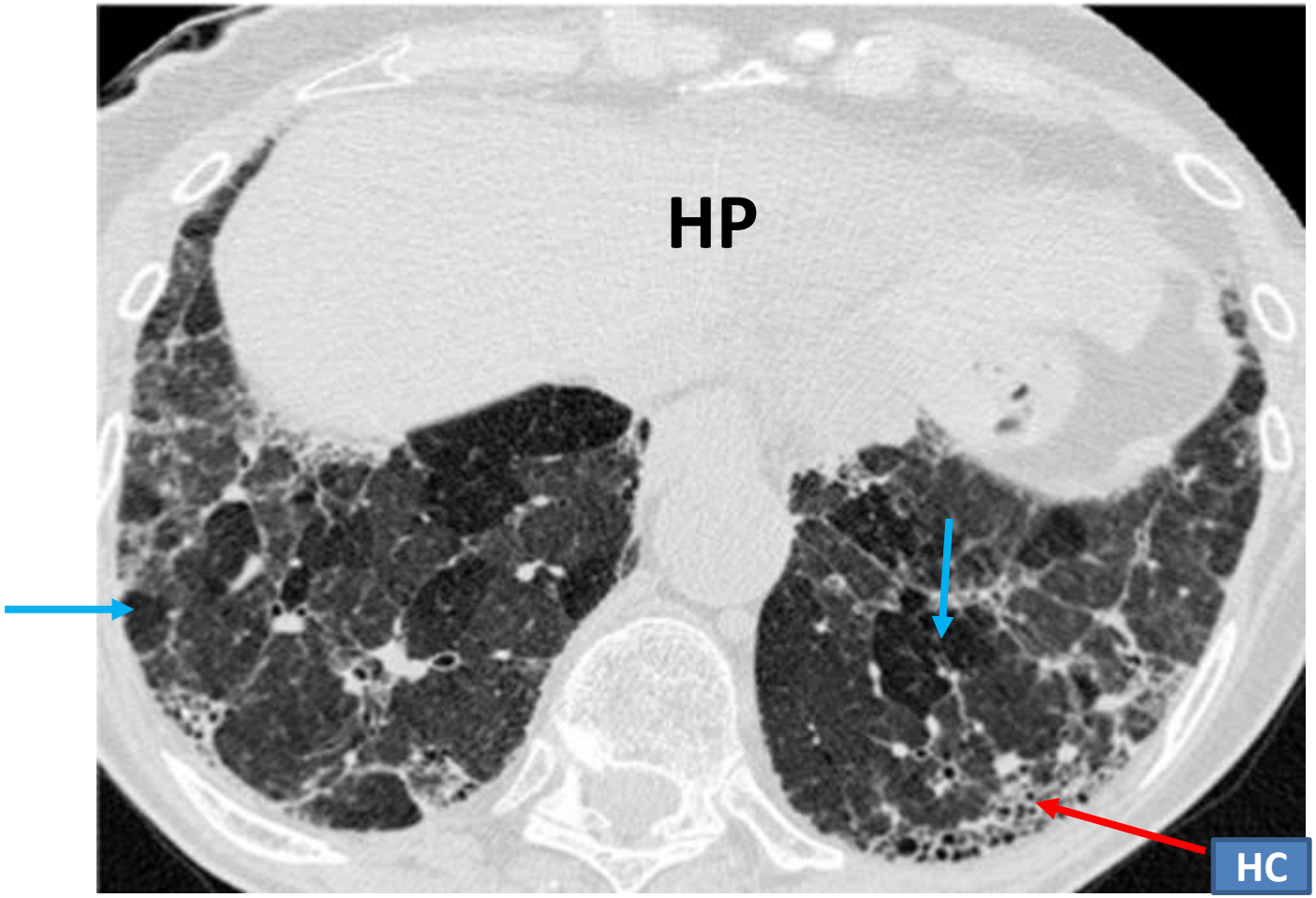
Features

Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts



www.thelancet.com/respiratory Published online November 15, 2017

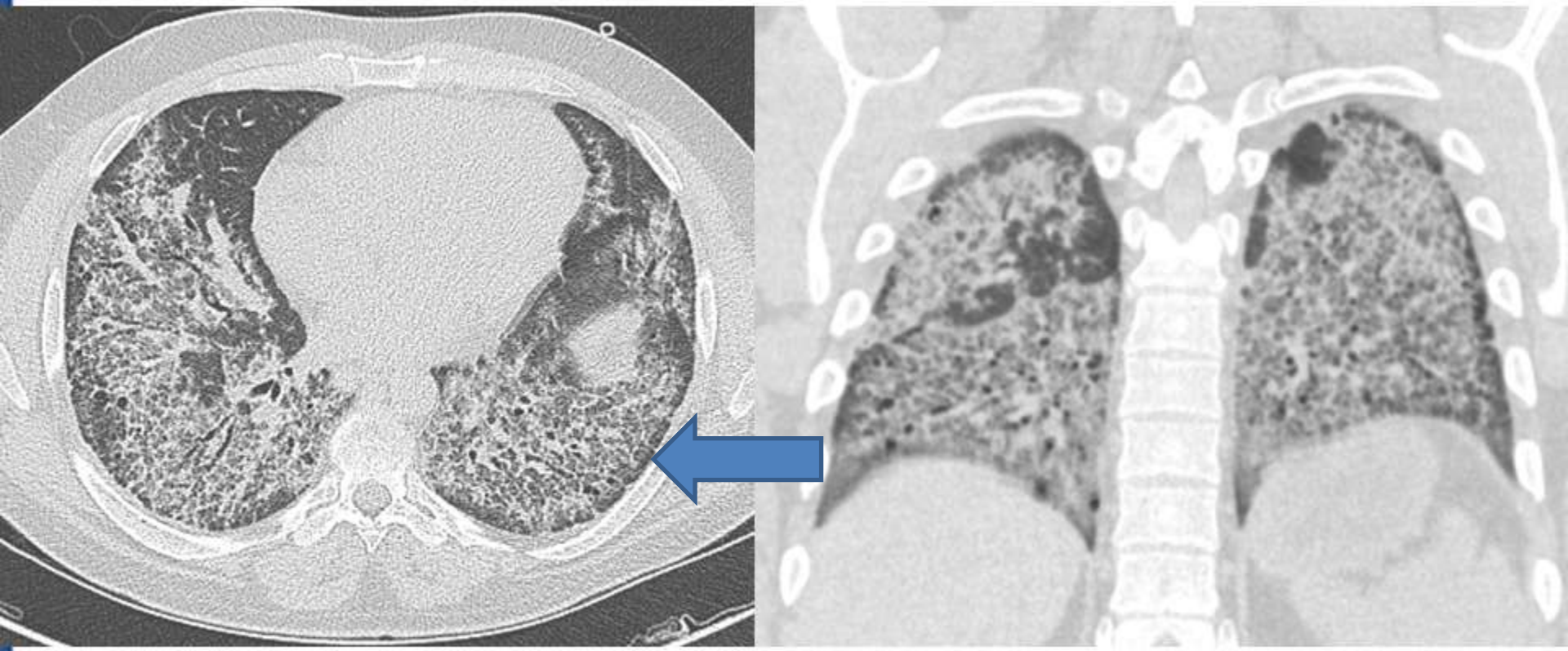
Inconsistent With UIP



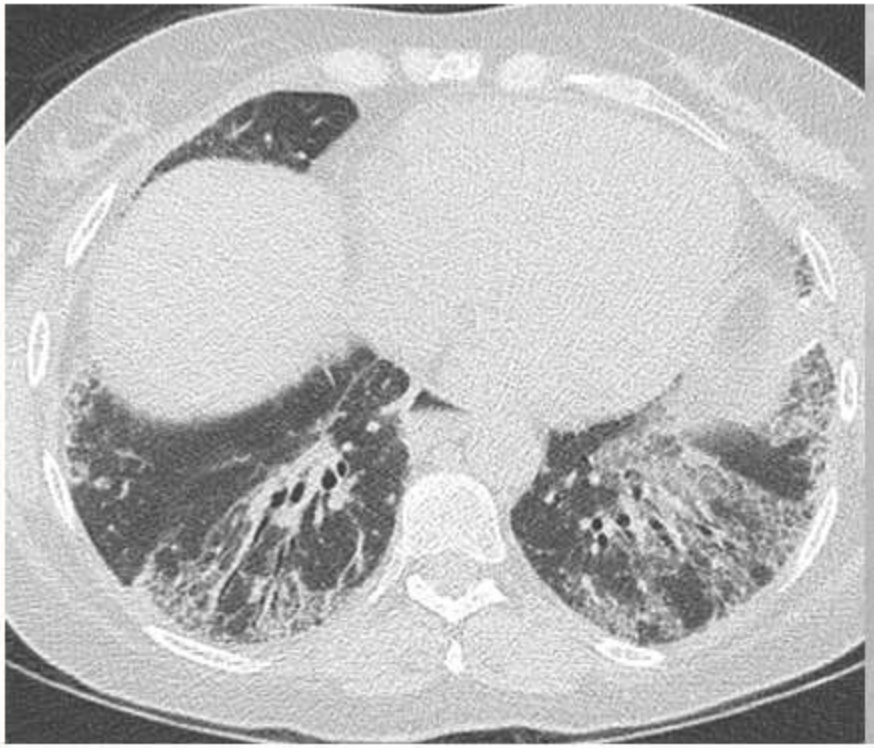
Distinct lobular pattern +HC

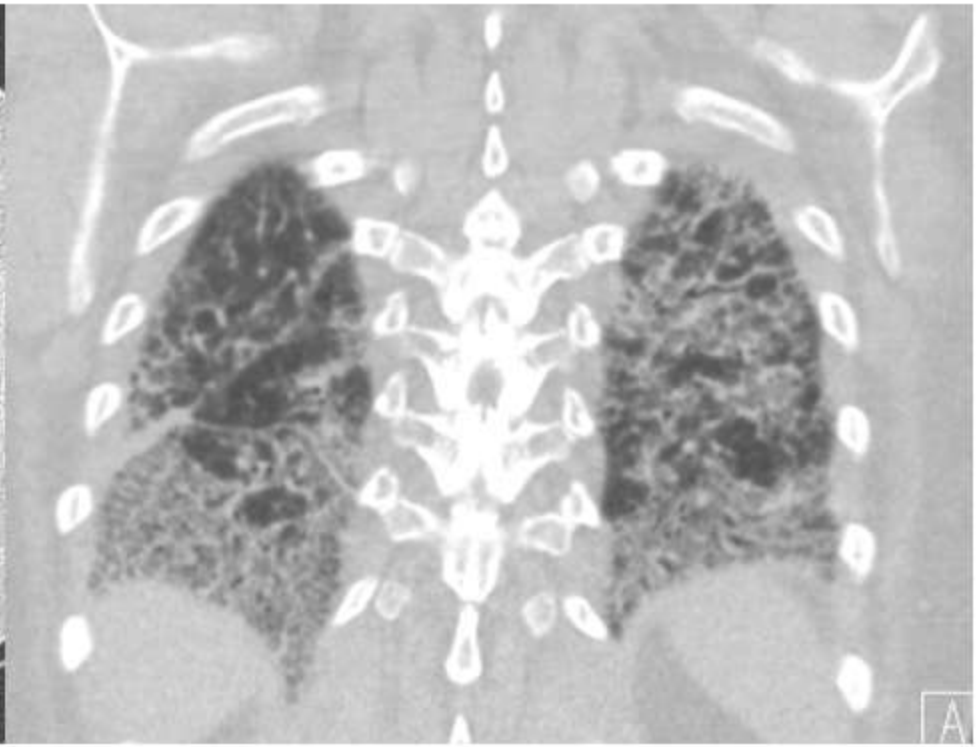
Slide courtesy D BOUROS

Fibrotic NSIP: subpleural sparing



MTX toxicity: GGO > reticular, peribronchovascular





Positive Predictive Value of UIP on HRCT for IPF

UIP pattern (honeycombing) on HRCT:

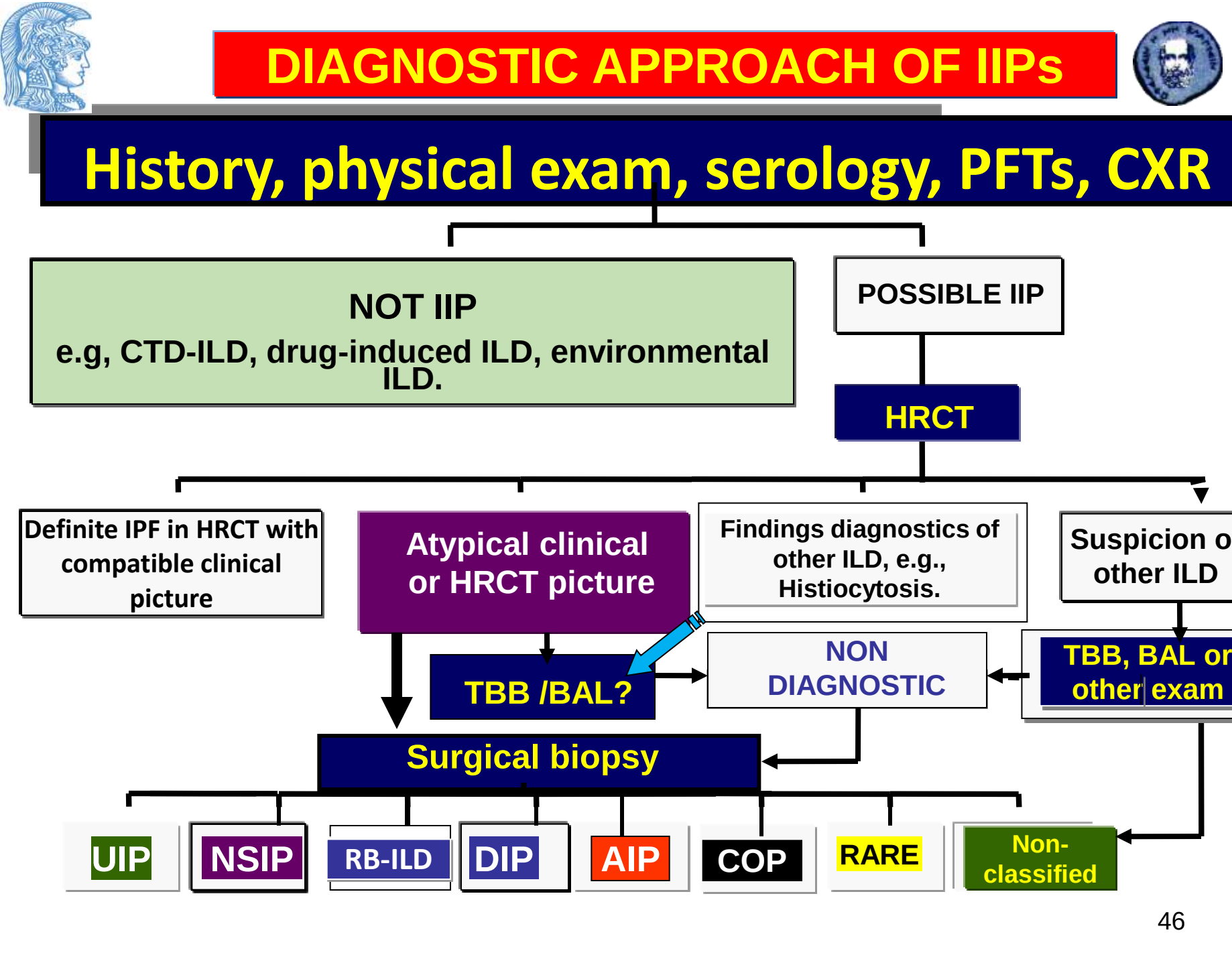
- PPV for IFP 90-100%

UCSF study: other HRCT classifications

- Possible UIP: 63% (94% Mayo)
- Inconsistent with UIP: 23%
  - Even if inconsistent, still can be IPF

Wells A, *Respir Res.* 2013;14(suppl 1):S2
Brownell R et al, *Thorax*. 2017 Jan 12., pii: thoraxjnl-2016-209671

DIAGNOSTIC APPROACH OF IIPs



Diagnosis of IPF- 2018 guidelines

For patients with newly detected ILD of apparently unknown cause who are clinically suspected of having IPF and have an HRCT pattern of UIP:

- We suggest NOT performing cellular analysis of their BAL fluid (*conditional recommendation, very low quality of evidence*).
- We recommend NOT performing SLB (*strong recommendation, very low quality of evidence*).
- We recommend NOT performing TBBx (*strong recommendation, very low quality of evidence*).
- We recommend NOT performing lung cryobiopsy (*strong recommendation, very low quality of evidence*).

NO

(ATS/ERS/JRS/ALAT 2018)

Diagnosis of IPF- 2018 guidelines

For patients with newly detected ILD of apparently unknown cause who are clinically suspected of having IPF and have an HRCT pattern of probable UIP, indeterminate, or an alternative diagnosis:

- We suggest cellular analysis of their BAL fluid (*conditional recommendation, very low quality of evidence*).
- We suggest surgical lung biopsy (SLB) (*conditional recommendation, very low quality of evidence*).
- The panel made no recommendation for or against transbronchial lung biopsy (TBBx).

- The panel made no recommendation for or against lung cryobiopsy.

(ATS/ERS/JRS/ALAT 2018)

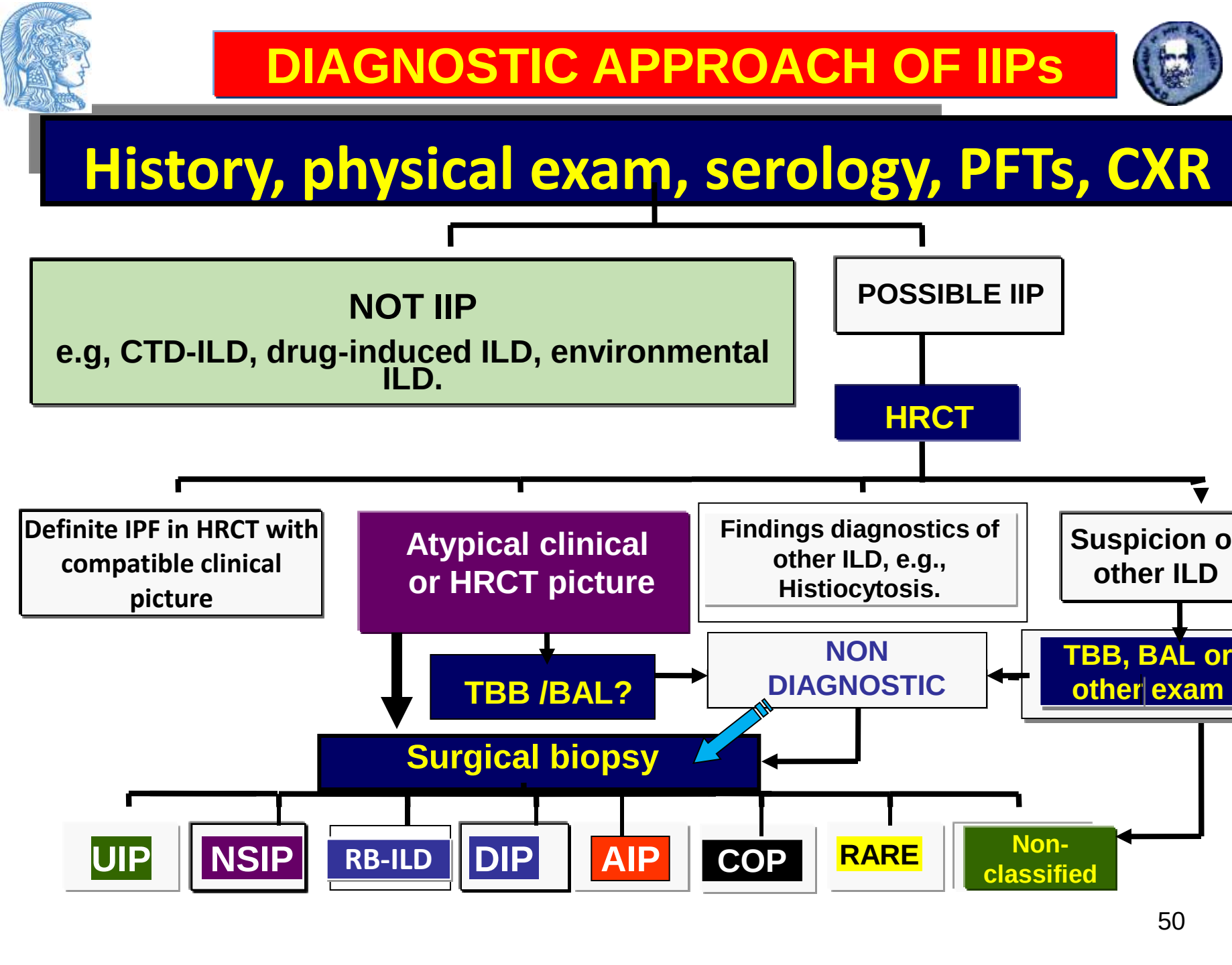
Diagnosis of IPF. 2018 guidelines

BIOMARKERS

We recommend NOT measuring serum MMP (matrix metalloproteinase)-7, SPD (surfactant protein D), CCL (chemokine ligand)-18, or KL (Krebs von den Lungen)-6 for the purpose of distinguishing IPF from other ILDs (*strong recommendation, very low quality of evidence*).

(ATS/ERS/JRS/ALAT 2018)

DIAGNOSTIC APPROACH OF IIPs



FLEISCHNER society 2017 white paper Diagnostic criteria for IPF. *Lancet RM 2017*

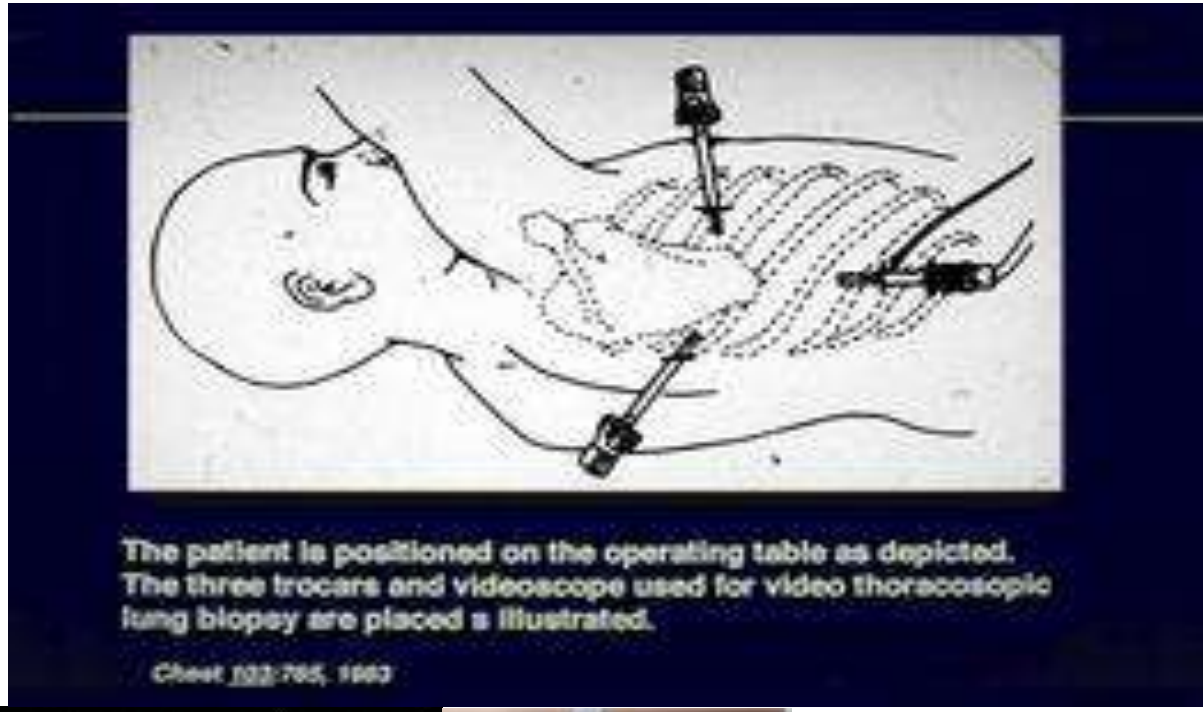
When can one make a confident diagnosis of IPF without biopsy?

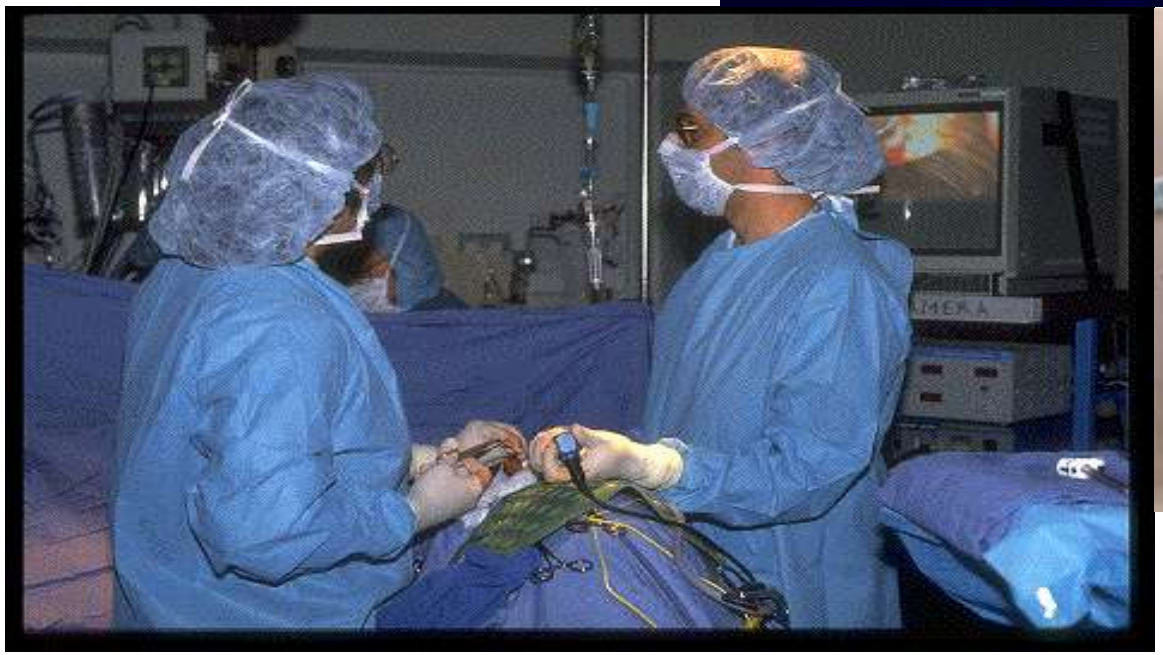
- Clinical context of IPF*, with CT pattern of typical or probable UIP

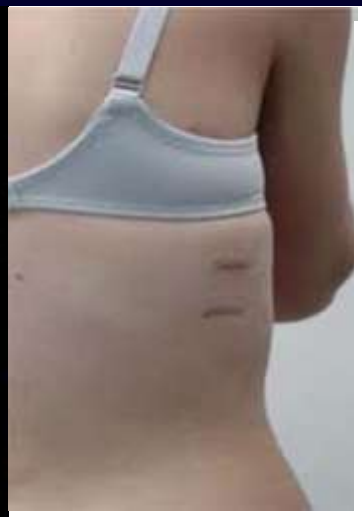
When is a diagnostic biopsy necessary to make a confident diagnosis of IPF?

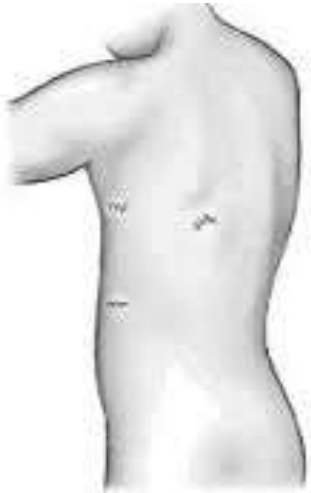
- Clinical context of IPF* with CT pattern either indeterminate or suggestive of an alternative diagnosis
- Clinical context indeterminate for IPF† with any CT pattern

Video-Assisted Thoracoscopic Surgery
VATS





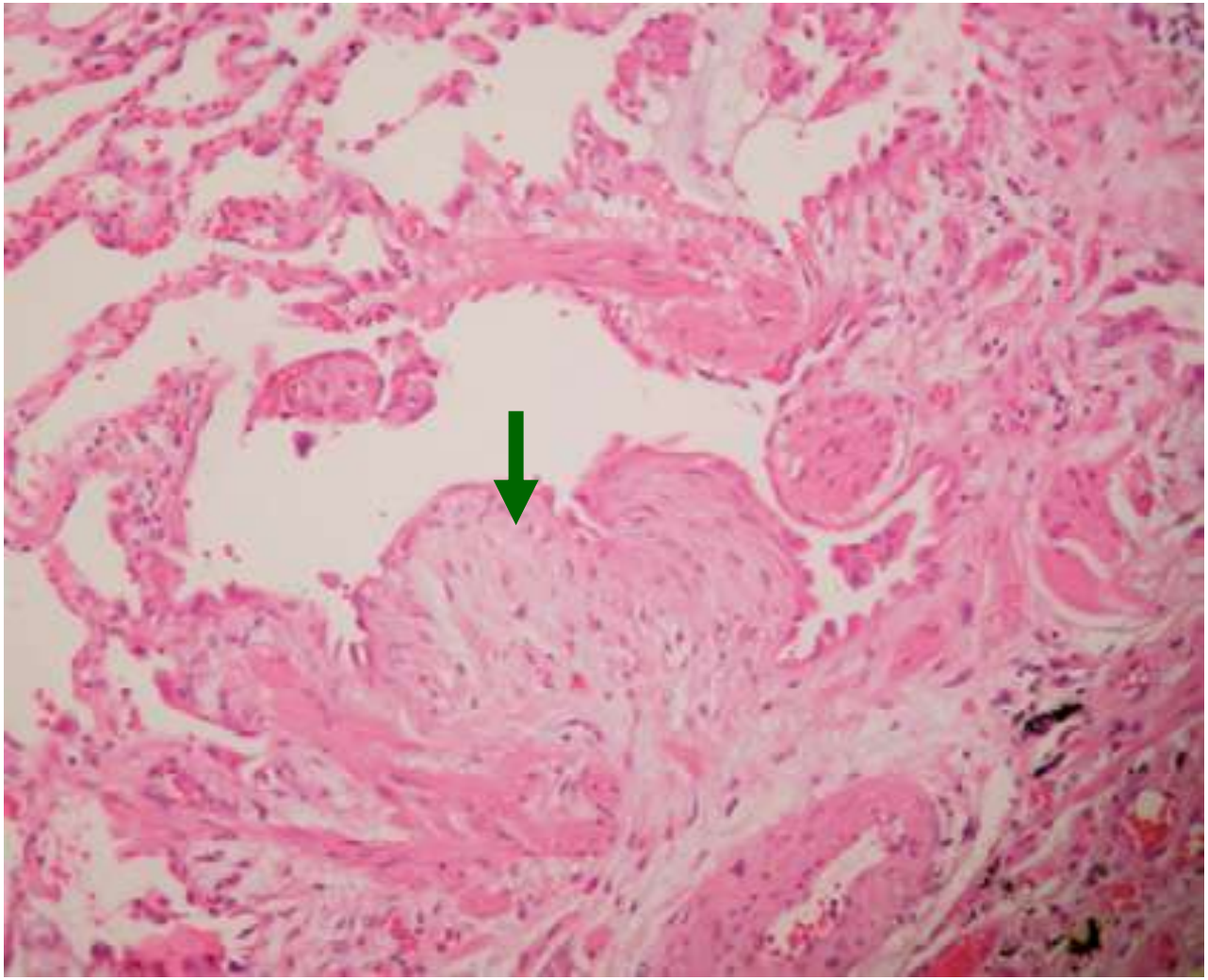




Histologic criteria of UIP

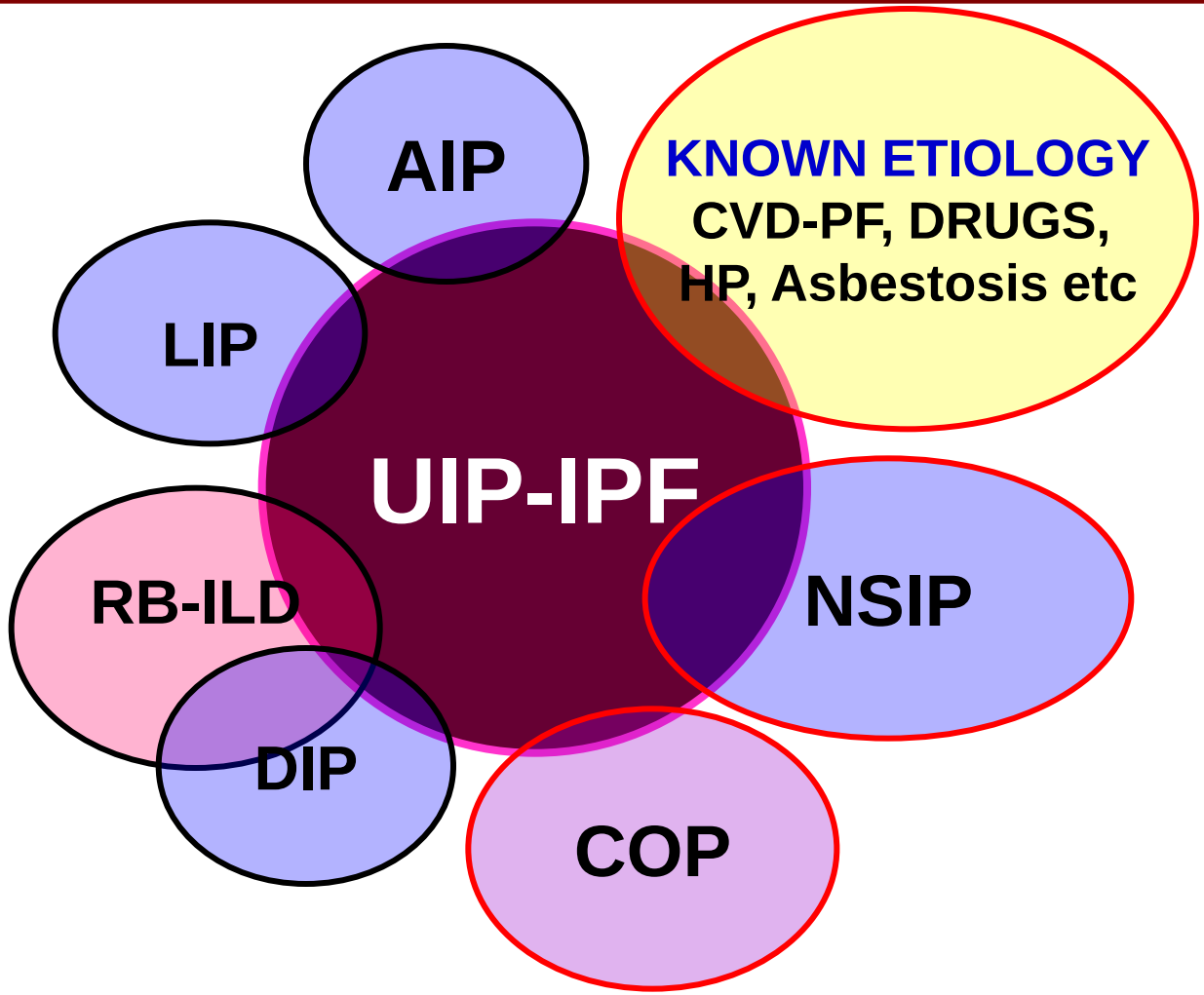
	Definite UIP-IPF	Probable UIP-IPF	Indeterminate for UIP-IPF
General comments	Patients show features with all four criteria, and do not show features that might suggest an alternative diagnosis (eg, non-UIP)	Patients show either honeycomb fibrosis only, or a severe fibrosing process that falls short of showing all four criteria for definite UIP-IPF and do not show features that might suggest an alternative diagnosis	Patients show evidence of a fibrosing process but with features that are more in favour of either a non-UIP pattern, or UIP in a setting other than IPF
Specific criteria	Dense fibrosis causing architecture remodelling with frequent honeycombing; patchy lung involvement by fibrosis; subpleural or paraseptal distribution, or both; fibroblast foci at the edge of dense scars	Honeycomb fibrosis only or; dense fibrosis causing architecture remodelling with frequent honeycombing; patchy lung involvement by fibrosis; fibroblast foci at the edge of dense scars may or may not be present	Patients have less compelling histological changes than those classified by the final column (eg, occasional foci of centrilobular injury or scarring, rare granulomas or giant cells, only a minor degree of lymphoid hyperplasia or diffuse inflammation, or diffuse homogenous fibrosis favouring fibrotic non-specific interstitial pneumonia); these features, and the differential diagnoses they call to mind, become part of the multidisciplinary discussion and decision with regard to a multidisciplinary diagnosis of IPF, or not

VATS biopsy shows UIP: **heterogeneous** appearance with alternating areas of normal lung, interstitial **inflammation**, **fibrosis**, **fibroblastic foci** and **honeycomb** change.



BOUROS D. Editorial. Lancet 2009;374:180-182

USUAL INTERSTITIAL PNEUMONIA AND IDIOPATHIC PULMONARY FIBROSIS



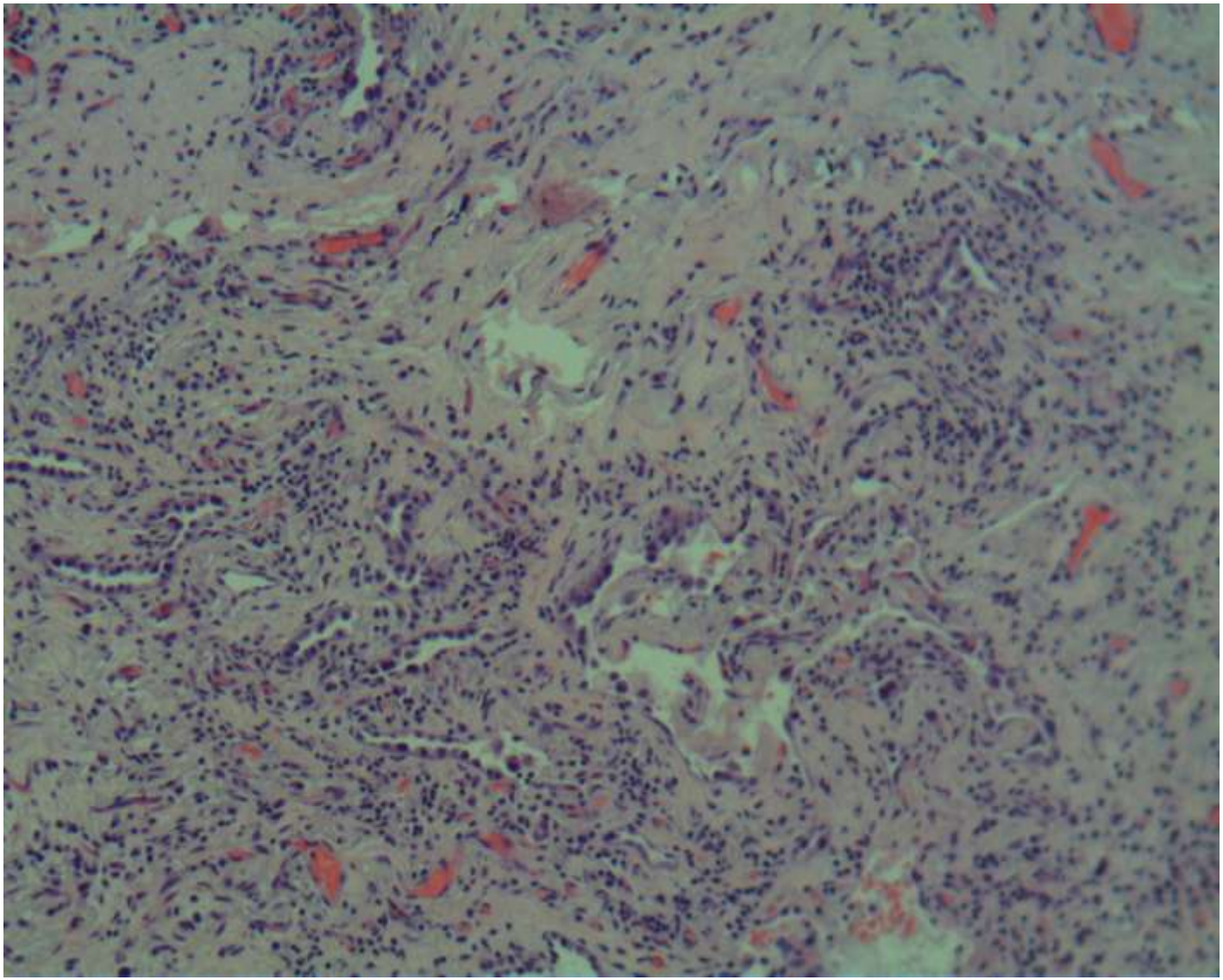
Most UIPs are "IPF", ALL UIPs ARE NOT IPF

Slide courtesy of Demosthenes Bouros

POINTING TO ANOTHER DIAGNOSIS

Features most consistent with an alternative diagnosis
Patients show either a UIP pattern with ancillary features strongly suggesting an alternative diagnosis, or a non-UIP pattern (see cell below)
Non-UIP pattern: patients with features of other fibrotic disorders—eg, fibrotic hypersensitivity pneumonitis, fibrotic non-specific interstitial pneumonia, fibrosing organising pneumonia, pleuroparenchymal fibroelastosis, pulmonary Langerhans cell histiocytosis, or smoking-related interstitial fibrosis; UIP pattern with ancillary features strongly suggesting an alternative diagnosis: eg, prominent diffuse alveolar damage or organising pneumonia (consider acute exacerbation of UIP), granulomas, (consider hypersensitivity pneumonitis, sarcoid, infection), marked interstitial inflammatory cell infiltrate away from areas of UIP (consider hypersensitivity pneumonitis)

Possible UIP pattern



No fibroblastic foci / honeycomb

Courtesy R. Trigidou

	ATS/ERS/JRS/ALAT clinical practice guideline [1]	Fleischner white paper consensus statement [2]
Histopathology pattern	**UIP**	**Definite UIP** Dense fibrosis with architecture remodelling Predominant subpleural or paraseptal distribution of fibrosis Patchy lung involvement by fibrosis Presence of fibroblastic foci
		Probable UIP Honeycomb fibrosis only Fibroblastic foci may or may not be present
	Fibrosis with or without architecture distortion Some histological features from the UIP pattern	**Indeterminate for UIP** Occasional foci of centrilobular injury or scarring Rare granulomas or giant cells Minor degree of lymphoid hyperplasia or diffuse inflammation Diffuse homogenous fibrosis favouring fibrotic nonspecific interstitial pneumonia
	Alternative diagnosis Histological findings indicative of other diseases	**Features most consistent with an alternative diagnosis** A UIP pattern with ancillary features strongly suggesting an alternative diagnosis A non-UIP pattern

Eur Respir J 2018; 52: 1801485

Diagnosis of IPF

Diagnosis of IPF requires the following:

1. **Exclusion of other known causes *(e.g., domestic and occupational environmental exposures, CTD, drug toxicity),***
   and either #2 or #3:
2. **The presence of the HRCT pattern of UIP**
3. **Specific combinations of HRCT and histopathology patterns**

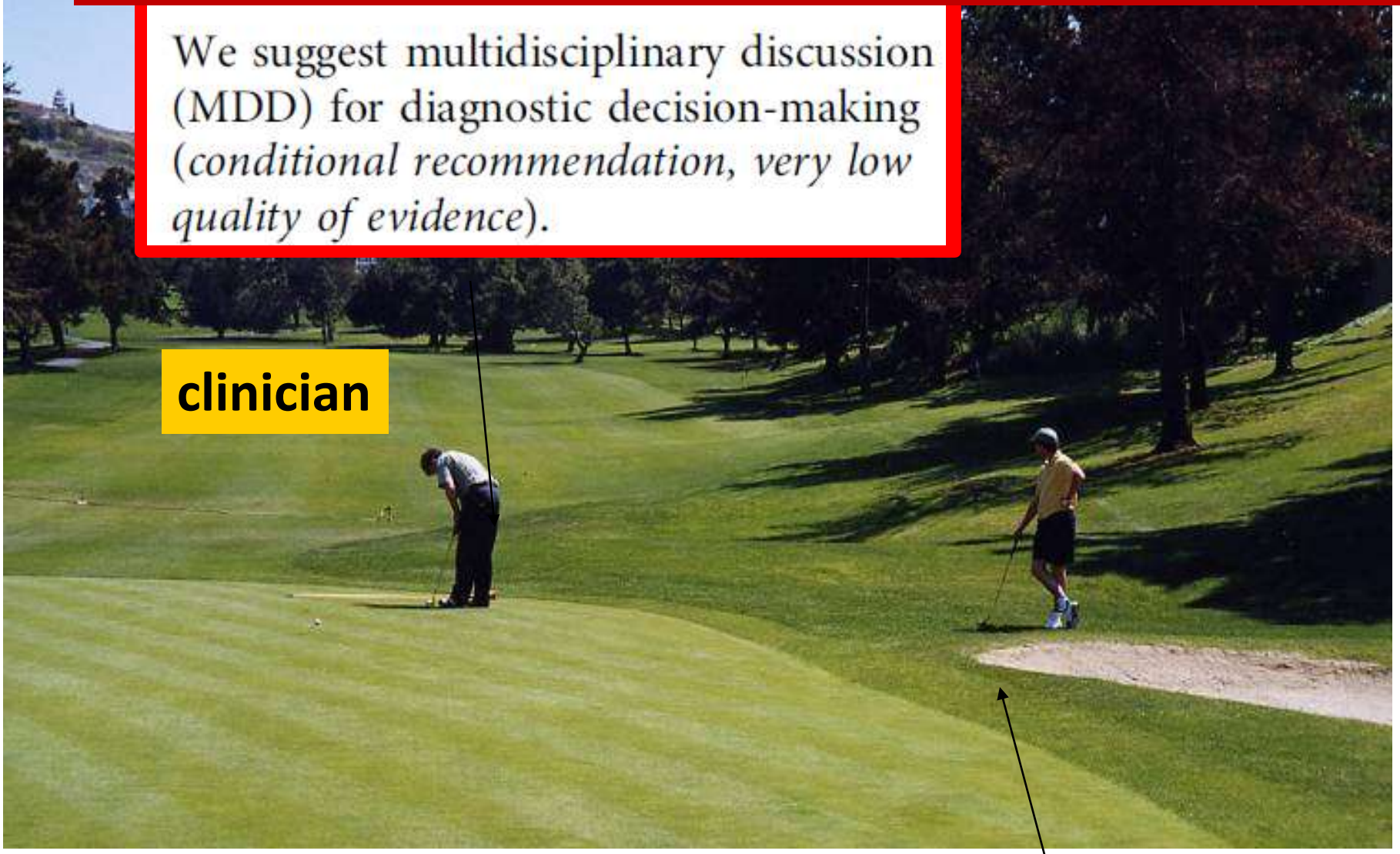
(ATS/ERS/JRS/ALAT 2018)

HRCT pattern	Histopathology pattern				
	UIP	Probable UIP	Indeterminate for UIP	Alternative diagnosis	No biopsy
UIP	IPF	IPF	IPF	Non-IPF	IPF
Probable UIP	IPF	IPF	IPF (Likely)	Non-IPF	IPF (Likely)
Indeterminate	IPF	IPF (Likely)	Unclassified *	Non-IPF	Unclassified *
Alternative diagnosis	IPF (Likely)	Non-IPF	Non-IPF	Non-IPF	Non-IPF

D. BOUROS et al. LANCET RM 2018

Diagnosis of IPF- 2018 guidelines

We suggest multidisciplinary discussion (MDD) for diagnostic decision-making (*conditional recommendation, very low quality of evidence*).



Approach to the Diagnosis of IPF

Clinical	Radiology	Pathology
• History • Physical • Laboratory • PFTs	• Chest X-ray • HRCT	• Surgical lung biopsy

Primary care physicians	Pneumonologist	Radiologist	Pathologist

Multidisciplinary discussion

GOLD STANDARD

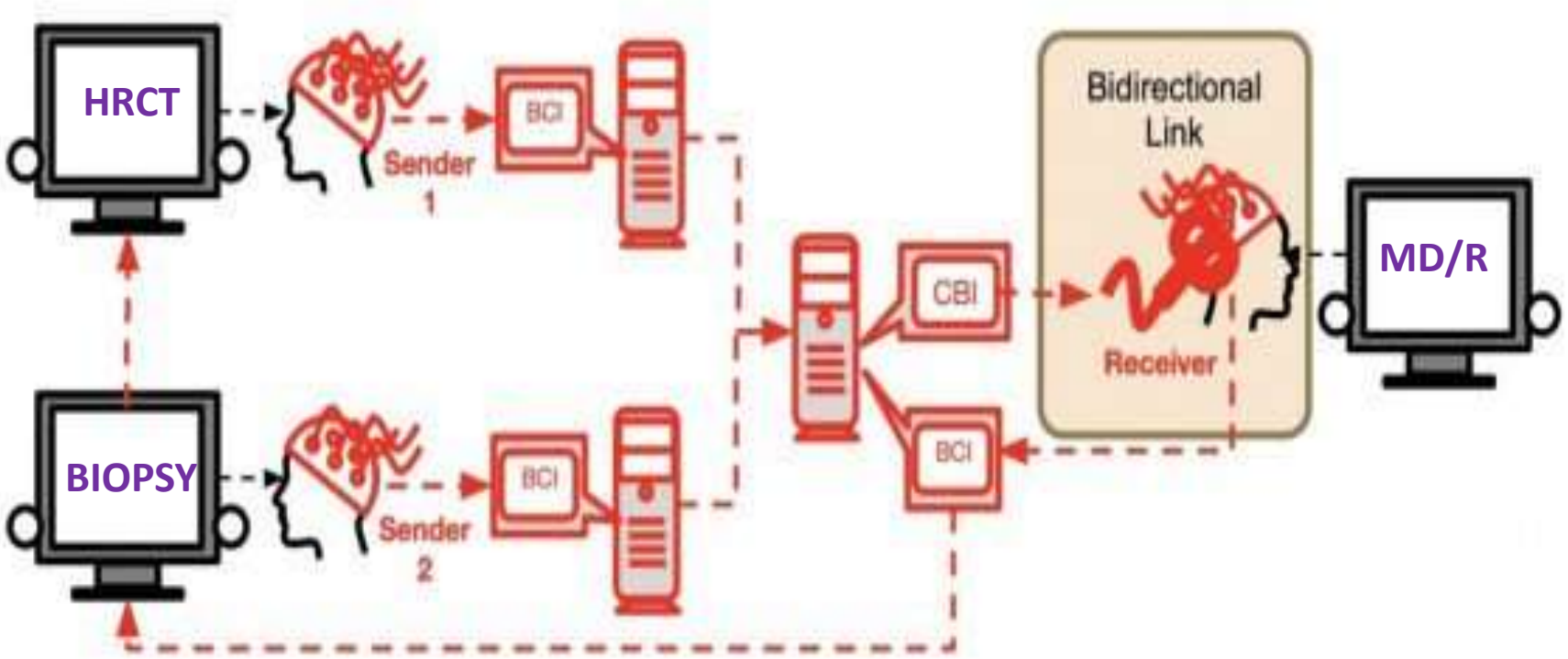
REFERENCE CENTER

2005 PILOT™

Pulmonary Fibrosis Identification: Lessons for Optimizing Treatment

BrainNet allows collaborative problem-solving using direct brain-to-brain communication.

The first "social network" of brains lets three people transmit thoughts to each other's heads



MIT Technology Review

PARTHENON-ACROPOLIS

QUESTIONS?